Oslo University Hospital

Comprehensive Cancer Centre

ANNUAL REPORT 2021

Oslo University Hospital

Comprehensive Cancer Centre (OUS CCC)

OECI Comprehensive Cancer Centre

UiO : University of Oslo

Oslo University Hospital Comprehensive Cancer Centre

OUS was designated as a Comprehensive Cancer Centre by OECI in April 2017. Postponed by one year, because of the pandemic, we started the preparation for the reaccreditation process in 2021. This includes revision of OUS Cancer Strategy from 2016 and a focus on areas we need to strengthen. The latter included initiating a project for an institutional educational program for cancer nurses and a focus on patient centred care and cancer rehabilitation with reference to the national initiative "pakkeforløp hjem" among others. For both projects, we expect a report in 2022. These projects exemplify the momentum we can achieve with the Cancer Centre Board in complex institutional processes involving several divisions and departments.

During the last years, the Comprehensive Cancer Centres (CCC) structure is more recognised as a key factor to improve quality, facilitate coordination and/or reduce variation in diagnosis, treatment, training/education and research in cancer care across university or other large and complex hospitals. Accordingly, both in the Europe's beating cancer plan and the European Missions cancer, further development of the CCC concept is addressed. In 2021 OUS CCC played an active role in two Joint Action programs within the EU4Health program on building CCC networks and a network of European Cancer Centre of Expertise.

2021 was the second year of the pandemic and OUS experienced for the second year in a row a reduced number of newly diagnosed cancer patients. The number of newly referred cancer patients to OUS was also lower than in the reference year, 2019 (-2,6 %). The pattern varies among the diagnoses and we have for some cancers experienced a 10 % or higher reduction (see later in this report for more details). This is an area we need to follow and not only the numbers for OUS but also the total numbers and distribution between the hospitals within the health region. With regard to the standardized cancer patient pathways (pakkeforløp) the flow-times were generally satisfactory in 2021 which reflects the priority of cancer patients during the pandemic, but probably also the reduction in the number of patients. With the improved flow-times for internal OUS pathways, we still have major challenges on pathways starting at local hospitals ending up in OUS with a delay in the transition phase between the hospitals involved.

A major achievement in 2021 was the further development of the national initiative in precision cancer medicine. OUS plays a key role in that program and for the InPreD molecular diagnostic network molecular diagnostics with the extended TSO-500 gene panel got started and the clinical trial, IMPRESS-Norway, opened for patient accrual April 1st. At the institutional level, a challenge in diagnostics is the delay to validate and set-up new test for accompanying biomarkers for treatments approved by NyeMetoder. The delay can be substantial and OUS CCC Board has initiated a dialogue with NyeMetoder to include the diagnostic work-up earlier in the health-technology assessment process.

OUS CCC receive annual survival data from the Cancer Registry on survival split into tumour groups and residence or patients who had received their main treatment at OUS. For patients who received main treatment at OUS the survival data is dependent on both medical treatment given and the characteristics of patients treated at OUS. For 2021 we observed improvement for all tumour groups and more than 10 % improvement in relative survival compared to the previous 5-year period for esophagus, stomach, pancreas, lung, myeloma, liver and melanoma. _The 5-year survival for patients from OUS's districts in Oslo, was 77,7 % and compared favourable to Norway in total (75,7 %) and South East Health Region (75, 6 %) . We need to look more into the data for South East Health Region and the fact that the data for OUS area is better than for the region in total.

A major task for OUS and the cancer area is the building of the hospital and proton center at The Radium Hospital. The clinical building is planned to open for patients in late April 2024 and the proton center in December 2024. In 2021 we started the process on how to organize the clinical activity and patient logistics in the new building. These include novel concepts such as a breast cancer center and prostate cancer center. In practical terms, that means that all activity, clinical and diagnostic, are located at The Radium Hospital. Regarding proton therapy, Varian was chosen as the vendour in 2019, and in fall 2021 a OUS delegation visited Varian's factory in Germany to name the cyclotron, Ellen Gleditsch, after the second female professor in Norway. Prof. Gleditsch was professor in chemistry and a research fellow at Madame Curie's laboratory in Paris and personally brought the first radioactive Radium samples for Paris to Oslo to establish radiotherapy in Oslo and Norway.

