Københavns Kommune
Kultur- og Fritidsforvaltningen
1008 - Direktør Michael Hermann Nielsens Mindelegat, afd. B - Sygdomsforskning

Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk)
Ansøgningsrunde 1. marts til 30. april
Indstilling til legatbestyrelsen (Kultur- og Fritidsudvalget)

Ansøger	**Projekt**
Sveina Björk Karlsdóttir	Den diagnos ske værdi af "Dermal-Op cal Coherens Tomography (D-OCT)" for klinisk mistænkte basalcellekarcinomer (BCC) i
Colm O´Rourke	Adapting a transcriptome-based strategy for precision chemoimmunotherapy in bile duct cancer
Viktor T. lemgart	Udvikling af A2M-IL-10 fusuoner til behandling af autoimmune sygdom
Annina Kurzay	ProS1-MerTK Signalling in CD4 T Cells: Implications for TIL Expansion and functionality
Magnus Nygaard Bech	Præhabilitering til patienter med blodkræft, der skal behandles med allogen knoglemarvs-transplantation – et national randomiseret
Lea Löffler	Molecular, Immunological, and Thrombophilia Studies in the GESUS
Lars Møller Pedersen	Klinisk betydning af ændringer i kropssammensætning under førstelinjebehandling af pati-enter med lymfekræft
Rasmus Haahr	CALIBRATE (Colchicine Assessment of Low-grade Inflammation and Biomarker Response in Atherosclerosis with Targeted Evaluation)
Lisbet Rosenkrantz Hölmich	DAHT, Dermoscopy Augmented Histology Trial. Increasing the diagnostic accuracy in histopathological melanoma- and skin lesion assessment through the inclusion of dermoscopic images and other clinical data
Sofie Louise Rygård	Randomized clinical multicenter trial of small thyroid cancers treated with hemi thyroidec-tomy or radiofrequency ablation
Karoline Lolk Revsbech	Betydning af hjemmeblodtryksmåling om natten hos personer med kronisk nyresygdom
Anders Møller Greve	Kunstig intelligens til præcisionsdiagnostik af blod, knoglemarvs- og
Pernille Koll	The OvaCure Collection – Etablering af 40 organoidkulturer til brug i international forskning i æggestokkræft
Marie Bredgaard Thuesen	Extending the applicability of the In Ovo Chicken chorioallantoic membrane (CAM) model using high dose proton radiation to study the
Christian Wejse	Prævalensen af tuberkulose- (TB-) infektion blandt migranter i Danmark: Et modelleringsstudium
Ada Colic	ARTHUR for Clinic on Demand: Anvendelse af robotassisteret ultralydsundersøgelse til akut vurdering af inflammatoriske forandringer hos patienter med reumatoid artrit (leddegigt).
Naomi Nadler Skjødt	Microbial and oncoimmunological features embedded in the tumor microenvironment in non-muscle invasive bladder cancer
Jakob Myllerup Jensen	Kan man opspore tilbagefald af kræft i mundsvælget ved hjælp af
Louise Adel Jensen	Molekylær Tumorprofilering af Arvelig Brystkræft til Forbedring af Rådgivning og Behandling

Tanja Fromberg Gorlen	Prognose og risiko for kræft hos patienter udredt for kæmpecellearteritis
Sara Fresnillo Saló	Exercise as combination partner for immune therapy of cancer
Christina Therkildsen	Tidlig opsporing af kræft med blodbaserede biomarkører
Trine Engelbrecht Hybel	Rethinking Diagnostics in Myelodysplasic Neoplasia: Integrating AI-Assisted Morphometrics for Improved Accuracy and Risk Stratification
Ivona Cudina	The application of spatial technologies to the investigation of localized
Lars Rolighed & Khalil Rafiqi	The Impact of Total Thyroidectomy on Parathyroid Function and Quality of
Morten Nielsen	En retrospektiv undersøgelse af immunrespons til sarkomer
Janne Minet Pedersen	Supraglottisk planocellulært karcinom i Danmark
Oliver S.K Harving	Infections of Intravascular Stents - Case report and Systematic review of
Gitte Holmen Olofsson	Gør en god behandling bedre: motion ved immunterapi af kræft

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- **Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)**
- **CV og publikationsliste**
- **Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside [Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk)] (der hvor du fandt det obligatoriske ansøgningsskema)**

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	Sveina Björk Karlsdóttir, læge, ph.d.-studerende
Arbejdssted/ Institution	Vejle Øjenafdeling, Sygehus Lillebælt
Adresse	Beriderbakken 4, 7100, Vejle
Tlf.nr.	53420448
e-mail	Sveina.bjork.karlsdottir@rsyd.dk

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel:

Den diagnostiske værdi af "Dermal-Optical Coherens Tomography (D-OCT)" for klinisk mistænkte basalcellekarcinomer (BCC) i øjenomgivelserne.

Formål:

Projektets formål er at undersøge om en hudskanner kan diagnosticere hudkræft i øjenregionen samt forbedre kirurgens vurdering af, hvor meget hud der bør fjernes ved operationen.

Problemstilling:

Basalcellekræft (BCC) i øjenregionen udgør en særlig udfordring, da området er både kosmetisk og funktionelt følsomt. Den nuværende diagnostiske proces og behandling indebærer mange tidskrævende trin. BCC ligner ofte godartede hudforandringer, hvilket nødvendiggør biopsi og en ventetid på svar er op til 16 dage. Behandlingen kræver kirurgisk fjernelse med en sikkerhedsmargin på 3 mm, hvilket kan kompromittere øjenlågets funktion og tårevejene, hvilket i værste fald kan føre til kroniske gener eller påvirke synsfunktionen. Frysemikroskopi under operationen kan forlænge indgrebet betydeligt, og der er en risiko for, at kræften ikke fjernes fuldstændigt ved første operation.

Baggrund:

BCC i øjenregionen rammer hvert år ca. 2600 danskere. Selvom BCC vokser langsomt, kan det forårsage omfattende vævsskader, der påvirker både øjenlågets funktion og udseende.
Diagnosen stilles ved en vævsprøve (biopsi) og først herefter kan operationen planlægges. Standardbehandling er kirurgisk fjernelse med en sikkerhedsmargin på 3 mm. Dette er særligt udfordrende i øjenregionen, hvor selv små vævsfjernelser kan påvirke øjenlågets funktion og tåreveje. Under operationen anvendes frysemikroskopi til at sikre, at alt kræftvæv er fjernet, hvilket gør proceduren både tidskrævende og kompleks.
En hudskanner, Dermal Optical Coherence Tomography (D-OCT), kan skabe detaljeret 3D-billeder af hudlagene, uden behov for invasive vævsprøver og har vist sit værd på andre dele af kroppen. I 2022 blev der i samarbejde mellem øjenlæger på Vejle Sygehus og producenten for skanneren, VivoSight, udviklet en specialdesignet skanningsprobe til øjenregionen, optimeret til de krumme og smalle overflader omkring øjnene.

Metoder:

210 patienter med mistænkelige hudforandringer i øjenomgivelserne inkluderes. Alle skannes med både standard D-OCT probe (læge 1) og specialudviklet øjenprobe (læge 2). Herefter gennemgår patienterne den sædvanlige forundersøgelse og biopsi. Ved bekræftet BCC foretages en ny skanning før operation for præcist at afgrænse tumoren.
Analyse: Skanningsresultaterne sammenlignes med histologiske fund fra biopsi og fjernet tumor. Skanningsbillederne vurderes af en afhængig læge for at sikre objektivitet.

Tidsplan

Det forventes at projektet er gennemførligt indenfor en ph.d.-periode på 3 år, jf. tabel.

År	2023				2024				2025				2026			
Kvartal	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Ph.d.-studerende				x	x	x	x	x	x	x	x	x	x	x	x	x
Planlægning, protokolbeskrivelse og godkendelser		x	x	x	x	x										
Patient rekruttering						x		x	x	x	x	x				
Ph.d.-kurser					x	x			x	x	x	x	x	x		
Artikler og afhandling												x	x	x	x	x

Forventede resultater og impact:

Det skal for første gang afklares, om denne skanning kan anvendes i øjenregionen. Vi forventer detaljeret viden om hudforandringer i øjenomgivelserne, herunder evnen til at skelne mellem godartede og ondartede forandringer samt vurdere, om teknologien kan integreres i operationsplanlægningen. Resultaterne kan potentielt forbedre diagnostik og behandling af BCC i et af kroppens mest sårbare områder. Hvis skanneren kan identificere kræft lige så effektivt som biopsier, kan ventetiden på diagnose og behandling forkortes til minutter. Hvis den også præcist kan afgrænse kræften, kan kirurgen fjerne mindst muligt sund hud, hvilket kan forbedre både øjenlågsfunktionen samt det kosmetiske resultat.

Øvrige projektdeltagere og samarbejdsrelationer

Projektet udføres på Øjenafdelingen, Sygehus Lillebælt i Vejle, der er anerkendt for sin ekspertise inden for øjennær hudkirurgi og har en stærk forskningsprofil.
Vi har et stærkt og erfarent forskerteam: Overlæge Nikolaj Carsting Bjerrum, en ekspert-kirurg indenfor øjennær hudkræftkirurgi; Overlæge, klinisk forskningslektor og hudlæge Mette Mogensen fra Hudafdelingen på Bispebjerg og Frederiksberg Hospital, der har 14+ års erfaring med anvendelse og udvikling af OCT-skanning af huden; Professor, overlæge, øjenlæge og patolog Steffen Heegaard fra Øjenafdelingen på Rigshospitalet, der er national og internationalt anerkendt ekspert i patologiske forandringer i øjet og øjenomgivelserne og hovedvejleder: Overlæge, klinisk forskningslektor og øjenlæge Flemming Møller, der er grundlægger af forskningsenheden i Vejle, og anerkendt for sin dybdegående forskningsindsigt og talrige videnskabelige publikationer.
Med en stærk institutionel forankring, et tværfagligt samarbejde mellem øjenlæger, hudlæger og patologer, dedikerede forskere og en høj patienttilgang er projektet realistisk, gennemførligt og har de bedste forudsætninger for succes. Kombinationen af ekspertise fra Sygehus Lillebælt, Bispebjerg og Frederiksberg Hospital samt Rigshospitalet styrker projektet videnskabelige kvalitet og sikrer en grundig evaluering af teknologien på tværs af specialer

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Projektets samlede budget er på 3.557.089 kr., hvoraf 2.247.316 kr. allerede er sikret gennem private fonde. Der resterer en manglende finansiering på 1.390.977 kr., som forventes dækket gennem yderligere fondsansøgninger. Vi arbejder aktivt på at sikre den fulde finansiering. Se CV for oversigt over bevillinger.

Curriculum Vitae og publikationsliste– Sveina Björk Karlsdóttir

Sveina Björk Karlsdóttir, Læge, Ph.d-studerende.

- Født, 27.01.1987
- Autorisations ID: 0BP5F
- E-mail: sveina.bjork.karlsdottir@rsyd.dk
- Tlf.: 5342 0448
- Adresse: Grønnegade 39.2, 7100 Vejle

Videnskabelig profil:

Tidligt i min hoveduddannelse i øjensygdomme påbegyndte jeg forskningstræning omhandlende hudkræft (basalcellekarcinom) i øjenregionen. Denne forskningstræning førte til en videnskabelig artikel samt præsentationer i form af posters og mundtlige fremlæggelser ved konferencer. Min interesse for forskningen dannede grundlag for udformningen af et Ph.d.-projekt, hvor jeg fortsat vil forske i hudkræft.

Uddannelse:

12/2023-nu:	Ph.d.-studerende, Syddansk Universitet.
2015:	Kandidat i Lægevidenskab, Aarhus Universitet.
2011:	Bachelor i Lægevidenskab Aarhus Universitet
2007:	Gymnasiel student fra Kvennaskólinn I Reykjavík, Island.

Ansættelser:

12/2023-nu:	Ph.d.-Studerende ved forskningsenheden på Øjenafdelingen Vejle, Sygehus Lillebælt.
12/2023-11/2026:	Forsknings orlov fra hoveduddannelse.
04/2023-11/2023:	1. Reservelæge i hoveduddannelse, Fase 4, Øjenafdelingen Vejle, Sygehus Lillebælt.
10/2022-03/2023:	1. Reservelæge i hoveduddannelse, Fase 3, Øjenlæge Rune Rask, Odense.
04/2021-09/2022:	1. Reservelæge i hoveduddannelse, Fase 2, Øjenafdeling E, Odense Universitetshospital.
04/2019-03/2021:	Reservelæge i hoveuddannelse, Fase 1, Øjenafdelngen Vejle, Sygehus Lillebælt • Barsel.
12/2018-03/2019:	Ansat i uklassificeret stilling, Øjenafdelingen Vejle, Sygehus Lillebælt.
11/2016-11/2018:	Reservelæge i introduktionsstilling på Øjenafdelingen Vejle, Sygehus Lillebælt • Barsel.
05/2016-10/2016:	KBU-læge, privatpraktiserende læge Anette Malling, Region Midtjylland.
07/2015-03/2017:	Ekstern vikar, Ortopædkirurgisk afdeling, Viborg Sygehus.
11/2015-04/2016:	KBU-læge, Mave-Tarmkirurgisk afdeling P, THG-AUH.
07/2015-10/2015:	PræKBU-læge, Medicinsk Endokrinologisk afdeling, THG-AUH.
07/2014-12/2014:	Lægevikar, Ortopædkirurgisk afdeling, Viborg Sygehus.
08/2013-01/2014:	Lægevikar, Alvehaugen Bu og Rehabiliteringscenter, Ulsteinvik, Norge.
01/2012-12/2012:	Forskningsassistent, Nyremedicinsk klinik, AUH Skejby.
06/2012-08/2012:	Lægevikar, Hjemmetjenesten, Sykkylven, Norge.
06/2010-08/2010:	Sygepleje assistent, Akut Modtagelsen, Landspítalinn Háskólasjúkrahús, Island.
01/2008-06/2008:	Portør, Akut Modtagelsen, Landspítalinn Háskólasjúkrahús, Island.

Publikationer:

10/2023:	Artikel i The Icelandic Medical Journal (10. Tbl. 109. Árg. 2023)- „Liprir pennar".
06/2022:	Karlsdóttir SB, Johannessen S, Bjerrum NC, Frydkjær-Olsen U, Blindbæk SL, Møller F, Wellejus C. Periocular basal cell carcinoma results and surgical outcome during a 5-year period in a larger Danish population. BMC Ophthalmol. 2022 Jun 28;22(1):282. doi: 10.1186/s12886-022-02494-9. PMID: 35761210; PMCID: PMC9237979.

Videnskabelige foredrag / Orale oplæg samt posters:

09/2019:	Oralt oplæg ved Dansk Oftalmologisk Selskab (DOS), videnskab og generalforsamling.
06/2022:	Posterpræsentation ved Nordic Congress of Ophthalmology (NOK).

Undervisning:

02/2025	Underviser på den regionale bacheloruddannelse i medicin (Kommunikation) i Odense.
02/2025:	Underviser på den regionale kandidatuddannelse i medicin (Oftalmologi) i Esbjerg.
03/2024:	Dansk Oftalmologisk Selskab (DOS) efteruddannelse, lab-kursus i øjenlågskirurgi til yngre-øjenlæger.
08/2021:	Basalcellekræft, Øjenafdelingen OUH

Konferencer og møder:

2024:	Dos Efteruddannelseskursus (Øjenlågskirurgi).
2023:	FAYO Årsmøde (Acute Ophthalmology).
2023:	Europian Society of Ophthalmic Plastic and Reconstructive Surgery, Napoli.
2023:	DOS januarmøde + DOS Efteruddannelseskursus (Vision Development and Eye Diseases in Childhood).
2022:	Nordic Congress of Ophthalmology (NOK), Reykjavík.
2022:	FAYO Årsmøde (Dilemmas in medical and surgical retina).
2021:	DOS Januarmøde.
2019:	DOS Efteruddannelseskursus (Neuro-oftalmologi, Strabismus og Orbita).
2019:	FAYO Årsmøde (Cornea).
2018:	FAYO Årsmøde (Uveitis).
2017:	DOS Efteruddannelseskursus (Corneale og Conjunctivale infektioner/inflammationer).

Curriculum Vitae og publikationsliste– Sveina Björk Karlsdóttir

Kurser:

01/2025:	„Train the Trainer“ kursus, for kommunikationsundervisning af medicinstuderende.
01/2025:	Ph.d-kursus: „Getting started on your teaching“.
03/2024:	REDCap database for clinical research.
03/2024:	Projektledelse, SDU Medarbejderkurus.
02/2024-03/2024:	Data management plan and responsible handling of research data.
02/2024:	Introduction to Health Research, SDU.
02/2024:	Fyraftensarrangement om hverdagsledelse ved Yngre Lægers Forening.
01/2024:	How to structure an oral presentation, SDU.
01/2024:	Responsible conduct of Research, SDU.
01/2024:	Projektstyring for Ph.d.-studerende, SDU Medarbejderkurus.
01/2024:	High impact Presentations Course, Dale Carnegie & Associates Inc., Island.
12/2023:	REDCap Projektadministration.
06/2023:	High impact Presentations Course, Dale Carnegie & Associates Inc., Island.

Professionel:

2024-nu:	Medlem af Dansk Kvindelige Lægers Forening.
2018-nu:	Medlem af Forening af Yngre Oftalmologer (FAYO).
2016-nu:	Medlem af Dansk Oftalmologisk Selskab (DOS).
2015-nu:	Medlem af Lægeforeningen.

Bevillinger og finansiering:

12/2024:	Øjenforeningen • 600.000 kr.
12/2024:	Sygehus Lillebælt Projektstøtte • 90.970 kr.
11/2024:	Tømrermester Jørgen Holm og Hustru Elisa F. Hansens Mindelegat • 50.000 kr.
06/2024:	Sygehus Lillebælt Projektstøtte • 75.000 kr.
06/2024:	Fabrikant Einar Willumsens Mindelegat • 40.000 kr.
05/2024:	Grosserer L.F. Foghts Fond • 223.000 kr.
05/2024:	Hans og Nora Buchards Fond • 50.000 kr.
04/2024:	Agnete Løvgreens Legat • 15.000 kr.
04/2024:	Synoptikfonden • 75.000 kr.
12/2023:	Ph.d.-skolen • 9.000 kr.
12/2023:	Sygehus Lillebælt Projektstøtte • 29.346 kr.
12/2023:	Sygehus Lillebælt Forskningsråds ph.d.-pulje • 500.000 kr.
12/2023:	Øjenforeningen • 390.000 kr.
10/2023:	Synoptikfonden • 100.000 kr.

Referencer:

- Cheflæge, Øjenafdelingen Vejle Sygehus, Marie Louise Høgsbro, e-mail: marie.louise.hoegsbro@rsyd.dk; Tlf.: 5142 9454.
- Privatpraktiserende læge Anette Malling, e.mail: amalling@dadlnet.dk; Tlf.: 2892 2203.

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Colm O'Rourke (lektor)**
Arbejdssted/ Institution	**Biotech Research & Innovation Centre, Department of Health & Medical Sciences, University of Copenhagen**
Adresse	**BRIC, Ole Maaløes Vej 5, 2200 Copenhagen N, Denmark**
Tlf.nr.	**31710291**
e-mail	**colm.rourke@bric.ku.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
Adapting a transcriptome-based strategy for precision chemoimmunotherapy in bile duct cancer
Formål
To develop a molecular assay that can predict chemotherapy benefit for patients with bile duct cancer before starting the treatment.
Problemstilling
Patients with advanced intrahepatic cholangiocarcinoma (iCCA) are all treated with chemotherapy, but only a subgroup benefits therapeutically, and treatment inevitably fails in all patients over time. This leads to toxicities from non-beneficial treatments in patients (often elderly and/or unwell) and loses time to pursue the increasing number of alternative treatments (targeted therapies, clinical trials). Since June 2024, all Danish patients are given chemotherapy plus immunotherapy based on international trials, even

though the addition of immunotherapy only appears to improve survival outcomes for <25% of patients. Current umbrella treatment protocols in unselected populations clearly result in non-beneficial treatment (rapid progression) and over-treatment (risk of adverse events, financial toxicity).

Baggrund

We recently demonstrated that pre-treatment immune functionality in tumor tissues is the critical determinant of chemotherapy outcome and identified an RNA signature that predicts chemotherapy benefit in diagnostic tissue biopsies (O'Rourke et al. Gut 2024). In this proposal, we will develop this signature into a prototype tool that can predict an individual's benefit from chemotherapy before treatment is initiated. We will determine if the minority benefiting from the addition of immunotherapy are those who would otherwise have rapid progression or long survival on chemotherapy alone. Further, we will identify recurrent actionable genetic alterations associated with those who rapidly progress on chemotherapy.

Metoder

We will perform whole transcriptome profiling and targeted mutational profiling on diagnostic biopsies from 470 patients with advanced intrahepatic cholangiocarcinoma.

Tidsplan

2-year duration (please see Gantt chart).

Forventede resultater og impact

This project will will generate a tool that can identify patients unlikely to benefit from chemo(immuno)therapy before starting treatment (avoiding unnecessary toxicities, minimizing health economy burden), and build support towards alternative treatment strategies for those currently doing worst on standard-of-care (improving patient outcomes).

Øvrige projektdeltagere og samarbejdsrelationer

Dr. Dan Høgdall (Denmark); Prof. John Bridgewater (England); Prof. Chiara Braconi (Scotland); Prof. Lorenza Rimassa (Italy); Prof. Teresa Macarulla & Dr. Tian Tian (Spain); Dr. Lara Heij (Germany); Prof. Jens Marquardt (Germany).

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Total budget: 2.881.012 DKK. **Amount with funding**: 1.913.222 DKK (supported by Kræftens Bekæmpelses, Lundbeckfonden). **Amount without funding**: 967.790 DKK. **Amount requested from Direktør Michael Hermann Nielsens Mindelegat, Afd. B**: 100.000 DKK (or parts thereof).

Direktør Michael Hermann Nielsens Mindelegat, Afd. B

6 MARCH 2025

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Til bedømmelseskomitéen,

Vi ansøger Direktør Michael Hermann Nielsens Mindelegat, Afd. B om forskningsmidler til at støtte vores studie med titlen: "***Tilpasning af en transkriptombaseret strategi for præcisionskemoimmunterapi ved galdevejskræft***".

Galdevejskræft er en aggressiv tumor, der opstår i galdevejene, med en gennemsnitlig overlevelse på ca. 12 måneder fra diagnosen. Det er derfor afgørende, at den rette patient matches med den rette behandling på det rette tidspunkt. Kemoterapi forbliver hjørnestenen i behandlingen, trods varierende effekt mellem patienter. Fra juni 2024 vil egnede danske patienter blive behandlet med kemoterapi plus durvalumab (anti-PD-L1), mens pembrolizumab (anti-PD-1) sandsynligvis snart vil blive godkendt som et alternativt immunterapiregime. På trods af banebrydende forsøg, der støtter disse nye behandlingsprotokoller, vurderes det, at kun ca. 1 ud af 4 patienter opnår langsigtet fordel af tilføjelsen af immunterapi. At forudsige en patients behandlingsfordel, før behandlingen påbegyndes, og identificere behandlingssvigt så tidligt som muligt, er kritiske udækkede behov for at optimere patientplejen (forhindre brug af toksiske behandlinger uden fordel og prioritere nye alternative behandlinger hurtigere).

Vores nylige studie påviste, at immunfunktionalitet er den dominerende faktor for kemoterapifordel og demonstrerede, at RNA-profiler fra biopsier kunne forudsige patientresultater før behandlingsstart (O'Rourke et al. Gut 2024). I samarbejde med førende onkologiske eksperter i hele Europa vil vi nu formelt udvikle denne test til et prototypeværktøj, der kan bruges til at understøtte behandlingsbeslutninger af klinikere på patient-til-patient-basis. Disse beslutninger omfatter prioritering af alternative behandlinger eller kliniske forsøg til patienter, som ikke vil have gavn af kemoterapi (bedre sygdomsbekæmpelse) eller udelukkelse af tilføjelse af immunterapi til patienter, der vil overleve i lang tid på kemoterapi alene (mindre bivirkninger for patienten, mindre økonomisk byrde for sundhedsvæsenet). Dette vil ultimativt forbedre den kliniske pleje og livskvaliteten for denne underforsynede patientgruppe i Danmark og internationalt.

Vi anmoder venligst Direktør Michael Hermann Nielsens Mindelegat, Afd. B om at bidrage med **100.000 DKK (eller dele deraf)** til molekylær profilering af biopsier fra patienter i kemoterapi (med eller uden immunterapi). Yderligere molekylær profilering af disse prøver er allerede finansieret af Kræftens Bekæmpelse og Lundbeckfonden (budget). Ekstraomkostninger (løn, infrastruktur, ressourcer) er dækket af interne midler i Andersen-gruppen.

På forhånd tak for jeres overvejelse.

Med venlig hilsen,

Colm O'Rourke, Associate Professor, Andersen group, BRIC, Department of Health & Medical Sciences, University of Copenhagen, 2200 DK. colm.rourke@bric.ku.dk

Lay project description

Dansk:

Alle patienter diagnosticeret med fremskreden galdevejskræft får kemoterapi med eller uden immunterapi som deres primære behandling. Denne 'one-size-fits-all' tilgang modsiges af vores viden om, at kemoimmunterapi ikke bremser tumorvækst i en undergruppe af patienter. Som følge heraf lider disse patienter af bivirkninger fra ikke-gavnlig standardbehandling og mister tid til at prøve alternative behandlinger. Gennemsnitlig overlevelse for disse patienter er kun cirka 12 måneder fra diagnosen, så det er afgørende at træffe den bedste behandlingsbeslutning for alle så hurtigt og effektivt som muligt. For nylig brugte vi patienters vævsbiopsier til at udvikle en molekylær test, der forudsiger behandlingsudbytte, før behandlingen påbegyndes. Nu vil vi optimere denne test yderligere for at gøre den klar til onkologer til brug på deres hospitaler. I dette forslag går vi sammen med internationale eksperter for at bygge netop denne prototype. Vi vil forudsige, hvilke patienter, der har gavn af kemoterapi, inden behandlingen påbegyndes, hvilke patienter, der ikke behøver for at få immunterapi med deres kemoterapi, og hvilke potentielle alternative behandlinger, der findes for patienter, der sandsynligvis ikke vil have gavn af kemoterapi. Opfyldelse af disse mål vil give læger et nyt værktøj til at optimere behandlingsplaner på patient-til-patient-basis, bremse kræften så længe som muligt og undgå unødvendige bivirkninger fra behandlinger, der ikke virker effektivt.

English:

All patients diagnosed with advanced bile duct cancer are given chemotherapy with or without immunotherapy as their primary treatment. This 'one-size-fits-all' approach is contradicted by our knowledge that chemoimmunotherapy does not slow tumor growth in a subgroup of patients. As a result, these patients suffer side effects from non-beneficial standard-of-care and lose time to try alternative treatments. Average survival of these patients is only approximately 12 months from diagnosis, so it is critical to make the best treatment decision for everyone as quickly and effectively as possible. Recently, we used patients' tissue biopsies to develop a molecular test that predicts treatment benefit before starting treatment. Now, we want to optimize this test further to make it ready for oncologists to use in their hospitals. In this proposal, we are teaming up with international experts to build exactly this prototype. We will predict which patients benefit from chemotherapy before starting the treatment, which patients do not need to get immunotherapy with their chemotherapy, and what potential alternative treatments exists for patients unlikely to benefit from chemotherapy. Accomplishing these aims will provide a new tool for doctors to optimize treatment plans on a patient-by-patient basis, slowing down the cancer for as long as possible and avoiding unnecessary side effects from treatments that do not work effectively.

Adapting a transcriptome-based strategy for precision chemoimmunotherapy in bile duct cancer

Associate Professor Colm J. O'Rourke, Professor Jesper B. Andersen

Research question: Patients with advanced intrahepatic cholangiocarcinoma (**iCCA**) are all treated with chemotherapy, but only a subgroup benefits therapeutically, and treatment inevitably fails in all patients over time[1,2]. This leads to toxicities from non-beneficial treatments in patients (often elderly and/or unwell) and loses time to pursue the increasing number of alternative treatments (targeted therapies[3], clinical trials[4]). Since June 2024, all Danish patients are given chemotherapy plus immunotherapy based on international trials[5,6], even though the addition of immunotherapy only appears to improve survival outcomes for <25% of patients[6]. Current umbrella treatment protocols in unselected populations clearly result in non-beneficial treatment (rapid progression) and over-treatment (risk of adverse events, financial toxicity). We recently demonstrated that **pre-treatment immune functionality in tumor tissues is the critical determinant of chemotherapy outcome** and identified an **RNA signature that predicts chemotherapy benefit in diagnostic tissue biopsies**[7]. In this proposal, we will develop this signature into a prototype tool (**$RPLS_{OPTI}$**) that can predict an individual's benefit from chemotherapy before treatment is initiated. We will determine if the minority benefiting from the addition of immunotherapy are those who would otherwise have rapid progression or long survival on chemotherapy alone. Further, we will identify recurrent actionable genetic alterations associated with those who rapidly progress on chemotherapy. Successfully accomplishing these aims will generate a tool that can identify patients unlikely to benefit from chemo(immuno)therapy before starting treatment (**avoiding unnecessary toxicities**, **minimizing health economy burden**), and build support towards alternative treatment strategies for those currently doing worst on standard-of-care (**improving patient outcomes**).

Hypotheses: (1) Expression of our previous RNA signature genes in diagnostic biopsies can be harnessed to identify patients who will not benefit from chemotherapy before starting treatment; (2) Patients with extreme outcomes on chemotherapy (either rapid progression or long survival) are the minority benefiting from the addition of immunotherapy; (3) Tumors that rapidly progress on chemotherapy have unique biology and distinct actionable alterations that could be exploited as alternative treatment strategies.

Objectives: (**O1**) To retrospectively train and validate an RNA signature ($RPLS_{OPTI}$) that accurately predicts patient outcomes on chemotherapy; (**O2**) To determine if the addition of immunotherapy benefits a subgroup of patients who would otherwise have poor, intermediate, or excellent outcome on chemotherapy alone; (**O3**) To identify recurrent actionable alterations over-represented among patients with limited benefit from chemotherapy.

State-of-the-art: Median survival of patients with advanced iCCA is ~12 months[6,8], so optimizing a patient's treatment strategy from diagnosis is critical to maximize outcome and quality-of-life (QoL). However, all iCCA patients are currently treated with chemo(immuno)therapy despite its heterogeneous benefit; ~22% of patients die within 4 months[8], ~11% of patients survive beyond 24 months[9], only 1 in 4 patients derive long-term benefit from the addition of immunotherapy[3], and these extreme differences cannot be explained by clinicopathologic characteristics. Our inability to predict chemo(immuno)therapy efficacy results in non-beneficial, toxic treatments being administered to patients who are often elderly and unwell, negatively impacting QoL. Further, this blind spot prevents advancement of clinical practice by delaying administration of the growing number of targeted drugs[2,10] until after chemo(immuno)therapy failure (when the disease has progressed, patients are less fit, and tumors may have been evolutionarily antagonized to more resistant phenotypes).

Compared to other cancers, BTC has remarkably high incidence of targetable genomic alterations (up to 45%) and response rates to drugs targeting these alterations[11], highlighting this rare cancer as a model disease for precision treatment. Yet, this precision treatment paradigm is not applicable to chemo(immuno)therapy, as these agents lack a specific target, and their efficacy is impacted by diverse biological processes. Recently, we identified a gene expression signature (RPLS) in pre-treatment biopsies that predicts chemotherapy outcome for patients with liver-origin BTC and liver-metastatic tumors[7]. This demonstrates that transcriptomics (RNA profiling) can overcome the limitations of DNA profiling and supports the use of a precision approach to chemo(immuno)therapy in BTC for the first-time. Our data indicate that key characteristics of the original RPLS signature warrant its further clinical development into an optimized format:

(1) Approximately one out of four iCCA biopsies fail molecular profiling (DNA-sequencing) due to insufficient tumor cell content[12]. In our study, we macrodissected tumor-adjacent stroma (no tumor cells) from our diagnostic biopsies and demonstrated that the RPLS signature could still differentiate outcomes on chemotherapy[7]. This suggests that $RPLS_{OPTI}$ will predict well even in biopsies with limited tumor cell content.

(2) The original RPLS signature predicted outcomes of liver tumors treated with systemic chemotherapy (iCCA, liver-metastatic colorectal cancer) but not liver tumors treated with targeted therapies ± immunotherapy (hepatocellular carcinoma)[7]. This suggests that $RPLS_{OPTI}$ will be predictive rather than just prognostic.

(3) The original RPLS signature predicted chemotherapy outcomes in biliary tumors arising inside the liver but not biliary tumors arising outside the liver[7]. Further, the RPLS signature predicted chemotherapy outcomes when measured in colorectal liver metastases but not when measured in the matched primary bowel tumors[7,13]. This supports a liver-specific mechanism(s) of chemoresistance and suggests that $RPLS_{OPTI}$ might be useful for predicting chemotherapy outcomes in other liver-metastatic cancers, increasing the pool of potential patient beneficiaries.

(4) The original RPLS signature identified novel biology associated with rapid progressor tumors, including preclinical support for the existence of specific vulnerabilities in tumors currently responding the worst to chemotherapy (for example, *KRAS* mutations and IL-6 signaling which are both therapeutically actionable events[7]). This suggests that $RPLS_{OPTI}$ will further support the potential for alternative treatment strategies in place of chemo(immuno)therapy in large real-world populations.

Research plan: Our proposal is broken into three inter-related objectives (**O**). Milestones (**M**) and deliverables (**D**) are specified per task (**Fig. 1 – Gantt, Fig. 2 – Study Design & Impact**).

O1: To retrospectively train and validate an RNA signature ($RPLS_{OPTI}$) that accurately predicts patient outcomes on chemotherapy.

- Our original RPLS signature is composed of 504 genes[7]. However, all these genes are likely not important for predicting chemotherapy outcome (requiring simplification by feature selection); some genes are likely more important than others (requiring weighting of individual genes relative to each other); and the final RPLS score for an individual biopsy is not yet interpretable in terms of outcome if that patient is started on chemotherapy (requiring establishment of reference ranges for RPLS scores and how they should be interpreted in terms of an individual's outcome on chemotherapy including confidence intervals).

- Retrospectively we have identified real-world training (n=110) and validation (n=230) cohorts to develop $RPLS_{OPTI}$ which advances our original RPLS signature. All patients were diagnosed with advanced iCCA and treated with gemcitabine plus cisplatin[8] in the first-line palliative setting.
- For each of these patients, we will perform whole transcriptome profiling (Tempo-seq) using their diagnostic FFPE biopsies.
- In the training cohort, we will perform Least Absolute Shrinkage and Selection Operator (LASSO) on the original 504 genes to identify the optimal combination for predicting overall survival on chemotherapy ($RPLS_{OPTI}$). This will include reference ranges for interpreting $RPLS_{OPTI}$ scores with predicted patient outcomes if chemotherapy is initiated (overall survival, but also: best RECIST, duration of response, progression-free survival).
- We will determine the predictive performance of $RPLS_{OPTI}$ in the validation cohort. This will include statistical metrics to quantify accuracy (sensitivity, specificity) in categorically differentiating rapid progressors (OS<6m) from long survivors (OS>23m), as well quantitatively determine risk of death (univariable and multivariable Cox regression analysis, including adjusting for baseline characteristics associated with outcomes). While overall survival is considered the primary outcome metric, others will also be co-evaluated (RECIST, duration of response, progression-free survival).

Outcome: We will develop $RPLS_{OPTI}$, an RNA-based support tool using diagnostic biopsies that can inform clinicians about predicted outcome on chemotherapy if this treatment is initiated for an individual. Identifying patients unlikely to do well on standard-of-care will empower earlier orientation to trials or rapidly emerging alternative treatments (molecularly matched targeted therapies).

Risks & mitigation: This objective is low risk, as it is a direct follow-up to our recent study[7]. Tempo-seq is compatible with high-quality transcriptome profiling from old FFPE biopsies with limited material and/or compromised RNA quality. Power calculations are not possible in this study design which draws from the general patient population (our previous study pre-specified analysis of extreme outcomes in the palliative setting). However, as the original RPLS signature (504 unweighted genes) successfully predicted outcomes across multiple cohorts (ranging in sample size from 70 to 244), we expect the proposed training (n=110) and validation (n=230) cohorts to be sufficiently powered. While we expect $RPLS_{OPTI}$ to improve further upon the performance of the original RPLS signature, we will include the original RPLS signature as a comparator for predictive performance in all analyses. REMARK guidelines for tumor marker prognostic studies[14]. Clinical supervision will be provided by a team of international experts in oncology and gastroenterology (see **Feasibility** section).

O2: To determine if the addition of immunotherapy benefits a subgroup of patients who would otherwise have poor, intermediate, or excellent outcome on chemotherapy alone.

- We will perform transcriptome profiling (Tempo-seq) on diagnostic biopsies from 130 patients treated with gemcitabine, cisplatin, and durvalumab. Based on the literature[6], we anticipate that <25% of these patients really derive long-term benefit from the addition of immunotherapy.
- We will calculate $RPLS_{OPTI}$ scores for each of these patients receiving chemoimmunotherapy (as a predictive metric of how they would have benefited from chemotherapy treatment alone).
- We will propensity score match patients receiving chemoimmunotherapy with patients receiving chemotherapy (validation cohort) for $RPLS_{OPTI}$ scores (predicted chemotherapy benefit) and other baseline characteristics associated with systemic treatment outcome.

- For patients with low $RPLS_{OPTI}$ scores (predicted long-term benefit from chemotherapy), we will compare survival curves between chemotherapy and chemoimmunotherapy regimens. If the chemoimmunotherapy arm has better survival, this means that the subgroup of patients benefiting from the addition of durvalumab were the patients already having the longest survival on chemotherapy alone.
- For patients with high $RPLS_{OPTI}$ scores (predicted rapid progression on chemotherapy), we will compare survival curves between chemotherapy and chemoimmunotherapy regimens. If the chemoimmunotherapy arm has better survival, this means that the subgroup of patients benefiting from the addition of durvalumab were the patients previously with worst outcomes on chemotherapy alone.

Outcome: We will determine the relationship (if any) between benefit from chemotherapy versus benefit from chemoimmunotherapy. This will advance our knowledge of the subgroup of patients specifically deriving outcome benefit from immunotherapy and, in the future, might support exclusion of immunotherapy for patients who do not derive benefit from immunotherapy (lower risk of adverse events, less financial toxicity).

Risks & mitigation: This objective is medium risk. Technically, no risks exist beyond those reported in O1. In our previous study, we identified immune checkpoint signaling to be associated with rapid progressor-like preclinical models, suggesting an association between this immune escape mechanism and poor chemotherapy outcomes. Conceptually, it is possible that sensitivity to chemotherapy is not exclusively associated with this escape mechanism in patients or that this escape mechanism is alone insufficient to confer sensitivity to checkpoint inhibitors. Nonetheless, reaching this negative conclusion is also important for the field and, in this scenario, we will repurpose the transcriptome data we generated to tailor a follow-up study specifically focusing on biomarker development of immunotherapy beneficiaries.

O3: To identify recurrent actionable alterations over-represented among patients with limited benefit from chemotherapy.

- Using biopsies from the validation cohort (n=230; O1), we will perform targeted DNA sequencing (Oncomine Comprehensive Assay Plus) to identify potentially actionable genetic alterations.
- We will identify recurrent genetic alterations associated with high $RPLS_{OPTI}$ scores (unlikely to benefit from chemotherapy) that might be serve as alternative treatment strategies in upcoming clinical trials.

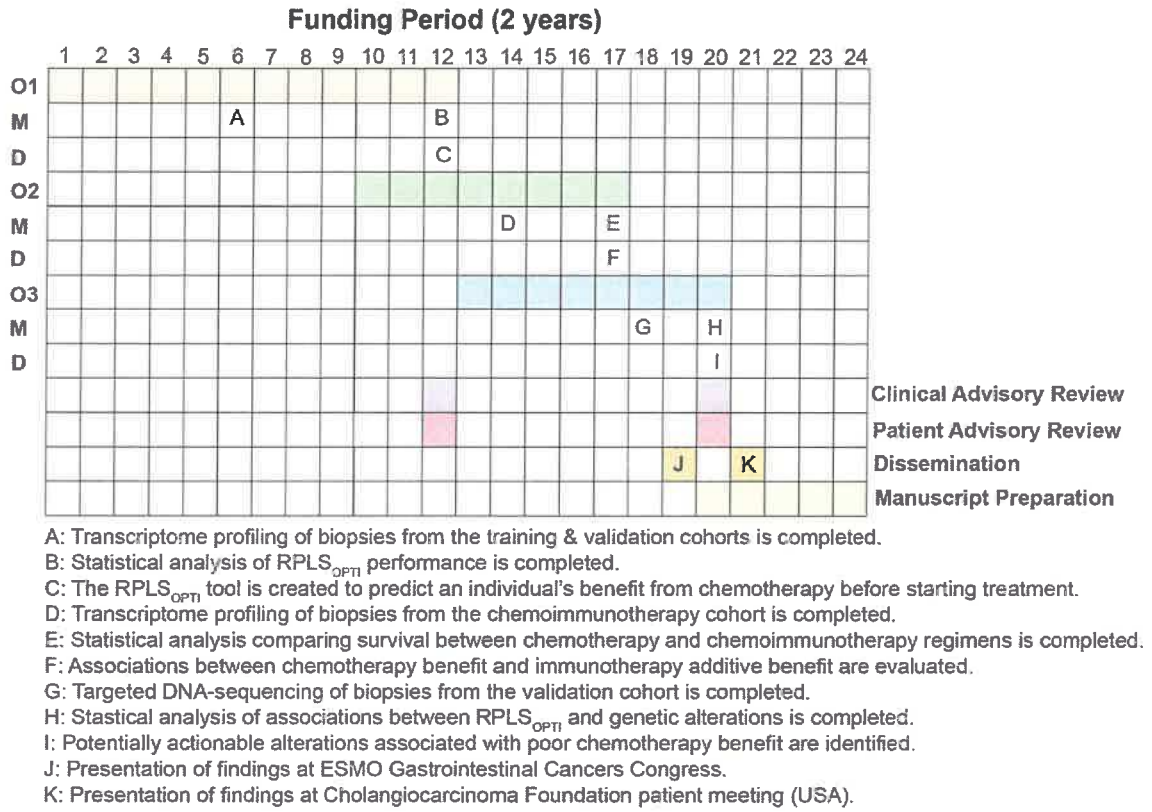
Outcome: We will identify potentially actionable genetic alterations associated with rapid progression on chemotherapy, building a knowledgebase of potential alternative treatment strategies for those patients currently doing the worst on chemotherapy.

Risks & mitigation: This objective is low-medium risk. Our previous study indicated *KRAS* mutations are associated with high RPLS scores (limited chemotherapy benefit)[7] and a subset of these variants are already therapeutically actionable. Our collaborator (Prof. Bridgewater, UCL, UK) is already conducting a clinical trial (SAFIR-ABC10 NCT05615818) in unselected patients to compare the efficacy of first-line chemoimmunotherapy compared to targeted therapy maintenance (including mutant KRAS inhibitors), emphasizing the unmet need for biomarkers in this setting (which we will develop). If no genetic alterations are significantly associated with high $RPLS_{OPTI}$ scores, we will conclude that alternative treatment options should be guided by individualized molecular profiling which is already recommended by ESMO[15].

Feasibility: This project is ambitious but feasible within 24 months due to: (1) the availability of diagnostic biopsies and clinical supervision from international expert collaborators (Dr. Dan Høgdall, Denmark; Prof. John Bridgewater, England (**Letter of Support**); Prof. Chiara Braconi, Scotland; Prof. Teresa Macarulla, Spain; Prof. Jens Marquardt, Germany; Dr. Lara Heij, Germany); (2) the prior expertise of our group in all necessary skills, including molecular profiling of patient samples and clinical biomarker discovery[16-21]; (3) the extensive prior work underlying this proposal, as reported in our

previous publication[7]; (4) the necessary support infrastructure available at our institute (laboratory space for sample processing and genomics, high-performance computational server for analysis; (5) the future ability to prospectively validate the $RPLS_{OPTI}$ signature via our expert collaborator network and professional organization, Precision-BTC-Network (https://precision-btc.eu/).

Dissemination: We will present our results to the scientific community at the ESMO Gastrointestinal Cancers Congress. Patients (Leverforeningen, DK; **Letter of Support**) and expert clinicians will provide active feedback on our study to ensure our study has maximal impact for patient care. Results will also be disseminated to lay audiences (including patients and caregivers) via Leverforeningen (DK), AMMF Cholangiocarcinoma charity (UK) and Cholangiocarcinoma Foundation (CCF, USA), as we have done previously.



A: Transcriptome profiling of biopsies from the training & validation cohorts is completed.
B: Statistical analysis of $RPLS_{OPTI}$ performance is completed.
C: The $RPLS_{OPTI}$ tool is created to predict an individual's benefit from chemotherapy before starting treatment.
D: Transcriptome profiling of biopsies from the chemoimmunotherapy cohort is completed.
E: Statistical analysis comparing survival between chemotherapy and chemoimmunotherapy regimens is completed.
F: Associations between chemotherapy benefit and immunotherapy additive benefit are evaluated.
G: Targeted DNA-sequencing of biopsies from the validation cohort is completed.
H: Stastical analysis of associations between $RPLS_{OPTI}$ and genetic alterations is completed.
I: Potentially actionable alterations associated with poor chemotherapy benefit are identified.
J: Presentation of findings at ESMO Gastrointestinal Cancers Congress.
K: Presentation of findings at Cholangiocarcinoma Foundation patient meeting (USA).

Figure 1: Gantt chart. D: deliverable; M: milestone; O: objective.

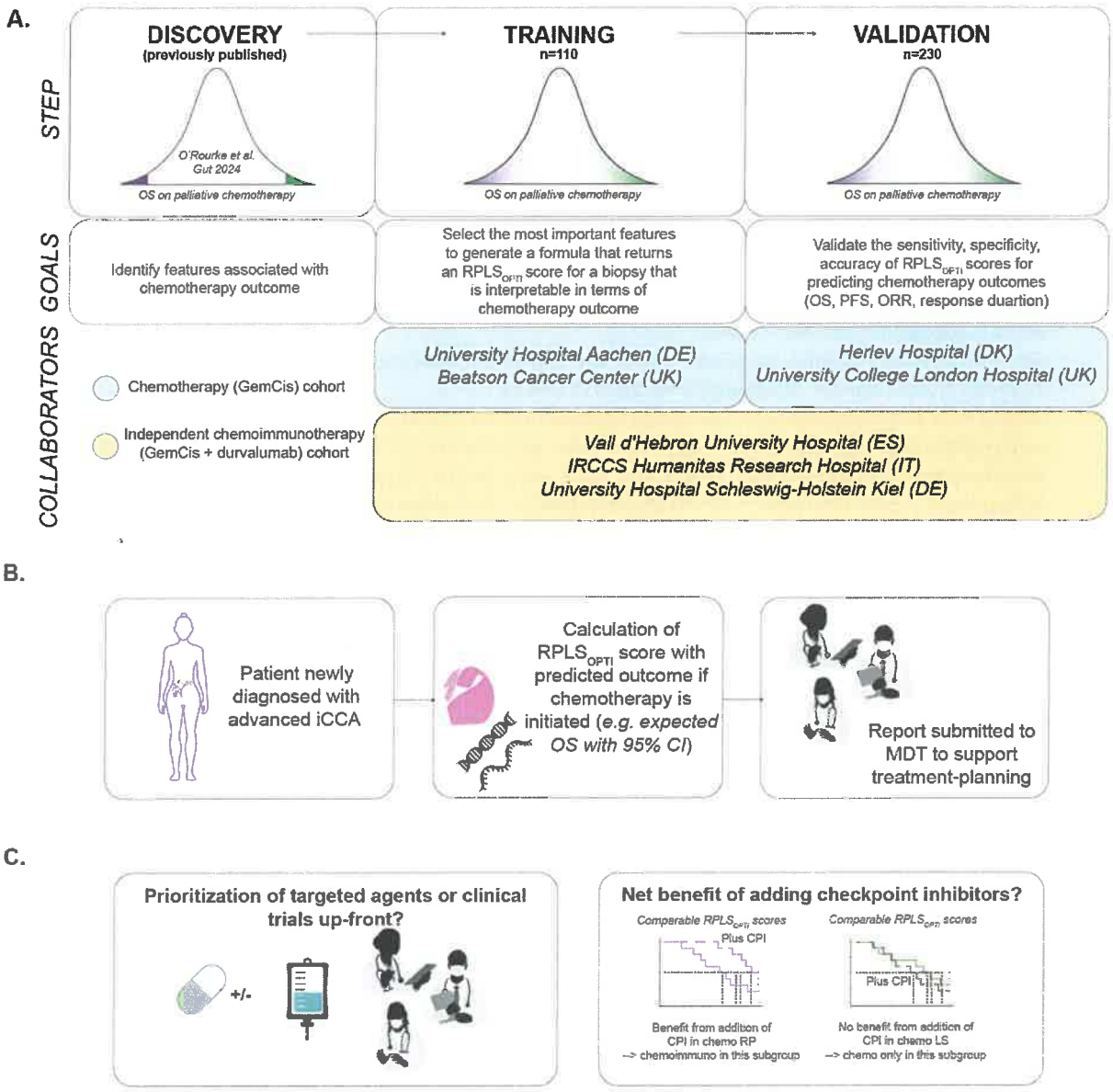


Figure 2: Proposal design & impact. (A) Overview of the study design, goals of each step, and international collaborators (contributing patient biopsies, clinical data, clinical advisory review). GemCis: gemcitabine plus cisplatin; ORR: objective response rate; OS: overall survival; PFS: progression-free survival. (B) We propose that when a patient is newly diagnosed by biopsy, this sample should undergo transcriptome profiling and the RPLS$_{OPTI}$ score should be calculated. This information would be provided as a written report to the multidisciplinary team (MDT), including the predicted patient benefit (with confidence intervals) if chemotherapy is initiated. This would enable the MDT to develop the optimal treatment plan on a patient-by-patient basis. (C) We envision that clinical adaptation of the RPLS$_{OPTI}$ score would have two major implications; for patients unlikely to benefit from chemotherapy, alternative targeted treatments or clinical trials should be used in first-line; for patient likely to greatly benefit from chemotherapy, omission of immunotherapy should be considered if our data support no additive benefit in this subpopulation. CPI: checkpoint inhibitors; LS: long survivor; RP: rapid progressor.

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UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES

Direktør Michael Hermann Nielsens Mindelegat, Afd. B

06 MARCH 2025

To the assessment committee.

This letter is in strong support of Dr. Colm J. O'Rourke, who is applying to the foundation for funding to advance his exciting project: "**Adapting a transcriptome-based strategy for precision chemoimmunotherapy in bile duct cancer**".

Colm has developed a transcriptomics-based score that at diagnosis can predict benefit from chemotherapy (Gem/Cis), which is the treatment most BTC patients still are offered in the clinical today. This study was published in the high impact journal, O'Rourke CJ. *et al.* GUT, 2024.
This gene signature (termed RPLS for rapid progressors versus long survivors) is exclusively predictive of outcome in intrahepatic BTCs, and importantly liver metastases from any primary cancer type (colon, lung, breast etc.). Of course, this score has limitations, as it cannot be longitudinally monitored during treatment to detect when chemoresistance inevitably arises in every patient. Therefore, Colm has initiated a collaboration with multiple oncology specialists across Europe, including the infamous BTC trial team at UCL, UK lead by Prof. John Bridgewater. His team has been responsible for most of the significant clinical trials in BTC, starting with ABC02 in 2010 investigating the efficacy of standard chemotherapy in more than 430 patients. Colm has access to unique samples, which will be essential to further develop the chemo-response score to a tool that can be used to facilitate rapidly changing treatment decisions for these patients. Envisioning follow-up from this study with prospective samples, Colm is establishing a collaboration with Prof. Rachna Schroff, Dept. of Medicine, University of Arizona, USA, utilizing the patient samples from the national randomized phase 3 trial (SWOG 1815).

Colm is an associate professor in my group (Andersen group) at BRIC and I am very pleased to support his research with my continued focus on his career development. I will support Colm in the form of space, infrastructure (access to BRIC core facilities) and of course any need for knowhow or help from me or other colleagues for this exciting project. This is a project, which I believe will have great societal impact and directly translatable to the clinic.

Sincerely,

Jesper B Andersen

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UCL CANCER INSTITUTE

JOHN BRIDGEWATER
PROFESSOR IN MEDICAL ONCOLOGY

11th February 2025

To the committee of Direktør Michael Hermann Nielsens Mindelegat, Afd. B,

I am enthusiastically writing this letter in support of Dr. O'Rourke's research proposal, entitled "Adapting a transcriptome-based strategy for precision chemoimmunotherapy in bile duct cancer".

Historically, cytotoxic agents have been the only treatment modalities for patients with advanced biliary tract cancer. However, benefit from chemotherapy is variable between patients and inevitably ceases to exert disease control over time in all patients. Molecular tools to predict which patients will benefit from chemotherapy before treatment and to identify the earliest timepoint in which disease progression occurs are critical unmet needs in our clinics.

The current proposal from Dr. O'Rourke builds upon his recent manuscript (Gut 2024) in which he and colleagues demonstrated the ability of pre-treatment tissue RNA profiles to predict chemotherapy outcome. Developing this text to be clinic-ready is a clear next step to predict chemo(immune)therapy benefit.

On behalf of the ABC trial team, I am happy to provide biopsy samples for use in this study, as well as clinical guidance to ensure this project achieves its full potential with maximum for patient care.

I hope the Direktør Michael Hermann Nielsens Mindelegat, Afd. B committee will give this impressive proposal the consideration it deserves.

With best wishes

John Bridgewater

Professor and consultant in Medical Oncology
Chair, NCRI UGI CSG
Lead, UGI Gel Consortium

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26.11.2024

"Tilpasning af en transkriptombaseret strategi for præcisionskemoimmunterapi ved galdevejskræft" af Dr. O'Rourke og Prof. Andersen ved Københavns Universitet

Galdevejskræft klassificeres som en sjælden sygdom i Danmark og de fleste andre lande, men forekomsten af disse aggressive tumorer er uhyggeligt stigende i de seneste år. Alle patienter har traditionelt fået kemoterapi, selvom mange patienter ikke har haft gavn af denne behandling. Med de nylige godkendelser af immunterapi og målrettede lægemidler er en væsentlig udfordring nu at afgøre, hvilken behandling der skal prioriteres. At træffe den rigtige behandlingsbeslutning for den rigtige patient på det rigtige tidspunkt er en tydelig hindring for at forbedre patientplejen.

Med udgangspunkt i teamets tidligere arbejde adresserer dette spændende projekt direkte det udækkede behov for værktøjer til behandlingsbeslutning og vil udvikle en prøve, der kan forudsige den enkelte patients fordel af kemoterapi (med eller uden immunterapi), inden behandlingen påbegyndes.

Leverforeningen Danmark støtter fuldt ud dette forskningsprojekt. Vi er glade for at bidrage med patientinput under projektet og offentliggøre resultaterne, når projektet er afsluttet.

Vi håber, at evalueringskomitéen finder dette vigtige projekt egnet til finansiering.

Med venlig hilsen
Leverforeningen Danmark

Lone McColaugh
Landsformand

BUDGET STATEMENT

The budget for this 2-year project is provided below.

We kindly request 100.000 DKK (or parts thereof) from Direktør Michael Hermann Nielsens Mindelegat, Afd. B towards molecular profiling of patient biopsies.

		Total (DKK)	Funded (DKK)	Not Funded (DKK)
Associate Professor salary (2 years)		1.318.492	1.318.492	0
Transcriptome profiling (Tempo-Seq)	Training cohort (n=110, chemotherapy)	155.760	155.760	0
	Validation cohort (n=230, chemotherapy)	325.680	325.680	0
	Validation cohort (n=130, chemoimmunotherapy)	184.080	113.290	**70.790**
Targeted DNA (Oncomine)	Validation cohort (n=230, chemotherapy)	897.000	390.000	**507.000**
Total		2.881.012	1.913.222	967.790

All other experimental costs, laboratory consumables, and salary are already funded by research grants (Danish Cancer Society, Lundbeck Foundation). Additional funding requests have been sent to: Torben & Alice Frimodts Fond, Frimodt-Heineke Fonden, Simon Spies Fonden, Tømrermester Jørgen Holm og hustru Elisa f. Hansens Mindelegat. In the unlikely event that unforeseen costs arise in these projects, they will be covered by additional internal funding from the Andersen group (BRIC, Department of Health & Medical Sciences, University of Copenhagen).

Pending positive evaluation of this proposal, payment can be made in coordination with our finance control office, Mr. Alfred Jensen (alfred.jensen@bric.ku.dk, +45 35 33 46 29):

CVR: 29979812 (SUND-BRIC)

Danske Bank, Holmens Kanal 2, DK-1090, København K

University of Copenhagen

IBAN: DK7302164069044336

SWIFT: DABADKKK

CURRICULUM VITAE – COLM O'ROURKE

PERSONAL DATA

Date of birth: 18th May 1989; Citizenship: Irish; ORCID research identifier: https://orcid.org/0000-0002-2224-2663

CURRENT POSITION(S)

Associate Professor of Liver Genomics & Biomarker Development, Andersen group, Biotech Research & Innovation Centre (BRIC), Department of Health & Medical Sciences, University of Copenhagen, DK.

EDUCATION & TRAINING

- Introduction to University Pedagogy, University of Copenhagen, DK (Oct 2022).
- Infinium array customer training, Illumina (University of Copenhagen), DK (July 2015).
- PhD clinical medicine, Institute of Molecular Medicine, Trinity College Dublin, IE (April 2015).
- Biobanking for translational research, Mater University Hospital, IE (March 2012).
- BA (Hons.) human genetics, Department of Genetics, Trinity College Dublin, IE (June 2010).

PROFESSIONAL EXPERIENCE

- Associate Professor, BRIC, University of Copenhagen (Feb 2025-)
- Assistant Professor, BRIC, University of Copenhagen (Feb 2019-Jan 2025).
- MSCA research fellow, BRIC, University of Copenhagen (Feb 2017-Jan 2019).
- Visiting researcher, FIMM, University of Helsinki, FI (Dec 2015-Feb 2016).
- Postdoc, BRIC, University of Copenhagen (Feb 2015-Jan 2017).
- Visiting researcher, National Cancer Institute, NIH, USA (Jan-Mar 2013).
- PhD student, Institute of Molecular Medicine, Trinity College Dublin, IE (Oct 2011-Jan 2015).
- Research assistant, Department of Genetics, Trinity College Dublin, IE (Oct 2010-June 2011).
- Summer intern, Department of Genetics, Trinity College Dublin, IE (July-Sep 2009).
- Undergraduate student, Department of Genetics, Trinity College Dublin, IE (Oct 2006-May 2010).

ACADEMIC ACTIVITIES

External funding:

-As **PI** (1.025.000 DKK)

- *"Developing a non-invasive tool to monitor chemotherapy benefit in biliary tract cancers"*, 100.000 DKK from Fabrikant Einar Willumsens Mindelegat (June 2024)
- *"Developing a non-invasive tool to monitor chemotherapy benefit in biliary tract cancers"*, 600.000 DKK from Læge Sofus Carl Emil Friis og Hustru Olga Doris Friis' Legat (July 2024)
- *"Developing a non-invasive tool to monitor chemotherapy benefit in biliary tract cancers"*, 75.000 DKK from Eva og Henry Frænkels MindeFond (September 2024)

- *"Developing a non-invasive tool to monitor chemotherapy benefit in biliary tract cancers"*, 200.000 DKK from Aase og Ejnar Danielsens Fond (September 2024)
- *"Developing a non-invasive tool to monitor chemo(immuno)therapy benefit in biliary tract cancers"*, 50.000 DKK from A.P. Møller Fonden (January 2025)

-As **co-PI** (>9.2m DKK)

- *"Tumor-macrophage dynamics and chemoresistance mechanisms in biliary tract cancers"*, >3.3m DKK from Kræftens Bekæmpelse (2023)
- *"Tumor phenotypes and sensitivities triggered by IL-6 activation in intrahepatic cholangiocarcinoma"*, 302.500 DKK from AMMF UK (2022)
- *"Inflammatory niche controlled by IL-6 promotes liver cancers"*, 1.5m DKK from NEYE-Fonden (2021)
- *"Dissecting the role of NRF1-mediated epigenome remodeling in metastatic intrahepatic cholangiocarcinoma"*, >1.9m DKK from Knæk Cancer (2020)
- *"Characterization of lysine demethylase family inhibitor-sensitive cholangiocarcinoma"*, >2.2m DKK from Novo Nordisk (2019)

-As **postdoc** (1.5m DKK):

- *"Epigenome-targeted therapy for cholangiocarcinoma"*, 1.5m DKK from MSCA Individual Fellowship (2017)

-As co-supervisor (>8.1m DKK):

- *"Characterization of the molecular landscape of patients with small bowel adenocarcinomas"*, 2m DKK from Luis-Hansen Fond (for clinical postdoc, 2024)
- *"Tumor-macrophage dynamics and chemoresistance mechanisms in biliary tract cancers"*, 225.000 DKK from Kræftforskningsfond (for PhD student, 2023)
- *"Understanding the impact of hypoxia on B cell-tumor crosstalk in intrahepatic cholangiocarcinoma"*, >1.5m DKK from Kræftens Bekæmpelse (postdoc, 2023)
- *"Tumor phenotypes and sensitivities triggered by IL-6 activation in intrahepatic cholangiocarcinoma"*, 225.000 DKK from Kræftforskningsfond (for PhD student, 2022)
- *"Exploiting the immunological tumor-host reaction for improved management of biliary tract cancer"*, >2.4m DKK from Lundbeck (for clinical postdoc, 2022)
- *"The impact of lysine demethylase (KDM) families 3 and 5 in epi-therapy-sensitive bile duct cancers"*, >1.6m DKK from Lundback (for postdoc, 2021)

Consortium roles:

-Young Investigator lead for Artificial Intelligence, Precision-BTC-Network (EU COST Action CA22125)

-Young Investigator lead for molecular profiling, European Network for the Study of Cholangiocarcinoma (EU COST Action CA18122).

-Member of Young Investigator Group (YIG-CCA, European Network for the Study of Cholangiocarcinoma).

-Member of 'precision medicine', and 'preclinical models' working groups in Precision-BTC Network.

-Co-founding member and bioinformatics lead of the national Danish small bowel cancer initiative (2023-present).

Research dissemination:

-local UCPH website

- https://www.bric.ku.dk/news/2022/the-immune-system-can-help-us-diagnose-cancer/
- https://www.bric.ku.dk/research-stories/research-stories-2020/tumor-microenvironment-could-play-an-important-role-in-gallbladder-carcinogenesis/
- https://www.bric.ku.dk/research-stories/research-stories-2020/biomarker-reveals-how-aggressive-biliary-tract-cancer-is-in-patients/

-CORDIS EU research results

- https://cordis.europa.eu/project/id/709161

-CURIS open access repository.

-national media (diagnostisktidsskrift.dk, radio4.dk, sciencenews.dk).

-Andersen group (@UCPHAndersen_Lab), personal (@ColmJJORourke), Young Investigator Group for Cholangiocarcinoma (YIG-CCA) social media.

-presentations at patient-focused (Leverforeningen, DK; AMMF, UK; CCF, USA) and professional meetings.

Invited presentations:

-Precision-BTC-Network meeting (oral-Spain; May 2025).
-OECI Academy (virtual; Feb 2025).
-Precision-BTC-Network meeting (oral-Poland; July 2024).
-Cholangiocarcinoma Foundation annual meeting (oral-USA; April 2023).
-EpiCPH meeting (oral-SUND, UCPH, DK; Feb 2023).
-EuroCholangioNet meeting (oral-Edinburgh; July 2022).
-EuroCholangioNet meeting (oral-virtual; July 2021).
-AMMF charity annual meeting (poster-virtual; May 2021).
-Digital Liver Cancer Summit (poster-virtual; Feb 2021).
-Cholangiocarcinoma Foundation annual meeting (oral-virtual; Feb 2021).
-International Liver Cancer Association meeting (oral-USA; Sep 2019).
-International Liver Congress (oral-Austria; April 2019).
-International Liver Cancer Association meeting (oral-London; Sep 2018).
-Metastasis as a Systemic Disease (poster-Denmark; Oct 2017).
-Marie Sklodowska Curie Actions Individual Fellowship meeting (oral-Belgium; Sep 2017).
-Dansk Selskab for Cancerforskning annual meeting (post-Denmark; April 2016).
-Illumina Methylation conference (oral-UK; May 2014).

Academic/clinical collaborations (ongoing):

-Prof. Johansen & Dr. Høgdall, Dept. Oncology, Herlev & Gentofte Hospital, DK.

