Oslo University Hospital

Comprehensive Cancer Centre

ANNUAL REPORT 2020

Oslo University Hospital

Comprehensive Cancer Centre (OUS CCC)

OECI Comprehensive Cancer Centre

UiO : University of Oslo

Oslo University Hospital Comprehensive Cancer Centre

The Comprehensive Cancer Centre (CCC) concept is vital for the consistent delivery of high-level quality of care, education and research within the cancer field. This annual report summarizes selected achievements of OUS-CCC in 2020.

2020 was the year of the pandemic. Although less seriously affected than most other countries, we experienced for the first time a reduction in the number cancer patients diagnosed or treated and we will follow the situation carefully evaluating the impact on the prognosis for our patients. With this perspective, I am very happy to report that we reached our goal to increase both the fraction (14.5 %) and number of patients (n= 1402) recruited to clinical trials in 2020.

For 2020, I would also highlight the breakthrough we experienced in molecular pathology/precision oncology in Norway with OUS-CCC as a key driver. This breakthrough includes the clinical study, IMPRESS-Norway, with participation from all hospitals in Norway with oncology department, and the affiliated national infrastructure (InPreD) for experimental molecular pathology. Both initiatives were designed, approved and funded in 2020. At the institutional level, gene panels for both solid tumours and myeloid malignancies are in use for standard molecular diagnostics, a major concern from the OECI audit team back in 2017, currently solved.

OUS has struggled with the national flow-time standards for Cancer Patient Pathways (CPP). A change took place in fall 2019 and the results for 2020 are overall very satisfying. Especially the flow-times for the three gynaecological pathways have improved substantially. Systematic and good work from several actors including coordinators, pathways leaders and the governance structure established with the CCC board, are key factors for this success. We will continue this work, and a focus for 2021 is pathways between hospitals where OUS will take an overall coordinating responsibility in the Health Region.

We started the CCC-reaccreditation process in 2020 and based on recently developed OECI quality standards, we will focus on five topics for 2021-22:

- An institutional model for training and education of nurses working with cancer patients
- An infrastructure for and systematic reporting from quality registers covering all cancer types
- Improvements in shared decisions making for patients
- Development of a management system with a data-dashboard presenting a compiled set of variables on cancer
- Action plan for cancer survivorship

Cancer research is a cornerstone for OUS CCC. I think we have three areas with special potential for therapy improvement. That is precision oncology, cellular immunotherapy and proton therapy. We are on the right track for all these areas, but we need to stay focused and be able to prioritize to achieve the full potential and improve therapy for our patients.

OUS CCC has an ambition to be a leading cancer centre in Europe. The new clinical building with a proton centre that will open in spring 2024 at the Radium Hospital is an important step to fulfil this ambition. In addition, as OUS-CCC includes cancer activity at several campuses, we will develop a comprehensive cancer plan also including Rikshospitalet and Aker.

Prof. Sigbjørn Smeland MD
Head, Division of Cancer Medicine
Chair, OUS CCC Board

Content

OUS CCC

Patient Treatment

Research

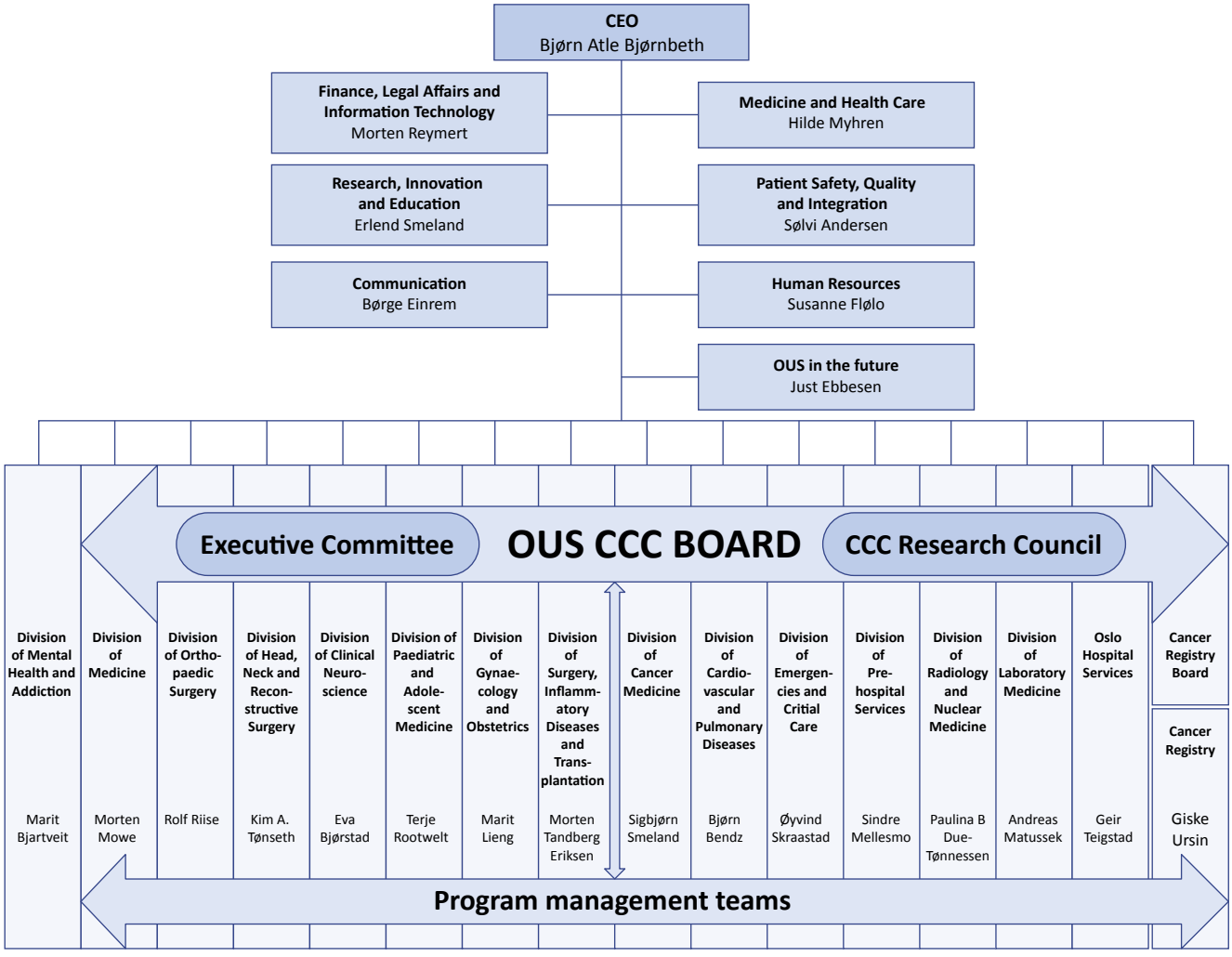
Cancer Strategy

Vision: OUS will be a leading cancer centre in Europe.
Mission: We are a complete cancer centre and the hub of Norwegian cancer care.
We are developing the hospital of the future in cooperation with our patients.

The OUS Cancer Centre's most important strategic measures from 2017-2022:

1. Strengthen the information, education and involvement for patients at all stages in illness
2. Develop standardised pathways for all patient groups
3. Gather the same type of patient treatment in one location in OUS and improve the infrastructure, including new buildings and a proton centre
4. Increase the use of personalised diagnostics as the basis for correct treatment, and to avoid over- and under-treatment
5. Further develop work-sharing with other hospitals
6. Develop existing and establish new prioritized areas of research with particular international impact or potential
7. Increase the number of clinical studies and patient accrual to trials
8. Establish national and enterprise-based quality registers for all cancer groups
9. Establish IT solutions which facilitate quality improvement and improve patient security, support patient pathways, and support research
10. Increased commitment to primary and secondary prevention of cancer in cooperation with the Cancer Registry
11. Establish institutional governance for the CCC
12. Set the agenda for public discussion of cancer in Norway

OUS Management Structure



CCC Board

The CCC board contributes to strengthening the line managements' power of action across organisational divides and where activities are located. This is strived for by strengthening the overall ability to coordinate work with operational challenges and the development and implementation of the cancer strategy. The work includes diagnostics, treatment, research, care, and rehabilitation.

Main focus areas in 2020:

- Cancer patient pathways (CPPs)
- Biobank
- Clinical quality registries
- Dialogues with pathway teams
- Developing the role of cancer coordinators
- Collaboration with other hospitals
- Precision medicine
- Myeloid gene panels
- New Radium Hospital
- Tools for shared decision making
- Cancer competence plans
- Cancer patients pathways home-to-home
- Governance systems focused on cancer

CCC Board

- Prof. Sigbjørn Smeland MD, Head, Division of Cancer Medicine (Chair)
- Assoc. Prof. Morten Tandberg Eriksen MD, Head, Division of Surgery, Inflammatory diseases and Transplantation
- Prof. Andreas Matussek, Head, Division of Laboratory Medicine
- Paulina Due-Tønnessen MD, Head, Division of Radiology and Nuclear Medicine
- Hilde Myhren, MD PhD, Medical Director, OUS
- Elin Henriksen, Head, Department of Gastro- and Paediatric Surgery
- Prof. Åslaug Helland MD, Head of Research, Division of Cancer
- Per Magnus Mæhle, Secretary, Division of Cancer Medicine

Professional council

- Torill Krøvel, Senior advisor, Staff Division of Surgery, Inflammatory diseases and Transplantation
- Prof. Giske Ursin, Director, The Cancer Registry of Norway
- Prof. Geir Tjønnfjord MD, Head, Department of Haematology
- Prof. Emeritus Gunnar Sæter MD, Senior Advisor, Division of Cancer Medicine
- Tove Nakken, Head, The OUS Patient Council
- Erik Rokkones MD, Head, Department of Gynaecological Cancer
- Prof. Stein Kaasa MD, Head, Department of Oncology
- Ying Chen MD, Head, Department of Pathology
- Prof. Kjetil Taskén MD, Head, Institute for Cancer Research, Division of Cancer Medicine
- Prof. Ellen Ruud MD, Head, Department of Paediatric Oncology and Haematology
- Ole-Jacob Norum, Head, Department of Cancer Orthopaedics
- Bjørn Wølstad-Knudsen, Union representative, Norwegian Union of Municipal and General Employees
- Aasmund Bredeli, Union representative, The Norwegian Medical Association
- Svein Erik Urstrømmen, Union representative, Norwegian Nurses Organisation

CCC Research Council

The CCC Research Council at OUS aims at contributing to comprehensive, optimal use and further development of the OUS potential within the field of cancer research. The scope of the Research Council includes clinical research, translation-research, foundation research and research-based innovation. The Research Council at OUS will work based on specific tasks from the CCC Board at OUS, but have several projects areas with an independent initiative.

Main focus areas in 2020:

- Inclusion in clinical studies
- Time allocated to clinicial research
- Precision Cancer Medicine
- Translational studies
- Biobank

CCC Research Board

- Prof. Åslaug Helland MD, Head of Research, Division of Cancer Medicine (Chair)
- Prof. Tom Hemming Karlsen MD, Head of Research, Division of Surgery, Inflammatory diseases and Transplantation
- Prof. Kristin Bjordal MD, Head, Department of Research Support, Oslo Hospital Services
- Prof. Kjetil Taskén MD, Head, Institute for Cancer Research, Division of Cancer Medicine
- Tove Nakken, Head, The OUS Patient Council
- Prof. Ellen Ruud MD, Head, Department of Paediatric Oncology and Haematology
- Prof. Bodil Bjerkehagen MD, Head, Department of Pathology, Division of Laboratory Medicine
- Prof. Stein Kaasa MD, Head, Department of Oncology
- Tom Børge Johannesen, PhD, Research Department, The Cancer Registry
- Prof. Dag Kvale MD, Institute leader, Med. Faculty, UiO
- Prof. Lars Eide, Head of Research, Division for Laboratory Medicine
- Prof. Emeritus Gunnar Sæter MD, Senior Advisor, Division of Cancer Medicine
- Anders Øverbye, PhD, UiO
- Per Magnus Mæhle, Secretary, Division of Cancer Medicine

SCIENTIFIC ADVISORY BOARD

- Prof. Josep Tabernero, Vall d'Hebron Institute of Oncology, Barcelona (Chair)
- Prof. Carl-Henrik Heldin, University of Uppsala and Chairman of the Board, The Nobel Institute
- Prof. Mef Nilbert, Director of Research, Danish Cancer Society, Copenhagen
- Prof. Kjeld Schmiegelow, Professor of Paediatrics and Paediatric Oncology, University Hospital Rigshospitalet, Copenhagen
- Prof. Jenny Chang-Claude, Division of Cancer Epidemiology, DKFZ Heidelberg
- Prof. Fabien Calvo, Chief Scientific Officer, Cancer Core Europe and Institut Gustave Roussy
- Prof. Inger Sandlie, Institute of Biosciences, University of Oslo

SAB visit

During 2020, the CCC Research Council planned for the SAB visit held in February 2021. The planning included a particular focus on five themes:

- Precision cancer treatment
- Molecular diagnostics
- Cancer biobank
- Increased clinical research activity and quality
- Immunotherapy including cell based techniques