Research and integration of research and clinics is a cornerstone for the CCC concept. In 2021 we were not able to further increase the number of patients recruited to clinical trials. The reason was lower activity from large phase III studies and not the number of clinical trials. We will still have a strong focus on this issue and aim to increase the number and to have more than 10 % of our patients recruited to a clinical trial.

Cellular Immunotherapy is a very promising field in cancer therapy. In 2021 we opened a centre for advanced cell therapy (ACT-center) at the Radium Hospital. In total 50 MNOK were donated from three donators to establish a state-of the art infrastructure for modern cell therapy. Combined with the strong expertise in this field, both the Institute for Cancer Research and the Section for Cell Therapy at the Department of Oncology, we will have the opportunity to bring novel and effective products from the laboratory to our patients.

In conclusion, 2021 has been an exciting and challenging year for OUS CCC. We have high ambitions, have made some major achievements, and but we still have to work hard on the reaccreditation to fulfil the criteria in all areas. We have been able to deliver high quality cancer care to our patients during the pandemic and with the new clinical building with a proton centre at The Radium Hospital, we will have the opportunity to further develop the OUS CCC.

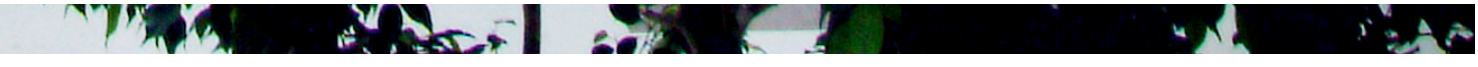
Prof. Sigbjørn Smeland MD
Head, Division of Cancer Medicine
Chair, OUS CCC Board

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 fraction 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

Developing a New Cancer Strategy Towards Reaccreditation as a CCC

In the early phase back in 2015 on our work towards reaching the status as a Comprehensive Cancer Centre, we were confronted by the question: What are the future ambitions and targets of the cancer activities in your hospital? Since we had no straight forward answer to this question we initiated the work on an institutional cancer strategy. A group of central leaders of cancer-related units from different divisions in the hospital made up the working group, and several more were involved during the process. The first cancer strategy of OUS was approved by the CEO in June 2016 and it was to be valid for five years. A core group of those leaders involved where chosen when the Cancer Centre Board was established with one of its task to coordinate the follow-up the ambitions from the cancer strategy.

Since 2016, OUS has reached several of the ambitions set up in the first strategy. A few mentioned below:

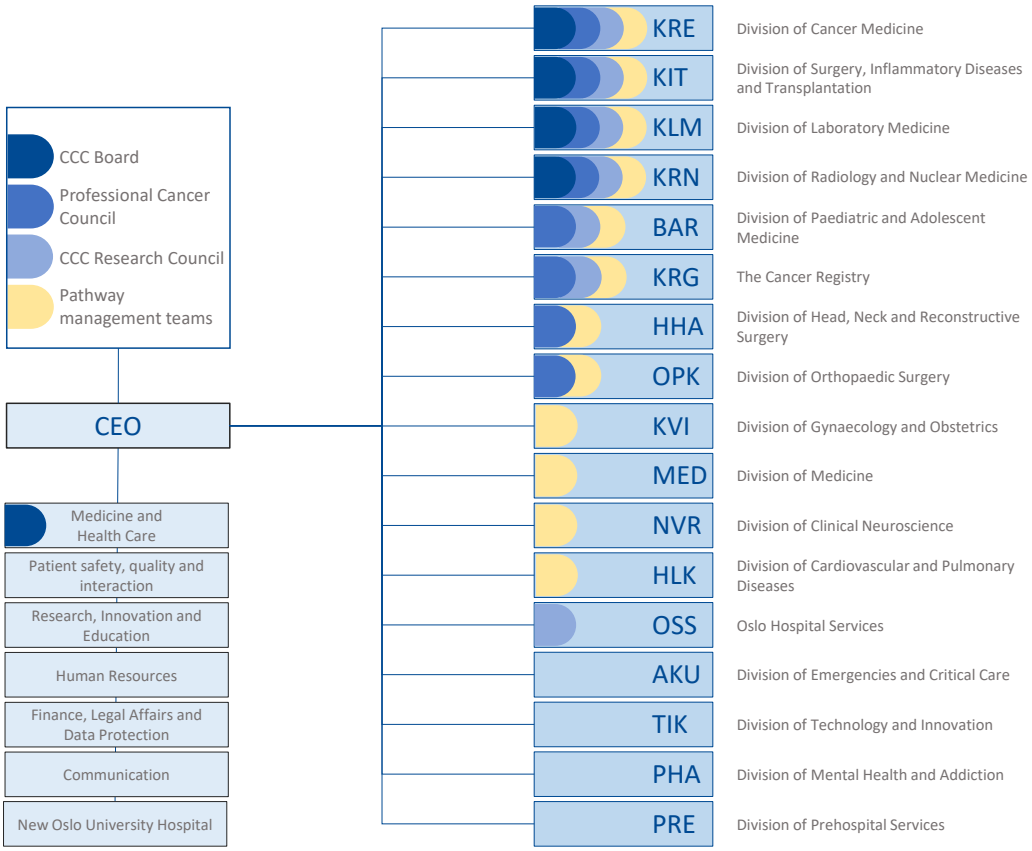
- Launched a program for establishing prospective biobanks for all tumour groups.
- Increased the proportion of patients included in clinical trials from round 8 % to > 14 %.
- Been a national instigator for establishing a program for precision cancer medicine.
- Developed a dashboard for following core indicators of cancer related activities and outcome indicators based on cancer diagnoses and not organizational affiliation.
- Elaborated documented, standardized pathways for all cancer pathways in the hospital.
- Further developed and matured the matrix-based model for organization of cancer centre coordination and development with the Cancer Centre Board as an arena for both problem solving and strategic development.
- Developed a model of specialized training and education for nurses working with cancer patients.
- Started the process of establishing a regional cancer coordinating network connected to processes and pathways across hospitals in HSØ Health region where OUS functions as the regional hub.
- A new clinical building and a proton centre at the Radium hospital (one of four hospital sites) is decided and will be ready in 2024.

The revised cancer strategy process begun in 2021 as a part of the CCC reaccreditation process. The new strategy process is based on the achievements in the first period. An advantage of this second cancer strategy process is the established Cancer Centre Board and Professional Council. Again all main divisions and departments have been engaged. The advices from the process during 2021 identified four headings:

- Prevention and early detection focus on the role of specialized health care
- Patient centred care integrated with oncology care throughout the whole patient trajectory, customizing all encounters and measures to the personal preconditions and wishes of the patients
- Precision medicine and new treatment methods, building on more precise diagnostics and combining knowledge from tumour biology, biostatistics and bioinformatics
- Progress in diagnostic and treatment technologies, deploying the potentials in information technologies, artificial intelligence as well as in surgical processes and radiation therapy including proton therapy

During the strategy discussions in 2021, continuation of the existing vision seems to have broad support: OUS – a leading cancer centre in Europe.

OUS Management Structure



Pathway Management Teams

There are 23 pathway management teams in OUS. These consist of professionals from the disciplines involved within the cancer pathways, often a surgeon, oncologist, radiologist, pathologist as well as patient pathway coordinators from the different departments.