-Prof. Mau-Sørensen, Dept. Oncology, Rigshospitalet, DK.
-Dr. Pommergaard, Dept. Surgery, Rigshospitalet, DK.
-Prof. Kristensen, Dept. Pathology, Rigshospitalet, DK.
-Prof. Braconi, University of Glasgow, UK.
-Prof. Bridgewater, University College London, UK.
-Prof. Matter, University Hospital Basel, SW.
-Prof. Rimassa, Humanitas University, IT.
-Prof. Shroff, University of Arizona, USA.

Academic collaborations with industry (ongoing):
-Misvik Biology (Finland), personalized experimental therapeutics (2020-present)
-Abzu (Denmark/Spain), explainable AI (2020-present)
-Adcendo (Denmark), antibody-based drug delivery (2024-present)

Research peer review:
-regular peer reviewer for Clinical Cancer Research, Journal of Hepatology.
-occasional peer reviewer for Biomarker Insights, Biomolecules, BMC Cancer, BMC Gastroenterology, BMC Medicine, Cancer Research, Cancer Research Communications, Cancers, Cellular & Molecular Gastroenterology & Hepatology, Cellular Oncology, Clinical Epigenetics, Clinics & Research in Hepatology & Gastroenterology, Current Oncology, Diagnostics, Discover Oncology, Experimental Hematology & Oncology, Expert Opinion on Pharmacotherapy, Gastroenterology, Gastro Hep Advances, Genes, Hepatology, International Journal of Molecular Sciences, JHEP Reports, Journal of Clinical Medicine, Journal of Gastrointestinal Cancer, Molecular Medicine, Oncogene, Pharmaceuticals, Scientific Reports, Targeted Oncology.

Funding peer review:
-Expert evaluator & rapporteur for EU COST action funding program (network medicine for curing diseases 2024).

Professional memberships:
-Dansk Selskab for Cancerforskning.
-European Association for Cancer Research.
-European Association for the Study of Cholangiocarcinoma.
-International Liver Cancer Association.

Administrative activities:
-Co-organizer of "Transcriptomics: Dos and Don'ts" session at International Liver Congress (Amsterdam, May 2025)
-Internal pre-submission reviewer of research grants at BRIC (2024-).
-Organizational and administrative roles for the Early Stage Innovation Board at BRIC (2023-)

-Internal pre-submission reviewer of postdoc grants at BRIC (2022-)
-Practical facilitator of EU-LIFE "*Epigenetics and Disease*" Scientific Workshop (BRIC, 2015)
-Responsible for managing and maintaining the Illumina iScan microarray system at BRIC

- Performed genomic microarray profiling for multiple groups at BRIC (Erler, Grønbæk, Jensen, Sandelin)
- Supported genomic microarray profiling for Forensics (UCPH), Pediatric Neuropathology (Rigshospitalet), and Pathology (Herlev University Hospital) departments

TEACHING & SUPERVISION ACTIVITIES

Research supervision (current):
-2 PhD (DISCOVER program, UCPH)
-2 postdoc (UCPH)
-1 clinical postdoc (UCPH/Herlev)

Research supervision (previous):
-2 PhD (UCPH)
-1 clinical PhD (UCPH /Herlev)
-1 visiting PhD (Biodonostia Institute, Spain)
-2 MSc (UCPH)
-1 BSc (DTU)
-1 summer medical student (EU COST short term scientific mission)

Teaching (undergraduate):
-Lecturer in basic pathology (microscopy, case studies) for undergraduate medical students (UCPH, 2022-present).

Teaching (PhD courses):
-Co-organized and moderated "*AI in biomedical research: concepts, perspectives, tools*" for MoMeD program (BRIC, June 2024)
-Designed and delivered a lecture on "*DNA methylation in cancer*" for PhD course "*Cancer Genomics: Current concepts and clinical applications*" at Graduate School of Health and Medical Sciences, UCPH (2018, 2022, 2025)

Teaching (international courses/initiatives):
-Expert molecular biologist for molecular tumor board as part of the European Association for the Study of the Liver's educational program for medical professionals (virtual, March 2024)
-Designed and delivered a presentation on "*How to write IMPACT*" for "*COST for MSCA*" program by Euro-Cholangio-Net (virtual, July 2023)
-Designed and delivered a PhD class on "*Essentiality & Druggability*" for *Euro-Cholangio-Net COST Action Multi-Omics Training School* (Poland, June 2022)

Teaching (high school courses):

-Designed and delivered a workshop on "*Big data in the clinics: the road to precision medicine*" for high-school teachers (BRIC, April 2018)

- https://www.bric.ku.dk/newslist/news/2018/bringing-genomics-into-the-class-room/

-Lecturer and practical demonstrator for high-school SRP program (BRIC, 2017-2018)

- https://www.bric.ku.dk/newslist/news/2017/srp2017/

Mentorship programs:

- Mentor to Dr. Ghada Nouairia, Karolinska Institute, SE (Precision-BTC-Network/ENSCCA/ICRN mentorship program, Dec 2024 – May 2025)

PRIZES & AWARDS

-Best presentation (chemotherapy and immunotherapy), Cholangiocarcinoma Foundation annual meeting (April 2023)

-International Junior Investigator Award (best oral), International Liver Cancer Association (Sep 2019)

-Young Investigator Travel Bursary, European Association for the Study of the Liver (April 2019)

-Young Investigator Travel Bursary, European Association for the Study of the Liver (April 2018).

ENTREPRENEURIAL ACTIVITIES

-Moderator of "Innovation Day" (BII, 2025)

-Organizer of "*From Spark to Breakthrough: Navigating Research Innovation*" (BRIC, 2024)

-Early Stage Innovation Board committee member (BRIC, 2023-).

-Completed the Rising Entrepreneurs in Bio Business and Life Science (REBBLS) primer course by the Life Science Start-Up Academy, DK (3-6 June 2021).

-Poster pitch of European patent application No. 19166515.7 at Danish IP Fair (Sep 2020).

-Submitted European patent application No. 19166515.7 (*Identification of PAN-GAMMA secretase inhibitor (PAN-GSI) theranostic response signatures for cancers*) in coordination with UCPH Tech Transfer Office (April 2019).

-Poster presentation of "*Epigenetic biomarkers in liver cancers*" at Biomarker AGORA (matchmaking event), DK (Oct 2017).

RESEARCH OUTPUT

42 peer reviewed articles focused on translational cancer research (with expertise in hepatobiliary cancers), including 13 first-author manuscripts in high-impact journals such as *Gut*, *Journal of Hepatology*, *Hepatology*, *Nature Reviews Gastroenterology & Hepatology*; 3 additional book chapters.

PUBLICATIONS (*equal contribution)

(42) Høgdall D, Schou JV, Andersen JB, **O'Rourke CJ**. *Personalized neoadjuvant chemotherapy for gastrointestinal cancers – shaping imprecision to be precise.* Clinical Cancer Research (in press).

(41) Olaizola P, Olaizola I, de Ara MF, Lapitz A, Izquierdo-Sanchez L, Fernandez-Barrena MG, Alvarez L, **O'Rourke CJ**, Lee-Law PY, Davies K, Gradinaru A, Jimenez-Aguero R, La Casta A, Riaño I, Macias RIR, Marin JGJ, Martinez-Chantar ML, Avila MA, Aspichueta P, Andersen JB, Boulter L, Bujanda L, Rodridgues PM, Perugorria MJ, Banales JM. *Targeting UBE2I-mediated protein hyper-SUMOylation halts cholangiocarcinoma progression and rewires the tumor-stroma crosstalk.* Hepatology 2024.

(40) Døssing RH, Broman JJA, **O'Rourke CJ**, Tabaksblat EM, Andersen JB, Hansen CP, Poulsen TS, Høgdall EVS, Schou JHV, Høgdall D. *Molecularly redefining small bowel adenocarcinoma to accelerate precision patient care – Protocol of a multicenter observational cohort biomarker study.* BMC Cancer 2024.

(39) Zhuraleva E, Lewinska M, **O'Rourke CJ**, Pea A, Rashid A, Hsing A, Taranta A, Chang D, Gao YT, Koshiol J, Andersen JB. *Mutational signatures define immune and Wnt-associated subtypes of ampullary carcinoma*. Gut 2024.

(38) Oliveira DVNP*, Biskul E*, **O'Rourke CJ**, Hentze JL, Andersen JB, Høgdall C, Høgdall EV. *Developing a DNA methylation signature to differentiate high grade serous ovarian carcinomas from benign ovarian tumors.* Molecular Diagnosis & Therapy 2024.

(37) **O'Rourke CJ**, Schou JHV, Andersen JB, Høgdall D. *Targeted therapies in biliary tract cancer – when precision becomes imprecise.* ESMO Gastrointestinal Oncology 2024.

(36) Keggenhoff FL, Castven D, Becker D, Stojkovic S, Castven J, Zimpel C, Straub BK, Gerber T, Langer H, Hahnel P, Kindler T, Fahrer J, **O'Rourke CJ**, Ehmer U, Saborowski A, Ma L, Wang XW, Gaiser T, Matter MS, Sina C, Derer S, Lee JS, Roessler S, Kaina B, Andersen JB, Galle PR, Marquardt JU. *PARP1 selectively impairs KRAS-driven phenotypic and molecular features in intrahepatic cholangiocarcinoma*. Gut 2024.

(35) **O'Rourke CJ***, Salati M*, Rae C, Carpino G, Leslie H, Pea A, Prete MG, Bonetti LR, Amato F, Montal R, Upstill-Goddard R, Nixon C, Sanchon-Sanchez P, Kunderfranco P, Sia D, Gaudio E, Overi D, Cascinu S, Høgdall D, Pugh S, Domingo E, Primrose JN, Bridgewater J, Spallanzani A, Gelsomino F, Llovet JM, Calvisi DF, Boulter L, Caputo F, Lleo A, Jamieson NB, Luppi G, Dominici M, Andersen JB, Braconi C. *Molecular portraits of patients with intrahepatic cholangiocarcinoma who diverse as rapid progressors or long survivors on chemotherapy*. Gut 2024.

(34) Gehl V*, **O'Rourke CJ***, Andersen JB. *Immunogenomics of cholangiocarcinoma*. Hepatology 2023.

(33) Rodrigues PM, Afonso MB, Simao AL, Islam T, Gaspar MM, **O'Rourke CJ**, Lewinska M, Andersen JB, Arretxe E, Alonso C, Santos-Laso A, Izquierdo-Sanchez L, Jimenez-Aguero R, Eizaguirre E, Bujanda L, Pareja MK, Prip-Buus C, Banales JM, Rodrigues CMP, Castro RE. *miR-21-5p promotes NASH-related hepatocarcinogenesis*. Liver International 2023.

(32) Jansson H, Cornillet M, Sun D, Filipovic I, Sturesson C, **O'Rourke CJ**, Andersen JB, Bjorkstrom NK, Sparrelid E. *Preoperative immunological plasma markers TRAIL, CSF1 and TIE2 predict survival after resection for biliary tract cancer*. Frontiers in Oncology 2023.

(31) Lapitz A, Azkargorta M, Milkiewicz P, Olaizola P, Zhuraleva E, Grimsrud MM, Schramm C, Arbelaiz A, **O'Rourke CJ**, La Casta A, Milkiewicz M, Pastor T, Vesterhus M, Jimenez-Aguero R, Dill MT, Lamarca A, Valle JW, Macias RIR, Izquierdo-Sanchez L, Perez Castano Y, Caballero-Camino FJ, Riano I, Krawczyk M, Ibarra C, Bustamante J, Nova-Camacho LM, Falcon-Perez JM, Elortza F, Perugorria MJ, Andersen JB, Bujanda L, Karlsen TH, Folseraas T, Rodrigues PM, Banales JM. Liquid biopsy-based protein biomarkers for risk prediction, early diagnosis, and prognostication of cholangiocarcinoma. Journal of Hepatology 2023.

(30) Duwe L, Munoz-Garrido P, Lewinska M, Lafuente-Barquero J, Satriano L, Høgdall D, Taranta A, Nielsen BS, Ghazal A, Matter MS, Banales JM, Aldana BI, Gao YT, Marquardt JU, Roberts LR, Oliveira RC, Koshiol J, **O'Rourke CJ**, Andersen JB. *MicroRNA-27a-3p targets FoxO signalling to induce tumour-like phenotypes in bile duct cells.* Journal of Hepatology 2023.

(29) Haefliger S, Hench J, **O'Rourke CJ**, Meyer-Schaller N, Uzun S, Saldarriaga J, Weber A, Mazzucchelli L, Jermann P, Frank S, Andersen JB, Terracciano L, Sempoux C, Matter MS. *Genetic and epigenetic analysis of hepatocellular adenomas with atypical morphological features.* Histopathology 2023.

(28) Høgdall D*, **O'Rourke CJ***, Andersen JB. *Molecular therapeutic targets for cholangiocarcinoma: Present challenges and future possibilities.* Advances in Cancer Research 2023.

(27) Høgdall D, **O'Rourke CJ**, Larsen FO, Zarforoushan S, Christensen TD, Ghazal A, Boisen MK, Munoz-Garrido P, Johansen JS, Andersen JB. *Whole blood microRNAs capture systemic reprogramming and have diagnostic potential in patients with biliary tract cancer.* Journal of Hepatology 2022.

(26) Zhuravleva E*, **O'Rourke CJ***, Andersen JB. *Mutational signatures and processes in hepatobiliary cancers.* Nature Reviews Gastroenterology & Hepatology 2022.

(25) Olaizola P, Lee-Law PY, Fernandez-Barrena MG, Alvarez L, Cadamuro M, Azkargorta M, **O'Rourke CJ**, Cabellero-Camino FJ, Olaizola I, Macias RIR, Marin JJG, Serrano-Macia M, Martinez-Chantar ML, Avila MA, Aspichueta P, Calvisi DF, Evert M, Fabris L, Castro RE, Elortza F, Andersen JB, Bujanda L, Rodrigues PM, Perrugorria MJ, Banales JM. *Targeting NAE1-mediated protein hyper-NEDDylation halts cholangiocarcinogenesis and impacts on tumor-stroma crosstalk in experimental models.* Journal of Hepatology 2022.

(24) Zimmer CL, Filipovic I, Cornillet M, **O'Rourke CJ**, Berglin L, Jansson H, Sun D, Strauss O, Hertwig L, Johansson H, von Set E, Sparrelid E, Dias J, Glaumann H, Melum E, Ellis EC, Sandberg JK, Andersen JB, Bergquist A, Bjorkstrom NLK. *Mucosal-associated invariant T-cell tumor infiltration predicts long-term survival in cholangiocarcinoma.* Hepatology 2022.

(23) Silva R, Moran B, Baird AM, **O'Rourke CJ**, Finn SP, McDermott R, Watson W, Gallagher WM, Brennan DJ, Perry AS. *Longitudinal analysis of individual cfDNA methylome patterns in metastatic prostate cancer.* Clinical Epigenetics 2021.

(22) Czauderna C, Poplawski A, **O'Rourke CJ**, Castven D, Perez-Aguilar B, Becker D, Heilmann-Heimbach S, Odenthal M, Amer W, Schmiel M, Drebber U, Binder H, Ridder DA, Schindeldecker M, Straub BK, Galle PR, Andersen JB, Torgeirsson SS, Park YN, Marquardt JU. *Epigenetic modifications precede molecular alterations and drive human hepatocarcinogenesis.* JCI Insight 2021.

(21) Oliveira DVNP, Hentze J, **O'Rourke CJ**, Andersen JB, Høgdall C, Høgdall EV. *DNA methylation in ovarian tumors – a comparison between fresh tissue and FFPE samples.* Reproductive Sciences 2021.

(20) Gonzalez-Romero F, Mestre D, Aurrekoetxea I, **O'Rourke CJ**, Andersen JB, Woodhoo A, Tamayo-Caro M, Varela-Rey M, Palomo-Irigoyen M, Gomez-Santos B, de Urturi DS, Nunez-Garcia M, Garcia-Rodriguez JL, Fernandez-Ares L, Buqye X, Iglesias-Are A, Bernales I, De Juan VG, Delgado TC, Goikoetxea-Usandizaga N, Lee R, Bhanot S, Delgado I, Perugorria MJ, Errazti G, Mosteiro L, Gaztambide S, Martinez de la Piscina I, Iruzubieta P, Crespo J, Banales JM, Martinez-Chantar ML, Castano L, Zubiaga AM, Aspichueta P. *E2F1 and E2F2-mediated*

repression of CPT2 establishes a lipid-rich tumor-promoting environment. Cancer Research 2021.

(19) Nepal C*, Zhu B*, **O'Rourke CJ***, Bhatt DK, Lee D, Song L, Wang D, Van Dyke AL, Choo-Wosoba H, Liu Z, Hildesheim A, Goldstein AM, Dean M, LaFuente-Barquero J, Lawrence S, Mutreja K, Olanich ME, Lorenzo Bermejo J, CGR Exome Stidues Group, Ferreccio C, Roa JC, Rashid A, Hsing AW, Gao YT, Chanock SJ, Araya JC, Andersen JB, Koshiol J. *Integrative molecular characterization of gallbladder cancer reveals microenvironment-associated subtypes*. Journal of Hepatology 2021.

(18) Mikkelsen SU, Safavi S, Dimopoulos K, **O'Rourke CJ**, Andersen MK, Holm MS, Marcher CW, Andersen JB, Hansen JW, Grønbæk K. *Structural aberrations are associated with poor survival in patients with clonal cytopenia of undetermined significance.* Haematologica 2021.
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(12) **O'Rourke CJ**, Lafuente-Barquero J, Andersen JB. *Epigenome remodeling in cholangiocarcinoma.* Trends in Cancer 2019.

(11) Lozano E, Macias RIR, Monte MJ, Asensio M, Del Carmen S, Sanchez-Vicente L, Alonso-Pena M, Al-Abdulla R, Munoz-Garrido P, Satriano L, **O'Rourke CJ**, Banales JM, Avila MA, Martinez-Chantar ML, Andersen JB, Briz O, Marin JJG. *Causes of hOCT1-dependent cholangiocarcinoma resistance to sorafenib sensitization by tumor-selective gene therapy.* Hepatology 2019.

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(5) **O'Rourke CJ***, Munoz-Garrido P*, Aguayo EL, Andersen JB. *Epigenome dysregulation in cholangiocarcinoma.* Biochimica et Biophysica Acta Molecular Basis of Disease 2018.

(4) Merino-Azpitarte M, Lozano E, Perugorria MJ, Esparza-Baquer A, Erice O, Santos-Laso A, **O'Rourke CJ**, Andersen KB, Jimenez-Aguero R, Lacasta A, D'Amato M, Briz O, Jalan-Sakrikar N, Huebert RC, Thelen KM, Gradilone SA, Aransay AM, Lavin JL, Fernandez-Barrena MG, Matheu A, Marzioni M, Gores GJ, Bujanda L, Marin JJG, Banales JM. *SOX17 regulates cholangiocyte differentiation and acts as a tumor suppressor in cholangiocarcinoma.* Journal of Hepatology 2017.

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(2) **O'Rourke CJ**, Knabben V, Bolton E, Moran D, Lynch T, Hollywood D, Perry AS. *Manipulating the epigenome for the treatment of urological malignancies.* Pharmacology & Therapeutics 2013.

(1) **O'Rourke CJ**, Murphy TM, Hollywood D, Perry AS. *Mining methylome databases.* Trends in Genetics 2013.

BOOK CHAPTERS

(3) **O'Rourke CJ**, Andersen JB. *Pharmacoepigenetics of cholangiocarcinoma.* Pharmacoepigenetics (2nd edition, Elsevier, 2024).

(2) **O'Rourke CJ**, Andersen JB. *Advances in the molecular characterization of liver tumors.* Blumgart's Surgery of the Liver, Biliary Tract, and Pancreas (7th edition, 2022)

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(1) **O'Rourke CJ**, Satriano L, Oliveira DVNP, Munoz-Garrido P, Andersen JB. *Therapeutic potential of pharmacoepigenetics in cholangiocarcinoma.* Pharmacoepigenetics (1st edition, Elsevier, 2019).

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Viktor T. Lemgart, PhD, Forskningschef**
Arbejdssted/ Institution	**Troya Therapeutics**
Adresse	**Ole Maaløes Vej 3, 2200 Copenhagen N**
Tlf.nr.	**21433235**
e-mail	**viktor@troya-tx.com**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
Udvikling af A2M-IL-10 fusioner til behandling af autoimmune sygdomme
Formål
Troya Therapeutics søger DKK 150.000 fra Direktør. Michael Hermann Nielsens Mindelegat, afd. B til udvikling af en ny og innovativ proteinbaseret behandling mod autoimmune og inflammatoriske sygdomme. Projektet sigter mod at udvikle A2M-IL-10, et fusionsprotein, der kombinerer IL-10 med alfa-2-makroglobulin (A2M) for at tilbyde en mere målrettet og sikker behandling af sygdomme som leddegigt, inflammatorisk tarmsygdom og multipel sklerose.
Problemstilling
Cirka 1% af den globale befolkning lider af immundrevne inflammatoriske sygdomme, som udgør en betydelig sundhedsmæssig byrde. Nu anvendte behandlinger, især biologiske

lægemidler som TNF-inhibitorer, har begrænsninger såsom høje omkostninger, hyppige injektioner og bivirkninger som øget risiko for infektioner og immunsystemundertrykkelse. Der er derfor behov for et mere målrettet alternativ.

Baggrund

Troya Therapeutics har udviklet en teknologi, der fusionerer A2M, en naturlig protease-inhibitor, med IL-10, et antiinflammatorisk cytokin. Teknologien beskytter IL-10 under cirkulation og aktiverer det kun i inflammatoriske områder, hvilket giver en mere præcis behandling med færre systemiske bivirkninger.

Metoder

Projektet gennemføres i fire faser:

1. Skalering af fusionsproduktion: Optimering af produktionen af A2M-IL-10 i cellelinjer.
2. Udvikling af in vitro assays: Evaluering af effekten og sikkerheden af fusionsproteinet i cellekulturer.
3. Præklinisk testning i dyremodeller: Vurdering af farmakokinetik, sikkerhed og effektivitet i mus og rotter.
4. Udvælgelse af førende kandidater: Screening og udvælgelse af de mest lovende fusionsproteiner.

Tidsplan

- Måneder 1-2: Skalering af produktionen og optimering af cellekulturforhold.
- Måneder 2-3: Udvikling af oprensningsmetoder.
- Måneder 3-5: Udvikling og optimering af in vitro assays.
- Måneder 5-7: Forberedelse og opsætning af dyreforsøg.
- Måneder 7-10: Udførelse af in vivo forsøg og dataindsamling.
- Måneder 9-12: Udvælgelse og screening af lead-kandidater.

Forventede resultater og impact

Vi forventer, at A2M-IL-10 vil kunne tilbyde en mere målrettet og sikker behandling mod autoimmune sygdomme. Det kan potentielt forbedre patienternes resultater og reducere de sundhedsmæssige omkostninger forbundet med behandling af inflammatoriske sygdomme.

Øvrige projektdeltagere og samarbejdsrelationer

Troya Therapeutics har et erfarent team inden for proteinproduktion og immunologi. Dr. Ulrik Nielsen er co-founder af Troya Therapeutics og har mere end 25 års erfaring inden for proteinengineering og biotekentreprenørskab. Dr. Seandean Harwood er co-founder, assisterende professor ved Aarhus Universitet og opfinder af A2M-teknologien.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Samlet beløb: 290.000 DKK
Ansøgt beløb: 150.000 DKK

- Produktionsomkostninger: 60.000 DKK
- Oprensning af fusionsproteiner: 40.000 DKK
- Udvikling af in vitro metoder: 50.000 DKK
- In vivo forsøg: 100.000 DKK
- Udvælgelse af lead-kandidater: 40.000 DKK

Samlet tid: 12 måneder

Vi er på nuværende tidspunkt finansieret ved et konverterbart lån på DKK 4 millioner fra Bioinnovation Institute, men søger konkret funding til det beskrevne projekt.

Viktor T. Lemgart

Research Director, Ph.D.

Head of Research at Troya Therapeutics with experience in drug development, project management, and biotech entrepreneurship.

viktor@troya-tx.com

+45 21433235

Copenhagen, Denmark

linkedin.com/in/viktortechenlemgart

EDUCATION

Industrial Ph.D. in Immuno-Oncology
Denmark's Technical University / Sanofi

05/2021 - 10/2023

Projects

- *In vivo* programming of cancer-specific T-cells and macrophages with mRNA lipid nanoparticles.
- Engineering novel CARs to achieve highly functional expression and target cell killing *in vitro* and *in vivo*.
- Harvard Medical School: Critical Issues in Tumor Microenvironment: Angiogenesis, Metastasis and Immunology.

MSc. Eng. in Biotechnology (Honors)
Denmark's Technical University

02/2019 - 12/2020 *GPA: 11.5/12.0*

Thesis

- Programming of cancer-specific T-Cells with mRNA lipid nanoparticles in collaboration with Tidal Therapeutics.

RESEARCH PROJECTS

Thomas Andresen Group (DTU Health Tech) and Tidal Therapeutics (A Sanofi Company) (02/2020 - 10/2023)

- Programming of Cancer Specific T-Cells with mRNA Lipid Nanoparticles and reprogramming of tumor-associated macrophages

Symphogen A/S (09/2018 - 01/2019)

- Mutual Stabilization of Antibodies in the Mixture

Stanford University (05/2018 - 09/2018)

- CRISPR/AAV-mediated Genome Editing to Cure Beta-Thalassemia by Concurrent Insertion of HBB and Knockout of HBA

Morten Sommer Group (Novo Nordisk Foundation Center for Biosustainability) (06/2017 - 05/2018)

- Expression of Human Hormones in E. Coli Nissle

WORK EXPERIENCE

Research Director
Troya Therapeutics

01/2025 - Present *Copenhagen, Denmark*

Tasks

- Define and execute the overarching research strategy to drive innovation, product development, and market differentiation
- Ensure the alignment of research priorities with company objectives, continuously optimizing resources, budgets, and timelines for maximum impact

Contact : CEO - Ulrik Nielsen - ulrik@troya-tx.com

Senior Scientist
Sanofi

10/2023 - 01/2025 *Cambridge, USA*

Tasks

- Managing projects on LNP-mediated *in vivo* reprogramming of immune cells for various applications
- Plan and direct the work of junior team members, including mentoring in designing suitable studies

Contact : Head of Non-Viral and Genome Editing - Christopher Borges - christopher.borges@sanofi.com

SKILLS

Project Management | Immunology | Protein Engineering | Cell Based Assays | Pharmacology

PATENTS AND PUBLICATIONS

Ionizable cationic lipids and lipid nanoparticles, and methods of synthesis and use thereof. Patent US2023/068090, filed June 7, 2023.

Identification of Pre-Existing Adaptive Immunity to Cas9 Proteins in Humans. Nature Medicine (2019).

Highly Efficient and Marker-free Genome Editing of Human Pluripotent Stem Cells by CRISPR-Cas9. Cell Stem Cell (2019).

Gene replacement of α-globin with β-globin restores hemoglobin balance in β-thalassemia-derived hematopoietic stem and progenitor cells. Nature Medicine (2021).

SGK1 inhibition induces fetal hemoglobin expression and delays polymerization in sickle erythroid cells. Blood Advances (2023).

Genomic discovery and functional validation of MRP1 as a novel fetal hemoglobin modulator and potential therapeutic target in sickle cell disease. Manuscript in review at Nature.

Reprogramming of human CAR-T cells in vivo using mRNA lipid nanocarriers. Manuscript in preparation.

Review on Reprogramming of T cells in vivo. Manuscript in preparation.

AMPKb1 Activators Induce Fetal Hemoglobin in Human Erythroid Cells and Sickle Mice. Manuscript in preparation.

In Vitro and In Vivo Activity of a Lipid Nanoparticle System for the In Vivo Generation of CAR T Cells. Abstract at ASH (2024).

Speaker at PEGS, PepTalk, Immuno-Oncology Summit, LNP Formulation Summit, and mRNA-based Therapeutics Summit.

LANGUAGES

Danish and Swedish
Native or Bilingual Proficiency

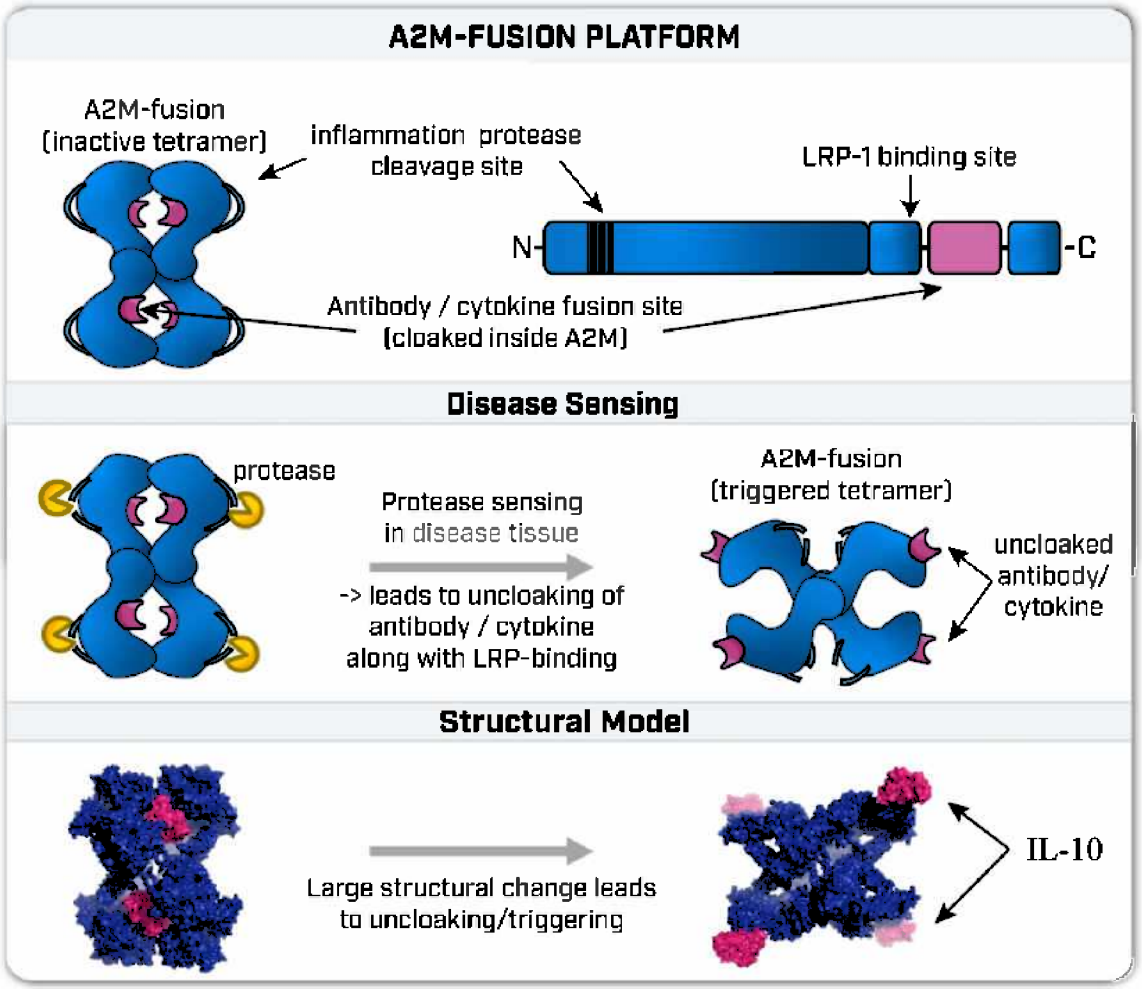
English
Native or Bilingual Proficiency

INTERESTS

I have always enjoyed sports both as an elite athlete and as a leisure. I won the youth Danish Championships in ski racing, played soccer on the youth elite team at FC Nordsjælland, and competed in golf. I always enjoy pushing myself physically and mentally. Currently, I enjoy Crossfit, Ultramarathons, and Triathlons with finishes in the Copenhagen IRONMAN and QMT 160 km trail run. My next goal is to complete a double IRONMAN.

Udvikling af A2M-IL-10 fusioner til behandling af autoimmune sygdomme

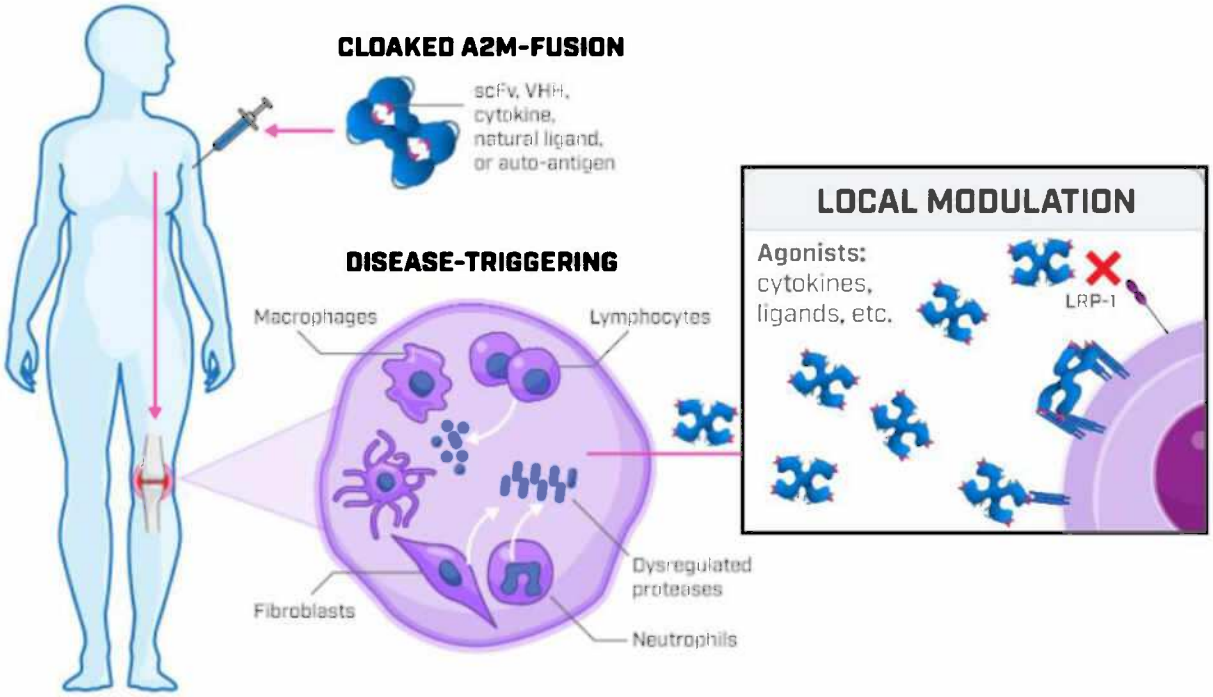
Illustrationer



Øverste panel: A2M tetrameren (blå) er fusioneret med IL-10 proteinet (pink). Det fremstilles og oprenses i sin "skjulte" konformation, som gemmer IL-10 fusionen, når den er i cirkulation.

Mellemste panel: Proteaser (gul), som udskilles i høje koncentrationer ved inflammation, kløver specifikt 'bait-regionen' af A2M. Denne kløvning udløser en konformationsændring, der eksponerer IL-10, der nu kan binde til receptoren og signalere.

Nederste panel: Strukturel model, der viser A2M tetrameren i dens skjulte tilstand (til venstre) og efter proteasekløvning, hvor IL-10 er eksponeret (til højre).



Venstre panel: Den skjulte A2M-IL-10 fusion injiceres systemisk. Når den når inflammationsstedet (her illustreret som det venstre knæ), aktiverer naturligt forekommende proteaser A2M, hvilket resulterer i en konformationsændring og eksponering af IL-10.

Højre panel: A2M-IL-10 fusionen er designet til lokal modifikation og signalering, hvor LRP-1 bindingsstedet er muteret for at forhindre internalisering.

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

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- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	Annina Kurzay, PhD student
Arbejdssted/ Institution	National Centre for Cancer Immunotherapy (CCIT), Onkologisk Afdeling, Herlev Hospital
Adresse	Borgmester Ib Juuls Vej 13, 2730 Herlev
Tlf.nr.	91990454
e-mail	annina.kurzay@regionh.dk

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
ProS1-MerTK Signalling in CD4 T Cells: Implications for TIL Expansion and functionality
Formål
T cells are immune cells that are capable of homing to tumours, where they detect and kill cancer cells. This response may not always be effective. Patient-specific immunotherapy boosts their anti-tumour activity with less systemic toxicity. Tumour infiltrating lymphocytes (TILs) are taken from tumour biopsies, expanded in vitro, and returned to the patient. This boosts the immune response and enhances the ability of T cells to eliminate cancer cells. At CCIT, this treatment was administered in a pioneer clinical trial and resulted in twice as long progression free survival. However, TIL product quality and phenotype are crucial for patient response and treatment outcome.
Problemstilling

Despite administering T cells with excellent cytotoxic ability when examined in the laboratory, patients relapse. Oftentimes this is caused by a suppressive tumour microenvironment, hindering proper T cell function.

We propose that MerTK signaling could improve the long-term remission directed by CD4 T cells in TIL- based ACT. Currently, we know very little about the dynamics of MerTK in clinical CD4 T cell cultures and its involvement in cell durability to prevent relapses. In this project proposal, we aim to unravel the molecular function of MerTK in anti-tumour T cells and its potential for ACT. ProS1-MerTK priming has potential to improve performance and function of ACT products, ultimately prolonging cancer patients' remission and/ or survival.

Baggrund

TAM (Tyro3, Axl, MerTK) tyrosine kinase receptors are key regulators of immune control. They are activated by binding phosphatidylserine residues on apoptotic cells via Protein S1 (ProS1). When activated, this pathway delivers co-stimulatory signal to the T cell, establishing full function in terms of cytokine production, proliferation and cancer cell killing. CD4 T cells are increasingly recognised as equally potent killers of cancer cells as CD8 T cells. Notably, long-term remission has been attributed to a highly activated population of CD4 T cells that maintained functionality, unlike CD8 T cells.

Metoder

We utilise common lab methods as flow cytometry, western blot, qRT-PCR, ELISA and FACS. Additionally, we utilise CRISPR-Cas9 based knockouts of the MerTK receptor and look at metabolism of cells using Seahorse technology.
We expand TILs as in clinical protocols from banked melanoma biopsies to assess ProS1 impact on product quality and performance.

Tidsplan

The project has been running for 2.5 year and is expected to be continued and finished within the next 6-12 months. We are focusing on essential and critical last experiments to gain deeper understanding of ProS1-MerTK signalling for ACT.

Forventede resultater og impact

Previously generated results in this project have resulted in multiple research articles in reputable journals and one review article. Collected data is unpublished, however currently under revision and all future data generated will be novel and original. Moreover, given the fact that modulation of costimulatory or inhibitory molecules in T cells is associated with impressive clinical responses, our data will be of great interest in the field of cancer immunology and immunotherapy. To this end, data from this study may lead to the development of novel strategies to improve immunological cancer treatments.

Øvrige projektdeltagere og samarbejdsrelationer

The project will benefit from collaborations with experts in cell differentiation and metabolism (Claus Desler, University of Copenhagen) and cancer immunotherapy (Ozcan Met, CCIT, Herlev Hospital).

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Budget for the requested amount for salary:
Salary 3 months: 120.000 DKK

Smaller amounts will be received with great gratitude! The salary of the PhD candidate was supported for the majority of the PhD studies by the 'European Union's Horizon 2020 research and innovation program' through the Marie Skłodowska-Curie grant agreement No. 955575. A number of larger and smaller funds will be applied for to cover the remaining operational costs. Additionally, funding from the Okologisk Afdeling, as part of our staff, is allocated to the project (Technician Tina Seremet works part-time on the project).

Curriculum Vitae: Annina Kurzay

Personal details & Contact

Address:	Store Kongensgade 21E, 1264 København K Denmark
Mobile:	+45 91 99 04 54
Email:	annina.kurzay@regionh.dk

Education

Københavns Universitet — **Copenhagen, DEN**

- PhD study at Faculty of Immunology and Microbiology — 01/22-present

Ruprecht-Karls Universität Heidelberg/ DKFZ — **Heidelberg, DEU**

- M.Sc. Molecular Biosciences, Major Cancer Biology, GPA 1.3 — 10/2018-05/2021

University of Aberdeen — **Aberdeen, GBR**

- B.Sc. Honours in Genetics (Immunology), graduation with a first-class degree — 09/2017-06/2018

University of Applied Sciences — **Rheinbach, DEU**

- B.Sc. Applied Biology, graduation with a GPA of 1.5 — 09/2015-07/2018

Research/Work experience

National Centre for Cancer Immunotherapy (CCIT-DK), Herlev — **Herlev, DEN**

PhD study in Per thor Straten's group as part of Marie Curie funded T-OP network — 01/22- present

- **Project Title:** ProS1-MerTK signalling in human CD4 T cells

Merck KGaA, Germany — **Darmstadt, DEU**

Internship in Healthcare R&D in the translational innovation platform (TIP) Oncology — 06/-10/2021

Focus: DNA damage response (DDR), group of Claudio Lademann

- Identification of novel therapeutic targets in DDR pathways using common cell culture models

University Medical Centre (UMM)/ German Cancer Research Centre (DKFZ) — **Mannheim, DEU**

Master's thesis internship in the research group of Viktor Umansky — 10/2020-05/2021

- **Project title:** Targeting myeloid-derived suppressor cells *in vitro* by the STAT3 inhibitor Napabucasin

Scientific assistant (HiWi):

- Genotyping of RET transgenic mice; general laboratory work

Hopp Kindertumoren Zentrum (KiTZ)/ German Cancer Research Centre (DKFZ)

Internship as part of master's program in the research group of Frank Westermann — **Heidelberg, DEU**

- **Project title:** *In silico* characterisation of novel rare molecular subtypes of neuroblastoma using published datasets — 05/2020-09/2020

Bioclinicum, Karolinska Institutet (KI) **Stockholm, SWE**

Internship as part of master's program in the research group of Andreas Lundqvist 09/2019-04/2020

- **Project title:** Overcoming therapy resistance: two novel strategies to improve anti-tumour immunity
- **Stipends:** ERASMUS+ Internship
  Stipendium Grundutbildning (KI)

Institute of Medical Research **Aberdeen, GBR**

Bachelor's thesis internship in the research group of Ian Fleming 01/2018-03/2018

- **Project Title:** Evaluating the mechanism of action of novel paclitaxel conjugates in cancer cells that express the $\alpha_v\beta_3$ integrin
- **Stipend:** DAAD Scholarship

SKILLS & ACHIEVEMENTS

Laboratory skills:

primary cell isolation & continuous cell culture, viability assays, suppression of T cell proliferation assays, Incucyte, flow cytometry, FACS, BCA assays, Western Blot, ELISA, DNA/RNA isolation, (RT)-PCR, Gel electrophoresis, CRISPR Cas9 knockout, enzyme activity assays, handling of mice, *in vitro* and *in vivo* experiments, Seahorse, TIL expansion, γδ T cell expansion and culture

Languages

- German: native
- English: fluent
- Danish: Intermediate

Certificates:

- Handling of laboratory animals (FELASA-B)
- Danish language module 3
- Advanced Latin proficiency certificate
- French proficiency diploma (DELF A2)

Bioinformatic skills:

Python (UMAP, tSNE, PCA, hierarchical clustering, HDBSCAN, differential gene expression analysis, data visualisation), R2 datasets

Other relevant IT knowledge:

- Proficient: Microsoft's Excel and Powerpoint, GraphPad's Prism, Treestar's FlowJo, ImageStudio, Biorender

Achievements:

- EU Horizon/Marie Curie stipend, Erasmus +, Stipendium Grundutbildning, DAAD Scholarship
- Finalist in best short electronic presentation (Research Symposium 2022, Herlev og Gentofte Hospital)
- Selected talk at annual GSI meeting 2023, Helsingør

References available upon request.

Nationalt Center for Cancer Immun Terapi
Onkologisk afdeling
Københavns Universitetshospital, Herlev
Borgmester Ib Juuls Vej 25C, 5. sal

2730 Herlev

Publikationsliste Annina Kurzay

1. Bitsch R*, Kurzay A*, Özbay Kurt F, De La Torre C, Lasser S, Lepper A, Siebenmorgen A, Müller V, Altevogt P, Utikal J, Umansky V (2022). *STAT3 inhibitor Napabucasin abrogates MDSC immunosuppressive capacity and prolongs survival of melanoma-bearing mice.* Journal for Immunotherapy of Cancer (Impact factor: 10.3)
   doi: 10.1136/jitc-2021-004384 *authors contributed equally

2. Rahbech A, Kurzay A, Saló SF, Seremet T, Debet R, Met O, Peeters M, Thor Straten P (2024). *MerTK Signaling in Human Primary T cells Modulates Memory Potential and Improves Recall response*. Journal for Leukocyte Biology (Impact factor: 3.6)
   doi: 10.1093/jleuko/qiae226

3. Groth C, Weber R, Lasser S, Özbay FG, Kurzay A, Petrova V, Altevogt P, Utikal J, Umansky V (2021). *Tumor promoting capacity of polymorphonuclear myeloid-derived suppressor cells and their neutralization.* International Journal of Cancer (Impact factor: 7.4)
   doi: 10.1002/ijc.33731

4. Yang Y, Neo SY, Chen Z, Cui W, Chen Y, Guo M, Wang Y, Xu H, Kurzay A, Alici E, Holmgren L, Haglund F, Wang K, Lundqvist A (2020). *Thioredoxin activity confers resistance against oxidative stress in tumor-infiltrating NK cells.* Journal of Clinical Investigation (Impact factor: 13.3)
   doi: 10.1172/JCI137585.

In revision:

5. Kurzay A, Saló SF, Rahbech A, Seremet T, Oelvang Madsen C, Chamberlain CA , Bülow Jensen E, Thy Luu V, Met Ö, Peeters MJW and thor Straten P. *ProS1-MerTK Signalling in CD4 T Cells: Implications for TIL Expansion and functionality*

In preparation:

6. Kurzay A, Saló SF, Rahbech A, Seremet T and thor Straten P. *ProS1-Tyro3 Signalling guards CD4 T helper polarization.*

CCIT DENMARK

Annina Kurzay
PhD Student, CCIT
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Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Magnus Nygaard Bech, fysioterapeut, videnskabelig assistent, MSc**
Arbejdssted/ Institution	**Rigshospitalet**
Adresse	**Blegdamsvej 9, 2100 København Ø**
Tlf.nr.	**28 51 31 59**
e-mail	**Magnus.nygaard.bech@regionh.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

Præhabilitering til patienter med blodkræft, der skal behandles med allogen knoglemarvstransplantation – et national randomiseret kontrolleret studie

Formål

Studiet undersøger effekten af en skræddersyet præhabiliteringsintervention, som supplement til den sædvanlige behandling, for patienter der skal behandles med allogen knoglemarvstransplantation sammenlignet med den sædvanlige behandling, målt på helbredsrelateret livskvalitet, indlæggelsestid, muskelmasse og muskelstyrke.

Problemstilling

Patienter med hæmatologiske kræftsygdomme oplever betydelige sygdomsrelaterede udfordringer. For mange patienter er allogen stamcelletransplantation (allo-HSCT) den eneste kurative mulighed. På trods af en 1-års overlevelsesrate på 75%, lider mange patienter af alvorlige bivirkninger, især fysisk dekonditionering. Dette begynder ofte ved diagnosen – op til et år før transplantation – og fortsætter længe efter. Effekterne inkluderer både kort- og langvarig fysisk inaktivitet, træthed og nedsat livskvalitet, hvilket understreger det presserende behov for effektive interventioner, der kan forebygge og lindre de følger der opstår efter så intensiv behandling som ved en allo-HSCT.

Baggrund

Allo-HSCT er en af de mest intense behandlingsformer inden for kræftbehandling på tværs af alle diagnosegrupper. Behandlingen er forbundet med forlænget - og tvungen - indlæggelse, og hermed en stor socioøkonomisk byrde, samt en bred vifte af både milde og svære bivirkninger herunder især fysisk dekonditionering. Patofysiologiske ændringer i muskelmasse og muskelfunktion har vist sig, at have betydelige sammenhænge med sygdomsprogression og langsigtet diagnose. Samtidig rapporterer patienterne om store rehabiliteringsbehov før, under og efter behandlingen, som ikke altid kan tilgodeses i det aktuelle behandlingsforløb. Ydermere ses det at mindst 35 % af kræftpatienter har utilstrækkeligt proteinindtag hvilket kan forhindre forbedringer i fysisk funktionsniveau via rehabilitering trods regelmæssig deltagelse. Flere studier har efterhånden vist, at et præhabiliteringsprogram inden en allo-HSCT er gennemførbart og sikkert, men endnu er der på international plan ikke gennemført et fuld-skala randomiseret, kontrolleret studie som dette.

Metoder

Studiet er et nationalt randomiseret kontrolleret studie med patienter rekrutteret fra Rigshospitalet og Århus Universitetshospital. Patienterne tilbydes præhabilitering fra 5-8 uger før allo-HSCT, og data indsamles ved T0; når der gives godkendelse til allo-HSCT, T1; 1-4

dage før allo-HSCT, og T2; tre måneder efter HSCT.
Interventionen består af gruppebaseret styrketræning 3x ugentligt samt ernæringsstøtte hver anden uge op til transplantationen.

Tidsplan

Studiet forventes at blive opstartet primo september 2025 og forventes afsluttet – inklusiv artikelskrivning og udgivelse – i september 2028.

Forventede resultater og impact

Dette projekt kan sætte en nye standard for præhabilitering i kliniske praksis på tværs af kræftdiagnoser og revolutionere behandlingsprotokoller. For patienterne forventes forbedre kliniske outcomes, øget livskvalitet og bedre fysisk funktion før, under og efter deres deres behandlingsforløb.

Øvrige projektdeltagere og samarbejdsrelationer

Projektet er et national studie inkluderende Århus Universitetshospital og Rigshospitalet. Fra Rigshospitalet deltager; Professor i hæmatologi, Henrik Sengeløv, overlæge i hæmatologi, Lone Smidstrup Friis, Professor i klinisk sygepleje, Mary Jarden, Forskningsleder i Afdeling for Ergo- og Fysioterapi, Jan Christensen, Klinisk diætist, Frederik Hansen udover ansøger MSc i fysioterapi Magnus Nygaard Bech.

Fra Århus Universitetshospital deltager; Overlæge i hæmatologi, Anne Roug, Forskningsleder i Afdeling for Ergo- og Fysioterapi, Nanna Rolving, Fysioterapeut og stud. Cand. I fysioterapi, Astrid Toft Christensen

Herudover lektor på Københavns Universitet, statistiker Anders Tolver.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Det samlede budget for studiet er 5.316.907 DKK. Heraf er 2.606.786 DKK finansieret **internt på Rigshospitalet** (aflønning af vejledergruppe samt operationelle omkostninger som software, hardware, testudstyr), af **Svend Andersen Fonden** (udstyr i form af DXA-scanner samt testudstyr) samt fra **Axel Muusfeldts Fond**, som er bevilliget til aflønning af TAP (teknisk administrativt personale) i form af kliniske diætister, projektfysioterapeut på Århus Universitetshospital samt udførsel af kliniske tests (DXA-scanninger).

Der ansøges derfor bredt om 2.710.121 DKK der skal dække aflønning af ansøger (Magnus Nygaard Bech) som projektleder i hele studieperioden samt supplerende aflønning af øvrigt TAP, der skal sikre driften af studiet. Herudover ansøges der også om rejseudgifter, artikeludgivelse, udførsel af resterende kliniske tests (fx. DXA-scanninger) samt indskrivning som PhD-studerende for ansøger Magnus Nygaard Bech.

Name	**MAGNUS NYGAARD BECH**
Address	**Edvard Griegs Gade 11, 3. tv. 2100 København Ø**
Phone	**0045 28513159**
E-mail	**Magnus.nygaard.bech@regionh.dk**
Date of birth	**2. APRIL 1991**

PROFILE

Currently I work as a physiotherapy-based research assistant at the Copenhagen University Hospital within the field of hematology and oncology.

My main working interests as a physiotherapist is to develop the best possible conditions for optimizing the physical function for the patients in a hospital setting. One of my key motivations is to be an active part of developing the best national in-hospital pre- and rehabilitation programs.

I am eager to seek knowledge and know-how and I rarely settle for mediocrity. I enjoy taking responsibility both in private and working areas, and do not hesitate to put in the extra effort necessary. Besides, I consider myself as a team-player both on and off field

CURRENT JOB DESCRIPTIONS

Research assistant at Department for Occupational- and Physiotherapy, Copenhagen University Hospital.
Operations Manager for the daily functioning of "Musclelab" – a science-based test-laboratory in collaboration between Center for Physical Activity Research and the Department for Occupational- and Physiotherapy, Copenhagen University Hospital.

MAIN EDUCATION

MSc in Physiotherapy from University of Southern Denmark from 2024
Physiotherapist from Metropolitan University College 2016

EXPERIENCE WITH DEVELPOMENT AND SCIENCE

I have spent years as the clinical responsible specialist in physiotherapy within the areas of hematology and oncology having the responsibility to maintain and develop working procedures of the highest standards and implement and promote evidence-based practice in the clinical setting.

Since 2018 I have been leading part of a science-based test-laboratory Muscle Lab including state of the art test-equipment (CPET, DXA-scanner, PowerRig etc.)
I have been responsible for evaluation and optimizing PhD-protocols while being operations manager for the daily functioning and coordination of tests. Further I have been performing tests and assessments for several PhD-studies gathering significant know-how within coordinating and performing clinical research in a hospital-setting.

Currently I am projectlead on a cohort-study regarding the changes in musclefunction for patients with blood cancer undergoing allogeneic stem cell transplantations that started in september 2023 and is still on-going.

Between January 2021 and May 2023 I was chosen to represent the Danish Association of Physiotherapy in an interdisciplinary national working group lead by the National Board of Health with updating the guidelines for treatment for Chronic Lymphocytic Leukemia and Lymphoma. The guidelines were published may 2023.

Member of National Interdisciplinary Hematological Research Network.

PUBLICATIONS

Grønset C, BECH MN, Jarden M, Høgdal N, Hutchings M, Suetta C, Christensen J. Effectiveness of exercise-based interventions on muscle mass, muscle strength, functional performance, aerobic capacity, and health-related quality of life in adults with malignant lymphoma undergoing chemotherapy: a systematic review of randomized controlled trials. Accepted for publication Acta Oncologica Jan 2025.

MOTIVATION

To kick off my future research career in a highly specialized and inspirational environment. Funding of this project will be a boost on short term but also a solid foundation for what will develop into further research and a PhD-thesis. The project could potentially set precedence for future national and international recommendations.

Rigshospitalet

Publicationlist, Magnus Nygaard Bech

(1) Groenset C, BECH MN, Jarden M, Høgdal N, Hutchings M, Suetta C, Christensen J. The effectiveness of exercise-based interventions on muscle mass, muscle strength, functional performance, aerobic capacity, and health-related quality of life in adults with malignant lymphoma undergoing chemotherapy: a systematic review of randomized controlled trials. Acta Oncol. 2025 Jan 28;64:129-142. doi: 10.2340/1651-226X.2025.42056. PMID: 39876686.

(2) Sundhedsstyrelsen (2023). Pakkeforløb for lymfeknudekræft og kronisk lymfatisk leukæmi. https://www.sst.dk/-/media/Udgivelser/2023/Kraeft/Pakkeforloeb-lymfeknudekraeft-lymfatisk-leukaemi/Pakkeforloeb.ashx

Center for Kultur- og Fritidsaktiviteter
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Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	Lea Löffler, PhD-studerende
Arbejdssted/ Institution	Hæmatologisk Afdeling, Sjællands Universitetshospital (SUH), Roskilde & Institut for Inflammationsforskning (IIR), Afdeling for Rygkirurgi, Led- og Bindevævssygdomme, Rigshospitalet (RH)
Adresse	Valdemar Holmers Gade 57, 2100 København Ø
Tlf.nr.	+45 60586939
e-mail	llof@regionsjaelland.dk

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

Molecular, Immunological, and Thrombophilia Studies in the GESUS Cohort

Formål

Studiet har til formål at undersøge hvordan en genetisk mutation (JAK2V617F) kan drive skjult inflammation i kroppen og dermed øge risikoen for blodkræft.

Baggrund & Problemstilling

Myeloproliferative neoplasier (MPN) er en gruppe blodkræftsygdomme, der opstår, når genetiske mutationer i blodets stamceller fører til ukontrolleret celleproduktion. Ny forskning viser, at særligt JAK2V617F mutationen findes hos en langt større del af befolkningen end tidligere antaget og kan være til stede i en præsygdomstilstand kaldet clonal hematopoiesis of indeterminate potential (CHIP). CHIP øger ikke kun risikoen for MPN, men også for hjertekarsygdomme og blodpropper, hvilket gør tidlig identifikation afgørende. Kronisk inflammation spiller en central rolle i denne proces, da den kan skabe et miljø, der accelererer overgangen fra CHIP til MPN. Næstvedundersøgelsen (GESUS) mellem 2010-2013 giver en unik mulighed for at undersøge disse sammenhænge, hvor man fandt at 3,1% havde mutationen. I opfølgende studier på GESUS så man en stærk sammenhæng mellem stigende mutationsbyrde og risikoen for MPN, samt en højere risiko for anden kræft, blodpropper og øget dødelighed. Vi vil derfor kortlægge kronisk inflammation i CHIP ved at analysere tromboinflammatoriske biomarkører for at forstå, hvordan inflammation påvirker sygdomsudviklingen. Dette vil vi undersøge på blodprøver taget mellem 2010-2013 af de JAK2 positive borgere samt deres matchede kontroller, og nu ved 12-15 års follow-up. Vi vil desuden følge kohorten i vores ambulatorie for at identificere risikofaktorer, der driver sygdomsprogressionen. Til sidst vil vi undersøge, om eksisterende anti-inflammatoriske lægemidler som interferon-alpha2, atorvastatin og colchicin kan reducere inflammation og potentielt sygdomsprogressionen.

Metoder

Studiet benytter de 629 JAK2-positive GESUS-borgere til at vurdere kronisk inflammation, risiko for MPN-progression og effekten af antiinflammatorisk behandling på hhv. 25 individer per lægemiddel. De 629 blev matchet 1:1 med kontroller uden mutationen. Blodprøver opbevares ved -80°C i forskningsbiobanker på SUH og Rigshospitalet indtil analyserne påbegyndes. Cytokinprofiler måles ved MSD-teknologi for at vurdere inflammatoriske niveauer, mens tromboinflammatoriske markører analyseres med Luminex-teknologi for indsigt i tromboserisiko. NET (neutrophil extracellular trap)-niveauer måles ved ELISA både ved baseline og opfølgning. Statistiske analyser udføres i R med t-tests, ANOVA og logistisk regression. Longitudinelle ændringer evalueres med mixed-effects modeller, og subgruppeanalyser gennemføres.

Tidsplan

Fra februar 2025 rekrutteres JAK2-positive GESUS-borgere til opfølgning i ambulatoriet på hæmatologisk afdeling. Samtidig påbegyndes cytokinprofilering, hvorefter der udføres trombofili- og NET-analyser, efterfulgt af komparative analyser.
Interventionsstudierne igangsættes efter etisk godkendelse, med forventet deltagerrekruttering fra slutningen af 2026/primo 2027. Alle data forventes indsamlet i sidste kvartal af 2027, og cytokinprofilering i interventionsgruppen vil foregå sideløbende.

Forventede resultater og impact

Studiets kliniske implikationer er betydelige. JAK2-CHIP er forbundet med øget risiko for blodpropper, hjertekarsygdomme og anden inflammatorisk sygdom, mens MPN ofte er underdiagnosticeret – cirka 10.000 danskere er uvidende om deres tilstand. Projektet vil ikke blot styrke forståelsen af CHIP-patogenese, men også bane vejen for tidlige interventionsstrategier. Studiet repræsenterer da et paradigmeskift i hæmatologi med potentiale til at omdefinere tidlig opsporing og behandling af MPN.

Øvrige projektdeltagere og samarbejdsrelationer

Professor Hans Hasselbalch (Hæmatologi, SUH) er hovedvejleder med ekspertise i myeloproliferative neoplasier. Professor Christina Ellervik (Klinisk Biokemi, SUH) vejleder i epidemiologi og statistik. Professor Claus Nielsen (Immunologi, Rigshospitalet) leder laboratoriestudierne.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Endnu ikke dækkende:	Detaljer	Beløb (kr.)
Laboratorieudgifter	Cytokinanalyser: MSD S-Plex	464.841
	Trombofilistudie: Luminex	194.990
	NET niveauer til 2x645 prøver	61.214
	Allerede modtaget til laboratorieudgifter	-100.000
Opfølgning på GESUS-kohorten	Opfølgende spørgeskemaundersøgelse	50.000
	Adgang til Danmarks Statistik	30.000
Publikations- & præsentationsudgifter	Open Access publikation, transport og hoteludgifter	60.000
Total		**761.045**

Allerede modtaget:	Detaljer	Beløb (kr.)
Novo Nordisk Fonden	Løn til PhD studerende, Lea Löffler	1.531.608
Novo Nordisk Fonden	Laboratoriedrift	100.000
Novo Nordisk Fonden	Løn til Bioanalytiker	240.000
Region Sjælland	Annuum & Tuition fee til PhD-skole	180.000
Total		**2.051.608**

Lea Löffler, Cand. Med.

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Tlf.: +4560586939. E-mail: llof@regionsjaelland.dk.
Orcid ID: 0009-0008-5903-4092

Beskæftigelse:

Siden 02/2025:	Ph.d.-studerende på Hæmatologisk Afd., Sjællands Universitetshospital Roskilde
09/2022-02/2024:	Forskningsassistent, Center for Surgical Science, Sjællands Universitetshospital Køge
08/2021-01/2025:	Lægesekretær og -vikar i Almen Praksis, Ole Abrahamson, Brønshøj
02/2020 – 06/2022:	Lægesekretær, Hudlæge Edgar Lauritzen, Nørrebro
10/2018-09/2023:	Sygeplejevikar (SPV), FADL

Uddannelse:

2021 – 2025:	Kandidat i medicin, Københavns Universitet
2018 - 2021:	Bachelor i medicin, Københavns Universitet
2015 - 2018:	Bachelor i geografi, Philipps University Marburg
2014 - 2017:	Bachelor i statskundskab, Philipps University Marburg
2011 - 2014:	STX, Deutsches Gymnasium für Nordschleswig

Tillidserhverv & frivilligt arbejde:

- Siden 2022: Delegeret for Lægernes Pension i listen 'Læger for Klimaet'
- Siden 2018: Frivillig hos 'Medicinstuderende/Læger for Kimaet'
- 09/2021-09/2023: Frivillig hos Mellemfolkeligt Samvirke
- 2017-2018: Bestyrelsesmedlem Amnesty Youth, Germany

Hæderspriser:

- Kræftens Bekæmpelse Skolarstipendium, 01.12.2022-30.11.2023
- Deutsches Gymnasium für Nordschleswig, årgangens højeste snit, 2014

Funding:

Modtaget 100.000 kr som hovedansøger til et studie med titlen: "Lokal interferon-α2a behandling før operation til patienter med tarmkræft af typen pMMR"

Publikationer:

- Gögenur M., Mashkoor M, Bräuner KB, **Löffler L**, Olsen ASF, Gundestrup A, Jakobsen PCH, Kleif J, Bertelsen CA, Gögenur I. *Refined algorithm for identifying recurrence among patients with non-metastatic colorectal cancer based on Danish national health data registries.* In Review.
- **Löffler L**, Mashkoor M, Gögenur I, Gögenur M. *Associations between pre-operative cholesterol levels with long-term survival after colorectal cancer surgery: a nationwide propensity score-matched cohort study.* Int J Colorectal Dis. 2024 Oct 10;39(1):159
- **Löffler L,** Gögenur I, Gögenur M. *Correlations between preoperative statin treatment with short- and long-term survival following colorectal cancer surgery: a propensity score-matched national cohort study*. Int J Colorectal Dis. 2024 Apr 27;39(1):60
- **Löffler**, L., Gögenur, I., Brix, S., & Gögenur, M. *Intratumoral induktion af type Iinterferonrespons i solide tumorer*. Ugeskrift for Laeger. 2024, 186(1), 43-47.

