Oslo universitetssykehus

UiO : Institutt for klinisk medisin
Det medisinske fakultet

Foto: Øystein Horgmo, UiO

ÅRSRAPPORTER FRA FORSKNINGSGRUPPENE 2021

Klinikk for kirurgi, inflammasjonsmedisin og transplantasjon (KIT)

Innholdsfortegnelse

Forord

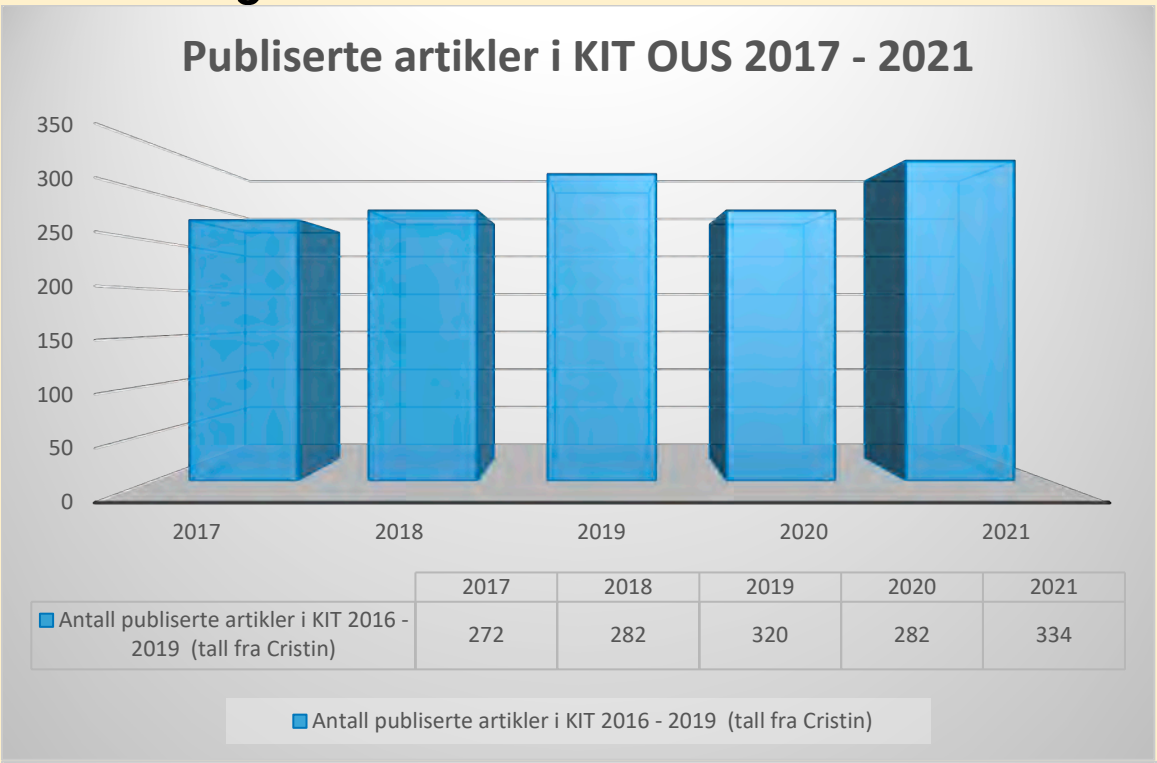
Både starten og slutten av forskningsåret 2021 var fortsatt i stor grad preget av koronavirus og nedstengning, men med en rolig periode som forsmak på normalisering midt i. Pustepausen med åpningen over sommeren og tidlig høst gav mulighet for gjennomføring av flere av tiltakene i handlingsplanen for forskning som hadde vært på vent, kanskje viktigst av alt KIT Masterclass og endelig en fysisk forskningsgruppeledersamling igjen. Til tross for mange nedstengninger har forskningsåret 2021 vært godt, med stabilt høy aktivitet i mange prosjekter. Noen forsinkelser har det blitt, men ikke mer enn at det har latt seg løse gjennom de støtteordningene som har vært. Og som antydet ved de mange tildelinger klinikken fikk i Helse-Sør Østs utlysning om forskningsmidler mangler det ikke på gode planer og prosjekter fremover, som tegn på en sunn og aktiv forskningsorganisasjon. Ledelsen er imponert over miljøene og vil takke alle dem som har stått på i den rare tiden.

Klinikkens to hovedsatsninger i 2021 var nettopp KIT Masterclass i tillegg til en ny runde med fokus på biobank og registerløsninger. KIT Masterclass ble utviklet av et faculty bestående av Sheraz Yaqub, Hanne Scholz og Espen Melum, og var et tilbud til det skiktet av våre yngre forskere som er i ferd med å utvikle egne, uavhengige karriereveier innen forskning, typisk sent i en post doc periode. Programmet løp over flere samlinger utover året, med «hjemmelekse» for deltakerne i intervallene. En av samlingene var knyttet til besøk ved Karolinska i Stockholm, og sentralt i programmet var også personlig mentor med egne møter med fokus på karriereutvikling for alle deltakerne, på to ulike tidspunkt. Programmet fikk svært gode tilbakemeldinger, og gjennomføringsansvarlig Steinar Heldal har måttet fortelle om tiltaket i tallrike fora i andre klinikker og for sentral ledelse.

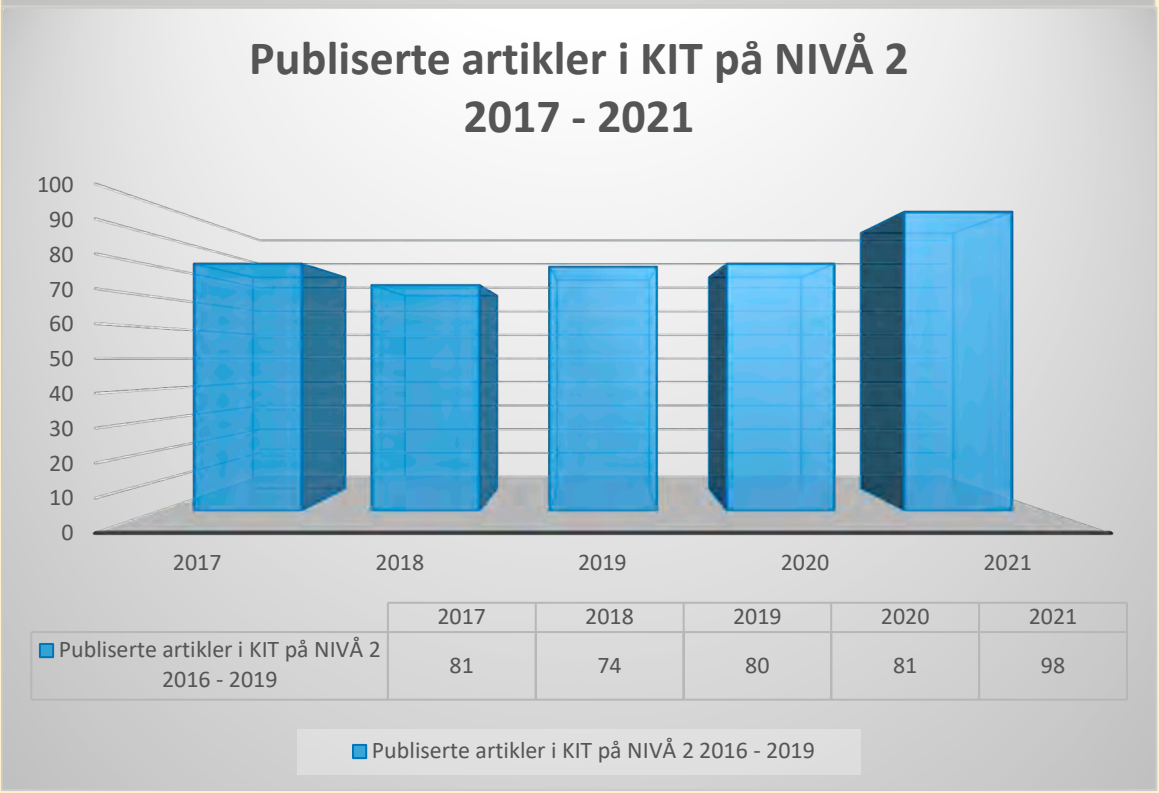
Pga. den kirurgiske virksomheten er KIT er en stor biobankaktør i OUS. Dette kommer egen forskning til gode, men er også essensiell infrastruktur for forskning i mange av andre sykehusets klinikker, særlig Kreftklinikken. Systemene knyttet til biobanking er stadig under utvikling og gjennomgående underfinansiert, og mye av klinikkens stimuleringsmidler for 2022 ble brukt for oppgraderinger både for biobanker og tilhørende registere. På sikt er det et mål for klinikken å samle flere av biobankene i bredere, tematiske satsninger, etter mønster av Kreftbiobanken (der også flere av klinikkens biobanker inngår). Eksempler er transplantasjonsbiobanken og biobanker knyttet til lever- og galleveissykdommer, der det er betydelige muligheter for synergi og samarbeid. Klinikken har lagt seg på en policy der samlingene drives av berørte miljøer selv, noe som nok gjør at prosessen med samling tar mer tid enn sentralt styrte initiativer, men opprettholder eierskapsfølelse til aktiviteten.

Forskningsgruppesamlingen hadde som tema både koronaforskning i KIT og også en mer fremtidsrettet komponent knyttet til industrisamarbeid og interessekonflikter. Flere miljøer i KIT har vært sentralt engasjert i forskning relatert til pandemien, og forskningen får også et spor videre i form av det EU finansierte SOLIDACT plattformen for klinisk utprøving som er forankret i klinikken med Marius Trøseid som prosjektleder. Innovasjonen i KIT spenner bredt, og inkluderer både legemiddelutprøving og utvikling knyttet til kirurgiske metoder. Med klinikkens protokollutvalg har man fått et system for håndtering av kliniske studier, og fra 2021 har man også fast tilgjengelig arealer for kliniske studier – som gledelig for det aller meste er helt fullbooket. I veien videre med innovasjonsarbeidet ble det i diskusjonene i forskningsgruppeledersamlingen viktig å få på plass intern veiledning i regelverk som også tar høyde for en «positiv» og stimulerende dimensjon rundt innovasjon og industrisamarbeid, og problemstillingen tas videre i handlingsplan for 2022 nettopp med denne orientering. Vi ønsker at forskerne våre skal ha et pro-aktivt forhold til innovasjon.

Forskningsaktivitet i KIT – 2021

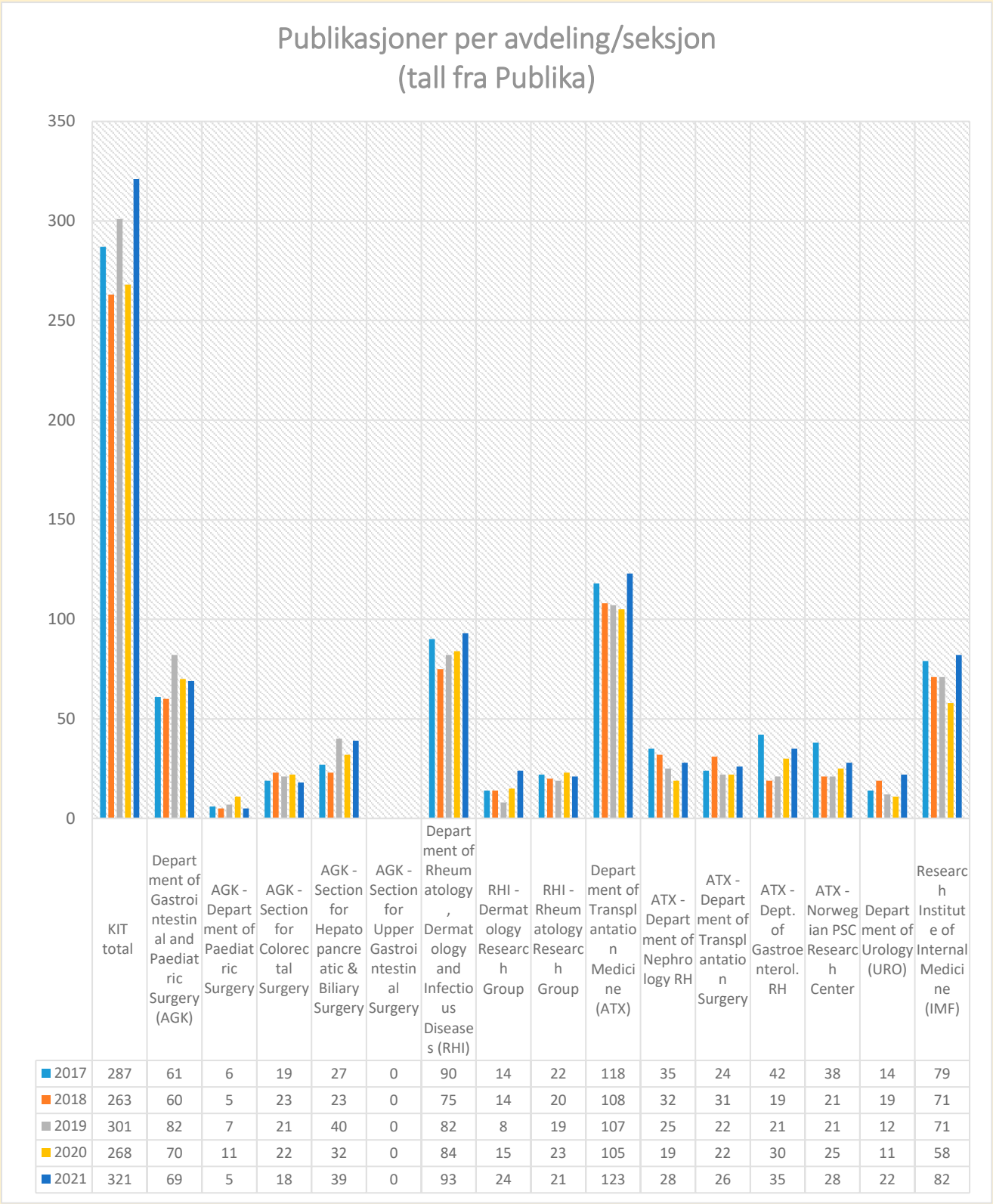


	2017	2018	2019	2020	2021
Antall publiserte artikler i KIT 2016 - 2019 (tall fra Cristin)	272	282	320	282	334