The most important work areas include:

- Patient logistics and pathway
- Multidisciplinary team meetings
- Integration of clinical research
- Quality improvement
- Documentation

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 2021:

- Collaboration with other hospitals
- Clinical quality registries and biobank
- Key cancer data indicators and dashboard
- Continuing educational programmes
- Precision medicine
- Cancer patient pathways (CPPs)
- Multidisciplinary team meetings
- Dialogues with pathway teams
- New Radium Hospital
- Tools for shared decision-making
- Cancer patient pathways home-to-home

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. Åslaug Helland MD, Head of Research, Division of Cancer
- Eli Gunhild By, CCC Quality director
- Prof. Andreas Matussek, Head, Division of Laboratory Medicine
- Paulina Due-Tønnessen MD, Head, Division of Radiology and Nuclear Medicine
- Hilde Myhren MD, Director of Medicine
- Prof. Stein Kaasa MD, Head, Department of Oncology
- Elin Henriksen, Head, Department of Gastro- and Paediatric Surgery
- Per Magnus Mæhle, Secretary, Division of Cancer Medicine

Professional Cancer Council

- *CCC Board*
- 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, Patient representative
- Erik Rokkones MD, Head, Department of Gynaecological Cancer
- Assoc. Prof. Bodil Bjerkehagen MD, Head, Department of Pathology
- Prof. Kjetil Taskén MD, Head, Institute for Cancer Research, Division of Cancer Medicine
- Anne-Grethe Bechensteen MD, Head, Department of Paediatric Oncology and Haematology
- Ole-Jacob Norum MD, Head, Department of Cancer Orthopaedics
- Torill Krøvel, Senior advisor, Staff Division of Surgery, Inflammatory diseases and Transplantation
- Bjørn Wølstad-Knudsen, Union representative, Norwegian Union of Municipal and General Employees
- Anne Marit Wang Førland MD, 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 2021:

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

CCC Research Council

- Prof. Åslaug Helland MD, Head of Research, Division of Cancer Medicine (Chair)
- Prof. Knut Jørgen Labori, Group leader, 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
- Espen Stang, Patient representative
- Monica Cheng Munthe-Kaas MD, Head, Department of Paediatric Oncology and Haematology
- Assoc. Prof. Knut Håkon Hole, Division of Radiology and Nuclear Medicine
- Prof. Bodil Bjerkehagen MD, Head, Department of Pathology, Division of Laboratory Medicine
- Prof. Stein Kaasa MD, Head, Department of Oncology
- Mari Nygård, Research Director, The Cancer Registry
- Prof. Dag Kvale MD, Institute leader, Institute of Clinical Medicine, 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
- 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 February 2021

OUS CCC had a very useful feedback session with our SAB, especially focusing on five select areas:

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

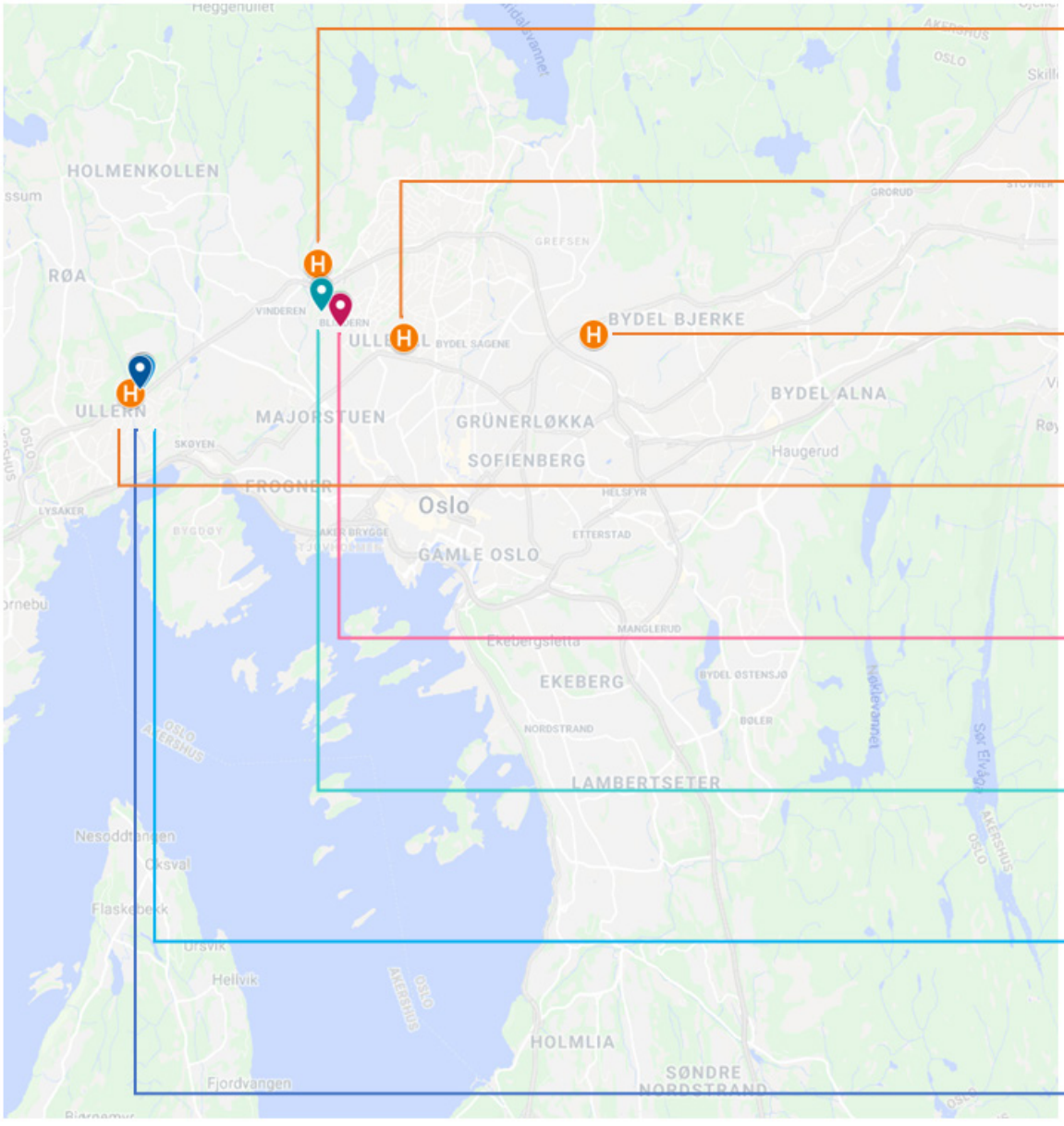
Collaborating Partners

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

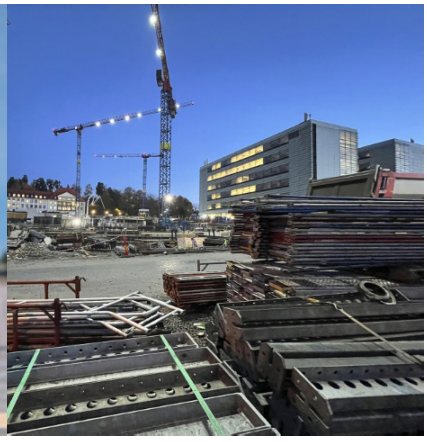
UiO : University of Oslo

inven2

OSLO CANCER CLUSTER

CANCER Registry of Norway





Major Events 2021

- ACT center for advanced cell therapy established, Feb
- Fridtjof Nansen Award for Excellence in Science to Harald Stenmark, Mar
- The national study IMPRESS-Norway was initiated, Apr
- CCC quality director Eli Gunhild By started, Jun
- Foundation stone laying ceremony Radium hospital, Aug
- Excellent Researcher Award OUS to Ragnhild Lothe, Aug
- Early Career Award OUS to Marina Vietri, Aug
- The National Cancer Nursing Conference Best Inpatient Ward Award to Karine Blom Kjerulf, Section for palliative medicine, Sep
- Cervical cancer awareness day event, Sep
- Kolbjørn Brambanis' Cancer Research Award to Muhammad Ali at Oncological Forum, Nov
- Young Researcher Award to Knut Smeland at Oncological Forum, Nov
- Dr Ragnar Mørks Cancer Research Award to Anita Sveen, Nov
- The Norwegian Cancer Society granted 84 MNOK to research projects in OUS CCC including research on tailored antibody-therapy, data-modelled precision colorectal therapy, mitochondrial dysfunction, early AI-based cancer diagnosis, Nov
- Key Cancer Data Dashboard prototype developed, Dec
- The MATRIX clinical research centre funding (128 mill NOK), Dec
- 104 MNOK in research funds from South Eastern Norway Regional Health Authority to 21 recipients in OUS CCC, in addition to a Career Grant to Åsmund Fretland, Dec
- OUS' Excellent Article Awards 2021 to Eivind Ask (Med), Jakob Skalleberg (Laryngoscope), June, Nina Haagenrud Schultz (NEJM) and Sebastian W. Schultz (Nature), Jan 2022




