

ÅRSRAPPORT FRA FORSKNINGSGRUPPENE 2022

Klinikk for kirurgi, inflammasjonsmedisin
og transplantasjon (KIT)



Innholdsfortegnelse

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Avdeling for gastro- og barnekirurgi (AGK)

- Barnekirurgi
- Kolorektal kirurgi
- Pancreaskreft
- Svlster i lever og galleveier
- Øsafagus- og ventrikkelsykdommer

Avdeling for revmatologi, hud og infeksjonssykdommer (RHI)

- Hud
- Klinisk immunologi og infeksjonsmedisin
- Epidemiologi og utkomme ved revmatisk sykdom
- Fibroserende inflammatoriske revmatiske sykdommer (Nor-FIORD)
- Klinisk barnerevmatologisk forskning

Avdeling for transplantasjonsmedisin (ATX)

- Forskningsgruppe for transplantasjonsonkologi
- Klinisk forskningsgruppe for primær skleroserende kolangitt
- Transplantasjonsmedisin
- Eksperimentell Celletransplantasjon
- Klinisk Effektforskning
- Forskningsgruppe for pasientraporterte resultater og helseøkonomi
- Nevroendokrine svulster

Avdeling for urologi (URO)

- Rekonstruktiv urologi og nevrourologi
- Prostatakreft

Institutt for indremedisinsk forskning (IMF)

- Aterosklerose og relaterte metabolske sykdommer
- Innflammasjonsmarkører for hjertekar- og metabolske sykdommer
- Eksperimentell leverforskning
- Inflammasjonssykdommers genomikk og metagenomikk
- Klinisk mikrobiologi og microbiota medisin

Forord / Preface

The most significant development related to research in 2022 was the vanishing of Covid-restrictions. Research has always had significant benefit from personal interactions, and particularly for difficult topics and development of complex ideas, there is a need to meet and discuss face-to-face. After the lifting of Covid-restrictions, group meetings, research seminars and informal and formal collaborative meetings – locally, nationally, and internationally – restarted, and over the course of the summer and fall, most activities returned to the normal functioning of pre-Covid times.

The action plan for research in KIT gave priority to the importance of re-activating international relations following Covid-19, and a program was developed for supporting a small research exchange program for KIT-researchers to visit international institutions with an emphasis on the acquisition of new methods and skills. This program will be implemented throughout 2023 and responds to the lack of international travels for our researchers during the pandemic.

Another key element to the action plan for research in 2022 was to support career development and clinical researchers by allowing a paid relief from clinical duties. The program was hugely popular, and amongst 23 applications, a total of 6 grant recipients were supported for a range of activities, such as protocol and grant application development, setting up clinical trials, writing manuscripts and articles, and improve research registries.

We also hosted several seminars, of which a particular mentioning should be done for the seminars on popular research communication and big data and artificial intelligence, in follow-up to plans made throughout 2021. The seminar related to collaborations between Department of pathology and KIT was also popular, and put the spotlight on the need for good and strong links between the surgical activities in KIT and the processing and biobanking of tissue samples by the Department of pathology.

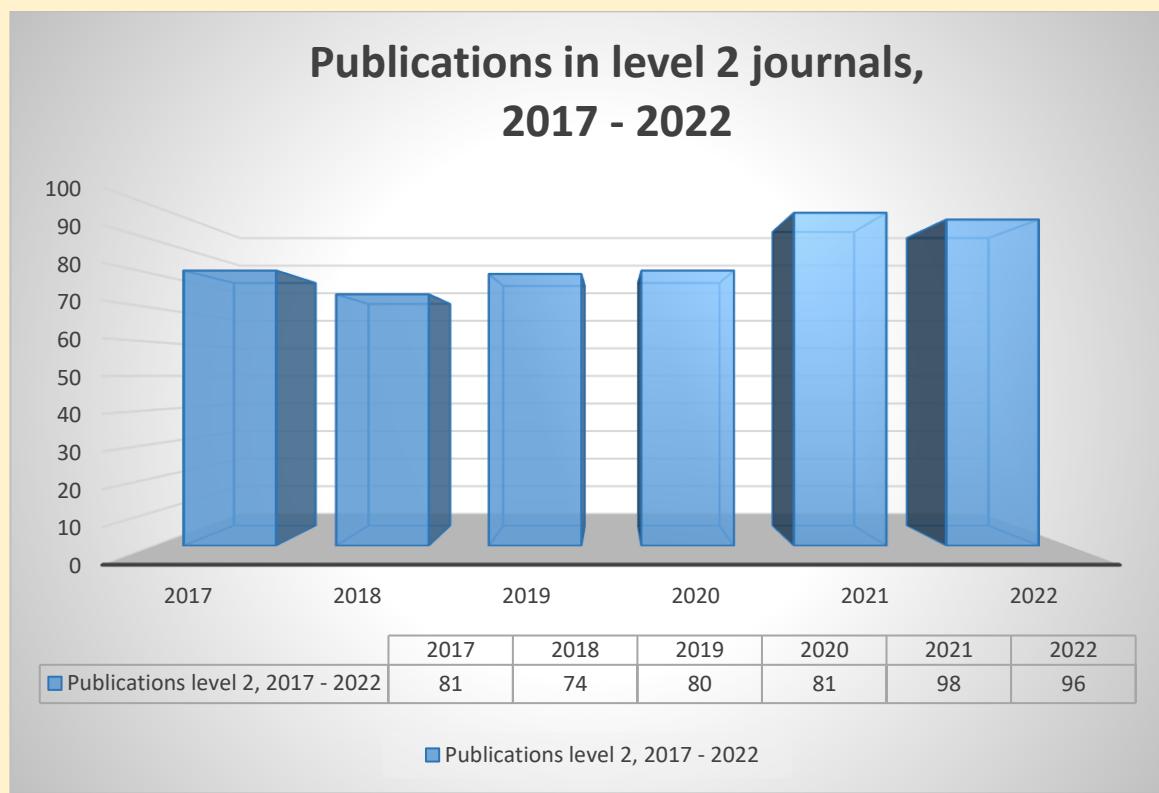
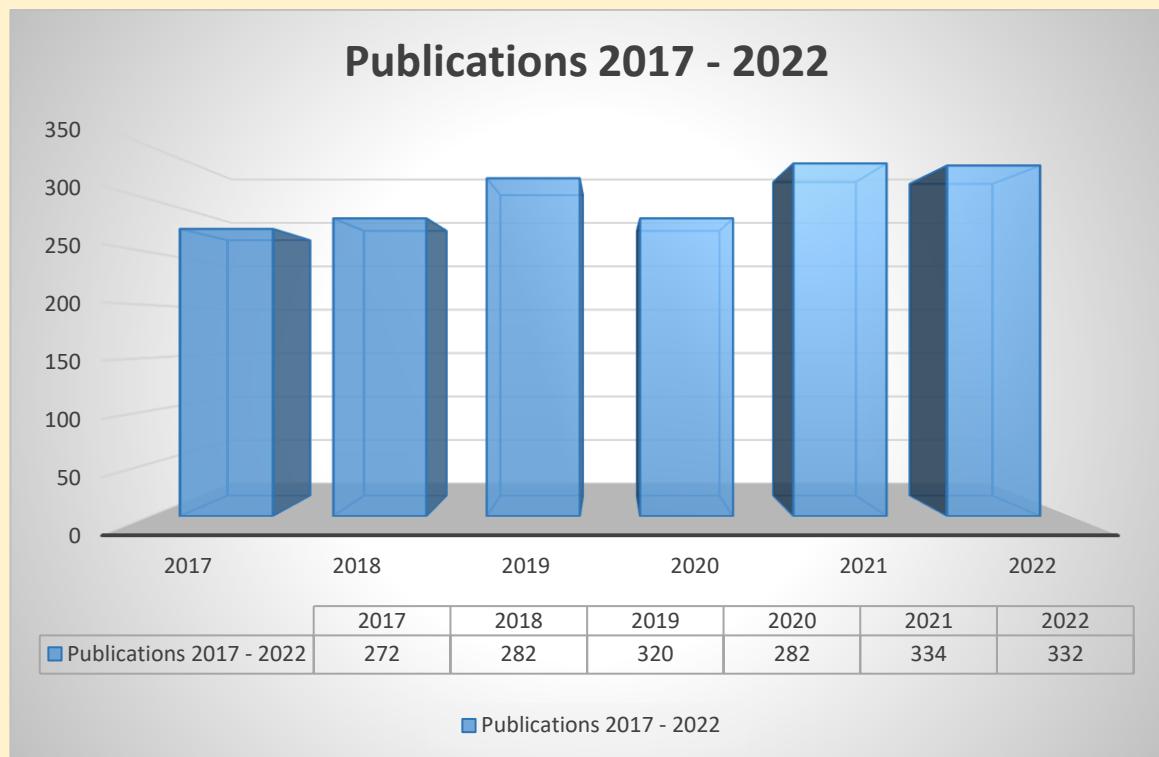
Extramural research grants continue to be the cornerstone of research support in KIT. We note with great interest that amongst comparable clinics within OUH, the fraction of resources in KIT spent for research from external funding sources vs internal funding is extremely high, with an overall number of 213% in 2022 (i.e. external research funds are 2.13 times higher than the baseline funding for research and researcher positions coming via OUH). The range for this number for similar divisions within OUH spans from 79% to 239%, with only one clinic having a higher fraction of extramural funding than KIT. Tremendous efforts are put down in obtaining research grants, and from a research leadership perspective we wish to thank our researchers for this work. We feel proud that the success rate for the South-Eastern Norway Regional Health Authority grants and fellowships program in 2022 was 34,3%, with a total of 11 applications granted (out of a total of 32).

Also per publication output, our researchers maintain high standards. Out of a total of 332 publications in 2022, 29,2% were published in level 2 journals. We remain involved in the competition for the OUH research awards, with Silje Fjellgård Jørgensen being awarded the OUH Early Career award in 2022, and a team from the Department of Urology the prize for best research article of the second half of 2022. There is little doubt that research in KIT has survived the pandemic, and we look forward to following developments into 2023.

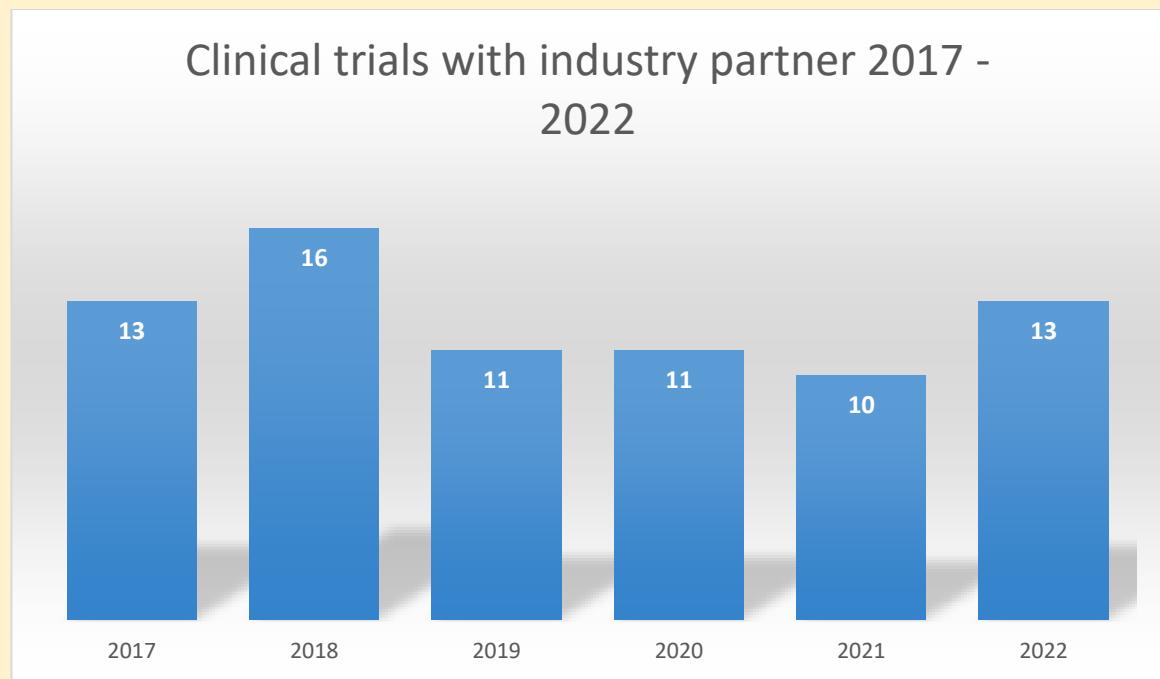
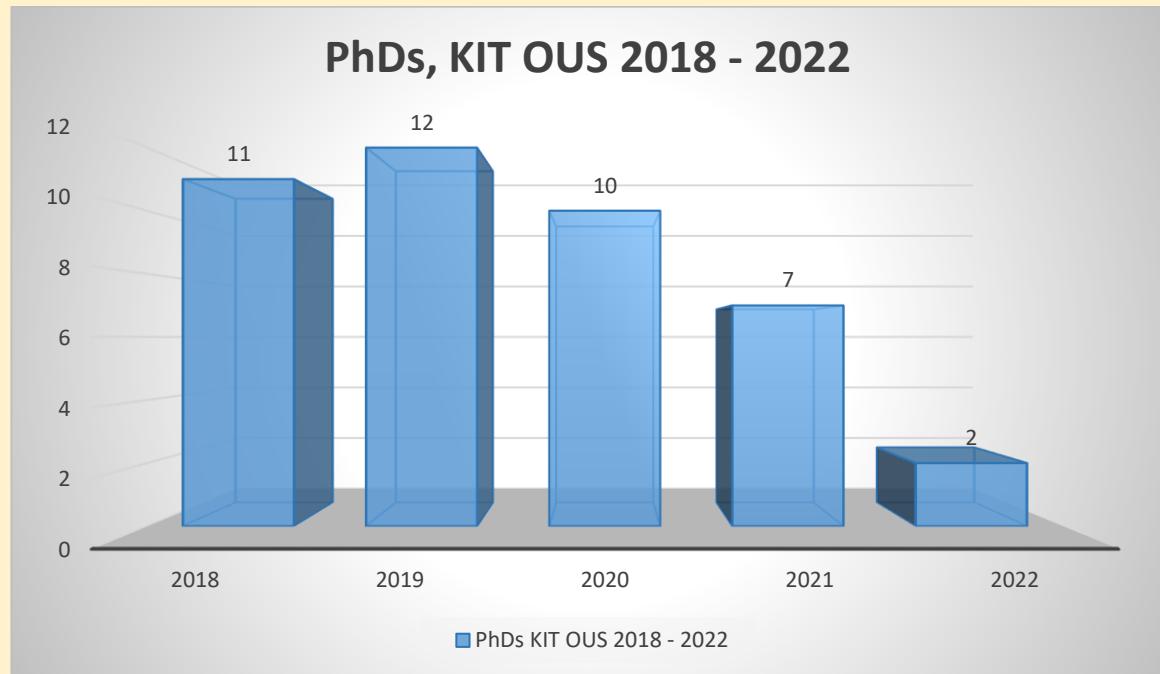
Tom Hemming Karlsen,

Forskningsleder v/KIT

Research Activity 2022

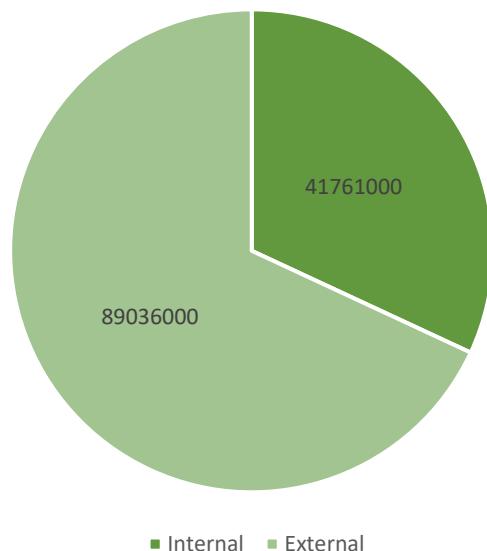


Research Activity – 2022

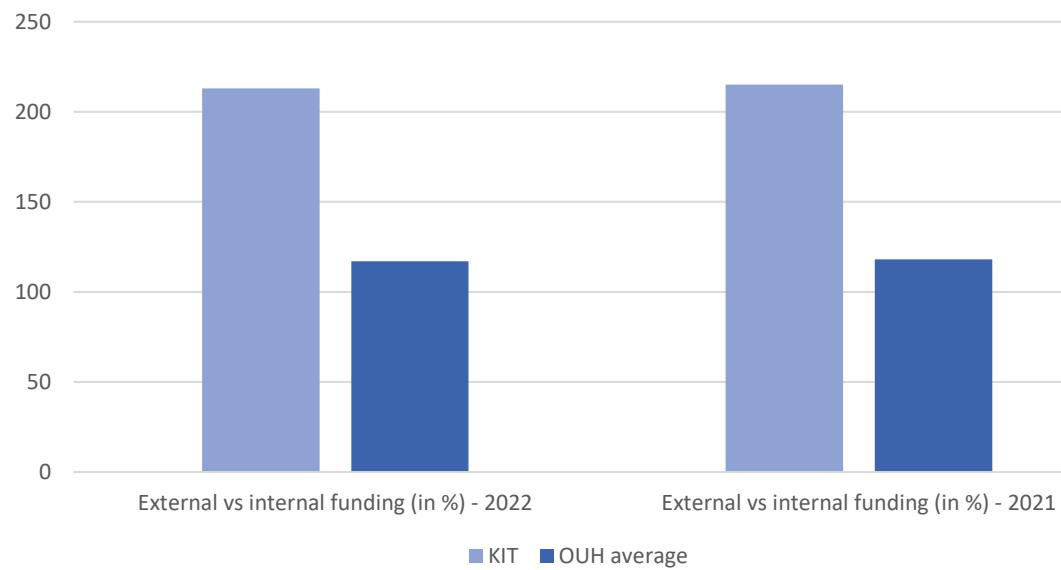


Research Activity – 2022

External vs internal research funding in KIT (in NOK)



External vs. internal research funding in KIT



The Research Committee in KIT (KIT-FU)

Members of the committee:

- Sheraz Yaqub, HPB-surgery
- Henriette Veiby Holm, Urology
- Bente Halvorsen, Research Institute of Internal Medicine (spring 2022)
- Ida Gregersen, Research Institute of Internal Medicine (autumn 2022)
- Hanne Scholz, Experimental Cell Transplantation
- Pernille Bøyesen, Rheumatology
- Ebbe Billmann Thorgersen, Surgical Oncology
- Astrid Klopstad Wahl, Health Sciences
- Tom Mala, Gastrointestinal surgery

and

- Tom Hemming Karlsen, Head of Research
- Morten Tandberg Eriksen, Head of Division
- Steinar Heldal, Head of Research Administration



Research groups

Department of Transplantation Medicine

Clinical PSC Research Group	Trine Folseraas
Neuroendocrine tumors	Espen Thiis-Evensen
Kidney Transplant Medicine	Trond Geir Jenssen
Transplant oncology	Pål-Dag Line
Clinical Effect Research within Gastroenterology	Mette Kalager
Experimental Cell Transplantation	Hanne Scholz
Patient Reported Outcomes and Health Economics	Marit Helen Andersen

Department of Rheumatology, Dermatology and Infectious Diseases

Dermatology Research Group	Olav Sundnes
Fibrotic Inflammatory Rheumatic Diseases (Nor-FIORD)	Anna-Maria Hoffmann-Vold
Paediatric Rheumatology Research Group	Berit Flatø
Epidemiology and outcomes in rheumatic diseases	Helga Sanner
Clinical immunology and infectious diseases	Børre Fevang
<i>Olafia Research group for venerology</i>	-

Research Institute of Internal Medicine

Immune regulation in atherosclerosis and other cardiometabolic diseases	Bente Halvorsen
Genomics and Metagenomics in Inflammatory Disorders	Johannes E. R. Hov
Inflammatory Biomarkers in Cardiovascular and Metabolic Disease	Thor Ueland
The Experimental liver research group	Espen Melum
Infectious Immunology	Marius Trøseid

Department of Urology

Prostate Cancer Research Group	Viktor Berge
Research group for reconstructive urology and neurourology	Henriette Veiby Holm

Department of Hepatic, Gastrointestinal and Paediatric Surgery

Colorectal surgery	Ole Helmer Sjo
Hepatobiliary malignancies	Sheraz Yaqub
Esophagus and stomach	Tom Mala
Pediatric surgery	Kristin Bjørnland
Pancreatic cancer	Knut Jørgen Labori
<i>Translational Cancer Therapy (part of Institute for Cancer Research)</i>	Kjersti Flatmark

Handlingsplan for forskning 2022, Klinikk for kirurgi, inflamasjonsmedisin og transplantasjon (KIT)