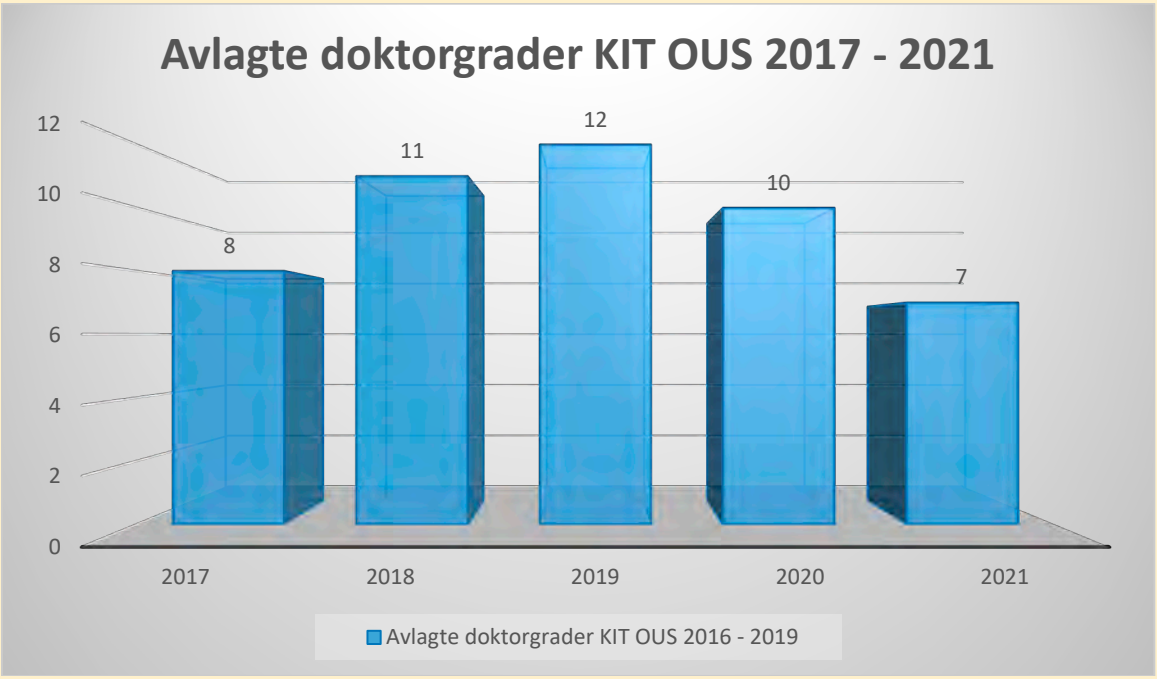
	2017	2018	2019	2020	2021
Publiserte artikler i KIT på NIVÅ 2 2016 - 2019	81	74	80	81	98

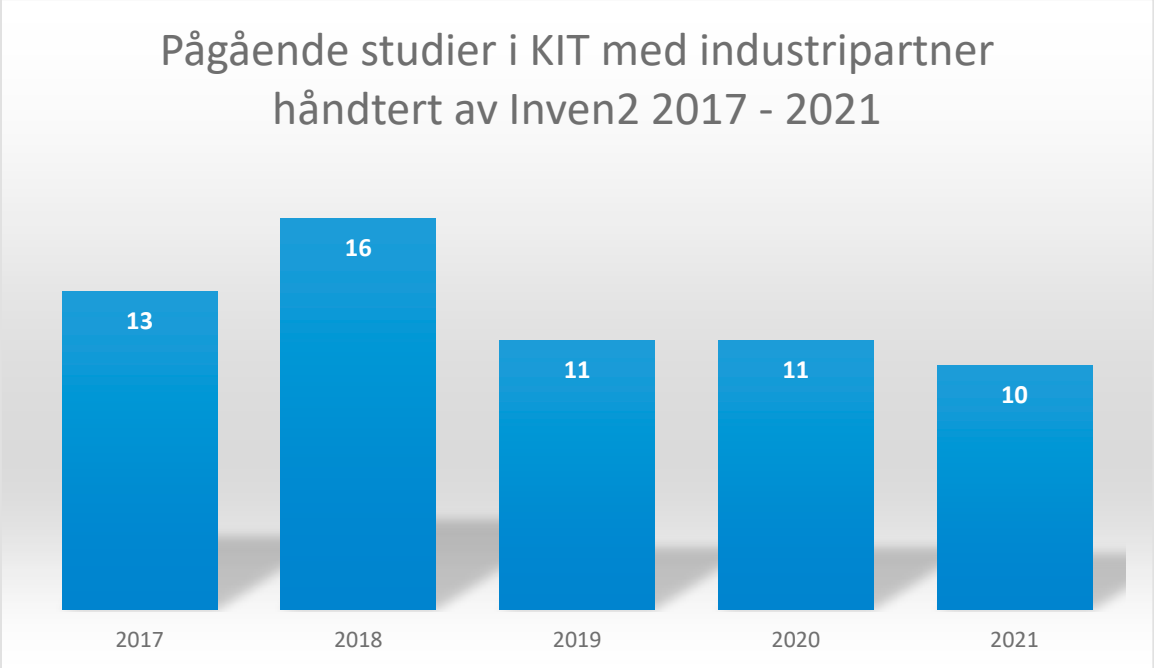
Forskningsaktivitet i KIT – 2021



	KIT total	Department of Gastrointestinal and Paediatric Surgery (AGK)	AGK - Department of Paediatric Surgery	AGK - Section for Colorectal Surgery	AGK - Section for Hepatopancreatic & Biliary Surgery	AGK - Section for Upper Gastrointestinal Surgery	Department of Rheumatology, Dermatology and Infectious Diseases (RHI)	RHI - Dermatology Research Group	RHI - Rheumatology Research Group	Department of Transplantation Medicine (ATX)	ATX - Department of Nephrology RH	ATX - Department of Transplantation Surgery	ATX - Dept. of Gastroenterol. RH	ATX - Norwegian PSC Research Center	Department of Urology (URO)	Research Institute of Internal Medicine (IMF)
2017	287	61	6	19	27	0	90	14	22	118	35	24	42	38	14	79
2018	263	60	5	23	23	0	75	14	20	108	32	31	19	21	19	71
2019	301	82	7	21	40	0	82	8	19	107	25	22	21	21	12	71
2020	268	70	11	22	32	0	84	15	23	105	19	22	30	25	11	58
2021	321	69	5	18	39	0	93	24	21	123	28	26	35	28	22	82

Forskningsaktivitet i KIT – 2021





Forskningsgrupper i KIT – 2021

Gruppenavn	Gruppeleder	Avdeling
Avdeling for transplantasjonsmedisin		
Eksperimentell Transplantasjon for Kreft	Svein Dueland	ATX
Klinisk transplantasjonskirurgi og eksperimentell immunologi	Einar Martin Aandahl	ATX
Klinisk PSC forskningsgruppe (NoPSC)	Trine Folseras	ATX
Nyretransplantasjonsmedisin	Anders Hartmann	ATX
Eksperimentell Celletransplantasjon	Hanne Scholz	ATX
Klinisk Effektforskning	Mette Kalager	ATX
Forskningsgruppe for livskvalitet og helseøkonomi	Marit Helen Andersen	ATX
Nevroendokrine svulster	Espen Thiis-Evensen	ATX
Avdeling for revmatologi, hud og infeksjonssykdommer		
Hud	Jon Anders Halvorsen	RHI
Klinisk mikrobiologi og mikrobiota medisin	Marius Trøseid	RHI
Olafiaklinikken	Anne Olaug Olsen	RHI
Revmatologi	Øyvind Molberg	RHI
Institutt for indremedisinsk forskning		
Atherosklerose og relaterte metabolske sykdommer	Bente Halvorsen	IMF
Inflammasjon og hjertesvikt	Arne Yndestad	IMF
Inflammasjonsmarkører for hjertekar- og metabolske sykdommer	Thor Ueland	IMF
Eksperimentell leverforskning (NoPSC)	Espen Melum	IMF
Inflammasjonssykdommers genomikk og metagenomikk (NoPSC)	Johannes Hov	IMF
Immunopathogenetic mechanisms in immunodeficiency and infectious disorders	Børre Fevang	IMF
Avdeling for urologi		
Infeksjon og inflammasjon i urologi	Truls E. B. Johansen	URO
Prostatakreft	Viktor Berge	URO
Avdeling for gastro- og barnekirurgi		
Barnekirurgi	Kristin Bjørnland	AGK
Kolorektal kirurgi	Arild Nesbakken	AGK
Pancreaskreft	Knut Jørgen Labori	AGK
Svulster i lever og galleveier	Sheraz Yaqub	AGK
Øsafagus- og ventrikkelsykdommer	Egil Johnson	AGK

Forskningsutvalget i KIT - 2021

Forskningsutvalget i Klinikk for kirurgi, inflammasjonsmedisin og transplantasjon (KIT-FU) bestod av følgende medlemmer i 2019:

- Anders Åsberg (Avdeling for transplantasjonsmedisin)
- Kristin Bjørnland (Avdeling for gastro- og barnekirurgi)
- Gro Wiedswang (Avdeling for gastro- og barnekirurgi)
- Sheraz Yakub (Avdeling for gastro- og barnekirurgi)
- Ida Gregersen (Institutt for indremedisinsk forskning)
- Einar Marin Aandal (Avdeling for transplantasjonsmedisin)
- Viktor Berge (Avdeling for urologi)
- Hanne Scholz (Avdeling for transplantasjonsmedisin)
- Michael Bretthauer (leder av protokollutvalget, Helsam, Avdeling for helseledelse og helseøkonomi)
- Magnus Løberg (Helsam, Avdeling for helseledelse og helseøkonomi)
- Astrid Klopstad Wahl (Helsam, Avdeling for tverrfaglig helsevitenskap)
- Steinar Heldal (forskningsadministrativ leder KIT OUS)
- Kine Yttersian (administrativ koordinator KIT UiO)
- Morten Tandberg Eriksen (klinikkleder KIT)
- Tom Hemming Karlsen (forskningsleder, leder for KIT FU)

Handlingsplan for forskning i KIT for 2021

PROSJEKT / TILTAK	ANSVAR	Ref. til spesifikke hovedmål i OUS forsk.strategi
NYE		
Biobank og register		
• Det lyses ut stimuleringsmidler til infrastrukturtiltak for biobank og registeraktivitet.	KIT-FU	2.b; 2.c
• Arbeidsgruppe ser på status for biobanking i KIT. • Gruppen gjennomgår planer for felles lagringsfasiliteter OUS og biobankenhet i KLM sett opp mot KITs nåværende biobankstruktur. • Arbeidsgruppens skal gi innspill til KITs representant i medvirkningsfasen i forprosjektet for Nye OUS knyttet til forskning/biobanking og som strategi for KIT på dette feltet frem mot nye sykehusbygg.	Arbeidsgruppe (foreløpig): Steinar Heldal	2.b; 2.c
Samarbeidsarena om stordata, biostatistikk og bioinformatikk		
• Arbeidsgruppe planlegger og gjennomfører samarbeidsarena/møteplass for (kliniske) forskere og de med bioinformatikk- eller biostatistisk kompetanse i KIT om hvordan vi bedre kan utnytte stordata og samarbeide rundt dette. • Arbeidsgruppen bes også å vurdere om det er hensiktsmessig å utarbeide en kort liste med tips til KITs forskere/forskningsgrupper om hvordan de kan nyttiggjøre seg av stordata, og i så fall utarbeide denne.	Arbeidsgruppe (foreløpig): Magnus Løberg, leder Sheraz Yaqub	3; 3.c; 2.a
Formidling og nyttiggjøring av forskningen vår		
• Arbeidsgruppe bes om å foreslå konkrete, lavterskel tiltak man kan gjøre i KIT (både klinikknivå og avdelings-/seksjonsnivå, i samarbeid med forskningsgruppene) for å: a) styrke formidling, forankring og nyttiggjøring av forskningsresultater internt i egen avdeling/seksjon/i KIT b) styrke den eksterne forskningsformidlingen fra KIT (utover tradisjonell vitenskapelig publisering)	Arbeidsgruppe (foreløpig): Hanne Scholz, leder Kristin Bjørnland Ida Gregersen	Kontinuerlig mål 6
PÅGÅENDE		
Karriereutvikling		
• Masterclass for future research leaders in KIT (Faculty bestående av: Sheraz Yakub, Hanne Scholz, Espen Melum og Steinar Heldal)	KIT Masterclass Faculty	4; 4.a
Kliniske studier		
• Etablere Protokollutvalget som permanent organisasjonsstruktur, og styrke rollen som lavterskel rådgivningstilbud • Drifte og videreutvikle Senter for kliniske studier i KIT og følge opp utvalgets rapport.	Protokollutvalget v/ Michael Bretthauer og Steinar Heldal	1.a; 1.
Helsefaglig forskning		
• Gjennomføre "Health Literacy Day" i klinikken i 2021	Astrid K Wahl	1.c; 2.c
Strategi for translasjonsforskning på nye RH		
• Arbeide for en organisering for, og samlokalisering i A-bygget av, de klinikknære translansjonsforskningsinstituttene.	IMF + forskningsleder/klinikkleder	2; 2.a; 2.c; 2.d; 5; 5.a; 5.b
LØPENDE AKTIVITETER og SAMARBEIDSMØTER		
Løpende innspill angående forskning og Nye OUS	KIT-FU	
Søknadspoliklinikker 2021	Forskningsledelsen	
Samarbeidsseminar KIT og Patologi	Forskningsledelsen	
Samarbeidsseminar KIT og OsloMet (Fakultet for helsefag)	A. K. Wahl / M. H. Andersen	
Nettverk for biobankingeniører og studie-/forskningssykepleiere i KIT	Forskningsledelsen	

Department of Gastrointestinal and Children Surgery (AGK)

- Barnekirurgi/ Pediatric Surgery
- Kolorektal kirurgi/ Colorectal Surgery
- Pancreaskreft/ Pancreatic Cancer
- Svulster 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. 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. I et translasjonsprosjekt studerer vi immunologiske faktorers betydning for utvikling av tarmbetennelse hos Hirschsprung pasienter.

About the group: The main focus is to study somatic and psychosocial long-term outcome in patients operated for congenital gastrointestinal and urogenital conditions and how surgical techniques and follow-up protocols influence these parameters. Patient reported outcomes are important outcome measures. All projects have a strong focus on interdisciplinary collaboration, and the group collaborates both nationally and internationally. Translational research includes studies on the immune system in the bowel of neonates and small children with Hirschsprung 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
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
Hoel, Anders	PhD student	OUS	a.t.hoel@ous-hf.no
Johansen, Hanna	Research Fellow	Helse sørøst	Hajoh3@ous-hf.no
Karlsen, Remi	Med student research fellow	UiO	r.a.karlsen@studmed.uio.no
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
Møinichen, Inger	Physiotherapist	OUS	umoinich@ous-hf.no
Røkkum, Henrik	Registrar	OUS	B26425@ous-hf.no
Skari, Hans	Consultant, PhD	OUS	Hans.skari@ous-hf.no
Stensrud, Kjetil	Consultant, PhD	OUS	kstensru@ous-hf.no
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
Helene Gjone	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 2021:

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 om langtidsresultater etter operasjon for anorektale misdannelser; 2: Bekkensenteret på Akershus universitetssykehus om nytte av oppfølging for voksne med anorektal misdannelser; 3: Nasjonal studie om nekrotiserende enterokolitt som ledes fra Helse Nord.

Disputas: Morten Kvello disputerte 17.12.21 med avhandlingen «Surgical and patient reported outcomes after novel techniques for gastrostomy insertion and fundoplication in children".

Pågående prosjekter. Det er tre pågående doktorgradsprosjekter: Audun Mikkelsen: Langtidsresultater etter operasjon for øsofagusatresi; Live Lundar: Uretraklaffer hos barn, Anders Telle Hoel: Anorektale misdannelser – overgang fra ungdom til voksne. Gruppen har to forskerlinjestudenter; Remi Andre Karslen (Resultater etter operasjon for Hirschpsrung sykdom) og Trine Arntzen (Prenatal diagnostikk ved øsofagusatresi). Begge hadde fulltidsår i 2019 og fortsetter på deltid. For øvrig er flere av gruppens medlemmer involvert i diverse kvalitetsstudier som omhandler de pasientkategorier barnekirurgisk avdeling behandler. Det er også medisinstudenter knyttet til noen av prosjektene,

Gruppens medlemmer var forfattere på 10 publikasjoner i 2021; i seks publikasjoner var førsteforfatter og/eller sisteforfatter fra vår forskningsgruppe.

Populærvitenskapelig aktivitet: Medlemmer i gruppen har holdt innlegg på pasientforeningsmøter og vært med på å starte en pasientforening (Hirschsprung).