Posterpræsentationer:

- Myeloid-derived suppressor cells in the peripheral blood of patients with colorectal cancer – a trial in progress. MAP Congress Paris, 2023
- Associations between pre-operative cholesterol levels with long-term survival after colorectal cancer surgery: A nationwide propensity score-matched cohort study. Danske Kræftforskningsdage, Odense, 2023
- Associations between pre-operative cholesterol levels with long-term survival after colorectal cancer surgery: A nationwide propensity score-matched cohort study. OHDSI EU Symposium, Rotterdam, 2023

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Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Lars Møller Pedersen, overlæge og klinisk forskningslektor**
Arbejdssted/ Institution	**Hæmatologisk Afdeling, Sjællands Universitetshospital**
Adresse	**Vestermarksvej 9, 4000 Roskilde**
Tlf.nr.	**47324803**
e-mail	**lmpn@regionsjaelland.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
Klinisk betydning af ændringer i kropssammensætning under førstelinjebehandling af patienter med lymfekræft
Formål
Undersøgelsen har til formål at vurdere, hvordan dynamiske ændringer i kropssammensætning under behandling af lymfekræft påvirker overlevelse, bivirkninger og behandling. Vi anvender CT-scanninger med brug af kunstig intelligens (AI) som gold-standard til automatiseret kvantificering af muskel-, fedt- og knoglemasse før og efter behandling. Vi vil analysere hvorvidt man ud fra ændringer i kropssammensætning kan identificere højrisikopatienter, som vil kunne profitere af individuelt tilrettelagte understøttende behandlinger.
Problemstilling

Den videnskabelige problemstilling er at undersøge hvilken indflydelse kropssammensætningen har for behandlingsforløb og prognosen på længere sigt. Vi har fokus på dynamiske ændringer i muskel- og fedtmasse i løbet af kræftbehandlingen, hvor tidligere undersøgelser kun har taget udgangspunkt i baseline kropskomposition ved diagnosetidspunkt. Den primære hypotese er, at især ændringer under behandling er associeret til graden af bivirkninger til og dosisintensitet af kemoterapi og dermed også den langsigtede prognose.

Baggrund

Diffust storcellet B-celle lymfom (DLBCL) er den hyppigste subtype af lymfekræft med ca. 500 årlige tilfælde i Danmark. Sygdommen er aggressiv, men kan ofte helbredes med moderne kemoimmunterapi. Trods fremskridt oplever cirka en tredjedel af patienterne tilbagefald. Behandlingen er desuden ofte forbundet med betydelige bivirkninger, som kan komplicere forløbet og påvirke behandlingsresultaterne. Skrøbelige patienter med lymfekræft er vist at have dårligere prognose ved undervægt, lav muskelmasse og generel svækkelse, hvorfor det er er vigtigt at fokusere på disse patient-relaterede faktorer i individuelt tilrettelagte programmer for understøttende behandling.
Kropssammensætning, særligt muskel- og fedtmasse, har vist stor betydning for behandling og prognose ved andre kræftsygdomme. Tab af muskelmasse er forbundet med flere bivirkninger, dårligere behandlingstolerance og kortere overlevelse, mens lav fedtmasse kan påvirke omsætningen af kemoterapi og energireserver. Selvom betydningen af lav muskel- og fedtmasse ved diagnose er kendt, er effekten af behandlingsrelaterede ændringer i kropssammensætningen stadig uafklaret.
Kemoterapi, binyrebarkhormon og kræftrelateret vægttab kan medføre betydelige tab af muskel-, fedt- og knoglemasse under behandling. Dette kan øge skrøbelighed og nedsætte immunforsvar, behandlingstolerance og overlevelse. Centrale videnskabelige spørgsmål omfatter, hvordan ændringer i kropssammensætning korrelerer med toksicitet, respons og overlevelse, samt om overvågning af disse ændringer kan identificere højrisikopatienter til tidlig individualiseret intervention som kostregulering, fysisk træning og tilpasning af kræftbehandlingen.

Metoder

Studiet er en retrospektiv undersøgelse af 100 patienter diagnosticeret med DLBCL i perioden 2017–2021. Ud fra CT-scanninger foretaget før og efter behandling beregner vi mål for muskelmasse, fedtmasse og knogletæthed. Vi udmåler efterfølgende specifikke ændringer samt kombinationer af ændringer i kropssammensætning. Ændringerne vurderes derefter i forhold til omfanget og graden af bivirkninger til behandlingen, om behandlingen kan gives til tiden og i fuld dosis, og sammenhæng med patientens prognose. Vi vil vurdere om vi kan udpege særlige grupper af patienter med tab af muskel, fedt og/eller knogle som har stor risiko for et ugunstigt sygdomsforløb.
Sideløbende vil gennemføre en såkaldt metaanalyse af eksisterende viden på området inddragende publicerede studier. Vores resultater vil kunne skabe ny viden til at udpege patienter, som vil have gavn af understøttende interventioner som ernæringsstøtte, fysisk

træning og behandlingsjusteringer for at optimere patientforløb. Resultaterne planlægges publiceret i anerkendte tidsskrifter og præsenteret på nationale og internationale konferencer.

Tidsplan

Studiet afvikles i perioden 2025-2026.

Opsætning af database og identifikation af patientkohorte: februar 2025 – marts 2025

Træning i CT-evalueringer: februar 2025 – april 2025

Pilotstudie med validering af CT-metode: marts 2025 – juni 2025

Gennemførelse af en parallel metaanalyse til syntese af eksisterende viden om kroppens sammensætning og dens betydning for patientudfald: februar 2025 – december 2025

CT-evalueringer: juli 2025 – februar 2026

Dataanalyse og publikation: februar 2026 – juni 2026

Forventede resultater og impact

Resultaterne planlægges publiceret i anerkendte tidsskrifter og præsenteret på nationale og internationale konferencer. Det er en yderst klinisk relevant problemstilling med potentielle muligheder for intervention i form af ernærings- og træningsstrategier.

Øvrige projektdeltagere og samarbejdsrelationer

Christiane Sophie Staxen, Afdeling for Hæmatologi, Sjællands Universitetshospital: studiedesign, indhentning af godkendelser fra relevante myndigheder og institutioner, CT-evalueringer, opsætning og administration af database, dataindsamling, dataanalyse, udarbejdelse af første artikeludkast.

Harald Alexander Kotiuszko Jørgensen, læge, radiolog, Afdeling for Radiologi, Sjællands Universitetshospital: bistand ved CT-evalueringer, manuskriptgennemgang.

Lars Møller Pedersen, klinisk forskningslektor, Afdeling for Hæmatologi, Sjællands Universitetshospital: primære vejleder og forsker, studiedesign, datafortolkning, manuskriptgennemgang.

Torsten Holm Nielsen, ph.d., læge: studiedesign, datafortolkning, manuskriptgennemgang.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Budget 2025-2026

	Finansieret	Søges fra Direktør Michael Hermann Nielsens Mindelegat	Total
Samlet år 2025-2026:	**860.000**	**400.000**	**1.260.000**
VIP-LØNUDGIFTER:			
Løn Christiane Sophie Staxen	620.000	400.000	1.020.000
Løn radiolog	50.000		50.000
ØVRIGE DRIFTSUDGIFTER:			
Publicering og kongresdeltagelse	70.000		70.000
Studieafgift til KU	120.000		120.000

Følgende finansiering er foreløbig sikret fra følgende eksterne fonde:

Fabrikant Einar Willumsens Fond	25.000
Grosserer L.F. Foghts Fond	100.000
Eva og Henry Frænkels Mindefond	62.500
Frimodt-Heineke Fonden	50.000
Region Sjællands Forskningspulje	150.000
Dansk Lymfomgruppe grant	25.000
Brødrene Hartmanns Fond	100.000
Dansk Kræftforskningsfond	250.000

Løbende driftsomkostninger dækkes af afdelingen.

CV

Lars Møller Pedersen

Education:
MSc in medicine Jan 1986, University of Copenhagen
Medical specialist Internal Medicine 1997
Medical specialist Hematology 1999
Current position (2021-):
Clinical associate research professor, consultant, head of lymphoma research, Department of Hematology, Zealand University Hospital.
All employments 2000-2021:
Consultant, Department of Hematology, Rigshospitalet, 2000 and Herlev University Hospital, 2001-06.
Clinical associate research professor, consultant, Department of Hematology, Odense University Hospital, 2006-2010.
Head of Department, Department of Hematology, Zealand University Hospital, Roskilde Hospital, 2011-16.
Associate professor, consultant, Department of Hematology, Herlev/Rigshospitalet, 2016-2021.
Clinical associate professor, consultant, head of lymphoma research, Department of Hematology, Zealand University Hospital, 2021-.
Other scientific qualifications:
https://orcid.org/0000-0002-9419-8841
Peer reviewed publications: 91 (Web of Science h-index: 31).
More than 50 peer reviewed abstracts and oral presentations at international conferences.
Chairman at several national and international meetings.
National coordinating, PI, and sponsor role in several national and international clinical trials.
Writing several protocols covering clinical trials and basic research.
Management experience:
Clinical associate research professor at the University of Southern Denmark and the University of Copenhagen.
Co-founder of the Danish Lymphoma Group (2000).
Board member of DHS, DLG and NLG.
Head of Clinical Research Unit, Roskilde Hospital and Herlev University Hospital.
Member of Independent Review Committees (IRC) in international clinical studies.
Invited peer reviewer in six international medical journals.
Chairman of the lymphoma committee in the Danish Medicines Council (Medicinrådet 2017-2022).
Member of the Danish Health Authority's expert panel for cancer ("second opinion").
International relations:
Nordic Lymphoma Group, member of the large cell group.
GELA (Groupe d'Etude des Lymphomes de l'Adulte), member of the board conducting the international trials PRIMA and MUNIN.

PET research (Memorial Sloan-Kettering Cancer Center, 3 months stay in research lab, 2005; Roswell Park Cancer Institute, Buffalo, New York, 3 months stay in research lab, 2007; and Mount Sinai Hospital, New York).
Academic Supervision:
PhD supervisor finalized: 7 PhD students.
PhD supervisor ongoing: 6

Publication list (20 selected including IF):

H-index 31
Citations 7.328
Number of peer reviewed publications: 91
Number of peer reviewed abstracts at international conferences: 52

Hutchings M, Jakobsen AL, Hansen M, **Pedersen LM**, Buhl T, Jurlander J, Buus S, Keiding S, Boesen AM, d'Amore F, Specht L. FDG-PET after two cycles of chemotherapy predicts treatment failure and progression-free survival in Hodgkin Lymphoma. **Blood (IF 22)** 2006; 107: 52-9. PMID: 16150944.

Hagenbeek A, Gadeberg O, Johnson P, **Pedersen LM**, Walewski J, Hellmann A, Link BK, Robak T, Wojtukiewicz M, Pfreundschuh M, Kneba M, Engert A, Sonneveld P, Flensburg M, Petersen J, Losic N, Radford J. First clinical use of ofatumumab, a novel fully human anti-CD20 monoclonal antibody in relapsed or refractory follicular lymphoma: results of a phase 1/2 trial **Blood (IF 22)** 2008; 111: 5486-95. PMID: 18390837.

Coiffier B, Lepretre S, **Pedersen LM**, Gadeberg O, Fredriksen H, van Oers MHJ, Wooldridge J, Kloczko J, Holowiecki J, Hellmann A, Walewski J, Flensburg M, Petersen J, Robak T. Safety and efficacy of ofatumumab, a fully human monoclonal anti-CD20 antibody, in patients with relapsed or refractory B-cell chronic lymphocytic leukemia: a phase 1-2 study. **Blood (IF 22)** 2008; 111: 1094-1100. PMID: 18003886.

Hagenbeek A, Gadeberg O, Johnson P, **Pedersen LM**, Walewski J, Hellmann A, Link BK, Robak T, Wojtukiewicz M, Pfreundschuh M, Kneba M, Engert A, Sonneveld P, Flensburg M, Petersen J, Losic N, Radford J. First clinical use of ofatumumab, a novel fully human anti-CD20 monoclonal antibody in relapsed or refractory follicular lymphoma: results of a phase 1/2 trial. **Blood (IF 22)** 2008; 111: 5486-95. PMID: 18390837.

Andersen NS, Pedersen L, Laurell A, Elonen E, Kolstad A, Boesen AM, **Pedersen LM**, Lauritzen G, Ekanger R, Nilsson-Ehle H, Nordström M, Fredén S, Jerkeman M, Eriksson M, Väärt J, Malmér B, Geisler C. Preemptive treatment with rituximab of molecular relapse after autologous stem cell transplantation in mantle cell lymphoma. **Journal of Clinical Oncology (IF 45)** 2009; 27: 4365-70. PMID: 19652064.

Salles G, Seymour JF, Offner F, Lopez-Guillermo A, Belada D, Xerri L, Feugier P, Catalano JV, Bouabdallah R, Brice P, Caballero D, Haioun C, **Pedersen LM**, Delmer A, Simpson D, Leppa S, Soubeyran P, Hagenbeek A, Casasnovas O, Tanin I, Ferme C, Gomes Da Silva M, Sebban C, Lister TA, Estell J, Milone G, Sonet A, Mendila M, Coiffier B, Tilly H.

Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomised controlled trial. **Lancet (IF 79)** 2011; 377: 42-51. PMID: 21176949.

Green TM, Young KH, Visco C, Xu-Monette ZY, Orazi A, Go RS, Nielsen O, Gadeberg OV, Mourits-Andersen T, Frederiksen M, **Pedersen LM**, Møller MB. Immunohistochemical Double-Hit Score Is a Strong Predictor of Outcome in Patients With Diffuse Large B-Cell Lymphoma Treated With Rituximab Plus Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone. **Journal of Clinical Oncology (IF 45)** 2012; 30:3460-3467. PMID: 22665537.

Sarkozy C, Seymour JF, Ferme C, Caballero D, Sebban C, Leppa S, Delarue R, **Pedersen LM**, Mounier C, Silva MG, Chassagne-Clement C, Maetevoet M, Salles G. Rituximab maintenance erases the poor prognosis associated with circulating lymphoma cells in patients with follicular lymphoma. **Blood (22)** 2014; 123:2740-2.

Abrahamsson A, Albertsson-Lindblad A, Brown PN, Baumgartner-Wennerholm S, **Pedersen LM**, D'Amore F, Nilsson-Ehle H, Jensen P, Pedersen M, Geisler CH, Jerkeman M. Real world data on primary treatment for mantle cell lymphoma: a Nordic Lymphoma Group observational study. **Blood (22)** 2014; 124: 1288-95. PMID: 24859361.

Brown PJ, Wong KK, Felce SL, Lyne L, Spearman H, Soilleux EJ, **Pedersen LM**, Møller MB, Green TM, Gascoyne DM, Banham AH. FOXP1 suppresses immune response signatures and MHC class II expression in activated B-cell-like diffuse large B-cell lymphomas. **Leukemia (12)** 2016; 30:605-16. PMID: 26500140.

Mylam KJ, Nielsen AL, Høilund-Carlsen PF, Alavi A, Gerke O, Braad PE, Mehlsen AB, Damgaard M, Hutchings M, **Pedersen LM**. Dual time point 18F-FDG PET/CT in the evaluation of patients with suspected malignant lymphoma. European Journal of **Nucl Med Mol Imaging (IF 9)** 2016; 43: 1824-36. PMID: 27102266.

Brown PJ, Wong KK, Felce SL, Lyne L, Spearman H, Soilleux EJ, **Pedersen LM**, Møller MB, Green TM, Gascoyne DM, Banham AH. FOXP1 suppresses immune response signatures and MHC class II expression in activated B-cell-like diffuse large B-cell lymphomas. **Leukemia (IF 12*)*** 2016; 30: 605-16.

Ahmad SM, Martinenaite E, Holmström M, Jørgensen MAa, Met Ö, Nastasi C, Klausen U, Donia M, **Pedersen LM**, Munksgaard L, Ødum N, Woetmann A, Svane IM, Andersen MH. The inhibitory checkpoint, PD-L2, is a target for effector T cells: Novel possibilities for immune therapy. **Oncoimmunology (IF 8)** 2017; 7: e1390641. PMID: 29308318.

Mylam KJ, Michaelsen TY, Hutchings M, Pulczynski EJ, **Pedersen LM**, Brændstrup P, Gade IL, Eberlein TR, Gang AO, Bøgsted M, de Nully Brown P, El-Galaly TC. Little value of surveillance magnetic resonance imaging for primary CNS lymphomas in first remission: Results from a Danish multicenter study. **British Journal of Haematology (IF 7)** 2017; 176: 671-3. PMID: 26913572.

Bachy E, Seymour JF, Feugier P, Offner F, López-Guillermo A, Belada D, Xerri L, Catalano JV, Brice P, Haioun C, Martin A, Casasnovas O, **Pedersen LM**, Dorvaux V, Simpson D, Leppa S, Gabarre J, da Silva MG, Glaisner S, Ysebaert L, Vekhoff A, Intragumtornchai T, Le Gouill S, Lister A, Estell JA, Milone G, Sonet A, Farhi J, Zeuner H, Tilly H, Salles G. Sustained Progression-Free Survival Benefit of Rituximab Maintenance in Patients with Follicular Lymphoma: Long-term Results of the PRIMA Study. **Journal of Clinical Oncology (IF 45)** 2019; 37: 2815-24. PMID: 31339826.

Hersby DS, Schejbel L, Breinholt MF, Høgdall E, Nørgaard P, Dencker D, Nielsen TH, **Pedersen LM**, Gang AO. Multi-site pre-therapeutic biopsies demonstrate genetic heterogeneity in patients with newly diagnosed diffuse large B-cell lymphoma. **Leukemia Lymphoma (IF 3)** 2023; 64:1527-35. PMID: 37328933.

Ludvigsen M, Campbell AJ, Enemark MB, Hybel TE, Karjalainen-Lindsberg ML, Beiske K, Bjerre M, **Pedersen LM**, Holte H, Leppä S, Jørgensen JM, Honoré B. Proteomics uncovers molecular features for relapse risk stratification in patients with diffuse large B-cell lymphoma. **Blood Cancer Journal (IF 13)** 2023; 13(1): 161. PMID: 37884514.

Tolley ER, Lewinter C, **Pedersen LM**, Nielsen TH. Efficacy of intravenous high-dose methotrexate in preventing relapse to the central nervous system in R-CHOP(-like)-treated, high-risk, diffuse large B-cell lymphoma patients and its effect on mortality: a systematic review and meta-analysis. **Haematologica (IF 11)** 2024; online ahead of print. PMID: 38497149.

Tolley ER Dr, Nielsen TH, Hersby DS, Østergaard S, Rasmussen M, Clausen MR, Al-Mashhadi AL, Egeberg KM, Haunstrup LM, Brieghel C, Niemann CU, El Galaly TC, **Pedersen LM**. Incidence and Characterization of Secondary CNS Lymphoma in 1,972 Patients with DLBCL - A Danish Nationwide Cohort Study. **Blood Advances (IF 8)** 2024; online ahead of print. PMID: 39571170.

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Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens min-delegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Rasmus Haahr, ph.d.-studerende**
Arbejdssted/ Institution	**Hjerteafdeling Y, Bispebjerg og Frederiksberg Hospital**
Adresse	**Bispebjerg Bakke 23, 2400 København NV**
Tlf.nr.	**+45 27843673**
e-mail	**Rasmus.haahr@regionh.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
CALIBRATE (Colchicine Assessment of Low-grade Inflammation and Biomarker Response in Atherosclerosis with Targeted Evaluation)
Formål
At undersøge, om man med en inflammationssænkende behandling (colchicin) kan mindske inflammation i blodkarrene og dermed reducere risikoen for hjerte-kar-sygdom hos patienter med stabil hjertesygdom.
Problemstilling
Vi ved, at inflammation spiller en vigtig rolle i udviklingen af blodpropper og hjertekarsygdom. Alligevel er inflammationssænkende behandling ikke standardbehandling i dag –

blandt andet fordi tidligere lægemidler har haft for mange bivirkninger. Et ældre lægemiddel, colchicin, ser dog lovende ud. Spørgsmålet er, hvor godt det virker – og hos hvem.

Baggrund

I de senere år er der kommet øget fokus på, at et lavt, men dog forhøjet niveau inflammation i blodkarrene kan føre til blodpropper i hjerte og hjerne. Colchicin er et gammelt, billigt og velkendt lægemiddel, som i lav dosis kan dæmpe betændelse og muligvis beskytte mod hjerte-kar-sygdom. Flere studier har vist effekt – men ikke hos alle patienter. Derfor undersøger vi nu, hvem der har gavn af behandlingen, og hvordan vi bedst måler effekten.

Metoder

Studiet er et lodtrækningsforsøg (randomiseret studie), hvor halvdelen af deltagerne får colchicin, og halvdelen får placebo. Vi måler inflammation i blodet med blodprøver og i blodkarrene med avancerede skanninger (PET/CT og CCTA/FAI) ved start, efter 3 og efter 6 måneder. Vi følger samtidig deltagerne tæt for bivirkninger og effekt.

Tidsplan

Efterår 2025: Opstart af projekt og inklusion af de første deltagere.

2025–2027: Løbende rekruttering og deltagelse i forsøget (6 måneder per deltager).

Efterår 2027: Sidste deltagere afslutter deres forløb.

2027–2028: Bearbejdning af data og analyser.

2028: Resultaterne offentliggøres og deles med fagfolk og offentlighed.

Forventede resultater og impact

Vi forventer at demonstrere en sænkning af inflammationen lokalt i karvæggen som globalt i kroppen, når man behandles med colchicin og således bekræfte at patienter med forhøjet inflammation i blodet har en hjerte-kar-beskyttende effekt af behandlingen. Vi forventer videre, at dette kan være et vigtigt skridt til at få etableret antiinflammatorisk behandling som en del af standardpakken til hjerte-kar-syge patienter, særligt og muligvis eksklusivt til patienter med tegn på øget inflammation.

Øvrige projektdeltagere og samarbejdsrelationer

Hovedvejleder: Professor Eva Prescott, Hjerteafdeling Y, Bispebjerg og Frederiksberg Hospital.

Bivejleder: Professor Rasmus Ripa, Klinisk Fysiologi og Nuklearmedicinsk afdeling, Bispebjerg og Frederiksberg Hospital.
Budget (herunder evt. finansiering fra offentlige/private råd og fonde)
Se vedhæftede ”Budget” og ”Ansøgte Fonde Opdateret 02.04.2025”.

CALIBRATE (Colchicine Assessment of Low-grade Inflammation and Biomarker Response in Atherosclerosis with Targeted Evaluation)

Om projektet(lægmands):

I 30 år har man vidst at betændelse (inflammation) spiller en vigtig rolle i udviklingen af åreforkalkning og i forlængelse heraf, i udviklingen blodpropper i hjertet og hjernen. Det var derfor en længerevarende og stor videnskabelig ambition, der blev opfyldt, da det i slutningen af 2010'erne lykkedes at demonstrere en beskyttende effekt af betændelsessænkende medicin til hjerte-kar-syge.

Næsten 10 år senere, er betændelsessænkede medicin dog stadig ikke en del af behandlingen til patienter med øget risiko for hjerte-kar-sygdom.

Og hvorfor ikke det?

En stor del af forklaringen findes i, at bivirkningsprofilerne på tidligere stoffer har været for store, til tider sågar farlige. En omstændighed, der afspejler, at immunsystemet som ansvarshavende i reguleringen af betændelsesniveauet i kroppen, ikke uden videre lader sig manipulere med.

Problemet blev altså snart forrykket fra at finde et middel, der kan sænke betændelsesniveauet, til at finde et der kan gøre det uden at have omfattende bivirkninger.

I netop den henseende har brug af lav dosis colchicin (et gammelt stof fra planten høsttidsløs) vist særdeles lovende takter; dels grundet en dokumenteret hjerte-kar-beskyttende effekt og stoffets velkendte, håndterbare og lave bivirkningsprofil, men dels også i kraft af colchicins økonomiske tilgængelighed. Idet hjerte-kar-sygdom er blandt de sygdomskategorier, der har den stejleste sociale slagside med over den dobbelte risiko for hjerte-kar-sygdoms-relateret død hos lavt uddannede sammenlignet med højtuddannede, er sidstnævnte en bestemt ikke ubetydelig omstændighed.

I forventningen til kommende stoffers indtog på markedet, som må forventes at være relativt dyre, fremstår colchicin som en gylden mulighed for en effektfuld, sikker og socialretfærdig behandling til hjerte-kar-sygdom.

En mulighed, der allerede har været benyttet, da man i begyndelsen af 2024 begyndte – under visse omstændigheder - at anbefale colchicin til hjerte-kar-syge i Europa.

Den tilstødende udfordring har imidlertid været, at der nogenlunde samtidigt med anbefalingerne – i slutningen af 2024 – udkom tre studier, der sådede tvivl om colchicins effekt, når den måles på en bred skare af alle hjerte-kar-patienter.

Og hvad så? Vi ved, at øget betændelse fører til øget død og hjerte-kar-sygdom, og vi ved at det kan forhindres, men hvilken behandling skal der til? Eller måske vigtigere, hvor meget af behandlingen og til hvem, skal behandlingen til?

Det er i besvarelsen af disse spørgsmål, vores studie vil gøre sig gældende.

Kontakt: Rasmus Haahr, rasmus.primholdt.haahr@regionh.dk TLF +45 27843673

Det er vores hypotese at colchicin virker beskyttende mod hjerte-kar-sygdom ved at sænke betændelsesniveauet i blodkarrene. Videre at patienter, der har minimalt forhøjet, men dog forhøjet betændelsesniveau i kroppen, har mest gavn af behandlingen. Vi tror også, at der er en afart af større effekt, ved større dosis colchicin, hvorfor vi også ønsker at teste dette.

Til formålet vil vi benytte os af PET/CT-teknologi, en avanceret billeddiagnostisk metode, hvor man udnytter radioaktive sporstoffer til at belyse funktion i kroppen (modsat normal billeddiagnostik, der kigger på struktur). I vores studie, er den funktion vi kigger på: betændelsesprocessen.

Vi kigger på betændelsesprocessen ved hjælp af et radioaktivt sukkerstof, kaldet FDG, der optages i celler med særlig høj sukkerstof omsætning (metabolisk aktivitet), hvilket bl.a. er gældende for de celler, der er ansvarlige for at hæve niveauet af betændelse. Vi injicerer FDG i patienterne, og ved hjælp af en scanner, der kombinerer billedtagning med registrering af mængden af radioaktivitet, kan vi således visuelt fremstille betændelsesprocessen og væsentligt for nærværende studie forandringer i samme.

Metode

For at undersøge, om colchicin kan mindske betændelse i blodårerne, gennemføres et videnskabeligt forsøg med 86 patienter, der tidligere har haft en blodprop i hjertet og har tegn på mild betændelse i kroppen (målt som blodprøve).

Patienterne deles tilfældigt i to grupper. Den ene gruppe får en lav dosis colchicin, mens den anden gruppe får en snydepille (placebo). Ingen ved, hvem der får hvad – heller ikke forskerne, før studiet er færdigt. Dette sikrer, at resultaterne er objektive og uden påvirkning fra forventninger.

Behandlingen varer seks måneder. I de første tre måneder tager deltagerne én tablet dagligt, hvorefter deltagerne i de sidste tre måneder tager to tabletter dagligt. Deltagerne bliver undersøgt før, under (efter 3måneder) og efter studiet (efter 6måneder) for at se, om colchicin påvirker betændelsen i blodårerne målt på blodprøver og med den beskrevne scanning.

Ved at sammenligne scanninger og blodprøver før, under og efter behandlingen vil vi kunne *portrættere* colchicins effekt på betændelsen i karvæggen. Videre vil vi kunne se om effekten afspejles i det generelle niveau af betændelse i kroppen og forhåbentligt afdække, hvem, der har brug for colchicin og hvorfor meget colchicin, de har brug for.

Kontakt: Rasmus Haahr, rasmus.primholdt.haahr@regionh.dk TLF +45 27843673

Curriculum Vitae – Rasmus Haahr

Jyllandsvej 10, 2.mf 2000 Frederiksberg

Phone: +45 27 84 36 74

E-Mail: rasmus.primholdt.haahr@regionh.dk

Authorization-ID: 0DWZM

Education

2014 - 2021	Cand. Med. at University of Copenhagen.

Postgraduate Work Experience

2025-	Ph.D.-student at dept. of Cardiology, Bispebjerg/Frederiksberg Hospital.
2024-2025	First year resident at dept. of Cardiology, Bispebjerg/Frederiksberg Hospital.
2024 Jan – Feb	Second year resident at dept. of Clinical Physiology and Nuclear Medicine, Bispebjerg/Frederiksberg.
2023	First year resident at dept. of Clinical Physiology and Nuclear Medicine, Bispebjerg/Frederiksberg.
2021-22	First year internship (KBU) at dept. of Neurology, Herlev Hospital and at General Practitioner “Dr. Kirsten Sander”

Pregraduat Work and teaching experience

2018-2021	Crossfit Trainer at CrossFit Copenhagen/Arca.
2019	Research Assistant at Infectious Diseases Dept, Rigshospitalet.
2014-2017	Substitute Nurse at FADL Copenhagen.
2012-2014	Substitute Teacher at Skivehus Skole.

Courses (beyond mandatory KBU and introduction courses)

2024	Course in basic echocardiography (FYC's EKKO 1).
2023	Theoretical Course for Doctors in Introduction Position in Clinical Physiology and Nuclear Medicine.

Other Positions

2024	Member of FYC (Society for young Cardiologist in Denmark)
2023	Member of YNK (Society for young Nuclear Physicians in Denmark)
2023	Union Representative (TR) for Junior Doctors at dept. of Clinical Physiology and Nuclear Medicine, Bispebjerg/Frederiksberg.
2023	Podcast Host at En Nobel Bogklub (2023-) 20 episodes
2017	Board member of COGITA (Society for medicine students with interest for philosophy and medical ethic’s)

Publications (4)

Haahr, R., Tetens, M. M., Dessau, R. B., Krogfelt, K. A., Bodilsen, J., Andersen, N. S., Møller, J. K., Roed, C., Christiansen, C. B., & Ellermann-Eriksen, S. Risk of Neurological Disorders in Patients With European Lyme Neuroborreliosis: A Nationwide, Population-Based Cohort Study. *Clinical Infectious Diseases*, *71*(6), 1511–1516 (2020).
DOI: 10.1093/cid/ciz997, Impact Factor: 8.2

Tetens, M. M., Haahr, R., Dessau, R. B., Krogfelt, K. A., Bodilsen, J., Andersen, N. S., Møller, J. K., Roed, C., Christiansen, C. B., Ellermann-Eriksen, S., Bangsborg, J. M., Hansen, K., Andersen, C. Ø., Lebech, A.-M., Obel, N., & Omland, L. H.
Assessment of the Risk of Psychiatric Disorders, Use of Psychiatric Hospitals, and Receipt of Psychiatric Medication Among Patients With Lyme Neuroborreliosis in Denmark. *JAMA Psychiatry*, *78*(2), 1–10 (2020).
DOI: 10.1001/jamapscychiatry.2020.2915, Impact Factor: 22.5

Tetens, M. M., Haahr, R., Dessau, R. B., Krogfelt, K. A., Bodilsen, J., Andersen, N. S., Møller, J. K., Roed, C., Christiansen, C. B., Ellermann-Eriksen, S., Bangsborg, J. M., Hansen, K., Benfield, T. L., Andersen, C. Ø., Obel, N., Omland, L. H., & Lebech, A.-M.
Changes in Lyme neuroborreliosis incidence in Denmark, 1996 to 2015. *Ticks and Tick-borne Diseases*. (2020).
DOI: 10.1016j.ttbdis.2020.101549, Impact Factor. 3.1

Gynthersen, R. M. M., Tetens, M. M., Ørbæk, M., Haahr, R., Fana, V., Hansen, K., Mens, H., Andersen, Å. B., & Lebech, A.-M.
Classification of patients referred under suspicion of tick-borne diseases, Copenhagen, Denmark. *Ticks and Tick-borne Diseases*. (2020).
DOI: 10.1016/j.ttbdis.2020.101591, Impact Factor: 3.1

Ongoing works (2)

2024	**Madsen, K. W., Haahr, R., Mkhitarjan, T., Wiinberg, N., Marstrand, J. R., Rosenbaum, S., Henriksen, A. C., & Marner, L.** Hemodynamic- and autonomic dysfunction in symptomatic carotid artery stenosis. Status: submitted
2024	**Haahr, R**., Holmager T, Prescott, E: Risk of HFrEF in Danish Patients with Reduced Myocardial Flow Reserve. Status: in writing

Kontakt: Rasmus Haahr, rasmus.primholdt.haahr@regionh.dk TLF +45 27843673

Forskningsbudget - CALIBRATE

	Estimeret 2025 pris til dit budget pr. år	Noter
Løn		
Ph.d.-løn 49.458,26 i 12 mdr	593.499,12 kr.	
Samlet over 3 år	1.780.497,36 kr.	1/3 er egen finansieret
Personalegrupper		
• Laboranter/bioanalytikere	117.132,00 kr.	Fuldt finansieret af Hjerteafdelingen og Nuklearmedicinsk afdeling
• Administrativt personale	26.400,00 kr.	Fuldt finansieret af Hjerteafdelingen og Nuklearmedicinsk afdeling
• Forskningsårsstuderende (12.000,00 i 6 mdr. + 5.180,00 i 6 mdr.)	103.080,00 kr.	Forventes finansieret af skolarstipendie.
Samlet Personale	246.612,00 kr.	Egen finansieret 3/3
Materiel		
· Forsøgsmedicin og Placebo	50.000,00 kr.	Pågående fondsansøgninger
· Radioaktiv Tracer (2.800 x 3 scanninger x 86 personer) + 5% forventet spild	758.520,00 kr.	Pågående fondsansøgninger.
· Biokemiske analyser (1200 x 3 prøveomgange x 86 personer) + 5% forventet spild	325.080,00 kr.	Pågående fondsansøgninger
Samlet Materiel	1.133.600,00 kr.	0/3 er egen finansieret
Drift		
• Studieafgift, ph.d.-studerende	50.000,00 kr.	Er finansieret
• IT-udstyr (Standard PC 5.150,00 med Dock 1.030,00)	6.180,00 kr.	Er finansieret
• Gebyr hos lægemiddelstyrelsen (40.898,00 ændring koster 10.322,00)	51.220,00 kr.	Er finansieret
• Gebyr hos Videnskabsetisk komite (Ny protokol 5.862,00 + tillægsprotokol 2.199,00)	8.061,00 kr.	Er finansieret
• Registeropkobling/Forsker Service/Bruger autorisation (10 timer + gebyr)	18.500,00 kr.	Er finansieret
• Udlandsophold/miljøskifte	150.000,00 kr.	Københavns Universitet finansierer 45.000
• Konferencedeltagelse (angiv antal konferencer årligt per deltager, destination/navn på konference hvis muligt)	2.500,00 kr.	Er finansieret
• Internationale møder/seminarer/workshops (angiv antal pr. år, forven-tede antal deltagere)	2.500,00 kr.	Er finansieret
• Publikationer (artikler, herun-der "Open Access" samt bøger)	25.000,00 kr.	Endnu ikke søgt fondsmidler
• Formidling af projektets resultater, f.eks. via websider, videoer, ...		
Samlet Drift	538.961,00 kr.	
Samlet ansøgte budget	300.000,00 kr.	
Egen Finansierng	1.274.072,12 kr.	
Samlet projekt budget	3.699.670,36 kr.	

Fondsoversigt

Fondsnavn	Søgt om støtte til:	Fået svar:	Støtte eller afslag
Fonden af 1870	FDG-Tracer	Afventer	
Kong Christian den Tiendes Fond	FDG-Tracer	Afventer	
Inge Levinsens Fond	FDG-Tracer	Afventer	
Danish Cardiovascular Academy	Løn	Afventer	
Karl F. Andersen Fond	FDG-Tracer	Afventer	
Dr. Thorvald Madsens Legat til fremme af lægevidenskabelig forskning	Materiel	Afventer	
Grosserer Andreas Collstrop og Søn Rudolf Collstrops Mindefond	Materiel	Afventer	

Herlev Hospital

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	Lisbet Rosenkrantz Hölmich, Lærestolsprofessor, Overlæge, Dr. Med.
Arbejdssted/ Institution	Plastikkirurgisk afd. Herlev Hospital
Adresse	Borgmester Ib Juuls vej 1, 2730 Herlev
Tlf.nr.	27 20 00 14
e-mail	Lisbet.Rosenkrantz.Hoelmich@reghionh.dk

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
DAHT, Dermoscopy Augmented Histology Trial. Increasing the diagnostic accuracy in histopathological melanoma- and skin lesion assessment through the inclusion of dermoscopic images and other clinical data across sectors
Formål
To increase the diagnostic accuracy of the pathologists who diagnose skin lesions suspicious of melanoma.
Problemstilling
Diagnosing melanoma has been proven difficult, even for experts within the field, and reproducing the diagnosis among colleagues has been found even more difficult due to inconsistent pathology assessments.
Baggrund
Denmark faces rising melanoma incidence (1-5) with surging biopsy rates (1,6) and concerning diagnostic variability among pathologists (7). Despite standardization efforts (8), subjective interpretation persists (9), leading to both overdiagnosis (10-14) and potentially compromised survival from underdiagnosis. Building on our previous work (1,15-19), we propose three sequential studies using technology and teledermoscopy to improve diagnostic accuracy by integrating dermoscopic images in the pathology assessment and directing pathologists' attention to clinically significant lesion areas (20).
Metoder
Existing Technology: Our research employs Dermloop Learn, a freely available mobile app providing dermoscopic image interpretation training. Additional platforms include Dermloop Capture (cross-specialty information sharing), Dermloop Tele (remote dermatologist consultations), and Dermloop Pathology (clinician-pathologist information exchange). **Case Database (Studies 1-2):** We established a database of 211 clinically suspected melanoma lesions referred in the cancer pathway to Herlev Hospital (2020-2021) with clinical/dermoscopic images, patient demographics, and digitized histological sections. A specialized DAHT platform facilitates standardized assessments based on an international standard: MPATH-Dx 2.0. **Study 1:** Diagnostic validation through a four-phased consensus process with four international dermatopathologists has been completed. All 211 cases were independently reviewed, with challenging cases discussed in consensus rounds. These consensus diagnoses serve as the gold standard for Study 2. The study has not yet been reported. **Study 2:** This phase evaluates the effect of structured training on pathologists' diagnostic performance. Participants will be randomized to either the intervention group with the

Dermloop Learn training program or the control group without training. Both groups will assess the 211 cases with a comparative analysis of diagnostic accuracy, confidence, and perceived complexity.
Study 3: This study examines how teledermoscopy enhances pathological sectioning. General practitioners will refer suspected lesions to teledermatologists, who mark suspicious areas on dermoscopic images. Surgeons will place adhesive markers on these areas prior to excision. Pathologists will determine if marked areas contain the most severe pathology and whether guided sectioning improves diagnosis.

Tidsplan

Study 1: Data collection completed; analysis is ongoing
Study 2: Case library completed; Platform ready Jun 2025; Recruitment Sep-Dec 2025; Analysis Jan-Jun 2026
Study 3: Platform development Jan-Apr 2026; Data collection May-Oct 2026; Analysis Nov 2026-Jun 2027

Forventede resultater og impact

The DAHT projects aim to transform melanoma diagnostics by integrating clinical, dermoscopic, and histopathological data across healthcare sectors. This approach enhances diagnostic precision, reduces pathologist variability, and mitigates both under- and overdiagnosis, directly benefiting patients through more accurate treatment decisions. Our three interconnected studies leverage expert consensus, digital training, and innovative lesion marking to create a standardized methodology that improves melanoma diagnostic reliability for patients, clinicians, and healthcare systems.

Øvrige projektdeltagere og samarbejdsrelationer

Local Team: L. Bønløkke Nervil, MD (Plastic Surgery, Herlev); N. Kvorning Ternov, MD, PhD (Plastic Surgery, Herlev); G.B.D. Rasmussen, MD, PhD, Consultant (Pathology, Herlev)
Danish Collaborators: T. Vestergaard, MD, PhD, Consultant (Dermatology, Odense); M. Tolsgaard, Prof. Dr.Med.Sci (Copenhagen Academy for Medical Education and Simulation)
International Experts: R.L. Barnhill, Prof., MSc (Institut Curie); D. Elder, Prof., MSc (Univ. of Pennsylvania); F. Watts, MD (Tissue Pathology, Sydney)
Companies/organisations: Melatech Aps (Software company); IMPSG (International network of pathologists)

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Budget Request: **111,132 DKK** for 2 months PI salary (55,566 DKK/month)
Main supervisor salary: Covered by Dept. of Plastic Surgery, Herlev
Equipment/programming: 540,000 DKK (from existing 22+ million DKK grant)

REFERENCES

1. Nervil GG, Vestergaard T, Klausen S, Tolsgaard MG, Ternov NK, Hölmich LR. Impact of skin biopsy practices: A comprehensive nationwide study on skin cancer and melanoma biopsies. J Eur Acad Dermatol Venereol. 12. oktober 2024;jdv.20371.
2. Helvind NM, Hölmich LR, Smith S, Glud M, Andersen KK, Dalton SO, m.fl. Incidence of In Situ and Invasive Melanoma in Denmark From 1985 Through 2012: A National Database Study of 24 059 Melanoma Cases. JAMA Dermatol. 1. oktober 2015;151(10):1087.
3. Nordcan 2.0 Incidence Denmark [Internet]. [henvist 16. januar 2025]. Tilgængelig hos: https://nordcan.iarc.fr/en/dataviz/trends?cancers=290&sexes=1_2&populations=208&age_start=0&age_end=17&mode=cancer&multiple_populations=0&multiple_cancers=1&years=1943_2023&key=total
4. Nordcan 2.0 incidence young danes [Internet]. [henvist 16. januar 2025]. Tilgængelig hos: https://nordcan.iarc.fr/en/dataviz/trends?cancers=290_520_180_240_160&sexes=1_2&populations=208&age_start=3&age_end=6&mode=cancer&multiple_populations=0&multiple_cancers=1&years=1990_2023
5. Cancer Over Time [Internet]. [henvist 16. januar 2025]. Tilgængelig hos: https://gco.iarc.fr/overtime/en/dataviz/trends?populations=752_208_32_36_246_191_218_233_250_276_352_356_376_392_410_428_440_8402_8401_8263_8262_8261_8260_840_800_756_764_724_792_634_630_705_616_372_203_380_470_554_528_474_414_112_152_48_156_188_124_40_196_578_170_608&sexes=2&types=0&multiple_populations=1&cancers=12
6. Nielsen JB, Kristiansen IS, Thapa S. Increasing melanoma incidence with unchanged mortality: more sunshine, better treatment, increased diagnostic activity, overdiagnosis or lowered diagnostic threshold? Br J Dermatol. 14. august 2024;191(3):365–74.
7. Elmore JG, Barnhill RL, Elder DE, Longton GM, Pepe MS, Reisch LM, m.fl. Pathologists' diagnosis of invasive melanoma and melanocytic proliferations: observer accuracy and reproducibility study. BMJ. 28. juni 2017;j2813.
8. Barnhill RL, Elder DE, Piepkorn MW, Knezevich SR, Reisch LM, Eguchi MM, m.fl. Revision of the Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis Classification Schema for Melanocytic Lesions: A Consensus Statement. JAMA Netw Open. 3. januar 2023;6(1):e2250613.
9. Elder DE. Melanoma Diagnosis in the Mihm Era—And Beyond. J Cutan Pathol. 3. november 2024;cup.14742.
10. Glasziou PP, Jones MA, Pathirana T, Barratt AL, Bell KJ. Estimating the magnitude of cancer overdiagnosis in Australia. Med J Aust. marts 2020;212(4):163–8.
11. Petty AJ, Ackerson B, Garza R, Peterson M, Liu B, Green C, m.fl. Meta-analysis of number needed to treat for diagnosis of melanoma by clinical setting. J Am Acad Dermatol. maj 2020;82(5):1158–65.
12. Nelson KC, Swetter SM, Saboda K, Chen SC, Curiel-Lewandrowski C. Evaluation of the Number-Needed-to-Biopsy Metric for the Diagnosis of Cutaneous Melanoma: A Systematic Review and Meta-analysis. JAMA Dermatol. 1. oktober 2019;155(10):1167.

13. Muzumdar S, Lin G, Kerr P, Grant-Kels JM. Evidence concerning the accusation that melanoma is overdiagnosed. J Am Acad Dermatol. oktober 2021;85(4):841–6.
14. Semsarian CR, Ma T, Nickel B, Scolyer RA, Ferguson PM, Soyer HP, m.fl. Do we need to rethink the diagnoses melanoma *in situ* and severely dysplastic naevus? Br J Dermatol. juni 2022;186(6):1030–2.
15. Vestergaard T, Prasad SC, Schuster A, Laurinaviciene R, Bygum A, Munck A, m.fl. Introducing teledermoscopy of possible skin cancers in general practice in Southern Denmark. Fam Pract. 5. september 2020;37(4):513–8.
16. Vestergaard T, Andersen MK, Bygum A. Acceptance of Teledermoscopy by General Practitioners and Dermatologists in Denmark. Dermatol Pract Concept. 12. april 2021;e2021033.
17. Gilling S, Mortz C, Vestergaard T. Patient Satisfaction and Expectations Regarding Mobile Teledermoscopy in General Practice for Diagnosis of Non-melanoma Skin Cancer and Malignant Melanoma. Acta Derm Venereol. 2020;100(8):adv00117-7.
18. Nervil GG, Ternov NK, Vestergaard T, Sølvsten H, Chakera AH, Tolsgaard MG, m.fl. Improving Skin Cancer Diagnostics Through a Mobile App With a Large Interactive Image Repository: Randomized Controlled Trial. JMIR Dermatol. 9. august 2023;6:e48357.
19. Nervil GG, Ternov NK, Lorentzen H, Kromann C, Ingvar Å, Nielsen K, m.fl. Teledermoscopic triage of melanoma-suspicious skin lesions is safe: A retrospective comparative diagnostic accuracy study with multiple assessors. J Telemed Telecare. 10. oktober 2024;1357633X241286003.
20. Ferrara G, Argenyi Z, Argenziano G, Cerio R, Cerroni L, Di Blasi A, m.fl. The Influence of Clinical Information in the Histopathologic Diagnosis of Melanocytic Skin Neoplasms. Westermark P, redaktør. PLoS ONE. 30. april 2009;4(4):e5375.

Short CV LR Hölmich
March 2025

POSITIONS
Chair of Plastic Surgery (2025-)
Consultant, dept. of Plastic Surgery, Herlev and Gentofte Hospital (2007-)

EDUCATION
1987 Medical Doctor, Copenhagen University (CU), 2006 Certified Plastic Surgeon
2009 Doctor of Medical Science (DMSc), CU

SCIENTIFIC FOCUS AREAS
Main interest is improved quality in cancer surgery, specifically melanoma and breast cancer. Special focus on new methods for diagnosis, follow-up, and identification of recurrence as well as survivorship aspects and late effects. Breast implant-related complications and abdominal wall reconstruction including rectus diastasis, and lymphedema are other focus areas. Methods of research are clinical, translational, and register-based studies—currently, 159 scientific publications, and 9 book chapters.

CLINICAL EXPERTICE
Melanoma and other skin cancer surgery, breast reconstruction, breast implant complications, abdominal wall reconstruction, massive weight loss surgery
a.o.

FUNDING
+24 mill. DKR as applicant/primary supervisor, and +38 mill DKR as co-applicant.

COMMISSIONS OF TRUST
Chairman of the Danish Melanoma Group and Database (2013-), board member of the Danish Breast Cancer Group (2016-21) and the Danish Multidisciplinary Cancer Groups (2019-22). President of Danish Society of Plastic and Reconstructive Surgery (2014-18). National member of the Global ALCL network (2017-). Member of the *EU SCENIHR Working group* (2012-2016). Expert consultant for the Danish Medico-Legal Council (2010-). Board member of the PhD programs Clinical Cancer Research and Surgical Sciences at CU, + several other positions.

SUPERVISION
Currently 11 Ph.D. students; primary supervisor for 5 and co-supervisor for 6, 3 in the pipeline. Finalized 8 PhDs, 21 candidate and 9 bachelor theses.

OTHER SCIENTIFIC ACTIVITIES
Reviewer of grant applications for several institutions. Regular peer-reviewer of manuscripts for several journals. Author of several clinical guidelines for melanoma treatment and for breast reconstruction in breast cancer. Participant in ACROBATIC – Danish Research Center for Cancer Surgery, and task force leader in Greater Copenhagen's Clinical Academic Group, Cancer Immunotherapy, CAGci.

10 selected publications Lisbet Rosenkrantz Hölmich

1. 159. Obinah MPB, Al-Halafi S, Dreisig K, Poulsen TS, Johansen C, Litman T, Bojesen SE, Høgdall E, Chakera AH, Hölmich LR, **Circulating Tumor DNA for Early Detection of Progression in High-Risk Melanoma Patients: A Study Protocol: An Exploratory Study for Validation of a Blood-Based Biomarker**, Acta Oncol, 2025, Accepted for publication 10.01. 2025 (IF 2.7)

2. 156. Hansen, SM, Johansen C, Obinah MP, Kasparian NA, Genter P, # Bidstrup PE, # Hölmich LR, **MELACARE Nurse-led follow-up after early-stage melanoma: protocol and feasibility**, Acta Oncol, 2024; 63(1), 909–914. PMID: 39582229 (IF 2.7)
3. 153. Nervil GG, Ternov NK, Lorentzen H, Kromann C, Ingvar Å, Nielsen K, Tolsgaard M, Vestergaard T, Hölmich LR, **Teledermoscopic triage of melanoma-suspicious skin lesions is safe: A retrospective comparative diagnostic accuracy study with multiple assessors**, J Telemed Telecare, 2024: 10:1357633X241286003, PMID: 39387164, online ahead of print (IF 3.5)
4. 152. Nervil GG, Vestergaard T, Klausen S,Tolsgaard MG, Ternov NK, Hölmich LR, **Impact of Skin Biopsy Practices: A Comprehensive Nationwide Study on Skin Cancer and Melanoma Biopsies**. J EUR Dermatol Venereol, 2024 oct; accepted, doi: 10.1111/jdv.20371, PMID: 39394835, online ahead of print (IF 8.4)
5. 137. Nervil GG, Tolsgaard M, Vestergaard T, Chakera A, Sølvsten H, Ternov NK, Hölmich LR**. Improving Skin Cancer Diagnostics Through a Mobile App With a Large Interactive Image Repository: Randomized Controlled Trial**, JMIR Dermatol, 2023; 9:6:e48357. PMID: 37624707 (IF 7.4)

6. 136. Helvind NM, Weitemeyer MBM, Chakera AH, Hendel HW, Ellebaek E, Svane IM, Kjærskov MW, Bojesen S, Skyum H, Petersen SK, Bastholt L, Johansen C, Bidstrup PE, Hölmich LR. **Stage-specific risk of recurrence and death from melanoma in Denmark from 2008 to 2021: A national observational cohort study of 25,720 stage IA-IV patients,** JAMA Dermatol, 2023; 159(11):1213-1222 PMID: 37650576 (IF 10.9)

7. 128. Helvind NM, Weitemeyer MBM, Chakera A, Hendel H, Ellebæk E, Svane IM, Kjærskov MW,Bojesen S, Skyum H, Petersen S, Bastholt L, Johansen C, Bidstrup P, Hölmich LR**, Earlier recurrence detection using routine FDG PET-CT scans in surveillance of stage IIB-IIID melanoma: A national cohort study of 1,480 patients**, Ann Surg Oncol., 2023; 30(4):2377-2388., PMID: 36752970 (IF 4.3)

8. 127. Rohaan MW, Borch TH, van den Berg JH, …..Hölmich LR, van Akkooi ACJ, van Houdt WJ, Wouters MWJM, van Thienen JV, Blank CU, Meerveld-Eggink A, Klobuch S, Wilgenhof S, Schumacher TN, Donia M, Svane IM, Haanen JBAG, **Tumor-Infiltrating Lymphocyte Therapy or Ipililumab in Advanced Melanoma**, N Engl J Med., 2022; 387(23):2113-2125. PMID 36477031 (IF 176.0)

9. 108. Helvind NM, Aros Mardones CA, Hölmich LR, Hendel HW, Bidstrup PE, Sørensen JA, Chakera AH, **Routine PET-CT scans provide early and accurate recurrence detection in asymptomatic stage IIB-III melanoma patients**, Eur J Surg Oncol, 2021; 47(12):3020-3027. PMID: 34120809 (IF 4.4)

10. 102. Gjorup CA, Dahlstroem K, Hendel HW, Drzewiecki KT, Klausen TW, Hölmich LR, **Factors associated with melanoma-related limb lymphoedema,** Acta Oncol, 2021; 60(6):779-784, PMID: 33793386 (IF 4.3)

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Sofie Louise Rygård, reservelæge**
Arbejdssted/ Institution	**Øre-, næse-, halskirurgiskafdeling, Aarhus Universitetshospital**
Adresse	**Palle Juul-Jensens Boulevard 165, 8200 Aarhus N**
Tlf.nr.	**51922819**
e-mail	**soryga@rm.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

Randomized clinical multicenter trial of small thyroid cancers treated with hemi thyroidectomy or radiofrequency ablation.

Formål

Vi ønsker at undersøge om varmebehandling er lige så god som operation til behandling af patienter med små kræftknuder i skjoldbruskkirtlen i forhold til et ukompliceret primært behandlingsforløb.

Problemstilling

For at kunne introducere en mindre invasiv metode til behandling af skjoldbruskkirtelkræft skal det undersøges i et klinisk lodtrækningsforsøg.

Baggrund

Omkring 500 personer rammes hvert år af kræft i skjoldbruskkirtlen i Danmark og antallet har været stigende gennem flere år. Kræft i skjoldbruskkirtlen behandles med operation, og i tilfælde af en lille kræftknude bliver patienter behandlet med kirurgisk fjernelse af halvdelen af kirtlen (hemithyroidektomi, HT). Selvom der ved operation er god helbredelse fra kræften og god overlevelse, er der relativt mange (20-25%) som oplever komplikationer såsom lavt stofskifte eller nerveskade. En ny og mindre invasiv behandling der i stigende grad bruges verden over, er radiobølge varmeablation (radiofrequency ablation, RFA). Ved RFA-behandling bliver kræftknuden ved hjælp af en ultralydsvejledt nål varmet op og på denne måde behandlet uden operation. Udfordringen med den nye behandling er, at den ikke er undersøgt i et lodtrækningsforsøg.

Metoder

Studiet vil være et multi-center, randomiseret, parallel-gruppe, stratificeret, non-inferiority forsøg.
Inklusionskriterierne vil være patienter på 30 år eller ældre med en enkelt knude på under 2 cm i diameter i skjoldbruskkirtlen, som bliver behandlet på Øre-, næse- og halskirurgisk afdeling, Aarhus Universitetshospital eller Rigshospitalet. Der skal være en mistanke om kræft, som er bekræftet ved en finnåls-prøve.
Patienter vil blive ekskluderet hvis en af følgende er opfyldt: spredning til lymfeknuder eller mistanke om spredning til lymfeknuder eller andre organer; tegn til lokal spredning ved gennemvækst af skjoldbruskkirtlens kapsel; knudens placering som gør den uegnet til RFA-behandling; tidligere kirurgi i området; hyperparathyroidsime (forhøjet biskjoldbruskkirtel-

hormon og kalk); hvis patienten er gravid; eller hvis patienten ikke er i stand til at give informeret samtykke.
Intervention: De inkluderede patienter vil blive fordelt 1:1 ved lodtrækning til enten standard behandling med HT eller den eksperimentelle RFA-behandling. Behandlingen vil foregå i løbet af en til to uger efter lodtrækningen.
Fordelingen vil være ligeligt (stratificeret) mellem behandlingsgrupper mht. de inkluderende centre (AUH og RH) samt mht. alder (under 60 år eller 60 år og ældre).
Der forventes at skulle inkluderes 88 patienter i forsøget – 44 i hver behandlingsgruppe.

Tidsplan

Der vil være et kontrolforløb efterfølgende som ligner de forløb, der tilbydes andre patienter i behandling for kræft i skjoldbruskkirtlen. Opfølgningen vil være op til 5 år efter behandlingen, og der vil i forbindelse med kontrolbesøg blive udført lægesamtale, ultralydsscanning af halsen, blodprøver, samt til nogle besøg også udfyldning af to forskellige spørgeskemaer.
Planen er at igangsætte forsøget efter opnået videnskabsetisk godkendelse i løbet af ultimo 2025, og det forventes at inklusionsperioden vil vare 3 år.

Forventede resultater og impact

Hvis det viser sig at varmebehandling er lige så god som standardbehandlingen med operation, vil andre patienter kunne tilbydes dette i fremtiden, med mulighed for at undgå en operation og de risici den medfører. Resultaterne fra dette forsøg vil have en stor national og international betydning for forbedring af behandlingen af patienter med kræft i skjoldbruskkirtlen. Der er ikke lavet et lignende forsøg tidligere.

Øvrige projektdeltagere og samarbejdsrelationer

Forsøget har udgangspunkt på Aarhus Universitetshospital, hvor ansøger vil fungere som forsøgsansvarlig sideløbende med at ansøger er i sit hoveduddannelsesforløb i øre-, næse- og halskirurgi.
Øre-, næse-, halskirurgisk afdeling på Rigshospitalet vil deltage i forsøget og vil inkludere patienter. Desuden deltager klinikere fra Odense Universitets Hospital i en sikkerheds-styregruppe og en repræsentant fra patientforeningen, Stofskifteforeningen, vil være involveret i forsøget fra planlægningen til afslutning. Derfor vil forsøget fremme det nationale samarbejde og derved højne kvaliteten af behandlingen af danske patienter med kræft i skjoldbruskkirtlen.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Samlet budget: 3.520.000 DKK (dækker løn til seniorforsker og en Ph.d.-studerende, operationelle udgifter og udgifter til formidling og publikation af resultater).
Bevilling fra Novo Nordisk Fonden (andel af bevilling givet til Lars Rolighed): 3.320.000 DKK
Manglende finansiering: 200.000 DKK (som vil dække frikøb af reservelæge 25% af fuldtid i 1 år).

Curriculum Vitae - Kompetencebaseret

Sofie Louise Rygård
Esbyvej 4
8240 Risskov
51 92 28 19
sofilosi@gmail.com / soryga@rm.dk
Født 1. november 1982
Cand. Med., Københavns Universitet, november 2013.

Medicinsk ekspert

Postgraduat klinisk erfaring

2024, aug. –	Læge, hoveduddannelse, Øre-, næse-, halskirurgisk afd., Aarhus
2023, okt. – 2024, aug.	Læge, vikar for speciallæge, Lægerne Vennelystparken, Aarhus
2022, okt. – 2023, okt.	Læge, introduktionsstilling, Øre-, næse-, halskirurgisk afdeling, AUH
2022, aug. – okt.	Læge, Almen Lægeklinik Randers
2020, maj – nov.	Læge, introduktionsstilling, Klinisk immunologisk afdeling, Rigshospitalet
2019, maj – 2020, maj	Læge, introduktionsstilling, Anæstesiologisk afdeling, Hvidovre Hospital
2019, jan. – maj	Læge, KBU, Mit Lægehus Rødovre
2015 - 2018	Klinisk assistent, Intensiv Terapiklinik, 4131, Rigshospitalet
2014, nov. – dec.	Læge, KBU, almen praktiserende læge, Annette Kristjansen
2014, maj – nov.	Læge, KBU, medicinsk afdeling, Amager Hospital
2014, jan. – maj	Læge, u-klassificeret stilling, Ortopædkirurgisk afdeling, Hvidovre Hospital

Prægraduat klinisk erfaring

2011 - 2012	Lægevikar, Urologisk afdeling, Roskilde Sygehus
2011 - 2012	Lægevikar, Hæmatologisk afdeling, Rigshospitalet
2008 - 2011	Ventilatør, Thorax-anæstesiologisk intensiv afd., Rigshospitalet

Uddannelse

2019	PhD grad, Københavns universitet, på baggrund af afhandlingen: *Red blood cell transfusion and long-term outcomes among patients with septic shock*
2006 - 2013	Lægevidenskab, Københavns Universitet

Akademiker

2015-2018	PhD-studerende, Institut for Klinisk Medicin, Københavns Universitet
2025, jan. –	Postdoc, Institut for Klinisk medicin, Aarhus Universitet

Bedømmer virksomhed

2017 – Peer-reviewer for Intensive Care Medicine (25 studier til dato), Acta Anaesthesiologica Scandinavica (9) og Journal of Systematic Reviews (6).

Andet akademisk arbejde

2023 – 2024 Ansvarlig for Journal Club på Øre-, næse-, halskirurgisk afdeling, AUH.

2022 – Medlem af en arbejdsgruppe til vurdering af kliniske retningslinjer omhandlende thyroideacancer. Samarbejde med klinikere og forskere fra Norge, Sverige og Danmark. Skal resultere i en publikation.

2019 Medlem af en arbejdsgruppe til udarbejdelse af kliniske retningslinjer for blodtransfusion under the European Society of Intensive Care Medicine. Resulterede i en publikation.

Kommunikator

Præsentation ved konferencer

- *Thyroid surgery in children – diagnostic evaluation, surgical treatment and pathological findings*, mundtlig præsentation, DSOHH årsmøde, april 2024
- *Surgical treatment, morbidity and mortality in patients with T1 and T2 thyroid cancer, mundtlig præsentation, Dansk Hoved-Hals Kirurgisk Selskabs årsmøde, november 2023*
- *Finansiering af kliniske forsøg på intensivafdelinger i Danmark 2005-2017*, poster og mundtlig præsentation, DASAIM årsmøde, København 2017.
- *Higher vs. lower haemoglobin threshold for transfusion in septic shock: subgroup analyses of the TRISS trial*, poster, Scandinavian Intensivist Meeting, Helsinki, Juni 2016 samt mundtlig præsentation, ESICM Lives, Milano, oktober 2016.
- *Long-term outcomes in patients with septic shock transfused at a lower versus a higher haemoglobin threshold: the TRISS randomised, multicentre clinical trial*, poster, Scandinavian Intensivist Meeting, Helsinki, Juni 2016 samt mundtlig præsentation, ESICM Lives, Milano, oktober 2016.
- *Red blood cell transfusion in ICU patients with septic shock – characteristics of patients, units given, timing and association to mortality*, poster, ESICM Lives, Barcelona 2014.

Anden undervisning

2019 – 2020	Undervisning af medicinstuderende (12. semester) i praktiske færdigheder, Hvidovre Hospital.
2018 og 2019	Underviser; 3 dages PhD kursus: *Clinical trial methodology*. PhD skolen, SUND, KU.
2015 - 2018	Formidling af forskning til intensivsygeplejersker og læger ved formaliseret undervisning
2010 - 2012	Underviser i anatomi, Danseuddannelsen ved Sara Gaardbo

Samarbejder

2018	Udveksling á 4 ugers varighed til Aarhus Universitet, Klinisk Epidemiologisk Afdeling – *erfaringsudveksling mellem klinisk epidemiologi og klinisk forskning samt fortsat samarbejde om epidemiologisk forskning omhandlende sepsis i Danmark.*
2017 - 2019	Medlem af Diversity Working Group, European Society of Intensive Care Medicine (ESICM) – *udarbejdelse af hensigtserklæring samt overvågning af diversitet i selskabet pba. seksualitet, etnicitet og faggruppe. Samarbejde med forskere fra hele verden.* Publikation*:* Weiss B and Task Force and Working Groups for Diversity and Equality of the ESICM*. Statement paper on diversity for the European Society of Intensive Care Medicine (ESICM).* ICM, 2019; 45(7):1002-1005.
2016 - 2018	Suppleant for tillidsrepræsentanten, Intensiv Terapiklinik 4131 – *fungerende TR i 3 måneder (som barselsvikar), februar – april 2017*

Leder/administrator/organisator

2023 - 2024	Ansvarlig for Journal Club, Øre-, næse-, halskirurgisk afd., AUH.
2019 - 2020	Anæstesiologisk vagthavende, Hvidovre Hospital – *organisering og prioritering af operationsprogram samt akutte problemstillinger. Teamleder til traumer.*
2018 og 2019	Organisator og administrator af et 3 dages kursus på PhD skolen under SUND, *Clinical trial methodology*

2016 - 2018	Koordinator og lokal investigator for ADRENAL-forsøget på intensiv terapiklinik, RH – *internationalt randomiseret klinisk forsøg med i alt 3800 patienter inkluderet.*

Sundhedsfremmer

2016 - 2020	Aktivt medlem af Danish Medical Group Against the Death Penalty, Amnesty International Denmark – *hjemmeside- og kommunikationsansvarlig.*
2008 - 2020	Studenterredaktør/senior-associeret, Fadls Forlag – *faglig assistance og gennemlæsning af udgivelser til de sundhedsvidenskabelige uddannelser og sundhedsfaglige bøger til det brede marked.*

Peer-reviewed publikationer

Som 1. forfatter:

- Rygård, SL, Grønlykke L, Perner A, et al. *Storage time of red blood cells among ICU patients with septic shock*. Acta Anaesthesiol Scand. 2019; 63(10):1366-1377.
- Rygård SL, Kjær MN, Perner A. *Statens investering i kliniske forsøg*. Ugeskr Læger. 2018; (180):V09170645.
- Rygård SL, Butler E, Granholm A, et al. *Low-dose corticosteroids for adult patients with septic shock: a systematic review with meta-analysis and trial sequential analysis*. Intensive Care Med. 2018; 44: 1003-16.
- Rygård SL, Jonsson AB, Madsen MB, et al. *Effects of shorter versus longer storage time of transfused red blood cells in adult ICU patients: a systematic review with meta-analysis and Trial Sequential Analysis*. Intensive Care Med. 2018; 44:204-217.
- Rygård SL, Holst LB, Perner A. *Blood Product Administration in the Critical Care and Perioperative Settings*. Crit Care Clin. 2018;34(2):299-311.
- Rygård SL, Jonsson AB, Madsen MB, et al. *Effects of red blood cell storage time on transfused patients in the ICU-protocol for a systematic review*. Acta Anaesthesiol Scand. 2017;61(10):1384-1397.
- Rygård SL, Holst LB, Wetterslev J, et al. *Higher vs. lower haemoglobin threshold for transfusion in septic shock: subgroup analyses of the TRISS trial.* Acta Anaesthesiol Scand. 2017;61(2):166-175.
- Rygård SL, Holst LB, Wetterslev J, et al. *Long-term outcomes in patients with septic shock transfused at a lower versus a higher haemoglobin threshold: the TRISS randomised, multicentre clinical trial.* Intensive Care Med. 2016; 42:1685-1694

Udvalgte medforfatterskaber:

- Barbateskovic M, Koster TM, …, Rygård SL, et al. *A new tool to assess Clinical Diversity In Meta-Analysis (CDIM) of interventions*. Journal of Clinical Edipemiology 2021; jul 135, s. 29-41
- Vlaar AP, Oczkowski S, de Bruin S, …, Rygård SL, et al. *Transfusion strategies in non-bleeding critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine*. Intensive Care Med. 2020; jan 7
- Jonsson AB, Rygård SL, Anhøj J, et al. *Use of red blood cells in Danish intensive care units: A population-based register study*. Acta Anaesthesiol Scand. 2019; 63(10):1357-1365.