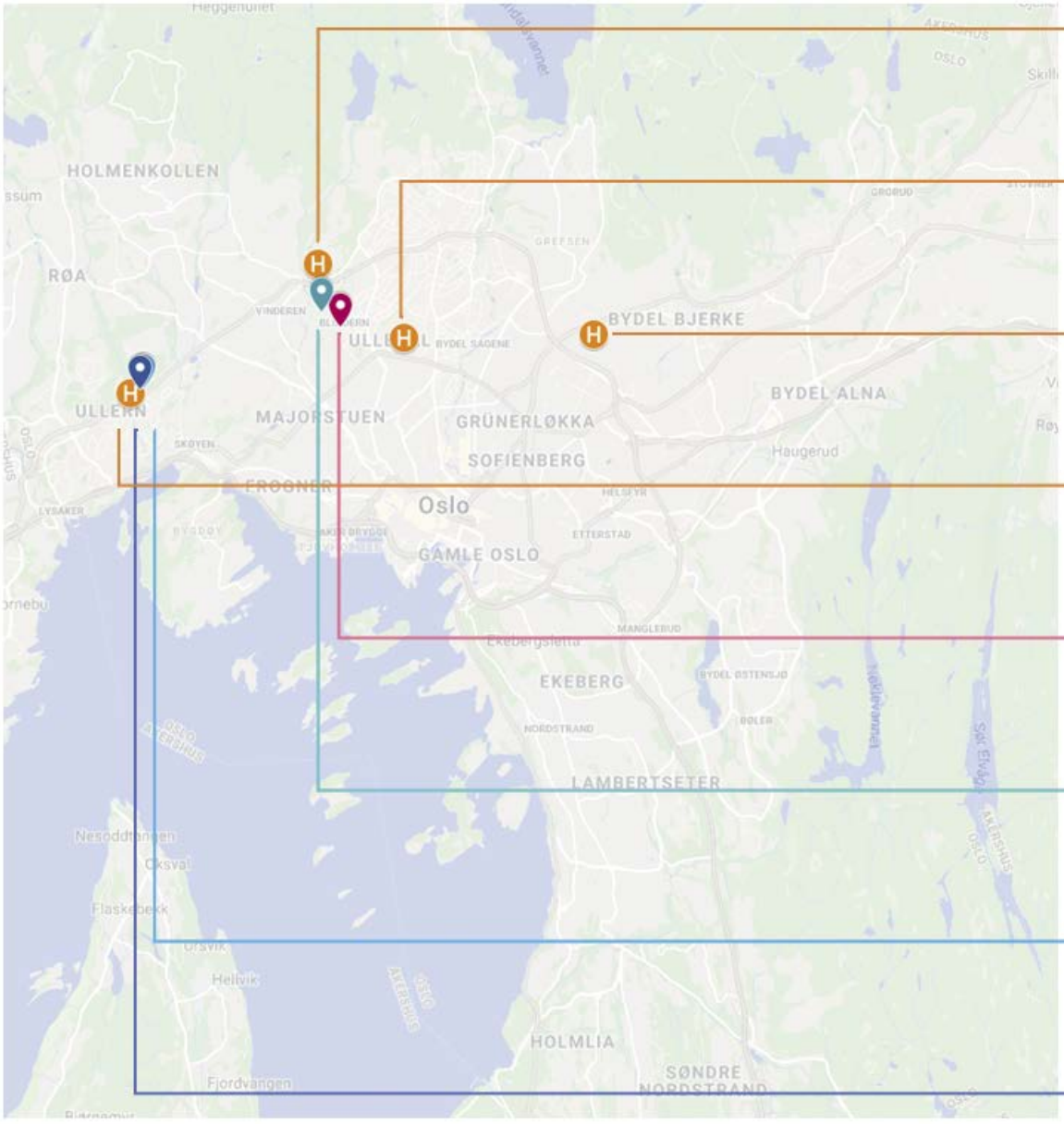
Collaborating Partners

University of Oslo (UiO)
OUS has close organizational links with a number of faculties at the University of Oslo, in particular the Faculty of Medicine and The Faculty of Natural Sciences. Around 100 of the Cancer division's employees are also employed by The University of Oslo's Faculty of Medicine, teaching medical students in six of the twelve semesters. Guest students are also received from other universities in Norway and from abroad. OUS is the major institution for specialized training in oncology for physicians and nurses in Norway. The close collaboration between the hospital and University of Oslo is an important platform for this.

Oslo Cancer Cluster (OCC)
OCC is an oncology research and industry cluster dedicated to improving the lives of cancer patients by accelerating the development of new cancer diagnostics and treatment. OCC is a national non-profit member organization with about 90 members, including OUS CCC along with other Norwegian and international companies, research and financial institutions, university hospitals and organizations – all working in the cancer field. OCC represent the entire oncology value chain, doing everything from exploratory research to selling therapeutics and diagnostics to global markets.

Cancer Registry of Norway
The Cancer Registry of Norway is part of South-Eastern Norway Regional Health Authority and is organized as an independent institution under Oslo University Hospital Trust, with its own board. The Cancer Registry of Norway, consisting of about 40 researchers, collects data and produces statistics of the cancer prevalence in Norway, and has an extensive research activity. They also got the administrative responsibility for the public screening programmes in Norway.

Inven2
Inven2 is Norway's largest player in the commercialization of research and is owned by the University of Oslo and Oslo University Hospital. Inven2 is the next generation of innovation company, established to safeguard and further develop Norwegian innovation, building bridges between outstanding research and the industry of the future.



Rikshospitalet

Ullevål Hospital

Aker Hospital

Radium Hospital

UiO : University of Oslo

inven2

OSLO CANCER CLUSTER

CANCER Registry of Norway

Major Events 2020

- Norwegian Cancer Society funded European Palliative Care Research Centre (PRC)
- Norwegian Cancer Society funded (15 mill NOK) to national expert group on pancreas cancer, led by OUS pathologist prof. Caroline Verbeke
- Norwegian Cancer Society funded (15 mill NOK) to national expert group on lung cancer, led by OUS oncologist prof. Åslaug Helland
- Advanced home hospital apartments for bone marrow transplant patients opened
- Pink ribbon research funding (25 mill NOK)
- OUS research article prize to Marina Vietri, Institute for Cancer Research (Vietri et al. 2020, Nature Cell Biology)

- Stein Kaasa, Head of Dept. of Oncology and Chair of European Palliative Care Research Centre (PRC) rewarded Vittorio Ventafridda memorial lecture from European Association for Palliative Care (EAPC)
- OUS researchers funded with 59 mill NOK from Norwegian Cancer Society
- OUS led study on precision medicine in oncology, IMPRESS-Norway, funded with 50 mill NOK from KLINBEFORSK program
- Public and private actors tied together in CONNECT to promote precision medicine in oncology
- OUS research article prizes from CCC, fall, to Jakob Skalleberg, Department of Otolaryngology, Head and Neck Surgery (Skalleberg et al. 2020, The Laryngoscope) and Eivind Heggernes, Institute of Cancer Research (Heggernes Ask et al. 2020, Med)

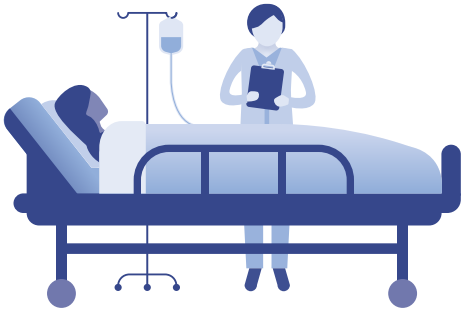
Core Activity Data

Patient Treatment

Number of cancer patients:
28 141

Total number of new cancer patients refferred to OUS:
9 646

Number of outpatient consultations:
122 560



Number of beds:
309

Number of over-night stays:
76 169

Number of chairs:
77

Chemotherapy treatments:
51 955

Radiotherapy: treatment series:
6 562

Radiotherapy: number of fractions:
98 513

Radiotherapy: number of patients:
6 530

* Number of radiology examination requests for cancer patients

MRI scans:
8 842

CT scans:
18 940

Radiology examinations:
62 129

Cytology:
9 892

Histology:
41 530

Molecular pathology:
13 896

Key Indicators in Research

Total number of peer-reviewed publications (with OUS-CCC first or last author):

768 (399)

Number of publications with impact factor >10 (with OUS-CCC first or last author):

104 (31)

Number of publications with impact factor >20 (with OUS-CCC first or last author):

42 (9)

Budget: estimate of research budget (by parameters):

750 mill. kr

Completed Ph.D. degrees:

23

Disclosures of Invention (DOFIs):

26

Active projects funded by EU (H2020):

12

Approx. Total number of FTEs in cancer research:

550

Number of active clinical trials:

223

Percentage of new patients included in clinical trials

14.5

Number of new patients included in clinical trials

1402

Patient Satisfaction

In 2020, 12 000 cancer patients replied to OUS' web-based survey. Results show overall high satisfaction scores (>90%). In addition, 2500 patients left valuable comments. The feedback conveys important information on what we should improve and what we should continue to do. Reports are provided monthly for continuous improvement. In 2020, the corona pandemic colored many of the comments.

«Fantastic personnel. I was taken seriously both as a human being and a patient with medical challenges. A calm atmosphere in the department despite the corona situation. Behavior and treatment approach provided reassurance"

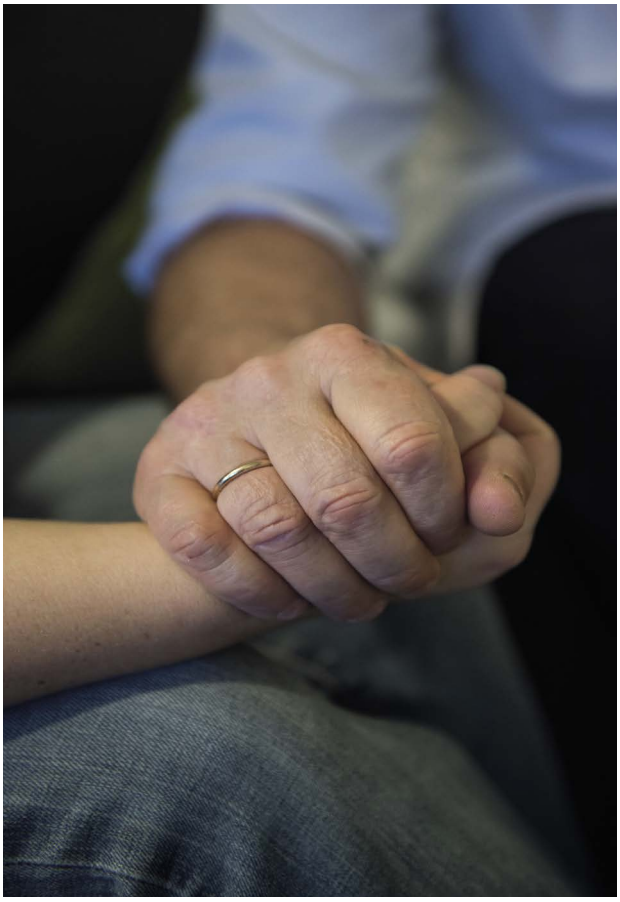
Breast cancer patient

«Phone consultations during the pandemic worked very well, however it's not the same as a physical consultations. This was a checkup consultation and thus it worked out well. The clinician was good at explaining and listening"

Prostate cancer patient

"I have been in contact with fantastic doctors and other health personnel at the hospital. I feel very confident that I am receiving the best possible medical treatment they can provide"

Lung cancer patient



Patient Reported Outcomes in the Cancer Registry of Norway (CRN)

Ylva Gjelsvik

As the number of cancer survivors in the population rises, it becomes increasingly important to gain more knowledge on the burden of adverse effects and the health related quality of life among people who have been treated for cancer. This information may also guide future cancer patients and their doctors in the treatment decision if they are faced with two or more options with similar expected survival effect, but different adverse effects.

Therefore, the CRN now collects patient reported outcomes on adverse effects and health related quality of life (HRQoL) through questionnaires consisting of PROMs (Patient Reported Outcome Measures) and PREMs (Patient Reported Experience Measures) instruments. The PROMs/PREMs data are included as part of the CRN's clinical registries, which already contain detailed data on the treatment of different cancer types. PROMs/PREMs results on hospital level are published in the yearly reports from the clinical registries.

Shortly after diagnosis, all patients diagnosed with prostate cancer, breast cancer, colorectal cancer or melanoma are invited to a longitudinal three-year national survey on health and quality of life. PROMs/PREMs collections among lung cancer, gynaecological cancer and lymphoma are being planned. The CRN uses validated PROMs instruments developed by the European Organisation for Research and Treatment of Cancer (EORTC). The EORTC QLQ-C30 is used for all cancer types together with the cancer specific modules (EPIC-26 is used as the cancer specific module for prostate cancer).

The survey is digital and everyone is invited through the official Norwegian health portal Helsenorge.no, or via an official digital mailbox (Digipost/e-boks). Participants log in safely by using for instance a bank issued electronic identity. The data collection is based on informed consent and Forskrift om befolkningsbaserte helseundersøkelser.

So far, the CRN reaches around 80% of cancer patients overall, except for colorectal cancer patients (69%). The response rates for breast cancer and prostate cancer patients invited in 2020 was 52% and 55%, respectively. The CRN is working together with clinicians and user organisations to improve the response rates.

Cancer Care and Research during the COVID-19 Pandemic

Treatment

The incidence of some cancers declined during 2020 (The Cancer Registry), and this is also seen in the activity reports from our CCC. We see a steep decline in newly diagnosed cancer patients in the spring and early summer 2020.

In addition, we have experienced a decline in number of lung cancer patients treated with radiotherapy. This might be due to many factors and will be investigated further.