Forskningsgruppe: Kolorektal kirurgi

Research group: Colorectal surgery

Avdeling: Avdeling for gastro- og barnekirurgi

Gruppeleder: Ole Helmer Sjo (fra primo mai 2021)

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 deltakelse 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 overordnete 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	Professor II	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	Ass 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
Ingeborg F. Backe	Study nurse / Master nursing	OUS	ingbac@ous-hf.no
Gro Wiedswang	Post doc / Senior consultant	OUS	uxgrie@ous.hf.no

Assosierte medlemmer / Associated members:

NAME	POSITION/TITEL/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Egil Johnson	Professor II / senior consultant	OUS and UiO	
Maria Magdalena Kowalewska-Hibyeli	Study nurse	OUS	
Tom Mala	MD PhD / senior consultant	OUS	
Ragnhild A Lothe	Professor	OUS and UiO	
Guro Elisabeth Lind	Ass Professor	OUS and UiO	
Anita Sveen	Ass 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	Ass Prof / senior consultant	OUS and UiO	

Aktivitet i 2021

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 2021 har samarbeidet med DNR blitt utvidet og videreutviklet.

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 2021 har forskningsgruppen også fokusert på å planlegge og initiere kliniske studier, både lokalt ved enheten samt gjennom deltakelse i multisenter studier. Enheten har deltatt i SCANDIV II (Scandinavisk multisenter studie på komplisert divertikulitt), TENTACLE (ESCP ledet multinasjonal studie på anastomoselekkasje etter cancer rektum operasjoner) og NORWAIT studien på rektum cancer etter komplett respons på neoadjuvant strålebehandling. Vi har deltatt i planlegging av den kommende 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 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.

Enheten har et stort materiale av TEM (Transanal Endoskopisk Mikrokirurgi) opererte pasienter gjennom mer enn to tiår, og har i 2021 arbeidet med analysering, i første omgang på pasienter behandlet for rektum cancer i tidlig stadium. Første publikasjon forventes i 2022, og kan evt. 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 har planlagt et PhD studie med dr. Fabian Ortega som kandidat, oppstart i løpet av 2022. Prosjektet har dessuten utviklet et kurs med simulatortrening på lik (“cadaver-kurs”), som er tiltenkt å bli nasjonalt obligatorisk «Kurs i kolorektal cancer med øvelser på modell» i ny spesialist utdannelsen i gastrokirurgi (ny struktur fra 2019). Oppstart på Ullevål er planlagt høsten 2022, med tilhørende muligheter for klinisk forskning.

Activity in 2021

Translation research on colorectal cancer is still a major focus area in multidisciplinary teams with dedicated researchers from clinical medicine and biology who cover fields in colorectal surgery. hepatobiliary surgery, oncology, radiology, pathology and molecular biology. Throughout 2021, the collaboration with DNR has been expanded and further developed.

Specific objectives have been to develop new diagnostic, prognostic, predictive and monitoring biomarkers for coloractal cancer. Continuous collection of fresh tumor tissue and normal high quality tissue, collection of formalin fixed tissue as well as blood / serum / bone marrow samples to our comprehensive biobank combined with very comprehensive continuously updated clinical database for colorectal primary cancer, liver metastases in unselected population-based patient register ensures optimal basis for both high clinical and translation research.

In 2021, the research group has also focused on planning and initiating clinical studies, both locally at the unit and through participation in multicenter studies. The unit has participated in SCANDIV II (Scandinavian multicenter study on complicated diverticulitis), TENTACLE (ESCP led multinational study on anastomotic leakage after cancer rectal surgery) and the NORWAIT study on rectal cancer after complete response to neoadjuvant radiation therapy. We have participated in the planning of the upcoming national Norwegian Stoma Trial which studies temporary and permanent stoma after surgery for rectal cancer. The unit participates in the national quality register NorGast with 100% inclusion of our colorectal cancer patients.

The research group has initiated several internal quality registers / studies on acute appendicitis, neoplasms in appendix after appendectomy, surgical results after construction of stoma, especially in connection with rectal cancer operations, use of ICG for testing of circulation during construction of intestinal anastomoses, results after surgery for IBD, rectal prolapse and endometriosis.

The device has a large material of TEM (Transanal Endoscopic Microsurgery) operated patients running over more than two decades. The unit has worked during 2021 with analysis of subgroups of patients, initially on those treated for rectal cancer in the early stages. The first publication is expected in 2022, and the works may be expanded to a PhD program.

LapcoNor is an ongoing national educational program in laparoscopic surgery for colorectal cancer that was established in 2015 and is led by Ole Sjo. The project has planned a PhD study with Dr. Fabian Ortega as a candidate, starting during 2022. The project has also developed a course with simulator training on corpses ("cadaver course"), which is intended to become a national mandatory "Course in colorectal cancer with exercises on model » in new specialist education in gastrointestinal surgery (new structure from 2019). Start-up course at Ullevål is planned for autumn of 2022, with associated possibilities for clinical research.

Forskningsaktivitet - publikasjoner 2021/publications 2021:

1. Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial.
   Bahadoer RR, Dijkstra EA, van Etten B, Marijnen CAM, Putter H, Kranenbarg EM, Roodvoets AGH, Nagtegaal ID, Beets-Tan RGH, Blomqvist LK, Fokstuen T, Ten Tije AJ, Capdevila J, Hendriks MP, Edhemovic I, Cervantes A, Nilsson PJ, Glimelius B, van de Velde CJH, Hospers GAP; RAPIDO collaborative investigators.
   Lancet Oncol. 2021 Jan;22(1):29-42. doi: 10.1016/S1470-2045(20)30555-6. Epub 2020 Dec 7.
   PMID: 33301740 Clinical Trial.
2. De novo transcriptomic subtyping of colorectal cancer liver metastases in the context of tumor heterogeneity.
   Moosavi SH, Eide PW, Eilertsen IA, Brunsell TH, Berg KCG, Røsok BI, Brudvik KW, Bjørnbeth BA, Guren MG, Nesbakken A, Lothe RA, Sveen A.
   Genome Med. 2021 Sep 1;13(1):143. doi: 10.1186/s13073-021-00956-1.
   PMID: 34470666 Free PMC article.
3. Metastatic heterogeneity of the consensus molecular subtypes of colorectal cancer.
   Eide PW, Moosavi SH, Eilertsen IA, Brunsell TH, Langerud J, Berg KCG, Røsok BI, Bjørnbeth BA, Nesbakken A, Lothe RA, Sveen A.
   NPJ Genom Med. 2021 Jul 14;6(1):59. doi: 10.1038/s41525-021-00223-7.
   PMID: 34262039 Free PMC article.
4. The expressed mutational landscape of microsatellite stable colorectal cancers.
   Sveen A, Johannessen B, Eilertsen IA, Røsok BI, Gulla M, Eide PW, Bruun J, Kryeziu K, Meza-Zepeda LA, Myklebost O, Bjørnbeth BA, Skotheim RI, Nesbakken A, Lothe RA.
   Genome Med. 2021 Sep 1;13(1):142. doi: 10.1186/s13073-021-00955-2.
   PMID: 34470667 Free PMC article.
5. Treatment outcomes and prognostic factors after chemoradiotherapy for anal cancer.
   Slørdahl KS, Klotz D, Olsen JÅ, Skovlund E, Undseth C, Abildgaard HL, Brændengen M, Nesbakken A, Larsen SG, Hanekamp BA, Holmboe L, Tvedt R, Sveen A, Lothe RA, Malinen E, Kaasa S, Guren MG.
   Acta Oncol. 2021 Jul;60(7):921-930. doi: 10.1080/0284186X.2021.1918763. Epub 2021 May 8.
   PMID: 33966592
6. Increased sensitivity to SMAC mimetic LCL161 identified by longitudinal ex vivo pharmacogenomics of recurrent, KRAS mutated rectal cancer liver metastases.
   Kryeziu K, Moosavi SH, Bergsland CH, Guren MG, Eide PW, Totland MZ, Lassen K, Abildgaard A, Nesbakken A, Sveen A, Lothe RA.
   J Transl Med. 2021 Sep 8;19(1):384. doi: 10.1186/s12967-021-03062-3.
   PMID: 34496878 Free PMC article.
7. Genomic and prognostic heterogeneity among RAS/BRAF^{V600E} /TP53 co-mutated resectable colorectal liver metastases.
   Berg KCG, Brunsell TH, Sveen A, Alagaratnam S, Bjørnslett M, Hektoen M, Brudvik KW, Røsok BI, Bjørnbeth BA, Nesbakken A, Lothe RA.
   Mol Oncol. 2021 Apr;15(4):830-845. doi: 10.1002/1878-0261.12885. Epub 2021 Jan 8.
   PMID: 33325154 Free PMC article.
8. 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. 2021 Dec 10. doi: 10.1002/1878-0261.13159. Online ahead of print.
   PMID: 34890102
9. Simultaneous Resection of Primary Colorectal Cancer and Synchronous Liver Metastases: Contemporary Practice, Evidence and Knowledge Gaps.
   Kleive D, Aas E, Angelsen JH, Bringeland EA, Nesbakken A, Nymo LS, Schultz JK, Søreide K, Yaqub S.

Oncol Ther. 2021 Jun;9(1):111-120. doi: 10.1007/s40487-021-00148-2. Epub 2021 Mar 23.
PMID: 33759076 Free PMC article. Review.

10. An international assessment of the adoption of enhanced recovery after surgery (ERAS®) principles across colorectal units in 2019-2020.
ESCP Enhanced Recovery Collaborating Group.
Colorectal Dis. 2021 Nov;23(11):2980-2987. doi: 10.1111/codi.15863. Epub 2021 Sep 30.
PMID: 34365718

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 translasjonsforskning. Gruppens medlemmer arbeider innen flere fagfelt som kirurgi, onkologi, gastroenterologi, patologi og molekylærbiologi. Hovedmålet er å bedre diagnostikk og behandling og derav prognosen 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:

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Aktivitet i 2021 / Activity in 2021:

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

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. Ongoing from March 2017. In April 2021 inclusion was completed, and 140 patients from 12 centers have been randomized. 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. Ongoing from January 2018-2020. Accrual completed in December 2020, 250 patients have been included in Oslo. 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. Ongoing from December 2018. In April 2021 inclusion was completed, and 258 patients from 31 centers have been randomized. Local-PI: professor Bjørn Edwin

Thesis defense:

1. Bart Baekelandt, MD:“Survival and patient reported outcome in surgically managed pancreatic and periampullary tumours”. Main supervisor: professor Trond Buanes. Jan 29, 2021
2. Harald Hugenschmidt, MD: “The impact of micrometastasis in presumed resectable pancreatic and periampullary cancers. Circulating tumour cells in the peripheral blood and disseminated tumour cells in the bone marrow as potential tools for risk-assesement before surgery”. Main supervisor: Consultant surgeon Gro Wiedswang. May 20, 2021

Ongoing PhD projects:

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

Forskningsgruppe: Svulster 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:

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Aktivitet i 2021 / Activity in 2021:

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. Due to the on-going pandemic, several meetings were held online (Zoom).
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 started recruiting patients in Q4 2021. 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, started December 2020.
- TESLA1 & TESLA2 trial: Liver Transplantation for Non-Resectable 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.
- CAMINO study: Investigate the value of MRI in assessing CRC liver mets compared to CT scan, and if MRI affects the surgical decision. The inclusion was completed in 2021.
- 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).

Planned projects:

- 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.
- The SYLMET trial; a multicentre, randomized controlled trial, comparing simultaneous and two-staged resection of primary colorectal cancer with synchronous liver metastases.
- PREPOSTEROUS; a single blinded trial, initiated by University of Helsinki, investigating the role of low-molecular heparin administered pre-operatively vs. post-operatively.

Forskningsgruppe: Øsofagus- og ventrikkelsykdommer

Research group: Diseases of esophagus and stomach

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

Gruppeleder: Egil Johnson (Tom Mala from 01.01.2022)

Om gruppen:
Hensikten med gruppen er:

1. Å evaluere (kvalitetssikre) eksisterende kirurgisk behandling av sykdommer i øsofagus og ventrikkel, så vel som brokk med siktemål å definere forbedringsområder (som robot-assistert kirurgi).
2. Å delta i forskningsstudier innen fagfeltet, både klinisk og molekylært for å forbedre behandlingen (f. eks biomarkører for tidlig deteksjon av kreft/type neoadjuvant/perioperativ behandling/type definitiv onkologisk behandling).
3. Arbeide for tettere nasjonalt og internasjonalt samarbeid innen forskning på kreft i spiserør og magesekk

About the group:

1. To evaluate by quality assurance existing surgical treatment of diseases of esophagus and stomach, as well as hernia, in order to improve treatment (e.g. robotic assisted surgery).
2. To participate in research studies within this field, both clinically and by molecularly in order to improve treatment (e.g. biomarkers for early detection of cancer/type of neoadjuvant/perioperative treatment/type of definitive oncologic treatment)
3. Work for a closer national and international cooperation within research on esophageal and gastric cancer

Hovedmedlemmer / Main members

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Activity in 2021:

Projects:
Establishment of a national database and biobank for patients resected for esophageal cancer as part of the NORECa project (Norwegian Esophageal Expert Consortium).
Continual monitoring of complications and survival following resection for esophageal- and gastric cancer – local registry.
Continuous local biobanking of blood samples and tumor tissue ((esophageal cancer (n= 500), gastric cancer (n=300)) since 2013 for research purposes. Analyses of biobank material have been ongoing since 2019.

Studies on esophageal cancer on biomarkers /local treatment of dysplasia and early cancer/total minimally invasive resection for more advanced cancer are ongoing (PhD study)

INNOVATION study. European randomised multicenter study, in which patients with HER-2 positive gastric cancer were randomized in three arms for i) chemotherapy (perioperative FLOTx4x2 eller CiFU/CiXel), ii) chemotherapy with trastuzumab or iii) chemotherapy with trastuzumab+pertuzumab. End point is overall survival. EORTC study. Inclusion is still ongoing.

INTENSE study. Effect of perioperative use of chemotherapy (FOLFIXFLIRIx4x2) in patients with resectable gastric and gastroesophageal junction adenocarcinoma. Inclusion is still ongoing.

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 (nivolumab plus ipilimumab) vs. Standard Chemotherapy for Gastric Cancer stage Ib-IVb, including esophagogastric junction adenocarcinoma, with high risk for recurrence (defined by ypN1-3 and/or R1 status) (VESTIGE).

The upper GI International Robotic Association (UGIRA) for contribution of patients to the International Registry for Robot-Assisted Minimally Gastrectomy (RAMIG) for gastric cancer. Recruitment of patients from OUS since 2021.

kiNETiC study – a Register based Randomized Controlled Trial- Ng-tube post–EsophagecTomy Complications. A Scandinavian multicenter study. Planned start 2022.

Keynote 061 (randomised study with palliative chemotherapy in 2. line for gastric cancer; standard chemotherapy vs. MK3475. MSD study. Inclusion from August 2015.
Keynote 180 (phase II study, palliative chemotherapy in 3. line for esophageal cancer; MK3474). MSD study. Inclusion from January 2016.
Keynote 181 (randomised phase III study, palliative chemoterapy in 2. line for esophageal cancer; standard chemotherapy vs MK3475). MSD study. Inclusion from January 2016.
Nordic NEC registry (registry study for all patients with neuroendocrine carcinoma of the GI-tract (GEP-NEC)). Inclusion from 2013. NNTG (Nordic Neuroendocrine Tumor Group). See reference 3 in the publication list.
ET-NEC. Nordic one armed phase II study for patients with GEP-NEC, Ki67 index 20-55%, first line treatment with everolimus and temozolomid. Inclusion from October 2014.
Medical student project: Hiatal gastroesophageal hernia – treatment at OUS, Ullevål – retrospective cohort study.