HOVEDPROSJEKTER OG TILTAK I 2022	ANSVAR	Ref. til hovedmål i OUS forsk.strategi
Stimulere klinisk forskning og flere kliniske studier		
<ul style="list-style-type: none"> • Utlyse 3-4 frikjøpsperioder for klinikere til forskning • Vurdere muligheter for utvidelse av/økt kapasitet i Senter for kliniske studier i KIT • Synliggjøre Protokollutvalgets tilbud om rådgivning • Gjennomgå prisfastsetting av tjenester i kliniske studier, og vurdere behov for maler/veiledninger ifm egeninitierte kliniske studier 	KIT-FU / Forsk.adm. Protokollutvalget	Hovedbruk av stim.midler 2022
Forskningsformidling		
<ul style="list-style-type: none"> • Arrangere kurs/seminar i forskningsmidling, med opplæring og trening spesielt i nye presentasjonsformater. • Vurdere/implementere tiltak for å styrke den eksterne forskningsformidlingen, og styrke formidling og nyttiggjøring av forskningsresultater internt i egen avdeling/sekksjon/i KIT. 	Arbeidsgruppe: Hanne Scholz, Steinar Heldal + andre ressurspersoner	
Helsefaglig forskning		
<ul style="list-style-type: none"> • Stimuleringsplan for karriereløp for helsefaglige forskere i KIT • Gjennomgå og formidle resultater fra "Health Literacy Day" i KIT. 	Astrid K. Wahl + andre ressurspersoner	
Internasjonalisering		
<ul style="list-style-type: none"> • Vurdere mulige internasjonaliseringstiltak med tanke på bruk av stimuleringsmidler i 2023 med blikk til UiOs «Circle U» satsning 	Arbeidsgruppe: Ebbe B. Thorgersen, Bente Halvorsen, + 1-2 yngre forskere	
Industrisamarbeid		
<ul style="list-style-type: none"> • Utarbeide enkle kjøreregler og internveileder for industrisamarbeid i KIT, basert på OUS' bestemmelser og andre styrende dokumenter, og de muligheter som Veksthuset for livsvitenskap gir. 	Arbeidsgruppe: Tom H. Karlsen, Olav Sundnes, Tom Mala, Michael Brethauer + andre ressurspersoner	
Karriereutvikling yngre forskere		
<ul style="list-style-type: none"> • Gjennomgå evaluering av Masterclass 2021 og foreslå endringer og tilpasninger ved en eventuell ny runde i 2023/2024 • Vurdere oppfølgingskurs for Masterclass deltakere • Utvide Søknadspoliklinikken til to trinn for yngre forskere 	Arbeidsgruppe: Steinar Heldal, Henriette V. Holm, Sheraz Yaqub, Hanne Scholz	
Samarbeidsarena om stordata, biostatistikk og bioinformatikk		
<ul style="list-style-type: none"> • Seminar om stordata i forskning i KIT, for forskere med kompetanse/interesse for bioinformatikk/biostatistikk. 	Arbeidsgruppe: Magnus Løberg, Sheraz Yaqub	
Strategi for translasjonsforskning på nye RH		
<ul style="list-style-type: none"> • Arbeide for best og mest mulig hensiktssmessig lokalisering av IMF i Nye OUS, fortrinnsvis gjennom samlokalisering med tematiske relevante translasjonsforskningssinstitutter. 	IMF + forskningsleder/klinikkleder	
LØPENDE AKTIVITETER og SAMARBEIDSMØTER		
Forskning og Nye OUS	KIT-FU	
Søknadspoliklinikker 2022	Forskningsledelsen	
Samarbeidsseminar KIT og Patologi	Forskningsledelsen	
Samarbeidsseminar KIT og OsloMet (Fakultet for helsefag)	Senter for helsefagforskning	
Nettverk for biobankingeniører og studie-/forskningssykepleiere i KIT	Forskningsledelsen	
Kjøpe plasser på kurs i medisinsk publisering og utlyse disse for forskere i KIT	Forskningsledelsen	

Avdeling for gastro- og barnekirurgi (AGK) / Department of Gastrointestinal and Children Surgery

- Barnekirurgi/ Pediatric Surgery
- Kolorektal kirurgi/ Colorectal Surgery
- Pancreaskreft/ Pancreatic Cancer
- Svlster i lever og galleveier/ Hepatobiliary malignacies
- Øsafagus- og ventrikkelsykdommer/ Diseases of esophagus and stomach

Forskningsgruppe: Barnekirurgi

Research group: Pediatric surgery

Avdeling: AGK

Gruppeleder: Kristin Bjørnland

Om gruppen: Hovedfokus er å studere somatiske og psykososiale forhold hos pasienter som er operert for gastrointestinale og urogenitale medfødte misdannelser, samt solide svulster utenfor sentralnervesystemet. Pasientrapporterte data vektlegges. Vi undersøker hvordan operasjonstekniske og behandlingsmessige faktorer påvirker somatiske, psykososiale og livskvalitet parametre. Forskningsprosjektene er tverrfaglige med bredt forskningssamarbeid nasjonalt og internasjonalt. Medlemmer i gruppen er også involvert i translasjonsforskning hvor man studerer immunologiske faktorers betydning hos pasienter med medfødt kolorektalsydom.

About the group: The main focus is to study somatic and psychosocial long-term outcome in patients operated for congenital gastrointestinal and urogenital conditions, as well as solid tumors outside of the central nervous system. Patient-reported outcomes are in focus. We examine how surgical techniques and follow-up protocols influence these parameters. All projects have a strong focus on interdisciplinary collaboration, and the group collaborates both nationally and internationally. Members of the group are also involved in translational research addressing the impact of immunological factors on patients with congenital colorectal disease.

Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Aksnes, Gunnar	Consultant, PhD,	OUS	Gunnar.aksnes@ous-hf.no
Arntzen, Trine	Med student research fellow	UiO	Trine.arntzen@studmed.uio.no
Bjørnland, Kristin	Consultant, Professor, Group leader	OUS, UiO	Kristin.bjornland@medisin.uio.no
Elveos, Marlene	Registrar	OUS	Mamely@ous-hf.no
Emblem, Ragnhild	Professor emerita	UiO	Ragnhild.emblem@medisin.uio.no
Engebretsen, Anders	Surgical registrar, PhD	OUS	anheng@ous-hf.no
Ertresvåg, Kjetil	Consultant	OUS	uxkjrt@ous-hf.no
Fosby, Marianne	Consultant	OUS	martei@ous-hf.no
Fyhn, Thomas	Registrar	UiO	t.j.fyhn@medisin.uio.no
Hameed, Rania	Consultant	Innlandet hospital	Rania.adel.hameed@sykehuset-innlandet.no
Hoel, Anders	PhD student	OUS	a.t.hoel@ous-hf.no
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Johansen, Hanna	Research Fellow	Helse sørøst	Hajoh3@ous-hf.no
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Kvello, Morten	PhD student	UiO	mkvello@gmail.com
Lundar, Live	Consultant/PhD Student, MD	UiO	Live.lundar@medisin.uio.no
Mikkelsen, Audun	Consultant/PhD Student, MD	UiO	Audun.mikkelsen@medisin.uio.no
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Røkkum, Henrik	Registrar	OUS	B26425@ous-hf.no
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Treider, Martin	Registrar	OUS	martintreider@gmail.com
Urdal, Andreas	Consultant	OUS	andurd@ous-hf.no

Associated members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/ AFFILIATION	E-MAIL
Andersen, Marit	Professor	UiO	Marit.andersen@medisin.uio.no
Austrheim, Astri	Stoma nurse	OUS	Astrid.ingerborg.austrheim@ous-hf.no
Birketvedt, Kirsti	Nutritionist	OUS	kbirkevt@ous-hf.no
Gjone, Helene	Consultant child psychiatrist, PhD	OUS	hegjon@ous-hf.no
Diseth, Trond	Consultant, Professor	OUS, UiO	tdiseth@ous-hf.no
Gulseth, Eirik	Nurse, research fellow	OUS	eirgul@ous-hf.no
Haugen, Guttorm	Professor, gynecologist	OUS, UiO	ghaugen@ous-hf.no
Jahnsen, Frode	Professor, pathologist	OUS, UiO	f.l.jahnsen@medisin.uio.no
Knatten, Charlotte	Consultant pediatrician, PhD	OUS	charlotte@knatten.org
Øresland, Tom	Professor emeritus	Ahus	Tom.oresland@medisin.uio.no

Forskningsaktivitet i 2022:

Internasjonalt samarbeid. Flere pågående prosjekter gjennom ERNICA, SIOPEN og The Nordic Pediatric Surgery Study Consortium om index tilstander i barnekirurgi.

Nasjonalt samarbeid med 1: barnekirurgisk avdeling, St Olavs Hospital; 2: Bekkensenteret på Akershus universitetssykehus.

Disputas: Thomas J Fyhn 22.03.22 "Small incisions, Big benefits? A randomized controlled trial comparing laparoscopic and open Nissen fundoplication in children.

Pågående prosjekter. Det er tre pågående doktorgradsprosjekter: Audun Mikkelsen: Langtidsresultater etter operasjon for øsofagusatresi; Live Lundar: Uretralklaffer hos barn, Anders Telle Hoel: Anorektale misdannelser – overgang fra ungdom til voksne. Gruppen har to forskerlinjestudenter; Remi Andre Karslen (Resultater etter operasjon for Hirschsprung sykdom) og Trine Arntzen (Prenatal diagnostikk ved øsofagusatresi). Andre prosjekter: Short- and long-term complications after resection of ganglioneuroma-a SIOPEN study. Oppfølging av ikke-operert hydronefrose. Appendicostomi – langstidsresultater. Mental helse og livskvalitet hos ungdommer med medfødte anorektale tilstander. Analblokking-foreldre erfaringer. Duodenalatresi – langstidsresultater og livskvalitet. Nekrotiserende enterokolitt – resultater etter kirurgisk behandling – en nasjonal studie. Resultater etter stapling av stomier som behandling av prolaps. Minimal invasiv kirurgi hos nyfødte – resultater.

Publikasjoner: Gruppens medlemmer var forfattere på 15 publikasjoner i 2022; hvorav 11 hadde førsteforfatter og/eller sisteforfatter fra barnekirurgisk forskningsgruppe.

Populærvitenskapelig aktivitet: Medlemmer i gruppen har holdt innlegg på pasientforeningsmøter for flere diagnosegrupper. Forskningsresultater har vært fremstilt på flere internasjonale og nasjonale konferanser for barnekirurger og pediatre.

Forskningsgruppe: Kolorektal kirurgi Ullevål

Research group: Colorectal surgery

Avdeling: Avdeling for gastro- og barnekirurgi

Gruppeleder: Ole Helmer Sjo

Om gruppen:

Forskningsgruppen er ansvarlig for all forsknings og kvalitetsforbedrende aktivitet ved kolorektal enheten i avdeling for gastro- og barnekirurgi. Gruppen har frem til 2021 vært ledet av prof. Emeritus Arild Nesbakken. Han er fremdeles ansvarlig for vår utstrakte deltagelse innen translasjonsforskning i samarbeid med Institutt for kreftforskning ved OUS – Radiumhospitalet, og i mangel av professorkompetanse ved enheten vår mentor innen forskning.

Gruppen har noen definerte deltakere med varierende forsknings kompetanse (se liste), men er prinsipielt åpen for alle enhetens/avdelingens leger og samarbeidspartnere med interesse for kolorektal forskning. Dette gjenspeiler seg i at alle kollegene inviteres til våre regelmessige forskningsgruppe møter. Viktige overordnede målsetninger er:

- 1: Engasjere flest mulig kolleger i forsknings- og kvalitetsforbedrende prosjekter (bredde).
- 2: Sikre at enheten deltar i forskning på høyt nivå (spisse).

Gruppen har arbeidet for at forholdene for forskningsarbeid legges til rette fra avdelingens side, og møter stor velvilje i dette fra ledelsen.

About the group (short description in English):

The research group is responsible for all research and quality-improving activity at the colorectal unit in the department of gastro- and pediatric surgery. Until 2021, the group has been led by Prof. Emeritus Arild Nesbakken. He is still responsible for our extensive activity on translational research in collaboration with the Department of Cancer Research at OUS-Radiumhospitalet, and in the absence of professor competence at our unit, he function as senior mentor in research.

The group has some defined participants with varying research competence (see list), but the group is principally open to all the unit's / department's doctors and partners with interest in colorectal research. Due to this all colleagues are invited to our regular monthly research group meetings. Important overall objectives are:

- 1: Engage as many colleagues as possible in research and quality improvement projects (breadth).
- 2: Ensure that the unit participates in high-level research (pointed).

The group has worked to ensure that the conditions for research work are facilitated by the department, and meets great goodwill in this from the management.

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Ole Helmer Sjo	Group leader / Senior consultant	OUS	olesjo@ous-hf.no
Arild Nesbakken	Adjunct Professor	OUS and UiO	arild.nesbakken@medisin.uio.no
Tuva Høst Brunsell	MD PhD research fellow	UiO	t.h.brunsell@medisin.uio.no

Morten Tandberg Eriksen	Associate Professor /Senior consultant	OUS and UiO	sbermo@ous-hf.no
Sigurd Folkvord	Post.doc	OUS	
Usman Saeed	PhD student	OUS	
Erlend Strønen	Post doc	OUS	
Tom-Andreas Wik	Senior consultant	OUS	uxwikt@ous-hf.no
Tom Glomsaker	Senior consultant	OUS	tomglo@ous-hf.no
Reidun Gustavsen	Study nurse		
Ingeborg F. Backe	Study nurse / Master nursing	OUS	ingbac@ous-hf.no
Gro Wiedswang	Post doc / Senior consultant	OUS	uxgrie@ous.hf.no

Assosierede medlemmer / Associated members:

NAME	POSITION/TITEL/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Egil Johnson	Adjunct Professor / senior consultant	OUS and UiO	
Tom Mala	MD PhD / senior consultant	OUS	
Ragnhild A Lothe	Professor	OUS and UiO	
Guro Elisabeth Lind	Adjunct Professor	OUS and UiO	
Anita Sveen	Associate Professor	OUS and UiO	
Aud Svindland	Professor emeritus	UiO	
Marianne G Guren	MD PhD / senior consultant	OUS	
Tormod K Guren	MD PhD / senior consultant	OUS	
Siri Rostoft	Adjunct Prof / senior consultant	OUS and UiO	

Forskningsaktivitet i 2022 / Research activity in 2022

Translasjonsforskning på kolorektal kreft er fremdeles et hoved satsings område i multidisiplinære team med dedikerte forskere fra klinisk medisin og biologi som dekker felt innen kolorektalkirurgi, hepatobiliær kirurgi, onkologi, radiologi, patologi og molekylær biologi. Gjennom 2022 har samarbeidet med DNR blitt utvidet med forbedring av rutiner for inkludering av kolorektal cancer pasienter til biobanking.

Spesifikke målsetninger har vært å utvikle nye diagnostiske, prognostiske, prediktive og monitorerende biomarkører for koloraktal kreft. Kontinuerlig innsamling av ferskt tumorvev og normalt vev av høy kvalitet, innsamling av formalin fiksert vev samt blod / serum /beinmargsprøver til vår omfattende biobank kombinert med svært omfattende kontinuerlig oppdaterte klinisk database for kolorektal primær cancer, levermetastaser i uselektert populasjonsbasert pasient register sikrer optimalt grunnlag for både klinisk forskning og translasjonsforskning på høyt nivå.

I 2022 har forskningsgruppen fortsatt sitt arbeid med å planlegge og initiere kliniske studier, både lokalt ved enheten samt gjennom deltagelse i multisenter studier. Enheten har deltatt i SCANDIV II (Scandinavisk multisenter studie på komplisert divertikulitt) og fulgt opp pasienter inkludert i NORWAIT studien på rektum cancer etter komplett respons på neoadjuvant strålebehandling. Forskningsgruppen har organisert oppstarten av den nasjonale Norwegian Stoma Trial som studerer avlastende og permanent stomi etter operasjon for rectum cancer. Enheten deltar i det nasjonale kvalitetsregisteret NorGast med 100 % inklusjon av våre kolorektal cancer pasienter.

Forskningsgruppen har initiert oppstarte av flere interne kvalitetsregister/studier på akutt appendicitt, neoplasier i appendix etter appendectomi, kirurgiske resultater etter anleggelse av stomier, særlig i forbindelse med rektum cancer operasjoner, bruk av ICG for testing av sirkulasjon ved anleggelse av tarm-anastomoser, resultater etter kirurgi for IBD, rektum prolaps og endometriose. I tillegg har gruppen initiert kvalitets/forsknings studier i

forbindelse med oppstart av robot assistert kolorektal kirurgi ved Ullevål, hvor spesielt behandling av rektum cancer er aktuell for klinisk forskning.

Enheten har en stadig voksende cohorte av TEM (Transanal Endoskopisk Mikrokirurgi) opererte pasienter gjennom mer enn to tiår, og har i 2022 fortsatt arbeidet med analysering, i første omgang på pasienter behandlet for rektum cancer i tidlig stadium. Første publikasjon forventes i 2023, og vil kunne utvides til et PhD program.

LapcoNor er et pågående nasjonalt utdanningsprogram i laparoskopisk kirurgi for kolorektal kreft som ble etablert i 2015 og ledes av Ole Sjo. Prosjektet hadde planlagt et PhD studie, men tiltenkt kandidat trakk seg dessverre ut av prosjektet før godkjenning. Man vil fortsette å søke om forskningsmidler til dette prosjektet, med utsatt oppstart til 2023-24.

Prosjektet har utviklet et kurs med simulatorøvelser på lik ("cadaver-kurs"), som sammen med det pedagogiske Tren-Treneren kurs for strukturert og standardisert opplæring i laparoskopisk kolorektal cancer kirurgi ble inkorporert i det nye nasjonale obligatoriske «Kurs i kolorektal cancer med praktiske øvelser på modell» for spesialist utdannelsen i gastrokirurgi (ny struktur fra 2019). Oppstart med 1. kurs på Ullevål er lagt til uke 3 i 2023, med tilhørende muligheter for klinisk forskning.

Kolorektal enheten ansatte i 2022 dr. Johannes Kurt Schultz som 1. amanuensis i stillingen etter prof. Emeritus Arild Nesbakken. Han tiltreder denne stillingen 01.01.2023.

Forskningsaktivitet – publikasjoner 2022/publications 2022:

1. Body mass index and pancreatic adenocarcinoma: A nationwide registry-based cohort study.
Saeed U, Myklebust TÅ, Robsahm TE, Møller B, Mala T, Skålhegg BS, Yaqub S. Scand J Surg. 2023 Mar;112(1):11-21. doi: 10.1177/14574969221127530. Epub 2022 Sep 29. PMID: 36173093
2. Risk and survival in colorectal cancer with increasing body mass index: A nationwide population-based cohort study.
Saeed U, Myklebust TÅ, Robsahm TE, Kielland MF, Møller B, Skålhegg BS, Mala T, Yaqub S. Colorectal Dis. 2023 Mar;25(3):375-385. doi: 10.1111/codi.16367. Epub 2022 Nov 17. PMID: 36222384
3. A clinical decision support system optimising adjuvant chemotherapy for colorectal cancers by integrating deep learning and pathological staging markers: a development and validation study.
Kleppe A, Skrede OJ, De Raedt S, Hveem TS, Askautrud HA, Jacobsen JE, Church DN, Nesbakken A, Shepherd NA, Novelli M, Kerr R, Liestøl K, Kerr DJ, Danielsen HE. Lancet Oncol. 2022 Sep;23(9):1221-1232. doi: 10.1016/S1470-2045(22)00391-6. Epub 2022 Aug 11. PMID: 35964620
4. E-cadherin is a robust prognostic biomarker in colorectal cancer and low expression is associated with sensitivity to inhibitors of topoisomerase, aurora, and HSP90 in preclinical models.
Bruun J, Eide PW, Bergsland CH, Bruck O, Svindland A, Arjama M, Välimäki K, Bjørnslett M, Guren MG, Kallioniemi O, Nesbakken A, Lothe RA, Pellinen T. Mol Oncol. 2022 Jun;16(12):2312-2329. doi: 10.1002/1878-0261.13159. Epub 2021 Dec 26. PMID: 34890102 Free PMC article.
5. Spatial analysis and CD25-expression identify regulatory T cells as predictors of a poor prognosis in colorectal cancer.
Bergsland CH, Jeanmougin M, Moosavi SH, Svindland A, Bruun J, Nesbakken A, Sveen A, Lothe RA. Mod Pathol. 2022 Sep;35(9):1236-1246. doi: 10.1038/s41379-022-01086-8. Epub 2022 Apr 28. PMID: 35484226 Free PMC article.

Forskningsgruppe: Pancreaskreft

Research group: Pancreatic cancer

**Avdeling: Department of Hepato-Pancreato-Biliary Surgery,
Division of Surgery, Inflammatory Diseases and Transplantation**

Gruppeleder: Knut Jørgen Labori

Om gruppen:

Forskningsgruppen arbeider med klinisk onkologisk forskning ved pancreaskreft, både innen kirurgisk og medikamentell behandling. En betydelig del av forskningen er kliniske studier og translasjonsforskning. Gruppens medlemmer arbeider innen flere fagfelt som kirurgi, onkologi, gastroenterologi, patologi og molekylærbiologi. Hovedmålet er å bedre diagnostikk og behandling og derav prognosene for pasienter med pancreaskreft. Translasjonsforskningen baserer seg på tumorvev og blodprøver fra pasienter som behandles ved OUS og arbeider med å kartlegge biologiske prosesser og identifisere biomarkører ved pancreaskreft. Det er utstrakt nordisk og internasjonalt samarbeid innen flere kliniske og translasjonsprosjekter. Forskningsgruppen har etablert en biobank for samling av tumorvev og blodprøver med tilhørende database og et klinisk register for pasienter som blir operert for pancreaskreft ved OUS.

About the group:

The research group is an interdisciplinary forum that perform clinical trials and translational research on pancreatic cancer and pancreatic cysts. The research group studies the importance of environmental and genetic factors in cancer development, prognostic and predictive factors, early diagnosis, and the efficacy of surgical- oncological- and symptomatic treatment. Patients with pancreatic tumors treated at Oslo University Hospital is requested consent for storage of biological material and clinical data for use in research. The research group has established a clinical data registry and a biobank with an associated database. This ensures a systematic, prospective registration of patients with pancreatic cancer who are being treated at the hospital. Clinical registry contains relevant clinical and histopathological data from routine diagnostics. Biobank database contains the results of clinical and molecular research.

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
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Assoserte medlemmer / Associated members:

NAME	POSITION/TITEL/ROLE	EMPLOYER/AFFILIATION	E-MAIL
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Åsmund Fretland	Consultant surgeon, MD PhD	OUS, AGK KIT/ Intervention Centre	aafret@ous-hf.no

Aktivitet i 2022/ Activity in 2022

Forskningsaktivitet/ Research activity:

Projects:

-Thematic pancreatic tumour project: Oslo University Hospital has established a multidisciplinary research program for patients undergoing investigation for a solid or cystic pancreatic or periampullary neoplasm. Through this project the research group has established a clinical data registry and a biobank with an associated database. Patients undergoing surgical resection are asked for written informed consent to approve sampling of blood and tumour tissue for biobanking and to collect clinical data during hospital admissions or outpatient clinic visits.

-Norwegian Cancer Society - National Group of Expertise for Research on Pancreatic Cancer (KNEP). KNEP consists of nine research groups which focus on pancreatic cancer and bundle their research activities in the context of a 5-years' project. The research group for pancreatic cancer at OUH is responsible for several of the work packages

-PREPAIRD-study: Personalized Surveillance for Early Detection and Prevention of Pancreatic Cancer in High-Risk Individuals. This is a national project to establish and evaluate a surveillance program for early detection and prevention of pancreatic cancer in individuals with a hereditary predisposition to the disease. Surveillance consists of a combination of annual imaging and evaluation of blood borne biomarkers. PI: Eli Marie Grindedal (from Research Group Inherited Cancer).