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling:	Karoline Lolk Revsbech, læge
Arbejdssted/ Institution	Afdeling for nyresygdomme/ Herlev og Gentofte Hospital
Adresse	Borgmester Ib Juuls Vej 1 Opgang 1, 9. etage 2730 Herlev
Tlf.nr.	Herlev Hospital: +45 3868 3868 / Forskningsenhed: +45 3868 2877
e-mail	karoline.lolk.revsbech@regionh.dk

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

Betydning af hjemmeblodtryksmåling om natten hos personer med kronisk nyresygdom.

Formål

Formålet med dette projekt er at undersøge om natlig hjemmeblodtryksmåling er et lige så pålideligt, mere gennemførligt, billigere alternativt til døgnblodtryk hos personer med kroniske nyresygdom (CKD).

Problemstilling

I et tværsnitsstudie vil vi undersøge overensstemmelsen mellem to forskellige metoder, døgnblodtryk og natligt hjemmeblodtryk. Ligeså vil forholdet mellem blodtrykket målt ved de to metoder og graden af organskade blive undersøgt, og vi vil desuden undersøge hvilken af de to målemetoder forsøgsdeltagerne foretrækker.

Baggrund

Forhøjet blodtryk er meget hyppigt forekommende hos personer med CKD, der samtidig har en høj forekomst af hjertekarsygdom og tidlig død. Det er centralt i behandlingen af CKD at sikre, at blodtrykket ikke er for højt, for at mindske fald i nyrefunktion og forebygge udvikling af hjertekarsygdom og tidlig død. Nøjagtige målinger af blodtrykket er derfor meget vigtigt. Blodtrykket målt derhjemme eller over 24 timer, er bedre til at forudsige, hvem der er i øget risiko for hjertekarsygdom og død, end blodtrykket målt i klinikken. Derudover har særligt blodtrykket om natten betydning for at forudsige denne risiko. Hidtil har det kun været muligt at måle natblodtryk ved døgnblodtryksmåling, hvor blodtrykket automatisk måles hver halve time i løbet af natten. Denne metode er mindre populær hos brugerne, da den kan påvirke søvnkvaliteten, og samtidig er døgnblodtryksapparatet dyrt. Der er for nyligt udviklet et hjemmeblodtryksapparat, der automatisk kan måle blodtryk 2-3 gange om natten ved hjælp af en timer, der indstilles efter ønske. Prisen er ca. 10% af et døgnblodtryksapparat og hyppigheden hvormed søvnen kan blive afbrudt væsentlig reduceret.

Dette projekt vil primært undersøge overensstemmelsen af natligt hjemmeblodtryk målt med døgnblodtryksmåling i forhold til hjemmeblodtryksapparatet med timer og associationen til organskade, der kan ses ved forhøjet blodtryk hos personer med CKD.

Metoder

Projektet er udformet som et tværsnitsstudie efterfulgt af et opfølgningsstudie. I alt skal indgå 500 personer med CKD, som får målt både døgnblodtryk og natligt hjemmeblodtryk. Forekomst af organskade findes ved at lave ultralydsskanning af hjertet samt måling af karstivhed og proteinindhold i urinen. De forskellige blodtryksmålemetoder vil blive sam-

menholdt med forandringer i hjertet, kar og nyrer. I tillæg spørges deltagerne om, hvilken metode de foretrak til måling af deres blodtryk. For at afklare hvilken type blodtryksmåling, der er bedst til at forudsige ens fremtidige risiko, vil deltagerne desuden blive fulgt i registre for progression af nyresygdom, hjertekarsygdom og død over en periode på 5 år.

Tidsplan

Forår og sommer 2025: fundansøgning, protokolskrivning og -godkendelse.
Efterår 2025 – efterår 2027: inklusion af patienter og dataindsamling.
2027 – 2028: Dataanalyse, artikelskrivning og sammenskrivning til ph.d.-afhandling.

Forventede resultater og impact

Det vurderes at op mod 10% af den voksne befolkning har CKD. Resultaterne af dette projekt vil potentielt kunne komme alle med CKD til gode, da både positive og negative fund vil bidrage med ny viden om den optimale måde at måle blodtrykket på.

Øvrige projektdeltagere og samarbejdsrelationer

Hovedvejleder:
Ditta Hansen, professor, overlæge og ph.d., afdeling for nyresygdomme, Herlev Hospital

Medvejledere:
Marie Frimodt-Møller, overlæge ph.d., afdeling for nyresygdomme, Herlev Hospital
Tine Willum Hansen, professor, overlæge, ph.d., Steno Diabetes Center Copenhagen

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

<u>Foreløbig finansiering:</u>
Ansættelse af seniorforsker i delestilling i 4 år, Herlev og Gentofte Hospital (942.384 kr.)
Augustinus Fonden (500.000 kr.)
Hørslev-Fonden (173.950 kr.)
Afdeling for nyresygdomme, Herlev Hospital (150.000 kr.)

Budget:

	price (DKK)	amount	covered (DKK)	not-covered (DKK)
equipment/analyses				
BP monitor both arms	9.450,00	2	18.900	0,00
UACR	5.5/analysis	1500	8.000	0
SphygmoCor		1	yes	0
ABPM (24h bloodpressure device)	10.500	20	yes	0
Home BP incl. Timer	1650	20	33.000	0
ECHO (apparatus)		1	yes	0
laboratory tests	150	500	75.000	0
establishment of biobank		500	65.000	0
Salary				
echocardioghapher	1200/ echo	500	0	600.000
ph.d.student studyfee		150.000	150.000	0
ph.d.student 3 years		**1.906.000**	**500.000**	**1.406.000**
ph.d.student travel	15.000/year		0	45.000
project nurse	267/h	1760	0	470.300
lab.technician	295/h	500	0	147.500
senior ph.d supervisor	19633/mth	48	942.384	0
Other				
Lunch for participants	100	500	0	50.000
patient transport			0	25.000
Total				
total covered/not-covered			**1.792.284**	**2.743.800**
TOTAL incl. covered, not-covered)		**4.536.084**		
Overhead (18%)		**816.495**		**816.495**
TOTAL (covered, not-covered, overhead)		**5.352.579**	**1.792.284**	**3.560.295**

Bilag

CV – Karoline Lolk Revsbech

Jyllandsvej 10, 2. mf
2000 Frederiksberg
karolinerevsbech@gmail.com +45 3023 9294

Uddannelse og kurser

2024	ALS (ERC-certificeret), Region Sjælland
2024	Fokuseret lungeultralyd, CAMES Region Hovedstaden
2021	Kandidat i medicin, Københavns Universitet

Postgraduate ansættelser

2024-25	Introduktionsstilling i intern medicin: Medicinsk afdeling, SUH Roskilde
2023-24	Introduktionsstilling i intern medicin: Afdeling for nyresygdomme, Herlev Hospital
2022-23	Introduktionsstilling i almen medicin: Lægehuset Stenløse og efterfølgende vikariat
2021-22	Klinisk basisuddannelse: - Ortopædkirurgisk afdeling, Hvidovre Hospital - Almen praksis, Lægerne Hall og Stengade, Glostrup

Prægraduate ansættelser

2019-20	Forskningsårsstuderende, Copenhagen Neuromuscular Center, Rigshospitalet
2017-21	Klinikassistent, Lægerne ved Trianglen, København
2014-16	Syeplejevikar, FADL København

Forskningserfaring

Under studiet tilbragte jeg et år som forskningsårsstuderende på Copenhagen Neuromuscular Center, Rigshospitalet. Jeg var dels ansvarlig for mit eget projekt, som resulterede i udgivelse af en artikel som førsteforfatter. Derudover var jeg involveret i adskillige andre projekter, både i den praktiske udførelse af disse samt i udarbejdelse af manuskript til artiklerne, hvilket har resulteret i syv medforfatterskaber.

Undervisning

2022-25	Div. oplæg i den kliniske hverdag som læge
2009-13	Tennistræner, Esbjerg Tennisklub

Præsentationer

2019	Oral præsentation: Paraspinal muscle involvement in LGMD2I patients
2019	Posterpræsentation: Quantitative MRI in patients with LGM2I

Øvrig erfaring

2024-25	Tillidsrepræsentant for yngre læger, medicinsk afdeling, SUH Roskilde
2023-24	Uddannelseskoordinerende yngre læge, afd. for nyresygdomme, Herlev Hospital

Publikationer

Revsbech KL, Rudolf K, Sheikh AM, Khawajazada T, de Stricker Borch J, Dahlqvist JR, Løkken N, Witting N, Vissing J. *Axial muscle involvement in patients with limb girdle muscular dystrophy type R9.* Muscle Nerve. 2022

Zhao Q, Naume MM, de Winter BCM, Krag T, Haslund-Krog SS, Revsbech KL, Vissing J, Holst H, Møller MH, Hornsyld TM, Dunø M, Hoei-Hansen CE, Born AP, Jensen PB, Ørngreen MC. *Paracetamol and its metabolites in children and adults with spinal muscular atrophy - a population pharmacokinetic model.* Br J Clin Pharmacol. 2025

Naume MM, Zhao Q, Haslund-Krog SS, Krag T, Winter BCM, Revsbech KL, Vissing J, Holst H, Møller MH, Hornsyld TM, Dunø M, Hoei-Hansen CE, Born AP, Bo Jensen P, Cathrine Ørngreen M. *Acetaminophen treatment in children and adults with spinal muscular atrophy: a lower tolerance and higher risk of hepatotoxicity.* Neuromuscul Disord. 2024

Løkken N, Nielsen MR, Stemmerik MG, Ellerton C, Revsbech KL, Macrae M, Slipsager A, Krett B, Beha GH, Emanuelsson F, van Hall G, Quinlivan R, Vissing J. *Can a modified ketogenic diet be a nutritional strategy for patients with McArdle disease? Results from a randomized, single-blind, placebo-controlled, cross-over study.* Clin Nutr. 2023

Løkken N, Revsbech KL, Jacobsen LN, Martinuzzi A, Martin MÁ, Díaz-Manera J, Dominguez-Gonzalez C, Brondani G, Musumeci O, Granata F, Stefan C, Merino-Sanchez C, Peralta CN, Khawajazada T, Alonso-Pérez J, Toscano A, Vissing J. *Muscle MRI in McArdle Disease: A European Multicenter Observational Study.* Neurology. 2022

Løkken N, Storgaard JH, Revsbech KL, Voermans NC, Van Hall G, Vissing J, Ørngreen MC. *No effect of oral ketone ester supplementation on exercise capacity in patients with McArdle disease and healthy controls: A randomized placebo-controlled cross-over study.* J Inherit Metab Dis. 2022

Andersen LK, Jakobsson AS, Revsbech KL, Vissing J. *Causes of symptom dissatisfaction in patients with generalized myasthenia gravis.* J Neurol. 2022

Salim R, Dahlqvist JR, Khawajazada T, Kass K, Revsbech KL, de Stricker Borch J, Munawar Sheikh A, Vissing J. *Characteristic muscle signatures assessed by quantitative MRI in patients with Bethlem myopathy.* J Neurol. 2020

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens min-delegat, afd. B - sygdomsforskning

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- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Anders Møller Greve, Afdelingslæge, PhD**
Arbejdssted/ Institution	**Afdeling for Klinisk Biokemi, Righospitalet**
Adresse	**Blegdamsvej 9, 2100 København Ø**
Tlf.nr.	**+45 3545 5543**
e-mail	**anders.moeller.greve@regionh.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
Kunstig intelligens til præcisionsdiagnostik af blod, knoglemarvs- og lymfekræft
Formål
1. Forbedre nøjagtigheden og effektiviteten af flowcytometrisk diagnostik af leukæmi, myelomatose og non-Hodgkin lymfom. 2. Identificere nye prognostiske markører og sammenhænge i flowcytometriske data, der ikke er mulige at opdage ved manuel fortolkning.
Problemstilling
Blodkræft (leukæmi), knoglemarvskræft (myelomatose) og lymfekræft (malignt lymfom) udgør en betydelig andel af kræftdiagnoser i Danmark og globalt. Præcis og hurtig diagnostik er afgørende for at kunne iværksætte effektiv behandling og forbedre patienternes overlevelse. Flowcytometri

er en grundsten i diagnostikken af disse sygdomme, da det muliggør hurtig og præcis karakterisering af celler ved hjælp af fluorescensmærkede antistoffer.

Den nuværende manuelle fortolkning af flowcytometriske data er dog tidskrævende og subjektiv, hvilket kan besværliggøre diagnostikken og føre til forsinkelser i behandlingen. Dette projekt har til formål at adressere disse udfordringer ved at udvikle og implementere et kunstig intelligens (KI)-værktøj, der kan afhjælpe dette.

Baggrund

Flowcytometri giver detaljeret information om cellers proteinprofil på kort tid, hvilket er afgørende for diagnostik, prognose og behandling af blod- og lymfekræft. Den manuelle fortolkning af disse data kræver dog ekspertise og er udsat for subjektivitet.

Med den stigende tilgængelighed af computerkraft og fremskridt inden for KI, er der nu mulighed for at udvikle værktøjer, der kan automatisere og forbedre fortolkningen af flowcytometriske data. Præliminære studier har vist, at KI-modeller kan opnå en hidtil uset nøjagtighed i diagnosticering af blod- og lymfekræft.

Implementeringen af et KI-værktøj vil føre til hurtigere og mere præcise diagnoser, hvilket vil forbedre patienternes overlevelse og livskvalitet. Desuden vil det effektivisere arbejdsgangene i laboratoriet og reducere behovet for unødvendige indlæggelser.

Metoder

Dette projekt vil anvende en kombination af retrospektiv dataanalyse og prospektiv klinisk validering.

- Retrospektiv modeludvikling og evaluering:
  - Vi vil anvende en stor database af flowcytometriske data fra Rigshospitalet til at træne og evaluere KI-modeller.
  - Vi vil udvikle modeller til diagnosticering og underklassificering af malignt lymfom, plasmacelledyskrasi og akut leukæmi.
  - Vi vil anvende metoder inden for forklarlig KI for at identificere vigtige mønstre i data og forbedre forståelsen af sygdomsmekanismer.
  - vi vil undersøge om KI kan bruges til at forudsige prognoser.
- Prospektiv diagnostisk sammenligning:
  - Vi vil evaluere KI-værktøjets ydeevne i en klinisk kontekst ved at sammenligne KI-assisteret diagnostik med standardmetoder for kronisk lymfatisk leukæmi (CLL).

Tidsplan

Projektet bliver udført som et Ph.d.-projekt, for Civilingeniør Elvin Iruthayam, over 4 år. Projektet startede oktober 2024 og forventes afsluttet september 2028.

Forventede resultater og impact

Projektet er et samarbejde mellem Afdeling for Klinisk Biokemi og MedTek Huset på Rigshospitalet. Forskerteamet har ekspertise inden for flowcytometri, KI og klinisk evaluering. Rigshospitalets unikke database og adgang til sundhedsregistre giver en enestående mulighed for at gennemføre dette projekt.

Vi forventer at udvikle et robust KI-værktøj, der kan implementeres i rutinemæssig diagnostik af blod- og lymfekræft. Dette vil føre til:

- Forbedret diagnostisk nøjagtighed og effektivitet.
- Identifikation af nye prognostiske markører.
- Forbedret patientbehandling og ressourceudnyttelse.

Øvrige projektdeltagere og samarbejdsrelationer

Elvin Iruthayam, Civilingeniør i Medicin & Teknologi (Ph.d.-studerende)
Marianne Benn, Professor, Afdeling for Klinisk Biokemi (Hovedvejleder)
David Kovacs Petersen, Leder, MedTek Huset (Med-vejleder)

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Udgifter i projektet

	Total (DKK)	**År 1***	**År 2***	**År 3***
Løn til 1 PhD studerende	1.223.040	407.680	407.680	407.680
Analyser	276.960	92.320	92.320	92.320
Total	1.500.000	500.000	500.000	500.000

***Bemærk budgettet er regnet i fuldtid, men selve projektet udføres på deltid over 4 år.**

Finansiering af projekt

Fond	Finansiering
Læge Sofus Carl Emil Friis og Hustru Olga Doris Friis' Legat	1.000.000 DKK
Den lægevidenskabelige del af det Sundhedsvidenskabelige Fakultets fond for videnskabeligt ansatte kandidater og studerende ved Københavns Universitet	294.000 DKK
** **Direktør Michael Hermann Nielsens mindelegat**	**206.000 DKK**

**** Direktør Michael Hermann Nielsens mindelegat ansøges om 206.000 DKK, for at dække den sidste del af finansieringen for hele Ph.d.-forløbet.**

CURRICULUM VITAE

Name: Anders Møller Greve
E-mail: anders.moeller.greve@regionh.dk
Date and place of birth: August 2nd, 1981, Copenhagen, Denmark.

EDUCATION

2001-2008	MD, University of Copenhagen, Denmark
2010-2014	PhD, University of Copenhagen, Denmark (January 24th, 2014)
2014-2015	Postdoctoral research, NHBLI, National Institutes of Health, Bethesda, Maryland
2017-2022	Specialist in clinical biochemistry, Board-certified on March 31st, 2022

POSITIONS

2008-2009	MD, Internal medicine, Bornholms Hospital.
2009-2010	MD (KBU), Internal medicine and General Practice, Nykøbing Falster Sygehus.
2010-2010	Research fellow, Department of Cardiology, Rigshospitalet.
2010-2011	PhD student, Department of Cardiology, Rigshospitalet.
2011-2012	PhD student, NHLBI, National Institutes of Health, Bethesda, Maryland.
2012-2013	Sick leave with my daughter Eleanor Dagmar Greve
2013-2014	PhD student, NHLBI, National Institutes of Health, Bethesda, Maryland.
2014-2015	Post doc, NHLBI, National Institutes of Health, Bethesda, USA.
2015-2017	MD, Department of Cardiology, Bispebjerg and Frederiksberg Hospital
2017-2020	MD, Department of Clinical Biochemistry, Rigshospitalet.
2020-2022	MD, Department of Clinical Biochemistry, Herlev and Gentofte Hospital.
2022-	MD (afdelingslæge), Department of Clinical Biochemistry, Rigshospitalet.

SCIENTIFIC AWARDS & HONORS

2014	Circulation Editors Pick (one of the most important papers published in 2012-2013).
2014	Top scored abstract, European society of cardiology congress, Barcelona.

BIBLIOMETRY

49 original articles (including 13 as first author), 2 reviews, 2 book chapters, 2 letters to the Editor, 1 editorial, 1 commentary.
Number of original articles published in journal with impact factor >20: 8 (hereof 4 as first author)
H-index (Google scholar, March 2025): 24
Total number of citations (Google scholar, March 2025): 1,664.

PhD SUPERVISION

2021-2023	PhD co-supervisor for Edina Hadziselimovic, MD. PhD obtained August 23rd, 2023.
2024-	PhD primary co-supervisor Elvin Iruthayam, MS (Enrolled PhD school).
2024-	PhD co-supervisor Søren Rønborg, MD (Enrolled PhD school).
2024-	PhD co-supervisor Anne-Sofie Rasmussen, MD (Enrolled PhD school).

INVITED TALKS

2012	Cardiology rounds, Medstar hospital, Washington DC.
2022	DANAK (Danish ISO accreditation foundation), Nyborg.

GRANTS >100,000 DKK

2023	Læge Sofus Carl Emil Friis og Hustru Olga Doris Friis' Legat	DKK 1.0M
2024	Det Sundhedsvidenskabelige Fakultets fond, Københavns Universitet	DKK 0.3M

REVIEWER
Reviewer for >10 top international journals including the New England Journal of Medicine, JACC and Circulation.

Original scientific contributions:

1. **Greve AM**, Gerdts E, Boman K, Gohlke-Baerwolf C, Rossebø AB, Hammer-Hansen S, Køber L, Willenheimer R, Wachtell K. Differences in cardiovascular risk profile between electrocardiographic hypertrophy versus strain in asymptomatic patients with aortic stenosis (from SEAS Data). Am J Cardiol. 2011 Aug 15;108(4):541-7.
2. **Greve AM**, Gerdts E, Boman K, Gohlke-Baerwolf C, Rossebø AB, Nienaber C, Ray S, Egstrup K, Pedersen TR, Køber L., Willenheimer R, Wachtell K. Prognostic importance of atrial fibrillation in asymptomatic aortic stenosis: the simvastatin and ezetimibe in aortic stenosis study. Int J Cardiol. 2013 Jun 5;166(1):72-6.
3. **Greve AM**, Boman K, Gohlke-Baerwolf C, Kesäniemi YA, Ray S, Egstrup K, Rossebø AB, Devereux RB, Køber L, Willenheimer R, Wachtell K. Clinical Implications of Electrocardiographic Left Ventricular Strain and Hypertrophy in Asymptomatic Patients with Aortic Stenosis: The Simvastatin and Ezetimibe in Aortic Stenosis Study. Circulation. 2012 Jan 17;125(2):346-53.
4. **Greve AM**, Gerdts E, Boman K, Gohlke-Baerwolf C, Rossebø AB, Devereux RB, Køber L, Ray S, Willenheimer R, Wachtell K. Impact of QRS Duration and Morphology on The Risk of Sudden Cardiac Death in Asymptomatic Patients with Aortic Stenosis: The Simvastatin and Ezetimibe in Aortic Stenosis Study. J Am Coll Cardiol. 2012 Mar 27;59(13):1142-9.
5. Bang CN, **Greve AM**, Boman K, Egstrup K, Gohlke-Baerwolf C, Køber L, Nienaber CA, Ray S, Rossebø AB, Wachtell K. Effect of Lipid Lowering on New-Onset Atrial Fibrillation in Patients with Asymptomatic Aortic Stenosis. The SEAS study. Am Heart J. 2012 Apr;163(4):690-6.
6. **Greve AM**, Olsen MH, Bella JN, Lønnebakken MT, Gerdts E, Boman K, Nieminen MS, Omvik P, Dahlöf B, Devereux RB, Wachtell K. Contrasting Hemodynamic Mechanisms of Losartan- versus Atenolol-based Antihypertensive Treatment; a LIFE study. Am J Hypertens. 2012 Sep;25(9):1017-23.
7. Bang CN, **Greve AM**, Abdulla J; Køber L, Gislason G, Kristian Wachtell. The Preventive Effect of Statin Therapy on New-Onset and Recurrent Atrial Fibrillation in Patients Not Undergoing Invasive Procedures - A Systematic Review And Meta-Analysis. Int J Cardiol. 2013 Aug 10;167(3):624-30.
8. Bang CN, Gislason GH, Køber L, Torp-Pedersen C, **Greve AM**, Wachtell K. Statins Reduce New-Onset AF in a First Time Myocardial Infarction Population and Shows a Type and Dose-Dependent Effect. *A Nationwide cohort study*. Eur J Prev Cardiol. 2014 Mar;21(3):330-8.
9. Bang CN, **Greve AM**, Dalsgaard M, Køber L, Gerdts E, Egstrup K, Wachtell K. Left atrial size and function as predictors of new-onset of atrial fibrillation in patients with asymptomatic aortic stenosis: The simvastatin and ezetimibe in aortic stenosis study. Int J Cardiol. 2013 Oct 3;168(3):2322-7.
10. Bang CN, Gislason GH, **Greve AM**, Bang CA, Lilja A, Torp-Pedersen C, Andersen PK, Køber L, Devereux RB, Wachtell K. New-onset Atrial Fibrillation in Associated with Cardiovascular Events Leading to Death in a First Time Myocardial Infarction Population of 89,703 Patients with Long-term Follow-up *A Nationwide Study*. J Am Heart Assoc. 2014 Jan 21;3(1):e000382.
11. **Greve AM**, Dalsgaard M, Bang CN, Egstrup K, Ray S, Boman K, Rossebø AB, Gohlke-Baerwolf C, Devereux RB, Køber L, Wachtell K. Stroke in patients with aortic stenosis: the Simvastatin and Ezetimibe in Aortic Stenosis study. Stroke. 2014 Jul;45(7):1939-46.
12. Bang CN, **Greve AM**, Køber L, Rossebø AB, Ray S, Boman K, Nienaber CA, Devereux RB, Wachtell K. Renin-angiotensin system inhibition is not associated with increased sudden cardiac death, cardiovascular mortality or all-cause mortality in patients with aortic stenosis. Int J Cardiol. 2014 Aug 20;175(3):492-8.
13. **Greve AM**, Dalsgaard M, Bang CN, Egstrup K, Rossebø AB, Boman K, Cramariuc D, Nienaber CA, Ray S, Gohlke-Baerwolf C, Okin PM, Devereux RB, Køber L, Wachtell K.

Usefulness of the electrocardiogram in predicting cardiovascular mortality in asymptomatic adults with aortic stenosis (from the Simvastatin and Ezetimibe in Aortic Stenosis Study). Am J Cardiol. 2014 Sep 1;114(5):751-6.
14. Ismail TF, Hsu LY, **Greve AM**, Gonçalves C, Jabbour A, Gulati A, Hewins B, Mistry N, Wage R, Roughton M, Ferreira PF, Gatehouse P, Firmin D, O'Hanlon R, Pennell DJ, Prasad SK, Arai AE. Coronary microvascular ischemia in hypertrophic cardiomyopathy - a pixel-wise quantitative cardiovascular magnetic resonance perfusion study. J Cardiovasc Magn Reson. 2014 Aug 12;16(1):49.
15. **Greve AM**, Bang CN, Berg RMG, Egstrup K, Rossebø AB, Boman K, Nienaber CA, Ray S, Gohlke-Baerwolf C, Nielsen OW, Okin PM, Devereux RB, Køber L, Wachtell K. Resting Heart and Risk of Adverse Cardiovascular Outcomes in Asymptomatic Aortic Stenosis: The SEAS Study. Int J Cardiol. 2015 Feb 1;180:122-8.
16. Hammer-Hansen S, Bandettini WP, Hsu LY, Leung SW, Shanbhag S, Mancini C, **Greve AM**, Køber L, Thune JJ, Kellman P, Arai AE. Mechanisms for overestimating acute myocardial infarct size with gadolinium-enhanced cardiovascular magnetic resonance imaging in humans: a quantitative and kinetic study†. Eur Heart J Cardiovasc Imaging. 2016 Jan;17(1):76-84.
17. Berg RM, Plovsing RR, **Greve AM**, Christiansen CB, Toksvang LN, Holstein-Rathlou NH, Møller K. Spontaneous blood pressure oscillations in mechanically ventilated patients with sepsis. Blood Press Monit. 2016 Apr;21(2):75-9.
18. Bang CN, **Greve AM**, La Cour M, Boman K, Gohlke-Bärwolf C, Ray S, Pedersen T, Rossebø A, Okin PM, Devereux RB, Wachtell K. Effect of Randomized Lipid Lowering With Simvastatin and Ezetimibe on Cataract Development (from the Simvastatin and Ezetimibe in Aortic Stenosis Study). Am J Cardiol. 2015 Dec 15;116(12):1840-4.
19. Nielsen OW, Sajadieh A, Sabbah M, **Greve AM**, Olsen MH, Boman K, Nienaber CA, Kesäniemi YA, Pedersen TR, Willenheimer R, Wachtell K. Assessing Optimal Blood Pressure in Patients With Asymptomatic Aortic Valve Stenosis: The Simvastatin Ezetimibe in Aortic Stenosis Study (SEAS). Circulation. 2016 Aug 9;134(6):455-68.
20. Hammer-Hansen S, Leung SW, Hsu LY, Wilson JR, Taylor J, **Greve AM**, Thune JJ, Køber L, Kellman P, Arai AE. Early Gadolinium Enhancement for Determination of Area at Risk: A Pre-Clinical Validation Study. JACC Cardiovasc Imaging. 2017 Feb;10(2):130-139.
21. Raphael CE, Cooper R, Parker K, Collinson J, Vassiliou V, Pennell D, de Silva R, Hsu LY, **Greve AM**, Nijjer S, Broyd C, Ali A, Keegan J, Francis D, Davies J, Hughes A, Arai AE, Frenneaux M, Stables R, Di Mario C, Prasad S. Mechanisms of Myocardial Ischaemia in Hypertrophic Cardiomyopathy: Insights from Wave Intensity Analysis and Magnetic Resonance. J Am Coll Cardiol. 2016 Oct 11;68(15):1651-1660.
22. LaRocca G, Aspelund T, **Greve AM**, Eiriksdottir G, Acharya T, Thorgeirsson G, Harris TB, Launer LJ, Gudnason V, Arai AE. Fibrosis as measured by the biomarker, tissue inhibitor metalloproteinase-1, predicts mortality in Age Gene Environment Susceptibility-Reykjavik (AGES-Reykjavik) Study. Eur Heart J. 2017 Dec 7;38(46):3423-3430.
23. Bang CN, **Greve AM**, Rossebø AB, Ray S, Egstrup K, Boman K, Nienaber C, Okin PM, Devereux RB, Wachtell K. Antihypertensive Treatment With β-Blockade in Patients With Asymptomatic Aortic Stenosis and Association With Cardiovascular Events. J Am Heart Assoc. 2017 Nov 27;6(12):e006709.
24. **Greve AM**, Bang CN, Boman K, Egstrup K, Forman JL, Kesäniemi YA, Ray S, Pedersen TR, Best P, Rajamannan NM, Wachtell K. Effect Modifications of Lipid-Lowering Therapy on Progression of Aortic Stenosis (from the Simvastatin and Ezetimibe in Aortic Stenosis [SEAS] Study). Am J Cardiol. 2018 Mar 15;121(6):739-745.

25. Hsu LY, Jacobs M, Benovoy M, Ta AD, Conn HM, Winkler S, **Greve AM**, Chen MY, Shanbhag SM, Bandettini WP, Arai AE. Diagnostic Performance of Fully Automated Pixel-Wise Quantitative Myocardial Perfusion Imaging by Cardiovascular Magnetic Resonance. JACC Cardiovasc Imaging. 2018 May;11(5):697-707.
26. Ta AD, Hsu LY, Conn HM, Winkler S, **Greve AM**, Shanbhag SM, Chen MY, Patricia Bandettini W, Arai AE. Fully quantitative pixel-wise analysis of cardiovascular magnetic resonance perfusion improves discrimination of dark rim artifact from perfusion defects associated with epicardial coronary stenosis. J Cardiovasc Magn Reson. 2018 Mar 8;20(1):16.
27. Hodges GW, Bang CN, Forman JL, Olsen MH, Boman K, Ray S, Kesäniemi YA, Eugen-Olsen J, **Greve AM**, Jeppesen JL, Wachtell K. Effect of simvastatin and ezetimibe on suPAR levels and outcomes. Atherosclerosis. 2018 May;272:129-136.
28. Park-Hansen J, Holme SJV, Irmukhamedov A, Carranza CL, **Greve AM**, Al-Farra G, Riis RGC, Nilsson B, Clausen JSR, Nørskov AS, Kruuse CR, Rostrup E, Dominguez H. Adding left atrial appendage closure to open heart surgery provides protection from ischemic brain injury six years after surgery independently of atrial fibrillation history: the LAACS randomized study. J Cardiothorac Surg. 2018 May 23;13(1):53.
29. Park-Hansen J, **Greve AM**, Clausen J, Holme SJ, Carranza CL, Irmukhamedov A, Sabah L, Lin Q, Madsen AS, Domínguez H. New-onset of postoperative atrial fibrillation is likely to recur in the absence of other triggers. Ther Clin Risk Manag. 2018 Sep 7;14:1641-1647.
30. Shanbhag SM*, **Greve AM***, Aspelund T, Schelbert EB, Cao JJ, Danielsen R, Þorgeirsson G, Sigurðsson S, Eiríksdóttir G, Harris TB, Launer LJ, Guðnason V, Arai AE. Prevalence and prognosis of ischaemic and non-ischaemic myocardial fibrosis in older adults. Eur Heart J. 2019 Feb 7;40(6):529-538. * Shared co-first authors
31. **Greve AM**, Bang CN, Boman K, Egstrup K, Kesäniemi YA, Ray S, Pedersen TR, Wachtell K. Relation of Lipid-Lowering Therapy to Need for Aortic Valve Replacement in Patients With Asymptomatic Mild to Moderate Aortic Stenosis. Am J Cardiol. 2019 Dec 1;124(11):1736-1740.
32. Kristensen AW, Berg RMG, **Greve AM**, Dahl RH, Perch M, Mortensen J. Survival in patients with scintigraphic evidence of pulmonary thromboembolism 12 weeks after double lung transplantation. J Heart Lung Transplant. 2020 Jul;39(7):719-721.
33. Kristensen AW, **Greve AM**, Dahl RH, Perch M, Mortensen J, Berg RMG. Evidence of unilateral diaphragmatic paralysis on lung scintigraphy after double lung transplantation: impact on lung function and survival. Scand J Clin Lab Invest. 2020 Oct;80(6):454-455.
34. Mohammad M, Kristensen AW, Hedsund C, **Greve AM**, Perch M, Mortensen J, Berg RMG. Prognostic impact of ventilation-perfusion defects and pulmonary diffusing capacity after single lung transplantation. Clin Physiol Funct Imaging. 2021 Mar;41(2):221-225.
35. Ramberg E, **Greve AM**, Berg RMG, Sajadieh A, Haugaard SB, Willenheimer R, Olsen MH, Wachtell K, Nielsen OW. Frequency and Impact of Hyponatremia on All-Cause Mortality in Patients With Aortic Stenosis. Am J Cardiol. 2021 Feb 15;141:93-97.
36. **Greve AM**, Christoffersen M, Frikke-Schmidt R, Nordestgaard BG, Tybjærg-Hansen A. Association of Low Plasma Transthyretin Concentration With Risk of Heart Failure in the General Population. JAMA Cardiol. 2021 Mar 1;6(3):258-266.
37. Hadziselimovic E, **Greve AM**, Sajadieh A, Olsen MH, Kesäniemi YA, Nienaber CA, Ray SG, Rossebø AB, Willenheimer R, Wachtell K, Nielsen OW. Association of Annual N-Terminal Pro-Brain Natriuretic Peptide Measurements With Clinical Events in Patients With Asymptomatic Nonsevere Aortic Stenosis – A Post Hoc Substudy of the SEAS trial. JAMA Cardiol. 2022 Feb 16:e215916. doi: 10.1001/jamacardio.2021.5916. Online ahead of print.
38. Madsen CV, Park-Hansen J, Holme SJV, Irmukhamedov A, Carranza CL, **Greve AM**, Al-Farra G, Riis RGC, Nilsson B, Clausen JSR, Nørskov AS, Kruuse C, Truelsen TC, Dominguez H.

Randomized Trial of Surgical Left Atrial Appendage Closure: Protection Against Cerebrovascular Events. Semin Thorac Cardiovasc Surg. 2022 Jun 28:S1043-0679(22)00147-2.
39. Pallisgaard J, **Greve AM**, Lock-Hansen M, Thune JJ, Fosbøl EL, Devereux RB, Okin PM, Gislason GH, Torp-Pedersen C, Bang CN. Atrial fibrillation onset before heart failure or vice versa: what is worst? A nationwide register study. Europace. 2023 Feb 16;25(2):283-290.
40. Berg RMG, Ronit A, Haase N, Møller MH, Kristiansen KT, Jonassen T, Wamberg C, Andreasen AS, Mohr T, Bestle MH, Jørgensen VL, Hammer NR, Mitchell AU, Smitt M, **Greve AM**, Nyeland ME, Jensen BW, Andreasen AH, Petersen J, Solem EJ, Winther-Jensen M, Plovsing RR. PaCO2 trajectories in mechanically ventilated patients with COVID-19: A population-based cohort study. Acta Anaesthesiol Scand. 2023 Mar 13. doi: 10.1111/aas.14233. Online ahead of print.
41. Hadziselimovic E, **Greve AM,** Sajadieh A, Olsen MH, Kesäniemi YA, Nienaber CA, Ray SG, Rossebø AB, Wachtell K, Nielsen OW. Association of high-sensitivity troponin T with outcomes in asymptomatic non-severe aortic stenosis: a post-hoc substudy of the SEAS trial. EClinicalMedicine. 2023 Feb 28;58:101875. doi: 10.1016/j.eclinm.2023.101875. eCollection 2023 Apr.
42. Madsen CL, Park-Hansen J, Irmukhamedov A, Carranza CL, Rafiq S, Lecoq RR, Camino NP, Modrau IS, Hansson EC, Jeppsson A, Hadad R, Moya-Mitjans A, **Greve AM**, Christensen R, Carstensen HG, Høst NB, Dixen U, Torp-Pedersen C, Køber L, Gögenur I, Truelsen TC, Kruuse C, Sajadieh A, Domínguez H. The Left Atrial Appendage Closure by Surgery-2 (LAACS-2) trial protocol Rationale and design of a randomized multicenter trial investigating if left atrial appendage closure prevents stroke in patients undergoing open-heart surgery irrespective of preoperative atrial fibrillation status and stroke risk. Am Heart J. 2023 Oct;264:133-142. doi: 10.1016/j.ahj.2023.06.003. Epub 2023 Jun 10.
43. **Greve AM**, Wulff AB, Bojesen SE, Nordestgaard BG. Elevated plasma triglycerides increase the risk of psoriasis: a cohort and Mendelian randomization study. Br J Dermatol. 2024 Jul 16;191(2):209-215. doi: 10.1093/bjd/ljae089.
44. Hadziselimovic E, **Greve AM**, Sajadieh A, Olsen MH, Nienaber CA, Ray SG, Rossebø AB, Wachtell K, Dominguez H, Valeur N, Carstensen HG, Nielsen OW. Development and validation of the ASGARD risk score for safe monitoring in asymptomatic nonsevere aortic stenosis. Eur J Prev Cardiol. 2024 Feb 28:zwae086. doi: 10.1093/eurjpc/zwae086. Online ahead of print.
45. Mohammad M, Hartmann JP, Carlsen J, **Greve AM**, Berg RMG, Mortensen J. Prognostic value of pulmonary diffusing capacity for carbon monoxide and ventilation-perfusion SPECT findings in pulmonary arterial hypertension. Exp Physiol. 2024 Jul;109(7):1040-1050. doi: 10.1113/EP091688. Epub 2024 May 9.
46. Madsen CL, Park-Hansen J, Hadad R, **Greve AM**, Domínguez H. The left atrial appendage closure by surgery 2 trial: statistical analysis plan for a randomized multicenter trial exploring if the closure of the left atrial appendage during open-heart surgery reduces stroke irrespective of patients' stroke risk and preoperative atrial fibrillation status. Trials. 2024 May 14;25(1):317. doi: 10.1186/s13063-024-08122-9.
47. Christoffersen M, **Greve AM**, Hornstrup LS, Frikke-Schmidt R, Nordestgaard BG, Tybjærg-Hansen A. Transthyretin Tetramer Destabilization and Increased Mortality in the General Population.
48. Nørskov A, Carlson A, **Greve AM**, Køber L, Gislason GH, Torp-Pedersen C, Bang C. The Association Between Chronic Kidney Disease and Third-degree Atrioventricular Block: A Danish Nationwide study. JACC Clin Electrophysiol. 2025 Feb;11(2):376-385. doi: 10.1016/j.jacep.2024.10.007.
49. Mohammad M, Kristensen AW, Hartmann JP, Wareham NE, Buttar SN, **Greve AM**, Lund TK, Jensen K, Schultz HHL, Perch M, Berg RMG, Mortensen J.

Survival in Patients With Evidence of Pulmonary Thromboembolism on Ventilation-Perfusion SPECT 12 Weeks After Double Lung Transplantation: A Retrospective Cohort Study. Clin Transplant. 2025 Feb;39(2):e70103. doi: 10.1111/ctr.70103.

Other Publications, Letters, Editorials and Reviews:

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Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Pernille Koll, Project & Communications Manager (vedlagt findes dog CV og publikationsliste på Professor Krister Wennerberg, OvaCures tætte partner i det pågældende projekt.**
Arbejdssted	**OvaCure**
Adresse	**Fruebjergvej 3, 2100 København**
Tlf.nr.	**22761035**
e-mail	**pernille@ovacure.org**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

The OvaCure Collection – Etablering af 40 organoidkulturer til brug i international forskning i æggestokkræft

Formål

Formålet med projektet er at udvide The OvaCure Collection – en banebrydende samling af patientafledte organoider fra æggestokkræfttumorer – fra de nuværende 18 kulturer til 40 inden juni 2026. Organoiderne stilles til rådighed for forskere i hele verden og skaber grundlag for ny, personaliseret behandling. Med støtte fra fonden vil vi dække essentielle udgifter til vækstthormoner, DNA-sekventering og transport.

Problemstilling

Æggestokkræft er den mest dødelige gynækologiske kræftform og diagnosticeres ofte for sent. På trods af sygdommens alvor og stigende forekomst, er forskningen stadig underprioriteret**.** Der mangler viden og finansiering, hvilket hæmmer udviklingen af nye og målrettede behandlinger.

Baggrund

I 2023 ansøgte vi fonden om støtte til at starte The OvaCure Collection. Vi fik desværre ikke en bevilling fra Direktør Michael Hermann Nielsens Mindelegat, men har alligevel formået at vække projektet betragteligt. Vi har nu etableret 18 unikke organoidkulturer fra æggestokkræftpatienter i samarbejde med førende forskningsinstitutioner i Danmark og Finland. Organoiderne skabes ud fra tumorvæv og repræsenterer en revolutionerende metode til præklinisk forskning og skræddersyet medicin.

Metoder

Organoidkulturer dannes ved at ekspandere tumorvæv indsamlet ved kirurgi. Vævet dyrkes i særligt vækstmedie med avancerede vækstthormoner og herefter foretages der DNA-sekventering for karakterisering. Organoiderne er 1000 gange større end det oprindelige væv og kan deles mellem forskningsgrupper, hvilket muliggør mere forskning samt samarbejde på tværs af lande og discipliner.

Tidsplan

Vi forventer at etablere 40 organoider mellem juni 2025 – 1. juni 2026

12. – 13. maj 2025 afholder vi desuden *OvaCure Innovation Challenge*, hvor The OvaCure Collection er omdrejningspunkt, og hvor Krister Wennerberg og Wojciech Senkowski deltager som facilitatorer og rådgivere for nye forskningsprojekter med organoider som udgangspunkt.

Forventede resultater og impact

Med verdens største samling af æggestokkræftorganoider, vil forskning i sygdommen blive lettere tilgængelig, hvilket vil gavne patienterne. The OvaCure Collection vil med andre ord understøtte udviklingen af præcisionsmedicin til en patientgruppe, der i dag mangler effektive behandlingsmuligheder. The OvaCure Collection vil samtidig styrke Danmarks position som international aktør inden for organoidforskning og skabe ny viden og grundlag for kommende forskningsbevillinger og kliniske afprøvninger.

Projektet adresserer samtidig FN's Verdensmål nr. 3 og 5 om sundhed og ligestilling, og bidrager til at modvirke den systematiske skævvridning i sundhedsforskningen, hvor kvindesygdomme er underrepræsenterede.

Øvrige projektdeltagere og samarbejdsrelationer

Adjuct Professor Johanna Hynninen og Professor Sakari Hietanen, Turku University Hospital. Lila Kallio, Director, Auria Biobank. Professor Sampsa Hautaniemi, Helsinki University.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

BRIC skal bruge omkring 600.000 kroner til vækstthormoner, dna-sekventering og transport til Auria Biobank i forbindelse med etableringen af de 40 organoider.

OvaCure har i år også søgt EP PerMed, der er et europæisk samarbejde for personaliseret medicin, samt Action for Women's Health, der er en amerikansk fond. Får vi en bevilling fra en af disse fonde, vil pengene blive delt mellem OvaCure, BRIC, Turku University Hospital og Helsinki University.

KRISTER WENNERBERG
Professor, Cancer Chemical Systems Medicine,
BRIC - Biotech Research & Innovation Centre, University of Copenhagen

Research statement

The overarching research goal in my group is to understand mechanisms of drug sensitivity and resistance in individual cancers with a particular focus on the subsets of cells that persist current therapies and drive cancer recurrence. We explore this using high throughput assays and patient-derived cell cultures with the aim to identify new effective stratified cancer precision medicine strategies that can be explored in clinical trials.

Current position(s)

2017- Professor, group leader, Biotech Research & Innovation Centre, University of Copenhagen

Education and training

1999 Ph.D. Uppsala University, Sweden, Medical Biochemistry, Mentor: Staffan Johansson

1995 B.Sc. Uppsala University, Sweden, Medical Sciences

Professional experience

2010-2020 FIMM-EMBL Group Leader, Institute for Molecular Medicine Finland, FIMM, University of Helsinki, Finland

2006-2009 Research Biologist, Southern Research Institute, Birmingham, AL, USA. Coordinator, Strategic Investment Program (internal drug discovery initiative) and Leader of Assay Development Group

2004-2006 Research & Development Scientist, Cytoskeleton, Inc., Denver, CO, USA

2000-2004 Postdoctoral Researcher, Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, USA. Mentors: Keith Burridge and Channing Der

Academic Activities

2022- Member of Steering group for the Chemical Biology Consortium Sweden.

2021- Member of the Innovative Therapies for Children with Cancer hematological malignancies committee

2021- Member of the executive board of the European Hematology Association Scientific Working Group on precision hematology

2019- Deputy director of the Danish Comprehensive Cancer Center national research center on Precision Medicine in Hematology

2018- Member of the Scientific Council of the Danish Comprehensive Cancer Center

Current supervisor of five PhD students, two of which will graduate this year. Three graduated PhD students 2017-2022.

More than 20 significant international invited lectures during the last 5 years, in Austria, Finland, Germany, Norway, Portugal, Switzerland, Sweden and USA.

International peer evaluation of funding and faculty tenure applications for more than 20 organizations, foundations and institutions. Peer-reviewing for more than 30 scientific journals.

Scientific and Societal Impact of Research

Published 141 peer-reviewed articles in journals such as Nature, Cancer Discovery, Nature Biotechnology, Cell, Cancer Cell. 11 850 citations, H-index 51 (Scopus, May 2023) ORCID iD: 0000-0002-1352-4220

Major Research Funding

Current research support from: Kræftens Bekæmpelse (DK) Novo Nordisk Foundation (DK), Innovationsfonden (DK), Danmarks Frie Forskningsfond (DK), European Commission (EU), National Cancer Institute (US)

Publications Krister Wennerberg.

Peer-reviewed scientific articles

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Shared senior authorships marked with ‡

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1. Bulanova D, Akimov Y, Senkowski W, Oikkonen J, Gall Mas L, Timonen S, Elmadani M, Hynninen J, Hautaniemi S, Aittokallio T, **Wennerberg K**. (2023) A synthetic lethal dependency on casein kinase 2 in response to replication-perturbing drugs in RB1-deficient ovarian and breast cancer cells. *Preprint. bioRxiv* doi: https://doi.org/10.1101/2022.11.14.516369

Invited scientific articles

1. **Wennerberg K**. (2016) Cancer cell drug response transcriptomes in 3D. *Cell Chem. Biol*. 23:1323-1324
2. Kriegbaum MC, **Wennerberg K**. (2020) Mitochondria in their prime drive venetoclax response in acute myeloid leukemia. *Cancer Cell.* 38:776-778

Awarded patents

1. Compounds and methods for altering lifespan of eukaryotic organisms (2013)

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	Marie Bredgaard Thuesen, forskningsårsstuderende og BSc.med
Arbejdssted/Institution	Institut for Klinisk Medicin, Århus Universitetshospital
Adresse	Palle Juul Jensens Blvd. 99, 8200 Århus N
Tlf.nr.	+45 31356490
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Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
Extending the applicability of the In Ovo Chicken chorioallantoic membrane (CAM) model using high dose proton radiation to study the tumor vascular response
Formål
Mit projekt har til formål at undersøge tumorbiologi og akutte stråleskader ved at gøre brug af innovativ billedteknologi og avanceret stråleterapi. Fokus vil være på behandlingseffekten af partikelstråling, en specifik type af stråleterapi, der bruges til behandling af visse former for kræft. Jeg vil anvende billedteknologi og histologiske vævssnit til at evaluere behandlingseffekten af partikelterapi vs. konventionel stråleterapi samt de akutte stråleskader, disse måtte forårsage på det raske omkringliggende væv. Projektet jeg vil beskæftige mig med, tager udgangspunkt i en vævsmodel baseret på befrugtede hønseæg. Denne model har vundet stigende popularitet inden for forskningen, da den understøtter en mere dyreetisk tilgang til forskning og ønskes i fremtiden at kunne reducere brugen af lidende mus og rotter i laboratorieforsøg.

Problemstilling

Kræft er en alvorlig sygdom med stigende forekomst og store konsekvenser for patienter og deres pårørende. Hver fjerde person estimeres at blive ramt af kræft i løbet af deres liv, hvilket øger behovet for fremskridt indenfor kræftbehandling- og forskning. Mit forskningsårsprojekt vil derfor fokusere på en ny form for strålebehandling, der har udvist lovende potentiale for fremtidig kræftbehandling, nemlig protonstråling.

Baggrund

Partikelterapi adskiller sig fra konventionel stråleterapi ved at anvende protonbestråling og er designet til at kunne levere en høj stråledosis til det kræftbærende område med samtidig skånsom stråledosis til det omkringliggende væv. Partikelterapi er derfor særligt velegnet til behandling af tumorer, der ligger tæt op ad væv eller organer, der i særlig høj grad skal beskyttes mod stråling. Den chorioallantoiske membran (CAM)-model, baserer sig på befrugtede hønseæg. CAM fungerer for kyllingefosteret som moderkagen gør hos et menneskebarn, og er således ansvarlig for at levere ilt og næringsstoffer nok til at ægget med tiden vil kunne udvikle sig til en kylling. Membranen er meget rig på blodkar, hvilket gør den velegnet til tumorvækst. Da kyllingen i sin fostertilstand endnu ikke har udviklet et velfungerende immunsystem, vil den ikke kunne afstøde tumorvævet, hvilket er endnu en vigtig fordel i forhold til andre dyremodeller.

Metoder

Udover strålebehandlingen vil jeg benytte avancerede billedteknologier, blandt andet optical coherence tomography (OCT), dynamisk PET og autoradiografi, til at vurdere strålebehandlingen. Autoradiografi gør det blandt andet muligt at generere billeder af de områder i vævet, hvor der er blevet afsat meget radioaktivitet. Min forskningsgruppe er blandt de første i verden til at anvende autoradiografi i forbindelse med CAM-modellen, hvilket giver en helt ny dimension til vores forståelse af tumorbiologi.

Tidsplan

Forskningsåret vil blive gennemført fra 1. september 2025 til 31. august 2026 ved Institut for Klinisk Medicin - Komparativ Medicinsk Laboratorium på Aarhus Universitetshospital.

Protocol	Phase 1		Phase 2		Phase 3 and 4									
Month	7	8	9	10	11	12	1	2	3	4	5	6	7	8
Participation in the research environment[a]														
Laboratory training[b]														
Preparatory pilot experiments														
Research year														
Data management														
Writing and publishing paper														

Table 1. Time schedule for the project

[a] Participating in project group meetings, performing laboratory work. [b] Laboratory training and literature research. **Phase 1 - Training:** Training in generation and handling of the CAM-model. **Phase 2 - Pilot experiments:** Working with pilot experiments to gain familiarity with all the techniques used in the model. **Phase 3 - Experiments:** Experiments adapted from the results of the pilot phase. **Phase 4 - Writing and publication:** Manuscript completion seeking publication in relevant journals.

Forventede resultater og impact

Det forventes at forskningsprojektet kan fungere som afsætningsrampe for fremtidig kræftforskning og at den benyttede vævsmodel (CAM-modellen) indenfor en overskuelig tidsramme vil kunne erstatte og eller nedsætte brugen af rotter og mus i kræftforskningsregi på Århus Universitetshospital. På kort sigt forventes det, at projektet på basalforskningsniveau kan give et større indblik i akutte stråleskader og behandlingseffekt af hhv. traditionel stråleterapi holdt op imod protonstråling af tumorvæv.

Øvrige projektdeltagere og samarbejdsrelationer

Hovedvejleder er Micheal Pedersen, Professor ved Institut for Klinisk Medicin på Århus Universitetshospital. Øvrige vejledere og samarbejdspartnere inkluderer post doc.; Morten Busk, onkologisk afdeling på Århus Universitetshospital, post doc.; Lars Thrane, Institut for Klinisk Medicin på Århus Universitetshospital, professor; Niels Bassler, fra Dansk Center for Partikel Terapi på Århus Universitetshospital samt stud.med; Emil Leth Villumsen.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Budget	Price per unit	Quantity	Sum	Seeking from your grant, in DKK
Scholarship	10.000	12	120.000	120.000
Publishing costs	10.000	1	10.000	10.000
Eggs, laboratory costs, utensils etc.	40.000	1	40.000	40.000
Analysis station and analysis software etc.	10.000	1	10.000	10.000
Total			**180.000 kr.**	**180.000 kr.**

Der er endnu ikke opnået bevilling fra anden side.

CV og publikationsliste (engelsk)

Der er endnu ikke foretaget nogle publikationer

Guldsmedegade 38, 1.tv 8000 Aarhus C
mariebredgaardthuesen@gmail.com
+45 31356490
Marie Bredgaard Thuesen

Curriculum Vitae

Marie Bredgaard Thuesen, Stud.Med.

My name is Marie Bredgaard Thuesen. I am 25 years old and curretnly studying a masters degree in medicine. I am passionate about my education and I always strive to perform at the top of my capabilities. I am a teamplayer and belive in the importance of open and encouraging communication to ensure good working enviroment and patient safety.

NOTEWORTHY UNIVERSITY ACTIVITIES

10 ETCS 6-week Clinical rotation in Tanzania at Haydom Lutheran Hospital
(2025)

Bachelor's thesis: "The role of TGF-ß-signaling in EndMT and atherosclerosis" - 12 (A)
(2022)

HIGHER EDUCATION

BSc.Med, Aarhus University, Nordre Ringgade 1, 8000 Aarhus
(2020 - 2024)

Higher General Exam in biotechnology, mathematics and physics
(2016 - 2019)

ACADEMIC AFFILIATIONS AND ACHIEVEMENTS

Extra at a simulation training program at Aarhus University Hospitals psychiatric ward
(2024 - 2025)

Instructor for surgical simulation training of hip fractures and cystoscopy at Concern HR, MidtSim
(2023 - 2025)

EXTRACURRICULAR COURSES

Courses:

- **Advanced CPR** *(2024)*
- **Advanced suturing** *(2024)*
- **Basic suturing** *(2024)*
- **Gynecology/obstetrics course** *(2024)*
- **Fire safety course** *(2022)*
- **Communication training** *(2022 and 2024)*
- **Basic CPR** *(2021)*

Projektbeskrivelse (engelsk)

Extending the applicability of the *In Ovo* Chicken chorioallantoic membrane (CAM) model using high dose proton radiation to study the tumor vascular response

Cancer is a severe disease with devastating health- and psychosocial consequences for patients and their relatives. And the incidence of cancer continues to increase, with one in four people having a lifetime risk of developing it.[1] This alarming situation underpins the need for advancements in cancer treatment technologies. My study will therefore focus on a novel form of radiotherapy that holds promising potential for future cancer treatment. For this to happen, I will use a unique model, called the CAM-model.

Background

The chorioallantoic membrane (CAM) model has seen a huge spike in popularity in recent years owing to its great advantages in economical, ethical, legal and versatile nature in a plethora of different fields[2-11]. Our group has successfully been able to establish the tissue model as a viable tumor-bearing model for oncological research. These efforts have been awarded with an in-house Reduce, Refine and Replace (3R) prize chosen from over 100 applicants, recognizing the model's huge untapped potential to be used as an alternative to traditional murine models[12]. Moving forward, I aim to refine our techniques in an effort to use patient derived xenografts (PDX) and do more experiments using other advanced techniques using the well-known tumor tissue MOC2. Aarhus University Hospital is the ideal place to utilize this model, owing to the many different and unique possibilities in radiation therapy provided particularly by the Danish Center for Particle Therapy and by the advanced research environments in both the Department of Oncology and Department of Nuclear Medicine.

The CAM model itself is derived from fertilized eggs of the domestic chicken *gallus gallus domesticus* and consists of the chorion and allantois, two extra-embryonal tissue layers that gradually fuse and provide a very well-vascularized, immunodeficient membrane capable of grafting different tumors including PDX for preclinical precision medicine research[2,13-19]. In normal development this membrane is responsible for gas exchange and calcium recruitment from the eggshell[2].

Aim

My long-term goal is to expand the use of the CAM model with various tumor types and PDX as a viable and desirable model used in preclinical oncological research at Aarhus University Hospital. I want to reduce the use of mice and heighten the scientific yield at the same time. Moreover, I aim to investigate the use of high dose proton radiation to study the tumor vascular response and acute radiation

damage. Hopefully, my study will help to enhance the quality of life and treatment of cancer patients. In time we plan to recruit one or more PhD students to realize this aim.

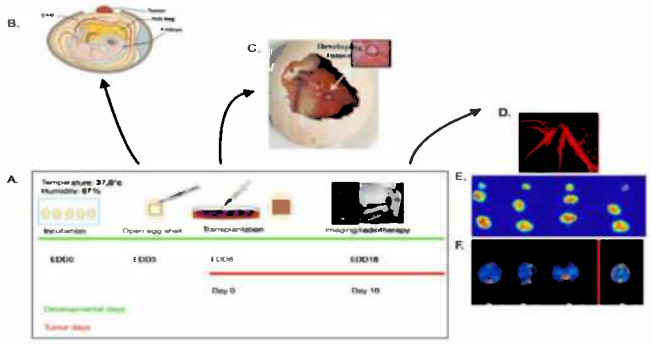

Figure 1. The chorioallantoic membrane (CAM) assay for cancer research
A) Illustration of the study design. Inspired by[20] **B)** Visualization of the anatomical structures of the chicken embryo model.[21] **C)** A tumor growth on the CAM. **D)** Optical coherence tomography (OCT) imagining of vessels in vivo. **E)** Autoradiography of a tumor to image the intra-tumoral distribution of FDG. **F)** PET scan of a tumor after administration of FDG. **D-F)** Images from in-house experiments.

I seek to develop the model and techniques already acquired further and use the experience with generation of the model obtained from international partners to establish a world first CAM model scaffold for high-dose proton radiation research in a cooperative effort between the Comparative Medicine Lab at Aarhus University, the Oncology Department and Danish Center for Particle Therapy, both at Aarhus University Hospital. The project aims to position the tumor-CAM model as a viable model to initially test acute radiation effects on vascularity using advanced *in vivo* optical coherence tomography(OCT) to evaluate differences in *in vivo* perfusion non-invasively at a micrometer resolution after different radiation regimes and homogenous vs. proton minibeam radiation therapy (pMBRT) to elucidate if effects on vascularity is why pMBRT develops fewer radiation related damages than traditional RT[22].
Using high dose proton radiation, we have so far managed to irradiate tumors grown on the CAM with the highest ever recorded doses (20 gy) while sparing the fetus with a tailored dose plan. This means our model could fill a significant hole in high dose radiotherapy on the CAM-model[23].

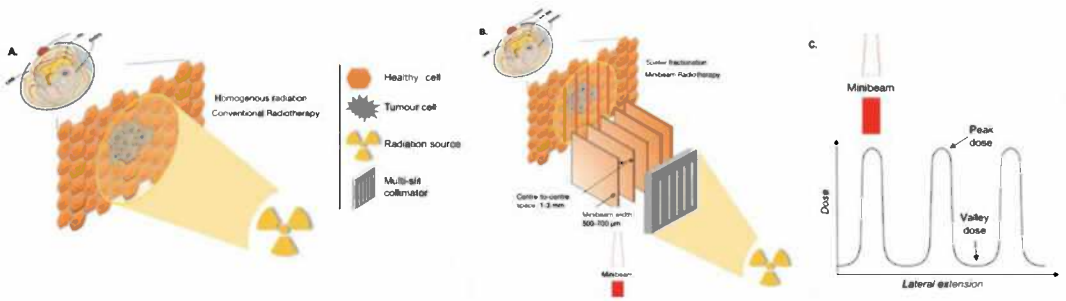

Figure 3. Homogenous radiation therapy (RT) vs proton minibeam radiation therapy (pMBRT).
A) Schematic representation of a homogenous beam of radiation and **B)** a pMBRT array, targeting a malignancy**. C)** Schematic representation of the microbeams dose distribution. Figure inspiration[24].

Note that we use pMBRT which usually has a field size of 500-700 µm and fields spaced 1 to 3 mm apart[25].

Alongside these *in vivo* bioimaging efforts, we aim to evaluate the radiation damage using both traditional histological and immunohistochemistry methods as well as advanced nuclear medicine techniques such as dynamic PET and autoradiography. Dynamic PET provides a measurement of how quickly and how well the tumor acquires tracers such as FDG or FAZA, and autoradiography provides the intra-tumoral distribution[26,27]. We are, to our knowledge, the first group in the world to have utilized the method of autoradiography in the tumor-bearing CAM model.

Time Schedule and personal contribution

The Research Year will be conducted from September 1, 2025, to August 31, 2026, at the Department of Clinical Medicine - Comparative Medicine Lab at Aarhus University with cooperative effort from the Oncology Department and Danish Center for Particle Therapy at Aarhus University Hospital. See table 1 for the detailed research year plan and timeline.

Protocol	**Phase 1**		**Phase 2**		**Phase 3 and 4**									
Month	7	8	9	10	11	12	1	2	3	4	5	6	7	8
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Materials and Methods for CAM generation

Fertilized Dekalb White eggs from a local breeder are marked, incubated at 37,8 °C and 67% humidity, and rotated regularly for the first three days. On embryonic development day (EDD) 3, the eggs are opened by creating a small hole at the blunt end of the egg, and 2 ml of albumen is removed to lower the embryo away from the shell membranes. A window is then made in the shell with a rotary tool, and the membranes are removed with tweezers to expose the fetus, which is checked for viability. Live embryos are sealed again with transparent film dressing and re-incubated. Dead embryos and unfertilized eggs are discarded according to local guidelines.

Tumor pieces are harvested from a mouse carrying a flank tumor or from cryostock. On EDD 8, the eggs are placed in a laminar flow hood, their film dressing is removed, and small areas on the CAM are scored near blood vessels. Tumor grafts are positioned onto these scored areas and the eggs are resealed and re-incubated to allow for development of the graft and fetus.

Perspectives - Ethical considerations

The Danish Animal Experiment Inspectorate does not consider experiments on unhatched eggs as animal experiments. I have, however, decided to pursue the highest standards of ethical conduct and will have continuous internal review from the Animal Welfare Committee at the Health Faculty of Aarhus University, or a similar body when available to ensure ethical standards.

Publication

The scientific results will be published in relevant journals with Marie Bredgaard Thuesen as first author and co-authorship following the Vancouver recommendations. Furthermore, we strive to present the scientific results at both national and international conferences.

Research Environment and Supervision

The project takes place at the experimental facilities at The Department of Clinical Medicine, Aarhus University; located at Aarhus University Hospital. Here, all facilities and expertise are available to handle the CAM model, including equipment to handle chicken embryos, mice tumor models, animal handling, imaging expertise, histological procedures, and data analyses. The main supervisor is Professor Michael Pedersen, Institute for Clinical Medicine – Comparative Medicine Lab, Aarhus University. The co-supervision consists of Stud. Med. Emil Leth Villumsen - Institute for Clinical Medicine – Comparative Medicine Lab, Aarhus University, post doc Morten Busk – Dept. Oncology, Experimental Clinical Oncology, Aarhus University Hospital, post doc Lars Thrane – Institute for Clinical Medicine – Comparative Medicine Lab, Aarhus University and Professor Niels Bassler – Danish Center for Particle Therapy, Aarhus University Hospital.