Meetings: There have been no group meetings locally but two meetings in the Scandinavian esophageal and gastric cancer group (SGICG).
Publications: 5 publications in international journals.

Popular science: Feature in NRK with Egil Johnson, where he was interviewed about the NORECa project.

Publications

Hauge T, Førland DT, Johannessen HO, Johnson E. Short- and long-term outcomes in patients
operated with total minimally invasive esophagectomy for esophageal cancer. Dis Esophagus.
2021 Sep 7:doab061. doi: 10.1093/dote/doab061. Epub ahead of print. PMID: 34491299.
Venizelos A, Elvebakken H, Perren A, Nikolaienko O, Deng W, Lothe IMB, Couvelard A, Hjortland GO, Sundlöv A, Svensson J, Garresori H, Kersten C, Hofsli E, Detlefsen S, Krogh M, Sorbye H, Knappskog S. The molecular characteristics of high-grade gastroenteropancreatic neuroendocrine neoplasms. Endocr Relat Cancer. 2021 Nov 11;29(1):1-14. doi: 10.1530/ERC-21-0152.
Elvebakken H, Perren A, Scoazec JY, Tang LH, Federspiel B, Klimstra DS, Vestermark LW, Ali AS, Zlobec I, Myklebust TÅ, Hjortland GO, Langer SW, Gronbaek H, Knigge U, Tiensuu Janson E, Sorbye H. A Consensus-Developed Morphological Re-Evaluation of 196 High-Grade Gastroenteropancreatic Neuroendocrine Neoplasms and Its Clinical Correlations. Neuroendocrinology. 2021; 111(9):883-894. doi: 10.1159/000511905. Epub 2020 Oct 1.Neuroendocrinology. 2021. PMID: 33002892.
Pommergaard HC, Nielsen K, Sorbye H, Federspiel B, Tabaksblat EM, Vestermark LW, Janson ET, Hansen CP, Ladekarl M, Garresori H, Hjortland GO, Sundlöv A, Galleberg R, Knigge P, Kjaer A, Langer SW, Knigge U. Surgery of the primary tumour in 201 patients with high-grade gastroenteropancreatic neuroendocrine and mixed neuroendocrine-non-neuroendocrine neoplasmsJ Neuroendocrinol. 2021 May; 33(5):e12967. doi: 10.1111/jne.12967. Epub 2021 Mar 26.

Melina Arnold , Eileen Morgan , Aude Bardot , Mark J Rutherford , Jacques Ferlay, Alana Little, Bjorn Møller, Oliver Bucher, Prithwish De, Ryan R Woods, Nathalie Saint-Jacques, Anna T Gavin, Gerda Engholm, Michael P Achiam, Geoff Porter, Paul M Walsh, Sally Vernon, Serena Kozie, Agnihotram V Ramanakumar, Charlotte Lynch, Samantha Harrison, Neil Merrett, Dianne L O'Connell, Tom
Mala, Mark Elwood, John Zalcberg, Dyfed W Huws, David Ransom, Freddie Bray, Isabelle Soerjomataram. 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) Gut. 2021 Nov 25;gutjnl-2021-325266. doi: 10.1136/gutjnl-2021-325266. Online ahead of print.

Department of Rheumatology, Dermatology and Infectious Diseases (RHI)

- Hud/ Dermatology Research Group
- Klinisk mikrobiologi og mikrobiotamedisin/ CliMic: Clinical microbiology and microbiota medicine
- Olafiaklinikken
- Revmatologi / Rheumatology

Forskningsgruppe: Hud

Research group: Dermatology Research Group

Avdeling: RHI

Gruppeleder: Olav Sundnes

Om gruppen
Vår forskning fokuserer på to kjerneområder; hudinflammasjon og hudkreft. Vi driver både translasjonell og klinisk forsking, 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 to 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
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Assosierte medlemmer / Associated members:

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

Aktivitet i 2021 / Activity in 2021

Forskningsaktivitet/ Research activity:

PhD-projects
▪ PhD-project Astrid Lossius, Early gene expression changes as predictors of therapeutic response to narrow-band UVB in atopic dermatitis, in progress (Main supervisors Holm) - completed 2021, dissertation februar 2022
▪ PhD-project Olav Gramstad, hereditary angioedema, in progress (Main supervisor Landrø)
▪ PhD-project Siri Hansen Stabell, Hidradenitis suppurativa, in progress (Main supervisor Sundnes)
PhD-project Karianne Haga , Gorlin syndrome in Norway, in progress (Main supervisor Hortemo)

Clinical trials and other research projects:
▪ GENTLEBULL study - topical gentamycin in epidermolysis bullosa (Sandanger)
▪ AP-GELP study - 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)
▪ An Observational Post-authorization Safety Study of Ustekinumab (Janssen) in the Treatment of Pediatric Patients Aged 12 Years and Older with Moderate to Severe Plaque Psoriasis (Sitek)
▪ Spesolimab in the treatment of hidradenitis suppurativa – Phase 2 Study (Boehringer Ingelheim) (Sundnes)
▪ Finger pulp blood flow in systemic sclerosis patients with digital ulcers treated with sympathetic blockade (Bergersen).

Populærvitenskapelig aktivitet/ Popular science:

Members of the research group have engaged frequently with the national media (NRK, VG, Dagbladet, Aftenposten) with interviews on topics involving dermatology as well as contributing with research communication to patient organisations (PEF and NAAF)

Innovasjonsaktivitet/ Innovation:

Investigator-initiated clinical trials
- GENTLEBULL study
- AP-GELP study

Selected Key Publications:

Occupation and cutaneous melanoma: a 45-year historical cohort study of 14·9 million people in five Nordic countries
Alfonso JH, Martinsen JI, Weiderpass E, Pukkala E, Kjaerheim K, Tryggvadottir L, Lynge E. Br J Dermatol. 2021 Apr;184(4):672-680. doi: 10.1111/bjd.19379.
Eczema distribution in girls and boys during infancy: A cohort study on atopic dermatitis
Endre KMA, Landrø L, LeBlanc M, Gjersvik P, Carlsen KL, Rehbinder EM. J Allergy Clin Immunol Pract. 2021 May 5:S2213-2198(21)00515-8. doi: 10.1016/j.jaip.2021.04.053. Epub ahead of print. PMID: 33964509.

Diagnosing atopic dermatitis in infancy using established diagnostic criteria: a cohort study
Endre KMA, Landrø L, LeBlanc M, Gjersvik P,..., Rehbinder EM. Br J Dermatol. 2021 Jan 28. doi: 10.1111/bjd.19831. Epub ahead of print. PMID: 33511639.

Factor VII activating protease (FSAP) is not essential in the pathophysiology of angioedema in patients with C1 inhibitor deficiency
Gramstad OR, Kandanur SPS, Etscheid M, Nielsen EW, Kanse SM. Mol Immunol. 2022 Feb;142:95-104. doi: 10.1016/j.molimm.2021.11.019. Epub 2021 Dec 29. PMID: 34973499.

Shifts in the Skin Microbiota after UVB Treatment in Adult Atopic Dermatitis
Lossius AH, Sundnes O, Ingham AC, Edslev SM, Bjornholt JV, Lilje B, Bradley M, Asad S, Haraldsen G, Skytt-Andersen P, Holm JO, Berents TL. Dermatology. 2022;238(1):109-120. doi: 10.1159/000515236. Epub 2021 Apr 22.PMID: 33887725

Contact allergy in patients with chronic venous leg ulcers
Lossius AH, Lorentzen M, Austad J, Bergersen TK (2021) Contact Dermatitis, 84 (6), 470-472 DOI 10.1111/cod.13770, PubMed 33368388

Rapid systemic surge of IL-33 after severe human trauma: a prospective observational Study
Sundnes O, Ottestad W, Schjalm C, Lundback O, la Cour Poulsen L, Mollnes TE, Haraldsen G, Eken T. Mol Med. 2021 Mar. DOI: 10.1186/s10020-021-00288-1 PMID: 33771098

A novel somatic mutation in GNB2 provides new insights to the pathogenesis of Sturge-Weber syndrome
Fjar R, Marciniak K, Sundnes O, Hjorthaug H, Sheng Y, Hammarstrom C, Sitek JC, Vigeland MD, Backe PH, Oye AM, Fosse JH, Stav-Noraas TE, Uchiyama Y, Matsumoto N, Comi A, Pevsner J, Haraldsen G, Selmer KK. Hum Mol Genet. 2021 Oct 13;30(21):1919-1931. DOI: 10.1093/hmg/ddab144 PMID: 34124757

Apremilast for genital erosive lichen planus in women (the AP-GELP Study): study protocol for a randomised placebo-controlled clinical trial
Skullerud KH, Gjersvik P, Pripp AH, Qvigstad E, Helgesen ALO (2021). Trials, 22 (1), 469. DOI 10.1186/s13063-021-05428-w, PubMed 34284808

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, inflammatory and metabolic diseases, including cardiovascular disease. 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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Sajan Raju	Post doc	UiO	sajan.raju@medisin.uio.no

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Birgitte Stiksrud	Senior researcher	OUS and UiO	birgitte.stiksrud@medisin.uio.no

Activity in 2020:

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. This project was finalized during 2019, with first paper accepted for publication (Gelpi M & Vestad B, et a.l Impact of HIV-related Gut Microbiota alterations in Metabolic Comorbidities. Clin Inf Dis 2020). PhD successfully defended November 2020 (Vestad).
- GutHeart (Targeting the gut microbiota to treat heart failure). The first adequately powered RCT targeting the gut microbiome aiming to improve cardiac function in heart failure patients, comprising n=150 patients. Also this ambitious project was finalized during 2020, with the main manuscript published (Awojemi, Mayerhofer et al, EbioMedicine 2021). PhD successfully defended November 2021 (Mayerhofer).
- 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 (Hoel H, et al. Soluble markers of IL-1 activation as predictors of first-time myocardial infarction in HIV-infected individuals. J Inf Dis 2019). We have also published a paper on inflammasome activation and cardiac involvement in COVID-19 (Hoel H, et al. J Int Med 2020). PhD successfully defended June 2021 (Hoel).
- 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 two years have been challenging due to the COVID-19 pandemic, but we have managed to keep the network alive through regular video meetings, hybrid meeting as well as a national meeting.
- 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.
- 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 2021.
- 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 baricintib for severe Covid-19 has stopped inclusions, whereas the first phase II trial on bemcentinib will be started in collaboration with BerGenBio during spring/summer 2022.

Forskningsgruppe: Olafiaklinikken

Research group: Olafiaklinikken

Avdeling: Avdeling for revmatologi, hud og infeksjonssykdommer

Gruppeleder: Usha Hartgill

Om gruppen:

Forskningsgruppen studerer smittemekanismer, utbredelse, diagnostikk og behandling av kjønnssykdommer. Olafiaklinikken i Oslo sentrum har et åpent poliklinisk tilbud for diagnostikk og behandling av kjønnssykdommer. Som Nordens største klinikk innen venerologi har vi opparbeidet er stor og unik database som gir svært gode forutsetninger for å drive epidemiologisk forskning. Med stort pasienttilfang er det godt tilrettelagt for forskning relatert til diagnostikk og behandling på områder der det er behov for ny kunnskap.

About the group:

Olafiaklinikken is the largest clinic for sexually transmitted infections (sti) in the Nordic region. The clinic is situated in central Oslo and provides a low threshold drop-in service for anyone wanting to test for a sti. We have unique access to a large patient population with a variety of background characteristics, symptoms, clinical findings and infections. Studies are focused on mechanisms of infection, as well as prevalence, diagnostics and treatment of stis.

We also hold the function as the National Advisory Unit on Sexually Transmitted Infections, and therefore our research focus is on clinical studies providing results to support evidence based medicine and guidance for treatment practice.

Hovedmedlemmer / Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Usha Hartgill	Senior consultant	OUS	ushhar@ous-hf.no
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Aktivitet i 2021 / Activity in 2021:

Evaluation På vei mot en multiresistent seksuelt overførbar infeksjon? Usha Hartgill, Karianne Nodenes, Harald Moi. Tidsskr Nor Legeforen 2021 doi: 10.4045/tidsskr.21.0441
En mann i 40-årene med analtumor og lymfeknutesvulst i lysken Svetlana Sharapova, Usha Hartgill, Premnaath Torayraju, Bettina Andrea Hanekamp, Sigurd Folkvord. Tidsskr Nor Legeforen 2021 doi: 10.4045/tidsskr.20.0722

Projects
- Evaluation of implementation of pre-exposure prophylaxis (PrEP) in subjects at particular risk of infection with HIV, Frank Olav Pettersen, Michelle Hanlon, Oslo universitetssykehus HF, Project period: 2017 – 2022, participating health region: HV HSØ

-Gonore-studien; 'Gonorrhoea - an 'urgent and major threat to public health': Diagnostic challenges, transmission, molecular epidemiology and antimicrobial resistance in Norway'. Linn Merete Brendefur Corwen and Patricia Merckoll er doktorgradsstudenter med hovedansvar for dette prosjektet. TTA er et forskningsnettverk etablert i Oslo Universitetssykehus med antimikrobiell resistens (AMR) som tematisk forskningsområde med bredt samarbeid nasjonalt og internasjonalt. Vår rolle i dette er gjennom forskning på resistensutviklingen ved gonore. Som en del av dette, har vi bl.a etablert samarbeid med referanselaboratoriet for gonokokker ved Folkehelseinstituttet som igjen vil legge til rette for og initiere mer forskning på gonore som også involverer de andre helseregioner.
-Turning the tide of Antimicrobial resistance (TTA) Fredrik Muller, Oslo universitetssykehus HF Prosjektperiode: 2016 – 2023 Deltakende helseregion: HSØ

Department of Transplantation (ATX)

- Eksperimentell transplantasjon for kreft / Experimental Transplantation and Malignancy
- Klinisk transplantasjonskirurgi og eksperimentell immunologi / Clinical transplantation surgery and experimental immunology
- Klinisk forskningsgruppe for primær skleroserende kolangitt / Clinical PSC Research Group
- Nyretransplantasjonsmedisin / Kidney Transplantation
- Eksperimentell Celletransplantasjon / Experimental Cell Transplantation
- Klinisk Effektforskning / Clinical Effectiveness Research Group
- Forskningsgruppe for livskvalitet og helseøkonomi / Quality of life and Health Economics
- Nevroendokrine svulster / Neuroendocrine tumors

Forskningsgruppe: Eksperimentell transplantasjon for kreft

Research group: Transplantation and Malignancy

Avdeling: Avdeling for transplantasjonsmedisin

Gruppeleder: Svein Dueland

Om gruppen:

Gruppen arbeider med levertransplantasjon hos pasienter med malign sykdom og spredning utelukkende til lever. Aktuelle pasienter har så omfattende sykdom i lever at vanlig leverkirurgi ikke er aktuelt. Behandlingsalternativet hos pasienter som er aktuelle for inklusjon i de ulike levertransplantasjonsstudiene er palliativ kjemoterapi. Median forventet overlevelse på kjemoterapi hos inkluderte pasienter har vært omtrent 1 år ved tidspunkt for levertransplantasjon. Forskningsgruppen består av transplantasjonskirurger, onkologer, radiologer, nukleærmedisinere, thoraxkirurg, gastrokirurg(leverkirurg)og sykepleier/forsker. Gruppen har etablert samarbeid med helseøkonomer.