Radiumhospitalet
P2 Besøkende


Rikshospitalet


HOVEDINNGANG
SENTRALBLOKKEN

Core Activity Data

Patient Treatment

Number of cancer patients:

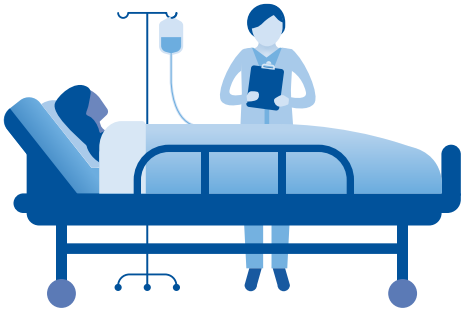
29 501

Total number of new cancer patients refferred to OUS:

11 172

Radiotherapy: treatment series:

6 960



Number of outpatient consultations:

123 575

Radiotherapy: number of fractions:

100 661

Number of beds:

263

Number of over-night stays:

76 182

Number of chairs:

77

Chemotherapy treatments:

41 562

Radiotherapy: number of patients:

6953

* Number of radiology examination requests for cancer patients

MRI scans:

12 362

CT scans:

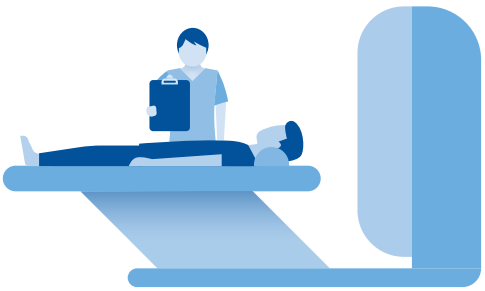
20 733

Cytology:

10 421

Histology:

40 970



Radiology examinations:

62 129

Molecular pathology:

14 734

Key Indicators in Research

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

863 (409)

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

151 (44)

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

57 (10)

Budget: estimate of research budget (by parameters):

91.8 mill. €

Completed Ph.D. degrees:

33

Disclosures of Invention (DOFIs):

40

Active projects funded by EU (H2020):

17

Approx. Total number of FTEs in cancer research:

650

Number of active clinical trials:

126

Percentage of new patients included in clinical trials

8.56

Number of new patients included in clinical trials

956

Foundation Stone Laying Ceremony for New Buildings at the Radium Hospital

The new clinic and proton therapy buildings at the Radium hospital will be ready for use in the spring and late autumn of 2024 respectively. Around 22,000 square meters of old buildings have been demolished to make way for the modern buildings, which together make up 44,000 square meters. The capacities in new buildings are listed in the table below.

Wards, beds	142
Infusion chairs	56
Intermediary unit, beds	5
Outpatient rooms, incl. special room	73
Post operative / intensive care	11
Special laboratories	21
Operating theatres	10
Radiology laboratories (incl. CT and MRI)	15
Treatment rooms proton	3

Unique Foundation Stone

The Radium Hospital history and mission are summarized in the foundation stone, which will function as an exhibition in the new main reception in 2024. The content consists of the following:

- Certificate from Madame Curie from 1924: the confirmation of the first shipment of radium. This is the start of cancer treatment at the Radium Hospital.
- A plate with the Radium hospital logo.
- A «Fuck Cancer» bracelet: Young Cancer and The Norwegian Cancer Society collaborate on this bracelet.
- The casting spoon used by King Haakon VII during the foundation stone laying for the Radium Hospital in 1929 and by Crown Princess Mette-Marit during the foundation stone laying for the Research Building in 2005.