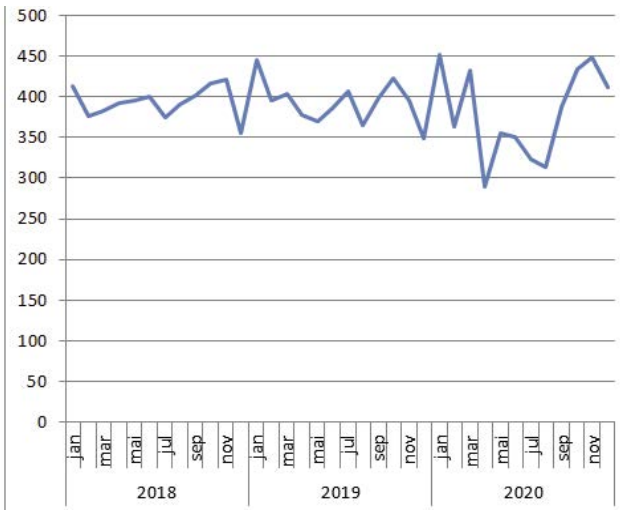


Figure. Number of newly diagnosed cancer patients

Research

With the uncertainty inflicted by the pandemic, inclusion was halted in many of our ongoing clinical trials in March 2020. However, this pause was only for some weeks, and our numbers indicate a high activity in clinical studies in 2020, with an all-time high inclusion rate.

Home offices and virtual meetings on Zoom, Skype, Teams etc have been dominating in 2020. This has had consequences for laboratory work, and many students, postdocs and researchers have experiences delays in their research progress. Although the numbers of publications for 2020 were high, the effects of the pandemic might appear in the numbers for 2021 and 2022.

Through a collaborative study with the Cancer Registry of Norway, we investigated the impact of COVID-19 in cancer patients in a population-based study using Norwegian registry data. The study was published in Frontiers in Oncology, and revealed that fatality rate of COVID-19 among cancer patients was similar to non-cancer patients, when adjusting for age and sex

Reduced Incidence of Pediatric Acute Lymphoblastic Leukemia during COVID-19 Lock-down in 2020

Kirsten Brunsvig Jarvis MD

On March 13th 2020 strict national lock-down measures were implemented as the first wave of coronavirus disease 2019 (COVID-19) hit Norway. At the department of pediatric hematology and oncology at Oslo University Hospital (OUS), the first lock-down period was remarkable calm. A retrospective review of all clinical pathways of cancer in children resulting in a cancer diagnosis from 01.01.2017 to 31.07.2020 found a stable rate of solid tumors in and outside the central nervous system in the first months after the lock-down, but there was a drop in the rate of new pediatric acute lymphoblastic leukemia (ALL) cases (1). In 2017, 2018, and 2019 there were 20, 31 and 22 new pediatric ALL cases respectively, an incidence of two per month (range 0-4). In the first 6 months of 2020, there were three new ALL cases, of which two occurred in the beginning of March 2020. In the first 4 months after the lock-down there were no new ALL cases.

We do not know why some children develop ALL, but there is a hypothesis that common infections may play a role. It is likely that with strict lock-down measures, there are fewer common infections in society, but this cannot be measured. However, as an indirect measure, numbers from the department of microbiology show an 82 and 76% decrease in airway pathogens found by PCR in deep nasal swabs in children <18 years at OUS in April and May 2020 compared to the previous two years, though the number of tests was stable. Our numbers are small and the findings may be coincidental; however, it would be very interesting to compare pediatric ALL rates with other regions with different degrees of lock-down once the pandemic is over.

1. Jarvis KB, Lind A, LeBlanc M, Ruud E. Observed reduction in the diagnosis of acute lymphoblastic leukaemia in children during the COVID-19 pandemic. Acta Paediatr. 2021;110(2):596-7.

Chemotherapy Management System

Karen Henjum MD, PhD

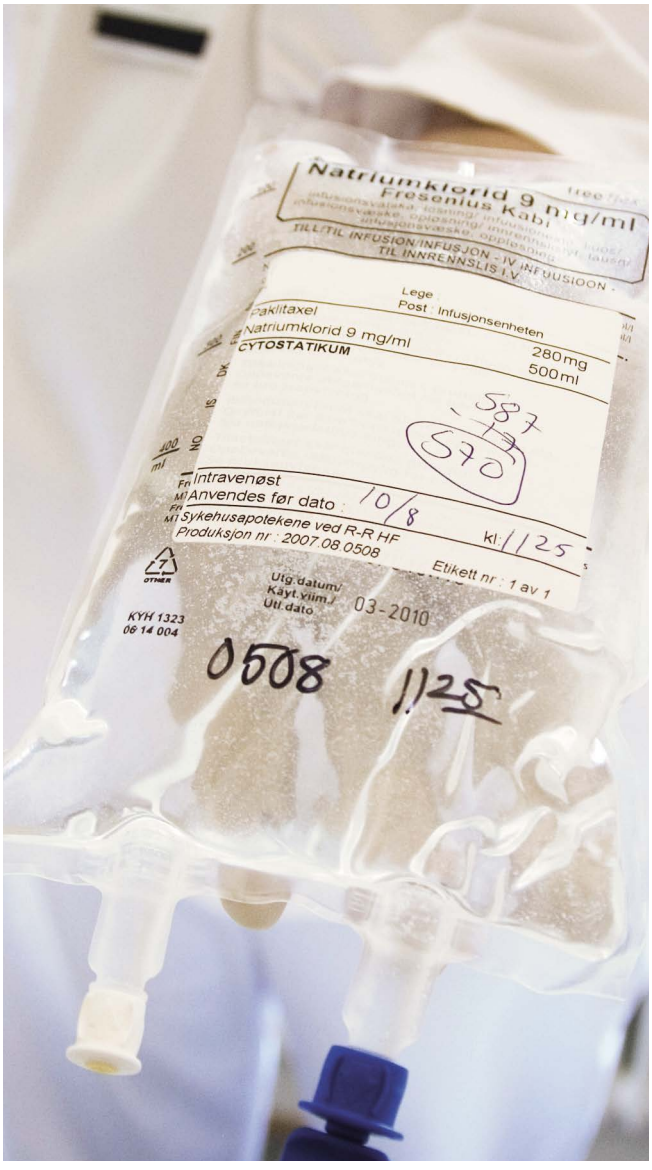
Chemotherapy Management System (CMS), a new cloud application for cancer treatment management, was introduced in 2016 in the healthcare trusts of Norway's South-East region.

It is a system for ordering, compounding and administration of parenteral cancer pharmacotherapy and is used by pharmacy staff, nurses, doctors and coordinators. Use of its barcode system supports a closed loop throughout the chain of medication management.

The Regional professional management of CMS (RPM) is organized under Oslo University Hospital (OUS) Cancer Clinic which governs and manages the professional quality of the database contents in the application. RPMs interdisciplinary team, comprised of pharmacists, nurses and doctors configure the basic data in the database. This is done in collaboration with Norway's top hematology and oncology consultants within all relevant fields of expertise. System managers and key decision makers in the South-East region trusts govern and contribute to the user functions in CMS where the prime goal is

to standardize, increase quality and reduce variation in the regions cancer treatment.

There are approximately 1550 specific active treatments in the applications library database. Oslo University Hospital has 1350 active users while the rest of the region has about 2700 users. Regionally in 2020 about 300.000 treatments have been administrated successfully using CMS.



Chemotherapy-Induced Nausea and Vomiting Guideline

Anne Grønstad, Cand. Pharm

Chemotherapy-induced nausea and vomiting (CINV) is one of the most frequently reported adverse events in patients receiving chemotherapy. CINV can lead to complications of treatment and also cause significant emotional and physical distress, disruptions to activities of daily living and influence the quality of life for the patient. The goal of antiemetic therapy is to prevent vomiting and minimize nausea both during and after the administration of chemotherapy.

The objective of the new guideline "chemotherapy-induced nausea and vomiting –medical treatment" is to provide health professionals with updated treatment recommendations for preventing and manage nausea and vomiting caused by antineoplastic agents or radiation therapy for cancer, and promote the use of these standardized, evidence-based recommendations across the hospital departments. The guideline applies for all the treatments for adult hematology, gynecological oncology and general oncology patients.

An important update in the guideline is the use of olanzapine as an option for antiemetic prophylaxis as standard treatment for adult patients who are treated with high emetic risk antineoplastic agents. This drug is also the first choice at breakthrough nausea.

The guideline is established by an interdisciplinary working group, comprised of doctors, nurses and pharmacists from various departments in the Oslo University Hospital Cancer Clinic.

There are approximately 1550 specific active treatments in the applications library database. Oslo University Hospital has 1350 active users while the rest of the region has about 2700 users. Regionally in 2020 about 300.000 treatments have been administrated successfully using CMS.

Cancer Patient Pathways (CPPs)

In Norwegian there is an idiom which in English translates to “dear child has many names”. One may say this about the cancer patients’ trajectories:

Cancer patient pathway (CPP) is the overarching term encompassing all patient activity and work processes.

The standardized CPPs (*pakkeforløp*) were politically implemented in 2015. These are based on medical guidelines and are measured by cancer specific normative times from received referral to start first treatment.

The documented CPPs are OUS specific flow charts showing logistics and responsibilities throughout the paths, created by the pathway management teams.

Standardized CPPs

E-learning course

There are many involved in carrying through OUS’ Standardized Cancer Patient Pathways. While some roles are responsible for smaller parts of the pathways, some are involved throughout the pathways. A new role-based e-learning course was created in 2020 to ensure common understandings of roles and responsibilities. The course encompasses an easily accessible overview of key concepts, tasks and advice adapted to the roles as clinician, cancer patient pathway coordinator, pathway management or other health personnel. The course had a successful launch, and will in 2021 be revised and implemented in other hospitals.

Results 2020

To carry out the standardized CPPs within the cancer specific normative times has also in 2020 been an area of focus. As seen in the figure, the share of standardized CPP patients within the set time frame from received referral to start treatment finally reached above the goal of 70% in 2020.

In 2021 the focus will be on keeping up the good results, as well as analyzing and improving pathways for patients who are referred to OUS later in their pathway.

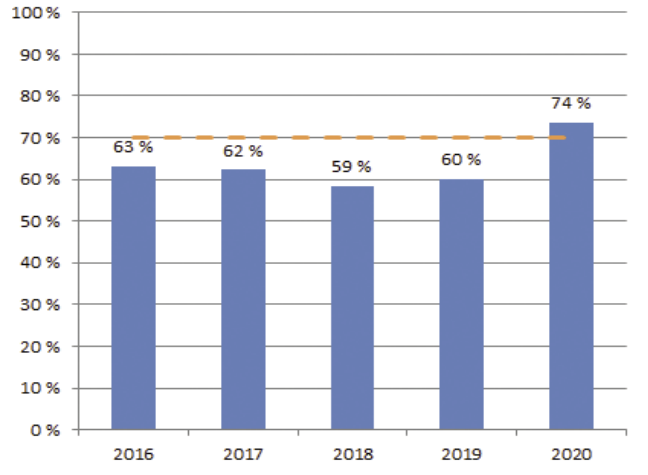


Figure. Share of standardized CPPs within target times.

Documented CPP for Anal Cancer

Marianne Grønlie Guren MD, PhD

Anal cancer is a relatively rare cancer treated mainly with radiotherapy and concomitant chemotherapy. The treatment is centralized, and all patients in the South-Eastern Norway Health Region are treated at Oslo University Hospital. A standardized patient pathway has been developed by a multi-disciplinary project group of all specialist and health care personnel groups involved in the diagnosis, staging, treatment and follow-up of these patients.

The patient care pathway describes details and practicalities of the referral, staging procedures, multidisciplinary team meeting, outpatient visits, radiotherapy planning and treatment, chemotherapy, response evaluation, treatment of recurrence and metastases, and follow-up. Personnel tasks are described, and there are links to relevant documents such as patient information, scoring systems, or toxicity management.

In the process, all relevant documents were reviewed and collected, and some were updated and revised. New guidelines such as the assessment of DPYD before treatment with chemotherapy (5-FU or capecitabine) were implemented. Areas of improvement were identified such as detailed description of local symptoms and tumor extent and symptom management, and the use of systematic scoring of treatment toxicity. The care pathway is implemented in the e-handbook at Oslo University Hospital. An audit is planned to assess the implementation of the care pathway and the areas of improvement.

CPP Coordinators

The cancer patient pathway coordinators are organized across all departments involved in cancer care. To ensure development and maintenance of competence within this important group, a competence plan was created in 2020. This plan encompasses topics such as communication with patients with different backgrounds or comorbidity, internal and external collaborative partners, and clinical system registration. All aimed at whether the cancer patient pathway coordinators are new in their role or advanced.

Two digital forums were held during the year.

In 2021 the working group will develop a guideline for the cancer patient pathway coordinators' communication across organizational units and hospitals.

Oslo universitetssykehus
OUS Kreftsenter CCC

KOMPETANSEPLAN FOR
FORLØPSKOORDINATORER KREFT

NY I STILLINGEN (I løpet av 6 måneder)

1. Pasienter og pårørende

Telefonkommunikasjon (Undervisning/veiledning) • Hvordan møte pasient på telefon	☐
Pasienttransport (eHåndbok) • Pasientreiser (Nitsy) (e-læring: pasientreiser.no) • Hotell (eHåndbok)	☐
Pasientrettigheter (internsertifisering henvisningsperioden) • Taushetsplikt • Lovpålagte frister	☐

2. Arbeidsmetodikk

Grunnleggende pakkeforløpskunnskap (e-læring: Rollebasert e-læring pakkeforløp kreft) • Forløpstider og pasientflyt mellom organisatoriske enheter • Retningslinjer for aktuelt pakkeforløp	☐
DIPS (Basisopplæring ved forespørsel til AKS (Avdeling for klinisk systemer)) • Hvordan bruke DIPS • Pakkeforløpskoding / DIPS Arena pakkeforløpsmodul • Registrering i sanntid • Dokumentasjon	☐

3. Strukturer

Fagrettet opplæring (hospitering / internundervisning) • Grunnleggende kunnskap: utredning, diagnose, symptomer • Ulike typer behandlinger • Oppfølging og kontroll	☐
MDT-møter • Pasientforløp kreft: Organisering av multidisiplinært teammøte (MDT-møte) (eHåndbok) • Administrering i DIPS (eHåndbok)	☐

Navn: .....