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Støttebrev

AARHUS
UNIVERSITET
INSTITUT FOR KLINISK MEDICIN

Comparative Medicine Lab

Michael Pedersen,
Professor

Date: 12-02-2025

Støttebrev vedr. Marie Bredgaard Thuesen

Jeg medgiver hermed mine varmeste anbefalinger af Marie Bredgaard Thuesen, medicinstuderende, Aarhus Universitet. Marie er for nyligt tilknyttet min forskningsgruppe i forbindelse med et studierelevant forskningsprojekt godkendt af Faculty of Heath, Aarhus Universitet. Marie

Maries planlagte projekt har til formål at erstatte onkologiske musemodeller med en 3R-replacement model (en tumormodel baseret på en ekstraembryonal membran i kyllingeæg). Ideen har allerede skabt opmærksomhed og er blevet tildelt Aarhus Universitets 3R pris 2025. Resultaterne fra Maries studie vil være vigtige i vores forsøg på at udvikle en helt ny form for tumor-model, hvor kræftpatienter i fremtiden vil kunne få gavn af en mere effektiv behandlingsstrategi.

Jeg betragter Marie som en flittig, energisk, imødekommende og dygtig studerende. Jeg anbefaler derfor Marie til den indsendte ansøgning.

Med venlig hilsen

Michael Pedersen

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Aarhus University Hospital
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DK-CVR-nr: 31-11-91-03

3R pris 2025 (engelsk)

AARHUS UNIVERSITY
HEALTH

The 3R Prize 2025

for Increasing Animal Welfare in Research

The Animal Welfare Body at AU Health works to strengthen that best practices for animal welfare are implemented and shared across the various research disciplines at the Department of Biomedicine and the Department of Clinical Medicine.

The Faculty of Health's 3R price is instituted to keep continued focus and awareness on animal welfare as an absolutely essential and mandatory prerequisite for keeping animals for research purposes, combining ethics, animal welfare and scientific excellence.

The Animal Welfare Body at AU Health has decided to award

Emil Leth Villumsen

The prize for best incorporating the use of the 3R principles to improve animal welfare in research at AU Health.

Congratulations!

On behalf of the Animal Welfare Committee at Health

Jakob le Fèvre Harslund
Chairman

On behalf of the Faculty of Health

Per Brønsted Hällsberg
Vice-dean for Research, Health

The principles of the 3Rs (Replacement, Reduction and Refinement) were first conveyed by Russel and Burch over 50 years ago. Today they provide the framework for performing more humane animal research to the benefit of the animals and the research itself. They are embedded in national and international legislation and regulations and additionally, at AU Health, the 3Rs are incorporated in the policies for using animals in research.

The 3R animal welfare principles seek to:

1) avoid or replace the use of animals,
2) minimize the number of animals used per experiment, and
3) minimize animal suffering and improve welfare.

Karakterblad (engelsk)

AARHUS UNIVERSITET

Aarhus University

Marie Bredgaard Thuesen
Guldsmedgade 38, 1. tv
8000 Aarhus C

AARHUS UNIVERSITET

Date 12.04.2025

It is hereby confirmed that Marie Bredgaard Thuesen, Civil Registration Number: 080200-5660, is enrolled as a student at Aarhus University.

Name of the education: **Bachelor's Degree Programme**

The student graduated on 14.01.2024.
The student has passed the following subjects.
The credits are shown in ECTS

	Marks	ECTS-scale	Credits
Bachelor's Degree Programme, Medicine	passed		180
Central Subject, Medicine	passed		180
1. semester	passed		30
Cell Biology	Pass		10
Genetics and Personalized Medicine	Pass		10
Science Studies, Health Psychology and Communication	Pass		10
2. semester	passed		30
Functional Anatomy and Histology	12	A	30
3. semester	passed		30
Molecular Principles of Cell and Organ Functions	7	C	20
Neuroscience	7	C	10
4. semester	passed		30
Epidemiology and biostatistics	10	B	10
Integration of Cell and Organ Functions	10	B	20
5. semester	passed		30
Immunology and Microbiology	10	B	15
BA Project and Elective Course	passed		15
BA Project	passed		10
BA Project: Membranes	12	A	10
Elective Course	passed		5
The Difficult Decisions	Pass		5
6. semester	passed		30
Pharmacology	10	B	10
Public Health	12	A	10
Pathology	10	B	10

AARHUS UNIVERSITET

Aarhus University

Marie Bredgaard Thuesen, Civil Registration Number: 080200-5660

Name of the education: **Master's Degree Programme in Medicine**

The student has not graduated.
The student has passed the following subjects.
The credits are shown in ECTS

	Marks	ECTS-scale	Credits
Master's Degree Programme in Medicine, Medicine			60
Central Subject, Medicine			60
2. semester	passed		30
Medicine and Surgery	4	D	20
Elective Courses	passed		10
Clinical neurophysiology	Pass		5
Psychoactive drugs in forensic medicine	Pass		5
1. semester	passed		30
Medicine and Clinical Practice 1	4	D	30

Vægtet karaktergennemsnit fra bacheloren (engelsk)

Calculation of weighted average from the bachelor:

Subject	ECTS Points	7-point scale	ECTS Scale	Weight
Cell Biology	*10*	*Passed*	*Passed*	-
Genetics and Personalized Medicine	*10*	*Passed*	*Passed*	-
Science studies, Health Psychology and Communication	*10*	*Passed*	*Passed*	-
Functional Anatomy and Histology	30	12	A	360
Molecular Principles of Cell and Organ Functions	20	7	C	140
Neuroscience	10	7	C	70
Epidemiology and biostatistics	10	10	B	100
Integration of Cell and Organ Functions	20	10	B	200
Immunology and Microbiology	15	10	B	150
BA Project and Elective Course. BA project: Membranes	10	12	A	120
The Difficult Decisions	*5*	*Passed*	*Passed*	-
Pharmacology	10	10	B	100
Public Health	10	12	A	120
Pathology	10	10	B	100
In total	**145**			**1460**

Text in "grey color" is not included in the calculations of weighted grade average

Weighted grade average:

$$\frac{Weight\ in\ total}{ECTS\ points\ in\ the\ periode} = \frac{1460}{145} = \mathbf{10,07}$$

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	Christian Wejse, PhD., professor ved Global Sundhed, Aarhus Universitet, overlæge og professor ved Infektionssygdomme, Aarhus Universitetshospital
Arbejdssted/ Institution	Institut for Klinisk Medicin - Infektionssygdomme, Aarhus Universitetshospital
Adresse	Degnebakken 3, 8210 Aarhus V
Tlf.nr.	51944519
e-mail	wejse@ph.au.dk

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

Prævalensen af tuberkulose- (TB-) infektion blandt migranter i Danmark: Et modelleringsstudium.

Formål

At estimere forekomsten af TB-infektion blandt migranter i Danmark. Formålet er at bidrage med et informationsgrundlag til fremtidige strategier for målrettet screening for TB-infektion og forebyggelse af TB-sygdom.

Problemstilling

WHO anbefaler at screene migranter fra lande med en høj incidens af TB, men alligevel har vi ikke nogen strategi for screening af migranter i Danmark. Vi mangler viden om, hvem det giver mest mening at screene.

Baggrund

TB er den infektionssygdom, som er skyld i flest dødsfald globalt. En fjerdedel af jordens befolkning er estimeret til at være inficeret uden kliniske tegn på sygdom. Uden behandling kan op til 10 % af disse infektioner udvikle sig til TB-sygdom i løbet af en persons levetid. Systematisk screening, tidlig diagnosticering og forebyggende behandling af højrisikogrupper er essentielle tiltag, som er nødvendige for at undgå fremtidige TB-sygdomstilfælde. I store dele af verden bærer migranter en større del af TB-byrden sammenlignet med den indfødte befolkning, særligt i lande med lav TB-incidens som f.eks. Danmark. Danmark udgør migranter omkring 75% af TB-notifikationerne, selvom de kun udgør 15,8% af den samlede befolkning. På trods af internationale anbefalinger udfører vi ikke systematisk screening af migrantgrupper i Danmark. Vi mangler viden om prævalensen af TB infektion blandt migranter, hvilket gør det svært at målrette eventuelle screeningsprogrammer til de grupper, der har mest brug for det.

Metoder

Prævalensen af TB blandt migranter i Danmark skal findes ved at sammenholde informationer om deres alder, indvandringstidspunkt og oprindelsesland med den infektionsrisiko, de har været udsat for i hhv. deres hjemlande og i Danmark. Dette bruges til at beregne den samlede risiko, de har været udsat for gennem tiden, dvs. den kumulerede risiko. For at beregne den kumulerede risiko, skal infektionsrisikoen i deres hjemlande og i Danmark estimeres. Da den er dynamisk over tid, genereres landespecifikke historiske tendenser over infektionsrisikoen fra 1934 og indtil nu. Gaussian process regression bruges til at estimere disse tendenser mhp. at generere estimater for landeår uden data og minimere usikkerheden af de endelige resultater. Migranternes alder antages at være den samlede

mængde tid, de har været udsat for en infektionsrisiko, og indvandringstidspunktet antages at være det tidspunkt, hvor infektionsrisikoen skifter fra risikoniveauet i deres oprindelsesland til risikoniveauet i Danmark. Demografiske data kommer fra Danmarks Statistik, og informationer om infektionsrisiko i de forskellige lande stammer fra publikationer, der afrapporterer nationale screeningsundersøgelser, og fra WHO's officielle estimater.

Tidsplan

Projektet udføres fra 1. september 2025 til 31. august.

Forventede resultater og impact

Vi forventer, at resultaterne af denne undersøgelse vil blive brug i planlægningen af offentlige sundhedstiltag, hvorfor der er potentiale for at forbedre vores håndtering af migranters helbredsproblemer. Derudover har det vist sig at være økonomisk hensigtsmæssigt at screene højrisikogrupper og tilbyde forebyggende behandling, hvorfor studiet også kan bidrage til at bibringe økonomiske besparelser på det offentlige sundhedsområde.

Øvrige projektdeltagere og samarbejdsrelationer

• Astrid Tausen, medicinstuderende, Aarhus Universitet, Aarhus, Danmark.
Universitetshospital, Aarhus, Danmark.

• Victor Næstholt Dahl, læge, PhD-studerende, Afdeling for Infektionssygdomme, Aarhus Universitetshospital, Aarhus, Danmark.

• Andreas Halgreen Eiset, læge, PhD, Institut for Biomedicin, Aarhus Universitetshospital, Aarhus, Danmark.

• Justin Denholm, Victoria State tuberculosis program, Peter Doherty Institute, Melbourne University, Australia

• Michael Søndergaard Nørbo, civilingeniør i computervidenskab, PhD-studerende med speciale i Python og machine learning, Computer Vision in Biosystems group hos Machine and Signal Processing Section, Aarhus Universitet

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Vi søger om 200.000 kr., men ethvert bidrag vil blive modtaget med største taknemmelighed. Samlet budget: 300.000 kr. Der ansøges om løn til den medicinstuderende, statistisk support, akademisk ophold ved Victoria State tuberculosis program, Peter Doherty Institute i Melbourne, open access publikationsgebyr samt en computer, som kan køre de avancerede analysemodeller. Resterende deltagere bidrager med in-kind finansiering af egen løn.

Curriculum vitae Christian Wejse

Personal data: Born 31. December 1969 in Thisted
Residence: Degnebakken 3, 8210 Aarhus V
Tel: 51944519. E-mail: wejse@ph.au.dk

Education:

20/6 - 1999	MD Aarhus University
30/5 - 2007	PhD, Faculty of Health, Aarhus University
14/8 - 2010	DTM&H (Diploma in Tropical Medicine and Hygiene), Johns Hopkins University, Baltimore, USA
1/10 - 2013	Infectious Disease Specialist

Employments:

2003-5	Field work Bandim Health Project in Guinea Bissau,
2007-2013	Specialisation, Inf.Dis Dept of Inf Dis, Aarhus/Randers
2011-22	Assoc.Prof (50%), Center for Global Health, Aarhus Univ.
2013-22	Staff specialist (50%), Dept of Inf Dis Aarhus
2019	Royal Melbourne Hospital/Doherty Institute, Melbourne Clinical observership/Research stay abroad 6 months
2022-	Consultant, Dept of Infectious Diseases, AUH.
2022-	Professor in Global Health, Aarhus University

Leave: Paternity leave 4 children born 1998, 2001, 2003 and 2007 in total 14 months, four of these after PhD (Jan-May 2008)
After PhD I have spent 5 years on clinical training for specialisation in infectious diseases with little time available for research.

Scientific qualifications/awards:
2007 – dd: Member of Scientific Steering Committee, Bandim Health Project
2008 - 2018: Chairman, Scientific Steering Committee Bandim HIV cohort in Guinea Bissau
2012 - 17: Member of IeDEA West Africa HIV cohort Executive committee
2010-22: Invited speaker at International Congress of Nutrition, INDEPTH Scientfic Conference, NSCMID, EurConfTropMedIntHealth, Eur Conf Clin Micr Inf Dis, Int Union Assoc Tub Lung Dis.
2011-22: Reviewer of PhD theses, 10 from Copenhagen and 3 from Aarhus (chairman)
2014-dd: Member of editorial board, Infection (Springer)
2016: Medicines for People award (by Universities Allied for Essential Medicines)
2018-22: Member of national medicine council for HIV
2020- : Editorial board member Journal of Migration and Health (Elsevier)
2021- : Assistant editor, PLoS Global Public Health
2021- : Academic chair for Aarhus in Circle-U Global Health Knowledge Hub.
2022- : Chairperson for ESGITM (ESCMID Study Group for Infections in Travelers and Migrants)
2023- : Chairperson for Danish Society for Migrant Health

Grants:
2003-2006: Aarhus University, PhD scholarship: *The role of vitamin D in pathogenesis and treatment of TB*. 1,4 mill.Dkr
2003-2005: Grant no.91163, Research Council for Developmental Research, *The role of vitamin D in pathogenesis and treatment of TB*. 1 mill. Dkr.
2004-2006: "*SuPARnostics - Establishing a TB Treatment Efficacy Marker*" (FP6-2003-LIFESCIHEALTH-3), 300.000 Euro as Specific Support Action for field work in Bissau.
2007-2009: Lundbeck Foundation: *The West African AIDS cohort study.*1 mill. Dkr.
2011-2016: PI for Bissau at "*IeDEA West-Africa HIV cohort collaboration*". NIH Grant #8300745, USD110,000 for the Bissau HIV cohort 2012-16

2016: Novo Nordisk Fonden: 845.000 Dkr for *"Clinical scoring tool for point-of-care diagnosis of tuberculosis - ClinPOC-TB"* ref nr NNF15OC0018034
2018: Danske Regioners Medicinpulje: 996.000 Dkr for "*Treating tomorrow's tuberculosis today"*
2021: Region Midts Sundhedsvidenskabelige Forskningsfond: 550.000 for "*The Clinical Significance of Non-Tuberculous Mycobacteria Isolation in Denmark"*. A3667
2021: Folkesundhed i Midten for "Hospitalsbaseret opfølgning af sårbare patienter i tværsektorielle screeningstilbud", 500.000 for post doc.
2022: Danish Research Council for Health: 2.87 mio Dkr for '*ENFORCE2 - Identifying the best COVID-19 vaccine technology for immune supressed individuals*. Sagsnummer: 2096-00144B
2022: Novo Nordisk Foundation: 485.000 for '*MatchPoints 2023: Global Health Challenges*'.
2023: Novo Nordisk Foundation: 5 mio kr for 'CohereMig - Coherence and co-creation in patient care coordination for migrant patients'. NNF23OC0082779
2024: Innovation Foundation: 24.5 mio kr for 'Saliva-based sOlution foR TB diagnosis (SORTS)', IFD 3146-00019B.

Leadership experience

Since 2003 leader of a team of 20 field assistants, data entry clerk and clinical staff in charge of a field trial site in Guinea-Bissau. Head of the TB research group since 2005 and a HIV research group since 2007. I have designed a wide range of projects and been principal supervisor for a very large number of MSc-, PhD-students and post docs. I have handled staff issues of the TB and HIV group on the site in Bissau and managed large research grants applied the same place such as coordination of large EU and NIH grants. Since 2013 I have been the founding director of Center for **Glo**bal **H**ealth at **A**arhus **U**niversity (GloHAU) from where I lead a large research group.

Scientific focus areas

Shortly after my PhD I built my own TB and HIV research unit at the Bandim project in Guinea Bissau where we continually identify new TB cases and include them in trials. I have also initiated an HIV cohort in the country, where we follow more than 10,000 HIV-infected. My primary focus has been to improve the clinical management of TB and HIV in low-income countries using epidemiological studies, development of clinical tools and testing of targeted interventions and new treatments. I have developed the first clinical score for TB which is today widely used as trial outcome and diagnostic tool. My current primary research focus is migrant health, which aligns with my clinical focus of running a migrants health clinic for complex patients with cross-cultural issues.

Supervision of students

Supervisor of 44 completed masterprojects and 3 ongoing projects. Supervisor for 18 completed PhD projects, currently supervisor of five enrolled PhD students, 3 of these as primary supervisor. Supervisor for four ongoing post docs mostly former PhD students. The majority have had research stays abroad, mainly in Africa.

Publications

256 in total (164 original articles (7 as first, 47 as last author), 15 case reports, 43 reviews, 3 metaanalyses, 15 editorials, 10 letters, 3 book chapters, 1 Health Technology Assessment, 2 Study Protocols).
H-index=36 (Scopus) Average IF: 5.8, median 3.5, total IF = 1306
ORCID ID: orcid.org/0000-0002-2534-2942 ResearcherID: C-8468-2014
Citations: +400 citations/year the past 5 years in total 5510 citations, herof 680 in 2023. 13 papers cited more than 100 times, primary PhD paper cited +350 times).

Publications Christian Wejse

263 in total (171 original articles (7 as first, 50 as last author), 15 case reports, 43 reviews, 3 metaanalyses, 15 editorials, 10 letters, 3 book chapters, 1 Health Technology Assessment, 2 Study Protocols).
H-index=38 (Scopus) Average IF: 5.8, median 3.5, total IF = 1330
ORCID ID: orcid.org/0000-0002-2534-2942 ResearcherID: C-8468-2014
Citations: +400 citations/year the past 5 years in total 5867 citations, herof 718 in 2024. 15 papers cited more than 100 times, primary PhD paper cited +350 times).
https://www.ncbi.nlm.nih.gov/myncbi/1XGRd8NhSI6kq/bibliography/public/

1: Christensen LS, Larsen LB, Johansen J, Andersen EA, **Wejse C**, Klug B, Hornsleth A. The fluctuating pattern of various genome types of respiratory syncytial virus in Copenhagen and some other locations in Denmark. *APMIS*. 1999 Sep;107(9):843-50. (IF=2.0)

2: **Wejse C**, Birkebaek NH, Nielsen LP, Andersen HM. Respiratory tract infections in cytomegalovirus-excreting and nonexcreting infants. *Pediatr Infect Dis J*. 2001 Mar;20(3):256-9. (IF=2.7)

3: Kronborg G, Weis N, Madsen HO, Pedersen SS, **Wejse C**, Nielsen H, Skinhoj P, Garred P. Variant mannose-binding lectin alleles are not associated with susceptibility to or outcome of invasive pneumococcal infection in randomly included patients. *J Infect Dis*. 2002 May 15;185(10):1517-20 (IF=6.0)

4. **Wejse C**, Østergaard L. Mollaret meningitis. *Ugeskr Laeger* 2004, Sep 27;166(40):3510

5. Møller HJ, Moestrup SK, Weis N, **Wejse C**, Nielsen HI, Pedersen SS, Attermann J, Nexø E, Kronborg G. Macrophage serum markers in pneumoccocal bacteremia: prediction of survival by soluble CD163. *Crit Care Med*. 2006 Oct;34(10):2561-6. (IF=6.3)

6. Roth A, Sodemann M, Gustafson P, **Wejse C**, Aaby P. Tuberculin reaction, BCG scar and lower female mortality: A prospective community study in Guinea-Bissau. *Epidemiology*. 2006 Sep;17(5):562-8. (IF=6.2)

7. **Wejse C,** Olesen R, Velez D, Bisseye C, Sodemann M, Aaby P, Rabna P, Worwui A, Chapman H, Diatta M, Adegbola RA, Hill PC, Ostergaard LJ, Williams S M, Sirugo G. DC-SIGN (CD209), Pentraxin 3 and Vitamin D Receptor gene variants associate with pulmonary tuberculosis risk in West-Africans. *Genes and Immunity* 2007 Sep;8(6):456-67 (IF=2.9)

8. **Wejse C**, Olesen R, Rabna P, Kaestel P, Gustafson P, Aaby P, Glerup H, Andersen PL Sodemann M. Serum 25-hydroxyvitamin D in a West African population of tuberculosis patients and unmatched healthy controls. *Am J Clin Nutr* 2007;86:1376–83 (IF=6.8)

9. **Wejse C**, Gustafson P, Nielsen J, Gomes VF, Aaby P, Andersen PL, Sodemann M. TBscore: Signs and symptoms from tuberculosis patients in a low-resource setting have predictive value and may be used to assess clinical course. *Scand J Infect Dis* 2008; 40:111-120 (IF=1.5)

10. Benn C, Friis H, **Wejse C**. Should micronutrient supplementation be integrated in the case management of tuberculosis? Editorial, *J Inf Dis* 2008, Vol. 197, No. 11: 1487-1489. (IF=6.0)

11. **Wejse C**. Tuberculosis and vitamin D- what is the evidence for interaction? Review. European Infectious Disease 2008 (2); 1:107-9

12. **Wejse C**, Maier C. Månedens billede: Zoster hos et barn. *UgeskrLaeger* 2008;170:3435 (IF=1.1)

13. **Wejse C**, Gomes VF, Rabna P, Gustafson P, Aaby P, Lisse I, Andersen PL, Glerup H, Sodemann M. Vitamin D as supplementary treatment for tuberculosis – a randomised double-blind placebo-controlled trial. *Am J Respir Crit Care Med*. 2009;179:843–850 (IF=13)

14. Raaby L, Bendix-Struve M, Nielsen J, **Wejse C**. Inter-observer variation of the Bandim TB-score. *Scand J Infect Dis*. 2009; 41:220-3. (IF=1.7)

15. Kristoffersen KB, Søgaard OS, **Wejse C**, Black FT, Greve T, Tarp B, Storgaard M, Sodemann M. Antibiotic treatment interruption of suspected lower respiratory tract infections based on a single procalcitonin measurement at hospital admission-a randomized trial. *Clin Microbiol Infect*. 2009 May;15(5):481-7. (IF=5.8)

16. **Wejse C**, Gomes VF, Rabna P, Aaby P, Lisse I, Andersen PL, Glerup H, Sodemann M. Improved vitamin D status despite allocation to placebo in a tuberculosis treatment trial: contamination bias? Author reply. *Am J Respir Crit Care Med*. 2009 Jul 15;180(2):189-90. (IF=13)

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Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens min-delegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Ada Colic, cheflæge**
Arbejdssted/ Institution	**Reumatologisk Afdeling, Sjællands Universitetshospital, Køge**
Adresse	**Lykkebækvej 1, 4600 Køge**
Tlf.nr.	**47 32 47 01**
e-mail	**adco@regionsjaelland.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
ARTHUR for Clinic on Demand: Anvendelse af robotassisteret ultralydsundersøgelse til akut vurdering af inflammatoriske forandringer hos patienter med reumatoid artrit (leddegigt).
Formål
Formålet med projektet er at evaluere værdien af at anvende robot-assisteret ultralyds-scanning af led ved undersøgelse af inflammationstegn hos patienter med reumatoid artrit.
Problemstilling
En af de anerkendte metoder for vurdering og monitorering af sygdomsforløbet hos patienter med reumatoid atrtit er ultralydsscanning af led – en teknik som er valideret for

detektion af inflammatoriske og destruktive forandringer hos patienter med reumatoid artrit.

Ultralydsscanning har inden for de sidste 20 år vundet anerkendelse og en stor popularitet blandt reumatologer verdenen over som en undersøgelse givende nøjagtige oplysninger om forandringer karakteristiske for reumatoid artrit, mens den er patientvenlig og kan gentages uden risici for patienter. Dens brede anvendelse er dog begrænset af behov for ultralydsapparater af høj kvalitet samt tilstedeværelse af nødvendige kompetencer hos det undersøgende sundhedspersonale.

Derfor vil vi vurdere en nyligt udviklet robot-assisteret ultralydsundersøgelse ved hjælp af ARTHUR Robot (Ropca Holdning Aps), som kan udføres uden behov for uddannet personale.

Baggrund

Reumatoid artrit er en kronisk inflammatorisk ledsygdom med stor betydning for patienters liv og for samfundet. Dens potentiale for at påføre patienter smerter, funktionsnedsættelse og invaliditet og hermed forbundne sociale og økonomiske omkostninger nødvendiggør tidlig opsporing og nøje monitorering af sygdomsforløbet med henblik på effektiv behandling af sygdommen.

Metoder

Der inkluderes 30 patienter med konstateret reumatoid artrit, som tilses i akut-funktionen Clinic on Demand i Reumatologisk Ambulatorium på Sjællands Universitetshospital i Køge. Patienternes fingerled (MCP- og PIP-led) og håndled scores klinisk for betændelsestegn (hævelse og ømhed; dorsalt/palmart/både dorsalt og palmart) og undersøges med en robot-assisteret ultralydsundersøgelse (der undersøges for synovialis-fortykkelse samt tilstedeværelse af Doppler signal i leddene). Undersøgelsens resultat bliver tilgængelig for den henvisende læge umiddelbart efter afslutning af ultralydsscanningen i en standardiseret rapportform med ultralydsbilleder og scoring af inflammation i ledsynovialis.

Patienternes alder, køn, sygdomsvarighed og behandling noteres. Desuden noteres, om oplysningerne fra undersøgelsen ved robot-assisteret ultralydsscanning har været tilstrækkelige for, at den kliniske beslutning kan tages efter undersøgelsen, eller om det har været nødvendigt at udvide undersøgelsen med ultralydsscanning udført ved en læge eller anden billeddiagnostisk modalitet (MR/knogleskintigrafi).

Resultaterne af studiet offentliggøres i abstract-form ved en af de internationale reumatologiske kongresser og efterfølgende i artikel-form i et af de peer-reviewede reumatologiske tidsskrifter.

Tidsplan
Projektperiode på 1 år med start 01.09.25 og afslutning 31.08.26 med metode (og tidsplan) som beskrevet ovenfor.
Forventede resultater og impact
Robot-assisteret ultralydsscanning forventes at kunne indgå i rutineevaluering af led hos patienter med reumatoid artrit, som behandles og følges for deres ledsygdom. Den kan prospektivt også bruges hos patienter mistænkt for betændelsestilstand i leddene for at objektivisere patienters symptomer. Undersøgelsen kræver ikke uddannet sundhedspersonale og kan udgøre en betydelig ressourcebesparelse i forhold til nuværende ultralydsled-evaluering, som kræver kompetent bemanding af ultralydsapparater. Efter undersøgelsen med robot-assisteret ultralydsscanning for patienter med reumatoid artrit vil der blive planlagt et opfølgende studie af en kohorte af patienter med andre artritformer.
Øvrige projektdeltagere og samarbejdsrelationer
Reumatologisk Afdeling på Sjællands Universitetshospital i Køge råder over ARTHUR robot forbundet med en GE LOGIQ E10 UL-enhed samt personale, som er forberedt på at vejlede patienter ved selvbetjening af robotten.
Budget (herunder evt. finansiering fra offentlige/private råd og fonde)
Projektet drives i praksis af en reumatologisk speciallæge i Reumatologisk Ambulatorium på Sjællands Universitetshospital i Køge med assistance fra en forskningssekretær til indsamling af data. Der er derfor behov for midler til VIP-løn til udførelse af studiet samt TAP-løn til dataindsamling, hvilket samlet beløber sig til 100.000 kr., som søges dækket gennem Direktør Michael Hermann Nielsens mindelegat, afd. B – sygdomsforskning.

CV

Ada Colic
Cheflæge
Uddannelsesansvarlig overlæge
Reumatologisk afdeling SUH Køge

Privat
Pileskellet 12
2000 Frederiksberg
Mobil 22207838

Cheflæge ved Reumatologisk afdeling SUH

April 2021 - nuværende

Konstituerende ledende overlæge ved Reumatologisk afdeling SUH

Nov.2020 – april 2021

Lægefaglig rådgiver til afdelingsledelse ved Reumatologisk afdeling SUH

Mar 2020 - Nov 2020

Uddannelsesansvarlig overlæge ved Reumatologisk afdeling SUH

Jan 2018 – nuværende

Uddannelsesansvarlig overlæge ved Medicin 1 Reumatologi NRS

Mar 2016 – Jan 2018

Uddannelsesansvarlig overlæge ved Medicinsk afdeling reumatologisk afsnit SVS Esbjerg

Okt 2009 – Mar 2016

Speciallægeuddannelse Overgangsblok ved Region Syd/speciallægepraksis Jannie Beier

Apr 2009 – Sept 2009

Overgangsblok ved Medicinsk afdeling M OUH

Sep 2008 – Mar 2009

Overgangsblok ved Reumatologisk afdeling C OUH

Sep 2006 – Sep 2008

Kursusstilling ved Reumatologisk afdeling C OUH

Mar 2006 – Aug 2006

Kursusstilling ved Geriatrisk afdeling G OUH

Sep 2005 – Feb 2006

Kursusstilling ved Kardiologisk afdeling B OUH

Mar 2005 – Aug 2005

Barsel

April 2004 – Mar 2005

Kursusstilling ved Reumatologisk afdeling C OUH

Sep 2003 – April 2004

1.reservelægestilling ved Reumatologisk afdeling ECS Esbjerg

Feb 2003 – Sep 2003

Introduksionsstilling ved Medicinsk afdeling ECS

Feb 2002 – Feb 2003

Introduktionsstilling ved Reumatologisk afdeling ECS

Aug 2000 – Feb 2002

Turnus ved Medicinsk afdeling ECS

Mar 1999- Aug 2000

Uddannelsesorlov + Barsel

Jun 1996 – Mar 1999

Turnus + reservelægestilling ved Ortopædkirurgisk afdeling Haderslev Sygehus

Mar 1995 – jun 1996

Reservelægevikar ved Ortopædkirurgisk afdeling Randers Sygehus

Nov 1994 – Mar 1995

Volontør for reservelæge ved Afdeling H OUH

Jun 1994 – Okt 1994

Forskningsstilling ved Institut for Social medicin Sarajevo Jugoslavien

Jun 1991 – Jun 1993

Vikar for forskningsstilling ved Institut for sygdomsforebyggelse Sarajevo

Jun 1990 – Jun 1991

Turnus ved Universitetshospital i Sarajevo

Jun 1989 – Jun 1990

Uddannelse

DPU Master i vejledning

Aug 2013 – Jun 2015

Kandidat ved Lægevidenskabelig Universitet

Aug 1983 – Mar 1989

Undervisning

Ekstern undervisningslektor ved CAMES (Copenhagen Academy for Medical Education and Simulation)

Apr 2017 – nuværende

Ekstern undervisningslektor i Reumatologi ved SDU Folkesundhedsvidenskab

Okt 2009 – Okt 2013

Underviser (reumatologi) på Fysioterapeut skole UC SYD

Aug 1999 – Aug 2003

Bestyrelsesposter

Medlem af bestyrelsen i Dansk reumatologisk selskab 2024-

Medlem af styregruppe DANIVAS (Dansk Vaskulitis database) /GCA 2021-

Medlem af styregruppe SLEDAN (Dansk lupus database) 2021 –

Medlem af Faglig råd RBGB 2021 –

Medlem af Specialeplansudvalg Dansk Reumatologisk selskab (DRS) 2020-

Medlem af NBV gruppe PsA under DRS 2022-2023

Medlem af NBV gruppe vaccinationer under DRS 2023-2024

Medlem af bestyrelsen i DSMU (Dansk selskab for medicinsk uddannelse) 2018-2021

TR SUH Køge Mar 2019 – Nov 2020

Kurser

Faglig kurser i sidste 5 år

EULAR 2023 Milano

EULAR online 2021

ACR 2019 Atlanta Nov 2019

ACR 2018 Chicago Okt 2018

ACR 2024 Washington November 2024

EULAR 2017 Madrid Jun 2017

EULAR 2023 Milano Jun 2023

Lederkurser

”Lederkommunikation der virker” i maj 2012 Middelfart

Aktiv medlem af Regionens Netværk for ledende overlæger, oversygeplejersker m.fl siden 2021 5 møder om året

Aktiv medlem af ” Det nære sundhedsvæsen” siden 2021 12 møder om året

Årsmøde i DSS regi (Dansk selskab for ledelse i Sundhedsvæsenet) 8-10 september 2021

Regionskursus Ledelse på forkant ”Ny leder- kom godt i gang” (47 timer) 23.01.2021-15.12.2021

Ledelse på forkant ”1.linje leder” (50 timer) 16.11.2021-21.06.2022

Ledelse på forkant ”Ledere af ledere” (50 timer) 28.11.2022-09.02.2023

Ledelseskommunikation - Planlæg og strukturer din kommunikation så du engagerer dine modtagere og skaber reel forandring 2022 (7+3 timer) 10.november 2022

Konflikthåndtering og ledelse- Hvordan det bliver lettere at være leder i svær situationer 2022 fra 15.02.2022 til 23.maj 2022

Stresshåndtering og ledelse – forebyg stress og skab bedre trivsel 2022 (16 timer) 07.09.2022-26.10.2022

DISPUK Narrativ coaching og vejledning startet 5.09.2022 1 års uddannelse

Ledelse af strategisk kompetenceudvikling MUS og GRUS 2023 (16 timer) 17-28.03.2023

Skab trivsel og stop stress i fællesskab 2023 06.09.2023

Arbejdspladsen sundhedsmiljø find en sund balance 16.maj 2023

Webinar Brugerinddragelse 08.11.2023

Individuel Strategisk sparring januar 2025

Ada Colic Publications list

1

Long-term Behavioral Changes During the COVID-19 Pandemic and Impact of Vaccination in Patients With Inflammatory Rheumatic Diseases.

Glintborg B, Jensen DV, Terslev L, Hendricks O, Østergaard M, Rasmussen SH, Jensen MP, Adelsten T, **Colic A**, Danebod K, Kildemand M, Loft AG, Munk HL, Pedersen JK, Østgård RD, Sørensen CM, Krogh NS, Agerbo JN, Ziegler C, Hetland ML.J Rheumatol. 2022 Oct;49(10):1163-1172. doi: 10.3899/jrheum.211280. Epub 2022 Jun 15.PMID: 35705237 **Free article.**

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Infliximab biosimilar-to-biosimilar switching in patients with inflammatory rheumatic disease: clinical outcomes in real-world patients from the DANBIO registry.

Nabi H, Hendricks O, Jensen DV, Loft AG, Pedersen JK, Just SA, Danebod K, Munk HL, Kristensen S, Manilo N, **Colic A**, Linauskas A, Thygesen PH, Christensen LB, Kalisz MH, Lomborg N, Chrysidis S, Raun JL, Andersen M, Mehnert F, Krogh NS, Hetland ML, Glintborg B.RMD Open. 2022 Nov;8(2):e002560. doi: 10.1136/rmdopen-2022-002560.PMID: 36418087 **Free PMC article.**

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Nationwide, large-scale implementation of an online system for remote entry of patient-reported outcomes in rheumatology: characteristics of users and non-users and time to first entry.

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5

Impact of the COVID-19 pandemic on treat-to-target strategies and physical consultations in >7000 patients with inflammatory arthritis.

Glintborg B, Jensen DV, Terslev L, Pfeiffer Jensen M, Hendricks O, Østergaard M, Engel S, Horskjær Rasmussen S, Adelsten T, **Colic A**, Danebod K, Kildemand M, Loft AG, Munk HL, Pedersen JK, Østgård RD, Møller Sørensen C, Krogh NS, Nørgaard Agerbo J, Ziegler C,

Hetland ML.Rheumatology (Oxford). 2021 Oct 9;60(SI):SI3-SI12. doi: 10.1093/rheumatology/keab500.PMID: 34146099 **Free PMC article.**

6

Self-protection strategies and health behaviour in patients with inflammatory rheumatic diseases during the COVID-19 pandemic: results and predictors in more than 12 000 patients with inflammatory rheumatic diseases followed in the Danish DANBIO registry.

Glintborg B, Jensen DV, Engel S, Terslev L, Pfeiffer Jensen M, Hendricks O, Ostergaard M, Horskjær Rasmussen S, Adelsten T, **Colic A**, Danebod K, Kildemand M, Loft AG, Munk HL, Pedersen JK, Østgård RD, Møller Sørensen C, Krogh NS, Agerbo J, Ziegler C, Hetland M.RMD Open. 2021 Jan;7(1):e001505. doi: 10.1136/rmdopen-2020-001505.PMID: 33402443 **Free PMC article.**

7

Absolute risk estimation of new-onset proteinuria in patients with systemic lupus erythematosus: a Danish nationwide cohort study.

Andersen M, Stockmarr A, Leffers HCB, Troldborg A, Voss A, Kristensen S, Deleuran B, Dreyer L, Johnsen L, **Colic A**, Jacobsen S.Clin Exp Rheumatol. 2023 Nov;41(11):2264-2268. doi: 10.55563/clinexprheumatol/rk2dxp. Epub 2023 Jun 28.PMID: 37382461

8

Comparative effectiveness of two adalimumab biosimilars in 1318 real-world patients with inflammatory rheumatic disease mandated to switch from originator adalimumab: nationwide observational study emulating a randomised clinical trial.

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9

Prevalence estimates of tuberculosis infection in adults in Denmark: a retrospective nationwide register-based cross-sectional study, 2010 to 2018.

Østergaard AA, Lillebaek T, Petersen I, Fløe A, Bøkan EHW, Hilberg O, Holden IK, Larsen L, **Colic A**, Wejse C, Ravn P, Nørgård BM, Bjerrum S, Johansen IS.Euro Surveill. 2024 Mar;29(12):2300590. doi: 10.2807/1560-7917.ES.2024.29.12.2300590.PMID: 38516789 **Free PMC article.**

10

Multifactorial intervention to prevent cardiovascular disease in patients with early rheumatoid arthritis: protocol for a multicentre randomised controlled trial.

Svensson AL, Christensen R, Persson F, Løgstrup BB, Giraldi A, Graugaard C, Fredberg U, Blegvad J, Thygesen T, Hansen IM, **Colic A**, Bagdat D, Ahlquist P, Jensen HS, Hørslev-Petersen K, Sheetal E, Christensen TG, Svendsen L, Emmertsen H, Ellingsen T.BMJ Open. 2016 Apr 20;6(4):e009134. doi: 10.1136/bmjopen-2015-009134.PMID: 27098820 **Free PMC article.** Clinical Trial.

11
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12
Changes in plasma IL-6, plasma VEGF and serum YKL-40 during Treatment with Etanercept and Methotrexate or Etanercept alone in Patients with Active Rheumatoid Arthritis Despite Methotrexate Therapy.
Knudsen LS, Hetland ML, Johansen JS, Skjødt H, Peters ND, **Colic A**, Grau K, Nielsen HJ, Ostergaard M.Biomark Insights. 2009 Sep 23;4:91-5. doi: 10.4137/bmi.s2300.PMID: 20029652 **Free PMC article.**

Enabling good transition processes from child to adult medical care: a study protocol.

Ravnbøl CI, Altweck L, Schmidt S, Bistrup L, Borgwardt S, Arnfred SM, Jeppesen P, von Bismarck P, Nellegaard JB, Prehn-Kristensen A, **Colic A.**Front Health Serv. 2025 Feb 27;5:1520013. doi: 10.3389/frhs.2025.1520013. eCollection 2025.PMID: 40083867 **Free PMC article.**

The DANIsh VASculitis cohort study: protocol for a national multicenter prospective study including incident and prevalent patients with giant cell arteritis and polymyalgia rheumatica.

Nielsen BD, Kristensen S, Donskov A, Terslev L, Dreyer LW, **Colic A**, Hetland ML, Højgaard P, Ellingsen T, Hauge EM, Chrysidis S, Keller KK.Front Med (Lausanne). 2024 Jul 3;11:1415076. doi: 10.3389/fmed.2024.1415076. eCollection 2024.PMID: 39026552 **Free PMC article.**

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Glintborg B, Jensen DV, Terslev L, Pfeiffer Jensen M, Hendricks O, Østergaard M, Engel S, Horskjær Rasmussen S, Adelsten T, **Colic A**, Danebod K, Kildemand M, Loft AG, Munk HL, Pedersen JK, Østgård RD, Møller Sørensen C, Krogh NS, Nørgaard Agerbo J, Ziegler C, Hetland ML.Rheumatology (Oxford). 2021 Oct 9;60(SI):SI3-SI12. doi: 10.1093/rheumatology/keab500.PMID: 34146099 **Free PMC article.**

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Svensson AL, Christensen R, Persson F, Løgstrup BB, Giraldi A, Graugaard C, Fredberg U, Blegvad J, Thygesen T, Hansen IM, **Colic A**, Bagdat D, Ahlquist P, Jensen HS, Hørslev-Petersen K, Sheetal E, Christensen TG, Svendsen L, Emmertsen H, Ellingsen T.BMJ Open. 2016 Apr 20;6(4):e009134. doi: 10.1136/bmjopen-2015-009134.PMID: 27098820 **Free PMC article.** Clinical Trial.

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Naomi Nadler Skjødt, læge, ph.d. studerende.**
Arbejdssted/ Institution	**Urologisk Afdeling, Sjællands Universitetshospital Roskilde / Center for Surgical Science(CSS), Sjællands Universitetshospital Køge**
Adresse	**Sygehusvej 10, 4000 Roskilde / Lykkebækvej 1, 4600 Køge**
Tlf.nr.	**60896072**
e-mail	**naon@regionsjaelland.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

Microbial and oncoimmunological features embedded in the tumor microenvironment in non-muscle invasive bladder cancer

Formål

Formålet med studiet er at undersøge, om ikke-muskelinvasiv blærekræft (NMIBC) har et særskilt mikrobiom samt onkoimmunologisk fænotype sammenlignet med normalt blærevæv, og om NMIBC-tilbagefald er forbundet med mikrobiel infiltration af blærevæv. Ved brug af banebrydende teknologier såsom Peptide Nucleic Acid Fluorescence in situ Hybridization (PNA-FISH) og multiplex digital spatial profiling (GeoMx, Nanostring), vil vi undersøge bakteriers indvirkning på immunssystemet lokalt i både sundt og sygt blærevæv fra patienter med NMIBC.
Vores hypotese er, at ubalance i blærens mikrobiom medfører genetiske mutationer og immunologiske reaktioner, der fører til tilbagefald af NMIBC.

Problemstilling

Op til 40 % af NMIBC-patienter oplever tilbagefald i blæren inden for fem år, som medfører, at behandling og opfølgning af disse patienter, forekommer blandt de kræftbehandlingsforløb, der er dyrest for samfundet. Derfor søges nye metoder til at følge samt forudsige hvilke patienter, som er i højere risiko for tilbagefald af deres sygdom.

Baggrund

Ca. 15% af alle kræftformer forventes at være associeret til mikrober, herunder vira, bakterier og parasitter. Et velkendt eksempel er humant papillomavirus (HPV) og livmoderhalskræft hos kvinder. Opdagelsen af denne sammenhæng førte til udviklingen af HPV-vaccinen, som har forebygget tilfælde af livmoderhalskræft verden over. I urinvejskirurgien er det velkendt, at infektion med parasitten Schistosoma haematobium fører til en højere forekomst af pladecelleblærekræft. Ny forskning har vist forskelle i urinmikrobiomet mellem raske forsøgspersoner og patienter med blærekræft. Disse undersøgelser er dog begrænset til analyse af ladt urin samt få inkluderede forsøgspersoner. Den tidligere opfattelse af urinvejene som et sterilt miljø er udfordret af nye studier, hvis resultater tyder på et separat blæremikrobiom, og dette har ført til stigende interesse for bakteriers indvirkning på sundhed og sygdom i blæren. Overfladisk blærekræft (NMIBC) rammer over 500.000 mennesker årligt på verdensplan og står for op til 75 procent af nydiagnosticerede blærekræfttilfælde. Sygdommen kan betragtes som en kronisk sygdom med hyppige tilbagefald, der kræver gentagen transurethral resektion af blæretumorer (TURB) og årelange kontrolforløb med kikkertundersøgelser. Over 1000 patienter får årligt konstateret og bliver behandlet for NMIBC i Danmark. Dette gør det til en af de dyreste kræftformer for samfundet på grund af gentagen operativ og medicinsk behandling samt kontrolomkostninger. Vi har i vores forskningsgruppe for første gang vist, at der findes bakteriel biofilm i blæren.
I dette studie, som er et delstudie under ansøgers Ph.d., vil vi undersøge, om vævsinfiltration af bakterier og dysbiose i urinvejene fører til hurtigere tilbagefald af NMIBC. Vi har planlagt et projekt, hvor vi vil undersøge onkoimmunologiske landskab, herunder identificere et muligt samspil mellem tumormikromiljøet og mikrobiomet på allerede udtaget blærevæv opbevaret i PatoBank.

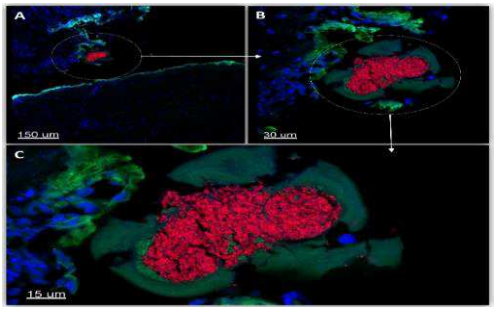

Figure 1 PNA-FISH farvning visualiserer biofilmbeklædt blæretumor. Nadler N, Kvich L, Bjarnsholt T, Jensen JB, Gogenur I, Azawi N. The discovery of bacterial biofilm in patients with muscle invasive bladder cancer. APMIS. 2021

Metoder

Dette er et eksplorativt studie, hvor vi ønsker undersøge, om NMIBC-væv er beklædt med biofilm og om denne mikrobielle og onkoimmunologiske signatur adskiller sig mellem patienter, der oplever blære-recidiv sammenlignet med recidivfrie patienter. Det estimerede antal patienter til inklusion er baseret på tidligere erfaringer fra mikrobiomstudier. Vævsprøver fra 50 patienter med en histologisk verificeret diagnose af NMIBC med og uden blærerecidiv vil blive inkluderet. 10 patienter med godartede vævsprøver vil blive inkluderet som kontrolpersoner. Vi vil analysere både tumorvæv og sundt væv fra hver enkelt person. Patienterne er tilfældigt udvalgt fra en etableret TURB-database på Urologisk Afdeling, Sjællands Universitetshospital (SUH), Roskilde.
Vævsprøver er indhentet fra Patologisk Afdeling, SUH, Roskilde. Biofilmanalyser og GeoMx analyser vil blive udført på Center for Surgical Science(CSS), SUH, Køge. Studiet er godkendt ved Videnskabsetisk Komité SJ-819. *Vævet vil blive analyseret for:* Biofilm ved hjælp af FISH-teknikker med en universel bakteriel probe.Spatiel analyse for regional og kvantitativ proteinkspression i tumorvæv ved hjælp af GeoMX™ Digital Spacial Profiler (Nanostring, USA), med fokus på biofilmadherente områder i vævet samt særligt immuncelleinfiltrede områder i vævet.

Tidsplan

Forventede resultater og impact

Resultaterne fra dette studie forventes at lægge grund for fremtidige prospektive studier, hvor der kan tages urin- og vævsprøver fra på diagnosetidspunktet og disse resultater kan indgå i et sygdomsnomogram som kan forudsige patienternes risiko for tilbagefald af sygdom.

Øvrige projektdeltagere og samarbejdsrelationer

Professor Jørgen Bjerggaard Jensen, formand for Dansk Blærecancer gruppe (DaBlaCa) og professor Ismail Gögenur, leder for CSS, som vejledere for ansøger samt Thomas Bjarnsholt, professor på Costerton Biofilm Center. Dette samarbejde demonstrerer gennemførbarheden af projektet.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Budgetposter	Projektets samlede udgiftsbehov	Tildelt finansiering fra andre fonde	Finansieret af Sjællands Uni. Hospital	Ansøges fra Direktør Michael Hermann Nielsens mindelegat	Udestående finansieringsbehov*
LØNUDGIFTER:	**829.683**	**474.000**	**120.000**	**105.447**	**127.236**
Vejledertimer til Ph.d. stud., 120 timer	120.000		120.000		
Ph.d. løn Naomi Nadler, 12 måneder	632.683	400.000	-	105.447	127.236
Patolog, 12 timer	12.000	12.000	-	-	-
Bioinformatiker, 37 timer	25.000	25.000	-	-	-
Laborant, 1 måned	40.000	37.000	-	-	-
APPARATUR:	**2.000.000**	-	**2.000.000**	-	-
GeoMx Digital Spatial Profiler, Nanostring	2.000.000		2.000.000	-	-
LABORATORIEANALYSER:	**226.032**	**226.032**	-	-	-
PNA FISH biofilm analyse, 450 pr vævsprøve, 96 prøver	43.200	43.200	-	-	-
GeoMx analyser, 10.581€ pr 12 prøver, 24 prøver	157.832	157.832	-	-	-
Skæring af vævsblokke, 250 pr vævsblok, 48 blokke	25.000	25.000	-		-
TOTALE UDGIFTER	**3.055.715**	**700.032**	**2.120.000**	**105.447**	**127.236**

Finansieringsplan for øvrig ekstern finansiering*	Ansøgt beløb	Tildelt beløb
Aase og Ejnar Danielsens Fond	196.334	150.000
Louis Hansen Fonden	619.270	150.000
MEDAC legat	25.000	25.000
Kræftens Bekæmpelse	150.000	150.000
Janssen	225.000	225.000
Christian Larsen og dommer Ellen Larsens Legat	127.236	-
Total	1.342.840	700.000

Curriculum vitae
Naomi Nadler Skjødt

Private
Kongedybs Allé 19, 1.
2300 København S
+45 60896072
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Work
Urologisk Afdeling, SUH
Sygehusvej 10, 4000 Roskilde
+45 47323500
naon@regionsjaelland.dk

EDUCATION

University of Copenhagen **2019-**	PHD STUDENT
University of Copenhagen **2012- 2016**	MASTERS DEGREE Medicine
University of Copenhagen **2015-2016**	PRE GRADUATE RESEARCH YEAR *"Do assisted reproductive technologies affect the epigenome of the newborn?"* Collection and epigenetic analysis of mesenchymal stem cells isolated from neonatal umbilical cord blood, conceived by assisted reproductive technologies.
University of Southern Denmark **2009-2012**	BACHELOR Medicine

WORK

Center for Surgical Science, ZUH **2025**	PHD STUDENT, full-time
2021-2022, 2024	MATERNITY LEAVE
Department of Urology **ZUH 2019-2025**	PHD STUDENT, part-time
Department of Urology, **ZUH 2017-2018**	RESIDENT
Øbro Lægehus **2017**	INTERN - KBU
Department of Internal Medicine **Amager Hospital** **2016-2017**	INTERN - KBU
Novo Nordisk Foundation **CBMR,** **University of Copenhagen** 2016-2017	RESEARCH ASSISTANT Collection and epigenetic analysis of sperm samples of expectant fathers as well as analysis of mesenchymal stem cells in the offspring's umbilical cord blood, this in order to elucidate the heredity of metabolic traits expressed by identical epigenetic traits.

COURSES

Faculty of Health and Medical Sciences, University of Copenhagen, 2023	Light Microscopy
Faculty of Health and Medical Sciences, University of Copenhagen, 2022	Intensive Medical Writing: Learn how to write papers that get published (online)
Sundhedsvidenskabelige Fakultet, Københavns Universitet, 2022	Statistical analysis of survival data
Section of Biostatistics, University of Copenhagen, 2021	Programming and Statistical Modelling in R
Section of Biostatistics, University of Copenhagen, 2020	Statistical analysis of survival data for biostatistical/statistical PhD Students
Section of Biostatistics, University of Copenhagen, 2020	Basic Statistics for Health Researchers, R.
Faculty of Health and Medical Sciences, University of Copenhagen, 2019	Responsible Conduct of Research

FUNDING

Det Frie Forskningsråd (FFS), Skolarstipendiat, 2015	*Do assisted reproductive technologies affect the epigenome of the newborn?"* - 172.800 kr.
Louis Hansen Fonden, 2021	*"Microbial and oncoimmunological features embedded in the tumor microenvironment in non-muscle invasive bladder cancer" - 150.000 kr.*
MEDAC legat, 2022	*"Microbial and oncoimmunological features embedded in the tumor microenvironment in non-muscle invasive bladder cancer" – 25.000 kr.*

Aase og Ejnar Danielsens fond, 2024	*"Microbial and oncoimmunological features embedded in the tumor microenvironment in non-muscle invasive bladder cancer" - 150.000 kr.*

PUBLICATIONS

Cancers	Azawi, N., Geertsen, L., **Nadler, N**., Mosholt, K. S. S., Axelsen, S. S., Christensen, J., Jensen, N. V., Fristrup, N., Dalton, S. O., Donskov, F., & Lund, L. *Cytoreductive Nephrectomy in Select Primary Metastatic Renal Cell Carcinoma Patients: A Comprehensive Nationwide Outcome Analysis*. 2024
Cancers	Guldhammer C, Vasquex J, Kristensen V, Norus T, **Nadler N**, Bjerggaard J, Azawi N:*Cystoscopy Accuracy in Detecting Bladder Tumors, 2023*
Cancers	Azawi N, Ebbestad F, **Nadler N**, Dalton S et al: *Lifestyle and Clinical Factors in a Nationwide Stage III and IV Renal Cell Carcinoma Study, 2023*
Annals of Internal Medicine	Marcucci M, Devereaux PJ, et al; **POISE-3 Trial Investigators** and Study Groups. *Hypotension-Avoidance Versus Hypertension-Avoidance Strategies in Noncardiac Surgery: An International Randomized Controlled Trial.*
Scandinavian Journal of Urology	Fode M, **Nadler N**, Lund L, Azawi N. *Feasibility of minimally invasive, same-day injection of autologous adipose-derived stem cells in the treatment of erectile dysfunction, 2023*
New England Journal of Medicine	Devereaux PJ, Marcucci M, Painter TW, Conen D, et al; ***POISE-3 Investigators***. *Tranexamic Acid in Patients Undergoing Noncardiac Surgery, 2022.*
European Urology Open Science	**Nadler, N**., Oedorf, K., Jensen, J. B. & Azawi, N.H: *Intraoperative Mitomycin C Bladder Instillation During Radical Nephroureterectomy Is Feasible and Safe, 2021.*
APMIS	**Nadler N**, Kvich L.A, Bjarnsholt T, Jensen J.B, Gögenur I, Azawi N.H: *The discovery of bacterial biofilm in patients with muscle invasive bladder cancer*, 2020.
Scandinavian Journal of Urology	Azawi N.H, Lindgren M.S, Ibsen I, Tolouee S, **Nadler N**; Dahl C, Fode M: *Novel technique: Retroperitoneal partial approach through a transperitoneal working space (Roskilde technique)*, 2019.

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Jakob Myllerup Jensen, Læge og Ph.d.-studerende**
Arbejdssted/ Institution	**Afdeling for Øre-Næse-Halskirurgi og Audiologi, Rigshospitalet**
Adresse	**Inge Lehmanns Vej 8**
Tlf.nr.	**35456464**
e-mail	**Jakob.myllerup.jensen@regionh.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
Kan man opspore tilbagefald af kræft i mundsvælget ved hjælp af blodprøver?
Formål
At undersøge om man ved hjælp af blodprøver kan opspore tilbagefald af HPV-positiv kræft i mundsvælget tidligere og mere effektiv en ved eksisterende metoder
Problemstilling
På trods af at prognosen for patienter med HPV-positiv kræft i mundsvælget er bedre end øvrige former for hoved-halskræft, oplever 10-15% af patienterne alligevel tilbagefald

efter endt behandling. Det er afgørende for patienternes videre forløb at tilbagefaldet konstateres hurtigst muligt.

Baggrund

Kræft i mundsvælget er en af de største undergrupper af hoved-hals-kræft og samtidig gruppen, hvor forekomsten stiger mest. Denne vækst skyldes især en stigning i humant papillomavirus (HPV)-positiv mundsvælgskræft, som i dag udgør op til 70% af alle tilfælde af mundsvælgskræft. Sammenlignet med de HPV-negative patienter, hvor tumoren typisk er forårsaget af tobak og alkohol, har de HPV-positive patienter en anden klinisk profil. De HPV-positive patienter er typisk yngre, har færre følgesygdomme og en bedre prognose end de HPV-negative patienter. Men trods dette vil 10-15% af de HPV-positive patienter opleve tilbagefald og 30% dør inden for 5 år efter deres diagnose.

Vores forskningsgruppe har de sidste 15 år arbejdet med patienter med HPV-positiv mundsvælgkræft, og vi har i et indledende forsøg vist, at vi er i stand til at påvise HPV-DNA i blodet hos disse patienter. Vores indledende forsøg viste også, at vi med næsten 100% følsomhed kan påvise HPV i blodet ved diagnosetidspunktet, samt at HPV-DNA koncentrationen i blodet faldt efter patienterne havde fået behandling for deres kræftsygdom. Hos patienter som helbredtes efter behandlign faldt HPV-DNA koncentrationen i blodet til nul. Hos patienter der efterfølgende fik konstateret et tilbagefald vi var i stand til at måle HPV-DNA i blodet op til 4 måneder før tilbagefaldet blev set ved en klinisk undersøgelse.
Studiet tyder derfor på, at måling af HPV-DNA i blodet kan detektere tilbagefald af kræftsygdommen tidligere end de kliniske kontroller, og åbner muligheden for tidligere behandling af disse patienter. Dette skal dog undersøges i et prospektivt studie, der skal vise om måling af HPV-DNA i blodet kan supplere det almindelige opfølgningsprogram ved at påvise HPV i blodet inden en klinisk eller radiologisk undersøgelse, for at undersøge om blodprøver kan detektere recidiv samtidig med eller før de faste kontroller i det allerede etablerede opfølgningsprogram.

Metoder

Dette studie er et prospektivt, single-arm forskningsimplementeringsprojekt, som undersøger værdien af at tilføje undersøgelsen af cirkulerende HPV-DNA (HPV-blodprøver) til det almindelige opfølgningsforløb i kontrolforløbet for patienter med HPV-positiv mundsvælgskræft. Studiet inkluderer nydiagnosticerede patienter med HPV-positiv planocellulært carcinom i mundsvælget. Patienterne får taget en blodprøve ved diagnose

inden påbegyndt behandling. Efter endt behandling følges patienterne med blodprøver ved hvert kontrolbesøg, dvs. efter 2 mdr., efter 6 mdr., og herefter ved 6. mdr. i tre år. Hvis en blodprøve efter endt behandling er positiv for HPV-DNA, kaldes patienten ind til en ekstra kontrol, og ekstra scanning, hvorved man kan be- eller afkræfte om den positive prøve skyldes et tilbagefald af den primære kræft.

Tidsplan

Studiet blev påbegyndt i april 2024, og inklusionen af patienter forløber planmæssigt. Inklusionen forventes at færdiggjort inden udløbet af 2025. efterfølgende skal alle patienterne følges med blodprøver ved deres kontrolbesøg.

Forventede resultater og impact

En tidlig konstatering af tilbagefald øger sandsynligheden for helbredelse, og patienter der behandles i et tidligere sygdomsstadie, gennemgår en mindre omfattende behandling forbundet med færre permanente bivirkninger, end patienter der diagnosticeres sent. Med dette studie håber vi at kunne hjælpe med at diagnosticere patienterne tidligere, end det i dag er muligt, og dermed øge deres overlevelse og livskvalitet. Hvis deres behandling og bivirkninger er mindre omfattende, fordi de diagnosticeres tidligere, kan vi yderligere bidrage positivt til et allerede økonomisk presset sundhedsvæsen.

Øvrige projektdeltagere og samarbejdsrelationer

Christian von Buchwald, Overlæge, Professor, Dr.med - Afdeling for Øre-Næse-Halskirurgi og Audiologi, Rigshospitalet

Christian Grønhøj, Afdelingslæge, Klinisk lektor, Dr.med **-** Afdeling for Øre-Næse-Halskirurgi og Audiologi, Rigshospitalet

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

<u>Første år</u>
Løn (inkl. pension) for Ph.d.-studerende – 600,000 DKK
Drift - blodprøvetagning og håndtering – 70.000 DKK
Drift - DNA oprensning – 105.000 kr.
Drift - ddPCR HPV analyse – 150.000 kr.

Andet år
Løn (inkl. pension) for Ph.d.-studerende – 600,000 DKK
Drift - blodprøvetagning og håndtering – 70.000 DKK
Drift - DNA oprensning – 105.000 kr.
Drift - ddPCR HPV analyse – 150.000 kr.

Tredje år
Løn (inkl. pension) for Ph.d.-studerende – 600,000 DKK
Drift - blodprøvetagning og håndtering – 70.000 DKK
Drift - DNA oprensning – 105.000 kr.
Drift - ddPCR HPV analyse – 150.000 kr.

Total: 2,775,000 DKK

Projektet er netop gået ind i sit andet år, og har inkluderet patienter planmæssigt. Der er allerede opnået bevilling fra Kræftens Bekæmpelse til løn alle tre år, og driftsudgifter til de to første år
Ved denne ansøgning søges derfor om midler til resterende driftsudgifter mhp. at færdiggøre projektet – Der søges derfor om et samlet beløb på 325.000 DKK
Et evt. bevilliget beløb mindre end dette vil naturligvis også modtaget med stor taknemmelighed.

Jakob Myllerup Jensen

Født 28. december 1994
Adresse Engvej 9, 3450 Allerød
Telefon 26 22 76 39
Mail Jakobsj10@gmail.com

Medicinsk ekspert

Uddannelse:

2022: Cand.med. fra Københavns Universitet

Udlandsophold under studiet: sep. - okt. 2020, Sisimiut, Grønland

2014: Matematisk-fysisk studentereksamen, Allerød Gymnasium

Post-graduate kurser:

2024: Introductory Course in Head and Neck Ultrasound – Rigshospitalet, Københavns Universitet, og CAMES (12 timer)

2024: Kursus i akut patient – Afdeling for Øre-Næse-Halskirurgi og Audiologi, Rigshospitalet (5 timer)

2024: Kursus i Bronkoskopi – CAMES (8 timer)

2024: Kursus i Basal hoved-hals ultralyd – CAMES og Dansk Ultralydsdiagnostisk Selskab (DUDS) (8 timer)

2024: Kursus i Almen kirurgi – CAMES (14 timer)

2024: Tubulation simulation – Afdeling for Øre-Næse-Halskirurgi og Audiologi, Rigshospitalet (2 timer)

2023: Avanceret suturkursus – Yngre Ortopædkirurger Danmark (YODA) (2,5 timer)

2022: Kursus i basal radiologi – Yngre Ortopædkirurger Danmark (YODA) (10 timer)

2022: Basalt suturkursus – Yngre Ortopædkirurger Danmark (YODA) (2,5 timer)

Konferencer og årsmøder:

2024: The Pediatric ENT symposium 2024, Danish ENT Academy (DENTA), København

2024: Årsmøde for Yngre Otologer (YO), Kolding – Tema: Kirurgi

2024: 7th Congress of European Otorhinolaryngology - Head and Neck Surgery (CEORL-HNS), Dublin

2024: Årsmøde for Dansk Selskab for Otorhinolaryngologi, Hoved- og Halskirurgi (DSOHH), Nyborg

2024: Årsmøde for Dansk Selskab for Hoved-Hals Onkologi (DSHHO), København

2022: 6th Congress of European Otorhinolaryngology - Head and Neck Surgery (CEORL-HNS), Milano

2022: Nunamed 2022 – Grønlandskmedicinsk konference, Nuuk

2021: Årsmøde for Dansk Selskab for Otorhinolaryngologi, Hoved- og Halskirurgi (DSOHH), Nyborg

2020: Head and Neck Cancer Research Symposium, MD Anderson Cancer Center, Houston, TX, USA

2020: 2020 Multidisciplinary Head and Neck Cancers Symposium (MHNCS), Phoenix, AZ, USA

2019: 7th World Congress of the International Academy of Oral Oncology (IAOO), Rom,

2019: 5th Congress of European Otorhinolaryngology - Head and Neck Surgery (CEORL-HNS), Bruxelles

2019: Årsmøde for Dansk Selskab for Otorhinolaryngologi, Hoved- og Halskirurgi (DSOHH), Nyborg

2018: EUROGIN2018 International multidisciplinary HPV congress, Lissabon

2018: 14th Congress of the European Society of Pediatric Otorhinolaryngology (ESPO), Stockholm

2018: 8th European Congress on Head and Neck Oncology (ECHNO), Rom

Professionel

Post-graduate ansættelser

Mar. 2025 – nu: Ph.d.-studerende, Afdeling for Øre-Næse-Halskirurgi og Audiologi, Rigshospitalet

Mar. 2025 – nu: Ekstern vikar, Afdeling for Øre-Næse-Halskirurgi og Audiologi, Rigshospitalet - Gennemsnit én døgnvagt per måned

Mar. 2024 – Feb. 2025: Introduktionsstilling, Afdeling for Øre-Næse-Halskirurgi og Audiologi, Rigshospitalet

Nov. 2023 – Feb. 2024: Uklassificeret stilling, Afdeling for Øre-Næse-Halskirurgi og Audiologi, Rigshospitalet

Maj 2023 – Okt. 2023: KBU - Almen praksis, Næstved lægecenter

Aug. 2022 – Jan. 2023: KBU - Ortopædkirurgisk afdeling, Slagelse Sygehus

Præ-graduate ansættelser

Feb. 2017 – Jun 2023: Forskningsassistent, Afdeling for Øre-Næse-Halskirurgi og Audiologi, Rigshospitalet, skolarstipendiat på fuld tid i perioden feb. 2018–jan 2019

Mar. 2021 – Feb. 2022: Operationsassistent, Charlottenlund Privathospital og Øre-Næse-Halsklinik

Jan. 2018 – Dec. 2018: Klinikassistent, ved speciallæge i almen praksis Amneh Hawwa

Okt. 2015 – Mar. 2017: Sygeplejevikar (SPV-vagt), FADL, København

Foreningsmedlemskaber:

2024 – nu - Dansk Ultralydsdiagnostisk Selskab (DUDS)

2022 – nu - Foreningen af Yngre Otologer (YO)

2022 – nu - Dansk Selskab for Otorhinolaryngologi, Hoved og Halskirurgi (DSOHH)

2022 – nu - Foreningen for Yngre Læger

2022 – nu - Lægeforeningen

2016 – 2022 - Studerendes Øre-Næse-Halskirurgiske Selskab (SØNHKS)

Akademiker

Min igangværende forskning har hovedsageligt fokus på

1) HPV og oropharynx cancer, herunder opsporing af recidiv af HPV-positiv oropharynx cancer ved måling af HPV-DNA i blodprøver, samt molekylær og genomisk karakterisering af aggressiv HPV-positiv oropharynx cancer
2) Pædiatriske øre-næse-halssygdomme, herunder hoved-halskræft hos børn, og medfødte kraniofaciale misdannelser

Jeg har aktuelt publiceret 39 artikler i internationale peer-reviewed tidsskrifter, heraf 10 publikationer som førsteforfatter - se vedlagte publikationsliste

H-indeks: 16 – citationer i alt: 665 - ORCID: 0000-0002-6636-6924

Jeg har desuden været medvejleder for i alt 8 medicinstuderende i forbindelse med deres bachelor- og kandidatopgaver, der er alle er blevet publiceret.