About the group:

The research group is exploring liver transplantation as a treatment option for patient with different malignant diagnoses, primarily patients with colorectal cancer. Patients that may be included in the different liver transplantation protocols have non-resectable liver only disease. The treatment option today for these patients is palliative chemotherapy with median expected overall survival of about one year at time of inclusion in the liver transplantation studies. Members of the research group are transplant surgeons, oncologists, radiologists, nuclear medicine specialists, liver surgeon and thorax surgeon. Research projects also include health economic expertise.

Hovedmedlemmer / Main members:

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

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Rune Horneland	Senior consultant	OUS	runhor@ous-hf.no
Mona-Elisabeth Revheim	Ass. Professor/Senior consultant	UiO and OUS	monar@ous-hf.no
Sheraz Yaqub	Post doc/senior consultant	OUS	shya@ous-hf.no

Collaboration
Internal (other groups, departments, clinicians, etc.):
- Trygve Syversveen and Mona-Elisabeth Revheim , Department of Radiology, OUS

National:
- Gudrun Bjørnelv , The Institute of Health and Society, UiO
- Eline Aas , The Institute of Health and Society, UiO

International:
- Professor Julia Johansen, Herlev University Hospital, Denmark
- Professor Eric Vibert; Hopital Paul Brousse Paris
- Professor Umberto Cillo, University of Padova

Activity in 2021:

We started in 2006 a pilot study (SECA-I) on liver transplantation (LT) in patients with colorectal cancer (CRC) with liver only metastases that had liver metastases that could not be resected. CRC patients were palliative chemotherapy is the only treatment option have median overall survival (OS) of about 2 years from time of starting first line chemotherapy. In the SECA-I study final 5-year OS was 44% and four patients are alive more than 10 years after LT and two other more than 5 years after resection of a pulmonary small metastatic lesion. All 23 patients included in the SECA-I study had a relapse of the malignant disease after LT, however they survived for long period of time after the relapse with median OS after relapse of 55 months. A patient has survived for more than 13 years after time of relapse.

The reason for the long OS from time of relapse is that the majority of relapses were small pulmonary metastases that increase at a slow rate. Many of the patients developing pulmonary metastases after the LT received surgical resection of the pulmonary metastases. Patients with multiple site of relapse should be considered for palliative chemotherapy. In genera, patients tolerate chemotherapy after LT, however one should pay increased attention to symptoms as diarrhea, mucositis and skin reactions when starting palliative chemotherapy.

OS after LT was related to clinical factors as: size of largest liver lesion, plasma tumor marker CEA levels, response to chemotherapy at time of LT and time from resection of the primary colorectal cancer and LT (Oslo Score). Furthermore, we have also shown that PET activity in liver metastases could predict OS after LT. By stricter selection criteria (SECA-II study), excluding patients with progressive disease at time of LT and at least one year from time of diagnosis, we have now reported estimated 5-years OS after LT of 83%. In contrast to SECA-I study where all 23 included patients had a relapse after LT, some patients in the SECA-II study have been observed for more than 8 years without a relapse. Also in the SECA-II study the most frequent site of relapse was pulmonary lesions that increased at a slow rate and many of the patients received surgical resection of the pulmonary metastases.

In a recent publication we have shown that Kaplan-Meier calculated 5-years OS of about 70-100 % may be obtained by using different selection criteria as Oslo Score 0-2, Fong Clinical Risk Score 0-2 or PET-MTV (metabolic tumor volume)<70cm^3.

We have published that the patients having general symptoms related to the malignant disease as appetite loss at time of LT had significant decreased OS at 3 years after LT compared to patients without appetite loss. Similar findings were also observed for patients having fatigue.

To expand the liver donor pool available for LT in CRC patients we have also used donor livers that are not routinely used in LT, in general these organs works well and may

represent an underutilized source of donor organs that may be used to expand donor organs for LT in CRC patients.
Furthermore, we have shown that the site of the primary tumor is of importance for OS after LT. Patients with primary tumor located in ascending colon have dismal prognosis after LT and should not be offered this treatment.
During the last year we have published several manuscripts indicting that CRC patients with high tumor load have increased OS after LT compared to resection of liver metastases.
There is increasing international interest in our results on LT in CRC patients. We have participated in an international expert group of researchers recommending guidelines for selection of CRC patients for LT.

Forskningsgruppe: Klinisk forskningsgruppe for primær skleroserende kolangitt

Research group: Clinical PSC Research Group

Avdeling: Avdeling for transplantasjonsmedisin

Gruppeleder: Trine Folseraas

Om gruppen:
Utredning og behandling av pasienter med primær skleroserende cholangitt (PSC) er en viktig del av det kliniske virke ved seksjon for gastromedisin på Rikshospitalet. Pasienter med PSC henvises fra hele landet og PSC er en av de vanligste indikasjonene for levertransplantasjon i Norge. Gallegangskreft (cholangiocarcinom) er en fryktet komplikasjon til PSC som rammer opptil 20% av pasientene, dessverre er det en utfordring å diagnostisere denne kreftformen tidlig nok til at kurativ behandling kan tilbys. Vår forskning har fokuserer på å forbedre utredning, oppfølging og behandling av PSC pasienter, inkludert bedret diagnostikk og behandling av gallegangskreft.

About the group:
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:

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Aktivitet i 2021 / Activity in 2021

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

Currently we have to ongoing PhD projects focusing on early detection and improved treatment of CCA.

In 2020 we published the first genomic characterization of PSC-associated CCA (PMID: 31925805). As an extension of this work we have performed a more comprehensive exome sequencing of a subset of the CCA tissue samples used in the previous effort, aiming for detection of a broader panel of targetable mutations that could provide PSC-CCA patients with better treatment options (manuscript in preparation).
In collaboration with the Epigenetics group at the Department of Cancer Prevention, Institute for Cancer Research at the Norwegian Radium Hospital we have used highly sensitive droplet digital PCR to analyze epigenetic biomarkers that provide early and accurate detection of CCA in patients with PSC. These methylation biomarkers have been analyzed using more than 300 bile samples collected from Norwegian, Swedish and Finnish PSC and CCA patients. Findings strongly suggest that analyzing aberrant DNA methylation utilizing bile as liquid biopsy material may improve and complement current detection methods for CCA. This work was published in Hepatology in 2021 (PMID: 34435693). We also have several other ongoing projects related to biomarker detection in CCA.

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 disease.

The biobank and database of the Norwegian PSC Research Center is steadily growing and currently include clinical data and biological samples on close to 950 Norwegian PSC patients. The NoPSC biobank represent a valuable source 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 to several registry studies outgoing from the International PSC Study Group (IPSCSG) and the European Network for the Study of Cholangiocarcinoma (ENSCCA).

Selected articles, 2021:

- Early and accurate detection of cholangiocarcinoma in patients with primary sclerosing cholangitis by methylation markers in bile.Hepatology, 75 (1), 59-73

- Defining Primary Sclerosing Cholangitis: Results From an International Primary Sclerosing Cholangitis Study Group Consensus Process. Gastroenterology, 161 (6), 1764-1775.

- Liver Metastases of Intrahepatic Cholangiocarcinoma: Implications for an Updated Staging System. Hepatology, 73 (6), 2311-2325.

- Primary sclerosing cholangitis and the risk of cancer, cardiovascular disease, and all-cause mortality: a systematic review and meta-analysis of cohort studies. Sci Rep, 11 (1), 10646.

- Fluctuating biomarkers in primary sclerosing cholangitis: A longitudinal comparison of alkaline phosphatase, liver stiffness, and ELF. JHEP Rep, 3 (5), 100328.

- Bile Acid Profiles in Primary Sclerosing Cholangitis and Their Ability to Predict Hepatic Decompensation. Hepatology, 74 (1), 281-295

Forskningsgruppe: Transplantasjonsmedisinsk forskningsgruppe

Research group: Research Group of Transplantation Medicine

Avdeling: Avdeling for transplantasjonsmedisin

Gruppeleder: Professor, overlege Trond Geir Jenssen

Om gruppen:
Gruppen utfører epidemiologiske og kliniske studier med endepunktsdata på pasienter som gjennomgår nyretransplantasjon, pankreastransplantasjon og øycelletransplantasjon. Data som publiseres er dels registerbasert (via et komplett 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).

About the group:
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
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Aktivitet i 2021 / Activity in 2021

Two of our candidates defended their thesis in 2021 (Hjørdis Thorsteinsdottir and Anders Haugen). A new PhD candidate started Sep 1 on a project financed by University of Oslo (Markus Herberg Hovd, cand.pharm.)

New projects started in 2021:

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?

Continued projects which started in 2020 and earlier:

1. Hypomagnesemia as a risk factor for development of posttransplant diabetes mellitus (PhD project Rasmus Kirkeskov Carlsen).
2. The microbiome and gut metabolism of mycophenolate acid.
3. Covid-19 vaccine study among kidney transplant recipients
4. EVITA (Epstein-Barr virus infection monitoring in renal transplant recipients)
5. BONTRAX – 10 years follow-up of bisphosphonate treatment in kidney transplant recipients

Other ongoing projects continued in 2021:

- 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 69 peer-reviewed papers were published in international journals in 2021.

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 joined an international network for surveillance of covid disease (incidence, vaccination and outcome) among patients with end-stage kidney disease (dialysis and kidney transplant patients). We have also published two reports on Fabry disease, an orphan disease in Southern Norway which is taken care of by our department.

Five representative papers published by our group in 2021 are cited below:

1. Langberg NE, Jenssen TG, Haugen AJ, Mjøen G, Birkeland KI, Åsberg A, Hartmann A, Dahle DO. Endothelial Dysfunction and 6-Year Risk of Mortality in Kidney Transplant Recipients. Transplant Direct. 2021 Dec 13;8(1):e1262. doi: 10.1097/TXD.0000000000001262. PMID: 34912949.

2. Witczak BJ, Pischke SE, Reisæter AV, Midtvedt K, Ludviksen JK, Heldal K, Jenssen T, Hartmann A, Åsberg A, Mollnes TE. Elevated Terminal C5b-9 Complement Complex 10 Weeks Post Kidney Transplantation Was Associated With Reduced Long-Term Patient and Kidney Graft Survival. Front Immunol. 2021 Oct 25;12:738927. doi: 10.3389/fimmu.2021.738927. PMID: 34759922.

3. Robertsen I, Åsberg A, Jenssen TG, Gence B, Tore Vethe N, Midtvedt K, Svensson MHS, Eide IA. Increased systemic exposure of once-daily tacrolimus in renal transplant recipients on marine omega-3 fatty acid supplementation. Transpl Int. 2021;34:1322-1324. doi: 10.1111/tri.13917. PMID: 33991364.

4. Pihlstrøm HK, Weedon-Fekjær MS, Bjerkely BL, von der Lippe C, Ørstavik K, Mathisen P, Heimdal K, Jenssen TG, Dahle DO, Solberg OK, Sigurdardottir S. Health-related quality of life in Norwegian adults with Fabry disease: Disease severity, pain, fatigue and psychological distress. JIMD Rep. 2021;62:56-69. doi: 10.1002/jmd2.12240. PMID: 34765399.

5. Aubert O, Yoo D, Zielinski D, Cozzi E, Cardillo M, Dürr M, Domínguez-Gil B, Coll E, Da Silva MI, Sallinen V, Lemström K, Midtvedt K, Ulloa C, Immer F, Weissenbacher A, Vallant N, Basic-Jukic N, Tanabe K, Papatheodoridis G, Menoudakou G, Torres M, Soratti C, Hansen Krogh D, Lefaucheur C, Ferreira G, Silva HT Jr, Hartell D, Forsythe J, Mumford L, Reese PP, Kerbaul F, Jacquelinet C, Vogelaar S, Papalois V, Loupy A. COVID-19 pandemic and worldwide organ transplantation: a population-based study. Lancet Public Health. 2021;6:e709-e719. doi: 10.1016/S2468-2667(21)00200-0. PMID: 34474014.

- Populærvitenskapelig aktivitet/ Popular science

- Trond G. Jenssen: Diabetesfri med nyre organer. Diabetes 2021:5:38-39
- Trond G. Jenssen: Diabetes og blodsukker er mer enn bare insulin: Historien om en bihormonell sykdom. Diabetes 2021;2:20-23
- Dagens Medisin 30.09.2021: Resultatet er nedsatt insulinfrigjøring. Trond G. Jenssen
- Dagens Medisin 28.09.2021: Tror vektsenkende legemidler kan bli en snakkis. Kåre Birkeland og Trond G. Jenssen
- DM Arena Diabetes/ Post EASD 07.10.2021: Foredrag av Kåre Birkeland og Trond Jenssen
- Dagens Medisin 09.09.2021: Må ikke unnlate å fortelle folk om risiko. Trond G. Jenssen
- Dagens Medisin 18.02.2021: Ny studie om covid-19 og diabetes: Må ses på som et worst case-scenario. Trond G. Jenssen
- Diabetes.no 14.12.2021: Vaksinen beskytter godt også mot omikronviruset. Trond G. Jenssen
- Diabetes.no 17.12.2021: Personer med diabetes burde prioriteres for vaksine. Trond G. Jenssen
- Diabetes.no 10.11.2021: Forskning i dag – behandling om 20 år? Trond G. Jenssen
- Diabetes.no 28.04-30.04.2021. Oppsummeringer fra Nasjonalt Diabetesforum 2021. Daglige webcasts Trond G. Jenssen og Kåre Birkeland
- Diabetes.no 31.08.2021: Slik kan vi løse diabetesutfordringene. Trond G. Jenssen og Kåre Birkeland
- Healthtalk.no 07.07.21: En «gamechanger» i behandlingen av kronisk nyresykdom. SGLT2-hemmer får grønt lys. Trond G. Jenssen
- Artikkel i Diabetesforum april 2021: Skyldes diabetes type 1 virus eller bakterier? Trond G. Jenssen
- Artikkel i Diabetesforum i januar 2021: Det er viktig at man ikke skremmer dem med diabetes. Trond G. Jenssen

- Populærevitenskapelige foredrag i 2021 for hhv. Diabetesforbundet og Landsforeningen for Nyresyke og Transplanterte (LNT). Trond G. Jenssen

- Innovasjonsaktivitet/ Innovation

- Enklere måling av nyrefunksjon (GFR): *Simplify-studien*. Ved professor Anders Åsberg
- HBM-studien (Home Based Monitoring): Enklere blodprøvetaking av pasienten selv i hjemmet. Ved professor Anders Åsberg og overlege Karsten Midvedt

Forskningsgruppe: Eksperimentell Celletransplantasjon

Research group: Experimental Cell Transplantation

Avdeling: Avdeling for transplantasjonsmedisin (ATX)

Gruppeleder: Hanne Scholz

About the group:

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).