Leders navn: .....

Sist oppdatert: 02.03.21

"The CPP coordinators are key for patients experiencing predictability and trust"
- Sigbjørn Smeland, Chair of OUS CCC Board


150
50

Head of CCC Research Council

OUS CCC Research Activity 2020

Research is a central and integrated part of the activities in Oslo University Hospital Comprehensive Cancer Center. The research activities comprise a broad range of different fields, from biochemistry and cell studies to studies of quality of life in cancer patients. There is extensive collaboration between different groups, departments including the Norwegian Cancer Registry and the University of Oslo, taking advantage of synergies and complementary competence.

Research within the OUS CCC is diverse and covers all major fields of cancer research. The past year was influenced by the pandemic, with home offices and restrictions in activities. Much of the laboratory work was postponed. We are therefore very pleased, that a total of 768 publications, indicate an increase from 2019. A substantial number of publications was in high impact journals, with 104 publications in journals with impact factor (IF) more than 10, and 42 in journals with IF more than 20.

In 2020, 1402 patients have been included in clinical trials, representing a substantial increase from the 1004 patients included in studies in 2019. The increase is due to an increase in inclusion in investigator initiated clinical trials.

The CCC research council meets every second or third months to discuss strategic research issues, and have representation from all major departments involved in research. This year, we have initiated a focused effort in the field of precision cancer medicine. A department of experimental diagnostics has been established, covering the gap between standard molecular pathology and research in precision medicine. This has been essential for the initiation of the clinical study IMPRESS-Norway, providing precision cancer medicine for patients based on molecular profile.

In addition, a new center for advanced cell therapy was planned and received essential funding. Cell and gene therapy are among the most dynamic research areas world-wide and can provide new therapies cancer patients.

Prof. Åslaug Helland MD
Head of Research, Division of Cancer Medicine
Chair, OUS CCC Research Council

Actions in Precision Medicine

Sigbjørn Smeland (Sponsor IMPRESS-N), Gro Live Fagereng (Coordinator), Kjetil Tasken (Strategic and international leader), Hege Russnes (Leader InPreD) and Åslaug Helland (National Principal Investigator, IMPRESS-N)

Several important steps towards implementation of precision cancer medicine has taken place in 2020 The infrastructure for precision diagnostics, InPreD, established in 2020 expanded molecular tumor testing to evaluate eligibility for patients to biomarker defined clinical trials. Through InPreD, a large next generation sequencing (NGS) panel was implemented at Section for Experimental Diagnostics, Dept. of Pathology in close collaboration with Sect. for Core Facilities (Genomics core facility and Bioinformatics Core Facility) and Section for Clinical Cancer Research. Through this, more than 500 genes are analysed on DNA / RNA level, with subsequent data analysis, interpretation and reporting. In addition, the planning and funding of the precision cancer medicine trial IMPRESS-Norway study progressed, and meetings with 20 different pharmaceutical companies were held. The pharmaceutical companies will provide drugs and funds for the patients included in the study, and the interest has been substantial. The Public Private partnership for implementation of precision cancer medicine, the CONNECT consortium, was established with more than twenty partners. Applications for funding of IMPRESS-Norway-related projects focusing on health economy, radiology, ethics, law and organisational aspect were submitted.

Accomplishments on some of the projects in 2020 are described in more detail below.

INPRED:

Aim:

Implement a national infrastructure for precision diagnostics / molecular pathology incl. tumour sequencing (InPreD) with TSO500 panel, WGS and RNAseq and organization of National molecular tumour board.

Status:

- National infrastructure for InPreD is initiated at all the University Hospitals including recruitment of key personnel.
- Logistics for TSO500 being piloted at OUS. Protocols / SOPs will be shared with partners at all University Hospitals.
- National molecular tumour board has been piloted autumn 2020
- Data management plan is under development
- OUS-CCC tasked with setting up National molecular tumour board for stratification of patients into PCM trials from 2021.
- TSO500 gene panel test available for Norwegian patients with advanced disease for stratification into clinical trials from Jan 2021.
- The diagnostic infrastructure has been supported by public funds in all health regions (70 mill NOK).

The TSO500 analyses are now reimbursed as part of the public health care, and the whole genome sequencing has funds from research grants. The implementation of the genomics has been led by Dr. Leonardo Meza-Zepeda, Dr. Susanne Lorenz and Dr. Hege Russnes. The bioinformatics analyses of the molecular data builds on competence already available at Oslo University Hospital, and Professor Eivind Hovig has been instrumental here, and the data analysis pipeline for TSO500 has been made available for the other InPreD nodes, and Ahus has already implemented it.

Leonardo A. Meza-Zepeda

Susanne Lorenz

Eivind Hovig

A MOLECULAR MULTIDISCIPLINARY TEAM MEETING (MOL-MDT-MEETING)

As an assignment from the national health authorities, OUS in charge of the establishment of a molecular MDT-meeting. This national tumour board meeting is a crucial part of the implementation of precision cancer medicine in Norway. In these meetings, experts from different disciplines take part such as molecular biologists (Vigdis Nygård), bioinformaticians (Daniel Vodak, Tonje Lien), medical geneticists (Teresia Wangensteen), oncologists (Tormod Guren) and pathologists (Hege Russnes) (OUS members indicated). In addition, the IMPRESS clinical study is represented by IMPRESS doctors /PIs and TMC/TSC members. The mol-MDT team represents an important establishment in Norwegian cancer care, and will lead to dissemination of knowledge in precision cancer medicine.

Hege Russnes*

Daniel Vodák*

Tormod Guren

Tonje G. Lien

Vigdis Nygaard

IMPRESS-NORWAY:

Aim:

Researcher-initiated national Precision Cancer Medicine trial building on harmonized molecular testing and national tumour board to provide equal access to drugs and clinical trials for cancer patients across Norway and piloting the implementation of precision cancer medicine.

Status:

- Trial Management Committee and Trial Steering Committee is established.
- First patient in April 2021
- Drug-specific manuals developed in dialog with the pharma companies
- Support from Roche with 8 drugs, process ongoing with several other companies. These provide free drugs and per-patient costs. More companies in internal process for participation.
- All hospital trusts with an oncology department are participating in the study.
- Concrete plan for aggregation of data between all the Nordic DRUP like Trials starting (data sharing and aggregation policy, alignment of eCRF-solutions), with DRUP and TAPUR.
- Sub-projects using data from IMPRESS-Norway being initiated e.g. using CT-images for automation of RECIST evaluation using AI. (TRAIN project, pending application)
- A national IMPRESS-team including IMPRESS-doctors and local personnel. Live Fagereng has been involved in all aspects of the diagnostics and the trial.
- The study has been supported by KlinBeForsk (60 mill NOK) and Kreftforeningen (16 mill NOK).

Through the study, patients who have progressed on standard treatment can benefit from precision cancer drugs provided by pharmaceutical companies. The interest has been very high.

INSIGHT / INCLUDE:

Aim:

Address the regulatory challenges for implementing precision cancer medicine including health economics.

Status:

Applications for funding of research using data from IMPRESS-Norway filed including support for:

- Developing statistical framework for small non-randomized clinical trials including optimalization of synthetic control groups.
- Cost – effectiveness analysis of the IMPRESS-Norway model.
- Suggest new reimbursement schemes for drugs with uncertain effect
- Ethical challenges embedded in the PCM-model
- Legal challenges for implementation of PCM
- Organizational challenges for implementation of PCM.

CONNECT:

Aim:

Public-private partnership driving the implementation of precision cancer medicine by jointly addressing key obstacles and piloting novel solutions to transform the current practice. CONNECT is operationalized via Working Groups engaging public and private partners as well as regulators and payers and is an arena for all relevant stakeholders to jointly address important issues and to ensure a balanced, broad, coordinated and informed approach and debate.

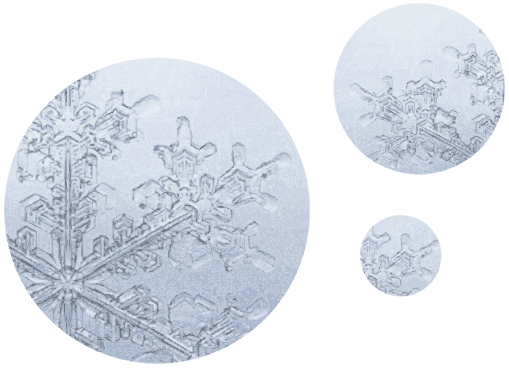
Status:

- Organization as project coordinated by Oslo Cancer Cluster and run with a Steering Committee with representatives from the public side and the industry
- Consortium contract completed and signed end 2020, foundation Jan 2021
- Activities for the four Working Groups interfacing InPreD, IMPRESs, INSIGHT (and related initiatives) defined and to be refined by the partners as the project start
- 27 public and private partners joined upon foundation or in first half 2021
- Open for additional partners to join as Partners

Funding:

Project partner fee and in-kind contribution.

PRC European Palliative Care Research Centre



The BrainMet Study

Improving treatment of patients with brain metastases

The BrainMet study is run by a Norwegian consortium with representatives from all health regions under the auspices of the European Palliative Care Research Center (PRC) – a Norwegian Cancer Society Center. The study is financed by Pink Ribbon (The Norwegian Cancer Society) and the South-Eastern Norway Regional Health Authority (HSØ).

The BrainMet study is running in its fourth year and we are now in the process to finalize a unique cohort study including more than 1000 patients with prospective assessment of anticancer treatments, palliative and supportive care (patient-centered care) and patient reported outcome measures (PROMS).

These data will inform us on how and where patients are treated, the clinical effects of anticancer treatments and how patient-centered care is delivered in hospitals and in community care. We are also selecting biopsies from brain metastases surgery and are in the process to analyze the biomaterial. The project aims to improve clinical, biological and patient-centered knowledge and thereby offer cancer patients with brain metastases better treatment and care in the future.

Patients with brain metastases experience multiple physical, mental and cognitive problems – also affecting the family members. In order to gain more knowledge about "the life" with brain metastases and thereby make the clinical interventions more personalized a comprehensive qualitative study is conducted and are in the process to be analyzed.

PRC, running the BrainMet study, is with its 26 collaborating centers one of the largest research networks in palliative care internationally. The overall objective is to improve the scientific evidence base and thereby to offer cancer patients optimal treatment and care.

Combining Advanced MRI Methods and Artificial Intelligence Approaches for Precision Diagnostic Imaging in Brain Cancer Patients

Siri Fløgstad Svensson, Elies Fuster i Garcia, and Kyrre E. Emblem

Department of Diagostic Physics, Division of Radiology and Nuclear Medicine

Artificial intelligence (AI) has changed the field of radiology. With the availability of large datasets and computational power, it can outperform experts in the most tedious and time-consuming image analysis tasks, as well as extract new information from acquired images. We develop and use these imaging tools to help support personalized cancer care by earlier diagnosis, more accurate monitoring of tumor evolution and response to therapy.

We apply advanced MRI methods and artificial intelligence for several tasks in precision medicine:

- Tumor classification, detection and segmentation
- Tracking tumor growth
- Evaluating treatment response
- Early detection of tumor progression

Advanced MRI techniques

Our group focus on advanced MR imaging techniques such as Vessel Architectural Imaging, providing new knowledge on vessel type dominance (arteries, capillaries and veins) and microvascular efficiency (1). We have now added MR Elastography to our state-of-the-art MR imaging protocol, enabling the assessment of biomechanical properties of brain tissue, such as stiffness and viscosity, by applying mechanical vibrations during the MRI scan (2). These advanced imaging techniques, illustrated in Figure 1, allows us to probe the tumor microenvironment and help stratify patients with brain cancer to receive the best treatment option for their tumor. Moving forward, we will use the added information obtained by these techniques and the power of AI in service of precision medicine:

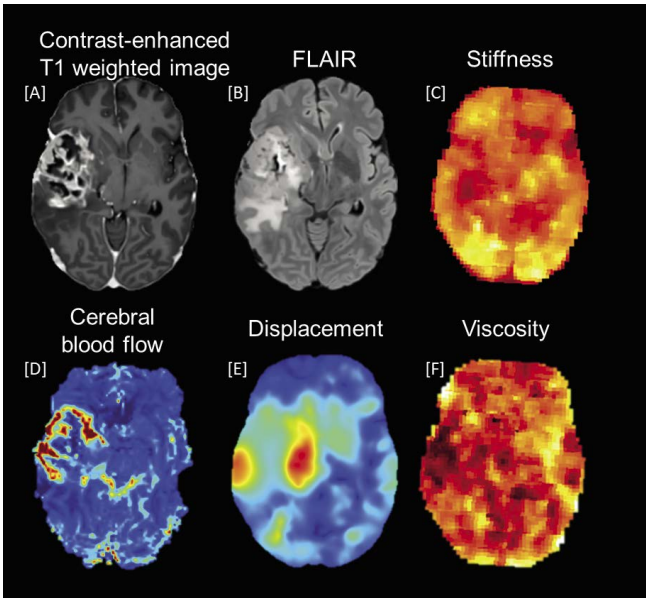


Figure 1. Anatomical and functional MRIs of a patient with glioblastoma. Maps of stiffness (C), cerebral blood flow (D), displacement (E) and viscosity (F) complement anatomical information (A and B) on the tumor and its surrounding tissue.