Clinical trials:

-NorPACT-1: Scandinavian multicentre un-blinded phase II randomized controlled trial. Patients with resectable adenocarcinoma of the pancreatic head are randomized to receive either surgery first (control) or neoadjuvant chemotherapy (=intervention) with four cycles FOLFIRINOX followed by resection. Accrual February 2018–April 2021, and 140 patients from 12 centers have been randomized. In December 2022 the database was locked for primary end point, results expected early 2023. PI: professor Knut Jørgen Labori

-NorPACT-2: NorPACT-2 is a single arm prospective study of borderline and locally advanced pancreatic cancer, in which eligible patients undergo neoadjuvant treatment possibly followed by surgical exploration and resection. Accrual January 2018–December 2020, 251 patients have been included in Oslo. In September 2022 the database was locked for primary end point. Results expected early 2023. PI: professor Knut Jørgen Labori

Bolt-on to NorPACT 1 and 2 is a translational research program based on tumour tissue and plasma (PIs: professor Elin Kure and professor Caroline Verbeke) that aims at identifying factors that are predictive of response to neoadjuvant therapy, the risk of distant cancer spread, and patient outcome.

-DIPLOMA trial: Pan-European, randomized controlled, multicenter, patient-blinded non-inferiority trial comparing minimally invasive distal pancreatectomy to open distal pancreatectomy for pancreatic cancer. Patients with resectable adenocarcinoma of the pancreatic body or tail are randomized to undergo either minimally invasive or open distal pancreatectomy. Accrual December 2018-April 2021, and 258 patients from 31 centers have been randomized. Results expected early 2023. Local-PI: professor Bjørn Edwin

Thesis defense: -

Ongoing PhD projects:

1. Ingvild Farnes, MD: "New treatment approaches for resectable, recurrent and locally advanced pancreatic cancer". Main supervisor: professor Knut Jørgen Labori.
2. Ammar Khan, MD: "Complex vascular procedures during pancreatic and hepatobiliary surgery". Main supervisor: professor Knut Jørgen Labori.
3. Tore Tholfsen, MD: "Optimization of outcomes in pancreatic surgery". Main supervisor: professor Bjørn Edwin.
4. Inger Marie Bowitz Lothe, MD: "Molecular profiling of precursor lesions and tumours from the pancreatic head". Main supervisor: professor Elin Kure.
5. Stina M. Stålberg, MD: "Plasma exosomes and their cargo in relation to tumor profiles in pancreatic and colorectal cancers". Main supervisor: professor Elin Kure.

Populærvitenskapelig aktivitet/ Popular science:

Foredrag på Årsmøtet for Pankreaskreft Nettverk Norge desember 2022:
«Kirurgiske studier for en mer persontilpasset behandling» Knut Jørgen Labori
«Nye forskningsprosjekter» Caroline Verbeke
«Forskningsprosjektet MyPath» Olav Dajani

Forskningsgruppe: Svlster i lever og galleveier

Research group: Hepatobiliary malignancies

Avdeling: Avd for gastro- og barnekirurgi, Seksjon for HPB kirurgi

Gruppeleder: Sheraz Yaqub

Om gruppen:

Gruppens primære mål er å tilby pasienter med kreft i lever og galleveier den fremste behandlingen og dermed inkludere dem i både kliniske og translasjons forskningsprosjekter. Gruppen har også et stort klinisk register som brukes for å evaluere/forbedre kvaliteten på behandlingen vi tilbyr.

About the group:

The main aim of the research group is to conduct clinical and translational studies for the treatment of hepatobiliary malignancies. The group has also register-based studies to evaluate and improve patient treatment.

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Sheraz Yaqub	Group leader / Consultant / Associate Professor	OUS and UiO	shya@ous-hf.no
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Aktivitet i 2022 / Activity in 2022:

The research group has regularly meetings every month where progress of on-going projects as well as new projects are presented. Both main and associated members are invited.

On-going projects:

- The ASAC study, Scandinavian multicentre, placebo-controlled, randomized trial, initiated by our group, investigating the role of aspirin as adjuvant after surgery for colorectal liver metastases (www.asac.no). The trial is funded by Research Council of Norway, Norwegian Cancer Society, and KLINBEFORSK.
- EXCALIBUR study; single centre, un-blinded, three-armed randomized trial for patients with high load of colorectal liver metastases, treated with 1)liver transplantation 2)liver resection 3)hepatic artery infusion of chemotherapy. The trial is funded by South-East Norwegian health care authority (HSØ) (www.excaliburstudy.com).
- Precision Medicine in Early Diagnostics and Therapy of Biliary Tract Cancer; is a collaborative project between several groups, led by Sheraz Yaqub.
- TESLA1 & TESLA2 trial: Liver Transplantation for Non-Resectionable Intrahepatic Cholangiocarcinoma (TESLA1) and perihilar cholangiocarcinoma (TESLA2) are prospective exploratory trials. These are collaborative studies between several groups at OUH-KIT treating patients with cholangiocarcinoma.
- NEW-COMET trial; double-blinded RCT on liver resection vs thermal ablation for colorectal liver metastases (n=260 patients). The study is funded by South-East Norwegian health care authority (HSØ).
- The EVIDENT trial (Ex vivo drug sensitivity testing of metastatic colorectal cancer) is a prospective, single-arm phase II study of metastatic CRC, in which patients will receive standard or experimental anticancer agents guided by a combination of molecular markers and PDO drug sensitivities led by Prof Ragnhild Lothe.
- PREPOSTEROUS; a single blinded trial, initiated by University of Helsinki, investigating the role of low-molecular heparin administered pre-operatively vs. post-operatively.
- LIVACOR trial; International multicentre randomized trial comparing simultaneous and two-staged resection of colon cancer with synchronous liver metastases with regards to Time to functional recovery. OUH is the Norwegian site that recruits patients.

Planned projects:

- The SYLMET trial; a multicentre, randomized controlled trial, comparing simultaneous and two-staged resection of primary colorectal cancer with synchronous liver metastases.

Forskningsgruppe: Øsofagus- og ventrikkelsykdommer

Research group: Diseases of esophagus and stomach

Avdeling: Avd. for gastro- og barnekirurgi, OUS, Ullevål

Gruppeleder: Tom Mala from 01.01.2022

Om gruppen:

Gruppen driver tværfaglig forskning knyttet til sykdommer i spiserør og magesekk. Det er etablert en stor biobank knyttet til kreft i spiserør og magesekk i samarbeid med Seksjon for molekylær onkologi (Prof. Guro Lund).

Forskningsgruppen har siste 1-2 årene utvidet samarbeidet nasjonalt med de andre regionssentra som driver øsofaguskirurgi. Samarbeidet inkluderer biobanking og registrering av kliniske data på nasjonalt nivå samt samarbeid om deltagelse i kliniske studier. Dette skjer gjennom det såkalte NORECa prosjektet (Norwegian Esophageal Cancer Consortium). Forskningsgruppen deltar også aktivt i det skandinaviske samarbeidsorganet for kreft i spiserør og magesekk som ledes fra Karolinska, Stockholm (SGICG). I tillegg har gruppen knyttet seg opp mot Upper GI Robotic Association (UGIRA) - en internasjonal organisasjon ledet fra Utrecht, Nederland i forbindelse med innføring av robotkirurgi som ny metode i denne sammenhengen.

Gruppen har ambisjoner om å videreutvikle samarbeidet med basalmedisinske forskningsmiljø spesielt innen tidlig diagnostikk og immunologisk mekanismer for effekt av neoadjuvant/adjuvant onkologisk behandling. Prosjekter pågår knyttet til biobanken sammen med seksjon for molekylær onkologi. For den kliniske forskningen er hovedmålene å redusere morbiditet og forekomst av komplikasjoner og å prøve bedre onkologiske resultat knyttet til kirurgien gjennom deltagelse i kliniske studier. Videre ønsker vi vurdere ulike onkologiske behandlingsregimer/tilnærmingar for å bedre overlevelse/mulighet for radikal kirurgi.

Siste året har vi også hatt fokus på forskning omkring akuttkirurgi i vår enhet. Vi har etablert en undergruppe av forskningsgruppen som vi på sikt ønsker utvikle til en egen forskningsgruppe knyttet til akutt gastrokirurgi. Gruppen har nå flere prosjekter så langt relatert til gallestensproblematikk. Samarbeid med andre sykehus planlegges.

About the group:

The group focuses on interdisciplinary research within the field of diseases of esophagus and stomach. A large biobank of samples from cancer in esophagus and stomach is established in cooperation with the Section for molecular oncology (Prof. Guro Lund).

Hovedmedlemmer / Main members

NAME	POSITION/TITLE/ROLE	EMPLOYER/ AFFILIATION	E-MAIL
Tom Mala	Adjunct Prof./Senior consultant Group leader from 01.01.22	OUS and UiO	tommal@ous-hf.no;
Egil Johnson	Prof. emeritus Group leader 2021	UiO	egil.johnsonmedisin.uio.no
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Activity in 2022:

Establishment of a national database and biobank for patients resected for esophageal cancer as part of the NORECa project (Norwegian Esophageal Expert Consortium).

Total histopathologic response after neoadjuvant chemo(radio)therapy for esophageal cancer -patient characteristics, diagnostics and survival. National study.

Prediction of postoperative outcome in esophageal cancer with body composition estimates based on AI-segmentation of preoperative CT.

Monitoring complications/survival after resection for esophageal- and gastric cancer – local registry.

Continuous local biobanking (blood/tumor tissue) for esophageal cancer, by now some 550 esophageal cancer patients and some 330 gastric cancer patients.

Studies on esophageal cancer on biomarkers /local treatment of dysplasia and early cancer.

INTENSE study. Effect of perioperative chemotherapy (FOLFOXFLIRx4x2) in patients with resectable gastric and gastroesophageal junction adenocarcinoma.

NEEDS study. Neoadjuvant chemoradiotherapy for squamous cell carcinoma of the esophagus versus definitive chemoradiotherapy with salvage surgery as needed. Multicenter study started in 2021.

VESTIGE study. Postoperative Immunotherapy vs. Standard chemotherapy for gastric cancer stage Ib-IVb, including esophagogastric junction adenocarcinoma, with high risk for recurrence.

The upper GI International Robotic Association (UGIRA) - International Registry for Robot-Assisted Minimally Gastrectomy and Esophagectomy (RAMIG and RAMIE) for cancer.

kiNETiC study – a Scandinavian Randomized Controlled Trial- Ng-tube post-EsophagecTomy.

Nordic NEC registry (neuroendocrine carcinoma of the GI-tract (GEP-NEC)) (NNTG).

Etablert "gallegruppa" som planlegges videreutviklet som egen forskningsgruppe for akuttkirurgi

PhD projects 2022:

1. Ingrid Vikan Sjurgard: "Molecular- and immuno-profiling of esophageal adenocarcinoma".
2. Tobias Hauge: "Esophageal Cancer and Barrett's Esophagus Targeted molecular profiling and long-term outcome following minimally invasive esophagectomy and endoscopic treatment"

Medical student projects 2022:

Hiatal gastroesophageal hernia – treatment at OUS, Ullevål – retrospective cohort study.

Publications

1. A national precision cancer medicine implementation initiative for Norway. Taskén K, et al. Nat Med. 2022.
2. Short- and long-term outcomes in patients operated with total minimally invasive esophagectomy for esophageal cancer. Hauge T, et al. Dis Esophagus. 2022.
3. Neoadjuvant Chemoradiotherapy and Surgery for Esophageal Squamous Cell Carcinoma Versus Definitive Chemoradiotherapy With Salvage Surgery as Needed: The Study Protocol for the Randomized Controlled NEEDS Trial. Nilsson M, et al. Front Oncol. 2022.
4. Improving public cancer care by implementing precision medicine in Norway: IMPRESS-Norway. Helland Å et al. J Transl Med. 2022.
5. Volumetric parameters from [18 F]FDG PET/CT predicts survival in patients with high-grade gastroenteropancreatic neuroendocrine neoplasms. Stokmo HL, J Neuroendocrinol. 2022.
6. Predicting satisfaction with outcome and follow-up care 5 years after bariatric surgery: A prospective evaluation. Kvalem IL, et al. Obes Sci Pract. 2022.
7. Targeted genetic and epigenetic profiling of esophageal adenocarcinomas and non-dysplastic Barrett's esophagus. Pinto R, et al. Clin Epigenetics. 2022.
8. Quality of life in patients with achalasia: Associations with Eckardt score and objective treatment outcomes after peroral endoscopic myotomy. Evensen H, et al. Endosc Int Open. 2022.
9. Early experience with total robotic D2 gastrectomy in a low incidence region: surgical perspectives. Mala T, et al.. BMC Surg. 2022.
10. International variation in oesophageal and gastric cancer survival 2012–2014: differences by histological subtype and stage at diagnosis (an ICBP SURVMARK-2 population-based study). Arnold M, et al. Gut. 2022.
11. Partial splenectomy after preoperative embolization in a patient with metastatic melanoma - A case report. Hauge T, et al. Int J Surg Case Rep. 2022.
12. Gastroscopy following vertical sleeve gastrectomy. Mala T et al. Tidsskr Nor Laegeforen. 2022.

Avdeling for revmatologi, hud og infeksjonssykdommer (RHI) / Department of Rheumatology, Dermatology and Infectious Diseases

- Hud/ Dermatology Research Group
- Klinisk immunologi og infeksjonsmedisin /
Immunopathogenetic mechanisms in immunodeficiency and
infectious disorders
- Epidemiologi og utkomme ved revmatisk sykdom /
Epidemiology and outcomes in rheumatic diseases
- Fibroserende inflammatoriske revmatiske sykdommer (Nor-
FIORD) / Fibrotic and inflammatory rheumatic diseases
- Klinisk barnerevmatologisk forskning / Pediatric
rheumatology research group

Forskningsgruppe: Hud

Research group: Dermatology Research Group

Avdeling: Revmatologi, hud og infeksjonssykdommer (RHI)

Gruppeleder: Olav Sundnes

Om gruppen

Vår forskning fokuserer på to kjerneområder; hudinflammasjon og hudkreft. Vi driver både translasjonell og klinisk forskning, og har flere pågående kliniske studier. Aktiviteten er tett knyttet opp til vårt kvalitets- og forskningsregister (Dermareg) og avdelingens biobank (RHI biobank).

About the group

Our research focuses on two main areas; skin inflammation and skin cancer. We perform both translational and clinical research, and our research registry (Dermareg) and biobank (RHI biobank) form the basis for the current research activity.

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER /AFFILIATION	E-MAIL
Jan Sitek	Senior consultant/head of section	OUS	jsitek@ous-hf.no
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Assoserte medlemmer / Associated members:

NAME	POSITION/TITEL/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Guttorm Haraldsen	Professor	UiO	
Karin Lødrup Carlsen	Professor	UiO	

Aktivitet i 2022 / Activity in 2022

Forskningsaktivitet/ Research activity:

PhD dissertations

Astrid Lossius - Atopic dermatitis, ultraviolet B treatment, and the IL-1 family of cytokines

PhD-projects

- PhD-project Olav Gramstad, hereditary angioedema, in progress (main supervisor Sundnes)
- PhD-project Siri Hansen Stabell, hidradenitis suppurativa, in progress (Main supervisor Sundnes)
- PhD-project Karianne Haga, Gorlin syndrome, in progress (Main supervisor Hortemo)

Ongoing clinical trials and other research projects:

- Treatment of Keratolytic Winter Erythema with systemic nitroxoline. A investigator-initiated phase 2a randomized placebo controlled crossover study of male and female adults from three Norwegian families (Sandanger)
- Treatment of genital lichen planus in women. Investigator-initiated RCT on oral treatment with the apremilast for genital erosive lichen planus (Helgesen)
- Moderate to Severe Atopic Dermatitis: Evaluation of Upadacitinib in Combination with Topical Corticosteroids in Adolescent and Adult Subjects (Abbvie) (Berents)

Selected Key Publications:

1. Brinchmann BC, Bugge MD, Nordby KC, Alfonso JH (2022) Firefighting and melanoma, epidemiological and toxicological associations: a case report. *Occup Med (Lond)*. 2022 Feb 22;72(2):142-144. DOI: 10.1093/occmed/kqab183. PMID: 35064261
2. Lossius AH, Sundnes O, Ingham AC, Edslev SM, Bjørnholt JV, Lilje B, Bradley M, Asad S, Haraldsen G, Skytt-Andersen P, Holm JØ, Berents TL Shifts in the Skin Microbiota after UVB Treatment in Adult Atopic Dermatitis. *Dermatology*. 2022;238(1):109-120. doi: 10.1159/000515236
3. Gjersvik P, Veierød MB, Thompson A, Grzyb K, Lilland KH, Vazov N, Roscher I, Bassarova AV (2022) Histopathologic reassessment of melanoma and other melanocytic skin lesions excised in 2009 and 2018-2019 *Tidsskr Nor Laegeforen*, 142 (15) DOI 10.4045/tidsskr.22.0204, PubMed 36286556
4. Kelleher MM, Phillips R, Brown SJ, Cro S, Cornelius V, .., Rehbinder EM, et al. (2022) Skin care interventions in infants for preventing eczema and food allergy *Cochrane Database Syst Rev*, 11 (11), CD013534 DOI 10.1002/14651858.CD013534.pub3, PubMed 36373988

5. Skjerven HO, Lie A, Vettukattil R, Rehbinder EM, LeBlanc M,..., Landrø L, et al. (2022) Early food intervention and skin emollients to prevent food allergy in young children (PreventADALL): a factorial, multicentre, cluster-randomised trial *Lancet*, 399 (10344), 2398–2411
DOI 10.1016/S0140-6736(22)00687-0, PubMed 35753340
6. Amandip Sangha; Mohammad Rizvi (2022) Structured digital care pathway for systemic acne treatment using isotretinoin. *BMJ Innovation*. (2022)
DOI: 10.1136/bmjinnov-2021-000917

Forskningsgruppe: Klinisk immunologi og infeksjonsmedisin

Research group: Immunopathogenetic mechanisms in immunodeficiency and infectious disorders

Avdeling: Department of Rheumatology, Dermatology and Infectious Diseases

Gruppeleder: Børre Fevang, MD, PhD

About the group: The research group focus on immunopathogenesis in primary and secondary immunodeficiency such as Common variable immunodeficiency (CVID) and selected infectious diseases, in particular the study of chronic inflammation characterising these disorders. The aim is to improve the understanding of disease mechanisms and to discover new targets for therapeutic intervention. The group works in a translational setting combining close contact to the Research Institute of Internal Medicine, OUH with access to a wide range of immunological methods.

Hovedmedlemmer / Main members:

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Børre Fevang	Group leader, senior consultant	OUH	borre.fevang@rr-research.no
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Ragnhild Øye Løken	Researcher, junior consultant	OUH	raloek@ous-hf.no

Aktivitet i 2022/ Activity in 2022

Forskningsaktivitet/ Research activity:

The group is currently working with several projects, including:

- Immunopathogenic mechanisms in CVID – a disease model for autoimmunity and persistent inflammation. Our group has for a long time used primary immunodeficiency in the form of CVID as a model for studying the immune system. In recent years we have been focusing on the interaction between gut microbiota, gut mucosa and local (intestinal) and systemic inflammation. Magnhild Eide Macpherson's PhD thesis defended in 2020 included work on the modulation of gut microbiota with rifaximin in CVID-patients and the anti-inflammatory effect of HDL in the same patients. This latter work has been extended into a study looking at fatty acids in relation to the gut

microbiome in CVID. The Post doc project of Silje Fjellgård Jørgensen that started in 2019 will include in-depth studies of epigenetic changes in gut mucosa from CVID-patients. We have started a new project focusing on granulomatous-lymphocytic interstitial lung disease (GLILD) in CVID where Mai Sasaki Aanensen Fraz has looked into differences between patients with stable and progressive disease. This project will include collaboration with several Nordic centers with our research group leading the network.

- Functional consequences of novel genetic variations in primary immunodeficiencies and immune dysregulation (FUNPID). High-throughput sequencing has revolutionized the diagnostics of primary immunodeficiencies, giving a definite genetic diagnosis in complicated clinical cases. However, novel genetic variations of uncertain significance tend to show up and in close collaboration with established partners at Oslo University Hospital and the University of Oslo we have established a research-based diagnostic pipeline for these patients. These findings give us an extraordinary opportunity to characterize both new disease entities and new immunologic mediators. We are currently looking into a family with a possible gain-of-function mutation in IL-1R8.
- Vaccine response in patients with CVID. Patients with primary immunodeficiencies like CVID have generally a poor response to vaccines. During the Covid-19 pandemic patients with CVID were however given mRNA vaccines as part of the mass vaccination program and several reports point to a significant immunological effect of these vaccines in the patient group. We have sampled patients with CVID and other primary immunodeficiencies to look at both humoral and cellular responses to the Covid-19 mRNA vaccine, and analyzes of this material started in 2022.

Forskningsgruppe: Epidemiologi og utkomme ved revmatisk sykdom

Research group: Epidemiology and outcomes in rheumatic diseases

Avdeling: Avdeling for revmatologi, hud- og infeksjonssykdommer (RHI)

Gruppeleder: Helga Sanner, MD, PhD, professor og enhetsleder

Om gruppen:

Forskningsgruppen fokuserer på deskriptiv epidemiologi (forekomst og sykdomsforløp) og analytisk epidemiologi (årsakssammenhenger inkludert genetisk predisposisjon) ved revmatisk sykdom oppstått i barne- og voksen alder. Vi undersøker også utkomme, inkludert organmanifestasjoner, pasientrapporterte utfallsmål og fysisk form ved revmatisk sykdom. Vi gjør dette ved å studere og koble ulike datakilder som inkluderer kvalitets- og forskningsregister, biobanker, helseundersøkelser, sentrale helseregister, coholt studier samt kliniske populasjonsbaserte kohorter. Vi jobber med epidemiologiske, registerbaserte og «stor data» analyser inkludert genetiske analyser og maskinlæring samt intervensjoner. Dette gjøres i nært samarbeid med relevante nasjonale og internasjonale ekspertgrupper og med tett brukermedvirkning.

About the group:

The research group focuses on descriptive epidemiology (incidence and disease course) and analytical epidemiology (causal relationships including genetic predisposition) in rheumatic diseases with juvenile and adult onset. We also focus on outcomes including organ manifestations, patient reported outcome measures and physical fitness in rheumatic disease. We achieve this by studying and combining various data sources that include quality- and research registries, biobanks, health surveys, central health registries, cohort studies and clinical cohorts. We work with epidemiological, register-based, and "big data" analyzes, including genetic analyzes and machinelearning as well as interventions. This is done in close collaboration with relevant national and international expert groups and with close user participation.