Præsentationer på konferencer og årsmøder:
2024: Mundtlig præsentation - 7th CEORL-HNS, Dublin, Irland
2024: Mundtlig præsentation – DSOHHs årsmøde 2024, Nyborg, Danmark
2024: Mundtlig præsentation – DSHHOs årsmøde 2024, København, Danmark
2022: Mundtlig præsentation - 6th CEORL-HNS, Milano, Italien
2022: Mundtlig præsentation - Nunamed 2022, Nuuk, Grønland
2021: Mundtlig præsentation – DSOHHs årsmøde 2021, Nyborg, Danmark
2020: Mundtlig præsentation – Head and Neck Cancer Research Symposium, Houston, TX, USA
2020: Poster præsentation – MHNCS 2020, Scottsdale, AZ, USA
2019: To mundtlige præsentationer - 7th World Congress of IAOO, Rom, Italien
2019: Mundtlig præsentation - 5th CEORL-HNS, Bruxelles, Belgien
2019: To mundtlige præsentationer – DSOHHs årsmøde 2019, Nyborg, Danmark
2018: Mundtlig præsentation - EUROGIN2018, Lissabon, Portugal
2018: Mundtlig præsentation - 14th Congress of ESPO, Stockholm, Sverige
2018: Poster præsentation - 8th ECHNO, Rom, Italien

Priser:
1st Place Junior Award ESPO 2018 (Bedste præsentation blandt oplægsholdere under 35 år)

Peer-reviewer for:
Ugeskrift for læger
International Journal of Cancer
BMC cancer
International Journal of Pediatric Otorhinolaryngology
Clinical Epidemiology
Journal of Oral Pathology and Medicine
World Journal of Surgical Oncology
Case Reports in Pathology

Leder/administrator

Jun. 2024 – nu: Medlem af styregruppen i DCCC ctDNA forskningscenter, som repræsentant for forskningsgruppen på Afdeling for Øre-Næse-Halskirurgi og Audiologi, Rigshospitalet

Nov. 2017 – Jun. 2022: Medlem af bestyrelsen i "Studerendes Øre-Næse-Halskirurgiske Selskab (SØNHKS)" – Formand i perioden 2019-2020 - før det, næstformand, og kasserer

Feb. 2019 – Jun. 2021: Medlem af "Advisory board: Frivillige for en røgfri fremtid" hos Kræftens Bekæmpelse – rådgivende udvalg for frivillig indsatsen i Kræftens Bekæmpelses kampagne "Røgfri Fremtid"

Feb. 2020 – Dec. 2020: Medlem af Røgfri Unge og Alkohol udvalget – Koordinerende udvalg for sundhedsformidler indsatsen i Kræftens Bekæmpelses kampagne "Røgfri Fremtid"

Kommunikator

Okt. 2024 – nu: Underviser på SØNHKS's kursus i Basal Øre-Næse-Hals undersøgelse (1 hold, 3 undervisningstimer)

Okt. 2021: Undervisningsvideo om audiometri, målrettet medicinstuderende - https://www.youtube.com/watch?v=NWcgHj4i7lc

Aug. 2020 – Jan. 2022: Tutor for nye medicinstuderende, årgang 2020/2021, Studievejledningen, Det Sundhedsvidenskabelige Fakultet, Københavns Universitet (2 hold, 30 undervisningstimer)

Sep. 2018 – Aug. 2021: Underviser i mave-tarm og hjerte-lunge anatomi på 4. semester af medicinstudiet, Biomedicinsk Institut, Københavns Universitet (12 hold, 300 undervisningstimer - derudover 20 timer som faglig støttelærer)

Sundhedsfremmer

Jun. 2021: Frivillig på "Cool Camp for kræftramte unge" hos Livskraft – én uges sommercamp for unge mellem 12 og 17 år med kræft

Aug. 2018 – Dec. 2020: Frivillig i kampagnen "Røgfri Fremtid" hos Kræftens Bekæmpelse – Information og tobaksforebyggende undervisning på folkeskoler og ungdomsuddannelser
Desuden mentor for nye sundhedsformidlere i perioden 2019-2020

Debatartikel, Politiken, 03-04-2018 - "*Giv HPV-vaccine til alle drenge*"

Publikationer

Jakob Myllerup Jensen (tidligere: Jakob Schmidt Jensen) - ORCID: 0000-0002-6636-6924

1. Myllerup Jensen J, Sjöstedt S, Carmona J, Ahlborn L, Vieira F, Nielsen, Kiss K, Grønhøj C, Von Buchwald C. **Genomic alterations in the stepwise progression from normal mucosa to metastasizing oral squamous cell carcinoma.** Front. Oncol. Published online 11-09-24

2. Justesen MM, Stampe H, Jakobsen KK, Andersen AO, Myllerup Jensen J, Nielsen KJ, Gothelf AB, Wessel I, Christensen A, Grønhøj C, von Buchwald C. **Impact of tumor subsites on survival outcomes in oral squamous cell carcinoma: A retrospective cohort study from 2000 to 2019.** Oral Oncol. 2024 Jan 10:149:106684. Doi: 10.1016/j.oraloncology.2024.206684.

3. Lauritzen BB, Sjöstedt S, Myllerup Jensen J, Kiss K, von Buchwald C. **Unusual cases of sinonasal malignancies: A letter to the editor on HPV-positive sinonasal squamous cell carcinoma.** Acta Oncol. 2023 Jun;62(6):608-613

4. Awada HN, Larsen MH, Kjær EKR, Schmidt Jensen J, Jakobsen KK, Scott S, Wessel I, Kehlet H, Grønhøj C, von Buchwald C. **Days alive and out of hospital following primary surgery for oral cavity squamous cell carcinoma.** Acta Oncol. 2022 Dec;61(12):1463-1672

5. Schnohr C, Schmidt Jensen J, Skovsen CF, Homøe, P, Niclasen B, Jensen RG. **Measurements of hearing impairment among Greenlandic school-children: association between self-reported data and clinical examinations.** BMC Pediatr. 2022 Oct 26;22(1)618

6. Christensen A, Grønhøj G, Schmidt Jensen J, Lelkaitis G, Kiss K, Juhl K, Charabi BW, Morten J, Kjær A, von Buchwald C. **Expression patterns of uPAR, TF and EGFR and their potential as targets for molecular imaging in oropharyngeal squamous cell carcinoma.** Oncol Rep, 2022 Aug;48(2):147

7. Petersen LØ, Schmidt Jensen J, Jakobsen KK, Grønhøj C, Wessel I, von Buchwald C. **Second primary cancer following primary oral squamous cell carcinoma: a population-based, retrospective study.** Acta Oncol. 2022 Aug;61(8):916-921

8. Andersen AØ, Schmidt Jensen J, Jakobsen KK, Stampe H, Nielsen KJ, Wessel I, Christensen A, Andersen E, Friborg J, Grønhøj C, von Buchwald C. **The impact of tobacco smoking on survival of patients with oral squamous cell carcinoma: a population-based retrospective study.** Acta Oncol. 2022 Apr;61(4):449-458

9. Jakobsen KK, Schmidt Jensen J, Todsen T, Kirkby, N, Lippert F, Vangsted AM, Klokker M, von Buchwald C. **Accuracy of anterior nasal swab rapid antigen tests compared with RT-PCR for massive SARS-CoV-2 screening in low prevalence population.** APMIS. 2022 Feb;130(2):95-100

10. Schmidt Jensen J, Schnohr C, Skovsen CF, Homøe P, Jensen RG. **Examination of hearing loss among school-aged children in Greenland.** Int J Pediatr Otorhinolaryngol. 2021 Oct;149:110865

11. Skovsen CF, Schmidt Jensen J, Jensen RG, Schnohr C. **Lower thriving among females with hearing impairment than males – a cross-sectional study of 185 primary and secondary students in Greenland.** International Journal of Circumpolar Health, 2021 Dec;80(1)1921995

12. Nielsen KJ, Jakobsen KK, Schmidt Jensen J, Grønhøj C, von Buchwald C. **The Effect of Prophylactic HPV Vaccines on Oral and Oropharyngeal HPV Infections – A Systematic Review.** Viruses, published online 2021 Jul 11

13. Carlander AF, Jakobsen KK, Bendtsen SK, Garset-Zamani M, Lynggaard CD, Schmidt Jensen J, Grønhøj C, von Buchwald C. **A Contemporary Systematic Review on Repartition of HPV-Positivity in Oropharyngeal Cancer Worldwide.** Viruses, published online 2021 Jul 9

14. Harwood, CD, Eriksen PRG, Clasen-Linde E, Schmidt Jensen J, Asdahl P, Rasmussen M, Hjalgrim LL, Heegaard S, von Buchwald C. **Clinicopathologic characteristics of Burkitt lymphoma of the head and neck in a non-endemic region-a Danish nationwide study**

15. Grønlund MP, Schmidt Jensen J, Hahn CH, Grønhøj C, von Buchwald C. **Risk Factors for Recurrence of Follicular Thyroid Cancer: A Systematic Review.** Thyroid, published online 2021 Jul 5

16. Jakobsen KK, Schmidt Jensen J, Todsen T, Tolsgaard MG, Kirkby N, Lippert F, Vangsted AM, Martel CJM, Klokker M, von Buchwald C. **Accuracy and cost description of rapid antigen test compared with reverse transcriptase-polymerase chain reaction for SARS-CoV-2 detection.** Danish Medical Journal, 2021 Jun 14;68(7):A03210217

17. Skovvang A, Schmidt Jensen J, Garset-Zamani M, Carlander A, Grønhøj C, von Buchwald C. **The impact of HPV genotypes on survival in HPV-positive oropharyngeal squamous cell carcinomas: a systematic review.** Acta Oto-Laryngologica, published online 2021 Jun 8;1-5

18. Lauritzen BB, Schmidt Jensen J, Grønhøj C, Wessel I, von Buchwald C. **Impact of delay in diagnosis and treatment-initiation on disease stage and survival in oral cavity cancer: a systematic review.** Acta Oncologica, published online 2021 May 27;1-8

19. Schmidt Jensen J, Grønhøj C, Garset-Zamani M, Westergaard-Nielsen M, Bjørndal K, Kiss K, Charabi B, von Buchwald C, Hjuler T. **Incidence and survival of salivary gland cancer in children and young adults in Denmark: A nation-wide study for the period 1990-2015.** International Journal of Pediatric Otorhinolaryngology, 2021 Apr;143:110637

20. Schmidt Jensen J, Jakobsen KK, Mirian C, Ghanizada M, Håkansson K, Wessel I, Grønhøj C, Rasmussen JH, von Buchwald C. **Impact of time to treatment initiation for patients with oral cavity squamous cell carcinoma: A semi-national, retrospective study.** Acta Oncologica, 2021 Apr;60(4):491-496

21. Kjær EKR, Schmidt Jensen J, Jakobsen KK, Wessel I, von Buchwald C, Grønhøj C. **The impact of Comorbidities on survival in head and neck squamous cell carcinoma patients in a nationwide setting: A nationwide case-control study spanning 35 years.** Frontiers in Oncology, 2021 Feb 17;10:617184

22. Ghanizada M, Jakobsen KK, Schmidt Jensen J, Wessel I, Tvedskov JF, Grønhøj C, von Buchwald C. **Comorbidities in oral cavity squamous cell carcinoma patients and the impact on survival: a population-based, case-control study.** Acta Oncologica, 2021 Feb;60(2):173-179

23. Schneider K, Jakobsen KK, Schmidt Jensen J, Wessel I, Christensen A, Specht L, Lelkaitis G, von Buchwald C, Grønhøj C. **Impact of p16-overexpression on overall and progression-free survival outcomes in oral cavity squamous cell carcinomas: A semi-national, population-based study.** Oral Oncol. 2020 Dec;111:105031

24. Herrlin Jensen A, Schmidt Jensen J, Kjær EK, Grønhøj C, Hjuler T. **Danish registry study showed increased incidence of paediatric haemangiomas and congenital vascular malformations from 1996 to 2015.** Acta Pædiatrica, 2020 Dec; 109(12):2727-2728

25. Lansner MW, Jakobsen KK, Schmidt Jensen J, Sandsten KE, von Buchwald, Christian. **Development of Depression in patients with Oral Cavity Cancer: A Systematic Review.** Acta Oto-Laryngologica, 2020 Oct;140(10):876-881

26. Bungum A, Schmidt Jensen J, Jakobsen KK, Christensen A, Grønhøj C, von Buchwald C. **Impact of surgical resection margins less than 5 mm in oral cavity squamous cell carcinoma: A systematic review.** Acta Oto-Laryngologica, 2020 Oct;140(10)869-875

27. Asheer J, Schmidt Jensen J, Jakobsen KK, Grønhøj G, von Buchwald C. **Rate of locoregional recurrence among patients with oropharyngeal squamous cell carcinoma with known HPV status: A systematic review.** Acta Oncologica, Acta Oncologica, 2020 Sep;59(9):1131-1136

28. Ellehauge E, Schmidt Jensen J, Grønhøj G, Hjuler T. **Trends of ankyloglossia and lingual frenotomy in hospital settings among children in Denmark.** Danish Medical Journal, 2020 May 1;67(5):A01200051

29. Schmidt Jensen J, Christensen JT, Håkansson K, Zamani M, Vogelius IR, Löfgren J, Fischer BM, Friborg J, von Buchwald C, Rasmussen JH. **High nodal FDG uptake increases risk of diastant metastasis in patients with oropharyngeal squamous cell carcinoma.** European Journal of Nuclear Medicine and Molecular Imaging, 2020 May;47(5):1039-1045

30. Stjernstrøm K, Schmidt Jensen J, Jakobsen KK, Grønhøj C, von Buchwald C. **Current status of Human Papillomavirus positivity in oropharyngeal squamous cell carcinoma in Europe: A systematic review.** Acta Oto-Laryngologica, 2019 Dec; 139(12):1112-1116

31. Schmidt Jensen J, Grønhøj C, Kjær EK, Charabi BW, von Buchwald C, Hjuler T. **Second primary cancers in pediatric head and neck cancer survivors in Denmark during 1980-2014: A nationwide study.** International Journal of Pediatric Otorhinolaryngology, 2019 Dec;127:109648

32. Jakobsen KK, Wingstrand VL, Schmidt Jensen J, Grønhøj C, Jensen DH, Karnov K, Agander TK, Specht L, von Buchwald C. **incidence and survival of hypopharyngeal cancer: A Danish nation-wide study from 1980 to 2014.** Acta Oncologica, 2019 Nov;58(11):1570-1576

33. Schmidt Jensen J, Jakobsen KK, Mirian C, Christensen JT, Schneider K, Nahavandipour A, Wingstrand, Irene Wessel VL, Tvedskov J, Frisch T, Christensen A, Specht L, Andersen E, Lelkaitis G, Grønhøj C, von Buchwald C. **The Copenhagen Oral Cavity Squamous Cell Carcinoma database: Protocol and report of establishing a comprehensive oral cavity cancer database.** Clinical Epidemiology 2019, 2019(11): 733-741

34. Grønhøj C, Schmidt Jensen J, Wagner S, Dehlendorff C, Friborg F, Andersen E, Wittekind C, Würdemann N, Sharma SJ, Gattenlöhner S, Klussmann JP, Buchwald C. **impact of Tobacco Smoking for Patients with Oropharyngeal Squamous Cell Carcinoma and known HPV and p16-status: a multicenter study.** Oncotarget 2019, 10(45):4655-4663

35. Zamani M, Grønhøj C, Schmidt Jensen J, von Buchwald C, Charabi B, Hjuler T. **Survival and Characteristics of Pediatric Salivary Gland Cancer: A Systematic Review and Meta-Analysis.** Pediatric Blood & Cancer 2018, 66(3):e27743

36. Schmidt Jensen J, Grønhøj C, Mirian C, Jensen DH, Friborg J, Hahn CH, Agander TK, Hjuler T. **Incidence and survival of thyroid cancer in children, adolescents, and young adults in Denmark: a nation-wide study from 1980 to 2014.** Thyroid 2018, 28(9): 1128-1133

37. Mirian C, Grønhøj C, Jensen DH, Jakobsen KK, Karnov K, Schmidt Jensen J, Hahn CH, Klitmøller TA, Bentzen J, Buchwald C. **Trends in thyroid cancer: retrospective analysis of incidence and survival in Denmark 1980-2014.** Cancer Epidemiology 2018, 55(8): 81-87

38. Schmidt Jensen J, Grønhøj C, Mirian C, Hjuler T. **Incidence and survival of head and neck squamous cell carcinoma in children and young adults in Denmark: a nationwide study from 1980 to 2014.** Acta Oncologica 2018, 57(10): 1410-1413

39. Schmidt Jensen J, Jensen DH, Grønhøj C, Karnov K, Nørregaard C, Agander TK, Specht L, Buchwald C. **Incidence and survival of oropharyngeal cancer in Denmark: A nation-wide, population-based study from 1980-2014.** Acta Oncologica 2018, 57(2): 269-275

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)

Navn og stilling	**Louise Adel Jensen, Ph.d. Studerende**
Arbejdssted/ Institution	**Syddansk Universitet (SDU) og Klinisk Genetisk Afdeling, Odense Universitets Hospital**
Adresse	**J. B. Winsløwsvej 4, 5000 Odense C**
Tlf.nr.	**+45 31201054**
e-mail	**Louise.Adel.Jensen@rsyd.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

Molekylær Tumorprofilering af Arvelig Brystkræft til Forbedring af Rådgivning og Behandling

Formål

Identifikation af nye molekylære undergrupper af arvelig brystkræft gennem helgenomsekventering og bioinformatisk analyse til klassificering af varianter af ukendt betydning for at reducere usikkerhed omkring patienters genetiske risiko og muliggøre bedre klinisk beslutningstagning.

Problemstilling

På trods af betydelige fremskridt indenfor genetisk analyse, er der mange genetiske varianter, som ikke kan klassificeres entydigt som sygdomsfremkaldende eller godartede, hvilket begrænser patientrådgivningen og behandlingsmulighederne.

Baggrund

Brystkræft er den mest almindelige kræftform blandt kvinder og rammer årligt omkring 4.000 danske kvinder. Af disse er ca. 10 % arvelige og ofte forbundet med mutationer i BRCA1- og BRCA2-generne. Disse mutationer kan medføre en op til 80 % livstidsrisiko for brystkræft hos bærere og bruges til at identificere personer, der kan have gavn af tæt opfølgning eller forebyggende behandling.

Imidlertid identificeres sygdomsforklarende mutationer kun i ca. 10 % af familier med mistanke om arvelig brystkræft. Dette efterlader mange patienter uden genetisk forklaring og skaber udfordringer for rådgivning og behandling. Ny forskning tyder på at arvelig brystkræft baseret på mutationssignaturer kan opdeles i flere molekylære undergrupper, herunder tumorer uden BRCA1/2-mutationer, men med BRCA-lignende karakteristika, de såkaldte BRCAX-tumorer.

Dette projekt har til formål at belyse disse undergrupper gennem molekylær profilering og klassificering af genetiske varianter af ukendt betydning. Denne indsats vil skabe ny viden, der kan forbedre behandlingsstrategier og klinisk rådgivning af patienter og deres familier.

Metoder

Projektet gennemføres i tre arbejdsfaser:

1. Prøveindsamling: Biologisk materiale indsamles fra patienter med arvelig brystkræft via samarbejde med nationale og internationale databaser og forskningskonsortier såsom ENIGMA.

2. Avanceret sekventering: Materialet analyseres ved hjælp af helgenomsekventering og long-read RNA-sekventering

3. Dataanalyse: Data behandles med avancerede bioinformatiske værktøjer, herunder HRDetect, der identificerer mutationssignaturer. Multifaktoranalyser integrerer genetiske data med kliniske oplysninger for at opdage undergrupper med fælles molekylære træk.

Tidsplan

Patientinklusion påbegyndtes 1. januar 2025. Sekventering og dataanalyse for ventes gennemført ved udgangen af 2025. Projektet forventes afsluttes juni 2026.

Forventede resultater og impact

Projektet forventes at give nye indsigter i molekylære undertyper af brystkræft, som i dag er mangelfuldt udforsket. Disse indsigter vil kunne bruges til at revurdere patienter og familier, som tidligere ikke har fået afklaring på kræftophobning i familier.

Øvrige projektdeltagere og samarbejdsrelationer

Professor Mads Thomassen (Vejleder, SDU og Odense Universitetshospital) Professor Thomas van Overeem Hansen (Medvejleder, KU og Rigshospitalet) Bioinformatiker Mark Burton (Klinisk Genom Center, Odense Universitetshospital) Det internationale forskningssamarbejde ENIGMA (Evidence-based Network for the Interpretation of Germline Mutant Alleles)
Budget (herunder evt. finansiering fra offentlige/private råd og fonde)
Fondsstøtte søgt hos Fonden: - Helgenomsekventering af 20 patienter: 60.000 kr. - Løn til ph.d.-studerende til forlængelse af projekt fra april til juni 2026: 50.000 kr.   o Samlet indeværende ansøgning: 110.000 kr. Allerede modtaget fondsstøtte til Projektet fra: Kræftens Bekæmpelse (500.000 kr.) Brødrene Hartmanns Fond til Medicinske Formål (48.000 kr.) Overlægerådets Forskningsfond – Ingemann O. Bucks Fond (48.000 kr.) Carl og Ellen Hertz's legat til dansk læge- og naturvidenskab (10.000 kr.) Fonden til Lægevidenskabens Fremme - A.P. Møllerfonden (48.000 kr.) Fru Astrid Thaysens Legat for Lægevidenskabelig Grundforskning (31.500 kr.)

Bilag: CV for Ansøger • Louise Adel Jensen

ORCID: 0009-0001-3763-7123

Januar 2023 – Nu: Ph.d.-projekt • Syddansk Universitet (SDU)

I projektet undersøger jeg forskellige metoder, herunder sekventerings- og analysemetoder, til at vurdere effekten af genetiske varianter for risikoen for udvikling af arvelig brystkræft.

Konferencer

Juni 2023: Præsentation • ENIGMA Konference, Wien

- Præsentation af projekt til sammenligning af Long-read RNA sekventeringsmetoder – Præliminære resultater og rekruttering af yderligere samarbejdspartnere.

Juni 2024: Præsentationer • ENIGMA Konference, Riga

- Præsentation af projekt til sammenligning af Long-read RNA sekventeringsmetoder – Præliminære resultater og diskussion af fremtidige perspektiver.

- Præsentation af resultater fra projekt om helgenomsekventeringsdata og sammenligning af analysesoftware. Præliminære resultater fra ShallowHRD vs. HRDetect manuskriptet.

Oktober 2024: Præsentation • DCCC Variant Fortolkningsnetværk, Sandbjerg Gods

- Præsentation af resultater fra sammenligning af software ShallowHRD og HRDetect.

November 2024: Præsentation • WYMM Tour: Oxford Nanopore, København

- Præsentation af præliminære resultater fra projekt til sammenligning af helgenomsekventeringsdata fra long-read og short-read protokoller.

November 2024: Poster-præsentation • Symposium: Genomics for Health, SDU Odense

- Poster over ENIGMA-projektet til sammenligning af Long-read metoder.

November 2024: Præsentation • Åben Forskerdag, Middelfart

- Præsentation af resultater fra artiklen *Validating ShallowHRD for Clinical Use: Correlation with HRDetect in familial Breast Tumors*, som er under review.

Vejledning

Forår 2024: Individuelt Studieprojekt, 15 ECTS, SDU • Sofie Sjølund Christensen
Titel: ”Splicing effect of *BRCA1* and *BRCA2* mutations in patient samples by comparison of short- and long-read RNA sequencing data”. Karakter: 10.

Forår 2025: Individuelt Studieprojekt, 15 ECTS, SDU • Matilde Skovbjerg Slot
Titel: ”Comparison of long-read and short-read sequencing of breast cancer patients to verify mutational signatures”. Forventes afsluttet d. 30. juni 2025.

Modtagne Fonde

- 2023: Carl og Ellen Hertz's legat til dansk læge- og naturvidenskab (10.000 kr.)
- 2023: Brødrene Hartmanns Fond – Medicinske Formål (48.000 kr.)
- 2024: Overlægerådets Forskningsfond - Ingemann O. Bucks fond (48.000 kr.)
- 2025: Fonden til Lægevidenskabens Fremme ved A.P. Møller Fonden (48.000 kr.)
- 2025: Fru Astrid Thaysens Legat for Lægevidenskabelig Grundforskning (31.500 kr.)

Internationalt Samarbejde • ENIGMA Konsortiet

Jeg er et aktivt medlem af ENIGMA konsortiet. Her samarbejder vi om forskning til klassifikation af genetiske varianter i brystkræft. Jeg arbejder i øjeblikket på et projekt, som undersøger forskellige long-read RNA-sekventerings protokollers evne til at detektere splejsningsevents i BRCA-generne.

Tidligere Uddannelse og Ansættelser

2017-2022: *BSc. og Cand. Scient i Biomedicine* • SDU

I min afhandling undersøgte jeg effekten af en mutation i et Parkinson's relateret gen i hjerneceller.

Valgfrie kurser: Epidemiologi, Sekventeringsteknikker, Etik, Mundtlig præsentation og GMP.

Datoer for afslutning: BSc. 30. juni 2020 og Master d. 30. juni 2022.

Efterår 2022: Videnskabelig Assistant • Odense Universitetshospital

Introduktion til analyse og fortolkning af genetiske data fra genom- og RNA-sekventering.

Efterår 2022: *Studiegruppevejleder* • SDU

Som vejleder introducerede jeg nye SDU-studerende til universitetet og assisterede med at forbedre gruppearbejder, f.eks. gene konflikthåndtering og feedback på opgaver.

2020-2022: *Bestyrelsesmedlem* • ABF Blommehaven

Som bestyrelsesmedlem i andelsboligforeningen har jeg opnået evner I planlægning, kommunikation og lederskab.

Bilag: Publikationsliste

- Publiceret: *Non-BRCA1/BRCA2 high-risk familial breast cancers are not associated with a high prevalence of BRCAness*. Lars v. B. Andersen, .., **Louise A. Jensen**, .., Mads Thomassen. Breast Cancer Research. 2023.
- Under Review ved Scientific Reports: *Validating ShallowHRD for Clinical Use: Correlation with HRDetect in familial Breast Tumors*. **Louise A. Jensen**, .., Mads Thomassen. 2025.
- Under udvikling: *Comparison of Long-Read RNA Sequencing Protocols for Comprehensive Splicing Analysis of the BRCA Genes – An ENIGMA study*. **Louise A. Jensen**, .., Mads Thomassen. 2025.

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- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	Tanja Fromberg Gorlen, afdelingslæge og klinisk assistent, ph.d.-studerende
Arbejdssted/ Institution	Copenhagen Centre for Arthritis Research (COPECARE) Afdeling for Rygkirurgi, Led- og Bindevævssygdomme HovedOrtoCenteret, Rigshospitalet, Glostrup
Adresse	Valdemar Hansens vej 17, 2600 Glostrup
Tlf.nr.	26243902
e-mail	Tanja.fromberg.gorlen@regionh.dk

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

Prognose og risiko for kræft hos patienter udredt for kæmpecellearteritis.

Formål

Igennem 2 delprojekter at beskrive sygdomsforløbene for patienter med kæmpecellearteritis (KCA) udredt via fast-track klinikken (FTK), bestemme karakteristika som er prædiktive for patienternes prognose og udforske sammenhængen mellem KCA og kræft. Specifikke formål for de to delprojekter, beskrives i metodeafsnittet.

Delprojekt 1

Titel: Behandlingsvarighed og prædiktorer for behandlingsprognosen hos patienter med KCA: en retrospektiv vurdering af patienter fra en fast-track klinik.

Formål: For kohorten af patienter diagnosticeret med KCA via FTK på Rigshospitalet, Glostrup i projektperioden, at bestemme: 1) Varighed af Prednisolon behandlingen, 2)

Andelen af patienter som stadig er i behandling med Prednisolon efter 1,2 og 3 år, og 3) Baseline patientkarakteristika som er prædiktive for varighed af Prednisolonbehandlingen.

Delprojekt 2

Titel: KCA og kræft: en retrospektiv undersøgelse af patienter fra en fast-track klinik.

Formål: For alle patienter undersøgt i FTK i projektperioden: 1) At bestemme hvor mange som blev diagnosticeret med kræft i relation til udredningsprocessen i FTK, 2) At bestemme hvor mange patienter som blev diagnosticeret med kræft i løbet af den efterfølgende opfølgning (2-5 år), og 3) At sammenligne incidensen af kræft-diagnoser imellem patienter med og uden samtidig KCA, både for kræft-diagnoser stillet ifm. den initiale udredning og for kræft-diagnoser stillet senere i opfølgningsforløbet.

Problemstilling

KCA er en alvorlig tilstand som kræver hurtig behandling, men hvor behandlingen med Prednisolon samtidig medfører betydelige bivirkninger. Diagnostik og behandling er udfordrende pga. den store variation i den kliniske præsentation og sygdomsvarighed. *Der er et stort behov for at få afklaret prognostiske faktorer for KCA,* således at man fremadrettet har mulighed for at lave mere individualiserede behandlings- og opfølgningsplaner for disse patienter.

Der mangler konkret viden til afklaring af, *om der er indikation for systematisk at screene for kræft hos patienter med nylig diagnosticeret KCA, og om der er en øget risiko for kræft hos patienter med KCA senere i sygdomsforløbet*, og deraf behov for øget opmærksomhed på evt. tegn på kræft i denne patientgruppe.

Baggrund

Kæmpecellearterit (KCA) er en alvorlig og kompleks gigtsygdom i form af vaskulit i store og mellemstore arterier (1). Det er den hyppigste systemiske vaskulitsygdom i Danmark, og kan potentielt have alvorlige følger, så som blindhed, blodpropper i hjernen og aortaaneurisme (2,3). Diagnosen kan være svær at stille, ikke mindst fordi symptombilledet undertiden er diffust med f.eks. vægttab og feber (4), og kan derfor og kan ligne andre tilstande, herunder kræft. Diagnosen bliver derfor ofte forsinket, trods mange forbedringer af den diagnostiske indsats (5).

KCA er i litteraturen blevet koblet til en øget risiko for kræft, men evidensen ikke er entydig (6–10), og der er ingen anbefalinger om egentlig screening for kræft i kliniske retningslinjer for KCA (11,12).

KCA behandles med højdosis Prednisolon med langsom aftrapning, ofte over flere år. Behandlingsbehovet er dog stærkt varierende. Nogen patienter kan trappes ud i løbet af 1-1,5 år, mens andre har behov for behandling igennem mange år (13,14), hvilket øger risikoen for langtidsbivirkninger, herunder bl.a. knogleskørhed og sukkersyge (15,16).

Diagnosen KCA kan stilles ved enten en biopsi af a. temporalis eller billeddiagnostiske metoder, primært ultralydsskanning og FDG-PET/CT (17). For at undgå komplikationer, herunder permanent synstab, er hurtig diagnose og behandling vigtig. Derfor er der i mange lande etableret såkaldte KCA fast-track klinikker (FTK), hvor patienter mistænkt for KCA undersøges med ultralydsskanning, ofte indenfor 48 timer fra henvisning. Studier tyder på at fast-track tilgangen reducerer forsinkelsen af diagnosen, risikoen for synskomplikationer og indlæggelsesbehovet (18,19), men det er usikkert om den hurtige diagnose og

behandling også kan have en betydning for langtidsprognosen, herunder varighed af Prednisolonbehandlingen.

Metoder

Design: Retrospektiv kohorteundersøgelse
Klinisk setting og deltagere: 01.09.18 åbnede KCA FTK på Afdeling for Rygkirurgi, Led- og Bindevævssygdomme, Rigshospitalet, Glostrup (RLB-Glostrup). I FTK ses henviste patienter indenfor få dage fra henvisning. Der laves ultralydsscanning af blodårerne, og efterfølgende vurderes pba. en samlet gennemgang af sygehistorie, objektive fund og ultralyd, om diagnosen kan stilles eller ej, eller om der er behov for yderligere undersøgelser. Fra 01.09.18 – 31.12.23 har næsten 700 patienter været undersøgt i FTK for mulig KCA på RLB-Glostrup, hvoraf ca. 40% er diagnosticeret med KCA (tidligere opgørelse fra det 1. år).
Fremgangsmåde: Der laves ekstensiv journalgennemgang for samtlige patienter som har været set i FTK på RLB-Glostrup i ovennævnte periode. Patient-kohorten følges fra henvisningstidspunktet til studiets slutdato eller patientens død, og data vedr. udrednings- og sygdomsforløbet registreres.
Statistik:
Delprojekt 1: Deskriptiv statistik anvendes til at beskrive demografiske data, kliniske fund, biokemiske markører og billeddiagnostik. Kaplan-Meier-metoden anvendes til at estimere overlevelseskurver mhp. at vurdere varigheden af Prednisolonbehandlingen.
For at vurdere baseline-variabler som er prædiktive for behandlingsprognosen, anvendes Cox-regression og logistisk regression til hhv. tidsafhængige og kategoriske outcomes.
Delprojekt 2: Deskriptiv statistik vil blive anvendt til at beskrive demografiske data, kliniske fund, biokemiske markører og billeddiagnostik. Afhængigt af datatyper og antagelser vil forskelle mellem subgrupper af patienter (med og uden KCA/med og uden cancer) blive testet ved hjælp af Welch's uparrede t-test, Mann-Whitney U-test eller Fisher's eksakte test.
Etik: Forskningsprojektet er af den videnskabsetiske komite i Region Hovedstaden vurderet ikke at være anmeldelsespligtig til de videnskabsetiske komiteer (Journal-nr.: F-24002418). Tilladelse til projekter i stedet indhentet fra Team for Journaldata, Region Hovedstaden (Journal-nr.: R-23073785).

Tidsplan

Projektperiode: 01.04.2025 – 31.03.2026
Relevante godkendelser er indhentet og database er oprettet.
Indtastning af data: 6 måneder
Dataanalyse og udarbejdelse af manuskripter: 4-5 måneder.

Forventede resultater og impact

Der er forventning om at der i det skitserede materiale vil være data på real-world patientforløb for ca, 280 patienter med KCA og en kontrolgruppe på ca. 420. Dette er et stort materiale i KCA-sammenhæng, og således stort potentiale for at ekstrahere viden om udrednings- og behandlingsforløbene samt eventuelle prognostiske markører.
De planlagte delprojekter forventes konkret at kunne bidrage med:

1) Viden om forekomsten af samtidig kræft hos patienter diagnosticeret med KCA fra diagnosetidspunktet og op til 5 år efterfølgende.
2) Real-world data på behandlingsvarighed hos patienter med KCA, der følger de nyeste strategier for udredning og behandling.
3) Viden om kliniske, biokemiske og billeddiagnostiske markører af betydning for prognosen, som kan bidrage til mere patientcentrererede og individualiserede behandlingsplaner i fremtiden.

Samlet set finder vi derfor at dette projekt har stort potentiale til at bidrage med ny viden som kan implementeres direkte i den kliniske hverdag mhp. at skabe de mest hensigtsmæssige udrednings- og behandlingsplaner for patienter med KCA.

Øvrige projektdeltagere og samarbejdsrelationer

Vejleder: Lene Terslev[1], overlæge, professor, MD, ph.d

Øvrige samarbejdspartnere:
Mikkel Østergaard[1], overlæge, professor, MD, ph.d., dr.med.
Uffe Døhn[1], overlæge, MD, ph.d.
Marie Celeste Heymonet[1], afdelingslæge, MD
[1]Copenhagen Centre for Arthritis Research (COPECARE),Afdeling for Rygkirurgi, Led- og Bindevævssygdomme, HovedOrtoCenteret, Rigshospitalet, Glostrup

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

	Udgift (DKK)	Forklaring
løn Tanja Gorlen	738.761	Løn, klinisk assistent (speciallæge) inkl. pension, 12 måneder.
TAP løn	225.000	TAP-løn til indtastning af data og statistisk assistance
Samlet budget	963.761	
Bevillinger modtaget	325.000	Modtaget fra Gigtforeningen og Beckett-fonden
Dækkes af arbejdsgiver	184. 690	
Søges her	**200.000**	
Søges anden fond	254.071	

Vedlagte bilag nedenfor:

Bilag 1: Curicullum Vitae for Tanja Fromberg Gorlen

Personlig data:

Navn: Tanja Fromberg Gorlen
Født: 9. Januar 1984, Oslo, Norge.
Sprog: Flydende dansk, norsk og engelsk.

Uddannelse

2021	Speciallæge i Intern Medicin: reumatologi.
2012	Cand.med., Københavns Universitet.

Ansættelser

Mar 2023 –	Klinisk assistent, Copenhagen Center for Arthritis Research, COPECARE, Afdeling for Rygkirurgi, Led- og Bindevævssygdomme, Rigshospitalet, Glostrup.
Nov 2021 – feb 2023	Graviditet og barsel.
Sep 2021 – okt 2021	Klinisk assistent, Copenhagen Center for Arthritis Research, COPECARE, Afdeling for Rygkirurgi, Led- og Bindevævssygdomme, Rigshospitalet, Glostrup.
Sep 2015 – aug 2021	Hoveduddannelse i Intern Medicin: reumatologi. (inklusiv 1 års barsel)
Maj 2015 – aug 2015	Reservelæge, uklassificeret, Reumatologisk afd., Gentofte Hospital
Apr 2014 – mar 2015	Introduktionsstilling i Intern Medicin: Reumatologi og kardiologi, Frederiksberg Hospital
Okt 2013 – mar 2014:	Introduktionsstilling i Almen Medicin hos Susanne Rygner, Hvalsø.
Sep 2013:	Vikariat, Ortopædkirurgisk afd., Hillerød Hospital.
Aug 2012 – aug 2013:	Klinisk basisuddannelse (ortopædkirurgi og almen medicin).

Kurser

Dec 2023	Ultralydskursus DRS, UL-scanning af spytkirtler v. Sjøgrens syndrom
Sep 2023	Ultralydskursus DRS niveau 3b (degenerative sygdomme i hofte og skulder).
Jun 2023	EULVIC: 5th European Large Vessel Vasculitis Imaging Course, Innsbruck, Østrig
Mar 2020	Ultralydskursus – DRS niveau 1.
Aug 2019	Dansk Idrætsmedicinsk Selskabs Diplomkursus Trin 1.
Maj 2016	Targeted Ultrasound Initiative, musculoskeletal ultrasound - Basic.
Maj 2016	TR2. Yngre lægers kursus for tillidsrepræsentanter.
Dec 2015	TR1. Yngre lægers kursus for tillidsrepræsentanter
Nov 2015	Targetet Ultrasound Initiative I, introduktionskursus muskuloskeletal UL-skanning.
Sep 2014	Muskuloskeletal MR - fokus på spondylartrit, v. Yngre Reumatologer.
Sep 2014	Led-score kursus
Juni 2014	Gentofte hospital, introduktionskursus i muskuloskeletal UL-skanning.
Jan 2014	Inspirationskursus i Reumatologi v. Yngre Reumatologer
Nov 2012	Crash-kursus i farmakologi ved Klinisk Farmakologisk afd., Bispebjerg Hospital.

Undervisning/vejledning

Apr 2025:	”Inflammatoriske reumatologiske sygdomme i almen praksis”, undervisning Almen Praksis, DGE-gruppe, København
Okt 2023 – Okt 2024:	Undervisning stud.med. på specialefokuseret kursus: ledsmerter og ledhævelser.
Okt 2023:	Undervisning i ”hands-on” ultralyd, DRS niveau 1 (HU-læger)

Forår 2009: Studenterunderviser i histologi på tandlægestudiets 2. semester

Foredrag

Apr 2024: Gigtforeningen: kredsforening Nordsjælland og København: Foredrag om Muskelgigt
Sep 2023: Gigtforeningen: kredsforening Bornholm: Foredrag om Muskelgigt.

Tillidshverv

Apr 2016 – okt 2020: Bestyrelsesmedlem og sekretær, Yngre Reumatologer (YR)
Maj 2016 – okt 2019: Repræsentant for YR i videreuddannelsesudvalget for reumatologi og ansættelsesudvalget for hoveduddannelsen i reumatologi i Region Øst.
Sep 2015 – aug 2016: Tillidsrepræsentant, Reumatologisk afd., Frederiksberg Hospital.

Administrativt

Dec 2020 – aug 2021: Uddannelseskoordinerende yngre læge (UKYL), Afdeling for Rygkirurgi, Led- og Bindevævssygdomme, Rigshospitalet, Frederiksberg.
Sep 2015 – aug 2016: Vagtplanlægger reumatologisk afdeling, Frederiksberg Hospital

Publikationsliste:

1. **Gorlen TF**, Brittain JM, Østergaard M, Fischer BM, Døhn UM and Terslev L (2024). Low incidence of malignancy in patients with suspected polymyalgia rheumatica or giant cell arteritis, examined with FDG-PET/CT. Front. Med. 11:1309905.

2. **Gorlen TF**, Gorlén T, Neergaard MA. Death in nursing homes: a Danish qualitative study. Int J Palliat Nurs. 2013;19(5):236-42.

3. Gorlen T, **Gorlen TF**, Vass M, Neergaard MA. Low confidence among general practitioners in end-of-life care and subcutaneous administration of medicine. Dan Med J. 2012;59(4):A4407.

Bilag 2: Referencer

1. Gonzalez-Gay MA. Giant cell arteritis and polymyalgia rheumatica: two different but often overlapping conditions. Semin Arthritis Rheum. 2004;33(5):289–93.
2. Vodopivec I, Rizzo JF. Ophthalmic manifestations of giant cell arteritis. Rheumatol Oxf Engl. 2018;57(suppl_2):ii63–72.
3. Jud P, Verheyen N, Dejaco C, Haas E, Szolar D, Meinitzer A, et al. Prevalence and prognostic factors for aortic dilatation in giant cell arteritis – a longitudinal study. Semin Arthritis Rheum. 2021;51(4):911–8.
4. Tomelleri A, van der Geest KSM, Khurshid MA, Sebastian A, Coath F, Pierscionek B, et al. Disease stratification in GCA and PMR: state of the art and future perspectives. Nat Rev Rheumatol. 2023;19(7):446–59.
5. van Nieuwland M, Colin EM, Boumans D, Vermeer M, Brouwer E, Alves C. Diagnostic delay in patients with giant cell arteritis: results of a fast-track clinic. Clin Rheumatol. 2024;43(1):349-355.
6. Hill CL, Cole A, Rischmueller M, Dodd T, Coleman M, Tucker G, et al. Risk of cancer in patients with biopsy-proven giant cell arteritis. Rheumatology. 2010;49(4):756–9.
7. Kermani TA, Schäfer VS, Crowson CS, Hunder GG, Gabriel SE, Ytterberg SR, et al. Malignancy Risk in Patients with Giant Cell Arteritis: A Population-Based Cohort Study. Arthritis Care Res. 2010;62(2):149–54.
8. Ungprasert P, Sanguankeo A, Upala S, Knight EL. Risk of malignancy in patients with giant cell arteritis and polymyalgia rheumatica: A systematic review and meta-analysis. Semin Arthritis Rheum. 2014;44(3):366–70.
9. Brekke LK, Fevang BTS, Diamantopoulos AP, Assmus J, Esperø E, Gjesdal CG. Risk of Cancer in 767 Patients with Giant Cell Arteritis in Western Norway: A Retrospective Cohort with Matched Controls. J Rheumatol. 2020;47(5):722–9.
10. Dar L, Ben-Shabat N, Tiosano S, Watad A, McGonagle D, Komaneshter D, et al. The Incidence and Predictors of Solid- and Hematological Malignancies in Patients with Giant Cell Arteritis: A Large Real-World Database Study. Int J Environ Res Public Health. 2021;18(14):7595.
11. Mackie SL, Dejaco C, Appenzeller S, Camellino D, Duftner C, Gonzalez-Chiappe S, et al. British Society for Rheumatology guideline on diagnosis and treatment of giant cell arteritis. Rheumatology. 2020;59(3):e1–23.
12. Hellmich B, Agueda A, Monti S, Buttgereit F, de Boysson H, Brouwer E, et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis. 2020;79(1):19–30.
13. Moreel L, Betrains A, Molenberghs G, Blockmans D, Vanderschueren S. Duration of Treatment With Glucocorticoids in Giant Cell Arteritis: A Systematic Review and Meta-analysis. JCR J Clin Rheumatol. 2023;29(6):291–7.
14. Moreel L, Betrains A, Molenberghs G, Vanderschueren S, Blockmans D. Epidemiology and predictors of relapse in giant cell arteritis: A systematic review and meta-analysis. Joint Bone Spine. 2023;90(1):105494.
15. Hoes JN, Jacobs JWG, Verstappen SMM, Bijlsma JWJ, Heijden GJMGV der. Adverse events of low- to medium-dose oral glucocorticoids in inflammatory diseases: a meta-analysis. Ann Rheum Dis. 2009;68(12):1833–8.

16. Mazzantini M, Torre C, Miccoli M, Baggiani A, Talarico R, Bombardieri S, et al. Adverse Events During Longterm Low-dose Glucocorticoid Treatment of Polymyalgia Rheumatica: A Retrospective Study. J Rheumatol. 2012;39(3):552–7.
17. Dejaco C, Ramiro S, Bond M, Bosch P, Ponte C, Mackie SL, et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice: 2023 update. Ann Rheum Dis. 2023;ard-2023-224543.
18. Diamantopoulos AP, Haugeberg G, Lindland A, Myklebust G. The fast-track ultrasound clinic for early diagnosis of giant cell arteritis significantly reduces permanent visual impairment: towards a more effective strategy to improve clinical outcome in giant cell arteritis? Rheumatology. 2016;55(1):66–70.
19. Monti S, Bartoletti A, Bellis E, Delvino P, Montecucco C. Fast-Track Ultrasound Clinic for the Diagnosis of Giant Cell Arteritis Changes the Prognosis of the Disease but Not the Risk of Future Relapse. Front Med. 2020;7:589794.

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael

Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Sara Fresnillo Saló**
Arbejdssted/ Institution	**Center for Cancer Immune Therapy (CCIT), Herlev Hospital**
Adresse	**Borgmester Ib Juuls Vej 13, DK-2730 Herlev**
Tlf.nr.	**+45 81903462**
e-mail	**sara.fresnillo.salo@regionh.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
Exercise as combination partner for immune therapy of cancer
Formål
This PhD project aims to investigate the impact of physical exercise on immune infiltration across clinically relevant murine cancer models.
Problemstilling
Checkpoint inhibitor (CPI) therapy, which consists in the administration of monoclonal antibodies that unleash T cells from inhibition in the tumor, has been approved for the treatment of a range of cancers. However, despite unprecedented response rates in melanoma, including curative responses in late-stage patients, only a fraction of patients responds to treatment. We believe exercise may represent a simple means to make tumors more permissive for immunotherapies like CPI.

Baggrund

In recent years, the landscape of cancer treatment has been reshaped by significant breakthroughs in immunotherapy. Thus, the well characterized capacity of the immune system to recognize and kill cancer cells is now successfully exploited clinically. Checkpoint inhibitor (CPI) therapy, which consists in the administration of monoclonal antibodies (mAb) that unleash T cells from inhibition in the tumor, has been approved for the treatment of a range of cancers including melanoma, renal cell carcinoma (RCC), and non-small cell lung cancer (NSCLC). However, despite unprecedented response rates in melanoma, including curative responses in late-stage patients, only a fraction of patients responds to treatment. The success of immunotherapy is intricately tied to the tumor microenvironment (TME), which refers to the surroundings in which a tumor exists, encompassing various factors like cells, blood vessels, and signaling molecules. Tumors that are infiltrated with immune cells tend to be more responsive to CPI therapy. Therefore, huge efforts are undertaken to study the molecular background for lack of immune infiltration, and ways by which immune cell infiltration can be augmented. We previously showed that voluntary exercise has a remarkable effect on immune infiltration and tumor growth across several murine models. This exercise-induced influx of immune cells into the tumor may represent a simple means to make tumors more permissive for immunotherapies like checkpoint inhibitors. Emerging research is bringing attention to the synergy between exercise and immunotherapy. In two separate studies, exercise revealed its potential to sensitize tumor models that were previously resistant to CPI therapy. A crucial player in the body's immune response against tumor cells are dendritic cells (DCs). These cells are responsible for recognizing and presenting tumor antigens to T cells, which then attack and destroy cancer cells. However, the function of DCs can be impaired in individuals with cancer, leading to a weakened immune response. Exercise could have a beneficial effect on the recruitment and function of DCs, potentially improving their ability to recognize and present tumor antigens. Understanding the relationship between exercise and DC function could lead to the development of new therapeutic strategies for cancer treatment.

Metoder

We will investigate the effects of exercise on tumor progression, immune infiltration, and survival across three mouse cancer models, using running wheels for voluntary exercise. Immune profiling will include flow cytometry, PCR, immunohistochemistry, and scRNAseq. Models showing improved outcomes with exercise will be further tested in combination with checkpoint inhibitor (CPI) therapy. To identify key immune mediators, we will perform cell depletion studies. Murine and human dendritic cells will be analyzed *in vitro* for exercise-induced functional changes. Experiments use C57BL/6 mice, treated with anti-PD-1 antibodies, with immune analyses performed via in-house and collaborative facilities.

Tidsplan
The project is expected to run for 3 years, divided in 3 work packages: Investigating the effect of voluntary exercise on tumor growth and immune cell infiltration (Month 1-11); Studying the synergy between voluntary exercise and CPI therapy (Month 12-27); Investigating the effect of exercise in dendritic cells (Month 28-36).
Forventede resultater og impact
By elucidating the synergistic effects of exercise and CPI on the tumor microenvironment, this study has the potential to inform the development of more effective treatment strategies against cancer. In addition to its scientific contributions, this project also holds significant implications for patient care and healthcare economics. Physical exercise represents a readily accessible and cost-effective intervention for cancer patients, offering potential benefits that extend beyond its direct impact on physical health.
Øvrige projektdeltagere og samarbejdsrelationer
The project is conducted in close collaboration with Ass. Prof. Daniel Hargbøl Madsen, Center for Cancer Immune Therapy (CCIT). The Ret mouse model is provided through a collaboration with Prof. Viktor Umansky, Clinical Cooperation Unit Dermato-Oncology, German Cancer Research Center (DKFZ), Heidelberg.
Budget (herunder evt. finansiering fra offentlige/private råd og fonde)
I am applying for 225.000 DKK to cover 6 months´ salary, smaller amounts of support will also be gratefully received. The project has been supported by Herlev Hospital´s PhD stipend and Dansk Kræftforskningsfond (covering 6 months' salary each).

CV for Sara Fresnillo Saló

Date of birth: 28/09/1998

EDUCATION:

2020-2022 **MSc in Immunology and Inflammation** – University of Copenhagen
2019-2020 **Erasmus Exchange Program: Biochemistry and Biotechnology** - Ghent University
2016-2020 **BSc in Biomedical Sciences** – Autonomous University of Barcelona

RESEARCH EXPERIENCE:

CCITdk – National Center for Cancer Immune Therapy, Herlev Hospital
04/23-now PhD student
Exercise as combination partner for immune therapy of cancer

CCITdk – National Center for Cancer Immune Therapy, Herlev Hospital
10/22-03/23 Research Assistant
Continuation of the Master thesis project and work on *High Intensity Aerobic Exercise Training and Immune Cell Mobilization in Patients With Lung Cancer (HI AIM) (NCT04263467)*

CCITdk – National Center for Cancer Immune Therapy, Herlev Hospital
09/21-10/22 Master thesis student
Characterization of CD4+ T cell responses against Rho C, a metastasis associated tumor antigen

Neuroscience institute (INc) of Autonomous University of Barcelona
02/20-06/20 Internship
Study of post-mortem delay in spontaneous dopamine accumulation in rat brain striatum incubated ex vivo.

SKILLS:

Languages: Catalan, Spanish, English (C1)
Certificates: FELASA (Function A, B, D), FACS course
Technical skills: Animal handling, cell culture, PBMC isolation, flow cytometry, RT-qPCR, T cell stimulation assays, western blotting, xCELLigence, EliSpot, chrome release assays.
Software: Microsoft Office Suite, SPSS, R studio, Pymol, NovoExpress, FlowJo and GraphPad Prism.

AWARDS/SCHOLARSHIPS:

Skolarstipendium from the Danish Cancer Society
Honorable mention by Generalitat de Catalunya in the General section of the University Entrance Exam (PAU)

PUBLICATION LIST

Fresnillo Saló, S., Schuhmacher, J., Rahbech, A., Pedersen, S., Brasso, K., thor Straten, P., Gouttefangeas, C. (2025). Vaccination Against RhoC in Prostate Cancer Patients Induces Potent and Long-Lasting CD4+ T Cell Responses with Cytolytic Potential in the Absence of Clinical Efficacy: A Randomized Phase II Trial. Vaccines.

Rahbech, A., Kurzay, A., **Fresnillo Saló, S**., Seremet, T., Debets, R., Met, Ö., Peeters, M. J. W., thor Straten, P. (2024). MerTK signaling in human primary T cells modulates memory potential and improves recall response. Journal of Leukocyte Biology.

Aehnlich, P., Velasco, M., Dam, S., **Fresnillo Saló, S**., Olsen, L., thor Straten, P., Desler, D., Olofsson, G.H. (2024). Glycolysis inhibition affects proliferation and cytotoxicity of Vγ9Vδ2 T cells expanded for adoptive cell therapy. Cytotherapy.

Aehnlich, P., Leuchte, K., Schöllkopf, C., **Fresnillo Saló, S**., Seremet, T.J., Høgdall, E., Met, Ö., Grønbaek, K., thor Straten, P. (2024). AXL in myeloid malignancies – an elusive target? Biomarker Research.

Yixin Fjæstad, K., Zedlitz Johansen, A., Linder, H., James Baker, K., Schattefor, M., Thorseth, M.L., Siersbæk, M., Perez-Penco, M., Rahbech, A., **Fresnillo Saló, S**., Engelholm, L., Svane, I.M., Hald Andersen, M., Junker, N., Grøntved, L., thor Straten, P., Hargbøl Madsen, D. (2024). β-adrenergic signaling blockade attenuates metastasis through monocyte-dependent activation of cytotoxic CD4 T cells. Nature Communications (manuscript under review)

Leuchte, K., Luu, T. V., **Fresnillo Saló, S**., Madsen, K., Ottosen, L. H., Skadborg, S. K., Kemming, J. S., Holmström, M. O., Chen, H., Olsen, L. R., Vinther, A., Andersen, M. H., Hadrup, S. R., thor Straten, P., Olofsson, G. H. (2025). Moving towards optimal immunity: Profiling interindividual differences of lymphocyte mobilization and reorganization of the CD8+ T cell compartment following acute high-intensity exercise. (submitted for publication)

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Christina Therkildsen, Forskningsleder**
Arbejdssted/ Institution	**Forskningsenheden for Tarmkræft, Gastroenheden, Hvidovre Hospital**
Adresse	**Kettegård Alle 36, 2650 Hvidovre**
Tlf.nr.	**38623507**
e-mail	**christina.therkildsen@regionh.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel:

Tidlig opsporing af kræft med blodbaserede biomarkører

Formål

Vores mål er at udvikle en kræftscreeningsmetode, der kan:

1. Opdage kræft tidligt ved at finde kræftmarkører i blodet, før symptomerne viser sig, så vi kan opstarte behandlingen tidligere og øge chancerne for helbredelse.

2. Identificere forskellige typer af kræft ved at finde markører, der kan se forskel på forskellige kræftformer, så patienterne hurtigere kan henvises til den rette specialist.

3. Gøre udredningen hurtigere ved at udvikle en blodprøve-analyse, da det er en nem og skånsom måde at screene for kræft, og dermed kan forbedre livskvaliteten for mennesker under udredning.

Problemstilling

Forestil dig at vi kunne opdage kræft før symptomerne overhovedet viser sig. At en simpel blodprøve kan måske give afgørende information, der fører til hurtigere behandling – og bedre chancer for helbredelse. Dét er ideen bag dette forskningsprojekt. Et forskningsprojekt, der har potentiale til at revolutionere, hvordan vi bekæmper kræft.

Det er her, vores forskningsprojekt kommer på banen. Vi arbejder på at udvikle en ny type screening, der er baseret på blodprøver. Disse blodprøver kan identificere specifikke "markører" – små tegn i blodet, der indikerer, om der er kræft til stede i kroppen. Nogle markører kan endda udpege, hvor i kroppen kræften sidder.

Baggrund

Kræft er en af de største sundhedsudfordringer i vores tid. Mange af os har oplevet, hvordan kræft kan påvirke vores liv – enten direkte eller gennem familie og venner. En stor udfordring ved kræft er, at den ofte opdages senere end man kunne ønske sig. Det gør behandlingen mere kompleks og mulighederne for helbredelse er mindre.

I dag screenes der for de mest hyppige former for kræft, så som tarmkræft, brystkræft og livmoderhalskræft. Der er dog en hel del kræftformer i de lidt mindre tilgængelige organer, som er svære at screene for med de nuværende metoder, da de er både ubehagelige og ikke uden risiko. Disse kræftformer kan yderligere være svære at opdage tidligt, fordi de giver tvetydige symptomer, såsom træthed og vægttab. Symptomer, der kan skyldes mange andre ting end kræft.

Metoder

Vi vil analysere blodprøver fra tre forskellige grupper af mennesker:

1. Fra en gruppe af patienter med kræft, men uden symptomer, vil vi udvælge de af vores biomarkører, der kan finde kræft på tidlige stadier.

2. Biomarkørerne vil blive testet i en anden kohorte for at teste om vores screeningsmetode kan hjælpe med at diagnosticere patienter med symptomer henvist i kræftpakkeforløb.

3. Endelig vil biomarkørerne blive testet i en gruppe af arveligt disponerede familier med en medfødt risiko for at udvikle forskellige former for kræft – for at se om vores screeningsmetode kan bruges som en kontrol-undersøgelse til tidlig opsporing af kræft.

Tidsplan

Forventede resultater og impact

Dette projekt har potentiale til at gøre en stor forskel for kræftpatienter. At leve med en risiko for kræft er mentalt en belastning – især, når der er tale om kræfttyper, som man ikke kan screene for.

Selve det at få en henvisning til et kræftpakkeforløb kan også være belastende – fx når man venter længe på en undersøgelse, der måske endda bliver udskudt pga. mangel på ressourcer. I begge tilfælde ville en blodprøve kunne tages hos egen læge og kun hvis der fortsat er begrundet mistanke for kræft sendes patienten videre til en hurtig udredning, mens de, der ikke er i risiko, kan undgå invasive og ikke risiko-frie undersøgelser.

Ved at opdage kræft tidligt kan vi:

Redde liv gennem tidlig behandling med bedre chancer for helbredelse.

Forbedre livskvaliteten ved hjælp af kombinationen af et accelereret diagnose-forløb og de mange undersøgelser, med medfølgende bekymring, som raske kan skånes for. Derudover forbedres livskvaliteten også via den ekstra kontrol, som familier med nedarvet risiko, kan have gavn af, da deres andre cancerformer opdages tidligere.

Hvad er det langsigtede mål?

Vores langsigtede mål er at udvikle en blodprøvebaseret screeningmetode, der kan bruges til at screene for forskellige typer af kræft. Vi forventer at vores forskning vil føre til, at kræft opdages tidligere og diagnosticeres mere effektivt, så færre mennesker dør af kræft.

Dette projekt er mere end bare forskning – det er et håb om en fremtid med bedre udsigter for flere kræftpatienter. En fremtid, hvor flere mennesker oplever, at kræft ikke er en dødsdom, men en sygdom, der kan behandles og overvindes og hvor flere mennesker med en nedarvet risiko ikke føler, at de lever med en dødsdom, men med håb og handlemuligheder. Vi er overbeviste om, at vores forskning vil bringe os et stort skridt nærmere denne fremtid.

Øvrige projektdeltagere og samarbejdsrelationer

Professor Inge Søkilde Pedersen ved Afsnit for Molekylær Diagnostik, Aalborg Universitetshospital.

Professor Niels Pallisgaard ved Afdelingen for Patologi, Næstved Sygehus.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Patientinklusion og indsamling af prøvemateriale er gennemført og prøverne er sendt til analyse i studiets første år (2024)

Udgifter til 1, herunder PhD-løn og indsamling af prøvemateriale, er dækket af Hvidovre Hospital (300.000 kr), Familien Erichsens Mindefond (50.000 kr.), Henrik Henriksens Fond (100.000 kr.), Bonnéns Fond (50.000 kr.), Else og Mogens Wedell-Wedellsborgs Legat (20.000 kr.), Sigurd Abrahamson og hustru Addies Mindelegat (100.000 kr.), A.D. Møller og hustru Chastines Fond (60.000 kr.) – i alt 680.000 kr.

Udgiftsposter	Projekt-år 2	Projekt-år 3	Total
Løn til Ph.d.-studerende (100%)	500.000	500.000	1.000.000
Løn til projektkoordinator (20%)	90.000	90.000	180.000
Løn til datamanager (20%)	90.000	90.000	180.000
DNA-oprensning (tumorvæv)	100.000	0	100.000
DNA-oprensning (blod)	100.000	0	100.000
Kortlægning af DNA-mutationer i tumorvæv	1.024.000	1.600.000	1.024.000 1.600.000
Kortlægning af DNA-methyleringer i tumorvæv			
Genfindelse af mutationer i blodprøve	560.000	200.000	760.000 200.000
Genfindelse af methyleringer i blodprøve			
TOTAL	2.584.000	2.560.000	5.144.000
Er dækket fra andre fonde*	2.148.000	1.000.000	3.148.000
MANKO d.d.	316.000	1.680.000	1.996.000

*** Projektet har opnået støtte fordelt på projekt-år 2 og 3 fra Kræftens Bekæmpelse (2.000.000 kr), IMK-fonden (268.000 kr), Juchumsen Fond (200.000 kr), Vissingfonden (295.000 kr.), Helsefonden (235.000 kr.) og Dansk Kræftforskningsfond (150.000 kr.) – i alt 3.148.000 kr.**

Direktør Michael Hermann Nielsens mindelegat ansøges om støtte til analyser i projekt-år 2 (2025): i alt DKK 300.000.