Classification, detection and segmentation
We have developed an automatic AI pipeline to pre-process structural and functional MRIs, where contrast-enhancing tumor, edema, and necrotic tissues on MRIs are detected and segmented automatically, using convolutional neural networks. The resulting AI-based segmentations can then be edited by experienced radiologists for iterative model improvements. Furthermore, such networks can be used to shed light on the tumor heterogeneity by mapping subregions of the lesions with differential imaging characteristics, coined habitats. The identification of such habitats in brain tumors is shown to improve the association to clinical outcomes such as patient overall survival (3), density or tissue stiffness. Our preliminary data show how a growing tumor change the entire architecture of the brain more than half a year before these changes are observed by traditional diagnostic means. This new information will allow physicians to make early decisions on treatment – a critical step for the patients in terms of improved quality of life and prolonged survival.

Tracking tumor growth and evaluation of therapy response
In recent years, numerous efforts focus on modelling tumor growth based on real patient data, using both mathematical models of evolution, and recently methods based on deep learning algorithms. Here, convolutional and recurrent deep learning networks are trained to predict future images in a longitudinal analysis by feeding previous images to the network. Currently, we are developing computational models to track the dynamics of tumor growth trained on real brain tumor data using a database of all patients with glioblastoma treated at Oslo University Hospital in the last 20 years.

Another approach in tracking tumor growth is a novel method we have developed to quantify tumor-induced tissue deformations from longitudinal, structural MRI. We derive so-called displacement biomaps that rely on a combination of robust automated processing pipelines, deep learning segmentation models, and non-linear registration and voxel tracking algorithms. This allows us to detect and quantify small structural changes in brain tissue and track any apparent evolution of the tumor microenvironment associated with early changes in angiogenesis, vascular architecture, cell density or tissue stiffness. Our preliminary data show how a growing tumor change the entire architecture of the brain more than half a year before these changes are observed by traditional diagnostic means. This new information will allow physicians to make early decisions on treatment – a critical step for the patients in terms of improved quality of life and prolonged survival.

The project is run by the MRI Research & Technology research group at the Department of Diagnostic Physics, Division of Radiology and Nuclear Medicine, led by Kyrre E. Emblem, (kemblem@ous-hf.no).

Grants:
European Union's Horizon 2020 Programme: ERC Grant Agreement No. 758657-ImPRESS, and Research and Innovation Grant Agreement No. 668039-FORCE, South-Eastern Norway Regional Health Authority (Grant Agreement No. 2017073 and 2013069), The Research Council of Norway FRIPRO (Grant Agreement No. 261984), European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement (No 844646-GLIOHAB).

References

1.Emblem, K. E. et al. Vessel architectural imaging identifies cancer patient responders [..]. Nat. Med 19, 1178-1183 (2013)
2.Svensson, S. et al. Robustness of MR Elastography in the Healthy Brain [..]. J Magn Reson Imaging Jan 5 (2021).
3.Juan-Albarracin, J. et al. ONCOhabitats: A system for glioblastoma heterogeneity [..]. Int. J. Med. Inform. 128, 53-61 (2019).

The NIPU-study

Dual-time PET to Identify redictive biomarkers for immunotherapy in the treatment of malignant mesothelioma

Vilde Haakensen, Eirik Malinen, Eivor Hernes

Malignant pleural mesothelioma is a rare and aggressive malignant tumour with median overall survival of 1 year and few treatment options. While immunotherapy (ipilimumab and nivolumab) improves overall survival, many patients do not respond. We seek to improve treatment response and elucidate mechanisms for resistance to treatment.

In the NIPU trial, a total of 118 patients will be randomised (1:1) to treatment with ipilimumab and nivolumab alone or in combination with the telomerase vaccine UV1. Telomerase is highly expressed in mesothelioma cells, but sparsely in normal cells. There is preclinical evidence to support the combination of telomerase vaccine and checkpoint inhibition to improve therapy response. We will develop a method of assessing immune cell infiltration in the tumour using positron emission tomography (PET) to identify a non-invasive biomarker of therapy response.

Highlights

- Adding UV1 to the combination of ipilimumab and nivolumab to improve therapy response
- Using dual-time PET to characterize immune cell infiltration in the tumour
- Identify mechanisms and biomarkers for therapy response

Main purpose

PET with 18F-Fluorodeoxyglucose (FDG) as tracer molecule is a non-invasive technique employing a positron-emitting tracer to create 3D images of glucose-uptake in the body. Effect of immunotherapy has been linked to the level of pre-existing immune cells in the tumour, with higher response rates in tumours with high levels of CD8+ T-cells. Immunotherapy and UV1 vaccine may lead to increased immune cell infiltration and tumour cell kill. Both tumour cells and immune cells consume glucose and may thus give a signal during a PET scan, and conventional PET is known to provide false-positive results at response evaluation due to high concentration of immune cells at the original site of the cancer[1]. However, the uptake kinetics of FDG (reflected by glucose consumption rates) may vary between different cell types, and we hypothesize that we can differentiate between cancer and immune cells by so-called dual-time PET[1].

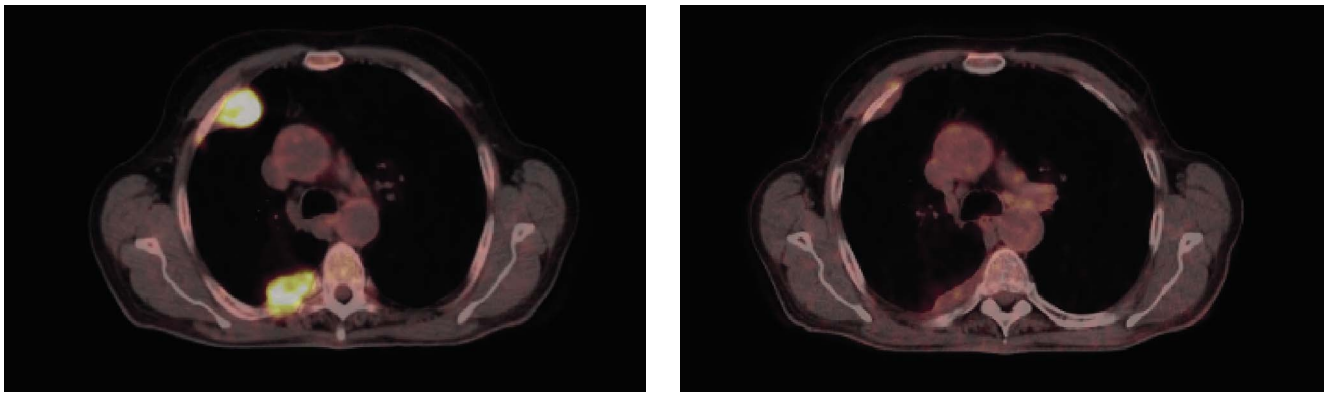


Figure. FDG-PET-image of a patient included in this study. Left: PET at baseline. Right: PET 6 weeks after start of treatment with ipi/nivo and UV1-vaccine. The images show conventional single-time scan at 60 minutes

This implies that the patient is scanned twice after injection of FDG, as opposed to once for conventional PET. For every PET-examination, scans will be performed both 60 minutes and 120 minutes after administration of FDG. We will develop methods for extracting image features and rates of FDG-uptake and correlate this with the presence of cell types (tumour cells and inflammatory cells) in biopsies at the same time point. This allows for exploration of tumour evolution and inflammatory responses to immunotherapy. For a subpopulation of patients (n=50), dual-time FDG-PET will be performed prior to treatment, after 5-6 weeks of treatment and at 1 year of treatment or at time of progression.

Project group

The clinical trial is sponsored by Oslo University Hospital (OUS) and headed by PI Åslaug Helland in Dept of Cancer Genetics and Dept of Oncology. Eirik Malinen (University of Oslo/OUS) and Eivor Hernes (Dept of Radiology and Nuclear Medicine, OUS) are responsible for the dual-time PET study and Mona-Elisabeth Revheim, Jarle Ellingsen and Ellen Husby are part of the multidisciplinary OUS nuclear medicine study team. Vilde Drageset Haakensen is supervisor for PhD students Saima J Farooqi and Solfrid M Thunold on the study. Maria Moksnes Bjaanæs, Henrik Horndalsveen, Lotte V Rogg og Hanne Marte Nymoen are clinicians in the study. Patients are included in the study from Norway, Sweden, Denmark, Australia and Spain. The NIPU-trial is supported by Ultimovacs, BMS and Helse Sør-Øst.

Trial Reference

EudraCT no.: 2019-002721-30

ClinicalTrials.gov: NCT04300244

Reference

[1] Schillaci O. Use of Dual-Point Fluorodeoxyglucose Imaging to Enhance Sensitivity and Specificity. Semin Nucl Med. 2012;42:267–80. https://doi.org/10.1053/j.semnuclmed.2012.02.003.

PRO-GLIO: PROton versus photon therapy in IDH-positive diffuse grade II and III GLIOmas

Petter Brandal, Cecilie E Kiserud, Tonje H Nordenmark, Katla Werlenius, Malin Blomstrand, Lars Bestum

The main therapeutic challenge of diffuse gliomas - astrocytomas and oligodendrogliomas - is their diffuse and infiltrative nature, at present rendering us unable to cure affected individuals. Patients with isocitrate dehydrogenase (IDH)-mutated diffuse gliomas grade II and III, nonetheless, have a relatively good prognosis and therapy therefore needs to be delicately balanced to achieve a maximal survival benefit without affecting quality of life significantly.

PRO-GLIO is/will

- one of the very first international interventional studies where patients are randomized to proton or photon radiotherapy
- a cooperative Norwegian-Swedish multi-institutional study
- show that proton radiotherapy of patients with IDH-positive diffuse gliomas yields a 2-year first intervention frees survival (FIFS) non-inferior to photon radiotherapy
- show that proton radiotherapy of patients with IDH-positive diffuse gliomas leads to a lower incidence and grade of neuropsychological side effects and a higher HRQOL when compared to photon radiotherapy
- establish that a considerable number of patients with IDH-positive diffuse gliomas have side effects from treatment and are in need of rehabilitation


Petter Brandal


Cecilie E. Kiserud


Tonje H. Nordenmark


Katja Werlenius


Malin Blomstrand


Lars Bestum

PRO-GLIO aims at establishing proton irradiation as standard radiotherapy for IDH-positive diffuse glioma grade II and III patients. First, PRO-GLIO will show that proton therapy is safe, despite the infiltrative nature of these neoplasms. Second, the HRQOL and neuropsychological investigating part of PRO-GLIO will show that patients irradiated with protons have a better outcome in this regard than those irradiated with photons. Also, PRO-GLIO will establish proton radiotherapy as a health economically beneficial alternative compared to photon radiotherapy for this patient group. Inclusion criteria are a diagnosis of grade II or grade III IDH-mutated diffuse glioma, good performance status, indication for radiotherapy and age between 18 and 65 years.

Funding

The study has received funding from The Norwegian Cancer Society (Kreftforeningen) and South-Eastern Regional Health Authority (Helse Sør-Øst), and is led from Oslo University Hospital (OUS) by oncology senior consultant and research group leader Petter Brandal.

Study group

PRO-GLIO is a Norwegian-Swedish cooperative study with OUS, Sahlgrenska University Hospital and Skandionkliniken as main study hubs. All Norwegian and Swedish institutions treating patients with IDH-positive diffuse gliomas grade II and III will include patients. In addition to dr Brandal, oncologist dr Kiserud at OUS, neuropsychologist dr Nordenmark at OUS, and oncologists dr Blomstrand and dr Werlenius are part of the PRO-GLIO steering group. Representative Mr Lars Bestum from the patient organization “Hjernesvulstforeningen” is also included in the steering group.

Next Generation Precision Medicine of Metastatic Colorectal Cancer

Anita Sveen, Ragnhild Lothe

Biomarker-guided therapy has improved the outcome from metastatic colorectal cancer (CRC), but only for a small proportion of patients. New precision medicine strategies beyond currently available therapies and known genomic markers are needed. Our approach to improve the rationale for stratified treatment is based on integrated genomics, transcriptomics, multiplexed immunohistochemistry, and ex vivo drug sensitivity testing of the patients' own cancer cells, all in the context of tumor heterogeneity (Figure 1).

2020 marked the final year of the K.G.Jebsen Centre for CRC research (2014-2020). This Centre has contributed to consolidation of the translational CRC research program at OUS, with results documented in 168 peer-reviewed publications (~25% in journals with impact factor >10), 20 successful PhDs, establishment of new technology platforms, and initiation of several clinical intervention studies. We look forward to further strengthen our transdisciplinary platform in the years to come, and to contribute to development of the next generation of treatment concepts in CRC.

Highlights in 2020:

- Publication of the initial study from our ex vivo drug screening platform, reporting on the largest study of inter-metastatic heterogeneity in drug sensitivities and gene expression among patient-derived organoids (PDOs) of multi-metastatic CRCs (Bruun et al., Clin Cancer Res 2020;26:4107-19).
- Approval of the protocol for the EVIDENT intervention study of metastatic CRC.
- Translation of the gene expression-based consensus molecular subtypes of CRC to metastatic cancers, and development of a new and improved subtyping framework (two manuscripts currently in revision).
- Comprehensive review of biomarker-guided treatment strategies against metastatic CRC published in Nat Rev Clin Oncol (Sveen, Kopetz, Lothe, 2020;17:11-32).