Website: <https://www.ous-research.no/sanner>

Hovedmedlemmer / Main members:

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Assosierede medlemmer / Associated members:

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Simon G Berger	PhD student	OUS and UiO	s.g.berger@studmed.uio.no

Activity in 2022

Research activity:

The research group was established in June 2022. We have monthly meetings where we focus on both on-going and planned projects including feedback on grant applications. Also, we have e-mail correspondence between meetings. 5/6 members in the group with PhD are main and/or co-supervisors for PhD students, and have regular meetings with their PhD students in addition to the group meetings. In 2022 we have worked on updating of our website. We have members with multidisciplinary background including a physiotherapist and a molecular biologist. We have expert collaborators within the fields of pediatrics, epidemiology, genetics, epigenetics and bioinformatics. In 2022 we have focused on funding, PREVENT-JIA: HSØ grant (åpen prosjekt støtte, NOK 9 mill) and grant from the DAM foundation (NOK 2.4 mill). Also, the SLE project biomarker development in SLE received HSØ funding (2.05 mill NOK). In 2022 we have published 10 original articles in peer reviewed journals, we have 5 oral presentation of abstracts on international congresses (PhD students H Haukeland, SR Moe and H Marstein) and been invited speaker on international congress and web meeting: (Researchers KS Berntsen and K Risum)

ONGOING PROJECTS (only supervisors from the group are mentioned)

NOR-SLE: Mapping and prospective follow-up of a large, population based SLE cohort from south-east Norway. PI K Lerang

- PhD student Sigrid Reppe Moe: Main supervisor Ø Molberg, co-supervisor: K Lerang
- PhD student Hilde Haukeland: Main supervisor K Lerang, co-supervisors: Ø Molberg and H Sanner

ANCA- associated vasculitis- establish population-based cohort and identify novel risk factors for clinical remission, relapse rate, organ damage and death. PI Øyvind Molberg

- PhD student Karin Kilian. Main supervisor Ø Molberg

Organ involvement in long-term juvenile dermatomyositis. PI Helga Sanner

- PhD student Henriette Marstein: Main supervisor H. Sanner
- PhD student Simon Girmai Berger: Co-supervisors K Schjander Bentsen and H. Sanner

PREVENT-JIA: Prospective evaluation of early-life modifiable environmental factors and genetic risk in juvenile idiopathic arthritis. PI Helga Sanner

- PhD student Sigrid V Hestetun: Main supervisor H. Sanner, Co-supervisor Anne Marit Selvaag
- Additionally, 2 PhD students and 1 postdoc funded in 2022 (HSØ/DAM) with planned start-up 2023

Translation and validation of pediatric Patient-Reported Outcomes Measurement Information Systems (PROMIS) modules. PI Kristine Risum

SELECTED PLANNED PROJECTS

- Biomarker development for early diagnosis of lupus nephritis using liquid biopsies. PI K Lerang. Funded postdoc (HSØ): Simin Jamaly
- PREDICT-JIA. Identifying early predictors for juvenile idiopathic arthritis at first admission to a pediatric rheumatology unit. PI Kristine Risum
- Behcets disease: a population-based study to describe epidemiology, disease manifestations, phenotypes, diagnosis and management. PI Birgir Gudbrandsson

Popular science:

- «Ny forskning på SLE» Foredrag av stipendiater SR Moe, H Haukeland og postdok K Lerang ved dialogseminar om bindevevssykdommer i regi av OUS og Norsk revmatikerforbund (NRF)
- «Hva er SLE?» Foredrag av stipendiat SR Moe ved SLE pasient konferanse i regi av NRF
- «SLE og siste nytt på behandlingsfronten» v/ postdoc K. Lerang. REVMA/DERMA
- «Juvenil spondylartritt» Innlegg på webinar med spondylartrittforbundet v/ H. Sanner and K. Risum



Publications 2022

1. Deakin CT, Bowes J, Rider LG, Miller FW, Pachman LM, Sanner H, Rouster-Stevens K, Mamyrrova G, Curiel R, Feldman BM, Huber AM, Reed AM, Schmeling H, Cook CG, Marshall LR, LL Wilkinson MG, Eyre S, Raychaudhuri S, Wedderburn LR, Juvenile Dermatomyositis Cohort and Biomarker Study, the Childhood Myositis Heterogeneity Study Group, and the Myositis Genetics Consortium (MYOGEN) (2022). Association with HLA-DR β 1 position 37 distinguishes juvenile dermatomyositis from adult-onset myositis
Hum Mol Genet, 31 (14), 2471-2481
DOI [10.1093/hmg/ddac019](https://doi.org/10.1093/hmg/ddac019), PubMed [35094092](https://pubmed.ncbi.nlm.nih.gov/35094092/)
2. Giancane G, Papa R, Vastert S, Bagnasco F, Swart JF, Quartier P, Antón J, Kamphuis S, Sanner H, Glerup M, De Benedetti F, Tsitsami E, Remesal A, Moreno E, De Inocencio J, Myrup C, Pallotti C, Koné-Paut I, Franck-Larsson K, Malmström H, Cederholm S, Pistorio A, Wulffraat N, Ruperto N, Paediatric Rheumatology International Trials Organisation (PRINTO) (2022)
Anakinra in Patients With Systemic Juvenile Idiopathic Arthritis: Long-term Safety From the Pharmachild Registry
J Rheumatol, 49 (4), 398-407
DOI [10.3899/jrheum.210563](https://doi.org/10.3899/jrheum.210563), PubMed [35105709](https://pubmed.ncbi.nlm.nih.gov/35105709/)
3. Mariette X, Barone F, Baldini C, Bootsma H, Clark KL, De Vita S, Gardner DH, Henderson RB, Herdman M, Lerang K, Mistry P, Punwaney R, Seror R, Stone J, van Daele P, van Maurik A, Wisniacki N, Roth DA, Tak PP (2022)
A randomized, phase II study of sequential belimumab and rituximab in primary Sjögren's syndrome
JCI Insight, 7 (23)
DOI [10.1172/jci.insight.163030](https://doi.org/10.1172/jci.insight.163030), PubMed [36477362](https://pubmed.ncbi.nlm.nih.gov/36477362/)
4. Marstein HS, Witczak BN, Godang K, Schwartz T, Flatø B, Bollerslev J, Sjaastad I, Sanner H (2022)
Adipose tissue distribution is associated with cardio-metabolic alterations in adult

patients with juvenile-onset dermatomyositis
Rheumatology (Oxford) (in press)
DOI [10.1093/rheumatology/keac293](https://doi.org/10.1093/rheumatology/keac293), PubMed 35575380

5. Saevarsottir S, Stefansdottir L, Sulem P, Thorleifsson G.....Sanner HKlareskog L, Askling J, Padyukov L, Pedersen OB, Thorsteinsdottir U, Jonsdottir I, Stefansson K (2022)
Multiomics analysis of rheumatoid arthritis yields sequence variants that have large effects on risk of the seropositive subset
Ann Rheum Dis, 81 (8), 1085-1095
DOI [10.1136/annrheumdis-2021-221754](https://doi.org/10.1136/annrheumdis-2021-221754), PubMed 35470158
6. Tollisen A, Selvaag AM, Aasland A, Ingebrigtsen T, Sagen J, Lerdal A, Flatø B (2022)
Personally Generated Quality of Life Outcomes in Adults With Juvenile Idiopathic Arthritis
J Rheumatol, 49 (10), 1138-1145
DOI [10.3899/jrheum.211245](https://doi.org/10.3899/jrheum.211245), PubMed 35569834
7. van Dijkhuizen EHP, Ridella F, Naddei R, Trincianti C, Avrusin I, Mazzoni M, Sutera D, Ayaz NA, Penades IC, Constantin T, Herlin T, Oliveira SK, Rygg M, Sanner H, Susic G, Sztajnbok F, Varbanova B, Ruperto N, Ravelli A, Consolaro A, Pediatric Rheumatology International Trials Organization (PRINTO) (2022)
Validity and Reliability of Four Parent/Patient-Reported Outcome Measures for Juvenile Idiopathic Arthritis Remote Monitoring
Arthritis Care Res (Hoboken) (in press)
DOI [10.1002/acr.24855](https://doi.org/10.1002/acr.24855), PubMed 35015379
8. Witczak BN, Bollerslev J, Godang K, Schwartz T, Flatø B, Molberg Ø, Sjaastad I, Sanner H (2022)
Body composition in long-standing juvenile dermatomyositis: associations with disease activity, muscle strength and cardiometabolic measures
Rheumatology (Oxford), 61 (7), 2959-2968
DOI [10.1093/rheumatology/keab805](https://doi.org/10.1093/rheumatology/keab805), PubMed 34718443
9. Witczak BN, Schwartz T, Barth Z, Taraldsrud E, Lund MB, Aaløkken TM, Flatø B, Sjaastad I, Sanner H (2022)
Associations between cardiac and pulmonary involvement in patients with juvenile dermatomyositis-a cross-sectional study
Rheumatol Int, 42 (7), 1213-1220
DOI [10.1007/s00296-021-05071-3](https://doi.org/10.1007/s00296-021-05071-3), PubMed 34984516
10. Zeng L, Walsh M, Guyatt GH, Siemieniuk RAC, Collister D, Booth M, Brown P, Farrar L, Farrar M, Firth T, Fussner LA, Kilian K, Little MA, Mavrakanas TA, Mustafa RA, Piram M, Stamp LK, Xiao Y, Lytvyn L, Agoritsas T, Vandvik PO, Mahr A (2022). Plasma exchange and glucocorticoid dosing for patients with ANCA-associated vasculitis: a clinical practice guideline
Practice Guideline, Feb 25;377
DOI: [10.1136/bmj-2021-064597](https://doi.org/10.1136/bmj-2021-064597), PMID: 35217581

Forskningsgruppe: Fibroserende inflammatoriske revmatiske sykdommer (Nor-FIORD)

Research group: Fibrotic and inflammatory rheumatic diseases

Department: Revmatologisk avdeling

Group leader: Anna-Maria Hoffmann-Vold

About the group:

The overall mission of this research group is to enable highly competitive translational and clinical research to foster the initiation of new clinical trials and translation of novel achievements into clinical use, benefiting patients with fibrotic and inflammatory rheumatic diseases. The research strategies of this group specifically focus on clinical and translational research, the use of existing registries, biobanks and core facilities and conduction of clinical trials. We anticipate societal benefit and optimized and personalized strategies for identification, monitoring, treatment and outcome assessment. We will promote transfer of knowledge and innovation-oriented processes from our projects to ensure that relevant results are effectively translated to clinical practice.

Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
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Phuong Phuong Diep	PhD-student	OUS	phudie@ous-hf.no

Activity in 2022

Research activity:

- The Oslo university hospital (OUH) Strategic Research area- Novel personalized management strategies for fibrosing diseases 2022- 2027 with Anna- Maria Hoffmann-Vold as Project leader. Collaboration with Convergence environments= UIO strategic research area with Mona-Elisabeth Rootwelt-Revheim as leader. The overall purpose of the environment is to develop personalized management strategies including early identification, treatment, monitoring, patient dialogue and outcome assessment in patients with fibrosing diseases.
- The ReSScue trial: Finalized phase 2 randomized clinical investigator initiated trial (KLINBFORSK)
- Senscisor 1199-225 – From 2018- Dec 2022, industry sponsored RCT

- I-FILE - 2021-2023: multicenter registry for home monitoring of ILD, initiated from Erasmus University in Rotterdam
- Connective tissue disease associated interstitial lung disease registry and cohort study (group leader)
- Molecular profiling of lung tissue in CTD-ILD in collaboration with UCLA and Zurich (USZ)
- ILD quantification on serial HRCT in collaboration with UCLA
- ERS/EULAR guideline development for CTD-ILD (Anna Hoffmann-Vold convenor and Jens Vikse task force member)
- Update of EULAR recommendation for treatment of SSc (Anna Hoffmann-Vold, task force member)
- COVID in systemic sclerosis registry from EUSTAR and OUS
- Ig coating of gut microbiota in early systemic sclerosis
- RA-ILD patient survey, international survey in 11 countries, initiated together with Heidelberg University
- Biomarker analysis for ILD progression in systemic sclerosis, multicenter study

Planned projects:

- Nor-mILDer home monitoring strategy trial of CTD-ILD, start estimated May 2023.

Thesis defense/completed degrees:

- Mona-Lovise Talaro Ramsli completed her Master's degree Nov 2022; The nurses contribution to quality of life in systemic sclerosis and proven pulmonary arterial hypertension – a study based on patients experiences and thoughts in meeting with nurses in their own treatment within the specialist health care in Norway.

Ongoing PhD projects:

- Hilde Jenssen Bjørkekjær, MD: "Optimizing pulmonary arterial hypertension (PAH) management in systemic sclerosis (SSc)". Main supervisor: Anna-Maria Hoffmann-Vold
- Henriette Didriksen, MD: "Lymphangiogenic biomarkers in Systemic Sclerosis". Main supervisor: Øyvind Molberg
- Imon Shoumitra Barua, MD: "Deciphering interstitial lung disease through advanced imaging of natural history; the nor-precision approach" Main supervisor: Anna-Maria Hoffmann-Vold
- Emily Langballe, MD: «Deciphering a contemporary approach to management for interstitial lung disease in rheumatic conditions». Main supervisor: Anna-Maria Hoffmann-Vold.
- Phuong Phuong Diep, MD, pulmonologist, "Evaluation of interstitial lung disease in patients with rheumatoid arthritis and other connective tissue diseases", co-supervisor:Anna-Maria Hoffmann-Vold

Awards:

- Anna Hoffmann-Vold received the Edith-Busch prize
- Phuong Phuong Diep "Best lecturer at Norwegian Respiratory Society annual meeting 2022"

Publications (first or last author):

- Hoffmann-Vold, A. M (7), Didriksen, H (1)

Co-author publications:

- Vikse Jens (2), Hoffmann-Vold AM (14), Fretheim Håvard (5), Henriette Didriksen (1)

Abstracts:

- Bjørkekjær H.J (3), Didriksen H (1), Vikse J (2), Carstens M.N (1), Barua I.S (2), Fretheim H (2), Hoffmann-Vold AM (7)

Grants:

- Research Funding for an investigator-initiated study entitled: "Risk stratification, treatment regimens and outcomes in systemic sclerosis associated pulmonary arterial hypertension".
- National funding for the IIS Nor-mILDer homemonitoring strategy trial (Åpen Prosjekt støtte, HSØ)
- Simon Fougner Hartmans Familiefond for home monitoring development

Popular science:

- Podcast production; "Revmatologi" with 13 episodes in 2022, Jens Vikse.
- Members of our group has been presenting webinars for patients in the Norwegian Rheumatology Association
- Hilde Jenssen Bjørkekjær was Interviewed by Medpage Today about the abstract presented at the ACR Convergence 2022 "Risk Stratification of Patients with SSc-PAH Using the Current and New Proposed Criteria in EUSTAR"
- Overview article about IgG4-RD to the Gastromedicines member magazine, "NGF-nytt" and "Revmatologen". Jens Vikse

Forskningsgruppe: Klinisk barnerevmatologisk forskning

Research group: Pediatric rheumatology research group

Avdeling: Avdeling for revmatologi, hud og infeksjonsmedisin

Gruppeleder: Berit Flatø

Om gruppen (kort beskrivelse på norsk):

Gruppen fokuserer sin forskning på diagnose, prognose og persontilpasset behandling ved barnerevmatolgske sykdommer. Målsettingen er å optimalisere diagnostikk, prediksjonsmodellering og målrettede behandlingsstrategier basert på pasientenes kliniske, personlige, genetiske og/eller molekylære profiler. Videre vil vi kartlegge sykdomsbyrden for pasienter, familie og samfunnet. Forskningsgruppen har en pågående nasjonal randomisert klinisk studie og pågående samt planlagte longitudinelle og randomiserte studier med fokus på videreutvikling av spesiell kompetanse innen målrettet behandling, effektive persontilpassede behandlingsstrategier, moderne bildediagnostikk hos barn (ultralyd, MR), og langtidsoppfølging. Vi har et etablert samarbeid om genetiske og molekylære risikofaktorer og medikament monitorering.

About the group (short description in English):

The research focus is diagnosis, prognosis, and tailored treatment strategies in pediatric rheumatic diseases. The work is aiming at optimized diagnosis, prediction models and targeted treatment strategies based on the patients' clinical, personal, genetic and/or molecular profile. Furthermore, we will describe the burden of the disease for the patients, their families and the society. This is achieved through ongoing and planned clinical trials, observational studies and translational biomedical research.

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Berit Flatø	Group leader / Professor	OUS og UiO	berit.flato@klinmed.uio.no
Anna Birgitte Aga	Post doc	OUS	aaga@ous-hf.no
Pernille Bøyesen	Post doc	OUS	boyper@ous-hf.no
Nina Krafft Sande	PhD student	OUS og UiO	ninamkrafft@hotmail.com
Siri Hetlevik	Post Doc	OUS	Siri.Opsahl.Hetlevik@ous-hf.no
Vibke Lilleby	Senior researcher/consultant	OUS	v lilleby@ous-hf.no
Imane Bardan	Stud med/ forsker	UiO	imane.bardan@studmed.uio.no
Irene Urnes Tjernlund	Research consultant	OUS	ireurn@ous-hf.no

Anita Tollisen	RN/researcher	OUS	anitatol@online.no
Name unknown	PhD Student	OUS og UiO	Oppstart 01.01.2004

Assosierede medlemmer / Associated members:

NAME	POSITION/TITEL/ROLE	EMPLOYER/AFFILIATION	E-MAIL
NN	NN	NN	NN
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Nils Bolstad	Post Doc	OUS	nilbol@ous-hf.no

Aktivitet i 2022/ Activity in 2022

Forskningsgruppen ble godkjent i september 2022

Forskningsaktivitet/ Research activity:

- Strategier mot persontilpasset behandling av juvenil idiopatisk artritt (JIA), MinJIA. En nasjonal randomisert studie av effekten ved ulike behandlingsstrategier og mulige risikofaktorer for behandlingssvikt. Datainnsamling pågår 110/201 pas er inkludert
- Betydningen av molekylære signaturer (basert på transcriptional, cellulær og genetisk risk) for sykdomsaktivitet og behandlingsrespons. En prospektiv studie av barn med JIA som starter behandling med TNF-hemmer. Samarbeid mellom medisinsk genetikk og revmatologi, OUS. Pågående datainnsamling
- Terapeutisk legemiddelmonitorering ved barnerevmatologisk sykdom. En prospektiv studie av JIA pas som starter med TNF- hemmer. Kartlegging av serum konsentrasjon/antistoff.
- Fysisk funksjon, livskvalitet og helseøkonomiske konsekvenser ved biologisk behandling av JIA, en prospektiv åpen forlengelsesstudie av MinJIA. Datainnsamling pågår.
- Validering og implementering av MR helkropp og UL ved JIA. Sammenligning av artrittfunn ved MR, ultralyd og klinisk undersøkelse. Datainnsamling avsluttet, analyser pågår.
- Optimalisert vedlikeholdsbehandling hos barn med JIA som er i vedvarende remisjon. Randomisert multisenter studie av sykdomsoppbluss ved ulike nedtrappingsstrategier.
- Langtidsforløpet ved revmatologisk sykdom som starter i barnealderen.
- Forståelse av leddforandringer på cellulært nivå. Prosjektet undersøker om genetisk fingeravtrykk fra leddvæskens hvite blodceller kan skille mellom undergrupper av barneleddgikt og forutsi deres behandlingsrespons. Datainnsamling pågår.

Populærvitenskapelig aktivitet/ Popular science:

Oppslag i Dagens Medisin.

Innovasjonsaktivitet/ Innovation:

Tollisen A, Selvaag AM, Aasland A, Ingebrigtsen T, Sagen J, Lerdal A, Flatø B. Personally Generated Quality of Life Outcomes in Adults With Juvenile Idiopathic Arthritis. *J Rheumatol*. 2022 Oct;49(10):1138-1145. doi: 10.3899/jrheum.211245. Epub 2022 May 15. PMID: 35569834.

Bardan I, Fagerli KM, Sexton J, Kvien TK, Bakland G, Mielnik P, Hu Y, Lien G, Flatø B, Molberg Ø, Kristianslund EK, Aga AB. Treatment response to tumor necrosis factor inhibitors and methotrexate monotherapy in adults with juvenile idiopathic arthritis: Data from NORDMARD. *J Rheumatol*. 2022 Nov 15:jrheum.220645. doi: 10.3899/jrheum.220645. Epub ahead of print. PMID: 36379571.

Li J, Li YR, Glessner JT, Yang J, March ME, Kao C, Vaccaro CN, Bradfield JP, Li J, Mentch FD, Qu HQ, Qi X, Chang X, Hou C, Abrams DJ, Qiu H, Wei Z, Connolly JJ, Wang F, Snyder J, Flatø B, Thompson SD, Langefeld CD, Lie BA, Munro JE, Wise C, Sleiman PMA, Hakonarson H. Identification of Novel Loci Shared by Juvenile Idiopathic Arthritis Subtypes Through Integrative Genetic Analysis. *Arthritis Rheumatol*. 2022 Aug;74(8):1420-1429. doi: 10.1002/art.42129. Epub 2022 Jul 15. PMID: 35347896; PMCID: PMC9542075.

Felbo SK, Wiell C, Østergaard M, Poggenborg RP, Bøyesen P, Hammer HB, Boonen A, Pedersen SJ, Sørensen IJ, Madsen OR, Slot O, Møller JM, Szkudlarek M, Terslev L. Do tender joints in active psoriatic arthritis reflect inflammation assessed by ultrasound and magnetic resonance imaging? *Rheumatology (Oxford)*. 2022 Feb 2;61(2):723-733. doi: 10.1093/rheumatology/keab384. PMID: 33895799.