Hovedmedlemmer / Main members:

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Activity in 2021

Ongoing projects:

1. Development of beta cell replacement therapy for type 1 diabetes
2. In vitro differentiate of human pluripotent stem cells into mature functional glucose regulatory islet cells
3. Create functional mini-pancreas for "organ on a chip" platform, together with the Centre of Excellence -Hybrid Technology Hub at IMB, UiO
4. Regenerative/repair of the endocrine compartment of the pancreas using adult stem cells
5. Development of the decidua stromal cells (DSC) ATMP product for the clinical trial: "Safety Trial, DSC vs. BAT in SR acute GvHD" and "DSC-COVID-19: An open-label study on the safety and efficacy of decidual stromal cells in respiratory failure induced by COVID-19"
6. Tissue engineering of vasculature and bioartificial pancreas using decellularization and 3D Bioprinting technology

Research activity:

Presentation at the International Pancreas & Islet Transplant Association's 2021 virtual congress

- Abadpour, Shadab; Niemi, Essi M.; Strid Orrhult, Linnea; Nogueira, Liebert Parreiras; Haugen, Håvard Jostein; Josefsen, Dag; Kvalheim, Gunnar; Krauss, Stefan; Gatenholm, Paul; Scholz, Hanne. 307.7: 3D Bioprinting of Functional Islets With Adipose-derived Stromal Cells in an Alginate/Nanocellulose Scaffold, Transplantation: December 2021 - Volume 105 - Issue 12S1 - p S25 doi: 10.1097/01.tp.0000804424.50335.7e

- Wang, Chencheng; Abadpour, Shadab; Aizenshtadt, Alexandra; Chera, Simona; Ghila, Luiza; Ræder, Helge; Scholz, Hanne. 402.2: High Glucose Concentration Increases KATP Channel Activity but Suppresses Mitochondrial Respiration Ability in Insulin-producing Cells Regenerated From Stem Cells, Transplantation: December 2021 - Volume 105 - Issue 12S1 - p S27 doi: 10.1097/01.tp.0000804436.14096.44

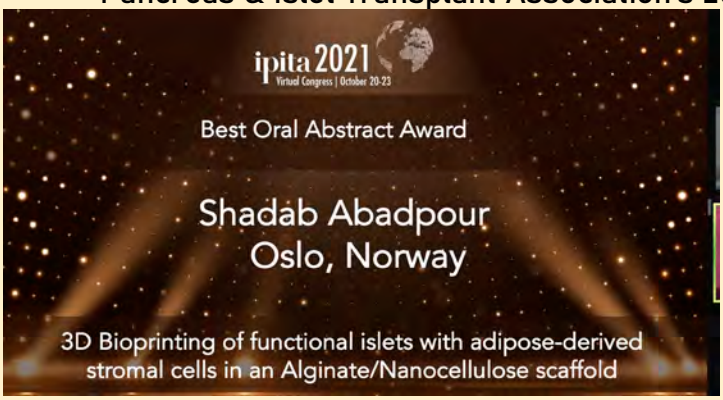
Publications 2021:

- Berishvili E, Casiraghi F, Amarelli C, Scholz H, Piemonti L, Berney T, Montserrat N. Mini-organs forum: how to advance organoid technology to organ transplant community. Transpl Int. 2021 Sep;34(9):1588-1593. doi: 10.1111/tri.13988. PMID: 34448263.
- Piemonti L, Andres A, Casey J, de Koning E, Engelse M, Hilbrands R, Johnson P, Keymeulen B, Kerr-Conte J, Korsgren O, Lehmann R, Lundgren T, Maffi P, Pattou F, Saudek F, Shaw J, Scholz H, White S, Berney T. US food and drug administration (FDA) panel endorses islet cell treatment for type 1 diabetes: A pyrrhic victory? Transpl Int. 2021 Jul;34(7):1182-1186. doi: 10.1111/tri.13930. Epub 2021 Jun 11. PMID: 34048106.
- Abadpour, S, Wang C, Niemi E.M, Scholz H. Tissue engineering strategies for improving beta cell transplantation outcome. Current Transplantation Report. Curr Transpl Rep (2021). doi.org/10.1007/s40472-021-00333-2
- Ghila L, Legøy TA, Mathisen AF, Abadpour S, Paulo JA, Scholz H, Ræder H, Chera S. Chronically Elevated Exogenous Glucose Elicits Antipodal Effects on the Proteome

Signature of Differentiating Human iPSC-Derived Pancreatic Progenitors. Int J Mol Sci. 2021 Apr 2;22(7):3698. DOI: 10.3390/ijms22073698. PubMed 33918250
- Nordheim E, Lindahl JP, Carlsen RK, Åsberg A, Birkeland KI, Horneland R, Boye B, Scholz H, Jenssen TG. Patient selection for islet or solid organ pancreas transplantation: experiences from a multidisciplinary outpatient-clinic approach. Endocrine Connections. 2021;10(2):230-9. doi: 10.1530/EC-20-0519 PubMed 33544090
- Zhou AX, Mondal T, Tabish AM, Abadpour S, Ericson E, Smith DM, Knöll R, Scholz H, Kanduri C, Tyrberg B. The long noncoding RNA TUNAR modulates Wnt signaling and regulates human β-cell proliferation. Am J Physiol Endocrinol Metab 2021 Apr 1;320(4):E846-E857.DOI: 10.1152/ajpendo.00335.2020 PubMed 33682459

Populærvitenskapelig aktivitet/ Popular science:

- Title: Music for stem cells: Aiming to cure diabetes with sound waves ABINO at Oslo Life Science Conference 2021 Feb. 18, 2021 4:00 PM–5:00 PM, Digital event
- Shadab Abadpour won Best Oral Abstract Award at the International Pancreas & Islet Transplant Association's 2021 virtual congress (IPITA2021).



Innovasjonsaktivitet/ Innovation:

The group has initiated a new project *Generation of insulin-producing cells from cholangiocyte organoids* funded by The Novo Nordic Foundation. In this project postdoc Shadab Abadpour will work together with postdoc Anna Frank (Dr. Espen Melum group) to develop novel (trans)differentiation protocols for cholangiocyte organoids using advanced methods including sequencing-based methods.

Forskningsgruppe: Klinisk Effektforskning – Avdeling for Kirurgi, Inflammasjonsmedisin 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 i 2020 27 medlemmer. 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 2020, the Group has 27 members. The Group conducts large randomized trials and epidemiologic studies to test end 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:

NAME	POSITION/TITLE/ROLE	EMPLOYER/ AFFILIATION	E-MAIL
Mette Kalager	Gruppeleder/ Professor	OUS & UiO	mkalager@hsph.harvard.edu
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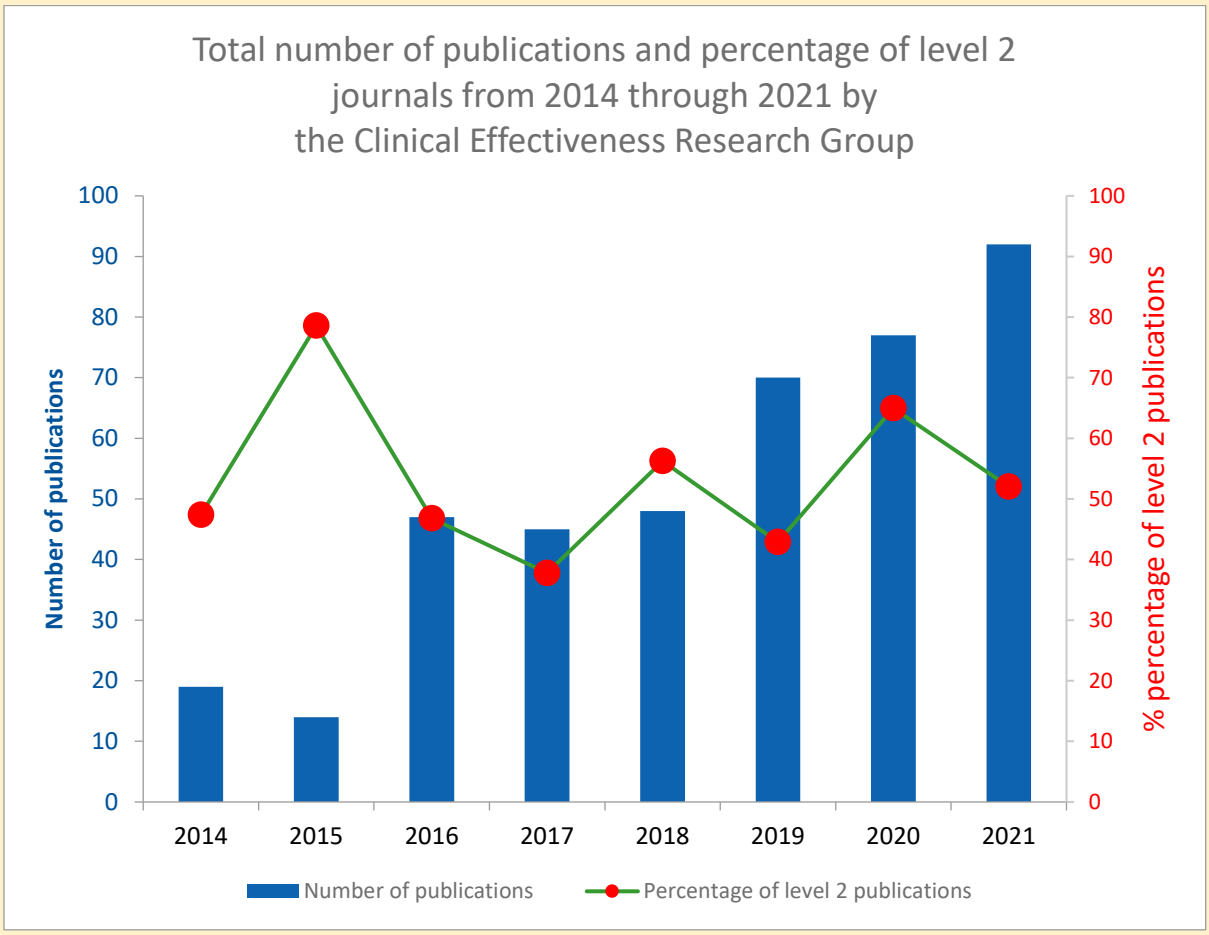
Aktivitet i 2021 / Activity in 2021

The Group has had an expansive growth from its four members in 2012 to 30 members in 2021. All but four members of the Group are funded by external grants.

Publications in 2021:

- The Group published 92 articles in peer-reviewed journals in 2021.
- Of all articles 52 % were published in level 2 journals (the top 20 % of journals).
- The mean impact factor of articles in 2021 is 9.1 and the cumulative impact factor is 831,2.



- The group members plays an active part in Norwegian media, TV and podcast debates with more than 50 comments and appearances in 2021.

Research activity:

Corona and the Rule of Law:

Corona and the Rule of Law is a research network, a collaboration between researchers from the University of Oslo, UiT The Arctic University of Norway and Inland Norway University of Applied Sciences. The Groups researchers have participated actively in this

initiative since the start of the Covid pandemic. The initiative contributes to public debate by providing interdisciplinary critical perspectives mainly in the following topics:
TB

- Children's rights
- Digital vaccine passports/COVID-19 certificates and COVID-19 tracking apps (Smittestopp)
- Border management (Sweden)
- The domestic practice on quarantine hotels
- The Emergency Powers Bill, politics and the rule of law
- Epidemiological knowledge and preventative measures
- Curfew legislation
- Migration, health and human rights

Artifical intelligence:

In 2021, the Clinical Effectiveness Research Group achieved two major goals in the research field of artificial intelligence (AI) in clinical medicine. We have completed an international, multicenter, prospective trial "EndoBRAIN International" in which we explored the possibility to reduce the burden of colonoscopy with the aid of AI. The other achievement is the launch of an international, multicenter, randomized controlled trial "ACCEPT" which is aimed at establishing the value of AI in colorectal cancer prevention. Both studies were designed in a very robust fashion with the inclusion of the large number of participants. We believe these landmark trials will play a crucial role in changing colonoscopy practice and colorectal cancer screening to the better.

Populærvitenskapelig aktivitet/ Popular science:

For some publications, please see link:
https://www.jus.uio.no/ikrs/forskning/forskningsnettverk/koronaogrettstaten/aktuelle-saker/mediebidrag.html

Forskningsgruppe: Forskningsgruppe for pasientrapportert resultat og helseøkonomi

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

Avdeling: Avd for transplantasjon

Gruppeleder: Marit Helen Andersen

Om gruppen:

Forskningsgruppe for pasientrapportert resultat og helseøkonomi er en veletablert forskningsgruppe som utgår fra Avdeling for transplantasjon ved Oslo universitetssykehus. Gruppen har som mål å fremme forskning på pasienterfarte resultater og helseøkonomi og fungerer som et støttende forskningsnettverk for å bidra til forskning av høy kvalitet.

Bruk av mål på pasientrapporterte utfall er blitt et sentralt verktøy i kliniske studier. Helseøkonomiske analyser er viktig som grunnlag for prioriteringer i helsevesenet. Medlemmene i forskningsgruppen representerer et bredt fagfelt med en felles metodeforankring

About the group:

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

Hovedmedlemmer / Main members 2021:

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Assosierte medlemmer / Associated members 2021:

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Unn Inger Møinichen	Fysioterapeut	OUS	umoinich@ous-hf.no
Ingrid Harg	RN/Master	OUS	Ingrid.harg@ous-hf.no
Kristian Heldal	PhD Master Nefrolog	OUS	hkri@ous-hf.no

Aktivitet i 2021 / Activity in 2021 (selected)

- PROM-conference for researchers in HSØ organized by Research group for Quality of Life and Health Economics and PROMINET (82 participants)
- 4 regular meetings for main group members prepared with agenda beforehand and report thereafter
- 12 publications in peer reviewed international journals (authors are main group members)
- Oral - and poster presentations at international conferences (transplant conferences, health literacy conferences, quality of life conferences)
- Active collaboration with network partners (PROMINET, LIVSFORSK, OsloMet, UiO): 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.
- 2 Applications to Helse Sør Øst, 1 application to DAM, 1 application to NFR, a application to Life Science at UiO.

Ongoing research projects (selected):

- Testing the effect of a new health communication intervention for renal transplant recipients. A randomized controlled study.
- Developing and testing a physical training intervention for renal transplant recipients
- Health literacy in the context of renal transplant recipients

Forskningsaktivitet/ Research activity:

Andersen MH, Urstad KH, Larsen MH, Henrichsen GF, Engebretsen E, Ødemark J, Stenehjem AE, Reisaeter AV, Nordlie A, Wahl AK (2021). Intervening on health literacy by knowledge translation processes in kidney transplantation: A feasibility study. J Ren Care, 48 (1), 60-68
DOI 10.1111/jorc.12379, PubMed 34053202

Astrup GL, Rohde G, Rimehaug SA, Andersen MH, Bernklev T, Bjordal K, Falk RS, Jørgensen NMH, Stavem K, Tollisen A, Amdal CD, (2021). Comparing the use of patient-reported outcomes in clinical studies in Europe in 2008 and 2018: a literature review. Qual Life Res
DOI 10.1007/s11136-021-02946-7, PubMed 34350566

Borge CR, Larsen MH, Osborne RH, Engebretsen E, Andersen MH, Holter IA, Leine M, Wahl AK (2021)
Exploring patients' and health professionals' perspectives on health literacy needs in the context of chronic obstructive pulmonary disease. Chronic Illn, 1742395321999441
DOI 10.1177/1742395321999441, PubMed 33705224

Dahl KG, Wahl AK, Urstad KH, Falk RS, Andersen MH (2021). Changes in Health Literacy during the first year following a kidney transplantation: Using the Health Literacy Questionnaire. Patient Educ Couns, 104 (7), 1814-1822
DOI 10.1016/j.pec.2020.12.028, PubMed 33454146

Gulseth E, Urdal A, Andersen MH, Diseth T, Aksnes G, Emblem R, Wæhre A (2021)
High satisfaction on genital self-perception and sexual function in healthy Norwegian male adolescents. J Pediatr Urol, 17 (4), 555.e1-555.e8
DOI 10.1016/j.jpurol.2021.02.015, PubMed 33750647

Urstad KH, Wahl AK, Moum T, Engebretsen E, Andersen MH (2021). Renal recipients' knowledge and self-efficacy during first year after implementing an evidence based educational intervention as routine care at the transplantation clinic. BMC Nephrol, 22 (1), 265
DOI 10.1186/s12882-021-02468-x, PubMed 34266414