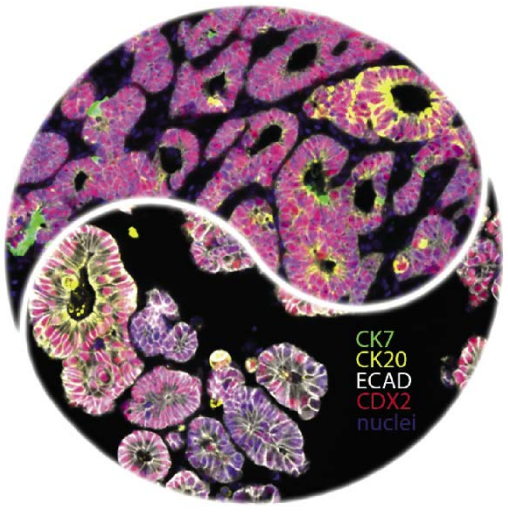


Figure 1. Fluorescent, multiplexed immunohistochemistry of a liver metastasis (top) and its corresponding tumor organoids (bottom)

EX VIVO DRUG SENSITIVITY TESTING OF METASTATIC CRC (EVIDENT)

We have established a pre-clinical pharmacogenomics platform of solid tumors, including cell lines and tumor organoids mainly of CRC. Results from the observational phase show that promising anti-cancer agents can be nominated to the majority (80%) of patients with hepatic CRC metastases, that heterogeneity of drug sensitivities among metastatic lesions from each patient is modest, and that there is strong correspondence in the gene expression and drug sensitivity profiles of PDOs (Bruun et al.). As of April 2021, 170 tumor organoid lineages from 90 patients have been established and screened for 47 drugs/drug combinations. These results have provided the foundation for the EVIDENT trial.

EVIDENT 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 (Figure 2). "Actionability" of ex vivo sensitivities will be interpreted in relation to our pre-existing PDO reference set, identifying potential "outlier" sensitivities, or for broadly acting drugs, strong activity relative to other drugs in the same patient and the same drug across patients. "Co-clinical" evaluation of first-line combination chemotherapies will also allow us to predict the true beneficiaries of standard treatment.

This study design represents a next generation of precision oncology trials, and patient inclusion is expected to start mid-2021.

Drug repurposing and mechanisms of response

Several possibilities for drug repurposing in CRC have been identified from our pre-clinical platform. Sensitivity to PARP inhibition was found in a small subset of microsatellite stable cell lines, and functional studies identified wild-type TP53 activity as the primary mechanism of response. A link to homologous recombination deficiency was shown by wild-type TP53-mediated suppression of RAD51 (Smeby et al., EBioMed 2020;59:102923).

Longitudinal profiling of a recurrent, KRAS mutated metastatic CRC showed evolution towards a phenotype with strong sensitivity to the pro-apoptotic agent LCL161 in PDOs from three consecutive hepatic resections. Sensitivity was associated with degradation of anti-apoptotic targets, induction of apoptosis, and a high inflammatory response (Kryeziu et al., submitted manuscript). Unpublished data from CRC cell lines with acquired resistance to BRAFV600E inhibition suggest potential for novel effective combination therapies.

Authors and Departments

Ragnhild A. Lothe, Anita Sveen, Kushtrim Kryeziu – Dept. Molecular Oncology, Inst. Cancer Res, KRE

Tormod K. Guren, Svein Dueland, Stein Kaasa – Dept. Oncology, KRE

Arild Nesbakken, Sheraz Yaqub, Kristoffer Lassen – Dept. Gastrointestinal Surgery, KIT

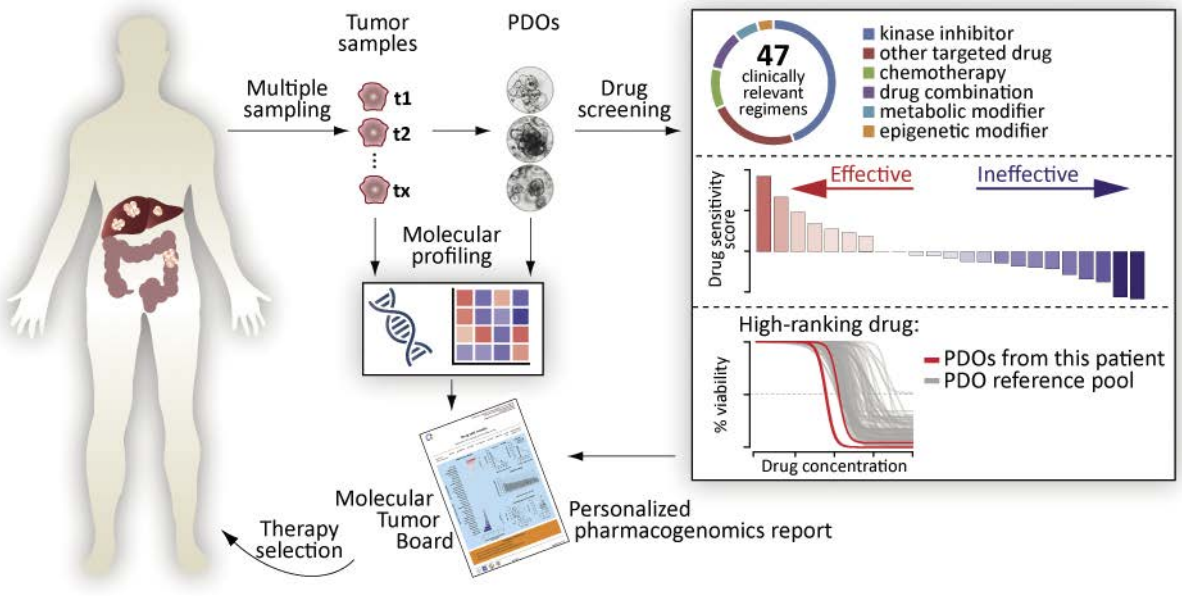


Figure 2. Workflow in the EVIDENT trial

Aspirin as Secondary Prevention for Colorectal Cancer Liver Metastases

The ASAC trial is an investigator-initiated, phase III, Scandinavian multicentre, randomized, placebo-controlled study comparing the clinical outcome of standard treatment with surgical resection of colorectal cancer liver metastasis (CRCLM) with adjuvant of low-dose acetylsalicylic acid (ASA/Aspirin). Several studies have shown beneficial effect of ASA on primary prevention of CRC. In a register-based study we showed that patients using Aspirin on a regular basis after diagnosis of CRC had an improved overall and cancer-specific survival (J. Clin. Oncol, 2016). The ASAC trial will include 800 patients operated for CRCLM which will be randomized to Arm#1 ASA 160 mg once daily or Arm#2 Placebo for a period of 3 years or till disease recurrence. The patients will be treated and followed up according to standard-of-care and national guidelines. There are 5 sites in Norway, 6 sites in Sweden and 3 sites in Denmark recruiting patients to the trial.

We have now included 400 patients and although the covid-19 pandemic has slowed the inclusion rate a bit, we are optimistic for recruiting the remaining 400 patients within the scheduled timeline.

The ASAC trial will be the first clinical interventional trial to assess the beneficial role of ASA in recurrence of CRC liver metastases and survival. Aspirin is an inexpensive, well tolerated, and easily accessible drug that could be a potent adjuvant in secondary prevention of CRC liver metastases if the study shows a beneficial effect. We will also determine the effect of ASA as adjuvant treatment on Health-related Quality of Life and the cost-effectiveness.

The trial is initiated by Oslo University Hospital, Norway and is funded by The Research Council of Norway, The Norwegian Cancer Society, and KLINBEFORSK.

More information about the study on www.asac.no.

The ASAC study team in Oslo: PI Sheraz Yaqub Assoc Professor & Consultant Surgeon, Study nurses (from left): Vilde Edvardsen, Kornelia Borgen, Victoria Bringsjord. Co-PI Prof Kjetil Taskén was not present.

ASAC TRIAL
Scandinavian Livermet Study

Experimental Transplantation and Malignancy Research Group

Pål-Dag Line
Division of Surgery, Inflammatory Diseases and Transplantation

The research group works with «transplant oncology», specifically to study how liver transplantation and transplant surgical techniques can be applied as treatment modalities for cancer patients where current standard of care fail to provide curative potential or probability of more than about 12-18 months. The research projects specifically involve patients with hepatocellular carcinoma, cholangiocarcinoma, non-resectable liver metastases from neuroendocrine cancer and colorectal cancer (CRLM). In the latter instance, we have been running a unique and world leading research program for the last 15 years.

Highlights

The first controlled trial on liver transplantation for CRLM (SECA-I) was published in 2013, and showed that an estimated 5-year survival of 60% could be obtained in patients where the expected survival on palliative chemotherapy was about 12 months [1]. This led to the development of improved patient selection criteria, and in the sequel SECA-II study, the estimated 5-year survival for non resectable CRLM was 83% [2]. Allocation of liver grafts are, due to organ scarcity, only justifiable if long term survival can be anticipated. Improved selection criteria, and the utilisation of other markers are essential in this context. PET-CT is commonly only used to exclude extrahepatic disease in hepatobiliary surgery and liver transplantation. Our group has shown that metabolic tumor volume (MTV) derived from preoperative PET-CT examinations is a sensitive marker predictive of postoperative cancer specific survival [3–5], and long-term survival based on distinct selection strategy has been documented [6].

Recurrence is a common problem after both liver resections and transplants for CRLM. The pattern of recurrence is however distinctly different, with pulmonary metastases being the most common site after transplant, whereas liver and multisite recurrences are prevalent after resection [7,8]. The pulmonary metastases seen after transplant are often resectable with curative intent, and contrary to a-priori assumptions, the immunosuppression does not accelerate the growth rate of pulmonary metastases in these patients [2,9]. Based on over 15 years of experience in the field, disease free survival is not a reliable parameter of treatment efficacy in transplanted CRLM patients, and the concept of transplantation for a highly selected group has gained international traction by many international centers and societies [10,11].

All our experiences so far has been focused on non-resectable disease, but it is unlikely that the patient selection factors do not also apply to resectable patients with bar prognosis, particularly those with high hepatic tumor load. We have recently confirmed this hypothesis [12], and more studies along the same line are underway.

Access to liver grafts is still a major problem. Our group has presented innovative surgical techniques where liver resection and auxiliary segmental liver transplantation combined with two stage hepatectomy can enable utilization of small segmental grafts from deceased or living donors [13,14].

The Experimental Transplantation and Malignancy Research Group has a broad translational focus throughout the project portfolio. Quality of life and the cost effectiveness aspect have been reported and is an area of continued research focus [15–18].

Main outcomes and future directions

- Through systematic biobanking, close cooperation with Institute for Cancer Research-OUS as well as international partners to elucidate possible molecular and immunological factors of significance for liver transplantation in CRLM
- The group is part of the consensus process for liver transplantation in CRLM of the International Hepato-pancreato-biliary association (IHPBA)
- A formal world-wide registry for liver transplantation in CRLM is being founded with headquarter in Oslo

Main collaborators

- Gudrun Bjørnelv, The Institute of Health and Society, UiO
- Eline Aas , The Institute of Health and Society, UiO
- Prof. Ragnhild Lothe, Institute for Cancer Research, OUS
- Prof. Julia Johansen, Herlev University Hospital, Denmark
- Prof. Eric Vibert; Hopital Paul Brousse Paris
- Prof. Umberto Cillo, University of Padova, Italy
- Prof. Roberto Hernandez Alejandro, URMC, Rochester NY, USA
- Ass.prof. Gonzalo Sapisochin, UHN Toronto General Hospital, Toronto, Canada

People involved and author group details

Research group members		Associate members	
Pål-Dag Line	Professor II / Senior consultan	Einar Martin Aandahl	Senior consultant
Svein Dueland	Senior consultant	Marit H. Andersen	Professor/RN PhD
Morten Hagness	Senior consultant	Mona-Elisabeth Revheim	Ass.prof./senior consultant
Jon Magnus Solheim	PhD student/consultant	Sheraz Yaqub	Post doc/senior consultant
Harald Grut	Senior consultant	Trygve Syversveen	Consultant
Tor Magnus Smedman	PhD student/consultant		
Maria Gjerde	Study nurse		

1. Hagness M, Foss A, Line P-D, Scholz T, Jörgensen PF, Fosby B, Boberg KM, Mathisen Ø, Gladhaug IP, Egge TS, Solberg S, Hausken J, Dueland S. Liver transplantation for nonresectable liver metastases from colorectal cancer. Ann Surg. 2013 May;257(5):800–6.

2. Dueland S, Syversveen T, Solheim JM, Solberg S, Grut H, Bjørnbeth BA, Hagness M, Line P-D. Survival Following Liver Transplantation for Patients With Nonresectable Liver-only Colorectal Metastases. Ann Surg. 2019 Jun 7;1.

3. Grut H, Dueland S, Line P-D, Revheim ME. The prognostic value of (18) F-FDG PET/CT prior to liver transplantation for nonresectable colorectal liver metastases. Eur J Nucl Med Mol I. 2017 Oct 12;4(Suppl 1):283.

4. Grut H, Stern NM, Dueland S, Labori KJ, Dormagen JB, Schulz A. Preoperative 18F-FDG PET/computed tomography predicts survival following resection for colorectal liver metastases. Nucl Med Commun. 2020;41(9):916–23.

5. Grut H, Revheim ME, Line P-D, Dueland S. Importance of 18F-FDG PET/CT to select patients with nonresectable colorectal liver metastases for liver transplantation. Nucl Med Commun. 2018 Apr 20;39(7):1–627.

6. Dueland S, Grut H, Syversveen T, Hagness M, Line P-D. Selection criteria related to long-term survival following liver transplantation for colorectal liver metastasis. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons. 2019 Nov 1;

7. Hagness M, Foss A, Egge TS, Dueland S. Patterns of recurrence after liver transplantation for nonresectable liver metastases from colorectal cancer. Ann Surg Oncol. 2014 Apr;21(4):1323–9.