Avdeling for transplantasjonsmedisin (ATX) / Department of Transplantation

- Forskningsgruppe for transplantasjonsonkologi /
Transplant oncology research group
- Klinisk forskningsgruppe for primær skleroserende
kolangitt / Clinical PSC Research Group
- Transplantasjonsmedisin / Transplantation Medicine
- Eksperimentell Celletransplantasjon / Experimental Cell
Transplantation
- Klinisk Effektforskning / Clinical Effectiveness Research
Group
- Forskningsgruppe for pasientrapporterte resultater og
helseøkonomi / Patient-reported Outcomes and Health
Economics
- Nevroendokrine svulster / Neuroendocrine tumors

Forskningsgruppe: Forskningsgruppe for transplantasjonsmedisin

Research group: Transplant oncology research group

Avdeling: Avdeling for transplantasjonsmedisin

Gruppeleder: Pål-Dag Line

Om gruppen (kort beskrivelse på norsk):

Forskergruppen for transplanasjonsonkologi studerer hvordan levertranplantasjon som terapi kan brukes ved bestemte kreftformer der alternativet bare er palliativ behandling. Målet er å tilby bedre pasienttilpasset behandling. Forskningsgruppen har vært pionerer på vedensbasis på levertransplantasjon innenfor transplantasjon av pasienter med levermetastaser fra tykk- eller endetarmskreft og fagfeltet transplantasjonsokologi er blitt en gren av levertransplantasjon med sterkt internasjonal utvikling. Vi har nå løpende forskningsstudier for kolorektale levermetastaser, intrahepatiske cholangiocarcinomer og hilære cholangiocarcinomer. Gruppen er også involvert i levermetastaser fra neuroendokrine svulster. Forskningsgruppen består av transplantasjonskirurger, onkologer, radiologer, nukleærmedisinere, thoraxkirurg, gastrokirurg/leverkirurg og helefaglig forsker. Gruppen har også etablert samarbeid med helseøkonomer.

About the group (short description in English):

The research group for Transplant Oncology is exploring liver transplantation as a treatment option for patient with primary or secondary liver malignancies that currently are treated by palliative care due to lack of surgical possibilities. The group has been leading the field of liver transplant for colorectal liver metastases (CRLM), and transplant oncology has become an emerging field in liver transplantation with international traction. The research group for transplant oncology is currently running prospective study protocols in liver transplantation in colorectal liver metastasis, intrahepatic cholangiocarcinoma and hilar cholangiocarcinoma and is also thightly involved in liver metastases from neuroendocrine tumors. Members of the research group are transplant surgeons, oncologists, radiologists, nuclear medicine specialists, liver surgeon and thorax surgeon and nursing. The research group also has sn established cooperation with academic expertise in health economics.

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/ AFFILIATION	E-MAIL
Pål-Dag Line	Group leader/Adjunct Professor/ Senior consultant surgeon	OUS / UiO	p.d.line@medisin.uio.no
Morten Hagness	Senior consultant surgeon	OUS	morten.hagness@ous-hf.no

Jon Magnus Solheim	PhD research fellow/senior consultant surgeon	UiO / UiO	uxsojc@ous-hf.no
Harald Grut	Post Doc, Senior consultant	Vestre Viken	hargru@ous-hf.no
Tor Magnus Smedman	PhD research fellow/consultant	UiO /OUS	torha@ous-hf.no
Maria Gjerde	Study nurse	OUS	mgjerde@ous-hf.no
Svein Dueland	Senior consultant	OUS	svedue@ous-hf.no

Assoserte medlemmer / Associated members:

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Mona-Elisabeth Revheim	Assoc. Professor/Senior consultant	OUS / UiO	monar@ous-hf.no
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Åsmund A Fretland	Senior consultant	OUS	aafret@ous-hf.no
Trygve Syversveen	Consultant	OUS	tsyversv@ous-hf.no

Collaboration

National:

- Gudrun Bjørnelv , The Institute of Health and Society, NTNU
- Eline Aas , The Institute of Health and Society, UiO
- Professor Ragnhild Lothe, UiO
- Professor Anita Sveen, UiO

International:

- Professor Julia Johansen, Herlev University Hospital, Denmark
- Professor Karen-Lise Spindler, Aarhus University, Denmark
- Professor Krishna Menon, King's College Hospital, London, UK
- Professor Silvio nadalin, Univeristy of Tübingen, Germany
- Professor Utz Settmacher, Univeristy of Jena, Germany
- Professor Umberto Cillo, University of Padova, Italy
- Professor Roberto Hernandez Alejandro, URMC, Rochester NY, USA
- Associate Professor Gonzalo Sapisochin, UHN Toronto General Hospital, Toronto, Canada

Activity in 2022:

The group contributed strongly during 2021 to develop the consensus guidelines of the International Hepato-Pancreato-Biliary Association (IHPBA), both as senior authors and providing a significant proportion of the data. During the last year we have solidified and broadened the evaluation on transplant for CRLM by publishing a new study on health-related quality of life ¹ and a new study on health economic aspects compared to standard of care palliative oncological therapy². Recurrence is common in these patients, but most patients develop lung metastases that in the majority may be offered curative intent treatment and we have published an updated paper on treatment and prognostic impact of recurrence on the long-term outcomes³. The long-standing work has led to invitation to numerous international meetings to give invited plenary and state of the art talks as well as commentaries and reviews⁴. The group of transplant oncology invented the RAPID concept in 2015, which allows transplantation of very small auxiliary grafts in combination with two-stage

hepatectomy. In a multicentric study we have evaluated the RAPID operation technique⁵.

The field of transplant oncology also encompasses other tumor forms and handling of malignant disease in the transplant recipient population. The group has been represented in a guideline publication on this topic and also contributed to a large multicentric study on liver transplantation in liver metastases from neuroendocrine cancer^{6,7}. We have also been able to show that selected patients with technically resectable disease may benefit from transplantation as compared to liver resection and this is a very controversial field requiring better predictive tools in liver resected patients^{8,9}. In 2022 we got 3-year HSØ funding for the project "Improved long term survival of patients with colorectal liver metastases by individualised risk assessment for allocation to surgical therapy". This project aims at improving the prediction of outcome in patients resected for CRLM to better understand if there is a subgroup that could benefit from transplant. The funding has enabled hiring of two post doc. Positions. We have also a long standing cooperation with Professor Ragnhild Lothe at the Institute for cancer research to elucidate basic molecular mechanisms relevant for treatment of patients liver transplanted for CRLM. In 2022 Anita Sveen and Pål-Dag Line got an open call grant from The Norwegian Cancer Society (2023-27) – Converting inoperable to curable metastatic cancer on behalf of the respective research groups.

One PhD student will defend his thesis in the summer of 2023, and the second will according to current planning deliver his thesis in the course of 2023.

Relevant papers from 2022

1 Smedman TM, Guren TK, Tveit KM, *et al.* Health-Related Quality of Life in Colorectal Cancer Patients Treated With Liver Transplantation Compared to Chemotherapy. *Transplant Int* 2022; 35: 10404.

2 Bjørnelv GMW, Zolic-Karlsson Z, Dueland S, Line P-D, Aas E. Cost-effectiveness of liver transplantation versus last-resort systemic therapy for colorectal liver metastases. *Brit J Surg* 2022. DOI:10.1093/bjs/znac022.

3 Dueland S, Smedman TM, Røsok B, *et al.* Treatment of relapse and survival outcomes after liver transplantation in patients with colorectal liver metastases. *Transplant Int* 2021; 34: 2205–13.

4 Line P-D. Liver transplantation for colorectal secondaries: on the way to validation. *Curr Opin Organ Tran* 2022; 27: 329–36.

5 Settmacher U, Ali-Deeb A, Coubeau L, *et al.* Auxiliary Liver Transplantation According to the RAPID Procedure in Non-cirrhotic Patients – Technical Aspects and Early Outcomes. *Ann Surg* 2022; Publish Ahead of Print. DOI:10.1097/sla.0000000000005726.

6 Salcedo M, Vinaixa C, Javle M, Trapero-Marugán M, Bustamante J, Line P-D. Evaluation and Management of Liver Transplant Candidates With Prior Nonhepatic Cancer: Guidelines From the ILTS/SETH Consensus Conference. *Transplantation* 2022; 106: e3–11.

7 Eshmuminov D, Studer DJ, Lopez VL, *et al.* Controversy Over Liver Transplantation or Resection for Neuroendocrine Liver Metastasis: Tumor Biology Cuts the Deal. *Ann Surg* 2022; Publish Ahead of Print. DOI:10.1097/sla.0000000000005663.

8 Lanari J, Hagness M, Sartori A, *et al.* Liver transplantation versus liver resection for colorectal liver metastasis: a survival benefit analysis in patients stratified according to tumor burden score. *Transplant Int* 2021; 34: 1722–32.

9 Dueland S, Yaqub S, Line P-D. No Strong Evidence on Liver Transplant for Colorectal Cancer Liver Metastasis Over Portal Vein Embolization Associated With Liver Resection—Reply. *Jama Surg* 2022; 157. DOI:10.1001/jamasurg.2021.5127.

Forskningsgruppe: Klinisk forskningsgruppe for primær skleroserede kolangitt

Research group: Clinical PSC Research Group

Avdeling: Avdeling for transplantasjonsmedisin

Gruppeleder: Trine Folseraa

Om gruppen:

Seksjon for gastromedisin på Rikshospitalet har nasjonalt behandlingsansvar for pasienter med leversydommen primær skleroserede kolangitt (PSC). Tilstanden representerer den vanligste årsaken til levertransplantasjon i Norge. Flere faktorer, inkludert betydelig økt risiko for gastrointestinal kreft, herunder særlig gallegangskreft, kompliserer oppfølgingen av og sykdomsforløpet til disse pasientene. Vår forskning har som hovedmål å bedre utredning, oppfølging og behandling av PSC pasienter, herunder har vi særlig fokus på bedret tidlig diagnostikk og behandling av gallegangskreft ved PSC. Forskningsgruppen administrerer og står for den daglige driften av NoPSC biobanken som utgjør en av verdens største biobankressurser for PSC og som i tillegg har innsamlet materiale fra en rekke andre leversydommer. Vi er involvert i administrasjonen av nasjonalt nettverk for autoimmune leversydommer som ledes av prof. Mette Vesterhus, og har dessuten et tett samarbeid med m.a. epigenetikkgruppen ved DNR ledet av prof. Guro Lind, den internasjonale PSC studiegruppen (IPSCSG) og det europeiske nettverket for cholangiocarcinom forskning (ENSCCA).

About the group (short description in English): Primary sclerosing cholangitis (PSC) constitutes an important part of the patients seen at Department of Gastroenterology, Oslo University Hospital, Rikshospitalet. The Clinical PSC Research Group focus their effort on improving diagnosis, treatment and follow-up of PSC patients. We collaborate closely with the Clinical Liver Research Group at Haraldsplass Deaconess Hospital in Bergen, led by Mette Vesterhus, the Epigenetics Group at the Department of Cancer Prevention, Institute for Cancer Research at the Norwegian Radium Hospital, led by Guro E. Lind, the International PSC Study Group (IPSCSG) and the European Network for the Study of Cholangiocarcinoma (ENSCCA).

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Trine Folseraa	PhD/Senior consultant	OUS	trine.folseraa@medisin.uio.no
Kirsten Muri Boberg	Adj.Professor/Senior consultant, Head of Section of Gastroenterology	OUS and UiO	kboberg@ous-hf.no
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Assoserte medlemmer / Associated members:

NAME	POSITION/TITEL/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Mette Vesterhus	Professor/Senior consultant	OUS/Haraldsplass Deaconess Hospital, UiB	Mette.Vesterhus@uib.no
Guro E. Lind	Professor	UiO	guro.elisabeth.lind@rr-research.no

Activity in 2022

Selected research activity:

Identification of molecular alterations in and biomarkers for PSC-associated cholangiocarcinoma (CCA).

Currently we have two ongoing PhD projects (Grimsrud and Breder) focusing on early detection and improved treatment of CCA.

- In collaboration with the Epigenetics group at the Norwegian Radium Hospital we have used highly sensitive droplet digital PCR to analyze epigenetic biomarkers in more than 300 bile samples that provide early and accurate detection of CCA in patients with PSC. Findings strongly suggest that analyzing aberrant DNA methylation utilizing bile as liquid biopsy material may improve and complement current detection methods for CCA. (Published in Hepatology in 2022; PMID: 34435693).
- By the end of 2022 we are about to finalize the first comprehensive mutational profiling of PSC-associated CCA tumors (exome sequencing, including copy number variation analysis). By this we have delineated both PSC specific and universal driver genes. Findings provide opportunities for better understanding carcinogenesis in PSC, as well as a platform for personalized therapy (manuscript under finalization).
- We are key collaborators in several projects outgoing from the European Network for Cholangiocarcinoma Research (ENSCCA), including a multicenter study on liquid biopsy protein biomarkers of CCA risk, early diagnosis and survival (under revision in Journal of Hepatology).

Continued systematic biobanking and registration of clinical data on PSC patients utilizing the infrastructure of the NoPSC biobank and the National network for autoimmune liver diseases.

- The biobank and database of the Norwegian PSC Research Center is steadily growing and currently include clinical data and biological samples on close to 1000 Norwegian PSC patients and more than 1000 disease controls. The NoPSC biobank represent a valuable resource for PSC research both nationally and internationally. We also contribute data, imaging and blood samples from PSC patients followed at Rikshospitalet to the National network for autoimmune liver disease, -a national multicenter study including a research registry and a prospective research biobank for non-transplant patients with PSC. In addition, we have contributed clinical data and biological samples to several multicenter

studies, including those outgoing from the International PSC Study Group (IPSCSG) and the ENSCCA.

Selected articles, 2022:

- Early and accurate detection of cholangiocarcinoma in patients with primary sclerosing cholangitis by methylation markers in bile. Hepatology. 2022
- Cholangiocarcinoma landscape in Europe: Diagnostic, prognostic and therapeutic insights from the ENSCCA Registry. J Hepatol. 2022.
- Algebraic topology-based machine learning using MRI predicts outcomes in primary sclerosing cholangitis. Eur Radiol. Exp. 2022
- Portal fibroblast with mesenchymal stem cell features form a reservoir of proliferative myofibroblast in liver fibrosis. Hepatology. 2022

Populærvitenskapelig aktivitet/ Popular science:

- Popular science article: Blodtype kan avsløre sykdomsrisiko. Verdens Gang 22.02.2022
- Popular science presentation; webinar: The role and impact of primary sclerosing cholangitis in bile duct disease and CCA. The International Cholangiocarcinoma Network Seminar Series. 03.10.2022.
- Popular science presentation; webinar: The role of primary sclerosing cholangitis in cholangiocarcinoma pathogenesis. The European Network for Cholangiocarcinoma biannual meeting. 08.07.2022.
- Several presentations at patient conferences and meetings for the patient group for autoimmune liver disease in Norway (autoimmunlever.no).

Forskningsgruppe:

Transplantasjonsmedisinsk forskningsgruppe

Research group:

Research Group of Transplantation Medicine

Avdeling:

Avdeling for transplantasjonsmedisin

Gruppeleder:

Professor, overlege Trond Geir Jenssen

Om gruppen (kort beskrivelse på norsk):

Gruppen utfører epidemiologiske og kliniske studier med endepunktsdata på pasienter som gjennomgår nyretransplantasjon, pankreastransplantasjon og øycelletransplantasjon. Data som publiseres er dels registerbasert (via et komplet nasjonalt endepunktsregister som oppdateres årlig (Norsk nyreregister) samt en lokal biobank, dels randomiserte kliniske studier som initieres av gruppen selv, og deltakelse i internasjonale multisenter-studier. Studiene fokuserer spesielt på immunterapi, farmakokinetikk, farmakokinetisk modellering og metabolisme, sistnevnte med fokus på benmetabolisme etter nyretransplantasjon og på post-transplantasjons diabetes (PTDM). Gruppen fikk i 2022 innvilget 17.6 mill kroner fra KLINBEFORSK for å starte en placebokontrollert randomisert og blindet intervensionsstudie med SGLT2-hemmeren dapagliflozin. Hensikten er å finne ut om behandlingen kan forlenger levetiden for den transplanterte nyren.

About the group (short description in English):

The research group carries out epidemiological and clinical outcome studies in kidney transplantation, pancreas transplantation and islet transplantation. Data from the Norwegian Renal Registry (which is updated yearly) together with data from a local biobank are generated, together with RCTs and observational studies. The studies focus on immunotherapy, pharmacokinetics, pharmacotherapeutic modelling and metabolism, in particular post-transplant bone disease metabolism and also post-transplant diabetes (PTDM).

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Trond Geir Jenssen	Group leader / Professor	OUS/UiO	t.g.jenssen@medisin.uio.no
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Ruth Strømmen	MD, PhD candidate	UiO	rutstr@ous-hf.no

I sum har forskningsgruppen 1,2 vitenskapelige stillinger ved UiO, 3 eksternt finansierte PhD-stillinger og 65 vitenskapelige publikasjoner i 2022 (se nedenfor).

Assoserte medlemmer / Associated members:

NAME	POSITION/TITEL/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Hanne Scholz	PhD, Chief Ex vivo islet lab	UiO	hanne.scholz@medisin.uio.no
Svein Olav Kolset	Professor	UiO	s.o.kolset@medisin.uio.no
Ida Robertsen	Associate Professor	UiO	Ida.robertsen@medisin.uio.no

Aktivitet i 2022/ Activity in 2022

Forskningsaktivitet/ Research activity:

Two new PhD candidates started on projects by Helse SørØst in 2022:

Inger Charlotte Kongerud, MD, on the project: Can SGLT2 inhibition preserve measured glomerular filtration rate (GFR) in kidney transplant recipients?

Ruth Strømmen, MD, on the project: Long term skeletal health in kidney transplant recipients.

New projects started in 2022:

TRAX study. An epidemiological study on bone health and plasma biomarkers after kidney transplantation.

Continued projects which started in 2021 and earlier:

1. SIMPLIFY study: Simplification of the plasma clearance of iohexol.
2. Patiromer PK study: Effect of patiromer on pharmacokinetics of immunosuppressive drugs in renal transplant recipients.

3. Hypomagnesemia as a risk factor for development of posttransplant diabetes mellitus (PhD project Rasmus Kirkeskov Carlsen).
4. The microbiome and gut metabolism of mycophenolate acid.
5. Covid-19 vaccine study among kidney transplant recipients
6. EVITA (Epstein-Barr virus infection monitoring in renal transplant recipients)
7. BONTRAX – 10 years follow-up of bisphosphonate treatment in kidney transplant recipients
8. Home Based Monitoring – patient centric sampling for analyses of tacrolimus, creatinine and hemoglobin.

Other ongoing projects continued in 2022:

- Post-transplant diabetes mellitus
- Kidney rejection and immunity
- Individualization of immunosuppression, also with home based blood sampling (MitraTip®)
- Biomarkers of outcomes after transplantation
- Measured GFR by iohexol plasma clearance vs. estimated glomerular filtration rate
- Evaluation and follow-up of kidney donors (ALDON Study)
- Long-term effects and safety with human pancreas transplantation.

In relation to these topics altogether 65 peer-reviewed papers were published in international journals in 2022.

Our biobank was expanded, and we have established valid measures for long-term outcome after transplantation (e.g., GFR, pharmacological and metabolic measures, inflammation parameters, etc.). We have received a EU grant as partner in a twinning project of the Horizon program: Diabetes, Obesity & the Kidney (DOKI), The research group received a large grant from KLINBEFORSK to start a randomized, blinded and placebo-controlled intervention study on the SGLT2 inhibitor dapagliflozin in kidney transplant recipients. The purpose of the study is to see whether SGLT2 inhibition can prolong the survival time for transplanted kidney grafts.

Five representative papers published by our group in 2022 are cited below:

1. Heldal TF, Åsberg A, Ueland T, Reisæter AV, Pischke SE, Mollnes TE, Aukrust P, Hartmann A, Heldal K, Jenssen T. Inflammation in the early phase after kidney transplantation is associated with increased long-term all-cause mortality. *Am J Transplant* 2022; 22(8): 2016-2027.
2. Tsarpali V, Midtvedt K, Lønning K, Bernklev T, Åsberg A, Fawad H, von der Lippe N, Reisæter AV, Røysland K, Heldal K. A comorbidity index predicts survival in older recipients of deceased donor kidney transplantation; a national prospective study. *Transplant Direct* 2022; 8(4): e1307.
3. Kvistne KE, Robertsen I, Skovlund E, Christensen H, Krogstad V, Wegler C, Angeles PC, Wollmann BM, Hole K, Johnson LK, Sandbu R, Artursson P, Karlsson C, Andersson S, Andersson TB, Hjelmesæth J, Jansson-Löfmark R, Åsberg A. Short- and long-term effects of body weight loss following calorie restriction and gastric bypass on CYP3A-activity - a non-randomized three-armed control. *Clin Transl Sci* 2022; 32.
4. Haugen AJ, Hallan S, Langberg NE, Dahle DO, Pihlstrøm H, Birkeland KI, Reisæter AV, Midtvedt K, Hartmann A, Holdaas H, Mjøen G. Increased risk of ischaemic heart disease after kidney donation. *Nephrol Dial Transplant*. 2022; 37(5): 928-936. Iled trial. *Clin Transl Sci* 2022; 15(1): 221-233.
5. Dahle DO, Skauby M, Langberg CW, Brabrand K, Wessel N, Midtvedt K. Renal Cell Carcinoma and Kidney Transplantation: A Narrative Review. *Transplantation*. 2022; 106(1): e52-e63.

Populærvitenskapelig aktivitet/ Popular science:

- Er det trygt for meg å besøke barnebarna? Trond G. Jenssen, *Diabetes*, Februar, 2022

- Om Hypoglykemi i «Thomas (37) ble brått revet bort». Trond G. Jenssen, Dagbladet, 14.august, 2022.
- Pankreas- og øycelletransplantasjon, Trond G. Jenssen. LNT-nytt, august, 2022
- Pasientene må få undersøkt føttene sine også i primærhelsetjenesten. Trond G. Jenssen, Dagens Medisin, 20. september, 2022.
- Studie: En av fire med kronisk nyresykdom hadde type 2 diabetes. Trond G. Jenssen, Dagens Medisin, 21. september, 2022
- DM Arena Diabetes/ Post-EASD 2022. Moderne behandling av nyresykdom ved diabetes. Trond G. Jenssen, Dagens Medisin, 29. september, 2022 (nettversjon)
- Gastroparese hos pasienter med diabetes: Flertallet passerer uoppdaget. Trond G. Jenssen, Dagens Medisin, 4. oktober, 2022
- Refusjon av ny nyrebeskyttende medisin. Trond G. Jenssen, HealthTalk, November 2022.
- Diabetespasienter bør sjekke nyrene på årskontrollen. Trond G. Jenssen, Mediaplanet, 17. desember 2022

Forskningsgruppe: Eksperimentell Celletransplantasjon

Research group: Experimental Cell Transplantation

Avdeling: Avdeling for transplantasjonsmedisin (ATX)

Gruppeleder: Hanne Scholz

About the group (short description in English):

The research group work on develop and establish new cell therapies for treating diabetes focus on experimental, translational and clinical studies. The research group consisting of members with a research background in medicine, biology, stem cell biology, tissue engineering, transplantation, and laboratory engineering.