Bemærk vores finansierings-strategi i øvrigt:

Tildelte forskningsmidler administreres af Hvidovre Hospitals regnskabsafdeling via en specifik forskningskonto tilknyttet projektet. Hvidovre Hospital egenfinansierer lokaler, drift og vedligehold af apparatur (dvs. pc'er, printere, centrifuger, frysere og 24/7 overvåget frysehus) + løn til forskningsansvarlig daglig leder, Christina Therkildsen - TOTALT: DKK 667.500/år

Evt. bevilling bedes indbetalt på Hvidovre Hospitals konto: 3100-3100333635/Mrk: F-21200-01-72-08

CVR: Hvidovre Hospital/ Region Hovedstaden: 29190623

CURRICULUM VITAE – CHRISTINA THERKILDSEN

NUVÆRENDE STILLING

Forskningsleder af Colorectal Cancer Forskningsenheden og leder af det danske HNPCC-register for arvelig tarmkræft, Gastroenheden, Hvidovre Hospital, Kettegård Allé 36, 2650 Hvidovre

PERSONLIGE OPLYSNINGER

Fødselsdato: 24.03.1982
Civil status: Gift, 2 børn

ANSÆTTELSER

2020 -:	Forskningsleder af Colorectal Cancer Forskningsenheden, Gastroenheden, Hvidovre Hospital
2020 -:	Medleder af "Tidlig Opsporing"-sporet i ctDNA Forskningscenteret, DCCC
2018 -:	Leder af HNPCC-Registret for arvelig tarmkræft, Gastroenheden, Hvidovre Hospital
2018-2020:	Seniorforsker i arvelig tarmkræft, Klinisk Forskningsenhed, Hvidovre Hospital
2014-2018:	Postdoc, Klinisk Forskningscenter, Hvidovre Hospital
2013-2014:	Postdoc, Department of Oncology and Pathology, Lund Universitet, Sverige
2008:	Forskningsassistent, Klinisk Forskningscenter, Hvidovre Hospital

UDDANNELSE

2019+2024:	Lederkursus, Region H
2018:	Laboratorieleder kursus, EMBO, Heidelberg, Tyskland
20082013:	PhD i Molekylær Diagnostik, Sundhedsvidenskabeligt Fakultet, Københavns Universitet
2007:	Cand.Scient. i Biokemi, Naturvidenskabeligt Fakultet, Københavns Universitet

UNDERVISNING/VEJLEDNING mm.

2024:	Inviteret oplægsholder ved Lynch Syndrome Expert Network Workshop, UK
2023:	Inviteret oplægsholder ved Royal College of Obstetricians and Gynaecologists, UK
2023:	Inviteret oplægsholder ved EHTG konferencen i Vilnius
2021+2024:	Forskerpraktik for gymnasieelever med høj-niveau biotech/biokemi, Christianshavns Gymnasium
2021:	Medorganisator og underviser ved ctDNA workshop for PhD-studerende, Odense
2019-2024:	Medorganisator af EHTG konferencer (Barcelona, Palma, Online og i Vilnius)
2018 -:	Vejleder for 8 PhD studerende (4 afsluttede og 4 igangværende)
2017 -:	Vært og organisator for de årlige nationale HNPCC-symposier
2015 -:	Vejleder for 4 specialer og 1 master (medicin, biokemi og diplomuddannelse)
2009-2017:	Underviser i Cancer Genetik ved gymnasiale erhvervsbesøg
2010:	Pædagogikum del 1, Københavns Universitet
2006:	Underviser i "Signal Transduktion", Molekylær Biomedicin, Københavns Universitet

VIDENSKABELIGE TILLIDSHVERV

2024:	Fakultetsmedlem for Extra-kolonisk kræft ved EHTG (Online)
2022-2023:	Chair ved EHTG konferencerne for sessionerne "Nye cancergener" og "Yngre forskere"
2022:	Gæste-editor ved Frontiers of Oncology – særudgave omkring Lynch syndrome
2020:	Styregruppemedlem i ctDNA forskningscenter under DCCC
2020:	Medlem af ekspert komite i udarbejdelsen af nationale HNPCC-retningslinjer under DCCG
2020:	Bedømmer for La Marató de TV3 (Catalan Biomedical Research Funding Program)
2020:	Ekstern eksaminator: 1 PhD-afhandling og 1 halvtidsevaluering, Karolinska Instituttet, Sverige
2019-2023:	Styregruppemedlem af The Young European Hereditary Tumour Group
2017 -:	Medlem af The International Mismatch Repair Consortium
2017 -:	Medlem af The International Society for Hereditary Gastrointenstinal Cancer
2010 -:	Reviewer for 10 videnskabelige tidskrifter

PUBLIKATIONER

56 videnskabelige artikler (10 førsteforfatter, 1 delt første- og 1 delt sidste-forfatter, 11 sidste-forfatter) H-index 22 (Google Scholar, Marts 2025)–Citationer 2.356

PUBLIKATIONER

56 videnskabelige artikler (10 førsteforfatter, 1 delt første- og 1 delt sidste-forfatter, 11 sidste-forfatter) H-index 22 (Google Scholar, Marts 2025) – Citationer 2.356

20 vigtigste publikationer

1. Frydendahl A, Widman AJ, Øgaard N et al. (2025) *Whole-genome sequencing of cell-free DNA reveals DNA of tumor origin in plasma from patients with colorectal adenomas.* Mol Oncol. Jan 20. doi: 10.1002/1878-0261.13803.

2. Mansvelders MSE, Kleif J, Andersen MR, Karstensen JG, **Therkildsen C**. (2024) *Use of Fecal Immunochemical Testing for Risk Stratification of Patients With Symptoms of Colorectal Cancer Referred for Diagnostic Colonoscopy.* Gastroenterology. Dec 12:S0016-5085(24)05757-3. doi: 10.1053/j.gastro.2024.11.018.

3. Øgaard N, Jensen SØ, Ørntoft MW et al. (2024) *Circulating tumour DNA and risk of recurrence in patients with asymptomatic versus symptomatic colorectal cancer.* Br J Cancer. Nov;131(10):1707-1715. doi: 10.1038/s41416-024-02867-5.

4. Medina JE, Annapragada AV, Lof P et al. (2025) *Early Detection of Ovarian Cancer Using Cell-Free DNA Fragmentomes and Protein Biomarkers.* Cancer Discov. Jan 13;15(1):105-118. doi: 10.1158/2159-8290.CD-24-0393.

5. Petersen MM, Kleif J, Liggett J….**Therkildsen C**. (2024) *Development of an algorithm combining blood-based biomarkers, fecal immunochemical test, and age for population-based colorectal cancer screening.* Gastrointest Endosc. Jun:S0016- 5107(24)03290-5. doi: 10.1016/j.gie.2024.06.015.

6. Widman AJ, Shah M, Frydendahl A et al. (2024) *Ultrasensitive plasma-based monitoring of tumor burden using machine-learning-guided signal enrichment.* Nat Med. Jun;30(6):1655-1666. doi: 10.1038/s41591-024-03040-4.

7. Bernstein I, **Therkildsen C**, Seppälä T. (2023) *Identification, risk stratification, and optimized management for Lynch Syndrome*. Front Oncol. Jun 8;13:1223568. doi: 10.3389/fonc.2023.1223568. IF:5.738

8. Dominguez-Valentin M, Haupt S, Seppälä T et al. (2023) *Mortality by age, gene and gender in carriers of pathogenic mismatch repair gene variants receiving surveillance for early cancer diagnosis and treatment: a report from the prospective Lynch syndrome database*. EClinicalMedicine, Mar 20;58:101909. doi: 10.1016/j.eclinm.2023.101909. IF:17.033

9. Rasmussen M, Sowter P, Gallon R … **Therkildsen C**. (2023) *Mismatch repair deficiency testing in Lynch syndrome- associated urothelial tumors.* Front Oncol. Apr 18;13:1147591. doi: 10.3389/fonc.2023.1147591. IF: 6.244

10. Petersen MM, Kleif J, Jørgensen LN … **Therkildsen C**. (2023) *Optimizing Screening for Colorectal Cancer: An Algorithm Combining Fecal Immunochemical Test, Blood- Based Cancer-Associated Proteins and Demographics to Reduce Colonoscopy Burden.* Clin Colorect Cancer. Feb;S1533- 0028(23)00006-3. doi: 10.1016/j.clcc.2023.02.001. IF: 4.035

11. Rasmussen M, Durhuus JA, Nilbert M, Andersen O, **Therkildsen C**. (2022) *Response to immune checkpoint inhibitors is affected by deregulations in the antigen presentation machinery: a systematic review and meta-analysis.* Journal of Clinical Medicine, Dec 31;12(1):329. PMID: 36615128. IF:4.964

12. Rasmussen M, Lim K, Rambech E, Andersen MH … **Therkildsen C.** (2021) *Lynch syndrome-associated epithelial ovarian cancer and its immunological profile.* Gynecol Oncol. Sep;162(3):686-93. PMID: 34275654. IF: 5.482

13. **Therkildsen C**, Jensen LH, Rasmussen M et al. (2021) *An Update on Immune Checkpoint Therapy for the Treatment of Lynch Syndrome.* Clin Exp Gastroenterol. May 24;14:181-197. IF: 3.53

14. International Mismatch Repair Consortium. (2021). *Variation in the risk of colorectal cancer in families with Lynch syndrome: a retrospective cohort study.* Lancet Oncol. Jun 7:S1470-2045(21)00189-3. IF: 33.75

15. Dominguez-Valentin M, Crosbie EJ, Engel C et al. (2021) *Risk-reducing hysterectomy and bilateral salpingo-oophorectomy in female heterozygotes of pathogenic mismatch repair variants: a Prospective Lynch Syndrome Database report*. Genet Med. Apr;23(4):705-712. IF: 8.90

16. Dominguez-Valentin M, Sampson JR, Seppälä TT et al. (2020) *Cancer risks by gene, age, and gender in 6350 carriers of pathogenic mismatch repair variants: findings from the Prospective Lynch Syndrome Database*. Genet Med. Jan;22(1):15-25. IF: 8.90

17. Suerink M, Rodríguez-Girondo M, van der Klift HM et al. (2019) *An alternative approach to establishing unbiased colorectal cancer risk estimation in Lynch syndrome*. Genet Med. Dec;21(12): 2706-2712. IF: 8.90

18. Walkowska J, Jönsson M, Kallemose T ... **Therkildsen C**. (2018) P*DL1 protein upregulation and B2M loss correlates with improved survival in CD8 infiltrated Lynch syndrome-associated colorectal cancer*. Oncoimmunology. Sep 26;8(1):e1515612. IF: 5.87

19. **Therkildsen C**, Eriksson P, Höglund M et al. (2018) *Molecular subtype classification of urothelial carcinoma in Lynch syndrome*. Mol Oncol. Aug;12(8):1286-1295. IF: 6.57

20. **Therkildsen C**, Ladelund S, Smith-Hansen L et al. (2017) *Towards gene- and gender-based risk estimates in Lynch syndrome; age- specific incidences for 13 extra-colorectal cancer types*. British J Cancer. Nov;117(11):1702-1710. IF: 5.94

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens min-delegat, afd. B - sygdomsforskning

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	Trine Engelbrecht Hybel, PhD Studerende
Arbejdssted/ Institution	Afdelingen for Blodsygdomme, Aarhus Universitetshospital & Institut for Klinisk Medicin, Aarhus Universitet
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e-mail	trihyb@rm.dk

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

Rethinking Diagnostics in Myelodysplasic Neoplasia: Integrating AI-Assisted Morphometrics for Improved Accuracy and Risk Stratification

Formål

The aim of this research project is to improve the diagnostics for patients with the rare and chronic cancer myelodysplastic neoplasia (MDS). We aim to develop a new system which makes it possible to distinguish MDS patients and patients with benign cytopenia, while the diagnostic process becomes faster, more precise, and gentler for the patients.

Problemstilling

MDS is a rare, hematological cancer characterized by dysplasia in the bone marrow (BM), resulting in various degrees of cytopenia. MDS significantly affects quality of life, causing fatigue, pain, and anxiety. Symptoms range from mild cases to severe BM failure and rapid progression to acute leukemia. Around 750 patients are referred and 250 are diagnosed annually in DK. While low-risk patients have a median life expectancy of 5-8 years, high-risk patients typically survive less than a year. Diagnosing MDS is challenging, often requiring repeated BM sampling, causing physical discomfort and prolonged uncertainty. Dysplasia, the hallmark of MDS, varies widely in degree and cellular diversity, making accurate identification challenging and prone to inter-observer variability. Traditional diagnostic methods often miss subtle or rare dysplastic changes. This uncertainty impedes clarification and treatment planning, resulting in prolonged and stressful diagnostic processes.

Baggrund

This research project aims to develop a novel and enhanced diagnostic scoring system for MDS using imaging flow cytometry (IFC), a technique which combines multiparameter flow cytometry with microscopy. IFC enables rapid image analysis of thousands of BM cells in suspension, improving sensitivity. By employing AI-assisted quantification of morphometrics, cell dysplasia can be detected across the three myeloid lineages implicated in MDS. The ultimate goal is to establish IFC as a routine diagnostic tool, enhancing diagnostic accuracy, enabling earlier intervention, and improving patient outcomes.

Metoder

Validation of IFC-panels. Development of the IFC-based diagnostic system involves assessment of dysplastic features in three myeloid lineages: erythropoiesis, megakaryopoiesis, and granulopoiesis. Three IFC panels have already been developed for immunophenotypic detection and have shown proof-of-concept results. Now, the panels will be applied and tested for combined myeloid dysplasia assessment on a larger cohort, including 40 MDS patients, 40 patients with cytopenia of undetermined significance, and 15 pathological controls.

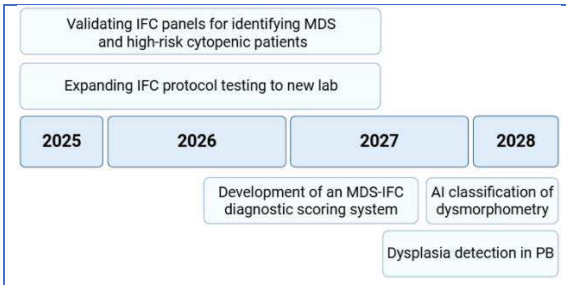
Expanding IFC protocol. To validate the robustness of the developed assays across different laboratories, the IFC protocols established by our group will be transferred to the research laboratory at the Department of Pathology and Laboratory Sciences, University of Western Australia (UWA), led by Professor Wendy Erber. This laboratory will serve as an additional site for inclusion of MDS patients and individuals with persistent cytopenia.

Dysplasia Detection in PB. BM sampling is invasive and painful, making the detection of dysplastic changes in blood samples an attractive alternative. To assess the plausibility of this, data from PB and BM samples will be compared to determine whether the dysmorphometric abnormalities identified in BM can also be detected in PB samples.

Development of Scoring System. We will develop an IFC-based diagnostic scoring system to evaluate morphometric abnormalities in the three myeloid lineages involved in MDS. Each parameter will be assessed for its ability to differentiate MDS and high-risk cytopenic individuals from controls and to distinguish high-risk from low-risk CCUS patients. We will also evaluate diagnostic performance (sensitivity, specificity, predictive values).

Tidsplan

The project will take place during the period 01-07-2025 – 30-06-2028:



Forventede resultater og impact

This IFC approach is expected to enhance diagnostic precision and timing, potentially enabling earlier detection. The platform will differentiate high-risk from low-risk cases, improving patient care, treatment personalization, and follow-up. Also, by detecting morphometric abnormalities in blood, we aim to develop a less invasive screening method.

Øvrige projektdeltagere og samarbejdsrelationer

The project is conducted in collaboration with national partner Prof. Kirsten Grønbæk, University of Copenhagen as well as international partners Scientist Matthew Rodrigues, Seattle, USA and Professor Wendy Erber's research group at the University of Western Australia.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

July 2025 - June 2028	Budget (DKK)	On hand from employer (DKK)	On hand from others (DKK)	Applied for from others (DKK)	Applied for from Direktør Michael Hermann Nielsens Mindelegat, Afd. B (DKK)
Salaries	5.727.597	1.729.587	2.872.410	1.125.600	
Running costs	1.548.558	688.000	630.558	130.000	**100.000**
Others	111.000		111.000		
In total	7.387.155	2.417.587	3.613.968	1.255.600	**100.000**

Curriculum Vitae & Publication List

Trine Engelbrecht Hybel

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EDUCATION

2021 —	Integrated PhD Student, Graduate School of Health, Aarhus University and Department of Hematology, Aarhus University Hospital.
2019-2023	MSc in Molecular Medicine, Aarhus University.
2016-2019	MSc in Molecular Medicine, Aarhus University.

PUBLICATIONS AND ABSTRACTS

- In total, 15 published articles in international peer-reviewed journals (7 as first author). Currently, 4 manuscripts-in-preparation (2 as first author).
- In total, 9 abstracts presented at national/international conferences (4 as first author) (*e.g.,* ASH 2024 and CYTO 2025).

TEACHING/DISSEMINATION

2021 — Instructor in the course Cancer Diseases in the master's degree in molecular medicine, Aarhus University (https://kursuskatalog.au.dk/en/course/107976/Cancer-Diseases).

- Lectures on "How to read scientific literature" and "CAR-T cell therapy".
- Planning and executing two-day laboratory visits at the Department of Hematology, Aarhus University.

2020 — Presentations of my research project at HemeLab meetings and department meetings at the Department of Hematology, Aarhus University Hospital.

2021 Presentation at the 66th Meeting of the Danish Society for Flow Cytometry on "Challenges in Establishing a 9-color Imaging Flow Cytometry Panel to Identify Leukemic Stem Cells in Acute Myeloid Leukemia".

2018-2019 Lectures at academic events by the Academic Committee of the Student Association of Molecular Medicine on "How to find and execute bachelor's and master's thesis projects".

CO-SUPERVISION

- Ongoing: 2 molecular medicine master's students.
- Previously: 1 molecular medicine master's student, 1 molecular medicine bachelor's student, 1 research year medical student, 1 research project medical student.

FUNDING

During the last 4 years: Obtained funding for **1.7 million DKK**, including a fully financed PhD fellowship from the Department of Clinical Medine, Aarhus University and kind donations from the Dagmar Marshall Foundation, Danish Lymphoma Group, Eva and Henry Frænkel Memorial Foundation, Toyota Foundation, Family Hede Nielsen Foundation, Aase and Ejnar Danielsens Foundation, Poul and Ellen Hertz' Foundation, Butcher Max Wørzner and wife Inger Wørzner's Memorial Grant.

ORGANIZATIONAL EXPERIENCE

2021-2022	Co-organizer of the course Cancer Diseases in the master's degree in molecular medicine, Aarhus University (https://kursuskatalog.au.dk/en/course/107976/Cancer-Diseases).
2020-2021	Member of the Organizing Committee of the Nordic Meeting in Tumor Microenvironment in Lymphoma (https://www.nordictumormicroenvironment.org).
2018-2019	Member of the Academic Committee of the Student Association of Molecular Medicine, Aarhus University.

SCIENTIFIC SOCIETIES

- Member of the *HemeLab* research network at the Department of Hematology, Aarhus University Hospital (https://clin.au.dk/hemelab)
- Member of the national community *The Danish Society of Flow Cytometry (DSFCM)*

DETAILED PUBLICATION DESCRIPTION

- Articles published in international peer-reviewed journals: 15 (7 as first author)
- Manuscripts in preparation: 4 (2 as first author)
- H-index (Scopus): 5. Citations: 87

First authorships

Imaging Flow Cytometry and Convolutional Neural Network-Based Classification Enable Discrimination of Hematopoietic and Leukemic Stem Cells in Acute Myeloid Leukemia
Trine Engelbrecht Hybel, Sofie Hesselberg Jensen, Matthew A. Rodrigues, Thomas Engelbrecht Hybel, Maya Nautrup Pedersen, Signe Håkansson Qvick, Marie Hairing Beck Enemark, Marie Bill, Carina Agerbo Rosenberg, Maja Ludvigsen. *International Journal of Molecular Sciences,* 2024 (PMID: 38928171)

High-Efficiency Enrichment of Megakaryocytes and Identification of Micromegakaryocytes from Human Bone Marrow by Imaging Flow Cytometry
Maya Nautrup Pedersen*, Trine Engelbrecht Hybel*, Jens Haugbølle Bjerre, Anne Sofie Borg Hammer, Anja Bille Bohn, Marie Bill, Carina Agerbo Rosenberg, Maja Ludvigsen. *Cells,* 2025 (*Shared first authorship, PMID: 40277913)

Characterization of the genomic landscape of HIV-associated lymphoma reveals heterogeneity across histological subtypes
Trine Engelbrecht Hybel*, Emma Frasez Sørensen*, Marie Hairing Enemark, Jonas Klejs Hemmingsen, Anita Tranberg Simonsen, Kristina Lystlund Lauridsen, Michael Boe Møller, Court Pedersen, Gitte Pedersen, Niels Obel, Carsten Schade Larsen, Fransesco d'Amore, Stephen Hamilton-Dutoit, Magnus Stougaard, Maja Ølholm Vase, Maja Ludvigsen. *AIDS*, 2024 (PMID: 39178160, *Shared first authorship)

Response to correspondence piece on 'Characterization of the genomic landscape of HIV-associated lymphoma reveals heterogeneity across histological subtypes'
Emma Frasez Sørensen*, Trine Engelbrecht Hybel*, Maja Ludvigsen. *AIDS*, 2024 (PMID: 40009213, *Shared first authorship)

Intratumoral expression of CD38 in patients with post-transplant lymphoproliferative disorder
Trine Engelbrecht Hybel*, Maja Ølholm Vase*, Eva Futtrup Maksten, Marie Beck Enemark, Kristina Lystlund Lauridsen, Stephen Hamilton-Dutoit, Claus Andersen, Michael Boe Møller, Søren Schwartz Sørensen, Bente Jespersen, Jan Kampmann, Francesco d'Amore, Maja Ludvigsen. *Acta Oncologica*, 2022 (PMID: 34474636, *Shared first author).

CD38 is a potential treatment target in lymphoma patients concurrently infected with human immunodeficiency virus
Trine Engelbrecht Hybel*, Maja Ølholm Vase*, Kristina Lystlund Lauridsen, Marie Beck Enemark, Michael Boe Møller, Court Pedersen, Gitte Pedersen, Stephen Hamilton-Dutoit, Niels Obel, Carsten Schade Larsen, Francesco d'Amore, Maja Ludvigsen. *Leukemia & Lymphoma*, 2022 (PMID: 35019824, *Shared first author)

Simulated Microgravity Influences VEGF, MAPK, and PAM Signaling in Prostate Cancer Cells
Trine Engelbrecht Hybel, Dorothea Dietrichs, Jayashree Sahana, Thomas J Corydon, Mohamed Z Nassef, Markus Wehland, Marcus Krüger, Nils E Magnusson, Johann Bauer, Kirsten Utpatel, Manfred Infanger, Daniela Grimm, Sascha Kopp. International Journal of Molecular Sciences, 2020 (PMID: 32070055)

Co-authorships

Progression of disease within 24 months (POD24) in follicular lymphoma in the rituximab era: incidence, clinicopathological risk factors, and outcome in a population-based Danish cohort
Marie Hairing Enemark, Jonas Klejs Hemmingsen, Maja Dam Andersen, Trine Engelbrecht Hybel, Mads Emil Bjørn, Pär Lars Josefsson, Lars Møller Pedersen, Maja Bech Juul, Robert Schou Pedersen, Michael Thorsgaard, Ida Blok Sillesen, Trine Lindhardt Plesner, Stephen Jacques Hamilton-Dutoit, Paw Jensen, Charlotte Madsen, Maja Ludvigsen. *Blood Cancer Journal*, 2024 (PMID: 39349431)

Differential tumor protein expression at follicular lymphoma diagnosis reveals dysregulation of key molecular pathways associated with histological transformation.
Marie Hairing Enemark, Katharina Wolter, Trine Engelbrecht Hybel, Maja Dam Andersen, Emma Frasez Sørensen, Linnea Meier Hindkaer, Kristina Lystlund Lauridsen, Charlotte Madsen, Trine Lindhardt Plesner, Stephen Hamilton-Dutoit, Bent Honoré, Maja Ludvigsen. *Scientific Reports*, 2024 (PMID: 39622932)

Tumor-Tissue Expression of the Hyaluronic Acid Receptor RHAMM Predicts Histological Transformation in Follicular Lymphoma Patients
Marie Beck Enemark, Trine Engelbrecht Hybel, Charlotte Madsen, Kristina Lystlund Lauridsen, Bent Honoré, Trine Lindhardt Plesner, Stephen Hamilton-Dutoit, Francesco d'Amore, Maja Ludvigsen. *Cancers*, 2022 (PMID: 35267625)

IDO1 Protein Is Expressed in Diagnostic Biopsies from Both Follicular and Transformed Follicular Patients
Marie Beck Hairing Enemark, Emma Frasez Sørensen, Trine Engelbrecht Hybel, Maja Dam Andersen, Charlotte Madsen, Kristina Lystlund Lauridsen, Bent Honoré, Francesco d'Amore, Trine Lindhardt Plesner, Stephen Jacques Hamilton-Dutoit, Maja Ludvigsen. *International Journal of Molecular Sciences*, 2023 (PMID: 37108483)

Proteomics identifies apoptotic markers as predictors of histological transformation in patients with follicular lymphoma
Marie Beck Hairing Enemark, Katharina Wolter, Amanda Jessica Campbell, Maja Dam Andersen, Emma Frasez Sørensen, Trine Engelbrecht Hybel, Charlotte Madsen, Kristina Lystlund Lauridsen, Trine Lindhardt Plesner, Stephen Jacques Hamilton-Dutoit, Bent Honoré, Maja Ludvigsen. *Blood Advances*, 2023 (PMID: 37824846)

Proteomics uncovers molecular features for relapse risk stratification in patients with diffuse large B-cell lymphoma
Maja Ludvigsen, Amanda Jessica Campbell, Marie Beck Enemark, Trine Engelbrecht Hybel, Marja-Liisa Karjalainen-Lindsberg, Klaus Beiske, Mette Bjerre, Lars Møller Pedersen, Harald Holte, Sirpa Leppä, Judit Meszaros Jørgensen, Bent Honoré. *Blood Cancer Journal*, 2023 (PMID: 37884514)

Proteomic Profiling Differentiates Lymphoma Patients with and without Concurrent Myeloproliferative Neoplasia
Johanne Marie Holst, Marie Beck Enemark, Martin Bjerregaard Pedersen, Kristina Lystlund Lauridsen, Trine Engelbrecht Hybel, Michael Roost Clausen, Henrik Frederiksen, Michael Boe Møller, Peter Nørgaard, Trine Lindhardt Plesner, Stephen Jacques Hamilton-Dutoit, Francesco d'Amore, Bent Honoré, Maja Ludvigsen. *Cancers*, 2021 (PMID: 34771688)

Three-Dimensional Growth of Prostate Cancer Cells Exposed to Simulated Microgravity
Dorothea Dietrichs, Daniela Grimm, Jayashree Sahana, Daniela Melnik, Thomas J Corydon, Markus Wehland, Marcus Krüger, Randy Vermeesen, Bjorn Baselet, Sarah Baatout, Trine Engelbrecht Hybel, Stefan Kahlert, Herbert Schulz, Manfred Infanger, Sascha Kopp. *Frontiers in Cell and Developmental Biology*, 2022 (PMID: 35252204)

Manuscripts in preparation

Revealing morphometric differences between hematopoietic and leukemic stem cells in acute myeloid leukemia: Machine learning-based analysis of im-aging flow cytometry data
Trine Engelbrecht Hybel, Sofie Hesselberg Jensen, Matthew A. Rodrigues, Thomas Engelbrecht Hybel, Maya Nautrup Pedersen, Signe Håkansson Qvick, Marie Hairing Enemark, Marie Bill, Carina Agerbo Rosenberg, and Maja Ludvigsen. Planned submission to *Cytometry Part A* by invitation.

Machine learning-assisted morphometric analysis enables determination of cell viability using imaging flow cytometry
Trine Engelbrecht Hybel, Carina Agerbo Rosenberg, Thomas Engelbrecht Hybel, Maya Nautrup Pedersen, Marie Hairing Enemark, Maja Ludvigsen

Exploring dysgranulopoieses in peripheral blood from patients with myelodysplastic neoplasm by imaging flow cytometry and machine-learning assisted morphometrics
Carina Agerbo Rosenberg, Naja Lorenzen, Trine Engelbrecht Hybel, Matthew Rodrigues, Jens Haugbølle Bjerre, Marie Bill, Maja Ludvigsen

Detection of IDO1 Protein in Diagnostic Lymphoma Biopsies from Immunodeficient Patients
Emma Frasez Sørensen, Trine Engelbrecht Hybel, Marie Beck Hairing Enemark, Maja Dam Andersen, Jonas Klejs Hemmingsen, Kristina Lystlund Lauridsen, Eva Futtrup Maksten, Claus Andersen, Michael Boe Møller, Søren Schwartz Sørensen, Bente Jespersen, Jan Kampmann, Court Pedersen, Gitte Pedersen, Niels Obel, Carsten Schade Larsen, Francesco d'Amore, Stephen Hamilton-Dutoit, Maja Ølholm Vase, Maja Ludvigsen

Department of CLINICAL MEDICINE, HEALTH
Aarhus University

Central Denmark Region

Department of Clinical Medicine
Aarhus University

Department of Hematology, Aarhus University Hospital

Palle Juul-Jensens Boulevard 35, C115-155

Maja Ludvigsen
Associate professor,
MSc PhD

Dato: 29.04.2025

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Regarding Trine Engelbrecht Hybels's funding application.

Rethinking Diagnostics in Myelodysplasic Neoplasia: Integrating AI-Assisted Morphometrics for Improved Accuracy and Risk Stratification

Molecular Medicine PhD student Trine Engelbrecht Hybel has been in my research group since her initial research project, September 2020, and now as a PhD student. During this, she has demonstrated a perceptive interest in Hematology with a translational research focus. Trine has built a strong interdisciplinary research environment around her projects, which has resulted in high impact findings, both with her as first author on 7 manuscripts (PMIDs: 38928171, 40277913, 39178160, 40009213, 34474636, 35019824, and 32070055) and as co-author on 8 manuscripts in several collaborative projects (PMIDs: 39349431, 39622932, 35267625, 37108483, 37824846, 37884514, 34771688, and 35252204)

During Trine's time in research, both in her master's thesis and during her PhD, she has worked in the laboratory and with a special focus on data management by AI – thereby combining laboratory experiments with improved data sciences. This has driven the research projects to discover biological findings not previously possible. Consistently, Trine has shown an independent approach to conduct and analyze results. She holds a permanent enthusiastic approach to acquainting herself with knowledge and keeps a profound translational interest in her search for solutions or explanations.

Trine has proved to excel in driving her research projects in collaboration with various professions, thus thriving in a multidisciplinary environment combining knowledge from both basic researchers focusing on the methodology and clinical researchers with focus on translating the research into the clinic. With this application, Trine aims at solidifying as an expert in the research field within the undersigned's research group, HemeLab, in a truly translational research project that aims to uncover the utility of imaging flow cytometry, a novel technology, to identify dysmorphometric characteristics of malignant cells. I trust Trine to succeed in this project which, prospectively, will improve diagnostics of MDS and other malignancies. The research study will be conducted in close collaboration with MD PhD Marie Bill and MSc PhD Carina Agerbo Rosenberg, as well as with our national collaborators, in particular prof. Kirsten Grønbæk, University of Copenhagen, and international collaborators, mainly Matthew Rodrigues, Seattle, USA and ass. prof. Kathy Fuller, Perth, Australia.

Thus, I am convinced that all practicalities are in place for Trine to succeed in her future research, both as to the practicalities regarding analysis set-ups in the different laboratories and in regard to the strong expertise delivered into this project. I hereby give Trine and this high-impact project my highest recommendations.

Maja Ludvigsen,
MSc PhD, associate professor

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens min-delegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Ivona Cudina, PhD fellow**
Arbejdssted/ Institution	**BRIC, Copenhagen University**
Adresse	**Njalsgade 169, 2300, Copenhagen**
Tlf.nr.	**+45 31712637**
e-mail	**ivona.cudina@bric.ku.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel
The application of spatial technologies to the investigation of localized scleroderma
Formål
The goal of this project is to uncover the cellular and molecular mechanisms driving morphea using advanced spatial and molecular technologies. We are applying spatial transcriptomics and multiplex immunofluorescence (IF) to non-lesional and lesional skin biopsies from morphea patients to generate high-resolution maps of gene and protein expression. Our central hypothesis is that distinct cellular niches promote disease progression through spatially organized signaling pathways. In preliminary work, we have identified phosphorylated STAT3 (pSTAT3) as being highly expressed in endothelial cells in more severe subtypes of morphea. This finding points to a potentially understudied role for endothelial activation and suggests that pSTAT3 may serve both as a marker and as a driver of disease severity.

Problemstilling

Localized scleroderma (morphea) is a chronic inflammatory connective tissue disorder with poorly understood pathogenesis and no reliable biomarkers to predict disease progression or treatment response. Despite clinical advances in other inflammatory diseases, morphea still remains understudied in terms of molecular pathways and spatial tissue dynamics, which are crucial for understanding the development of the lesions and disease progression.

Baggrund

Localized scleroderma (also known as morphea) is a is a chronic inflammatory connective tissue disorder that mostly affects the skin and underlying tissues. The condition is characterized by an initial perivascular lymphocytic infiltrate that leads to over deposition of collagen fibers, resulting in thickened, hardened, and often disfiguring skin lesions (1). The Clinical presentation of morphea can be highly variable, from small, superficial plaques to widespread, deeply infiltrating lesions affecting fascia and muscle (2). Even though morphea is a distinct disease from systemic sclerosis, they still share key features such as immune dysregulation and excessive extracellular matrix deposition. The disease can be particularly aggressive in children and middle-aged adults, and there are currently no reliable biomarkers to predict progression or treatment response (1, 3).
Immune-mediated processes are central to morphea pathogenesis. Th1-, Th2-, and Th17-related cytokine activity has been observed, with negatively impacted regulatory T cell populations (1,2). Despite the rise of biological treatment in inflammatory/rheumatic group of diseases, the cellular and molecular drivers of lesion development in morphea and variability between clinical subtypes remain poorly understood (4). Endothelial cells, fibroblasts, epithelial cells and immune cells interact in complex spatial arrangements within the skin, contributing to repeated cycle of inflammation and fibrosis. Understanding these cell-to-cell interactions in situ is crucial step into identifying the key pathways involved in the disease progression and ultimately developing potential targeted therapies.

1. Papara C, De Luca DA, Bieber K, Vorobyev A, Ludwig RJ. Morphea: The 2023 update. Front Med (Lausanne). 2023;10:1108623.
2. Fett N, Werth VP. Update on morphea. J Am Acad Dermatol. 2011;64(2):217–228.
3. Mertens JS, Seyger MM, Thurlings RM, Radstake TR, de Jong EM. Morphea and eosinophilic fasciitis: an update. Am J Clin Dermatol. 2017;18(4):491–512.
4. Kinkhabwala A, Herbel C, Pankratz J, Yushchenko DA, Rüberg S, Praveen P, et al. MACSima imaging cyclic staining (MICS) technology reveals combinatorial target pairs for CAR T cell treatment of solid tumors. Sci Rep. 2022;12:1911.

Metoder

We will focus on spatial and functional profiling of lesional and non-lesional skin from morphea patients:

-Spatial Transcriptomics (ST):
Using the Curio Seeker platform, we will generate spatially resolved transcriptomic maps from frozen skin biopsies. This technique will allow us to profile the transcriptomes of cells in their native tissue context at near single-cell resolution. Our aim is to identify unique gene expression signatures associated with fibrotic regions, perivascular zones, and immune infiltrates (5).

-Multiplex Immunofluorescence (IF):
We will use a high content IF platform to detect and localize key proteins, including pSTAT3, in the same biopsy samples. This technique enables detection of multiple markers simultaneously, capturing cellular phenotypes and post-translational modifications such as phosphorylation (6). Co-staining with endothelial, immune, epithelial and stromal markers will give a better insight to define spatial map of cells in different regions of the skin.

-In Vitro Validation:
To test hypotheses arising from spatial analyses, we will perform in vitro validation experiments.

1. Curio Bioscience. Seeker Whole Transcriptome Spatial Mapping. [Internet]. [cited 2025 Apr 29]. Available from: https://curiobioscience.com/seeker/
2. Kinkhabwala A, Herbel C, Pankratz J, Yushchenko DA, Rüberg S, Praveen P, et al. MACSima imaging cyclic staining (MICS) technology reveals combinatorial target pairs for CAR T cell treatment of solid tumors. Sci Rep. 2022;12:1911.

Tidsplan

Month 1-39 (PhD project): ethical permits, sample collection, optimization of modern techniques and troubleshooting, building initial hypothesis based on the explorative work, merging spatial data (multiplex-IF and ST)

Month 39-42: In vitro validation of key hypotheses and initiation of in vivo studies, including the development of a mouse model

Forventede resultater og impact

This study will be the first to apply spatial transcriptomics and multiplex IF to morphea lesions, providing a novel systems-level view of its pathogenesis. This is also one of the first spatial transcriptomics studies with higher resolution to be applied on skin tissues. By focusing on certain activation pathways, we hope to observe early events in lesion formation and uncover new therapeutic targets. The integration of transcriptomic, proteomic, and spatial data will generate insight into cellular interactions in morphea, which may be applicable to other fibrotic or inflammatory conditions.

Øvrige projektdeltagere og samarbejdsrelationer

The project is conducted under the supervision of Cord Herbert Brakebusch, with collaborations involving Thomas Krieg´s lab in Cologne, Germany. Additional technical support will be provided by several BRIC facilities.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Salary (month 1-39) : 28,896.97/ month (on 1/2023) + non-pensionable PhD Fellow support

Funding of salary : Brakebusch group and financial support by the Marie Sklodowska-Curie COFUND DISCOVER from the Research Executive Agency (REA) under the power delegated by the European Commission

Project expenses: Brakebusch group

The amount I am asking for:

Salary (month 39-42): 102 390 DKK

Project expenses: 10000 DKK

Total: 112 390 DKK

Ivona Ćudina

Date of birth: 10/01/1997

Nationality: Croatian

Gender: Female

CONTACT

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europass

WORK EXPERIENCE

15/04/2023 – CURRENT

PhD fellow Copenhagen University (Medical university)

Brakebusch group
EU HORIZON 2020: DISCOVER fellowship

Title: "The application of spatial technologies to the investigation of diseases with unknown pathogenesis"

- Conducted research on skin samples from patients with morphea, focusing on investigating potential pathogenesis.
- Utilized advanced spatial technologies, including multiplex immunofluorescence (spatial proteomics) and spatial transcriptomics, to analyze and interpret complex biological data.
- Developed new approaches to treatment options by identifying key molecular pathways involved in the disease.
- Collaborated with an interdisciplinary team to enhance the understanding of morphea and improve patient outcomes.

Project in collaboration with: Thomas Krieg´s group (University of Cologne, Germany)

15/01/2023 – 14/04/2023

Higher education research assistant Copenhagen University (Medical university)

Brakebusch group
EU HORIZON 2020: DISCOVER fellowship

Title: "The application of spatial technologies to the investigation of diseases with unknown pathogenesis"

- Conducted research on skin samples from patients with morphea, focusing on investigating potential pathogenesis.
- Utilized advanced spatial technologies, including multiplex immunofluorescence (spatial proteomics) and spatial transcriptomics, to analyze and interpret complex biological data.
- Developed new approaches to treatment options by identifying key molecular pathways involved in the disease.
- Collaborated with an interdisciplinary team to enhance the understanding of morphea and improve patient outcomes.

01/06/2022 – CURRENT

MEDICAL DOCTOR Croatian Institute of Public Health (Hrvatski zavod za javno zdravstvo - HZJZ)

"Healthy living" promotion

https://zivjetizdravo.eu/
Opportunity to process and use statistics, also primary prevention of obesity and sexually transmitted diseases. Creation of national programs and campaigns.

20/10/2021 – 31/05/2022 Zagreb

GENERAL PRACTITIONER (MEDICAL DOCTOR) Health Center Zagreb – Centar

EDUCATION AND TRAINING

2015 – 2021 Zagreb, Croatia

DOCTOR OF MEDICINE The University of Zagreb, School of Medicine

Overall GPA - 4.585
ECTS 360/ 6 years
The course of medical studies lasts six years, thus uniting the undergraduate and the graduate level into one single whole (0+6), which has already been accepted by the majority of European universities. The curriculum leading to the Doctor of Medicine degree at the University of Zagreb School of Medicine comprises mandatory general premedical courses, as well as four major groups of professional courses: basic medical sciences, pre-clinical medicine, clinical medicine and public health.

Introduction to R and R modelling Copenhagen university (PhD course)

Introduction to python coding Copenhagen university (PhD course)

08/2022 Croatia

DATABASE USAGE BASICS CERTIFCATE educational program SRCE

CURRENT

INTRODUCTION TO STATISTICS Stanford- online classes/ Coursera

2022 Croatia

BASICS OF USING SPREADSHEETS CERTIFICATE/ ADVANCED COURSE educational program SRCE

LANGUAGE SKILLS

MOTHER TONGUE(S): Croatian

OTHER LANGUAGE(S): English | Danish | German | Italian

DIGITAL SKILLS

Microsoft Office: proficient user of Word, Excel and Powerpoint

CONFERENCES AND SEMINARS

05/2024 Odenske, Denmark

Invited speaker: Novel insight into the pathogenesis of morphea by using multiplex IF

Annual singel cell conference

03/2022

OPENING LECTURE AT THE CONGRESS OF EMERGENCY MEDICINE, RIJEKA

"Tommorow I work in ER"

06/2022

OPENING LECTURE AT THE CONGRESS OF EMERGENCY MEDICINE, VODICE

"Tommorow I work in ER"

Link https://hitna2022.conventuscredo.hr/program-kongresa/

PROJECTS

2018 – CURRENT

ANUAL TENNIS TOURNAMENT AT THE SCHOOL OF MEDICINE, ZAGREB

As the leader of tennis club, I had an opportunity to engage with different students and include them in this tournament with the aim of promoting healthy lifestyles as well as meeting new people/ new friends.

2019 – 2021

IMPORTANCE OF INTERMITENT BLOOD GLUCOSE MONITORING IN REDUCTION OF GLUCOVARIABILITY AND IMPROVMENT OF PARAMTERES RELATED TO COMPLICATIONS OF DABETES MELLITUS

The written theme was the subject of my bachelor/masters thesis, which was conducted in Vuk Vrhovac University Clinic for Diabetes, Endocrinology and Metabolic Diseases, Merkur.

2019 – 2021

TOMMOROW I WORK IN ER

The project "Tomorrow I'm working in the emergency room" was started less than 4 years ago by the leaders of the
Student section for anesthesiology, resuscitation and intensive care medicine. In the 9 lectures we held in the 2020./2021. academic year, the number of participants ranged from 150 to 380 per lecture. The scope of the project was shown by the figure of 250 doctors of medicine who attended the aforementioned lectures.

2021

PAIN SYMPOSIUM

This Symposium was focused on pain as one of the main problems of almost all branches of medicine. Every medical student, as well as students of related sciences, are familiar with the concept of pain, but with this project, we wanted to bring that term even closer. The goal was to show what all types of pain exist, which specialization in medicine deal with the issue of pain and most importantly, how to help a patient who has exactly that symptom.

2021

ANESTHESIOLOGY AND INTENSIVE MEDICINE MONTH

Idea was to connect the targeted topics of this demanding specialization via 10 different lectures.

HONOURS AND AWARDS

2020 School of Medicine in Zagreb

DEAN'S AWARD FOR THE BEST STUDENT IN SCHOOL OF MEDICINE ZAGREB

Overall GPA 5.0 in academic year 2019./2020.

2021 University of Zagreb, Croatia

CHANCELLOR'S AWARD FOR SOCIALLY USEFUL WORK

During the Academic year 202o./2021. I had an opportunity to be one of the organizers of different activities (volunteering and teaching lessons) for which I was awarded with this prestige award.

Link http://www.unizg.hr/fileadmin/rektorat/Istrazivanja/Znanstvena_postignuca/Nagrade/Rektorova/2020_2021_Dobitnici_Rektorove_nagrade.pdf

2021 University of Zagreb, Croatia

DEAN'S AWARD FOR THE BEST RESEARCH PAPER

"Comparison of the number of biopsies and operative resections of prostate and lung cancer in University Hospital Center Zagreb before and during the COVID-19 pandemic"

The research was conducted in University Hospital Center Zagreb, in Pathology and Citology department with the leadership od proffessor Marijana Ćorić.

Link https://mef.unizg.hr/dodijeljene-dekanove-nagrade-najboljim-studentima-fakulteta-u-protekloj-akademskoj-godini/

2021 Croatian Society of Pathology

SERGEJ SALTYKOW AWARD FOR THE BEST STUDENT RESEARCH PAPER

BEST RESEARCH PAPER IN PATHOLOGY RESEARCH

"Comparison of the number of biopsies and operative resections of prostate and lung cancer in UHC Zagreb before and during the COVID-19 pandemic"

THE HEAD OF TENNIS CLUB (MEDICAL STUDENTS CLUB)

From an early age, I have been active tennis player and as part of the activities of the my school, I was one of the founders of the Tennis Club at the School of Medicine in Zagreb. As part of these, I won several gold and silver medals and was a member of the most awarded tennis team in the history of the University.

THE HEAD OF THE SECTION FOR ANESTHESIOLOGY AND REANIMATOLOGY

In the last two semesters of college, I became the head of the Student Section for Anesthesiology and resuscitation, as part of which I organize in February 2021. an interdisciplinary " Pain Symposium", with more than 300
participants and officially recognized by Croatia Medical Committee. During the COVID-19 pandemic in cooperation with prof.dr.sc. Visnja Nesek Adam and the Clinical Hospital "Sveti Duh" I participate in the organization of volunteering of medical students. As part of the activities of the student section, I participate in the implementation of the project: "Tomorrow
I work in the emergency room "and" Month of Anesthesiology and Intensive Care Medicine ", with the aim of additional education of young doctor/ students.

MEMBER OF "SPORTMEF" ORGANISATION

SPORTMEF stands for sports organisation of students in School of Medicine in Zagreb. We held multiple projects and volunteering activities; with emphasis on our biggest project: "162 stairs".

Link https://mef.unizg.hr/humanitarna-utrka-162-stube-2-4-subota-u-12-sati/

School of Medicine in Zagreb: 2018./2019., 2019./2020.

TUTOR IN THE DEPARTMENT: MEDICAL MICROBIOLOGY AND PARASITOLOGY

Student teachers/ tutors are recruited among top students who have completed Medical Microbiology and Parasitology course with excellence. Their duties include helping with teaching/learning of labs and other practicals and working with other students. Tutors must know the macroscopic and microscopic appearance of the preparations, understand the functioning of microbiological tests (PCR, antibiogram, electron microscope, culture on a nutrient medium), and present the functioning of those to other colleagues.

School of Medicine in Zagreb; 2018./2019. , 2019./2020.

TUTOR IN THE DEPARTMENT: PATHOPHYSIOLOGY

Student teachers/ tutors are recruited among top students who have completed the Pathophysiology course with excellence. Their duties include helping with teaching/learning of labs and other practicalls and working with other students. Also, during the time the student teachers must observe one specific, officially given, topic and analyze the same.
The topic I observed was: "Two-way musculoskeletal inter-regulation according to Wolff's law."

VOLUNTEERING

2018 – 2021 Zagreb, Croatia

INTERNSHIP AND VOLONTEERING IN VUK VRHOVAC UNIVERSITY CLINIC FOR DIABETES, ENDOCRINOLOGY AND METABOLIC DISEASES, MERKUR UNIVERSITY HOSPITAL

My main focus during the studies was diabetology/ obesity and I had an opportunity to learn and to "work" with the best clinicans in diabetology in the Republic of Croatia. I spent a lot of weeks each year in this clinic in order to grow and learn as a proffessional.

2020 – 2021 Zagreb

VOLUNTEERING OF MEDICAL STUDENTS IN CLINICAL HOSPITAL HOLY SPIRIT, ZAGREB

I was one of the main organizers and one of the volunteers in the actions which were made in order to help the medical stuff during the pandemic of coronavirus. Those actions included: triage, volunteering in the ER and micriobiology testing and sampleing.

PUBLICATIONS

2019

Increased Apolipoprotein A1 Can Suggest the Presence of Latent Autoimmune Diabetes and a Lower Cardiovascular Risk Compared with Type 2 Diabetes

SPOMENKA LJUBIC, ANAMARIJA JAZBEC, IVANA ANTAL, IVONA CUDINA, MARTINA TOMIC i MARIJANA VUCIC LOVRENCIC
Diabetes 2019 Jun; 68(Supplement 1)

2020

Increase in triglycerides seems to overwhelm glucovariability in development of diabetic retinopathy

S. Ljubic, I. Cudina, A.Jazbec, M. Tomic, D. Rahelic
DIABETES TECHNOLOGY & THERAPEUTICS, 23 VOLUME
140 HUGUENOT STREET, 3RD FL, NEW ROCHELLE, NY 10801 USA: MARY ANN LIEBERT, INC, 2021.

https://scholar.google.com/scholar?oi=bibs&cluster=9632796525624477543&btnI=1&hl=en

2020

Decreased Serum Vitamin D Level Implies Increased Cardiovascular Risk in Diabetes

SPOMENKA LJUBIC, ANAMARIJA JAZBEC, IVONA CUDINA, MARTINA TOMIC i DARIO RAHELIC
Diabetes 2020 Jun; 69(Supplement 1)

2020

Efficacy of a fixed combination of insulin degludec and glp-1 receptor agonist liraglutide (Xultophy) in patient with type 2 diabetes

IVONA ĆUDINA, LESTER TONI DOBRIĆ, DARIO RAHELIĆ, SPOMENKA LJUBIĆ
2020 E-poster in Book of Abstracts of the 20th Zagreb International Medical Summit for students and young doctors; Liječnički vjesnik, Volume 142, Supplement 5, 2020

2020

Multimodalne mogućnosti utjecaja na razvoj demencije

Dobrić LT, Kalinić D, Bazina Martinović A, Cudina I, Mimica N
E-poster in Abstracts of the Croatian Congress on Alzheimer's Disease (CROCAD-20v) with International Participation; Neurologia Croatica, Volume 69, Supplement 2, 2020

https://www.researchgate.net/publication/ 345729070_Multimodalne_mogucnosti_utjecaja_na_razvoj_dem

2020

The role of MRI in diagnosis of Alzheimer's disease

Lester Toni Dobrić , Ivona Ćudina , Marijana Radić , Fran Borovečki

E-poster in Book of Abstracts of the 16th International Biomedical Croatian Student Summit; Liječnički vjesnik, Volume 142, Supplement 3, 2020

ISSN 1849-2177

2020

The potential of virtual reality in the treatment of phobias

Lester Toni Dobrić , Kristijan Harak , Ivona Ćudina , Robert Gečević , Robert Likić

E-poster in Book of Abstracts of the 16th International Biomedical Croatian Student Summit; Liječnički vjesnik, Volume 142, Supplement 3, 2020

ISSN 1849-2177

2020

Primary eosinophilic central nervous system vasculitis: a case report

Ivona Ćudina , Lester Toni Dobrić , Marijana Radić , Fran Borovečki

E-poster in Book of Abstracts of the 16th International Biomedical Croatian Student Summit; Liječnički vjesnik, Volume 142, Supplement 3, 2020

ISSN 1849-2177

2020

Immunotherapy in advanced non-small cell lung cancer treatment

Robert Gečević, Lester Toni Dobrić , Ivona Ćudina , Robert Likić

E-poster in Book of Abstracts of the 16th International Biomedical Croatian Student Summit; Liječnički vjesnik, Volume 142, Supplement 3, 2020

ISSN 1849-2177

2020

Hemolytic anemia as side effect of usage of antimicrobial drugs in people with glucose 6 phosphate dehydrogenase deficiency

Ivona Ćudina , Robert Gečević , Lester Toni Dobrić , Kristijan Harak , Robert Likića

2020 E-poster in Book of Abstracts of the 16th International Biomedical Croatian Student Summit; Liječnički vjesnik, Volume 142, Supplement 3, 2020

ISSN 1849-2177

2021

Ruptured blood blister-like aneurysm of rare location successfully treated by flow- diversion device: case report

L.T. Dobric , I. Cudina , K. Toljan , I. Jovanovic , I. Peric , J. Ljevak , Z. Poljakovic
EUROPEAN JOURNAL OF NEUROLOGY 28, 591-591, 2021

2021

Usporedba TNM klasifikacije i stadija karcinoma pluća u KBC-u Zagreb prije i za vrijeme pandemije

Marin Glavčić, Ivona Ćudina, Pero Hrabač, Marijana Ćorić

https://doi.org/10.26800/LV-143-supl3-KI01

2021

Usporedba TNM klasifikacije karcinoma prostate u KBC-u Zagreb prije i za vrijeme COVID-19 pandemije

Ivona Ćudina, Marin Glavčić, Marijana Ćorić, Pero Hrabač

https://doi.org/10.26800/LV-143-supl3-KI02

2022

The use of adalimumab in the treatment of a patient with a severe case of spondyloarthritis

Ivona Ćudina, Iva Žagar (mentor), Porin Perić, Lester Toni Dobrić

2022

Perioperative physiotherapy- text book for students

I am one of the autors of this textbook thast is currently being published for physiotherapy students in croatian language.
theme: "Postoperative lung complications and treatment"

Nesek Adam V. and authors

2022

Time above range emerged as valuable predictor of albuminuria in patients with latent autoimmune diabetes after follow-up period

S Ljubic, I Cudina, A Jazbec, M Tomic, T Bulum, D Rahelic

2021

Comparison of TNM classification of lung cancer in UHC Zagreb before and during the COVID-19 pandemic

Cudina I, Glavcic M, Hrabac P, Coric M

Journal Name: Liječnički vjesnik | **Volume, Issue and Pages**: Vol. 143, Supplement 3, KI01

2021

Comparison of TNM classification of prostate cancer in UHC Zagreb before and during the COVID-19 pandemic

Authors: Glavcic M, Cudina I, Hrabac P, Coric M | **Journal Name**: Liječnički vjesnik | **Volume, Issue and Pages**: Vol. 143, Supplement 3, KI02

2024

Cystatin C seems to be superior to homocysteine as reliable markers of early diabetic nephropathy

Write here the description...

Authors: S Ljubic, A Jazbec, I Cudina, M Tomic, T Bulum, D Rahelic | **Journal Name**: DIABETOLOGIA

The application of spatial technologies to the investigation of localized scleroderma

Localized scleroderma (also known as morphea) is a is a chronic inflammatory connective tissue disorder that mostly affects the skin and underlying tissues. The condition is characterized by an initial perivascular lymphocytic infiltrate that leads to over deposition of collagen fibers, resulting in thickened, hardened, and often disfiguring skin lesions (1). The Clinical presentation of morphea can be highly variable, from small, superficial plaques to widespread, deeply infiltrating lesions affecting fascia and muscle (2). Even though morphea is a distinct disease from systemic sclerosis, they still share key features such as immune dysregulation and excessive extracellular matrix deposition. The disease can be particularly aggressive in children and middle-aged adults, and there are currently no reliable biomarkers to predict progression or treatment response (1, 3).

Immune-mediated processes are central to morphea pathogenesis. Th1-, Th2-, and Th17-related cytokine activity has been observed, with negatively impacted regulatory T cell populations (1,2). Despite the rise of biological treatment in inflammatory/rheumatic group of diseases, the cellular and molecular drivers of lesion development in morphea and variability between clinical subtypes remain poorly understood (4). Endothelial cells, fibroblasts, epithelial cells and immune cells interact in complex spatial arrangements within the skin, contributing to repeated cycle of inflammation and fibrosis. Understanding these cell-to-cell interactions in situ is crucial step into identifying the key pathways involved in the disease progression and ultimately developing potential targeted therapies.

Project Aim and Hypothesis

The goal of this project is to uncover the cellular and molecular mechanisms driving morphea using advanced spatial and molecular technologies. We are applying spatial transcriptomics and multiplex immunofluorescence (IF) to non-lesional and lesional skin biopsies from morphea patients to generate high-resolution maps of gene and protein expression. Our central hypothesis is that distinct cellular niches promote disease progression through spatially organized signaling pathways.

In preliminary work, we have identified phosphorylated STAT3 (pSTAT3) as being highly expressed in endothelial cells in more severe subtypes of morphea. This finding points to a potentially understudied role for endothelial activation and suggests that pSTAT3 may serve both as a marker and as a driver of disease severity.

Methodological Approach

We will focus on spatial and functional profiling of lesional and non-lesional skin from morphea patients:

1. **Spatial Transcriptomics (ST)**:
   Using the Curio Seeker platform, we will generate spatially resolved transcriptomic

maps from frozen skin biopsies. This technique will allow us to profile the transcriptomes of cells in their native tissue context at near single-cell resolution. Our aim is to identify unique gene expression signatures associated with fibrotic regions, perivascular zones, and immune infiltrates (5).

2. **Multiplex Immunofluorescence (IF)**:
   We will use a high content IF platform to detect and localize key proteins, including pSTAT3, in the same biopsy samples. This technique enables detection of multiple markers simultaneously, capturing cellular phenotypes and post-translational modifications such as phosphorylation (6). Co-staining with endothelial, immune, epithelial and stromal markers will give a better insight to define spatial map of cells in different regions of the skin.

3. **In Vitro Validation**:
   To test hypotheses arising from spatial analyses, we will perform in vitro validation experiments.

Significance and Impact

This study will be the first to apply spatial transcriptomics and multiplex IF to morphea lesions, providing a novel systems-level view of its pathogenesis. This is also one of the first spatial transcriptomics studies with higher resolution to be applied on skin tissues. By focusing on pSTAT3 in endothelial cells, we hope to observe early events in lesion formation and uncover new therapeutic targets. The integration of transcriptomic, proteomic, and spatial data will generate insight into cellular interactions in morphea, which may be applicable to other fibrotic or inflammatory conditions.

References

1. Papara C, De Luca DA, Bieber K, Vorobyev A, Ludwig RJ. Morphea: The 2023 update. Front Med (Lausanne). 2023;10:1108623.
2. Fett N, Werth VP. Update on morphea. J Am Acad Dermatol. 2011;64(2):217–228.
3. Mertens JS, Seyger MM, Thurlings RM, Radstake TR, de Jong EM. Morphea and eosinophilic fasciitis: an update. Am J Clin Dermatol. 2017;18(4):491–512.
4. Kinkhabwala A, Herbel C, Pankratz J, Yushchenko DA, Rüberg S, Praveen P, et al. MACSima imaging cyclic staining (MICS) technology reveals combinatorial target pairs for CAR T cell treatment of solid tumors. Sci Rep. 2022;12:1911.
5. Curio Bioscience. Seeker Whole Transcriptome Spatial Mapping. [Internet]. [cited 2025 Apr 29]. Available from: https://curiobioscience.com/seeker/
6. Kinkhabwala A, Herbel C, Pankratz J, Yushchenko DA, Rüberg S, Praveen P, et al. MACSima imaging cyclic staining (MICS) technology reveals combinatorial target pairs for CAR T cell treatment of solid tumors. Sci Rep. 2022;12:1911.

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	Lars Rolighed, Medical Doctor, PhD, Clinical associate professor
Arbejdssted/ Institution	Aarhus University Hospital, Department of OtoRhinoLaryngology
Adresse	Palle Juul-Jensens Blvd. 165, indgang J, plan 2 J219, 8200 Aarhus
Tlf.nr.	+45 81 49 12 15
e-mail	kharaf@rm.dk

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)
Projekttitel The Impact of Total Thyroidectomy on Parathyroid Function and Quality of Life
Formål To improve postoperative outcomes and quality of life in thyroidectomy patients by using intraoperative PTH monitoring to guide individualized care and prevent hypoparathyroidism.
Problemstilling

Currently, there is a lack of precise, individualized guidelines for postoperative management of thyroidectomy patients. Although parathyroid hormone (PTH) has a short half-life and can be measured intraoperatively (ioPTH), this potential early predictor of hypoPT is not systematically used to guide postoperative care.

There is a clear need for evidence on how ioPTH monitoring can be applied as a clinical decision-making tool—to identify low-risk patients who may safely avoid unnecessary blood tests and hospitalization, and to tailor early supplementation strategies for high-risk patients.

Baggrund

Total thyroidectomy (TT) is a widely used surgical procedure, but it carries a significant risk of impairing parathyroid gland function, potentially leading to hypoparathyroidism (hypoPT). This condition causes low calcium levels in the blood and may result in both acute symptoms and long-term complications such as reduced quality of life, kidney impairment, and increased dependency on lifelong medication.

Metoder

The project includes two cohort studies and two randomized controlled trials. Study 1 investigates incidence and risk factors retrospectively. Study 2 prospectively examines the association between ioPTH decrease and patient-reported quality of life. Study 3 tests if low-risk patients can safely avoid routine postoperative blood tests. Study 4 assesses early, high-dose supplementation in high-risk patients

Tidsplan dec/2025 – dec/2028

Forventede resultater og impact

This PhD project represents state-of-the-art research, with the potential to establish groundbreaking standards in postoperative patient management and quality care. We aim to reduce the risk and impact of hypoparathyroidism after thyroid surgery by improving postoperative care. Studies 1 and 2 explore how parathyroid function affects quality of life, laying the groundwork for personalized follow-up. Study 3 tests whether routine blood tests can be safely skipped in low-risk patients, while Study 4 evaluates if early high-dose supplementation benefits high-risk patients. Together, these results could shape future clinical guidelines and improve outcomes globally.

Øvrige projektdeltagere og samarbejdsrelationer

Khalil Rafiqi, MD, Department of Otorhinolaryngology, Head and Neck Surgery
Aarhus University Hospital
Rasmus Reinke, MD, PhD, Department of Otorhinolaryngology, Aarhus University Hospital
Jacob Lilja-Fischer, MD, Department of Otorhinolaryngology, Aarhus University HospitalLars Rejnmark, MD, PhD, DrMSc, Professor, Department of Endocrinology and Internal Medicine, Aarhus University Hospital

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Budget (all in DKK)

Salary	2026	42.000 per month	x 12	504.000
	2027	43.000 per month	x 12	516.000
	2028	44.000 per month	x 12	528.000
			Salary total	1.548.000

Fee	Aarhus University	40.000	x 3	120.000
IT	Hardware and software			30.000
Publication fee		20.000	x 3	60.000
Conference attendance		25.000	x 3	75.000
International course and/or workshop		10.000	x 2	20.000
Local meetings		3500	x 2	7.000
			Budget total	1.860.000

CV

Curriculum Vitae
Lars Rolighed. Aarhus, January 2025
H-index: 29
Citations (2025): 2502

Birth 19th of July 1978

Graduate from Medical School at Aarhus University 2004

2014 PhD Graduate with the title *Effects of vitamin D treatment in primary hyperparathyroidism*.

2014 Staff specialist, Department of Surgery, Aarhus University Hospital.

2016 Consultant Surgeon, Department of Otorhinolaryngology, Aarhus University Hospital (80%).

2016 Consultant Surgeon, Department of Surgery, Aarhus University Hospital (20%).

2016 Associate Professor, Department of Otorhinolaryngology, Aarhus University Hospital.

2018 Member of Faculty, PARAT programme in European Society of Endocrinology

2024 Fellow of the European Board of Surgery (FEBS) in Endocrine Surgery

Significant Grants

2024 Borregaard Clinical Ascending Investigator Grant (5 year), Novo Nordisk Fonden

Scientific production (66 publications):

62 original papers and 4 reviews.

Co-author of two Danish National Guidelines: *Primary hyperparathyroidism, Adrenal incidentalomas*.

Keynote speaker at "3rd Annual symposium in Endocrine Surgery", Yale University Hospital, USA 2015.

6 international oral presentations and 15 national oral presentations

29 international poster presentations

Performing reviews for several international medical journals

Opponent at 2 PhDs:

- Mikkel Pretorious 2023, Norway: *Management of mild primary hyperparathyroidism*
- Erling J Setså 2024, Norway: *Recurrent laryngeal nerve injury and nerve recovery by EMG, accelerometry and direct laryngoscopy*

Teaching experiences:

Head responsible teacher at courses of Learning, Guidance and Mentoring for young medical doctors.

Teaching clinics for medical students.

Theoretical and clinical lessons in 2nd, 4th, and 5th year at Medical School, Aarhus University.

Coordinating education for young doctors, 2014-2015, Department of Surgery, Aarhus University Hospital.

Teaching laparoscopic operations for future surgeons and gynaecologists, 2013-2016.

Teaching lessons on PhD course in *Bone Biology*, Aarhus University.

Instructor in open and laparoscopic surgery, International Workshop of Surgery, Davos, Switzerland 2015.
Local morning teaching in several Departments, for young doctors, clinical nurses, etc. > 30 times.
Large experience in clinical teaching during surgical procedures.
Responsible for parathyroid teaching at national course in Paraclinics for future ENT specialist doctors.