Wahl AK, Osborne RH, Larsen MH, Andersen MH, Holter IA, Borge CR (2021)
Exploring health literacy needs in Chronic obstructive pulmonary disease (COPD): Associations between demographic, clinical variables, psychological well-being and health literacy
Heart Lung, 50 (3), 417-424
DOI 10.1016/j.hrtlng.2021.02.007, PubMed 33618148
Amdal, Cecilie Delphin; Pe, Madeline; Falk, Ragnhild Sørum; Piccinin, Claire; Bottomley, Andrew & Arraras, Juan Ignacio [Vis alle 16 forfattere av denne artikkelen] (2021). Health-related quality of life issues, including symptoms, in patients with active COVID-19 or post COVID-19; a systematic literature review. Quality of Life Research. ISSN 0962-9343. DOI: 10.1007/s11136-021-02908-z.
Chen X, Badian RA, Hynne H, Amdal CD, Herlofson BB, Utheim ØA, Westgaard KL, Fineide F, Jensen JL, Utheim TP (2021). Alterations in meibomian glands in patients treated with intensity-modulated radiotherapy for head and neck cancer. Sci Rep, 11 (1), 22419
DOI 10.1038/s41598-021-01844-9, PubMed 34789830
Singer S, Hammerlid E, Tomaszewska IM, Amdal CD, Bjordal K, Herlofson BB, Santos M, Silva JC, Mehanna H, Fullerton A, Brannan C, Gonzalez LF, Inhestern J, Pinto M, Arraras JI, Yarom N, Bonomo P, Baumann I, Galalae R, Nicolatou-Galitis O, Kiyota N, Raber-Durlacher J, Salem D, Fabian A, Boehm A et al. (2021). Methodological approach for determining the Minimal Important Difference and Minimal Important 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 Qual Life Res
DOI 10.1007/s11136-021-02939-6, PubMed 34272632
Westgaard KL, Hynne H, Amdal CD, Young A, Singh PB, Chen X, Rykke M, Hove LH, Aqrawi LA, Utheim TP, Herlofson BB, Jensen JL (2021). Oral and ocular late effects in head and neck cancer patients treated with radiotherapy Sci Rep, 11 (1), 4026
DOI 10.1038/s41598-021-83635-w, PubMed 33597629
Miriam Evensen, Søren Toksvig Klitkou, Mette Christophersen Tollånes, Simon Nygaard Øverland, Torkild Hovde Lyngstad, Stein Emil Vollset, Jonas Minet Kinge, (2021). Parental income gradients in adult health: a national cohort study. *BMC Medicine* s. 1-14. doi: 10.1186/s12916-021-02022-4

Innovasjonsaktivitet/ Innovation:

Centre of Patient Reported Outcomes Research at Dep of Transplant Medicine, OUS, was established January 2021 aiming to stimulate and strengthen clinical PROM research within chronic kidney disease and kidney transplantation. In the centre two users representing The Norwegian organization for kidney patients and kidney recipients (LNT) collaborate systematically with the 6 researchers in planning and performing research project (www.protx.no).

Forskningsgruppe: Nevroendokrine svulster

Research group: Neuroendocrine tumors

Avdeling: Department for organ transplantation

Gruppeleder: Espen Thiis-Evensen

Om gruppen
Består av personer med interesse for nevroendokrine neoplasmer, hovedsakelig fra avdelinger som involvert i utredning, diagnostikk og behandling av nevroendokrine neoplasmer ved Oslo universitetssykehus

About the group
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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Håvard Bjørke Jenssen	LIS/ phd student	OUS	haajen@ous-hf.no

Activity in 2021:

Projects ongoing or finished in 2021:
1. Explain-study. Nordic study evaluating multiple tumor markers. Included 26 patients. Manuscript no 2. submitted
2. Evaluation of the treatment effect of the chemotherapy combination temozolomide/capecitabine5FU. Study started, data collection, 103 patients included.
3. The feasibility and outcome of D3-resection in patients with small intestinal tumors. Cooperation with Akershus University Hospital. Ongoing inclusion, so far 23 patients included.
4. Prevalence and incidence of neuroendocrine neoplasms in Norway. Data collected, data analyses in preparation
5. Radiofrequence ablation of pancreatic neuroendocrine tumors. Study sinitiated
6. Prognostic factors for development of disseminated disease in appendiceal neureondocrine tumors. Multinational study. Data collected. 4 patients included, paper submitted
7. The importance of serum concentration level of everolimus for treatment effect and occurrence of adverse events in treatment of patients with neuroendocrine tumors. Patients being included
8. An Open-Label Phase 2 Study of Surufatinib in Patients with Neuroendocrine Tumours in Europe. Inclusion active
9. Quality of live in PRRT treated patients, paper submitted
10. Carcinoid heart disease. Registration and evaluation of outcome after heart surgery. Data collection
12. Screening of individuals from families with high incidence of small intestinal NETs. Protocol in preparation.
13. Participation in the IMPRESS-study
14. Artificial intelligence in interpreting CT scans from patients with liver metastases
15. The effect of liver transplantation versus resection in patients with neuroendocrine tumors. Multicenter study. Paper submitted.
16. Blood-markers as prognosis of treatment with PRRT in patients with neuroendocrine neoplasms

Popular science

We have given a number of lectures for patients and had a number of posts in the membership magazine for the patient group with neuroendocrine cancer.

Other

Establishment of a new patient ebiobank.

Publikasjoner/ Publications

Janson ET, Knigge U, Dam G, Federspiel B, Grønbaek H, Stålberg P, Langer SW, Kjaer A, Arola J, Schalin-Jäntti C, Sundin A, Welin S, Thiis-Evensen E, Sorbye H. Nordic guidelines 2021 for diagnosis and treatment of gastroenteropancreatic neuroendocrine neoplasms. Acta Oncol. 2021 May 17:1-11. doi: 10.1080/0284186X.2021.1921262. Epub ahead of print. PMID: 33999752.

Department of Urology (URO)

- Infeksjon og inflammasjon i urologi/ Infections and inflammation in urology

- Prostatakreft/ Prostate Cancer

Research group: Infections and inflammation in urology

Department: Urology

Group leader: Truls E. Bjerklund Johansen

ABOUT THE GROUP:

The group represents a wide international research network of urologists, urology departments, universities, medical societies as well as physicians from related fields of medicine. The group overlaps with the European Section of Infections in Urology, a full section of the European Ass. of Urology. Our vision is to provide evidence-based answers to all relevant knowledge gaps in the field of genitourinary tract infections that has real-life impact on patients. Our mission is to build a sustainable, transparent, independent international research network capable to identify, design, organize and run research projects which target real life knowledge gaps related to urinary tract infections. Our strategic plan is to develop a full functional research network with adequate resources for long-term maintenance and development.

Main members:

NAME	POSITION/TITLE/ROLE	EMPLOYER/AFFILIATION	E-MAIL
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Riccardo Bartoletti	Ass. Member/ professor	Pisa, Italy	riccardo.bartoletti@hotmail.com
Tamara Perepanova	Ass. Member/ professor	Moscow, Russia	perepanova2003@mail.ru

Activity in 2020:

All our studies are based upon the annual Global Prevalence study on Infections in Urology, which is being run in about 130 countries and numerous side studies ie the SERPENS study on urosepsis, the GPIU.com study on cystitis and the GPIU side study on infective complications after prostate biopsy. SERPENS is the world`s largest study on urosepsis and results are due I 2021. The study focuses on risk factors, diagnostic criteria, disease course, mortality and post-sepsis morbidity. Results published by the group in 2020 and results that will be published in 2021, have led to a change in international guidelines recommendations on prostate biopsies. In 2020 the group has contributed with numerous publications related to Covid and to the diagnosis and follow-up of cystitis by means of a new symptom-score (ACSS) which is already approved by FDA. The group provides open access to research data on inflammation and infection in urology through its living textbook at http://books.publisso.de/publisso_gold/book/52

Selected publications by group members in 2020

Validation of the American English Acute Cystitis Symptom Score. Alidjanov JF, Naber KG, Pilatz A, Wagenlehner FM. Antibiotics (Basel). 2020 Dec 19;9(12):929. doi: 10.3390/antibiotics9120929. PMID: 33352734 Free PMC article.

Hyperbaric Oxygenation in the Treatment of Fournier's Gangrene: A Systematic Review. Schneidewind L, Anheuser P, Schönburg S, Wagenlehner FME, Kranz J. Urol Int. 2021;105(3-4):247-256. doi: 10.1159/000511615. Epub 2020 Dec 7. PMID: 33285541 Free PMC article. [Infectious diseases]. Kranz J, Wagenlehner FME. Urologe A. 2020 Dec;59(12):1461-1462. doi: 10.1007/s00120-020-01372-w. PMID: 33284371 Free PMC article. German. No abstract available.

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Forskningsgruppe: Prostatakreft

Research group: prostate cancer

Avdeling: Urologisk avdeling

Gruppeleder/groupleader: Viktor Berge

Om gruppen:

Forskningsgruppen i prostata kreft består av urologer og onkologer (hovedmedlemmer) og leger og basalforskere fra andre avdelinger og institutter (assosierte 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:

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:

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Eivor Hernes	PhD, consultant in nuclear medicin		

Aktivitet i 2021 / Activity in 2021

Forskningsaktivitet/ Research activity:

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 2021. Kirsti Aas, MD, defended her PhD thesis in February with the title *Prostate Cancer without Distant Metastases Treatment and Mortality in Norway 2001-16.* The PhD student Maciej Jacewicz is almost there preparing publication of his third paper.
Eduard Baco (MD, PhD) finished recruiting patients in the FARP (Focal prostate Ablation versus Radical Prostatectomy) study. This is a randomized controlled study not done before and the results are awaiting with great excitement.
The STORM (Salvage Treatment of OligoRecurrent Nodal Prostate Cancer Metastases) study also finished inclusion of patients. This is a randomized multisenter international study lead by Reino Heikkilä (MD, PhD).
The SPCG-17 study is recruiting well at our department with over 70 patients recruited so far into active surveillance for low risk and intermediate risk cancer prostate.
Last year our department arranged a national course for urological candidates about prostate cancer where many members in our group participated as teachers.

Populærvitenskapelig aktivitet/ Popular science:

Members in our group has been presenting lectures for PROFO, the Norwegian society for prostate cancer paitients

Innovasjonsaktivitet/ Innovation:

During the last year we intensified the work for changing our PROMS form into a digital format. We have collaborated with the University of Oslo and TSD (Tjeneste for sensitive data) we are now ready to go digital. The link for the digital PROMS will be sent to patients scheduled for radical prostatectomy together with the link for informed consent for inclusion in the registry and biobank. This link will be opened by the patients with two factor authentication.
Last year our group worked hard for expanding our radical prostatectomy register to also include patients treated with radical radiation therapy. We are on the right track, but not finished yet.

Research Institute for Internal Medicine (IMF)

- Immunregulering i aterosklerose og andre kardiometabolske sykdommer / Immune regulation in atherosclerosis and other cardio metabolic diseases
- Innflammatoriske biomarkører ved kardiovaskulære og metabolske sykdommer / Inflammatory Biomarkers in Cardiovascular and Metabolic Disease
- Eksperimentell leverforskning / Experimental hepatology (NoPSC)
- Inflammasjonssykdommers genomikk og metagenomikk / Genomics and metagenomics in inflammatory diseases (NoPSC)
- Immunopathogenetic mechanisms in immunodeficiency and infectious disorders

Forskningsgruppe: Immunregulering i aterosklerose og andre kardiometabolske sykdommer

Research group: Immune regulation in atherosclerosis and other cardio metabolic diseases

Avdeling: Institutt for Indremedisinsk Forskning

Gruppeleder: Bente Halvorsen

Om gruppen:

Vårt overordnede fokus i forskningen er på kardiovaskulær sykdom og relaterte metabolske sykdommer som diabetes, fedme og fettlever som er viktige årsaker til sykelighet og død over hele verden. Mer konkret er aterosklerose en tilstand som karakteriseres ved en kronisk inflammatorisk fenotype, mens hjerteinfarkt og hjerneslag, de direkte konsekvensene av aterosklerose, er akutte inflammatoriske tilstander. Disse lidelsene har mange fellestrekk, som for eksempel dyslipidemi og inflammasjon. Ved å studere disse prosessene ved hjelp av translasjonsforskning, der vi forbinder basal forskning og klinikk, ønsker vi å bygge et fundament for utvikling av ny diagnostikk og behandling for disse sykdommene. Vår forskningsgruppe arbeider i krysningen mellom molekylærbiologi og biokjemi, og kardiovaskulær, cerebrovaskulær og endokrin medisin. Vårt overordnede mål er å avdekke nye terapeutiske mål og biomarkører. Gruppen bruker et bredt spekter av metoder, alt fra analyser av blod og vevsprøver fra pasienter, til studier i genetisk modifiserte mus ved hjelp av avansert celle- og molekylærbiologi. Gruppen består av personer med forskjellig bakgrunn og inkluderer leger, ernæringsfysiologer, biokjemikere, molekylærbiologer og ingeniører. Den tverrfaglige kompetanse er en stor styrke i vår forskningsgruppe.

About the group:

Our overall research focus is on cardiovascular disease and related metabolic diseases such as diabetes, obesity and fatty liver which are major causes of morbidity and mortality worldwide. More specifically, atherosclerosis is a condition characterized by a chronic inflammatory phenotype, while myocardial infarction and stroke, the direct consequences of atherosclerosis, are acute inflammatory conditions. These disorders have many common features, such as dyslipidemia and inflammation. By studying these processes using a translational approach, where we connect basic research and clinic, we want to build a foundation for the development of new diagnostics and treatment for these diseases. Our research group works at the intersection between molecular biology and biochemistry, and cardiovascular, cerebrovascular and endocrine medicine. Our overall goal is to uncover new therapeutic goals and biomarkers. The group uses a wide range of methods, ranging from analysis of blood and tissue samples from patients, to studies in genetically modified mice using advanced cell and molecular biology. The group consists of people with different backgrounds and includes doctors, nutritionists, biochemists, molecular biologists and engineers. This interdisciplinary competence is a great strength of our research group

Hovedmedlemmer / Main members:

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Activity in 2021

Research activity:

As for all other parts of society, also our research has also this year been influenced by the Covid-19 pandemic. The pandemic results in new research opportunities, as we are involved in the analysis of NorSolidarity, the Norwegian part of the WHO-initiated treatment study of Covid-19 patients. Sequencing and metabolic mapping of the patients are key tasks for personnel in our group and some of the first results indicate that critical Covid-19 is associated with distinct leukocyte phenotypes and transcriptome patterns. The biobank with material from Covid-19 patients will in the coming years prove to be valuable for further understanding of the pandemic.

Despite much focus and effort has been dedicated to these tasks, we have also been able to pursue our regular research ranging from work on human mutations in the Sigirr genes, the role of complement in atherosclerosis, and deciphering the role of ENDOV. Below are some selected examples from advances in some of our projects during 2021:

T cells in obesity We investigate T cell function in metabolic regulation during obesity development to seek new treatment options. T cells can modulate macrophage function and adipocyte differentiation, which affects energy storage and utilization, leading to healthy or dysregulated metabolism. In 2021 we have performed several advanced animal studies leading us closer to pinpoint important mechanisms of how T cells affect whole body metabolism.

EU- projects We are actively participating in two EU projects. During 2021, *AtheroMacHete*, a long lasting project aiming to decipher the heterogeneity of macrophages in atherosclerotic plaques and to determine different functions of the cell types their contribution to disease development came to an end. Another project, *PainFact*, has the objective to investigate the connection of chronic pain, pain sensitivity and development of cardiovascular disease. In 2021 we conducted a large scale animal study to provide data and further material for the whole consortium in this project.