Major aims:

- To develop novel strategies for beta cell replacement therapy
- To develop novel strategies for tissue engineering and regeneration of islet cells

Our research focused on developing beta cell replacement therapy for type 1 diabetes and understanding human islet cell biology. The human islet consists mainly of insulin-producing beta cells and glucagon producing alpha cells responsible for the fine-tune regulation of our blood glucose level in our body. The laboratory aims to improve the care for diabetic patients and has a clear and strong focus on clinical translation based on experimental research. Scholz is head of the Cell Therapy Laboratory for islet isolation and mesenchymal stromal/stem cell preparation that holds international standards. The group work in close collaboration with the Nordic Network for Clinical Islet transplantation and Uppsala group (led by Prof. Olle Korsgren). The research group is integrated in the Centre of Excellence -Hybrid Technology Hub at Institute of Basic Medical Sciences, UiO for developing organoids and the organ on a chip technology.

The lab is funded by the Research Council of Norway, UiO:Life Science, South-Eastern Norway Regional Health Authority, University of Oslo, The Norwegian Diabetes Association, Oslo Diabetes Research Center, Novo Nordisk Fonden.

Hanne Scholz is a board member of the Nordic Network for Clinical Islet Transplantation (NNCIT), MC member of the EU Horizon 2020 COST Action CA17116 (SPRINT), Officer (secretary) of the International Pancreas and Islet Transplantation Association (IPITA 2021-2025), and Councillor of the European Society for Organ Transplantation (ESOT 2019-2023).

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Stefan Krauss	Professor/Director CoE-HTH-Organ on chip	UiO	s.j.k.krauss@medisin.uio.no

Aktivitet i 2022/ Activity in 2022

Projects:

- Clinical beta cell replacement therapy program
- Adipose-derived stromal cells preserve pancreatic islet function in a 3D bioprinted scaffold
- Generation of beta cells from human induced pluripotent stem cells (hiPSCs)
- Determination of insulin secretion from islet organoids
- Generation of insulin-producing cells from cholangiocyte organoids
- Decidua Stromal Cells (DSC) for Steroid-Refractory Acute Graft-versus-host Disease After Hematopoietic Stem Cell Transplantation (HSCT)
- Development of a novel cell therapy based on decidual stromal cells (DSC) for treatment of patients with type 1 diabetes
- Deep learning-based analysis of stem cell differentiation pathways (islets)
- Metabolism on chip

Publikasjoner/ Publications:

1. S Sämfors, EM Niemi, K Oskarsdotter, CV Egea, A Mark, H Scholz, P Gatenholm. Design and biofabrication of a leaf-inspired vascularized cell-delivery device, *Bioprinting*, Volume 26, 2022, e00199, ISSN 2405-8866, Doi: 10.1016/j.bioprint.2022.e00199.
2. S Abadpour, EM Niemi, LS Orrhult, C Hermanns, R de Vries, LP Nogueira, HJ Haugen, D Josefson, S Krauss, A Apeldoorn, P Gatenholm, H Scholz. Adipose-derived stromal cells preserve pancreatic islet function in a transplantable 3D bioprinted scaffold, *bioRxiv* doi: <https://doi.org/10.1101/2022.05.30.494035>
3. Berney T, Andres A, Bellin MD, de Koning EJP, Johnson PRV, Kay TWH, Lundgren T, Rickels MR, Scholz H, Stock PG, White S, International Islet Transplant Centers (2022) A Worldwide Survey of Activities and Practices in Clinical Islet of Langerhans Transplantation *Transpl Int*, 35, 10507 DOI 10.3389/ti.2022.10507
4. C Olsen, E Wiborg, E Lundanes, S Abadpour, H Scholz, SR Wilson. On-line reduction of insulin disulfide bonds with photoinduced radical reactions, upstream to nano liquid chromatography-mass spectrometry. *Separation Science Plus* (2022) <https://doi.org/10.1002/sscp.202200022>
5. SA Brinch, E Amundsen-Isaksen, S Espada, C Hammarström, A Aizenshtadt, PA Olsen, L Holmen, M Høyem, H Scholz, G Grødeland, ST Sowa, A Galera-Prat, L Lehtio, I Meerts, R Leenders, A Wegert, S Krauss, J Waaler; The Tankyrase Inhibitor OM-153 Demonstrates Antitumor Efficacy and a Therapeutic Window in Mouse Models. *Cancer Research Communications* 8 April 2022; 2 (4): 233–245. Doi:10.1158/2767-9764.CRC-22-0027
6. Kwak D, Combriat T, Wang C, Scholz H, Danielsen A, Jensenius AR. Music for Cells? A Systematic Review of Studies Investigating the Effects of Audible Sound Played Through Speaker-Based Systems on Cell Cultures. *Music & Science*. January 2022. doi:10.1177/20592043221080965
7. Ghila L, Furuyama K, Grey ST, Scholz H, Chera S. Editorial: Beta-Cell Fate: From Gene Circuits to Disease Mechanisms. *Front Genet*. 2022 Feb 25;13:822440. doi: 10.3389/fgene.2022.822440. eCollection 2022.
8. Carrasco M, Wang C, Søviknes AM, Bjørlykke Y, Abadpour S, Paulo JA, Tjora E, Njølstad P, Ghabayen J, Nermoen I, Lyssenko V, Chera S, Ghila LM, Vaudel M, Scholz H, Ræder H (2022) Spatial Environment Affects HNF4A Mutation-Specific Proteome Signatures and Cellular Morphology in hiPSC-Derived β-Like Cells *Diabetes*, 71 (4), 862–869 DOI 10.2337/db20-1279
9. Ward C, Odorico JS, Rickels MR, Berney T, Burke GW 3rd, Kay TWH, Thaunat O, Uva PD, de Koning EJP, Arbogast H, Scholz H, Cattral MS, Stratta RJ, Stock PG; International Pancreas and Islet Transplant Association Beta-Cell Replacement Therapy Monitoring Task Force. International Survey of Clinical Monitoring Practices in Pancreas and Islet Transplantation. *Transplantation*. 2022 Jan 10. doi: 10.1097/TP.00000000000004058. PMID: 35019897.

Populærvitenskapelig aktivitet/ Popular science:

NRK radio Hanne Scholz was a guest on the Abels Forgård radioshow and podcast talking about 3D printing of organs.

https://radio.nrk.no/podcast/abels_taarn/sesong/202203/l_1e994fa7-9813-4a47-994f-a798138a478e

Innovasjonsaktivitet/ Innovation:

SPARK is a two-year UiO:Life Science innovation program to further develop ideas within health-related life sciences for the benefit of patients and society.

Project leader: Metabolism on chip

Dr. Shadab Abadpour, Dept. of Transplantation and Institute for Surgical Research, OUS / Hybrid Technology Hub-Centre of Excellence, UiO

Team members: Dr. Aleksandra Aizenshtadt, Dr. Mathias Busek, Chencheng Wang, Prof. Steven Ray Haakon Wilson, Prof. Stefan Krauss, Dr. Hanne Scholz

Forskningsgruppe: Klinisk effektforskning – Avdeling for Kirurgi, Inflamasjonsmedisin og Transplantasjon, Oslo Universitetssykehus og Institutt for Helse og Samfunn, Universitetet i Oslo

Research group: Clinical Effectiveness Research Group - Division of Transplantation medicine, Inflammation and Surgery, Oslo University Hospital and Institute of Health and Society, University of Oslo

Avdeling: Avdeling for transplantasjonsmedisin, KIT

Gruppeleder: Mette Kalager

Om gruppen: Forskergruppen ble startet i 2012 av Michael Bretthauer og Mette Kalager og har 36 medlemmer i 2022. Gruppen gjennomfører store randomiserte og epidemiologiske studier for å vurdere effekter av ulike diagnostiske og terapeutiske intervensjoner.

Målet med forskningen er å finne ut om kliniske intervensjoner og behandlinger virker, hvilken behandling eller diagnostikk som virker best, og hvilke bivirkninger og komplikasjoner de har. Gruppen har inkludert mer enn 400.000 deltagere i pågående studier. Gruppen samarbeider med de fleste sykehusene i Norge og mange ledende forskingsinstitusjoner i utlandet.

About the group: The research group was established by Michael Bretthauer and Mette Kalager in 2012. In 2022, the Group has 36 members. The Group conducts large randomized trials and epidemiologic studies to test and compare diagnostic and therapeutic clinical interventions.

The main goal of the research is to find if clinical interventions and treatments work, what works best, and what side effects and complications they have. Currently more than 400.000 participants are enrolled in ongoing studies. The group collaborates with most hospitals in Norway and with many leading research institutions worldwide.

HOVEDMEDLEMMER / MAIN MEMBERS:

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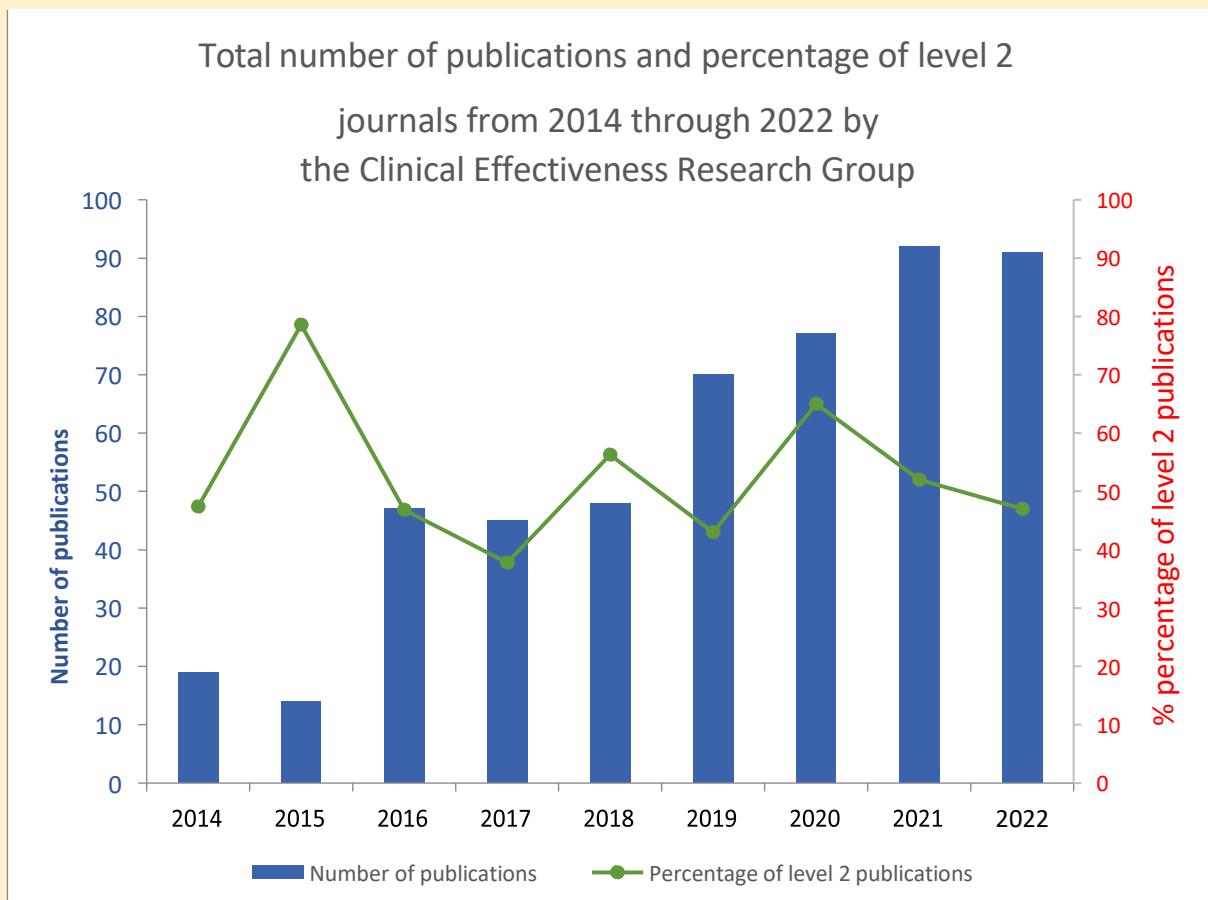
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Aktivitet i 2022 / Activity in 2022

The Group has had an expansive growth from its four members in 2012 to 36 members in 2022. All but four members of the Group are funded by external grants.

Publications in 2022:

- The Group published 91 articles in peer-reviewed journals in 2022.
- Of all articles, 47 % were published in level 2 journals (the top 20 % of journals).
- The mean impact factor of articles in 2022 is 9.1 and the cumulative impact factor is 831,2.
- For a full list of publications, see the group website at <https://www.med.uio.no/helsam/forskning/grupper/klinisk-effektforskning/publikasjoner/>



Populærvitenskapelig aktivitet/ Popular science:

The group members plays an active part in Norwegian media, TV and podcast debates with more many comments and appearances in 2022. For more details, see the group website at

<https://www.med.uio.no/helsam/forskning/grupper/klinisk-effektforskning/index.html>

Forskningsgruppe: Forskningsgruppe for pasientrapporterte resultater og helseøkonomi

Research group: Research group for patient reported outcomes and health economics

Avdeling: Avd for transplantasjon

Gruppeleder: Marit Helen Andersen

Om gruppen (kort beskrivelse på norsk):

Forskningsgruppe for pasientrapporterte resultater og helseøkonomi er en aktiv, veletablert forskningsgruppe som utgår fra Avdeling for transplantasjon ved Oslo universitetssykehus HF, men har medlemmer fra andre klinikker og flere har bistilling ved Universitetet i Oslo. Gruppen har som mål å fremme klinisk forskning på pasienterfarte resultater og helseøkonomi og fungerer som et støttende forskningsnettverk for å bidra til forskning av høy kvalitet. Medlemmene i forskningsgruppen representerer et bredt fagfelt med en felles metodeforankring.

About the group (short description in English):

Research group for Patient Reported Outcomes and Health Economics is aiming to be a research network and communicate methodological issues within patient reported outcomes studies and health economics research. The group is multidisciplinary and has varied research activities related to a wide span of research questions within different patient groups

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Jintana B. Andersen	PhD-student	OUS	eborosun@ous-hf.no
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Activity in 2 (selected)

- PROM-conference for researchers in HSØ organized by Research group for patient reported outcomes and health economics, and PROMINET (92 participants)
- 5 regular meetings for main group members prepared with agenda
- 14 publications in peer reviewed international journals (authors are main group members)
- Oral – and poster presentations at international conferences (transplant conferences, cancer conferences, health literacy conferences, quality of life conferences)
- Active collaboration with national and international network partners (PROMINET, LIVSFORSK, OsloMet, UiO, EORTC): planning and performing research projects, funding, courses/teaching, recruiting master and PhD-candidates, supervision of candidates, external scientific committee work etc. Collaboration with professor Richard Osborne, Australia, within health literacy research.
- WP leader in an EU-project related to statistical analyses and interpretation of HRQoL in clinical trials/studies, SISAQOL-IMI
- HSØ funding new research projects: postdoc (1), phd (2)

Publications (14)

1. Wahl AK; Hermansen Å; Tschauder MB; Osborne RH; Helseth S & Jacobsen R (2022). The Parent Health Literacy Questionnaire (HLQ-Parent). Adaptation and validity testing with parents of children with epilepsy. Scandinavian Journal of Public Health. ISSN 1403-4948. doi: 10.1177/14034948221123436.
2. Osborne RH; Cheng CC; Nolte S; Elmer S; Besancon S, Budhathoki SS, Debussche x,8, Dias S, Kolarčík P;10, Loureiro MI;9, Maindal H; Nascimento D; Smith AJ;13, Wahl A, Elsworth GR; Hawkins M (2022). Health literacy measurement: embracing diversity in a strengths-based approach to promote health and equity, and avoid epistemic injustice. BMJ Global Health. ISSN 2059-7908. 7(9). doi: 10.1136/bmjgh-2022-009623.
3. Tyrdal MK, Veierød MK, Bragelien M; Røe C; Natvig B; Wahl AK & Robinson HS (2022). Neck and back pain: Differences between patients treated in primary and specialist health care. Journal of Rehabilitation Medicine. ISSN 1650-1977. 54. doi: 10.2340/jrm.v54.363.

4. Larsen EH; Mellblom A; Ruud E; Wahl AK & Lie HC (2022). Prepared for survivorship? Multidisciplinary healthcare professionals' experiences with adolescents' transition off cancer treatment: A focus group study. *European Journal of Oncology Nursing*. ISSN 1462-3889. 58. doi: 10.1016/j.ejon.2022.102150.
5. Borge CH; Larsen MH; Osborne RH; Engebretsen E; Andersen MH & Holter IA et al (2022). How to co-design a health literacy-informed intervention based on a needs assessment study in chronic obstructive pulmonary disease. *BMJ Open*. ISSN 2044-6055. 12 (10). doi: 10.1136/bmjopen-2022-063022.
6. Smedman TM; Guren TK; Tveit MK; Thomsen M; Andersen MH & Line PD (2022). Health-Related Quality of Life in Colorectal Cancer Patients Treated With Liver Transplantation Compared to Chemotherapy. *Transplant International*. ISSN 0934-0874. 35. doi: 10.3389/ti.2022.10404.
7. Larsen MH; Mengshoel AM; Andersen MH; Borge CH; Ahlsen B & Dahl KG et al (2022). "A bit of everything": Health literacy interventions in chronic conditions – a systematic review. *Patient Education and Counseling*. ISSN 0738-3991. 105 (10), s. 2999–3016. doi: 10.1016/j.pec.2022.05.008.
8. Wahl AK; Andersen MH; Ødemark J; Reisæter AV; Urstad KH & Engebretsen E (2022). The importance of shared meaning-making for sustainable knowledge translation and health literacy. *Journal of Evaluation In Clinical Practice*. ISSN 1356-1294. doi: 10.1111/jep.13690.
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10. Singer S; Hammerlid E; Tomaszewska IM; Amdal CD; Bjordal K & Santos M et al (2022). Methodological approach for determining the Minimal Important Difference and Minimal Imrotenat Change scores for the European Organisation for Research and Treatment of Cancer Head and Neck Cancer Module (EORTC QLQ-HN43) exemplified by the swallowing scale. *Quality of Life Research*. ISSN 0962-9343.
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14. Kling J; Asphaug L; Feragen KB. Cost-effectiveness analysis of a psychosocial web-based intervention for adolescents distressed by a visible difference: Results from a randomized controlled trial in Norway. *Scand J Psychol*. 2022 Nov 11. doi: 10.1111/sjop.12885. Epub ahead of print. PMID: 36367227.

Forskningsgruppe: Nevroendokrine svulster

Research group: Neuroendocrine tumors

Avdeling: Department for organ transplantation

Gruppeleder: Espen Thiis-Evensen

Om gruppen:

Gruppen består av personer med interesse for nevroendokrine neoplasmer, hovedsakelig fra avdelinger som er involvert i utredning, diagnostikk og behandling av nevroendokrine neoplasmer ved Oslo universitetssykehus.

About the group:

The group is comprised of persons with an interest for neuroendocrine neoplasias at Oslo University Hospital.

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/ AFFILIATION	E-MAIL
Espen Thiis-Evensen	Gruppeleder, lege	OUS	ethiisev@ous-hf.no
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Vera Dahle	Kreftsykepleier, medlem		vdahlel@ous-hf.no
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Aktivitet i 2022/ Activity in 2022

Forskningsaktivitet/ Research activity:

Name	Type	Description		No. of patient	
Carcinoid heartdisease	retrospective observational	Markers of succesfull heart valve surgery	local	19	
Impress	intervasjon	Genetic analysis to tailor therapy	National	2	
Artificial intelligece in-radiology	retrospective observational	AI in describing liver mnetastases	Local	80	
Livertransplantation in NET	retrospective observational	Effect of livertransplantaion in NET	International	16	
Livertransplantation in NE	prospective interventional	Effect of livertransplantaion in NET	Local	26	
RFA-PNET	Prospective interventional	Radio frequency ablation of pancreatic NET	National	2	
Prevalence and Incidence NEN	retrospective observational	Prevalence and incidence	Local	NEN in Norway -93-21	
PRRT efficacy markers	prospective observational	serum markers for effect of PRRT	National	106	
EvNET	prospective observational	Serumcons. Of related to everolimus-side effects	Local	20	
Explain	prospective observational	New serum biomarkerst in NET	Nordic	25	
D3 resection in SiNET	prospective interventional	Extended glandel resection in SiNET	Regional	30	
Tem/cap	retrospective observational	Efficay og temozolomid/capecitabine in NET	Local	115	
Appendix-NET	retrospective observational	Which treatment of appendix_NET 1-2 cm	European	4	
QoL in PRRT m Uppsala	prospective observational	Quality of life after PRRT	Nordic	12	
SiNET Grade 2	retrospective observational	SINET grade 3, treatment effects	Nordic	16	
Familial SiNET	prospective interventional	GaPET in screening of relatives ti SiNET patients	Local	30	
Total No of pts.				484	

Publikasjoner/ Publications

- Thiis-Evensen E, Kjellman M, Knigge U, Gronbaek H, Schalin-Jäntti C, Welin S, Sorbye H, Del Pilar Schneider M, Belusa R; Nordic NET Biomarker Group. Plasma protein biomarkers for the detection of pancreatic neuroendocrine tumors and differentiation from small intestinal neuroendocrine tumors. *J Neuroendocrinol*. 2022 Jul;34(7):e13176. doi: 10.1111/jne.13176. Epub 2022 Jul 13. PMID: 35829662.
- Eshmuminov D, Studer DJ, Lopez Lopez V, Schneider MA, Lerut J, Lo M, Sher L, Musholt TJ, Lozan O, Bouzakri N, Sposito C, Miceli R, Barat S, Morris D, Oehler H, Schreckenbach T, Husen P, Rosen CB, Gores GJ, Masui T, Cheung TT, Kim-Fuchs C, Perren A, Dutkowski P, Petrowsky H, Thiis-Evensen E, Line PD, Grat M, Partelli S, Falconi M, Tanno L, Robles-Campos R, Mazzaferro V, Clavien PA, Lehmann K. Controversy Over Liver Transplantation or Resection for Neuroendocrine Liver Metastasis: Tumor Biology Cuts the Deal. *Ann Surg*. 2022 Aug 17. doi: 10.1097/SLA.0000000000005663. Epub ahead of print. PMID: 35975918.