8. Line P-D, Ruffolo LI, Toso C, Dueland S, Nadalin S, Hernandez-Alejandro R. Liver transplantation for colorectal liver metastases: What do we need to know? Int J Surg Lond Engl. 2020;

9. Grut H, Solberg S, Seierstad T, Revheim ME, Egge TS, Larsen SG, Line PD, Dueland S. Growth rates of pulmonary metastases after liver transplantation for unresectable colorectal liver metastases. Bjs. 2018 Feb;105(3):295–301.

10. Hibi T, Rela M, Eason J, Line PD, Fung J, Sakamoto S, Selzner N, Man NK, Ghobrial RM, Sapisochin G. Liver Transplantation for Colorectal and Neuroendocrine Liver Metastases and Hepatoblastoma. Working Group Report from the ILTS Transplant Oncology Consensus Conference. Transplantation. 2020;1.

11. Line P-D, Dueland S. Liver transplantation for secondary liver tumors: the difficult balance between survival and recurrence. J Hepatol. 2020;

12. Dueland S, Yaqub S, Syversveen T, Carling U, Hagness M, Brudvik KW, Line P-D. Survival Outcomes After Portal Vein Embolization and Liver Resection Compared With Liver Transplant for Patients With Extensive Colorectal Cancer Liver Metastases. Jama Surg. 2021;156(6).

13. Line P-D, Hagness M, Berstad AE, Foss A, Dueland S. A Novel Concept for Partial Liver Transplantation in Nonresectable Colorectal Liver Metastases: The RAPID Concept. Ann Surg. 2015 Jul;262(1):e5-9.

14. Nadalin S, Settmacher U, Rauchfuß F, Königsrainer A, Line PD. RAPID procedure for Colorectal Cancer Liver Metastasis. Int J Surg. 2020;

15. Vidnes TK, Wahl AK, Andersen MH. Patient experiences following liver transplantation due to liver metastases from colorectal cancer. Eur J Oncol Nurs. 2013 Jun 1;17(3):269–74.

16. Andersen MH, Dueland S, Hagness M, Vidnes T, Finstad ED, Wahl AK, Foss A. Quality of life following liver transplantation in patients with liver metastases from colorectal carcinoma. Scand J Caring Sci. 2012 Dec;26(4):713–9.

17. Dueland S, Line PD, Hagness M, Foss A, Andersen MH. Long-term quality of life after liver transplantation for non-resectable colorectal metastases confined to the liver. Bjs Open [Internet]. 2018 Oct 25;3(2):180–5. Available from: https://www.readcube.com/

18. Bjørnelv GMW, Dueland S, Line PD, Joranger P, Fretland ÅA, Edwin B, Sørbye H, Aas E. Cost-effectiveness of liver transplantation in patients with colorectal metastases confined to the liver. Brit J Surg. 2018 Oct 16;93(1):465–10.

The Microbiome as a Colorectal Cancer Screening Biomarker (CRCBiome)

Trine Rounge and Paula Berstad

Section for Integrative Genomics at the Research Department, Cancer Registry of Norway (link) vision is to integrate data from population-based surveys, cancer screening, national registries, and clinical studies with omics analyses of related biological samples to understand cancer development and develop cancer biomarkers.

One of the large projects initiated is a prospective biomarker study (CRCbiome)(link), nested within a large, randomized colorectal cancer screening trial in Norway. The study aims to add knowledge essential for the development of biomarkers that improves the accuracy of non-invasive tests. The recruitment of screening participants who tested positive on a fecal immunochemical test (FIT) was completed in 2021.

We collected data on demography, diet, lifestyle and screening findings (link). Fecal follow-up samples are still collected 2 and 12 months after colonoscopy. Sequencing the gut microbiome identifies bacteria and viruses present in the fecal samples and what they can do. National registries will give us detailed prescription the participants' drug histories and cancer-relevant outcomes. The data collection and classification of precancerous lesions is funded by the Norwegian Cancer Society, analyses of differences in sex and prescription drug use are funded by Southern and Eastern Norway Regional Health Authority and identification of viruses is funded by EU Scientia Fellow program.

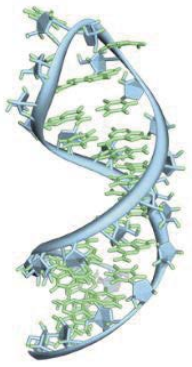
The JanusRNA study - Identification of Early Cancer Biomarkers

Hilde Langseth and Trine B Rounge

The aim of this project is to investigate miRNA and other circulating RNAs as early markers and potential screening biomarkers for cancer. The potential of miRNAs as cancer biomarkers is recognized, however little is known about circulating miRNA expression prior to cancer diagnosis.

Material and methods: we have produced non-coding RNA sequencing data from pre-diagnostic serum samples from the Janus Serum Bank Cohort. We have included patients with lung cancer (n=404), colorectal cancer (n=488), breast cancer (n=206) and prostate cancer (n=332) with a sample collected within 10 years prior to cancer diagnosis, and a large control group of 673 healthy individuals. In addition we have produced data from patients with testicular, ovarian and gallbladder cancer.

The project is initiated and lead by the Cancer Registry of Norway and is performed in close collaboration with the Norwegian Sequencing Centre at Oslo University Hospital, the University of Oslo. We have developed and optimized a RNA sequencing method for samples with low input RNA.



The sequencing depth is 18 mill sequences and we have identified more than 600 unique miRNAs per sample in addition to a number of other non-coding RNAs. Results published on the healthy control group shows that RNA expression levels are significantly affected by age and smoking.

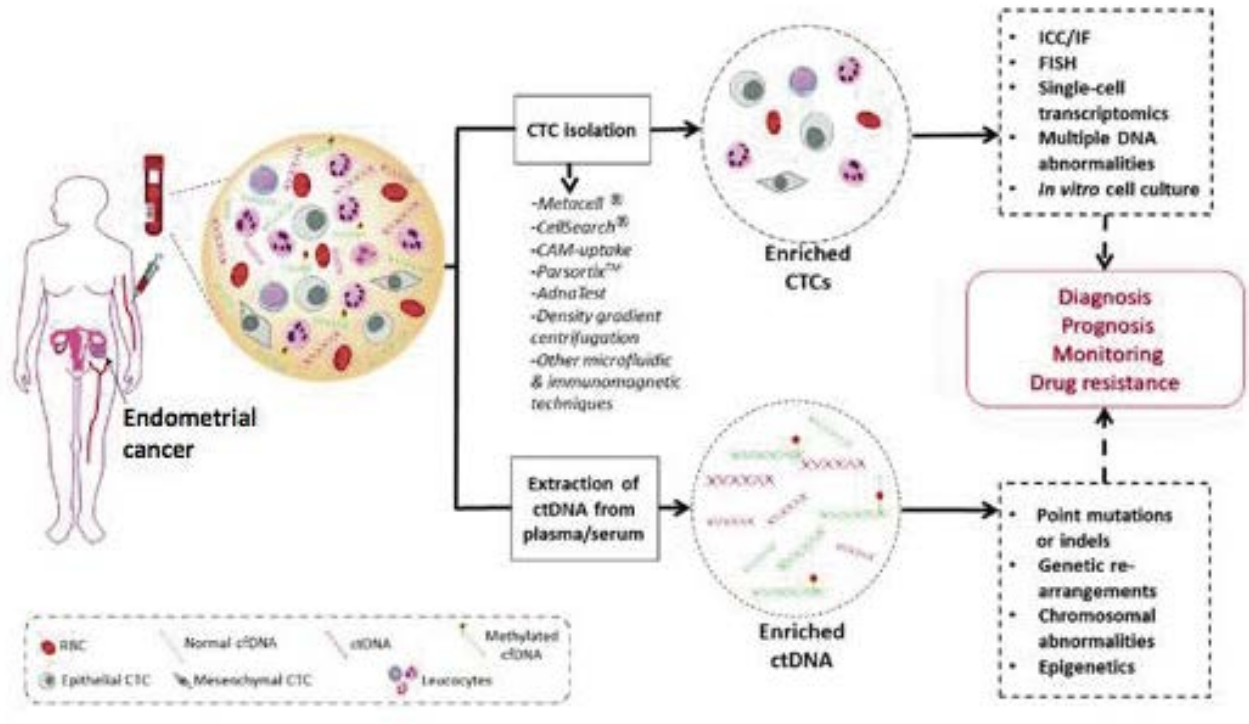
For lung cancer the results showed dynamic changes in differentially expressed circulating RNAs specific to histology and stage. The greatest number of differentially expressed RNAs was identified around 7 years before diagnosis for early-stage lung cancer and 1–4 years prior to diagnosis for locally advanced and advanced-stages. The majority of differentially expressed RNAs were associated with cancer-related pathways.
Project web page: https://www.kreftregisteret.no/en/Research/Projects/Identification-of-early-cancer-biomarkers/

Circulating Tumor DNA Potential Method to Better Characterize Patients with High-Risk Disease

Kristina Lindemann and Therese Sørlie

Endometrial cancer is the 4th most common cancer in women in Norway and the incidence has doubled over the last 20 years. Most women are cured with surgery alone, but some remain still after optimal surgery at high risk for relapse. There is no consensus on the optimal treatment for these high-risk patients, partly because the routine description of the tumor is not sufficient to be able to estimate the patient's risk of relapse. As a result, some patients are under-treated while others are probably overtreated. Our project will investigate whether the detection or characterization of circulating tumor DNA can be established as a new method to better characterize patients with high-risk disease. The prospective biobank at Oslo University Hospital (OUS) has enabled us to identify suitable patients for this project and together with Prof. Camilla Krakstad and senior researcher Erling Høivik at Haukeland University Hospital, we have now built a cohort of 50 patients for whom we have access to matched tumor and plasma samples. The primary tumors will be analyzed by whole exome sequencing for in-depth genomic characterization of mutations, copy number changes and structural aberrations. Analysis of ctDNA will be conducted by Prof. Therese´s Sørlies group at the Institute of Cancer Research. Detected ctDNA will be amplified and subjected to mutation analysis on the IonTorrent Next Generation Sequencing System using the Oncomine Pan-Cancer Cell-Free Assay and validation of specific mutations by droplet digital PCR. We aim to assess the proportion of patients with detectable ctDNA as well as the association with clinical characteristics and oncological outcome. The matched samples will be able to tell us if changes in ctDNA mirrors the molecular characteristics of the primary tumor, which will be important as we also lack non-invasive markers for response to treatment.

This project is funded by a grant from the Rakel and Otto Bruun Foundation and by institutional funds.



Modified from Asante et al. Cancer Letters 2020

Norwegian ITCC-Accreditation

Heidi Glosli

Oslo University Hospital, and thereby Norway, was granted ITCC-accreditation in November 2020. ITCC is an abbreviation for Innovative Therapies for Children with Cancer. ITCC, a European consortium, was established 2003 as a non-profit organization. The main aim of ITCC is to develop novel therapies for the treatment of paediatric and adolescent cancers in cooperation with regulatory bodies, pharmaceutical enterprises, parents and patients. The consortium gathers 63 paediatric oncology departments with expertise in conducting early phase clinical trials in children and adolescents, and also includes 25 research laboratories in Europe. The ITCC was established as a European category 1 network for paediatric research at the European medicines agency in 2011. The structure comprises several committees taking care of and contributing to various issues in the development of novel therapeutic strategies in paediatric oncology.

Lately, sponsors of academic as well as pharma-initiated studies have required ITCC-accreditation when selecting relevant sites for conducting clinical trials, especially in relation to early phase studies. This is because ITCC-accreditation indicates good quality and solid experience in conducting clinical trials with innovative therapy. The Norwegian ITCC accreditation increases the chance for Norwegian patients to be offered novel treatment in their own country. By attending studies, patients can be offered novel treatment 5-7 years prior to regular market authorization and by attending studies in their own country they can stay at home close to family and friends, and take part in their regular life to a greater degree.

“Barnekreftforeningen” has provided a substantial grant to support Norwegian ITCC-accreditation.

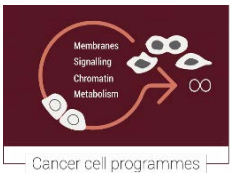
CanCell

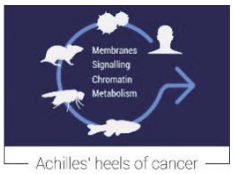
– Centre for Cancer Cell Reprogramming – Centre of Excellence

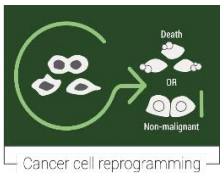
Harald Stenmark and Anders Øverbye

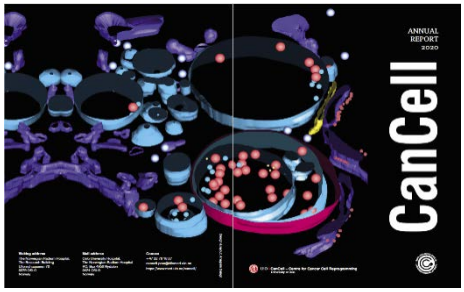
CanCell is a Centre of excellence, awarded by Norwegian Research Council (NFR) in December 2017. It numbers 125 researchers and technical staff distributed among six research groups at two locations – Institute for Cancer Research (Enserink, Rusten, Wesche and Stenmark) and Institute for Basic Medical Sciences (Eskeland and Simonsen. The Centre is led by Professor Harald Stenmark and co-director Professor Anne Simonsen, and has an average annual internal and external funding of 91 MNOK until 2027, of which 16.7 MNOK is granted by NFR. Anders Øverbye is the administrative coordinator. In addition, seven prominent investigators are associated with CanCell, including Åslaug Helland, Eivind Hovig and Yngvar Fløisand from OUS CCC.