Complications of the Covid vaccines. During the spring2021, Norway and Denmark stopped the ChAdOx1 nCoV-19 vaccination after several reported cases of vaccine-induced syndrome of severe thrombosis and thrombocytopenia with fatal outcome. Through an intensive collaboration with other groups at the hospital, we were heavily involved in this work.

Samples from vaccine-induced immune thrombotic thrombocytopenia (VITT) patients allowed us to investigate mechanisms in this severe syndrome and we report immune complexes (ICs) with multi-pathway triggers, innate immune response cytokines, activation of neutrophils in the blood, and extensive formation of neutrophil extracellular traps (NETs) surrounded by IgG in a thrombus ectomized from the sagittal sinus vein. Our results shed light on the underlying mechanisms in this rare adenoviral vector vaccine-induced syndrome of severe thrombosis and thrombocytopenia and suggest that antibody-mediated thrombus formation in VITT patients is accompanied by a massive innate immune activation with particular activation of neutrophils, at least partly induced by IC-mediated mechanisms with NET formation as a major pathogenic event.

Complement activation in cardiovascular disease. Since a couple of years, we are interested in the role the complement pathway plays in cardiovascular disease. By using the biobank of our consultant Mona Skjelland we were able to measure that the complement system is activated in patients with carotid atherosclerosis. Furthermore, we published a paper on a partial activation of this system in heart failure patients.

The role of DNA repair enzymes in cardiovascular disease. For many years we have been studying the DNA Glycosylase, Neil3 and its relation to development of atherosclerosis. During 2021 we have extended our findings in this field by demonstrating that mice deficient in Neil3 have increased gut permeability, which contributes to a pro-atherogenic metabolic

phenotype. These findings further demonstrate that Neil3 have functions beyond the traditional role in DNA damage repair.
In another project focusing on DNA damage and cardiovascular disease, we published evidence of a pathophysiological mechanism that connects mitochondrial DNA damage to cardiac dysfunction via reduced NAD+ levels and loss of mitochondrial function and communication. Using a transgenic model, we demonstrate that high levels of cardiomyocyte mtDNA damage cause a reduction in NAD+ levels due to extreme DNA repair activity, causing impaired activation of NAD+-dependent SIRT3, and ultimately mitochondrial dysfunction.

Popular science:

Members from our group, Xiang Yi Kong, Ida Gregersen and Maria Belland Olsen, have during 2021 established the podcast “Labprat” where they every week present research from our field in a form accessible for all. The podcast is free and available on most platforms, and have during the year become among the most popular in the field of medical sciences here in Norway.

Forskningsgruppe: Innflammatoriske biomarkører ved kardiovaskulære og metabolske sykdommer

Avdeling: Research Institute of Internal Medicine

Gruppeleder: Thor Ueland, Group Leader, Research Scientist; PhD

About the group:

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 focusing on cardiovascular disease and risk, 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. A focus in these studies is investigating the impact of Wnt signaling and secreted Wnt antagonist in these conditions.

We have a close collaboration with the endocrine unit, analyzing inflammatory markers in patients characterized by growth hormone deficieny (GHD) and excess (acromegaly) as well as gluccocorticoid excess (Cushing syndrome). We also have a tight collaboration with the women and children center evaluating the impact of systemic inflammation in pregnancy on future cardiovascular and metabolic risk. These studies investigate the association between hormones and inflammatory mediators and impact on metabolic disturbances in different target tissues such as adipose tissue and bone with special focus on glucose metabolism.

We have a tight collaboration with the Psychosis Research Centre Thematically Organized Psychosis Research (TOP) group, analyzing inflammatory biomarkers in patients with schizophrenia and bipolar disorder. In these studies we focus on markers in serum/plasma as well as mRNA levels in circulating immune cells that may reflect neuroinflammation and further, investigate associations with immune-related candidate risk genes within the major histocompatibility complex, identified by genome-wide association studies (GWAS).

In addition, we have strong collaborations with other clinical research, national and international.

Hovedmedlemmer / Main members:

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Activity in 2021:

31 publications from main group members in 2021

Selected articles for 2021:

1: Lekva T, Roland MCP, Estensen ME, Norwitz ER, Tilburgs T, Henriksen T, Bollerslev J, Normann KR, Magnus P, Olstad OK, Aukrust P, Ueland T. Dysregulated non-coding telomerase RNA component and associated exonuclease XRN1 in leucocytes from women developing preeclampsia-possible link to enhanced senescence. Sci Rep. 2021 Oct 5;11(1):19735. doi: 10.1038/s41598-021-99140-z. Erratum in: Sci Rep. 2021 11:22572. PMID: 34611223

2: Holm S, Kared H, Michelsen AE, Kong XY, Dahl TB, Schultz NH, Nyman TA, Fladeby C, Seljeflot I, Ueland T, Stensland M, Mjaaland S, Goll GL, Nissen-Meyer LS, Aukrust P, Skagen K, Gregersen I, Skjelland M, Holme PA, Munthe LA, Halvorsen B. Immune complexes, innate immunity, and NETosis in ChAdOx1 vaccine-induced thrombocytopenia. Eur Heart J. 2021 42:4064-4072. PMID: 34405870

3: Aarsetøy R, Ueland T, Aukrust P, Michelsen AE, de la Fuente RL, Pönitz V, Brügger-Andersen T, Grundt H, Staines H, Nilsen DWT. Angiopoietin-2 and angiopoietin-like 4 protein provide prognostic information in patients with suspected acute coronary syndrome. J Intern Med. 2021 290: PMID: 34237166.

4: Reponen EJ, Tesli M, Dieset I, Steen NE, Vedal TSJ, Szabo A, Werner MCF, Lunding SH, Johansen IT, Rødevand LN, Andreassen OA, Ueland T. Adiponectin Is Related to Cardiovascular Risk in Severe Mental Illness Independent of Antipsychotic Treatment. Front Psychiatry. 2021 12:623192. PMID: 34122163

5: Ueland T, Astrup E, Otterdal K, Lekva T, Janardhanan J, Prakash JAJ, Thomas K, Michelsen AE, Aukrust P, Varghese GM, Damås JK. Secreted Wnt antagonists in scrub typhus. PLoS Negl Trop Dis. 2021 15:e0009185. PMID: 33914733

6: Broch K, Anstensrud AK, Woxholt S, Sharma K, Tøllefsen IM, Bendz B, Aakhus S, Ueland T, Amundsen BH, Damås JK, Berg ES, Bjørkelund E, Bendz C, Hopp E, Kleveland O, Stensæth KH, Opdahl A, Kløw NE, Seljeflot I, Andersen GØ, Wiseth R, Aukrust P, Gullestad L. Randomized Trial of Interleukin-6 Receptor Inhibition in Patients With Acute ST-Segment Elevation Myocardial Infarction. J Am Coll Cardiol. 2021 77:1845-1855. PMID: 33858620.

7: Ueland T, Abraityte A, Norum H, Varathalingam S, Gullestad L, Aukrust P, Andreassen AK. Circulating regulators of the wingless pathway in precapillary pulmonary hypertension. Respirology. 2021 26:574-581. PMID: 33830565.

8: Ueland T, Dyrhol-Riise AM, Woll BM, Holten AR, Petteresen F, Lind A, Dudman SG, Heggelund L, Holter JC, Aukrust P. Increased inflammatory markers reflecting fibrogenesis are independently associated with cardiac involvement in hospitalized COVID-19 patients. J Infect. 2021 82:186-230. PMID: 33516748

9: Sikkeland LIB, Qiao SW, Ueland T, Myrdal O, Wyrożemski Ł, Aukrust P, Jahnsen FL, Sjåheim T, Kongerud J, Molberg Ø, Lund MB, Bækkevold ES. Lung CD4+ T-cells in patients with lung fibrosis produce pro-fibrotic interleukin-13 together with interferon-γ. Eur Respir J. 2021 57:2000983. PMID: 33154027.

10: Ueland T, Heggelund L, Lind A, Holten AR, Tonby K, Michelsen AE, Jenum S, Jørgensen MJ, Barratt-Due A, Skeie LG, Nordøy I, Aanensen Fraz MS, Quist-Paulsen E E, Pischke SE, Johal SK, Hesstvedt L, Bogen M, Fevang B, Halvorsen B, Müller F, Bekken GK, Mollnes TE, Dudman S, Aukrust P, Dyrhol-Riise AM, Holter JC. Elevated plasma sTIM-3 levels in patients with severe COVID-19. J Allergy Clin Immunol. 2021 147:92-98. PMID: 32971109

Forskningsgruppe: Eksperimentell leverforskning

Research group: Experimental hepatology

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.

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.

Hovedmedlemmer / Main members:

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Activity in 2021

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 2021 the group consisted of the group leader, three senior researchers, three postdocs, five PhD students, the lab manager, one full-time technician and one part-time technician. Following Anne Pharo's retirement, Oda Helgesen Ramberg took over the lab-manager responsibility. The 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. In 2021 our use of techniques from regenerative medicine further increased and we also started using sequencing-based methodologies. Together with patient material, animal models and in vitro assays these additional techniques give us a comprehensive and complete scientific toolbox for achieving our aims.

During the last years one of our major lines of research has been to clarify the regulatory role of unconventional T-cells in bile duct inflammation and in 2021 we published a report demonstrating the presence of antigens activating natural killer T (NKT)-cells in bile. Similarly, we also demonstrated in another project that antigens for mucosal associated

invariant T (MAIT)-cells are also present in bile and are defined by the microbiome. The role of the immune system during cholestasis has been a key interest in the team focusing on NKT-cells and in 2021 we expanded these projects by investigating the temporal and spatial development and specifically the contribution of the immune system using tissue transcriptomics. Another major topic of our immunology studies has been the role of CD100, which we have found to regulate cholangitis in a familiar form of PSC, and in 2021 a large collaborative paper reporting on a novel mutation in CD100 causing disease in mice and humans were published in Science Translational Medicine. In our studies using germ-free animals we have performed a range of large animal experiments to evaluate the effect on bacterial metabolites on immune system development. To aid the characterization of immune cells from these mice we have started using high-dimensional flowcytometry with 25-colors using the BD Symphony located at the flow-cytometry core facility. The organoid and bile-duct-on-a-chip projects were further strengthened last year by the recruitment of Enya Amundsen-Isaksen as an engineer and the recruitment for the first postdoc in the Research Council of Norway funded project DUCTchip was initiated at the end of the year.

A major event for the group was the excellent defense and celebration of Natalie Lie Berntsen's thesis on June 4th with the title "*The role of natural killer T cells in biliary immunology and disease".* Professor Ye Oo from the University of Birmingham acted as the first opponent and Professor Susanna Cardell for the University of Gothenburg as the second opponent, and their complementary background in NKT-cells, immunology in general and hepatology led to a very interesting discussion. After being awarded a combined position with research and clinical work from her department, previous PhD student Elisabeth Schrumpf rejoined the group to work on unconventional T-cells in our ongoing projects, while at the same time developing her own research agenda related to unconventional T-cells and skin inflammation. 2021 also marked the well-deserved retirement of lab-manager Anne Pharo, who has been instrumental in establishing all current methods in the group and especially those related to experimental animal models. Although Anne will be greatly missed by all group-members, she leaves a strong and solid foundation for smooth running of the lab that we will build on in the years to come. We wish her a very happy retirement.

In June the INFLAMMABILE grant was funded by the Research Council of Norway grant with 12 mill NOK. In this project we will examine bile duct inflammation in PSC patients and mouse models at different time points using spatial sequencing and 3D immunohistochemistry. The grant was a collaboration with Brian Chung in the genomics group at NoPSC and the grant now funds a senior scientist position in the experimental group that Brian started in December. Markus Jördens joined the team working on sequencing based techniques in September as a PhD student funded by the German Krebshilfe foundation and his project will also encompass examination of the spatial transcriptome of cholangiocarcinoma.

Innovation:

Submitted our first DOFI

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 betennelsessykdommer, med et særlig fokus på leversykdommen primær skleroserende cholangitt. Vi studerer tarmfloraen særlig ved hjelp av genetiske (sekvensering) og biokjemiske (metabolittundersøkeleser) 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. 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.

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Activity in 2021:

Research activity:

The overall research agenda and strategies are 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 over 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. In 2021, the final version of our first full metagenomic (i.e. sequencing of all microbial genes) in PSC was published. The study identified major metabolic alterations of the microbiome in patients with this disease, in particular related to essential nutrients like some B vitamins (B6) and amino acids. Following these observations, corresponding differences in these metabolites in blood were seen, suggesting that microbiome sequencing followed by targeted metabolomics may be on way to identify altered microbial functions in disease. Ongoing work starts at the other end, by unbiased screening for alterations of microbial metabolites in blood. Similar strategies have been or are employed in other disease states where we are we have been 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. Significant progress was made in 2021 related to the importance of e.g. vitamin B6. In parallel, we have now together with the Melum group initiated an agenda using experimental animal models 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. We are now initiating a first clinical trial in PSC based on our own observations (vit B6 supplementation). Clinical trials targeting the gut are important in our Strategic research area. In 2021, a unit for microbiota therapy was established in our department, in collaboration with other groups at the hospital. This will be important for the further development of clinical microbiota medicine at our hospital.

Notably, the group activities also try to answer other questions, including 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 2021 include the successful PhD defense of Cristiane Mayerhofer and her thesis "Targeting the Gut Microbiota in Heart failure. Our first hybrid version of the National Microbiota Conference (no. 8 since 2014) was also successful hosted in November 2021.The Strategic research area of Oslo University Hospital – "Personalized microbiota therapy in clinical medicine" hired an expert in fecal microbiota transplantation in part time position and with this we have gained significant momentum towards our goal in this area.

Popular science:

The group contributed to a limited number popular science activities in 2021, including a microbiota-focused podcast by our institute podcast team ("Labprat"): https://labprat.podbean.com/e/12-mikrobiota-vare-trofaste-følgesvenner/ (Norwegian). The group leader Hov was also featured in a full-page on the future of medicine and gut microbiota in The Times https://www.thetimes.co.uk/article/why-the-future-of-medicine-

is-all-in-your-gut-n5vq9d9dd (April 13, 2021, paywall). He has also contributed to a series of patient-directed digitial information videos on autoimmune liver diseases available at YouTube, e.g. https://www.youtube.com/watch?v=hiAbC9NeyQ0

Research group: Immunopathogenetic mechanisms in immunodeficiency and infectious disorders

Avdeling: Research Institute for Internal Medicine

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 HIV 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 clinic, in particular Section of Clinical Immunology and Infectious Diseases at OUS, with access to a wide range of immunological methods through extensive collaboration with other groups

Hovedmedlemmer / Main members:

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

NAME	POSITION/TITEL/ROLE	EMPLOYER/AFFILIATION	E-MAIL
Stig S Frøland	Professor emeritus		s.s.froland@medisin.uio.no

Activity in 2021:

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.
- Targeting the NLRP3 inflammasome in HIV infection. The research institute has a strong track record on HIV-research, and this has been continued with Hedda Hoel's PhD project that have looked at the NLRP3 inflammasome as a driving force of the systemic inflammation seen in HIV-infected patients. Hoel successfully defended her PhD in June, with a thesis that also included work on Covid-19. The NLRP3 inflammasome has been studied in cardiovascular disease by other groups at our institute, and the current project is an excellent example of how immunological insight gained from the study of one disease can be applied to new diagnoses. The project is led by Marius Trøseid who is also the main supervisor.
- Functional consequences of novel genetic variations in primary immunodeficencies 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.