Avdeling for urologi (URO) /

Department of Urology

- Rekonstruktiv urologi og nevrourologi/ Reconstructive urology and neurourology
- Prostatakreft/ Prostate Cancer

Forskningsgruppe:

Forskningsgruppe for rekonstruktiv urologi og nevrourologi

Research group:

Research group for reconstructive urology and neurourology

Avdeling:

Urologisk avdeling

Gruppeleder:

Henriette Veiby Holm

Om gruppen:

Forskningen er primært fokusert på klinisk forskning på pasienter med urethrastruktur, følgetilstander etter behandling for bekkenlidelser inkl. kreft hos kvinner og menn, inkl. pasienter med urinlekkasje etter prostatakreftbehandling og pasienter med medfødte lidelser (hypospadi, blæreekstrofi), samt neurologiske pasienter med dysfunksjon av nedre urinveier. Gjennom tverrfaglige samarbeidspartnere vil ytterligere fagfelt være inkludert, som f.eks. nyrecancer med cavatrombe.

Seksjon for rekonstruktiv urologi og nevrourologi med tilhørende forskningsgruppe er i en unik situasjon, i verdensammenheng, vedrørende pasientmateriale fra hhv. hele landet og helseregionen. Vi er den eneste avdeling/seksjon i Norge som har komplett kompetanse på urethrakirurgi og har ambisjon om å utvide forskningen på dette feltet. Vi får pasienter fra hele Helse Sør Øst med sequelae etter bekkenkirurgi/strålebehandling, inkl. menn med urininkontinens eller andre tilstander etter prostatakreftbehandling. Vi har også ansvar, sammen med Sunnaas sykehus, for oppfølging av alle pasienter med ryggmargsskade/ryggmargsbrokk og nevrogen blæredysfunksjon og forskning på denne pasientgruppen. Det er av stor interesse å redusere byrden ved nevrogen blæredysfunksjon og vi forsker bl.a. på metoder for å forhindre utvikling av alvorlig blæredysfunksjon etter akutt ryggmargsskade.

I tillegg har vi nær kontakt med andre spesialiteter ved og utenfor OUS, og samarbeider jevnlig med fysikalmedisiner, neurologer, barnekirurger, plastikkirurger, transplantasjonskirurger, gynekologer, psykiatere og fysioterapeuter. Ovennevnte forskningsprosjekt på ryggmargsskadde er i tett samarbeid med Sunnaas.

About the group:

The research group primarily focuses on clinical research on patients with urethral stricture, sequelae after treatment for pelvic disorders/LUTD including cancer in women and men, with a large group of patients with urinary incontinence after prostate cancer treatment and patients with congenital disorders (hypospadias, bladder extrophy), and neurological patients with LUTD. Multidisciplinary studies on other fields will also be included in the group.

Section of reconstructive urology and neurourology and research group has a unique situation, in a global context, regarding patient material from the whole country and the health region,

respectively. We are the only department/section in Norway that has complete expertise in urethral surgery and we have the ambition to expand the research in this field. We serve patients from all over Helse Sør Øst with sequelae after pelvic surgery/radiation therapy, including men with urinary incontinence or other conditions after prostate cancer treatment. We are also responsible, together with Sunnaas hospital, for follow up of all patients with spinal cord injury/myleomeningocele and neurogenic bladder dysfunction and research on this patient group. It is of great interest to reduce the burden of neurogenic bladder dysfunction and we are doing research on methods to prevent the development of severe bladder dysfunction following acute spinal cord injury.

In addition, we have close contact with other specialties at OU and elsewhere, and collaborate regularly with Sunnaas/physical medicine & rehabilitation, as well as neurologists, pediatric surgeons, plastic surgeons, transplant surgeons, psychiatrists and physiotherapists. We have an ongoing research project with Sunnaas.

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Henriette Veiby Holm	Group leader, Consultant urologist	OUS	hveiby@ous-hf.no
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Kari Bø	Professor, physiotherapist	Norges idrettshøyskole	karib@nih.no

Aktivitet i 2022/ Activity in 2022

Forskningsaktivitet/ Research activity:

Forskningsaktiviteten for gruppen i 2022 gjenspeiles i at ingen av hovedmedlemmene har avsatt tid til forskning i stillingen.

Internasjonalt samarbeid: Flere pågående prosjekter gjennom GURS (Society of Genitourinary Reconstructive Surgeons) og NUF (Nordisk Urologisk Forening) som omhandler urethrakirurgi, implantatkirurgi og senfølger etter prostatakreftbehandling.

Pågående prosjekter:

- Multisenter, internasjonal prospektiv studie på menn operert for urininkontinens (SATURN).
- Multisenter, internasjonal prospektiv studie på menn behandlet for urethrastruktur med medikamentgivende blokkeballong (OPTILUME).
- Opprettelse av register, inkl. validering av spørreskjema, for pasienter med erektil dysfunksjon operert med penisimplantat (PHOENIX). Under utarbeidelse.
- Randomisert studie: Forebygging av blæredysfunksjon hos ryggmargsskadde (SCIBOT). Studie gjennomført, manuskript under skriving.
- Langtidsoppfølging etter gjennomført randomisert nordisk studie (første i verden) vedrørende to måter å behandle urethrastruktur, som viser at den ene metoden gir sjeldnere penile plager/sekssuell dysfunksjon, enn den andre metoden (SUPS).
- OUS-studie av pasienter operert med AdVance slynge for urinlekkasje med oppfølging på >12 år. Presentert på NUF2022, manuskript skrevet og klart til innsendelse.
- OUS-studie av pasienter operert med urethral sfinkterprotese AMS800 for urinlekkasje med oppfølging på >10 år, nylig REK-godkjent.
- OUS-studie med prospektiv oppfølging av pasienter som får Botox i blæren for å evaluere effekt, tilfredshet, komplikasjoner.
- OUS-studie om bruk av ultralyd med kontrast til mer presis diagnostisering ved priapisme.
- Redaktør og forfatter av internasjonal bok (MRW, Major Reference Work): Female Genitourinary and Pelvic Floor Reconstruction, Springer forlag. Ferdigstilt 2022, er under produksjon.

Populærvitenskapelig aktivitet/ Popular science:

- Intervju om prematur ejakulasjon, Dagbladet (Ole Jacob Nilsen)
- Intervju om overaktiv blære og urinlekkasje, Norsk Ukeblad (Henriette Veiby Holm)
- Foredrag for leger i spesialisering, urologer, uroterapeuter, fysioterapeut etc.

Innovasjonsaktivitet/ Innovation:

- Oppstart av meget lovende minimal invasiv behandling av urethrastruktur med medikamentgivende blokkeballong Optilume DCB, som første senter i Norge.
- Utredning av mulig forskningsprosjekt med InVivo Bionics av ny revolusjonerende nanoteknologi for kontinuerlig blæretrykksmåling.

Forskningsgruppe: Prostatakreft

Research group: prostate cancer

Avdeling: Urologisk avdeling og Avdeling for kreftbehandling

Gruppeleder/groupleader: Viktor Berge

Om gruppen (kort beskrivelse på norsk):

Forskningsgruppen i prostata kreft består av urologer og onkologer (hovedmedlemmer) og leger og basalforskere fra andre avdelinger og institutter (assosierede medlemmer), engasjert i prostata kreft forskning ved Oslo Universitets sykehus. Hovedområdet i klinisk forskning er utkomme studier og livskvalitets studier etter primær behandling og salvage behandling av prostata kreft. Et annet viktig område er studier av nye diagnostiske metoder og fokal behandling av prostata kreft.

Hovedområdet i translasjonsforskning som gruppen er involvert i, er deteksjon og validering av nye potensielle biomarkører i tumorvev, blod og urin. Siktemålet med denne aktiviteten er reduksjon av overdiagnostikk og overbehandling, forbedring av diagnostikk og bedre behandling av høy risiko kreft

About the group (short description in English):

The Research group of prostate cancer consists of urologists and oncologists (main members) and physicians and scientists from other departments and institutes (associated members), engaged in prostate cancer research at Oslo University Hospital (OUH). Main topic of clinical research is new diagnostic methods, outcomes studies and Quality of Life studies after primary treatment and salvage treatment of prostate cancer.

The main aims for our translational research are detection and validation of new putative biomarkers in tumor tissue, blood and urine. This effort focuses on achieving a more personalized treatment of patients, in order to reduce overdiagnosis and overtreatment of prostate cancer, but also to improve diagnosis and treatment of high-risk prostate cancer.

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Viktor Berge	Group leader / Adjunct Professor, consultant in urology	OUH and UiO	vikber@ous-hf.no
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Eduard Baco	Associate professor/consultant in urology	OUH and UiO	BACE@ous-hf.no urology
Shivanthe Sivanesan	PhD student/ consultant in urol	UiO and OUH	shisiv@ous-hf.no
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Fredrik Ottosson	Consultant in urology	OUH	freott@ous-hf.no
Wolfgang Lilleby	PhD/consultant in oncology	OUH	WLL@ous-hf.no
Henriette Veiby Holm	PhD/ consultant in urology	OUH	hveiby@ous-hf.no
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Lars Fredrik Qvigstad	Consultant in urology	OUH	larqvi@ous-hf.no
Åsmund Nybøen	Bioengineer, department of pathol	OUH	ANC@ous-hf.no
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Assosierte medlemmer / Associated members:

NAME	POSITION/TITEL/ROLE	EMPLOYER/AFFILIATION	E-MAIL
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Activity in 2022

The last year has been an active year for our research group. Main members in the group have authored or coauthored 18 publications about prostate cancer during 2022, the same number as last year.

At the NUF meeting in Helsinki our group was well represented and one of our abstract even won the prize for best abstract: "Functional outcomes at 12 months after focal ablation versus radical prostatectomy for intermediate risk prostate cancer. Interim analysis of randomized control trial" presented by ass. professor Eduard Baco.

The randomized double blind study PeP-RALP was launched by PhD student Shivanthe Sivanesan in December. This is a pilot study targeting perioperative stress induced prostate cancer recurrence.

The research registry for prostate cancer is continuously improving; the latest change is inclusion of HIFU patients.

A satisfying trend is that the registry is utilized by increasing numbers of urologist at the department, both in presentations at meetings and congresses and in publications. At the Surgical Fall Meeting last year no other department of urology presented more abstracts than ours.

The SPCG-17 study is recruiting well with 105 included patients at the end of 2022 into active surveillance for low risk and intermediate risk cancer prostate.

Our group is also engaged in upstart of the SPCG 19 study: A randomized, controlled, open-label, prospective, multicenter intervention trial of immediate curative therapy versus conservative treatment in older patients with non-metastatic, high-risk prostate cancer.

Several members in our group have during 2022 been engaged in planning of the new prostate cancer center at Nye DNR.

Institutt for indremedisinsk forsking (IMF) / Research Institute for Internal Medicine

- Aterosklerose og relaterte metabolske sykdommer /
Atherosclerosis and other cardio metabolic diseases
- Inflamasjonsmarkører for hjertekar- og metabolske
sykdommer / Inflammatory Biomarkers in Cardiovascular
and Metabolic Disease
- Eksperimentell leverforskning / Experimental hepatology
(NoPSC)
- Inflamasjonssykdommers genomikk og metagenomikk /
Genomics and metagenomics in inflammatory diseases
(NoPSC)
- Klinisk mikrobiologi og microbiota medisin / CliMic: Clinical
microbiology and microbiota medicine

Forskningsgruppe:

Aterosklerose og relaterte metabolske sykdommer

Research group:

Atherosclerosis and other cardio metabolic diseases

Avdeling:

Institutt for Indremedisinsk Forskning

Gruppeleder:

Bente Halvorsen (permisjon 01.08-2022-31.07.23)

Konstituert Gruppeleder, Tuva B. Dahl (01.08-2022-31.07.23)

Om gruppen (kort beskrivelse på norsk):

Hjerte- og karsykdom, diabetes, fedme og fettlever, er viktige årsaker til morbiditet og dødelighet over hele verden. De deler mange fellestrek, som dyslipidemi og kronisk betennelse, og i vår forskningsgruppen studerer vi disse prosessene. De siste årene har vi også studert disse mekanismene i Covid-19 og sammenhengen mellom Covid-19 og risiko for kardiovaskulær sykdom. Ved å utforske immunmedierte mekanismer gjennom translasjonsforskning, som knytter grunnforskning til klinikk, ønsker vi å bygge et fundament for å utvikle bedre diagnostikk og behandling for kardiovaskulær og metabolsk sykdom. Vår forskning kombinerer moleylærbiologi, biokjemi, kardiovaskulær, cerebrovaskulær og endokrin medisin. Forskningsgruppen bruker ulike metoder og innfallsvinkler, fra analyser av blod og vevsprøver fra pasienter, til studier i genmodifiserte mus og cellekultursystemet ved hjelp av avansert celle- og molekylærbiologiske metoder.

Gruppen består av personer med ulik faglig bakgrunn, fra leger, ernæringsfysiologier, biokjemikere og ingeniører, og denne tverrfagligheten er en stor styrke for forskningen.

About the group (short description in English):

Cardiovascular disease and related metabolic disorders such as diabetes, obesity and fatty liver disease are major causes of morbidity and mortality worldwide. They have many common features, such as dyslipidemia and inflammation. In our research group, we focus on immune-mediated mechanisms in these conditions. The last years we have also studied these mechanisms in Covid-19, and the association between Covid-19 and risk of cardiovascular disease. By exploring these processes through translational research, connecting basic science and the clinic, we wish to build a foundation for the development of new diagnostic and treatment targets for cardiometabolic disease. Our research group works in the cross-section between molecular biology and biochemistry, and cardiovascular, cerebrovascular, and endocrine

medicine. Our ambitious goal is to delineate novel therapeutic targets and biomarkers. The group uses different research approaches, ranging from analyses of blood and tissue samples from patients to studies in genetically modified mice and cell culture systems, using advanced cellular and molecular biology.

The group consists of people with different educational background and includes medical doctors, nutritionists, biochemists, and engineers. Such multidisciplinary competence is a great strength of our research group.

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Bente Halvorsen	Group leader/ Professor On sabbatical 22/23	OUS/Uio	b.e.halvorsen@medisin.uio.no
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Organization:

From August 2022 the research group leader Bente Halvorsen has been on sabbatical in Prof. Peter Libbys lab at Brigham and Womens Hospital. Harvard School of Medicine, Boston., MA, USA. The acting group leader has in this period been Dr. Tuva B. Dahl. The group has in 2022 revised the group organization and split the group into three research Teams headed by Tuva B. Dahl, Ida Gregersen and Xiang Yi Kong, receptively. These Teams have biweekly meetings, while the whole research group meets monthly.

Achievements

Two doctoral candidates from the group defended their thesis in 2022:

- Camilla Huse, MSc, title: "Regulation of immune cells in atherosclerosis and its clinical implications - The role of A-to-I editing and interleukin 6 receptor inhibition"
- Tom Rune Karlsen, MD, title: "Missing NEIL3: a kick in the gut and a punch to the heart"

Professor Bente Halvorsen received the Nikkila Lecture award by the Scandinavian Society of Atherosclerosis Research.

PhD Xiang Yi Kong received the best pitch award in the KiT Masterclass course.

Aktivitet i 2022 / Activity in 2022

Forskningsaktivitet/ Research activity:

To increase our knowledge of the underlying pathology of cardiovascular disease and related metabolic disorders such as diabetes, obesity and fatty liver disease the group runs a large span of interconnected translational projects to study the immunological and molecular mechanisms in obesity, metabolic disorders, cardiovascular disease and Covid-19.

We study the following processes in these conditions to improve our understanding of the underlying ethiology and to identify new biomarkers and treatment targets:

- Regulation and role of innate and adaptive immune response
- DNA repair mechanisms and genome stability
- Pain sensitivity and vascular inflammation
- Fish oil supplements and cardiometabolism

In 2022 we have studied:

Cardiovascular and metabolic disease:

DNA repair enzymes:

In 2022 the group has finalized a long project to study the role of the DNA repair enzyme Neil3 in atherosclerosis. NEIL3-deficient mice develop increased atherosclerosis compared to control mice, and we have further found that NEIL3 is important for hematopoiesis and telomere maintenance in mice. We have also studied the role of the DNA repair enzyme, SMUG1 in fatty liver disease and found that SMUG1 modulates fat metabolism favoring net lipogenesis resulting in development of a fatty liver phenotype in mice.

T cells in obesity and metabolic disease:

One of the group's largest projects aims to decipher the role of T cells in development of obesity and metabolic disease. We study a transgenic mouse model with altered T cell activation, which is a unique model to explore this association. In 2022 we have performed extensive immune characterization of our model, including single cell RNA sequencing and CyTOF analysis, as well as adaptive T cell transfer experiments and bone marrow transplantation experiment to determine the role of immune cells these conditions. The first paper has in 2022 been assigned a revision in EBioMedicine.

Clinical material and add-on studies to clinical intervention trials:

In addition to a wide spectrum of animal models to study cardiometabolic disease, we study molecular mechanisms in patient material, as a bridge between the lab and the clinic. In 2022 we have published several papers describing altered immune status in patients with cardiovascular disease. Particularly, in blood from patients with acute myocardial infarction we have found increased potential of circulating factors to active macrophages ex vivo. Further, we have characterized the immune cell profile of STEMI patients receiving anti IL-6 treatment (from the ASSAIL trial) to identify molecular mechanisms for the beneficial effects of tocilizumab in this group.

Covid-19 and covid-19 sequalae

In several publications, we have in 2022 described different features of altered immune regulation in patients with Covid-19. We have studied DNA repair mechanisms in circulating lymphocytes and shown that markers of cellular senescence are associated with reduced lung function 3 months after infection. Further, we have measured and found several inflammatory mediators to be associated with mortality and disease severity (CCL19, CCL20), and cardiac involvement (CXCL16) in hospitalized patients with Covid-19. Further we have studied how the treatment of hospitalized patients with the anti-viral drugs Remdesivir and Hydroxychloroquine, affects the immune response and metabolism.

Other projects – cooperations

Experience and expertise possessed by our group members lead to fruitful collaborations also in 2022. To mention a few, we planned and performed a pre-clinical study in mice in collaboration with NTNU, where a synthetic peptide was used as a potential new treatment after myocardial infarction. In a different collaboration with Nofima and Division of Clinical Nutrition we are now finalizing a pre-clinical study where we found that certain dietary lipids can dampen the development of atherosclerosis in mice. Of clinical collaborations, we are now studying the role of immune cells and inflammation in brain abscesses.

EU-project – Painfact

We are actively participating in an EU-funded project, PainFACT, investigating the link between pain sensation and immune response. The sensation of pain is an evolutionary adaptation for organism to identify danger. It is a hallmark for injury, inflammation, and pathogen invasion, and is mediated through nociceptor sensory neurons. A cross-talk between nociceptors and the immune system is well known, especially the capability of immune modulators to sensitize nociceptors, thus increasing an individual's sensation of pain. The PainFACT consortium integrates pre-clinical and clinical data to investigate the correlation between pain sensitivity/threshold and risk of cardiovascular events. In 2022, we have further processed biological material from a large-scale pre-clinical study and made them suitable for downstream analysis to be conducted by the consortium.

Populærvitenskapelig aktivitet/ Popular science:

Members from our group, Xiang Yi Kong, Ida Gregersen and Maria Belland Olsen, have during 2022 published the podcast "Labprat" every other week, researcher and user representatives have been invited to present research from the group and the institute, as well as related topics, in a popular science format. The podcast is free and available on most platforms. In September group members attended the Research Festival ("Forskerfestival") arranged by UiO at The Norwegian Museum of Science and Technology where they promoted the podcast, as well as the research group and Institute to the public and school classes.

The group has also published popular science papers in Biologen and Aftenposten together with a user representative from LHL Covid.

Publications 2022

1. Use of High-Dose Androgens Is Associated with Reduced Brain-Derived Neurotrophic Factor in Male Weightlifters. Bjørnebekk, A., M. Scarth, S.P. Neupane, L.T. Westlye, I.R. Hullstein, P.M. Thorsby, and B. Halvorsen. *Neuroendocrinology*, 2023. 113(1): p. 36-47.
2. Corrigendum: Circulating T cell activation and exhaustion markers are associated with radiation pneumonitis and poor survival in non-small-cell lung cancer. Berg, J., A.R. Halvorsen,

M.B. Bengtson, M. Lindberg, B. Halvorsen, P. Aukrust, Å. Helland, and T. Ueland. *Front Immunol*, 2022. 13: p. 1051156.