Guidance:

Main supervisor for 1 Post. Doc.:

- Sofie Louise Rygård 2025-: *Improving treatment and outcome for patients with small cancers in the thyroid gland*

Main supervisor for 2 PhD students:

- Rasmus Reinke 2024: *Use of fluorescence in thyroid operations*
- Nichlas Udholm 2025-: *Hemithyroidectomy and minimal invasive treatments on the thyroid gland*

Co-supervisor for 4 PhD students:

- Henriette Ejlsmark-Svensson 2018: *Primary hyperparathyroidism – comorbidity, cardiovascular status and health related quality of life*
- Lise Sofie Bislev 2018: *Cardiovascular- and musculoskeletal effects of vitamin D treatment*
- Ali Abood 2024: *Autofluorescence-guided thyroid surgery: impact on parathyroid preservation and hypoparathyroidism*
- Anne Louise V Svenningsen 2025-: *Bisphosphonate vs. Placebo Prior to Parathyroidectomy in Primary Hyperparathyroidism*

Main supervisor and examination for 1 medical research-year student:

- Elizabeth Harregaard Vlk 2021: *Outcome and prognosis after adrenal metastasectomy*

Co-supervisor for 1 medical research-year student:

- Niels Frederik Jakobsen 2014: *Studies on familiar hypocalciuric hypercalcemia*

Main supervisor (and examination) for 5 medical students in specialist research paper.

- Erik Posselt Gunnersen 2021: *Clinical evaluation of autofluorescence used in thyroid operations to identify the parathyroid glands*
- Jakob Egsgaard Thomsen 2018: *Hypothyroidism after hemithyroidectomy and associated risk factors*
- Line Klestrup 2020: *Use of Fluorescence during Thyroidectomy to Reduce Postoperative Hypoparathyroidism*
- Samantha Nelson 2020: *Surgical treatment of primary aldosteronism – biochemical and clinical effects*

- Simon Kjeldsen 2020: *Transient and persistent hypoparathyroidism in patients undergoing total Thyroidectomy*

Informal supervisor in several research projects. Clinical mentor for several young doctors.
Head teacher on several courses in Guidance for young doctors.
Course in Supervision for PhD main supervisor 2021
Course in guidance for consultant doctors 2021

Surgical experience:

Approximately 15 years of surgical experience. Performed over 1000 endoscopies, more than 600 laparoscopic procedures, and more than 2000 open procedures. Endocrine operations: approximately 350 adrenalectomies, 900 thyroidectomies, and over 1300 parathyroidectomies.

Memberships:

European Society of Endocrine Surgeons
European Society of Endocrinology
Danish Bone Society
Danish Society of Otorhinolaryngology
Danish Head and Neck Surgical Society
Danish Society of Endocrinology
International Society of Technologies for Endocrine Surgery

Attendance in clinical courses

National mandatory courses for young doctors.
Supplementary national courses in Endoscopy and Laparoscopy (MIUC I, II, and III).
Open and laparoscopic surgery, Davos, Switzerland.
Course in Definitive Surgical Trauma Care (DSTC).
Course in Endocrine surgery, IAES, Greece.
Several courses in Statistics.
Course in Good Clinical Practice (GCP).
Mandatory courses for PhD students.
1st TOETVA Cadaver Course, Vienna, Austria

Prizes:

Winner 2013 President´s Poster Competition Award at The American Society for Bone and Mineral Research, Baltimore, USA.

Attendance and presentations in national and international scientific meetings

Danish Surgical Society

Danish Endocrine Society

Danish Bone Society

Danish Society of Otorhinolaryngology

Danish Head and Neck Surgical Society

European Calcified Tissue Society

European Society of Endocrine Surgeons

European Society of Endocrinology

American Thyroid Association

American Society of Bone and Mineral Research

International Osteoporosis Foundation

International Parathyroid meeting

Scandinavian meeting in Endocrine Surgery

International Federation of Head and Neck Oncologic Societies

1st International meeting on Parathyroid fluorescence

1st Expert Workshop on Parathyroid Disorders

2nd Expert Workshop on Parathyroid Disorders, Member of Faculty

Publikationsliste

Selected publications

Primary hyperparathyroidism: intraoperative PTH-measurements.
Rolighed L, Heickendorff L, Hessov I, Garne JP, Roth SA, Christiansen P.
Scand J Surg. 2004;93(1):43-7.
PMID: 15116819

BMD improvements after operation for primary hyperparathyroidism.
Rolighed L, Vestergaard P, Heickendorff L, Sikjaer T, Rejnmark L, Mosekilde L, Christiansen P.
Langenbecks Arch Surg. 2013 Jan;398(1):113-20. Epub 2012 Nov 7.
PMID: 23132462

Bone involvement in primary hyperparathyroidism and changes after parathyroidectomy.
Rolighed L, Rejnmark L, Christiansen P.
Eur Endocrinol. 2014 Feb;10(1):84-87.
PMID: 29872470

Muscle function is impaired in patients with "asymptomatic" primary hyperparathyroidism.
Rolighed L, Amstrup AK, Jakobsen NF, Sikjaer T, Mosekilde L, Christiansen P, Rejnmark L.
World J Surg. 2014 Mar;38(3):549-57.
PMID: 24101026

Vitamin D treatment in primary hyperparathyroidism: a randomized placebo controlled trial.
Rolighed L, Rejnmark L, Sikjaer T, Heickendorff L, Vestergaard P, Mosekilde L, Christiansen P.
J Clin Endocrinol Metab. 2014 Mar;99(3):1072-80. Epub 2014 Jan 13.
PMID: 24423366

No beneficial effects of vitamin D supplementation on muscle function or quality of life in primary hyperparathyroidism: results from a randomized controlled trial.
Rolighed L, Rejnmark L, Sikjaer T, Heickendorff L, Vestergaard P, Mosekilde L, Christiansen P.
Eur J Endocrinol. 2015 May;172(5):609-17. Epub 2015 Feb 2.
PMID: 25646406

Health related quality of life improves one year after parathyroidectomy in primary hyperparathyroidism: A prospective cohort study.
Ejlsmark-Svensson H, Sikjaer T, Webb SM, Rejnmark L, Rolighed L.
Clin Endocrinol (Oxf). 2018 Sep 29. doi: 10.1111/cen.13865. [Epub ahead of print]
PMID: 30267589

Hypoparathyroidism and mortality after total thyroidectomy: A nationwide matched cohort study.
Reinke R, Udholm S, Christiansen CF, Almquist M, Londero S, Rejnmark L, Rasmussen TB, Rolighed L.
Clin Endocrinol (Oxf). 2024 Apr;100(4):408-415. doi: 10.1111/cen.15037.
PMID: 38375986

Publication list Lars Rolighed (66):

Primary hyperparathyroidism: intraoperative PTH-measurements.
Rolighed L, Heickendorff L, Hessov I, Garne JP, Roth SA, Christiansen P.
Scand J Surg. 2004;93(1):43-7.
PMID: 15116819

Study of the quality of colonoscopies.
Rolighed L, Andersen L.
Ugeskr Læger. 2008 Jun 16;170(25):2232-4.
PMID: 18565311

Vitamin D status, physical performance and body mass in patients surgically cured for primary hyperparathyroidism compared with healthy controls - a cross-sectional study.
Amstrup AK, Rejnmark L, Vestergaard P, Sikjaer T, Rolighed L, Heickendorff L, Mosekilde L.
Clin Endocrinol (Oxf). 2011 Jan;74(1):130-6.
PMID: 21044111

Vitamin D treatment in primary hyperparathyroidism.
Rolighed L, Bollerslev J, Mosekilde L.
Curr Drug Saf. 2011 Apr;6(2):100-7. Review. PMID: 21524245

The effect of adding PTH(1-84) to conventional treatment of hypoparathyroidism: a randomized, placebo-controlled study.
Sikjaer T, Rejnmark L, Rolighed L, Heickendorff L, Mosekilde L; Hypoparathyroid Study Group.
J Bone Miner Res. 2011 Oct;26(10):2358-70.
PMID: 21773992

Mild Primary Hyperparathyroidism and Metabolism of Vitamin D.
J. Bollerslev, L. Rolighed and L. Mosekilde.
IBMS BoneKey 2011 July;8(7):342-351.

Vitamin D supplementation did not prevent influenza-like illness as diagnosed retrospectively by questionnaires in subjects participating in randomized clinical trials.
Jorde R, Witham M, Janssens W, Rolighed L, Borchhardt K, de Boer IH, Grimnes G, Hutchinson MS.
Scand J Infect Dis. 2012 Feb;44(2):126-32. Epub 2011 Oct 25.
PMID: 22026455

Renal stones and calcifications in patients with primary hyperparathyroidism: associations with biochemical variables.
Starup-Linde J, Waldhauer E, Rolighed L, Mosekilde L, Vestergaard P.
Eur J Endocrinol. 2012 Jun;166(6):1093-100. Epub 2012 Apr 3.
PMID: 22474170

Increased presence of capillaries next to remodeling sites in adult human cancellous bone.
Kristensen HB, Andersen TL, Marcussen N, Rolighed L, Delaisse JM.
J Bone Miner Res. 2013 Mar;28(3):574-85.
PMID: 22991221

BMD improvements after operation for primary hyperparathyroidism.
Rolighed L, Vestergaard P, Heickendorff L, Sikjaer T, Rejnmark L, Mosekilde L, Christiansen P.
Langenbecks Arch Surg. 2013 Jan;398(1):113-20. Epub 2012 Nov 7.
PMID: 23132462

PTH(1-84) replacement therapy in hypoparathyroidism: a randomized controlled trial on pharmacokinetic and dynamic effects after 6 months of treatment.

Sikjaer T, Amstrup AK, Rolighed L, Kjaer SG, Mosekilde L, Rejnmark L.
J Bone Miner Res. 2013 Oct;28(10):2232-43.
PMID: 23649554

Understanding coupling between bone resorption and formation: are reversal cells the missing link?
Andersen TL, Abdelgawad ME, Kristensen HB, Hauge EM, Rolighed L, Bollerslev J, Kjærsgaard-Andersen P, Delaisse JM.
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RET C611Y GERMLINE VARIANT IN MULTIPLE ENDOCRINE NEOPLASIA TYPE 2A IN DENMARK 1930-2021
Cancer 2025

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	Morten Nielsen, læge PhD
Arbejdssted/ Institution	Afdeling for kræftbehandling, Herlev og Gentofte Hospital
Adresse	Borgmester Ib Juuls Vej 1
Tlf.nr.	23838983
e-mail	morten.nielsen.03@regionh.dk

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

En retrospektiv undersøgelse af immunrespons til sarkomer

Formål

Vi ønsker med dette projekt at lave en detaljeret retrospektiv opgørelse over patienter som har haft udvalgte undertyper af sarkom samt lave supplerende analyser af kræftvævet fra disse patienter for at identificere molekylærbiologiske og genetiske karakteristika i både kræftceller og i tumormikromiljøet. Formålet er at skabe ny viden som på sigt kan give anledning til at afprøve immunterapi til patienter med sarkom.

Problemstilling

Sarkomer er en gruppe af sjældne kræftformer som opstår i bløddele og knogler. Selvom sygdommen er sjælden, er sarkomer en af de hyppigste kræftformer hos børn og unge. Prognosen er alvorlig og der er et stort behov for at forbedre behandlingsmulighederne. Vores hypotese er, at genetiske ændringer (herunder genfusioner) i sarkomer kan genkendes af immunsystemet og udnyttes til kræftbehandling.

Vi ønsker med dette studie at

- Kortlægge tidligere patienters sygdomsforløb mhp. at skabe viden om prognose, behandlingsrespons og naturforløb for udvalgte fusionsdrevne sarkomer
- Undersøge kræftvæv fra patienter med fusionsdrevne sarkomer for tegn på at immunsystemet kan genkende kræftcellerne

Baggrund

Der er i Danmark omkring 300 nye tilfælde af sarkom om året. Prognosen for patienter med sarkom er generelt dårlig og for patienter med spredt kræftsygdom er behandlingerne udelukkende lindrende og livsforlængende.

Nogle undertyper af sarkom har komplekse genetiske karakteristika mens andre opstår pga. velbeskrevne genfusioner som danner kræftfremmende fusionsproteiner. Begge typer genvarianter kan dog potentiels genkendes af immunsystemet og udnyttes til at målrette kræftbehandling. Vi har selv i et tidligere studie vist, at kræftceller fra flere typer af sarkom kan genkendes af patienternes egne immunceller (Nielsen et al 2020). Af særlig interesse er de såkaldt fusionsdrevne sarkomer som opstår pga. en bestemt translokation i arvemassen som danner et nyt gen med potentiale til at gøre cellen til en kræftcelle.

Metoder

Data udtrækkes fra kliniske systemer samt databaser (herunder Landsregistret for patologi og Dansk Sarkomdatabase) og bearbejdes/analyseres i statistikprogrammet R. Ansøger har

allerede erfaring med større dataudtræk fra Sundhedsplatformen. Vi har allerede indsamlet data fra kliniske systemer (Sundhedsplatformen og Midt-EPJ) for patienter med CIC-rearrangeret sarkom.

Når patientforløbene er kortlagt, vil vi undersøge allerede indsamlet kræftvæv fra de inkluderede patienter for tegn på at immunsystemet kan genkende kræftcellerne. Vi planlægger følgende analyser

- Immunhistokemi mhp. at identificere infiltration af immunceller, udtryk af immunmodulerende molekyler mm.
- Målrettede genanalyser/sekventering mhp. at karakterisere biologiske signaturer
- Kortlægning af DNA fra fusionsgener mhp. at identificere potentielle områder som kan genkendes af immunsystemet

Analyser vil blive lavet af samarbejdspartnere på patologisk afdeling, Rigshospitalet, samt Aarhus Universitetshospital eller af eksterne firmaer.

Tidsplan

Vi har allerede påbegyndt indsamling af retrospektive data fra kliniske systemer for udvalgte undertyper af sarkom. Vi forventer at have identificeret de relevante patientgrupper samt have de nødvendige tilladelser på plads i løbet af 2025 hvorefter analysearbejdet kan påbegyndes.

- Maj 2025 til december 2025: Analysere dataudtræk fra kliniske systemer samt identificere undergrupper til videre analyse
- Januar 2026 – december 2026: Udføre undersøgelser og analyser på arkivvæv

Forventede resultater og impact

Vi håber på, at disse data vil skabe ny viden om immunterapi til patienter med sarkom. Forhåbentlig kan dette danne grundlag for efterfølgende afprøvning immunterapi (vacciner og/eller celleterapi) i kliniske forskningsprojekter til disse patienter.

Øvrige projektdeltagere og samarbejdsrelationer

Projektet er forankring på Afdeling for kræftbehandling, Herlev Hospital.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Analyser af arkivvæv: 50.000

- Fremskaffelse af prøver, opstartsgebyr og oprensning af DNA
- Analyser (fx Nanostring, nCounter Pancancer IO 360 Panel)

Diverse driftsomkostninger (herunder evt. løn): 50.000

Samlet ansøgt beløb: 100.000 DKK (der søges løbende yderligere støtte til projektet)

CV – Morten Nielsen

Education

2019 PhD graduate, Clinical Cancer Research, University of Copenhagen
2012 MD (cand.med.), Faculty of Health Science, University of Copenhagen

Clinical employment

2024 - Department of Oncology, Hospital of North Zealand.
2020 - 2024 Department of Oncology, University Hospital Herlev.
2019 - 2020 Dept of lung and infectious diseases, Hospital of North Zealand.
2014 - 2015 Resident. Department of Oncology, University Hospital Herlev.
2013 - 2014 Assistant regional doctor. Aasiaat Sygehus, Greenland. *6 months*.
2013 - 2013 General Practice, Lægerne på Strandboulevarden 33.
2012 - 2013 Internship. Department of Orthopedic Surgery, Bispebjerg Hospital.
2012 - 2012 Resident. Department of Medicine, Nykøbing Falster Sygehus.

Scientific employment

2020 - Clinical research fellow (part time). National center for cancer immune Therapy, Department of Oncology, University Hospital Herlev.
2015 - 2019 Clinical research fellow. Center for Cancer Immune Therapy, Department of Oncology, University Hospital Herlev. *4 years*.
2008 - 2009 Pregraduate scholarship. Department of Neuroanaesthesiology, Rigshospitalet

Scientific presentations

Poster presentations at ASCO, ESMO, ESMO I/O, SITC, CIMT

Sub-investigator in clinical trials

LTX-315 and ACT in Advanced Soft Tissue Sarcoma; NCT03287674
Adoptive Cell Therapy Across Cancer Diagnoses; NCT03296137
TIL Therapy for Metastatic Ovarian Cancer; NCT03287674
Vemurafenib and TIL Therapy for Metastatic Melanoma NCT02354690
TIL Therapy for Metastatic Ovarian Cancer NCT02482090
Peginterferon and TIL Therapy for Metastatic Melanoma NCT 02379195

Academic teaching

2017 - External lecturer at Copenhagen University, Faculty of Health, Master of Science (MSc) in
Immunology and Inflammation
2019-2022 External lecturer the PhD course “Mechanisms of Cancer”
2018-2020 External lecturer at Danish Institute for Study abroad in Scandinavia.

Grants

2020-2025 Herlev and Gentofte Hospital, 5 years part time (20%) research grant

Publications

2023 **Nielsen M**, Monberg TJ, Sundvold V, Albieri B, Hovgaard D, Petersen MM, Krarup-Hansen A, Met Ö, Camilio K, Clancy T, Stratford R, Sveinbjornsson B, Rekdal Ø, Junker N, Svane IM. *LTX-315 and adoptive cell therapy using tumor-infiltrating lymphocytes generate tumor specific T cells in patients with metastatic soft tissue sarcoma.* Oncoimmunology 2023.

2022 **Nielsen M**, Presti M, Sztupinszki Z, Jensen AVP, Draghi A, Chamberlain CA, Schina A, Yde CW; Wojcik J, Szallasi Z, Crowther MD, Svane IM, Donia M. *Coexisting alterations of MHC class I antigen presentation and IFNg signaling mediate acquired resistance of melanoma to post-PD-1 immunotherapy.* Cancer Immunology Research 2022.

2022 Gokuldass A, Schina A, Lauss M, Harbst K, Chamberlain CA, Draghi A, Westergaard MCW, **Nielsen M**, Papp K, Sztupinszki Z, Csabai I, Svane IM, Szallasi Z, Jönsson G, Donia M. *Transcriptomic signatures of tumors undergoing T cell attack.* Cancer Immunology, Immunotherapy 2022.

2021 Draghi A, Chamberlain CA, Khan S, Papp K, Lauss M, Soraggi S, Radić HD, Presti M, Harbst K, Gokuldass A, Kverneland A, **Nielsen M**, Westergaard MCW, Andersen MH, Csabai I, Jönsson G, Szallasi Z, Svane IM, Donia M. *Rapid identification of the tumor-specific reactive TIL repertoire via combined detection of CD137, TNF, and IFNγ, following recognition of autologous tumor-antigens.* Frontiers in immunology 2021

2021 Kverneland AH, Chamberlain CA, Borch TH, **Nielsen M**, Mørk SK, Kjeldsen JW, Lorentzen CL, Jørgensen LP, Riis LB, Yde CW, Met Ö, Donia M, Svane IM. *Adoptive cell therapy with tumor-infiltrating lymphocytes supported by checkpoint inhibition across multiple solid cancer types.* JITC 2021

2020 Gokuldass A, Draghi A, Papp K, Borch TH, **Nielsen M**, Westergaard MCW, Andersen R, Schina A, Bol KF, Chamberlain CA, Presti M, Met Ö, Harbst K, Lauss M, Soraggi S, Csabai I, Szállási Z, Jönsson G, Svane IM, Donia M. *Qualitative Analysis of Tumor-Infiltrating Lymphocytes across Human Tumor Types Reveals a Higher Proportion of Bystander CD8 $^{+}$ T Cells in Non-Melanoma Cancers Compared to Melanoma.* Cancers 2020;12:3344; doi 10.3390/cancers12113344

2020 **Nielsen M**, Krarup-Hansen A, Hovgaard D, Petersen MM, Loya AC, Westergaard MCW, Svane IM, Junker N. *In vitro 4-1BB stimulation promotes expansion of CD8+ tumor-infiltrating lymphocytes from various sarcoma subtypes.* C Immunol Immunother 2020; doi: 10.1007/s00262-020-02568-x

2020 Kverneland AH, Pedersen M, Westergaard MCW, **Nielsen M**, Borch TH, Olsen LR, Aasbjerg G, Santesgoets SJ, van der Burg SH, Milne K, Nelson BH, Met Ö, Donia M, Svane IM. *Adoptive Cell therapy in Combination With Checkpoint Inhibitors in Ovarian Cancer.* Oncotarget 2020; 11(22):2092-2105.

2018 Pedersen M, Westergaard MCW, Milne K, **Nielsen M**, Borch TH, Poulsen LG, Hendel HW, Kennedy M, Briggs G, Ledoux S, Nøttrup TJ, Andersen P, Hasselager T, Met Ö, Nelson BH, Donia M, Svane IM. *Adoptive Cell Therapy with Tumor-Infiltrating Lymphocytes in Patients with Metastatic Ovarian Cancer: A Pilot Study.* Oncoimmunology 2018; 7: e1502905

2018 Andersen R, Borch TH, Draghi A, Gokuldass A, Rana MAH, Pedersen M, **Nielsen M**, Kongsted P, Kjeldsen JW, Westergaard MCW, Radic HD, Chamberlain CA, Holmich LR, Hendel H, Larsen MS, Met Ö, Svane IM, Donia M. *T cells isolated from patients with checkpoint inhibitor-resistant melanoma are functional and can mediate tumor regression.* Ann Oncol 2018; 29: 1575-1581.

2016 **Nielsen M**, Staalsøe JM, Ullum H, Secher NH, Nielsen HB, Olsen NV. *The Gly16 Allele of the Gly16Arg Single-Nucleotide Polymorphism in the β2-Adrenergic Receptor Gene Augments Perioperative Use of Vasopressors: A Retrospective Cohort Study.* Anesth Analg 2016; 122: 1385-93.

2011 Staalsø JM, **Nielsen M**, Edsen T, Koefoed P, Springborg JB, Moltke FB, Laursen H, Nielsen HB, Olsen NV. *Common Variants of the ACE Gene and Aneurysmal Subarachnoid Hemorrhage in a Danish Population: A Case-control Study.* Journal of Neurosurgical Anaesthesiology 2011; 23(4):304-9.

2009 Jensen MK, **Nielsen M**, Koefoed P, Nielsen HB, Ullum H, Haastrup E, Romner B, Moltke FB, Olsen NV. *Haplotype structure of the Beta 2-adrenergic receptor gene in 814 Danish Caucasian subjects and association with body mass index.* Scandinavian Journal of Clinical & Laboratory Investigation. Scand J Clin Lab Invest 2009; 69: 801–808.

2008 **Nielsen M**, Olsen NV. *Genetic polymorphisms in the cytochrome-P450 system and efficacy of 5-hydroxytryptamine type 3 receptor antagonists for postoperative nausea and vomiting*. British Journal of Anaesthesia 2008; 101: 441-445

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Janne Minet Pedersen, læge**
Arbejdssted/ Institution	**Øre-, Næse- og Halskirurgisk afdeling Aarhus Universitetshospital**
Adresse	**Mandalsvej 16B, 8200 Aarhus Nord**
Tlf.nr.	**20911250**
e-mail	**janne.minet@gmail.com**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel:

Supraglottisk planocellulært karcinom i Danmark

Formål

Formålet med projektet er at forbedre forståelsen og behandlingen af supraglottisk strubekræft og avanceret strubekræft i Danmark gennem en omfattende national analyse baseret på Den Danske Hoved-Hals Kræft database (DAHANCA). Resultaterne vil danne grundlag for optimering af behandlingsstrategier og potentielt opdatering af nationale retningslinjer.

Problemstilling

På trods af fremskridt i kræftbehandling har patienter med supraglottisk strubekræft fortsat dårlig prognose sammenlignet med andre undergrupper. Der mangler opdateret, nationalt dækkende viden om behandlingsresultater og sygdomsforløb. Eksisterende viden bygger primært på ældre, institutionsbaserede studier. Patientgruppen er ofte præget af sociale og helbredsmæssige udfordringer, hvilket fører til sen diagnostik og begrænsede behandlingsmuligheder.

Baggrund

Strubekræft udgør 16% af hoved-hals-cancere i Danmark. Den supraglottiske undertype adskiller sig med hensyn til symptomer, spredningsmønster og behandlingsudfald. Tidligere studier er institutionsbaserede og er af ældre dato. De nuværende nationale behandlingsretningslinjer stammer fra 2014. DAHANCA-databasen tilbyder en enestående mulighed for et nationalt overblik over udviklingen fra 1971 til 2020, herunder ændringer i incidens, overlevelse og behandlingsstrategier.

Metoder

Projektet består af tre nationale studier:

1. **Studie 1** undersøger forekomst, demografiske kendetegn og overlevelse hos patienter med supraglottisk strubekræft fra 1971 til 2020.
2. **Studie 2** analyserer mønstre for tilbagefald og effekten af supplerende kirurgisk behandling hos patienter behandlet med helbredende sigte fra 1986 til 2020.
3. **Studie 3** fokuserer på behandlingsresultater og mønstre for tilbagefald hos patienter med fremskreden kræft i struben fra 2011 til 2020.

Alle studier baseres på data fra DAHANCA databasen. Der forventes at indgå omkring 4500 patienter i det første studie, 3500 i det andet og 800 i det tredje. Data analyseres med fokus på overlevelse, patientkarakteristika, behandlingsform og mønstre for tilbagefald.

Tidsplan

	Prior to PhD	Year 1 – 2025/2026	Year 2 – 2026/2027		Year 3 – 2027/2028	
Study 1	Data collection[JP]		Analysis [JP]	Writing [JP]		
Study 2	Data collection[JP]		Analysis [JP+TK+co.]	Writing [JP+TK+co.]		
Study 3		Data collection[JP]		Analysis JP+TK+co.	Writing JP+TK+co.	
PhD courses		*9,4 ECTS*	*17,7 ECTS*		*3,6 ECTS*	
Teaching		*50 hours*	*50 hours*		*50 hours*	
PhD Thesis				Writing Thesis		

JP = Janne Pedersen (under supervision af TK). TK = Thomas Kjærgaard. Co. = medvejledere.

Der planlægges et forskningsophold på én måned ved Universitetet i Brescia i Italien.

Forventede resultater og impact

Projektet forventes at bidrage med:

- Opdateret viden om sygdommens udvikling og behandlingsudfald i Danmark over fem årtier.
- Identifikation af risikoprofiler for tilbagefald og forslag til optimering af opfølgningsprogrammer.
- Forskningsbaseret grundlag for revidering af nationale behandlingsretningslinjer.
- Øget opmærksomhed på social ulighed i sundhed, idet mange patienter tilhører udsatte grupper.

Resultaterne vil blive præsenteret på internationale konferencer og i videnskabelige tidsskrifter.

Øvrige projektdeltagere og samarbejdsrelationer

Projektansvarlig: Janne Minet Pedersen, læge og kommende ph.d.-studerende.
Hovedvejleder: klinisk lektor, overlæge og ph.d. Thomas Kjærgaard, Øre-, Næse- og Halskirurgisk afdeling, Aarhus Universitetshospital.

Medvejledere:
- Professor Jens Overgaard, Onkologisk afdeling, Aarhus Universitetshospital.
- Professor, overlæge og ph.d. Jesper Grau Eriksen, Onkologisk afdeling, Aarhus Universitetshospital.
- Læge og ph.d. Nina Munk Lyhne, Øre-, Næse- og Halskirurgisk afdeling, Aalborg Universitetshospital

Internationalt samarbejde: Forskningsophold og samarbejde med Universitetet i Brescia, Italien.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Budget expectations for the PhD project

	Year 1	Year 2	Year 3	All
Salary	596,400	613,200	625,200	1,834,800
Study fee	40,000	40,000	40,000	120,000
Conferenceres and publication fees		10,000	20,000	30,000
Stay abroad			30,000	30,000
All				**2,014,800**

Sources of funding (current or expected)

Source	Amount
The Danish Cancer Society (current)	1,500,000
External funding (expected)	514,800
Total	**2,014,800**

Vi har fået bevilliget de ovenstående 1,5 mio. kroner fra Kræftens Bekæmpelse til projektet.
Der søges støtte fra Direktør Michael Hermann Nielsens mindelegat på 454.800 kr. Mindre beløb påskønnes også.
Vi er i gang med at søge større fra andre fonde til at dække udgifter til konferencer, publikationer samt udlandsophold.

CV

PERSONAL INFORMATION

Age: 32 years

PHONE NUMBER:
+45 20 91 12 50

E-MAIL:
janne.minet@gmail.com

ADDRESS:
Mandalsvej 16B, 8200 Aarhus N.

COURSES

MANDATORY

Audio-Vestibulogy.
11/25/2024.

Pediatric Bronchoscopy.
11/16/2023.

Diagnostic Ultrasound in the Head and Neck region.
5/10/2023.

Radiotherapy.
9/27/2022, 9/28/2022.

The Oncological Toolbox.
9/19/2022, 9/20/2022.

Supervision.
12/8/2021, 12/9/2020, 1/12/2021.

Learning.
10/9/2020, 9/11/2020.

Acute communication, treatment and transportation.
8/13/2020, 8/14/2020, 9/10/2020, 9/11/2020.

Communication.
3/4/2020, 3/5/2020, 8/17/2020.

JANNE MINET PEDERSEN

RESIDENT PHYSICIAN

EDUCATION

08.01.2016 - 07.01.2019	**Aarhus University. Master's Degree in Medicine.**
01.08.2013 - 01.08.2016	**Aarhus University. Bachelor's Degree in Medicine.**

THE SEVEN ROLES OF A DOCTOR

MEDICAL EXPERT

04.01.2024 -	**Resident physician, Department of Ear, Nose and Throat and Head and Neck Surgery, Aarhus University Hospital.** Residency.
04.01.2023 - 03.31.2024	**Junior Doctor, Department of Ear, Nose and Throat and Head and Neck Surgery, Aarhus University Hospital.** Introductory Position.
06.01.2022 - 03.31.2023	**Junior Doctor, Department of Oncology, Aarhus University Hospital.** Introductory Position.
09.01.2020 - 08.31.2021	**Junior Doctor, Department of Surgery, Regional Hospital Horsens.** Introductory Position.
02.01.2020 - 07.30.2020	**Junior Doctor, General Practice, Thorning Doctors,** KBU.
08.01.2019 - 01.31.2020	**Junior Doctor, Diagnostic Center, Regional Hospital Silkeborg,** KBU.
Aug. 2016 - Nov. 2018	**Surgical Assistant, Department of Orthopedic, Aarhus University Hospital, SPV-attendant.**
Jan. 2017 – June 2017	**Pregraduate Surgical Training, "Surgical DreamTeam", Department of Surgery, Regional Hospital Horsens.**

COLLABORATOR/COMMUNICATOR

02.04.2021 - 08.31.2021	**Deputy Union Representative, Department of Surgery, Regional Hospital Horsens.**
09.01.2020 - 08.31.2021	**Mentor for Medical Students, Department of Surgery, Regional Hospital Horsens.**
12.01.2013 - 11.30.2018	**Nursing Substitute/FADL-attendant, Region Midt.** Working hours: 1300 hours.

LEADER/ADMINITRATOR/ORGANIZER

Jan. 2021 - Aug. 2021	**Member of the Hygiene Committee, Regional Hospital Horsens.**

ELECTIVE

LapBasis, MidtSim.
3/10/2021, 3/24/2021.

Endoscopy, MidtSim.
11/24/2021.

Open and laparoscopic surgery on Pigs, Department of Surgery, Regional Hospital Horsens.
10/22/2020.

Laparoscopic surgery on pigs, "Surgical DreamTeam".
4/11/2017.

Basic Flap and Papilla Reconstruction, SAKS Plastic Surgery.
3/17/2016

REFERENCER

Stefano Londero.
Chief Physician.
Department of Ear, Nose and Throat and Head and Neck Surgery,
Aarhus University Hospital.
E-mail: stelon@rm.dk
Phone: +45 21 55 46 77

Mehmet Öztoprak.
Chief of Residents,
Department of Surgery,
Regional Hospital Horsens.
E-mail: mehmoezt@rm.dk
Phone: +45 78 42 62 28.

PUBLICATIONS

"The Diagnostic Value of PET/CT and MRI in Head and Neck Cancer of Unknown Primary".
Signe Bergliot Nielsen/Mads Bøgh, Camilla Molich Hoff, Ate Haraldsen, Mathias Hald, Janne Minet Pedersen, Edith Nielsen, Mette Hjørringgaard Madsen, Jens Overgaard, Thomas Kjærgaard.
Under submission

"Diagnostic outcome in patients with squamous cell carcinoma lymph node metastasis and no primary tumor at initial clinical examination."
Signe Bergliot Nielsen, Mathias Hald, Janne Minet Pedersen, Ate Haraldsen, Camilla Molich Hoff, Edith Nielsen, Christian Godballe, Jens Overgaard, Thomas Kjærgaard.
Under preparation.

10.01.2019 - 01.31.2020 **Moderator at Junior Doctors Meetings, Regional Hospital Silkeborg.**

09.01.2017 - 10.01.2017 **Change and Process Management, Elective course 9th Semester (5 ECTS credits).**

Aug. 2016 – Aug. 2017 **Board Member, Students' General Surgery Society (SAKS).**

HEALTH PROMOTER

10.01.2020 - 08.31.2021 **Invers feedback, Initiator/responsible, Department of Surgery, Regional Hospital Horsens.**

EDUCATOR

06.01.2022 – 03.31.2023 **Academic Presentation, Department of Oncology, Aarhus University Hospital.**
Confrontation time: 30 minutes.

08.01.2019 - 01.31.2020 **10 Clinical Minutes, Diagnostic Center, Regional Hospital Silkeborg.**
Confrontation time: 30 minutes.

01.08.2019 - 31.01.2020 **Bedside Teaching, 7th and 9th Semester Medical Students, Regional Hospital Silkeborg.**
Confrontation time: 2 Hours.

Aug. 2016 – Aug. 2017 **Instructor in Basic and Advanced Suturing.**
Course for medical students, SAKS Aarhus.
Confrontation time: 40 Hours.

Aug. 2016 – Aug. 2017 **Instructor in Laparoscopy.**
Course for medical students, SAKS Aarhus.
Confrontation time: 30 hours.

ACADEMIC/RESEARCHER

May 2024 – oct. 2024 **DAHANCA database.**
Updating patient data on larynx cancer.

Sep. 2023 – dec. 2023 **RedCap.** Data entry and review of medical records for PhD student Signe Bergloit Nielsen. Head and Neck cancer of unknown Primary.

04.01.2023 – **Journal Clubs,** Department of ENT and Head and Neck Surgery, Aarhus University Hospital.

PROFESSIONAL

2023 – **The Association of Young Otologists**, member.

2023 – **The Danish Laryngological Society**, member.

11.30.2023 **360 Degree Evaluation,** Department of ENT and Head and Neck Surgery, Aarhus University Hospital.

Thomas Kjærgaard

Born 10.01.1976

Senior Consultant, PhD, Associate Professor
Dept. of ORL-HNS, Aarhus University Hospital
Palle Juul-Jensens Boulevard 99
8200 Aarhus N, Denmark
& Aarhus University

thokjae@rm.dk; tel. +45 31506029
https://orcid.org/0000-0002-5090-4812

CURRENT POSITIONS

2011 -	Associate professor, Aarhus University
2014 -	Consultant, member of staff, Dept. of ORL-HNS, Aarhus University Hospital (AUH)

EDUCATION

1997 - 2003	Medical doctor, Faculty of Health, Aarhus University (authorization: February 1st, 2003)
2010	Specialist in otorhinolaryngology, head and neck surgery (authorization: August 24th, 2010)
2006 - 2010	PhD, University of Bergen, Norway: ”Structural, functional, and subjective characteristics of the nasal airway” (defense: December 15th, 2010, Diploma: January 10th, 2011)
2016 - 2020	Fellowship, International Federation of Head and Neck Oncologic Societies (2020: MD Anderson Cancer Center, Huston, Texas)

RESEARCH INTERESTS & SCIENTIFIC FOCUS AREAS
Transoral robotic surgery
Head and Neck Cancer
Health economics
Transoral laser microsurgery
Central airway stenosis

INTERNATIONAL RELATIONS (Clinical and/or research collaboration)
Cesare Piazza, Professor Chief of the Department of Otorhinolaryngology - Head and Neck Surgery ASST Spedali Civili of Brescia School of Medicine, University of Brescia, Italy
Giorgio Peretti, Professor Chief of the Department of Otorhinolaryngology - Head and Neck Surgery, Genova School of Medicine, University of Genova, Italy
Isabel Vilaseca, Professor Head of the Functional Unit of Head Neck Tumors, Hospital Clínic. Barcelona School of Medicine. University of Barcelona, Spain
Se-Heon Kim, Professor, M.D., Ph.D., Department of Otorhinolaryngology, Yonsei University College of Medicine, Korea
Dr. Jeffrey N. Myers, Professor, Department of Head and Neck Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX
Dr. Boudewijn Plaat, Department of Otorhinolaryngology, University Medical Center Groningen, Netherlands

LEADERSHIP
Main and co-supervisor on PhD-projects
Associate professor
Chairman and member of national and international boards
Head of Robotics Division and Endoscopic Division, Dept. ORL-HNS, AUH
Co-founder of AROS Healthcare
Founder and owner of the ENT- and Sleep-division, AROS Private Hospital

COMMISSIONS OF TRUST

2012 - 2024 Member of board, Danish Laryngological Society
2012 - 2023 Member of board, Danish Glottis Study Group
2014 - 2020 Chairman of board, Danish Laryngological Society
2017 - Member of board, Danish Head and Neck Cancer Group (DAHANCA)
2018 - Member of board, Danish Society of Otorhinolaryngology, Head & Neck Surgery
2020 - Chairman of board, AROS Private Hospital, Aarhus
2021 - 2024 Chairman of board, Danish Society of Otorhinolaryngology, Head & Neck Surgery (National Society)
2021 - Member of board and Danish representative, Nordic Association of ORL
2022 - Member of board and Danish representative, UEMS MJC, Head & Neck Surgery
2022 - Member of board and Danish representative, UEMS, ORL

SUPERVISION, PhD

2012 - 2016 *PhD co-supervisor:* Nina Munk Lyhne: Glottic cancer –past, present and future.
2013 - 2017 *PhD co-supervisor:* Alexander Fjældstad: Testing olfactory function and mapping the structural olfactory networks in the brain.
2016 - 2020 *PhD co-supervisor:* Camilla Sloth Mehlum: Laryngeal intraepithelial neoplasia: epidemiology and preoperative assessment of malignant transformation.
2021 - 2024 *PhD main supervisor:* Signe Bergliot Nielsen: Diagnostic work-up and treatment of cancer of unknown primary in the head and neck
2024 - *PhD co-supervisor:* Mathilde Aalling, Dysphagia and quality of life in patients with oral squamous cell carcinoma before and after treatment
2023 - *PhD co-supervisor:* Anne Katrine Bak Poulsen: OCT/OFDI in Airways
2024 - *PhD main supervisor:* Mathias Hald: Socioeconomic aspects of oropharyngeal carcinoma in the HPV era

SUPERVISION, other

2014 - 2016 Research year: Claes Karstensen: DNA methylation profiles in laryngeal carcinoma and the impact of HPV
2024 - Research Year: Mads Bøgh: 3D Ultrasound and MRI in Evaluating Resection Margins during Salivary Gland Cancer Surgery
2011 - 2024 > 20 pregraduate supervisorships

RESEARCH FUNDING

Previous and ongoing research programs: >5 mill. DKK
Implementation of the transoral robotic program, AUH: >2 mill. DKK

OTHER ACADEMIC & SCIENTIFIC ACTIVITIES

Peer-reviewer for several international journals: >100 reviews
Author/co-author on >40 publications
Textbook authorship in *Lærebog for Øre-næse-halssygdomme og hoved-hals-kirurgi,* Munksgaard forlag, 3. udgave.
Course director and invited speaker

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens min-delegat, afd. B - sygdomsforskning

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	Oliver S.K Harving, BA Medicin, Stud. Med KA, KU
Arbejdssted/ **Institution**	*Københavns Universitet.* Arbejdssted for forskningsprojektet: *Diagnostisk Center, Afd. for Røntgen og Skanning, Rigshospitalet.* Afdeling for Røntgen og Skanning Blegdamsvej 9 2100 København Ø
Adresse	Korfuvej 12. st.tv
Tlf.nr.	+4527208525
e-mail	ostockfleth@gmail.com

Se projektbeskrivelse og CV nedenfor.
På forhånd tak for vurderingen og muligheden for at ansøge.
De bedste hilsner
Oliver Harving. Stud.med.

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

Infections of Intravascular Stents - Case report and Systematic review of literature.

Formål

Formålet med projektet er at udfærdige en systematisk litteraturgennemgang og klinisk kasuistik vedrørende infektion intravaskulære stents. Det er projektets formål at kunne publicere fundene og dermed understøtte klinisk beslutningstagning og bidrage til grundlaget for fremtidige evidensbaserede retningslinjer.

Problemstilling

Der eksisterer i dag begrænset og spredt evidens på området, og der foreligger ingen konsensusbaserede retningslinjer for håndtering af denne potentielt livstruende komplikation.
Der er derfor manglende viden om både forekomst, risikofaktorer, diagnostiske tilgange, behandling og kliniske udfald ved stentinfektioner. Det vil forskningsprojektet adressere.

Baggrund

Infektion i intravaskulære stents er en alvorlig komplikation med høj morbiditet og mortalitet.
Området er aktuelt underbelyst og baserer sig primært på enkeltstående kasuistikker og ældre reviews, hvilket understreger behovet for ny og opdateret evidens.
Samtidig er den kliniske relevans stigende i takt med den øgede anvendelse af endovaskulære procedurer og udbredelsen af stents til stadig mere komplekse og komorbide patientgrupper, heriblandt cancerpatienter med eksempelvis tumortryk på -eller indvækst i kar (som det fx ses ved Vena Cava Superior-syndrom).
Baggrund for legatansøgers rolle i projektet, skrevet af Hovedvejleder Mikkel Taudorf:
Projektet vil udføres som et selvstændigt, prægraduat forskningsprojekt af legatansøger Oliver Harving, som vil have hovedansvaret for projektets gennemførelse. Målet er publicering i peer-reviewed tidsskrift, med legatansøgeren som hovedforfatter.
Oliver står for projektets design, udførelse og rapportering.
Oliver kommer ydermere til at deltage aktivt i det kliniske miljø og modtage faglig oplæring i relevante interventionsprocedure, hvilket understøtter både det akademiske og kliniske udbytte i relation til det behandlede forskningsemne.

Metoder

Projektet udføres i to integrerede dele:
1. Kasuistik

Et konkret patientforløb fra Rigshospitalet (patientsamtykke er indhentet). Kasuistikken beskriver i detaljer symptomatologi, diagnostik, behandlingsstrategi og outcome. Denne del tjener som illustrativ case, der fremhæver steninfektionsforløbets relevans i praksis.

2. Systematisk litteraturgennemgang
Den systematiske gennemgang planlægges og udføres i overensstemmelse med PRISMA-retningslinjerne. Litteratur identificeres via en struktureret søgestrategi i relevante databaser (bl.a. PubMed), og inklusions- og eksklusionskriterier defineres a priori. Artikler screenes uafhængigt af to forskere (legatansøgeren værende den ene). Data vil blive udtrukket systematisk og underlagt kritisk vurdering med brug af anerkendte værktøjer til evidensvurdering (fx 'JBI ').
Litteraturgennemgangen vil tilsigte at indhente viden om blandt andet følgende nøgleparametre:
1) Forekomst, 2) Patienternes præmorbiditet, 3) Risikofaktorer for stentinfektion, 4) Ætiologi og mulig patofysiologi, 5) Klinisk præsentation og symptomprofil, 6) Anvendte diagnostiske modaliteter, 7) Behandlingsstrategier (konservativ, kirurgisk, endovaskulær mv.), 8) Kliniske outcomes.
Fundene vil blive systematiseret i både tabelform og narrativ syntese. Reviewet vil samtidig diskutere tendenser, usikkerheder og svaghed i data, samt komme med forslag til videre forskning og eventuelle anbefalinger baseret på litteraturgennemgangen.

Tidsplan

Projektet vil forløbe fra 1/7-25 til 1/6-26.
Der søges legatmidler til finansiering af 6 måneders forskningsstipendiat i perioden 1/7-2025 til 31/12-2025.

Forventede resultater og impact

Projektet gennemføres som henblik på publikation i et peer-reviewed tidsskrift, som eksempelvis 'EJVES (Impact Factor 5.7) ' eller 'JVIR (Impact Factor 2.8) '.
Projektet vil bidrage med vigtig viden til et vældigt underbelyst område og vil kunne være med til at danne grundlag for fremtidige kliniske retningslinjer, hvilket vil højne både patientsikkerheden og behandlingskvaliteten.

Øvrige projektdeltagere og samarbejdsrelationer

-Forskningsgruppen Lars Lönn-lab
- Hovedvejleder; Overlæge, Ph.d og Klinisk lektor Mikkel Taudorf

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Periode	Normal månedlig indkomst (før orlov)	Indkomst under forskningsorlov (kun netto arbejde)	Samlede estimerede udgifter (6 måneder)	Samlet indkomst under orlov (6 måneder)	Finansieringsbehov (beløb der skal dækkes)
1/7/25 - 31/12/25	13.208 DKK	3.118 DKK	79.246 DKK	18.706 DKK	**60.540 DKK**

CV:

Kontakt
Navn: Oliver Stockfleth Krahne Harving
Mail: ostockfleth@gmail.com

Uddannelse
Stud.med KA, Københavns Universitet
Bachelor i Medicin, KU.
Bachelorprojekt ved 'Department of Neuroscience, (KU)': "Endogen bioelektricitets rolle i cancer – et scoping review' (karakter: 12)
HF (Højere forberedelseseksamen), Gns; 11.9

Erhvervserfaring (udvalgt):
Røntgen og Ultralydsklinikken, Amagerbrogade (i nuværende stilling 5+ år, 200+ timer/år)
Stud.med i speciallægepraksis:
• Patientmodtagelse, klargøring og information
• Selvstændigt udført ultralyd under supervision (MSK, abdominal, thyroidea m.fl.)
• Assisteret ved kontrastundersøgelser (bl.a. HSG, kolon- og oesophagusgennemlysning)
Anbefaling kan rekvireres ved: Speciallæge i radiologi, Ph.d., Dr.med, Kristoffer Lindskov Hansen
Lindskov@gmail.com

Medicinsk konsulent, DEXA-bodyscan (2022–nu):
• Underviser i anatomi og scanningsanalyse
• Foredragsholder for sundhedsfaglige samarbejdspartnere
• Udarbejdelse af rapporter, heriblandt litteratursøgninger og evidensgennemgange
• Uddannet DXA-operatør
Certificeret DXA-operatør, Herlev Hospital
(certificeret 2021)

Ekstracurriculært:
• Frivillig vaccinatør, Holbæk Hospital (2023)
• Frivillig klinik, interventionsradiologisk afd., Rigshospitalet (2022–23)

Sprog:
Dansk (modersmål), Svensk (grundlæggende) Engelsk (flydende, inkl. medicinsk engelsk)

Center for Kultur- og Fritidsaktiviteter
Kultur- og Fritidsforvaltningen

Ansøgningsskema til Direktør Michael Hermann Nielsens mindelegat, afd. B - sygdomsforskning

Ansøgningen skal indeholde:

- Obligatorisk ansøgningsskema. (Det er valgfrit, om ansøgningen skrives på dansk eller engelsk.)
- CV og publikationsliste
- Ansøgningsskema, CV og publikationsliste sendes digitalt i ét samlet dokument ved at bruge kontaktboksen nederst på følgende hjemmeside Legat til sygdomsforskning | Københavns Kommunes hjemmeside (kk.dk) (der hvor du fandt det obligatoriske ansøgningsskema)

Oplysninger om ansøger (CV og publikationsliste vedlægges som bilag)	
Navn og stilling	**Gitte Holmen Olofsson, Post Doc**
Arbejdssted/ Institution	**National Center for Cancer Immune Therapy (CCIT-DK)** **Oncology department, Herlev Hospital**
Adresse	**Borgmester Ib Juuls Vej 13, 2730 Herlev**
Tlf.nr.	**+45 28998505**
e-mail	**gitte.holmen.olofsson@regionh.dk**

Projektbeskrivelse (projektbeskrivelsen må max fylde 2 sider, skriftstørrelse 12)

Projekttitel

Gør en god behandling bedre: motion ved immunterapi af kræft

Formål

Projektets formål er at undersøge, hvorvidt højintens træning kan mobilisere og aktivere immunsystemet og derved skabe en bedre effekt af immunterapibehandling for kræftpatienter. Som en vigtig del af studiet, vil vi undersøge om tilstedeværelsen af forskellige proteiner og celler, i både blod og kræftvæv, viser eller kan forudsige effekten af træningen.

Problemstilling

Med dette projekt håber vi på at vise, at motion ikke bare er ”sundt” men også ”terapeutisk” i forbindelse med immunterapi. I så fald, kunne motion tænkes at blive en standarddel af immunterapi behandlingen – en sund måde at øge responsraten og antal patienter der kureres for deres sygdom. Men, før vi kan gøre dette, er vi nødt til at forstå de underliggende mekanismer og det er netop hvad dette projekt vil undersøge.

Baggrund

Indtil 1980’erne var hvile betragtet som standardanbefalingen til kræftpatienter. Omfattende forskning har dog siden vist, at træning kan lindre både psykosociale og fysiske bivirkninger ved kræftbehandling. I de senere år har man desuden påvist, at træning kan reducere kræftforekomst og forbedre behandlingen på tværs af forskellige kræftformer. Især har højintensiv træning vist sig at have en stor effekt på immunsystemet, ved at mobilisere immunceller, styrke deres funktion og reducere kronisk inflammation – disse mekanismer forsinker aldring af immunceller, samt mindsker risikoen for infektioner og kræftprogression.

Vi har desuden tidligere vist, at mus med kræft som motionerer, har en reduceret vækst af kræftknuder og at det primært skyldes en aktivering af deres immunsystemet. Derfor har vi startet et klinisk forsøg kaldet HI AIM, hvor lungekræft patienter kombinere træning med deres immunterapi behandling. Patienterne har gennemført et superviseret 6-ugers træningsforløb med højintense intervaltræning. Vi har for nylig afsluttet rekruttering af 54 patienter med en imponerede adherence på 85%, og alle blodprøver opbevares i vores biobank klar til analyse.

Metoder

Nu hvor inklusions- og interventionsfasen af studiet er afsluttet, er næste skridt de eksperimentelle analyser af prøverne: I denne ansøgning søger jeg midler til at anskaffe reagenser, der er nødvendige for at udføre serumanalyser af immunmodulerende proteiner og til at karakterisere hvilke immunceller der aktiveres ved træning. Disse analyser vil give vigtig

indsigt i de immunologiske mekanismer bag træningsinduceret immunmodulation hos kræftpatienter, og kan i sidste ende bidrage til at integrere træning som supplement til immunterapi.

Tidsplan

Vi forventer at projektet vil tage ca. 1,5 år at udføre. Selve forsøgene vil tage cirka 9 måneder at udføre, og dernæst 3 måneder til analyser og samskrivning af artiklen. Vi afsætter ca. 6 måneder til publikation, inklusive review.

Forventede resultater og impact

Vi forventer at dette projekt bidrager med vigtig ny viden om hvordan motion påvirker immunsystemet i patienter med kræft, hvilket understreger potentialet af en terapeutisk tilgang til motion i klinisk onkologi. Vores data vil præsentere motion som en sund og billig kombinations-partner med immunterapi; en dyr behandling med lav responsrate.

På et mere overordnet plan, er min forskning er drevet af at et ønske om at forstå hvordan træning påvirker immunsystemet hos kræftpatienter. Mit langsigtede mål er at etablere træning som en integreret del af kræftbehandling, fordi det har potentialet til at forbedre effektiviteten af den eksisterende behandling. Men, før vi kan gøre dette, er vi nødt til at forstå de underliggende mekanismer og det er netop hvad dette studie fokusere på. Vi forventer at resultaterne vil have stor bevågenhed fra andre forskere og klinikere, samt have bred samfundsmæssig interesse, og bidrage til en øget forståelse for effekt af motion i patienter med kræft.

Øvrige projektdeltagere og samarbejdsrelationer

Projektet er et stort tværfagligt projekt, på tværs af fire afdelinger på Herlev Hospital. I henhold til de experimentielle analyser, vil denne del involvere Post Doc Katharina Leuchte og PhD studerende Sara Fresnillo Saló. Begge er tilknyttet projekt på ekstern funding, og vi forventer desuden at tilknytte en specialestuderende med opstart i efteråret 2025.

I andre dele af projektet, samarbejder vi desuden med Prof. Sine Reker Hadrup fra DTU, Prof. Lars Rønn fra KU og lektor Claus Deslar fra KU.

Budget (herunder evt. finansiering fra offentlige/private råd og fonde)

Jeg ansøger hermed om 100.000 DKK som støtte til projektet, men enhver form for støtte blive modtaget med stor taknemmelighed.

Projekt er desuden støttet af Fam. Erichsens mindefond (100.000), og min Post Doc løn er dækket af Det Frie Forskningsråd (FFS) frem til sommeren 2027.

CV

Personal information

Name: Gitte Holmen Olofsson (former Andersen)
Address: Alfred Christensens vej 25 st., 2850 Nærum, Denmark
Date of birth: 13-01-1985.
Researcher ID (ORCID): 0000-0002-7060-8754

Current and previous positions

2018 -	Postdoctoral fellow, National Center for Cancer Immune Therapy (CCIT-DK), Herlev Hospital
2014-2018	PhD student at Center for Cancer Immune Therapy, Herlev University Hospital
2012-2014	Research assistant at Center for Cancer Immune Therapy, Herlev University Hospital
2010-2011	Novo Nordisk A/S, Global Public Affairs department, Bagsværd, Denmark. Consultant. Data management and data analysis

Education

2018	Ph.D. degree in Immunology and infectious Diseases, from University of Copenhagen. Thesis title: 'Vγ9Vδ2 T cells as cancer cell killers and antigen presenting cells'. Primary supervisor: Professor Per thor Straten. Co-supervisor Professor Søren Skov.
2010-2012	Master of Science (M.Sc.) in Molecular Biomedicine at University of Copenhagen. Master thesis title: 'Gamma-delta T cells and PD-L1-specific T cell immunity', supervisor Professor Mads Hald Andersen and Professor Per thor Straten.
2006-2010	Bachelor of Science in Molecular Biomedicine.
2010	Bachelor thesis at Prof. Hinrich Abken, Center for Molecular Medicine Cologne, Germany. Bachelor thesis title: 'Tumor infiltrating lymphocytes genetically modified with a 3rd generation CAR'.
2009	International student at University of Auckland, New Zealand
2008	Exchange student at University of Western Ontario, Canada.

Clinical Project Manager:

I was qualified as Clinical Project Manager in 2020 (see below). Currently, initiator and principal investigator (PI) of the clinical trials HI AIM and INHALE.

2020	Course in 'Clinical Project Management - Module 2: Lead your project team, by IMPLEMENT learning institute, Atrium.
2019	Course in 'Clinical Project Management - Module 1: Mange your project' by IMPLEMENT learning institute, Atrium.

Presentations

2025 Jan	Invited speaker, Scandinavian Sports Medicine Congress 2025, Copenhagen, DK.
2024 June	Invited speaker, 10th World Congress on 'Cancer research and Therapy', Prague, CZ.
2022 Oct.	Selected for oral presentation at the 15th International Society of Exercise and Immunology (ISEI) symposium, Tucson, USA.
2022 Aug.	Selected to participate in the SITC 2022 Women in Cancer Immunotherapy Network (WIN) Leadership Institute, Seattle, Washington, USA.
2021 Oct.	Invited speaker at 'Krop & Kræft Netværksmøde' annual meeting 2021.
2019 June	Invited speaker at 'Exercise Minisymposium', Herlev Hospital.
2017 Oct.	Selected for oral presentation at the 2nd World Immunotherapy Council (WIC) Young Investigator Symposium. SITC meeting, Washington, USA
2017 Mar.	Selected for oral presentation at Cellular Therapy, Erlangen, Germany.
2016 Oct.	Winner of poster prize, Herlev Hospital Forsknings Day, Herlev, Denmark.
2016 June	Selected for oral presentation at 8th Gamma delta Conference, London, UK
2015 May	Selected for oral presentation at DIS yearly meeting, Århus, Denmark.
2013 Oct.	Winner of poster prize, DCS cancer symposium 2013 in Copenhagen.
2013 April	Selected for oral presentation at 'CITIM' meeting, Krakow, Polen.
2012 May	Oral presentation at 'Tumor Immunology Meets Oncology' meeting, Halle Germany.

Supervision

Co-supervisor of PhD students at University of Copenhagen: Thy Viet Luu, scholar of the Marie Curie ITN T-OP programme (https://www.itn-top.eu/itn-top), Sara Fresnillo Saló and former PhD student Pia Aehnlich. Practical supervisor of five former master students and one bachelor student. Main supervisor of two current and four former student assistants hired for processing of samples in our clinical trials.

Fellowships and funding:

2024	Grant from Familien Erichsens Mindefond.
2022/2023	Grant from the Region Hovedstadens Forskningsfond til Sundhedsforskning 2022.
2022	Awarded travel grant from the Danish Cancer Society (Kræftens Bekæmpelse)
2020/2021	Grant from the 'Karen A. Tolstrups Fond' supporting the HI AIM project.
2020	Grant from'Dr. phil Ragna Rask-Nielsens Grundforskningsfond'
2017/2018	Awarded the 'Dansk Kræftforsknings Fond' grant for 6 months' salary.
2016	Awarded travel grant from the Danish Cancer Society (Kræftens Bekæmpelse)
2014	Awarded travel grant from the Danish Cancer Society (Kræftens Bekæmpelse)
2013	Awarded the Capital Region research grant for 6 months' salary.
2011/2012	Awarded the Danish Cancer Society 1 year Scholarship as support to master thesis.

List of publications and manuscripts:

1. Katharina Leuchte; Thy Viet Luu; Sara Fresnillo Saló; Kasper Madsen; Lise Heide-Ottosen; Signe Koggersbøl Skadborg; Janine Sophie Kemming; Morten Orebo Holmström; Hongjin Chen; Lars Rønn Olsen; Anders Vinther; Mads Hald Andersen; Sine Reker Hadrup; Per thor Straten; **Gitte Holmen Olofsson.** 'Profiling interindividual differences of lymphocyte mobilization and reorganization of the CD8+ T cell compartment following acute high-intensity exercise' *Submitted to Immunity, 2025.*

2. Velasco Santiago M, Aehnlich P, Hulen TM, Mølgaard Jensen K, **Holmen Olofsson G**, Met Ö, thor Straten P, Overcoming antigen loss in CAR T therapy with Vγ9Vδ2-CAR T-cells, Immuno-Oncology and Technology (2025), doi: https://doi.org/10.1016/j.iotech.2025.101053

3. Aehnlich, P.; Santiago, M.V.; Dam, S.H.; Saló, S.F.; Rahbech, A.; Olsen, L.R.; Straten, P. thor; Desler, C.; **Olofsson, G.H.** Glycolysis Inhibition Affects Proliferation and Cytotoxicity of Vγ9Vδ2 T Cells Expanded for Adoptive Cell Therapy. *Cytotherapy* 2024, doi:10.1016/j.jcyt.2024.04.072.

4. **Holmen Olofsson G**.; Mikkelsen, M.K.; Ragle, A.-M.; Christiansen, A.B.; Olsen, A.P.; Heide-Ottosen, L.; Horsted, C.B.; Pedersen, C.M.S.; Engell-Noerregaard, L.; Lorentzen, T.; et al. High Intensity Aerobic exercise training and Immune cell Mobilization in patients with lung cancer (HI AIM)-a randomized controlled trial. *BMC Cancer* 2022, *22*, 246, doi:10.1186/s12885-022-09349-y.

5. **Holmen Olofsson G**, Idorn M, Carnaz Simões AM, Aehnlich P, Skadborg SK, Noessner E, et al. Vg9Vd2 T Cells Concurrently Kill Cancer Cells and Cross- Present Tumor Antigens. Front Immunol. 2021;12 June:645151.

6. Jensen, A. W. P., Carnaz Simões, A. M., thor Straten, P., & **Holmen Olofsson, G.**(2021). Adrenergic Signaling in Immunotherapy of Cancer: Friend or Foe? *Cancers*, *13*(3), 1–15. https://doi.org/10.3390/cancers13030394.

7. **Holmen Olofsson G,** Pedersen SR, Aehnlich P, Svane IM, Idorn M, thor Straten P. The capacity of CD4+ Vγ9Vδ2 T cells to kill cancer cells correlates with co-expression of CD56. Cytotherapy. 2021;0:1–8. doi:10.1016/j.jcyt.2021.02.003.

8. **Holmen Olofsson, G**., Jensen, A. W. P., Idorn, M., & thor Straten, P. (2020). Exercise Oncology and Immuno-Oncology; A (Future) Dynamic Duo. *International Journal of Molecular Sciences*, *21*(11), 1–15. https://doi.org/10.3390/ijms21113816.

9. Aehnlich, P., Carnaz Simões, A. M., Skadborg, S. K., **Holmen Olofsson, G.**, & thor Straten, P. (2020). Expansion With IL-15 Increases Cytotoxicity of Vγ9Vδ2 T Cells and Is Associated With Higher Levels of Cytotoxic Molecules and T-bet. *Frontiers in Immunology*, *11*(August). https://doi.org/10.3389/fimmu.2020.01868.

10. Peeters, M. J. W., Dulkeviciute, D., Draghi, A., Ritter, C., Rahbech, A., Skadborg, S. K.,… **Holmen Olofsson, G.**, … thor Straten, P. (2019). MERTK Acts as a Costimulatory Receptor on Human CD8+ T Cells. *Cancer Immunology Research*, canimm.0841.2018. https://doi.org/10.1158/2326-6066.CIR-18-0841.

11. Idorn, M., Skadborg, S. K., Kellermann, L., Halldórsdóttir, H. R., **Holmen Olofsson, G.**, Met, Ö., &

thor Straten, P. (2018). Chemokine receptor engineering of T cells with CXCR2 improves homing towards subcutaneous human melanomas in xenograft mouse model. *Oncoimmunology*, *7*(8), e1450715. https://doi.org/10.1080/2162402X.2018.1450715.

12. Pedersen, L., Idorn, M., **Olofsson, G. H.**, Lauenborg, B., Nookaew, I., Hansen, R. H., … Hojman, P. (2016). Voluntary Running Suppresses Tumor Growth through Epinephrine- and IL-6-Dependent NK Cell Mobilization and Redistribution. *Cell Metabolism*, *23*(3), 554–562. https://doi.org/10.1016/j.cmet.2016.01.011.

13. Hjortsø, M. D., Larsen, S. K., Kongsted, P., Met, Ö., Frøsig, T. M., **Andersen, G. H.**, … Andersen, M. H. (2015). Tryptophan 2,3-dioxygenase (TDO)-reactive T cells differ in their functional characteristics in health and cancer. *OncoImmunology*, *4*(1), e968480. https://doi.org/10.4161/21624011.2014.968480.

14. Munir, S., **Andersen, G. H.**, Svane, I. M., & Andersen, M. H. (2013). The immune checkpoint regulator PD-L1 is a specific target for naturally occurring CD4+ T cells. *Oncoimmunology*, *2*(4), e23991. https://doi.org/10.4161/onci.23991.

15. Munir, S, **Andersen, G. H**., Woetmann, A., Ødum, N., Becker, J. C., & Andersen, M. H. (2013). Cutaneous T cell lymphoma cells are targets for immune checkpoint ligand PD-L1-specific, cytotoxic T cells. *Leukemia*, *27*(11), 2251–2253. https://doi.org/10.1038/leu.2013.118.

16. **Andersen, G. H.*,** Munir, Shamaila*, Met, Ö., Donia, M., Frøsig, T. M., Larsen, S. K., … Andersen, M. H. (2013). HLA-restricted CTL that are specific for the immune checkpoint ligand PD-L1 occur with high frequency in cancer patients. *Cancer Research*, *73*(6), 1764–1776. https://doi.org/10.1158/0008-5472.CAN-12-3507. ** congributed equally to the study.*

Publications in national and non-peer reviewed journals

1. **Podcast** episode: 'Cancer, immuntherapi og træning'. LydDoping – Dansk Sportsmedicin. May 2024.

2. **Holmen Olofsson G.** 'Skal kræftpatienter kombinere træning og behandling med immunterapi?'. Dansk Sportmedicin, May 2024. Article.

3. **Holmen Olofsson G.** 'γδ T-celler kan både dræbe tumorceller og krydspræsentere tumor antigener'. Best Practive Nordic (BPN), September 2021.

4. 'Dansk forsøg: Kan benhård træning forbedre behandling af lungekæft' by Thomas Hoffmann, Jounalist, Videnskab.dk. June 2021. Interview about the HI AIM clinical trial.

5. 'Kemo og kondicykel', by Janni Brixen, Journalist, News and Communication at the Danish Cancer Society. May 2021. Interview about the HI AIM clinical trial.