Our vision is to uncover the "Achilles' heels" of cancer and target these for reprogramming cancer cells into harmless cells. In 2020, the centre published 37 articles, among these six were collaborative efforts related to the core activities – discovery of cancer programmes, detecting weaknesses in cancer cells and a novel approach to successfully reprogram cancer cells (Tadele et al 2020). The Centre is dedicated to enable young researchers to have opportunities to excel in their research careers, with initiatives such as a Young Scientist forum (workshops, talks, and career development), junior grants (seed grants to exciting collaborative projects) and an Equality Forum (to enhance and promote cultural, age and gender equality).









Annual Report 2020 http://cancell.no

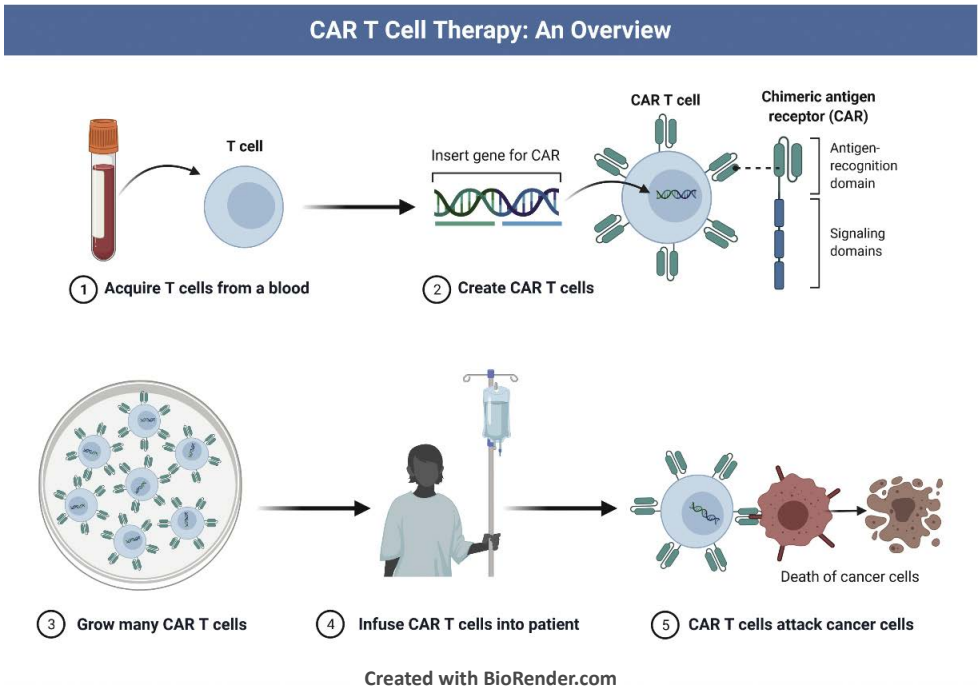
Anne Simonsen and Harald Stenmark

Development of CAR-T Immunotherapy

Benjamin Cauliier, Sebastien Walchli and Jorrit Enserink

One of the long-term goals of CanCell is to translate basic cancer biology knowledge to develop new forms of therapy. For example, we recently developed a compound that depletes c-Myc from cells, which is a transcription factor that plays a key role in survival and proliferation of a large variety of cancers (Tadele et al, 2020). A more recent project is focused on the development of new immunotherapy tools. Immunotherapy has revolutionized the way cancer is being treated. Multiple immunotherapy strategies exist or are currently under development. For instance, a recently approved form of cell-based immunotherapy includes synthetic receptors known as chimeric antigen receptors (CARs) expressed on immune cells. Thus, CARs lead to tumour recognition by the immune cells. These "living drugs" have been very successful in the treatment of certain refractory B-cell malignancies. Here, the receptor detected the common B-cell antigen CD19, and was fused to specific domains of the T-cell receptor signaling complex. This CD19 CAR was expressed in T cells derived from the patient (autologous), and transfusion of these recombinant T cells back into the patient resulted in killing of the cancer cells, eventually leading to complete remission of some patients. A major challenge of this strategy is the identification of cancer cell-specific antigens that are not expressed on essential healthy tissues.

- A major challenge in the development of CAR-based immunotherapy is the identification of cancer cell-specific antigens.
- We have recently identified an antigen that appears to be uniquely expressed on the surface of a wide variety of cancer cells.
- In a collaborative translational project, the Enserink (CanCell) and Wälchli/Inderberg (Translational Research Unit) groups are currently developing novel CAR- and antibody-based cancer immunotherapies that target this antigen.
- The work is sponsored by the Norwegian Cancer Society and is carried out by two Scientia Fellows (Marie Curie program)-supported postdocs, Jonathan Arias and Benjamin Caulier.



We recently identified an intracellular protein, which (for still unknown reasons) translocates to the surface of cancer cells. We confirmed that this protein is not present on the surface of healthy tissues, such as PBMCs and various untransformed cell lines, suggesting that the target is safe. In collaboration with pathologists we screened large cancer databases and found that this protein is found on the surface of several types of cancer for which few treatment options exist, such as certain aggressive forms of lung and breast (?) carcinoma. Importantly, this target could not have been detected by usual detection system such as RNAseq, since its quantity is likely not varying but rather its location. It thus represents a new type of cancer markers that can be called “moving targets”. Encouraged by these findings, we developed a CAR against this protein and demonstrated anti-cancer activity in CAR-expressing immune cells. We are currently optimizing the molecular architecture of this CAR to increase its efficacy against cancer cells, after which we will analyze a large panel of cancer cell lines to determine the indication of this new immunotherapy tool. We will also screen a wide variety of healthy tissue types to make sure that no essential tissues will be harmed by the CAR-expressing immune cells. This pre-clinical study will be completed by animal experiments where xenograft murine models will be treated with CAR T cells, and the curative efficiency will be monitored.

The Enserink group (Cancer Molecular Medicine) aims to better understand the basic biology of cancer cells and to develop new strategies for cancer treatment. The group currently consists of 23 members and makes use of model organisms, such as budding yeast and fruit flies, as well as drug combination screens in primary cancer cells. Jorrit Enserink is also a member of the Accreditation Committee of OECI.

The Wälchli/Inderberg Translational Research unit (Cellular Therapy) is developing next generation immunotherapy solutions, such as vaccines, receptor-redirected immune cells and innovative universal cell systems. It is also running the immunomonitoring service for industrial and academic clinical trials. The Unit is currently composed of 18 members, including specialist engineers, students and postdoc researchers. It has the capacity to independently run pre-clinical studies of immunotherapeutic products and has already completed four pre-clinical validations (TCR and CAR) and tested one TCR in human.

InvaCell

Camilla Raiborg and Harald Stenmark

The project "Mechanisms of cancer cell invasion, InvaCell, is a collaboration between Institute for Cancer Research, OUS, and Institut Curie, Paris. It is led jointly by Harald Stenmark at OUS and Philippe Chavrier at Institut Curie. InvaCell is funded by a donation from Mr Trond Paulsen through the Radium Hospital Foundation.

InvaCell focuses on protrusions formed by cancer cells, termed invadopodia. The tips of these structures secrete enzymes that degrade extracellular matrix and thereby enable cancer cells to invade tissues away from the primary tumour.

The principal objective of InvaCell is to understand how invadopodia are regulated, so that their functions in cancer cell invasion and metastasis can be inhibited.

Highlights 2020

- Discovery of molecular pathway that controls invadopodia formation
- Identification of a novel matrix degradation programme based on the invadopodia components
- Third joint symposium organized as an on-line conference with good participation

Results 2020

A joint scientific paper from InvaCell was published in the prestigious Journal of Cell Biology (Pedersen et al., 2020). In this paper, the InvaCell teams showed that the Protrudin protein is essential for formation of invadopodia, cellular protrusions that cancer cells use to invade host tissues. The paper also characterized other proteins that act in concert with Protrudin, and it showed evidence that the Protrudin pathway is upregulated in metastatic cancers. This identifies the Protrudin pathway as an attractive target of future cancer therapy directed against metastasis. The paper was dedicated a commentary article in Journal of Cell Biology and was selected for a special issue of Journal of Cell Biology with focus on Cancer Cell Biology.

The group at Institut Curie has published a paper that identified a novel matrix degradation programme based on the invadopodia components, MT1-MMP and TKS5, which supports the survival of tumour cells in nutrient-deplete conditions. Also this paper was published in Journal of Cell Biology (Zagryazhskaya-Masson et al., 2020).

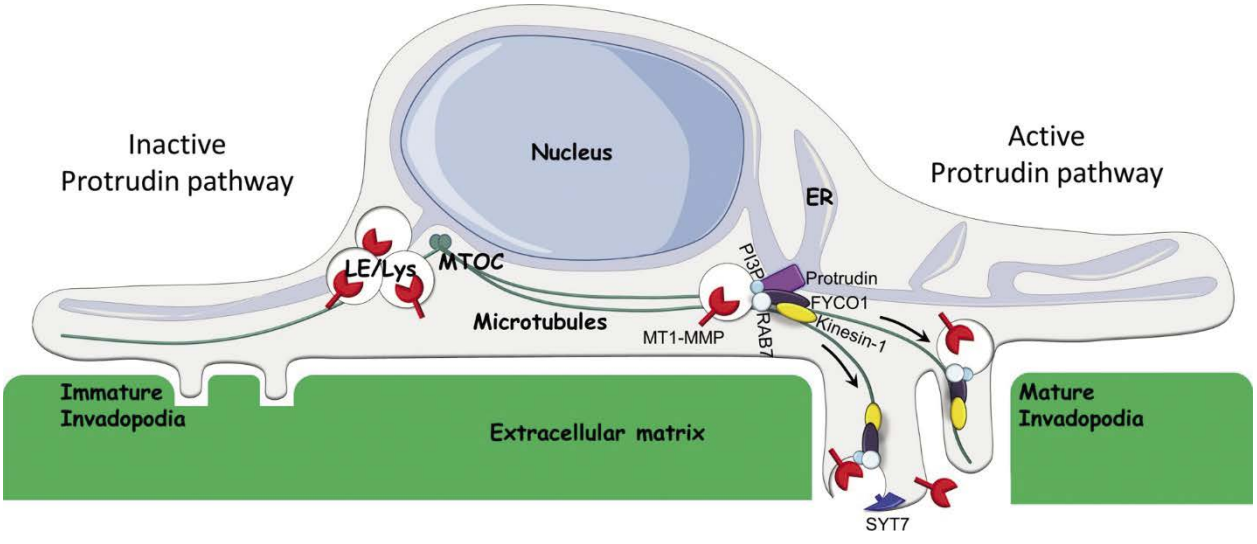
Group details

The InvaCell team at OUS is led by Harald Stenmark and consists of senior scientist Camilla Raiborg, scientist Eva Wenzel, scientist Nina Marie Pedersen, PhD student Liv Dammann Anker, and head technician Ling Wang. The InvaCell team at Institut Curie is led by Philippe Chavrier.

Publications

Pedersen NM, Wenzel EM, Wang L, Antoine S, Chavrier P, Stenmark H and Raiborg C (2020). Protrudin mediated ER-endosome contact sites promote MT1-MMP exocytosis and cell invasion. Journal of Cell Biology 219: e202003063

Zagryazhskaya-Masson A, Monteiro P, Macé AS, Castagnino A, Ferrari R, Infante E, Duperray-Susini A, Dingli F, Lanyi A, Loew D, Génot E, Chavrier P (2020). Intersection of TKS5 and FGD1/CDC42 signaling cascades directs the formation of invadopodia. Journal of Cell Biology 219: e201910132



KG Jebsen Centre for B-Cell Malignancies

June Myklebust and Ludvig Munthe

The center aims to identify new biomarkers and to develop and test new therapies for patients with leukemia (B-ALL and CLL), lymphoma and multiple myeloma. The center has a very extensive clinical program. Last year, the Centre had 25 clinical studies with active recruitment of patients, whereas 32 trials had ended inclusion of patients and were in follow up. The majority of studies were researcher-initiated, and researchers at the Centre have played a key role in the process for implementation of precision medicine in Norway (IMPRESS-Norway).
The Centre published 46 articles in 2020 in recognized international journals. The results included evaluation of new treatment strategies for patients with lymphoma, multiple myeloma and cold agglutinin disease (Leppä, Blood Adv; Kolstad, Blood Adv; Fajgenbaum, Am J Hematol; Schjesvold, Haematologica; Kaiser, Ann Hematol and Berentsen, Blood). An international study discovered that patients with CLL had high risk of developing COVID-19 lethal disease (Mato, Blood). Translational research within the Centre led to development of a functional precision medicine assay for CLL by ex vivo screening of cancer drugs (Skånland, Leukemia). Results from sequencing projects revealed that mutations in antigen-presentation molecules were associated with higher risk of relapse in lymphoma (Wise, Blood Adv), and identified genomic alterations in cold agglutinin disease (Małecka, Blood Adv). Tumor microenvironment studies revealed a key role of macrophages, with an adverse prognostic role in lymphoma (Autio, Haematologica), and as powerful mediators of tumor cell killing in a preclinical model (Haabeth, Blood Adv), warranting further investigation.
Several researchers at the Centre won major research grants including funding for new clinical studies from several companies, a research project funded by the Norwegian Cancer Society, an innovation project and a research project funded by NFR, two new research projects funded by HSØ, and as partner in an EU project (ERA PerMed).
Several of the center's researchers have an active role in the media and have put important challenges in current cancer treatment on the agenda through participation and notices in NRK, Aftenposten, and Dagens Medisin.


SIEMENS
220.0
-288.0
SOMATOM Force

Oslo University Hospital

Comprehensive Cancer Centre

02770

www.oslo-universitetssykehus.no/oslo-university-hospital

E-mail: oushfkreftstyret@ous-hf.no