3. Circulating T Cell Activation and Exhaustion Markers Are Associated With Radiation Pneumonitis and Poor Survival in Non-Small-Cell Lung Cancer. Berg, J., A.R. Halvorsen, M.B. Bengtson, M. Lindberg, B. Halvorsen, P. Aukrust, Å. Helland, and T. Ueland. *Front Immunol*, 2022. 13: p. 875152.
4. SMUG1 regulates fat homeostasis leading to a fatty liver phenotype in mice. Carracedo, S., L. Lirussi, L. Alsøe, F. Segers, C. Wang, Z. Bartosova, P. Bohov, N.B. Tekin, X.Y. Kong, Q.Y. Esbensen, L. Chen, A. Wennerström, P. Kroustallaki, D. Ceolotto, A. Tönjes, R.K. Berge, P. Bruheim, G. Wong, Y. Böttcher, B. Halvorsen, and H. Nilsen. *DNA Repair (Amst)*, 2022. 120: p. 103410.
5. Blood Milieu in Acute Myocardial Infarction Reprograms Human Macrophages for Trauma Repair. Fontaine, M.A.C., H. Jin, M. Gagliardi, M. Rousch, E. Wijnands, M. Stoll, X. Li, L. Schurgers, C. Reutelingsperger, C. Schalkwijk, N.M.S. van den Akker, D.G.M. Molin, L. Gullestad, J. Eritsland, P. Hoffman, M. Skjelland, G. Andersen, P. Aukrust, J. Karel, E. Smirnov, B. Halvorsen, L. Temmerman, and E.A.L. Biessen. *Adv Sci (Weinh)*, 2022: p. e2203053.
6. Omicron Variant Generates a Higher and More Sustained Viral Load in Nasopharynx and Saliva Than the Delta Variant of SARS-CoV-2. Granerud, B.K., T. Ueland, A. Lind, A. Søraas, B. Fevang, A.K. Steffensen, H. Al-Baldawi, F. Lund-Johansen, P. Aukrust, B. Halvorsen, T.B. Dahl, S. Dudman, F. Müller, and J.C. Holter. *Viruses*, 2022. 14(11).
7. CXCL16 associates with adverse outcome and cardiac involvement in hospitalized patients with Covid-19. Gregersen, I., T. Ueland, J.C. Holter, M.B. Olsen, A.E. Michelsen, S.L. Murphy, A.A. Tveita, K.N. Henriksen, H. Hoel, L.B. Nordberg, A.R. Holten, T. Edvardsen, K. Yang, L. Heggelund, M. Trøseid, F. Müller, A.B. Kildal, A.M. Dyrhol-Riise, A. Barratt-Due, T.B. Dahl, P. Aukrust, and B. Halvorsen. *J Infect*, 2022. 85(6): p. 702–769.
8. Pro-inflammatory cytokines in cystic glioblastoma: A quantitative study with a comparison with bacterial brain abscesses. With an MRI investigation of displacement and destruction of the brain tissue surrounding a glioblastoma. Hassel, B., P. Niehusmann, B. Halvorsen, and D. Dahlberg. *Front Oncol*, 2022. 12: p. 846674.
9. Interleukin-6 inhibition in ST-elevation myocardial infarction: Immune cell profile in the randomised ASSAIL-MI trial. Huse, C., A.K. Anstensrud, A.E. Michelsen, T. Ueland, K. Broch, S. Woxholt, K. Yang, K. Sharma, I.M. Tøllefsen, B. Bendz, B.H. Amundsen, J.K. Damås, E.S. Berg, E. Bjørkelund, A. Quiles-Jiménez, V. Bjerkeli, C. Bendz, O. Kleveland, K.H. Stensaeth, A. Opdahl, N.E. Kløw, G. Andersen, R. Wiseth, B. Halvorsen, L. Gullestad, I. Seljeflot, P. Aukrust, L. Osnes, and T.B. Dahl. *EBioMedicine*, 2022. 80: p. 104013.
10. NEIL3-deficient bone marrow displays decreased hematopoietic capacity and reduced telomere length. Karlsen, T.R., M.B. Olsen, X.Y. Kong, K. Yang, A. Quiles-Jiménez, P. Kroustallaki, S. Holm, G.T. Lines, P. Aukrust, T. Skarpengland, M. Bjørås, T.B. Dahl, H. Nilsen, I. Gregersen, and B. Halvorsen. *Biochem Biophys Rep*, 2022. 29: p. 101211.
11. Duodenal inflammation in common variable immunodeficiency has altered transcriptional response to viruses. Kaarbø, M., M. Yang, J.R. Hov, K. Holm, M.M.L. de Sousa, M.E. Macpherson, H.M. Reims, A.B. Kran, B. Halvorsen, T.H. Karlsen, P. Aukrust, K.E.A. Lundin, B. Fevang, M. Bjørås, and S.F. Jørgensen. *J Allergy Clin Immunol*, 2022.

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14. Markers of cellular senescence is associated with persistent pulmonary pathology after COVID-19 infection. Lekva, T., T. Ueland, B. Halvorsen, S.L. Murphy, A.M. Dyrhol-Riise, A. Tveita, A.K. Finbråten, A. Mathiessen, K.E. Müller, T.M. Aaløkken, O.H. Skjønsberg, T.V. Lerum, P. Aukrust, and T.B. Dahl. *Infect Dis (Lond)*, 2022. 54(12): p. 918-923.
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16. Targeting the Inflammasome in Cardiovascular Disease. Olsen, M.B., I. Gregersen, Ø. Sandanger, K. Yang, M. Sokolova, B.E. Halvorsen, L. Gullestad, K. Broch, P. Aukrust, and M.C. Louwe. *JACC Basic Transl Sci*, 2022. 7(1): p. 84-98.
17. DNA Repair Mechanisms are Activated in Circulating Lymphocytes of Hospitalized Covid-19 Patients. Olsen, M.B., C. Huse, M.M.L. de Sousa, S.L. Murphy, A. Sarno, T.S. Obermann, K. Yang, J.C. Holter, M.J. Jørgensen, E.E. Christensen, W. Wang, P. Ji, L. Heggelund, H. Hoel, A.M. Dyrhol-Riise, I. Gregersen, P. Aukrust, M. Bjørås, B. Halvorsen, and T.B. Dahl. *J Inflamm Res*, 2022. 15: p. 6629-6644.
18. Epitranscriptome in Ischemic Cardiovascular Disease: Potential Target for Therapies. Quiles-Jiménez, A., T.B. Dahl, M. Bjørås, I. Alseth, B. Halvorsen, and I. Gregersen. *Stroke*, 2022. 53(6): p. 2114-2122.
19. Markers of extracellular matrix remodeling and systemic inflammation in patients with heritable thoracic aortic diseases. Seim, B.E., M.F. Holt, A. Ratajska, A. Michelsen, M.M. Ringseth, B.E. Halvorsen, M. Skjelland, J.P. Kvitting, R. Lundblad, K. Krohg-Sørensen, L.T.N. Osnes, P. Aukrust, B. Paus, and T. Ueland. *Front Cardiovasc Med*, 2022. 9: p. 1073069.
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Ueland, A. Lind, B. Fevang, S.L. Murphy, C. Huse, A.B. Nygaard, A.K. Steffensen, H. Al-Baldawi, M. Holberg-Petersen, L.L. Andresen, C. Ågnes, T. Ranheim, Y. Schanke, M. Istre, J.A. Dahl, A. Chopra, S. Dudman, M. Kaarbø, J.T. Andersen, E.B. Vaage, T.T. Tran, J.T. Vaage, A.E. Michelsen, F. Müller, P. Aukrust, B. Halvorsen, T.B. Dahl, J.C. Holter, and F. Lund-Johansen. *Front Immunol*, 2022. 13: p. 964525.

23. Persistent T-cell exhaustion in relation to prolonged pulmonary pathology and death after severe COVID-19: Results from two Norwegian cohort studies. Trøseid, M., T.B. Dahl, J.C. Holter, A.B. Kildal, S.L. Murphy, K. Yang, A. Quiles-Jiménez, L. Heggelund, K.E. Müller, A. Tveita, A.E. Michelsen, S. Bøe, A.R. Holten, H. Hoel, A. Mathiesen, T.M. Aaløkken, B. Fevang, B.K. Granerud, K. Tonby, K.N. Henriksen, T.V. Lerum, F. Müller, O.H. Skjønsberg, A. Barratt-Due, A.M. Dyrhol-Riise, P. Aukrust, B. Halvorsen, and T. Ueland. *J Intern Med*, 2022. 292(5): p. 816-828.

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25. Anti-PF4/polyanion antibodies in COVID-19 patients are associated with disease severity and pulmonary pathology. Ueland, T., I. Hausberg, T.V. Mørberg, T.B. Dahl, T.V. Lerum, A. Michelsen, T. Ranheim, K. Nezvalova Henriksen, A.M. Dyrhol-Riise, P.A. Holme, T.M. Aaløkken, O.H. Skjønsberg, A. Barratt-Due, M.T. Ahlén, P. Aukrust, and B. Halvorsen. *Platelets*, 2022. 33(4): p. 640-644.

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Forskningsgruppe:

Inflammasjonsmarkører for hjertekar- og metabolske sykdommer

Research group:

Inflammatory Biomarkers in Cardiovascular and Metabolic Disease

Avdeling:

Institutt for indremedisinsk forskning

Gruppeleder:

Thor Ueland

Om gruppen (kort beskrivelse på norsk):

Vår forskning fokuserer på måling og bruk av betennelsesmarkører i ulike sykdomspopulasjoner preget av systemisk inflammasjon.

Våre fokusområder er kardiovaskulær sykdom og risiko, nevropsykiatriske lidelser, infeksjonssykdommer og metabolske endokrine sykdommer (hypofysesykdom).

Mange sykdomstilstander som er assosiert med lav grad av kronisk inflammasjon. Inflammasjonen kan føre til detekterbare endringer i inflammatoriske proteiner som kan måles i biologisk væske slik som serum og plasma, noe som gjør dem verdifulle biomarkører.

Måling av disse biomarkører kan derfor være nyttig for å oppdage sykdommer i tidlig fase og/eller tilby informasjon om mekanismer for sykdom. Disse kan også representerere behandlingsmål eller være nyttig i vurderingen av behandlingstiltak og forutsi utfall.

Hvilke markører vi måler i forskjellige prosjekter, er avhengig av populasjon og endepunkt og kan være hypotesedrevet tematiske markører eller være basert på mer untargeted omics teknologi i mindre discovery kohorter.

Gruppen består av forskere og stipendiater som fokuserer på inflamasjons markører målt i blod ved forskjellige sykdommer hvor inflamasjon kan være medvirkende i sykdomsprogresjon, samt utgjøre behandlings mål. Medlemmene har stort sett biokjemisk eller molekylær biologisk bakgrunn.

About the group (short description in English):

Many disease states are associated with low-grade chronic inflammation that may result in detectable changes in inflammatory proteins that can be measured in biological fluid such as serum and plasma, making them valuable biomarkers. Measurement of these biomarkers may be therefore be useful for detecting diseases before they present and/or offer information on the mechanisms of disease, they may represent treatment targets or be helpful in evaluating treatment responses and predicting outcomes.

Our research focuses on measurement and use of inflammatory markers in different populations characterized by low-grade systemic inflammation, but also in populations with markedly enhanced systemic inflammation. Main research populations are cardiovascular disease, infectious disease, neuropsychiatric disorders, and metabolic endocrine disease.

We have a close collaboration with the department of cardiology and analyzing inflammatory markers in blood and tissue in well characterized cross-sectional cohorts and clinical trials in patients with heart failure, acute coronary syndromes and aortic stenosis. In these studies we evaluate biomarkers, reflecting a wide range of inflammatory processes, as predictors of adverse outcome and treatment responses.

In addition, we have close local collaborations with the endocrine unit, the Psychosis Research Centre Thematically Organized Psychosis Research (TOP) group and Clinical immunology and infectious diseases, mainly evaluating markers that may promote or reflect cardiac involvement. We have strong collaborations with other clinical research, national and international.

Our approach to markers depends on population and outcome measures but can be targeted with more established thematic markers or untargeted omics in discovery cohorts.

Hovedmedlemmer / Main members:

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One each PhD student and post doc incoming			

Assosierede medlemmer / Associated members:

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Aktivitet i 2022/ Activity in 2022

Forskningsaktivitet/ Research activity:

48 articles on pubmed for 2022, 15 in journals > 10. Of the 48, the central members of the group had 13 first or last position on the articles, and 4 second authorships.

Forskningsgruppe: Eksperimentell leverforskning

Research group: Experimental hepatology

Avdeling: Norsk senter for PSC / Institutt for indremedisinsk forskning

Gruppeleder: Espen Melum

Avdeling: Norsk senter for PSC / Institutt for indremedisinsk forskning

Gruppeleder: Espen Melum

Om gruppen:

Hovedmålet med forskningen i gruppen er å forstå mekanismer som regulerer betennelse i gallegangene med fokus på immunologi. I tillegg driver vi basal forskning relatert til funksjonen til natural killer T-celler og mucosal associated invariant T (MAIT)-celler. I studiene våre er organoider og sekvenseringsbaserte teknikker stadig viktigere og vi arbeider med å utvikle en bile-duct-on-a-chip.

About the group:

The main aim of our research is to understand mechanisms regulating cholangitis with a clear focus on immunology. In addition to the cholangitis focused studies, we are also doing basic research related to the function natural killer T-cells and mucosal associated invariant T (MAIT)-cells. Organoids and sequencing-based techniques are of increasing importance in our studies and we are aiming to develop a bile-duct-on-a-chip.

Hovedmedlemmer / Main members:

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Aktivitet i 2022/ Activity in 2022

Forskningsaktivitet/ Research activity:

The experimental liver research group is focusing on experimental and translational studies related to primary sclerosing cholangitis (PSC). Our laboratory activities take place at the Research institute of Internal Medicine. In 2022 the group consisted of the group leader, two senior researchers, four postdocs, five PhD students, the lab manager, one researcher and two technicians. The overall main aim of our research is to understand mechanisms regulating cholangitis with a clear focus on immunology and the interaction of the immune system with the microbiome and what role the cholangiocytes play in propagation of the inflammatory process.

Our strong collaboration with the Hybrid-technology-hub on establishing a bile-bile-duct-on-a-chip was in 2022 strengthened by the recruitment of Henry W. Hoyle who joined the group in June. Henry has an ideal background for the project with a combination of molecular biology and physics. He defended his PhD thesis at the University of Durham before joining NoPSC. His main responsibility will be to improve the chip design and its integration with cholangiocyte organoids and immune cells. The organoid and bile-duct-on-a-chip projects were also strengthened in 2022 by Yuliia Boichuk who contacted us through the Science of Ukraine initiative where NoPSC offered to help Ukrainian scientists. Yuliia was one of the two Ukrainian colleagues that joined NoPSC. She has a solid background in molecular biology and long experience with advanced cell culture and was therefore an ideal fit for the ongoing work on organoids and chip-based technologies. At the end of the year her position was prolonged by a grant from "Fondsstiftelsen" at Oslo university hospital.

In an extensive follow-up study to our 2021 paper on CD100 in Science Translational Medicine we have in 2022 investigated the direct interaction of cells from CD100 mutated mice with cholangiocytes and discovered a clear Th17 profile. These data were presented at the International Liver Congress in London as an oral presentation and was well received. The large projects addressing the timing of introduction of the microbiome in the NOD.c3c4 mouse model was concluded in 2022 with detailed characterization of the immune phenotype using high-dimensional flowcytometry with 25-colors using the BD Symphony located at the flow-cytometry core facility.

In 2022, we published a report demonstrating the presence of antigens for mucosal associated invariant T (MAIT)-cells in the bile of patients with PSC and that these antigens were largely defined by the microbiome. Using organoids as a platform for detailed studies on the role of interaction of NKT cells with cholangiocytes we were able to further dissect the antigen production potential of cholangiocytes themselves. These observations will be followed up in relevant mouse models with genetically altered antigen presentation specifically in the bile ducts.

We have expanded our work on using 10x technology to examine the single cells and spatial transcriptomics in two different mouse models that we have used for many years in the group; NOD.c3c4 mice with spontaneous bile duct inflammation and induced bile duct inflammation following direct injection of oxazolone in the bile ducts. These two projects will be part of the PhD work of Markus Jördens and will accompany studies using the same methodologies in a large panel of PSC patients. In new a PhD project, which was awarded funding by The South-Eastern health authorities, we will also use sequencing-based technologies to potentially define antigens for PSC. In this project, we have recruited Lisa Bynjulfsen as a PhD student, and she will be supervised by senior scientist Brian Chung as the main supervisor.

Forskningsgruppe: Inflammasjonssykdommers genomikk og metagenomikk

Research group: Genomics and metagenomics in inflammatory diseases

Avdeling: Institutt for indremedisinsk forskning / Research institute of internal medicine (and Norwegian PSC Research Center, Department of Transplantation Medicine)

Gruppeleder: Johannes R. Hov, j.e.r.hov@medisin.uio.no

Om gruppen:

Forskningsgruppen studerer i hvilken grad tarmfloraen påvirker kroniske betennelsesssykdommer, med et særlig fokus på leversykdommen primær sklerosende cholangitt (PSC) og inflammatorisk tarmsykdom (IBD) som er assosiert med PSC. Vi studerer tarmfloraen særlig ved hjelp av genetiske (sekvensering) og biokjemiske (metabolittundersøkelser) metoder, og benytter tverrsnittsstudier, oppfølgingsstudier og behandlingsforsøk. Vi undersøker også betydningen av tarmfloraen eksperimentelt i dyremodeller. Hovedmålet er å lete etter sykdomsårsaker, men med et særlig fokus på å etablere klinisk tarmfloramedisin som et eget felt med vekt på biomarkører og behandling

About the group:

The research group is studying the influence of the gut microbiome on inflammatory diseases, with a particular emphasis on the liver disease primary sclerosing cholangitis (PSC) and on inflammatory bowel disease (IBD), which is associated with PSC. We use genetic and metabolomic methods, and cross-sectional, longitudinal and interventional designs. We also investigate the gut microbiota experimentally in animal models. The main aims are to identify causes of diseases and to establish microbiota medicine as a clinical field with an emphasis on biomarkers and therapy.

Hovedmedlemmer / Main members:

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Aktivitet i 2022/ Activity in 2022

Forskningsaktivitet/ Research activity:

The overall research agenda and strategies are still well-defined with a balance between the major focus on the liver disease primary sclerosing cholangitis (PSC) and associated conditions, and a more general focus on the strategic research area Personalized treatment in clinical microbiota medicine.

The first step of our translational research program is to characterize in detail microbiome in the disease by using metagenomic (sequencing-based) and metabolomic methodology. We study this in detail in PSC as well as recurrent PSC after liver transplantation, and the closely associated inflammatory bowel diseases. As part of the ERC Starting Grant project StopAutoimmunity, we published in 2022 (first author Mikal J Hole) our first study using recurrent PSC as disease model, by looking at overlapping features of the mucosal microbiota composition before and after liver transplantation. This study provides a strong rationale for further search for markers of microbial functions in PSC and rPSC. In ongoing work we therefore perform unbiased screening for alterations of microbial metabolites in blood. Similar strategies have been or are employed in other disease states where we are involved for the last decade, including inflammatory bowel diseases, immunodeficiencies and heart failure.

In the next steps, clinical relevance is established by investigations of altered microbial functions as biomarkers. We now follow up on several interesting findings, including new data on the importance of e.g. vitamin B6. In parallel, we now work extensively together with the Melum group to use experimental animal models in germ-free, gnotobiotic or conventional setting to investigate cause and effect of microbial alterations observed in PSC. This is crucial to establish a rationale for e.g. therapeutic trials. Clinical "proof-of-concept" trials are needed to establish feasibility and mechanistic evidence of a role of the gut microbiome and the protocol for our first clinical trial in PSC based on our own observations (vit B6 supplementation) is near-completed. Clinical trials targeting the gut are also important in our Strategic research area.

Notably, the group activities also try to answer other questions, including autoimmunity in PSC, molecular mechanisms of PSC and rPSC, including modern methods of spatial and tissue transcriptomics, molecular aspects of the GPR35, with clinical translation as an important goals. Finally, important milestones in 2022 include the successful PhD defense of Christopher Storm Ligaard and his thesis "Clinical interventions of the human gut microbiota". The 9th National Microbiota Conference was also successful hosted in November 2021.

Populærvitenskapelig aktivitet/ Popular science:

The group leader contributed to a podcast on the gut microbiota and your health: (<https://www.roche.no/historier/fremidtids-helse-podkast-sesong-2/>). He was also interviewed for an article at forskning.no: Do we have bacteria living in our blood (in Norwegian): <https://forskning.no/bakterier-blod/har-vi-bakterier-som-lever-i-blodet/2010762>

Forskningsgruppe: Klinisk mikrobiologi og mikrobiotamedisin

Research group: CliMic: Clinical microbiology and microbiota medicine

Avdeling: Reumatologi, hudsykdommer og infeksjonssykdommer (RHI)

Gruppeleder: Marius Trøseid

About the group:

Marius Trøseid is leading a research group on Clinical Microbiology and Microbiota Medicine (CliMic) at Department of Rheumatology, Dermatology and Infectious diseases at Oslo University Hospital, Rikshospitalet. In this environment, we have developed a sequencing-based microbiota profiling pipeline including bioinformatics methods and applied it in multiple conditions, including HIV and cardiovascular disease. We have also established a regional research network (ReMicS: Regional research network for clinical Microbiota Science) and are hosting a yearly national microbiota conference (www.microbiota.no). Our scientific focus is the role of the gut microbiota in chronic infectious and inflammatory diseases. The aim is to better understand the contribution of the gut microbiome in order to lay the foundation for clinical microbiota medicine, i.e. medical practice based on stratification or modulation of gut microbial composition or function. More recently, the scientific focus has also included COVID-19 research, as part of the managing team of the Nordic branch of the WHO solidarity trial (NOR solidarity), and as collaborator in the Horizon 2020 consortium EU-RESPONSE (European Research and Preparedness Network for Pandemics and Emerging Infectious Diseases).

Hovedmedlemmer / Main members:

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Activity in 2022:

ONGOING AND COMPLETED PROJECTS

- COMicS (Copenhagen-Oslo Co-morbidity and Microbiota Study in HIV infection). Planned as the largest prospective microbiome study in HIV-infected individuals. Several papers on 16s DNA microbiota data have been published. We are currently analyzing full metagenomic sequencing data in this cohort, which will spark new insight and papers from this unique cohort.
- Targeting the NLRP3 inflammasome in HIV infection. The aim is to explore whether inflammasome activation is enhanced during HIV infection, and if so, if inflammasome activation could explain increased cardiovascular risk in HIV-infected individuals. Several papers have been published from this ongoing project based on circulating inflammasome markers, whereas in vitro data are currently analyzed and will be published during 2023.
- In collaboration with Johannes Hov group we have established the regional research network ReMicS (Regional research network for clinical Microbiota Science), encompassing > 25 research groups. The last years have been challenging due to the COVID-19 pandemic, but we have managed to keep the network alive through regular video meetings and hybrid meeting, and the network is now back with physical meetings.

- Also in collaboration with Johannes Hov group, we have got funding for a Focused research area at Oslo University Hospital, where the main goal is to establish a therapeutic feces donor bank with relevance for ongoing microbiota research, including clinical treatment of *C Difficile* infection, ESBL eradication and biological cancer treatment by transferring microbiota from responders to non-responders.
- We have received funding through the Era-Net for managing a WP on multi-level integrated bioinformatics in the SCRATCH consortium (Microbiota-based SCreening of Anal Cancer in HIV-infected individuals), aiming to improve diagnostic screening of HIV-associated anal cancer, taking microbiota profiling one step closer to clinical practice. Microbiota analyses and bioinformatics have been finalized, and first manuscript submitted.
- We have also received NRC funding for the project “Targeting the gut heart axis”, and have hired a post doc bioinformatician who started in 2020. A common theme in this project and SCRATCH is to develop integrated multi-level bioinformatics on metagenomics, metabolomics and lipidomics analyses, that have been analyzed during 2022.
- Trøseid has recently taken the role as chief investigator for the novel pan-European adaptive platform trial for COVID and emerging pandemics, EU SolidAct, set up to run phase II and phase III trials in around 15 European countries, with OUH as sponsor. Recently, the first phase III trial evaluating baricitinib for severe Covid-19 was published, whereas the first phase II trial on bemcentinib was started in collaboration with BerGenBio during summer 2022.