The Proton Building

The establishment of proton treatment is central to the further development of the Radium Hospital as a specialized cancer hospital. Radiation therapy with protons is more precise and therefore gentle than traditional radiation therapy as it spares healthy tissue to a greater extent without reducing the radiation dose to the tumour. This results in fewer side effects and long-term damage. The treatment is particularly suitable for children, young people and for patients who will live a long life after cancer treatment. The treatment is already available abroad, but will finally become a reality in Norway in the summer of 2024. The offer will be established first in Oslo and then in Bergen.

Ellen Gleditsch, the Cyclotron

The cyclotron is the source of the high-energy proton particles serving all three treatment rooms. The cyclotron is produced by Varian and has been given the name Ellen Gleditsch. Ellen Gleditsch was the second woman professor in Norway.- Her life and work is a pretty incredible story. Ellen Gleditsch traveled the world, had a research stay at Yale and was a research fellow at Madame Curie laboratory and personally made sure that radium was sent to Norway. This was the start of the Radium Hospital. In addition, the name «Ellen» has a meaning that can be associated with the Radium Hospital; namely «a strong and shining light», says Sigbjørn Smeland, Head of Division of Cancer Medicine.

Breast Cancer Centre in 2024

Breast cancer is the most common form of cancer among women, and accounts for 22 percent of all cancer cases in women in total in Norway. In 2020, 3424 women and 31 men were diagnosed, according to the Cancer Registry. Establishment of a breast cancer center at the Radium Hospital is part of the development plans for OUS. When the center opens in 2024, all breast cancer-related activity at OUS will be gathered at the Radium hospital, including diagnostic (radiology and pathology) as well as oncology and surgery.

- Today, patients with breast cancer in Oslo usually the patient flow and the internal logistics in OUS is complex, often with several actors involved, says Stein Kaasa, Head of Department of Oncology.

The establishment of a separate breast cancer center at the Radium Hospital means that breast cancer patients in OUS will have a “one door entery” for diagnosis, treatment and follow-up. The breast cancer center will also include education and research, clinical and translational, which the gathering of professional groups will contribute to.

- Professional meetings across specialties are first and foremost beneficial for patients, but also very stimulating for employees. I therefore hope that the breast cancer center can become an arena for education, continuing education and not least recruitment, says Ellen Schlichting, Head of Section for breast and endocrine surgery.

Prostate Cancer Centre

Kristin Rennesund

In 2024 a new Prostate Cancer Center will appear in new premises in OUS localized at Radium hospital. It will gather all diagnostics, treatments and follow up of prostate cancer patients. By gathering all disciplines and interdisciplinary collaboration, it is expected that one can optimize the patient course within all stages of the prostate cancer disease. Co-location and proximity to the Cancer research Institute and the Norwegian Cancer Registry will strengthen the possibility of research in prostate cancer.

The quality register, currently owned by the urology department, will be expanded to a common register in the center. All surgical and oncological radical treatment will be registered in the new registry. This gives us the opportunity to evaluate patient treatment.

Audit Anal Cancer CPP

Jørgen Smedby

Anal cancer is a relatively rare cancer with increasing incidence. The majority of patients are treated with radiotherapy and concomitant chemotherapy with the aim to achieve cure and preserve the best possible quality of life. The treatment is centralized, and all patients in the South-Eastern Norway Health Region are treated at Oslo University Hospital.

A standardized cancer patient pathway (CPP) has previously been developed by a multi-disciplinary project group of all personnel groups involved in the diagnosis, treatment and follow-up of these patients. The CPP describes details and practicalities of the complete patient trajectory and was implemented in 2021.

A multi-disciplinary group has performed an audit this year to assess the implementation of the CPP and detect areas of improvement. The audit included the healthcare trajectories of all patients referred with newly diagnosed anal cancer during a four-month period and examined specific parameters encompassing radiological and pathological diagnostics, treatment planning, patient communication and toxicity scoring and management. Most aspects of the patient pathway had been satisfyingly implemented, especially regarding the diagnostic work-up and patient care during treatment. However, for some patients the time between clinical decision making and start of treatment was longer than specified in the CPP. In most cases this was due to medical reasons, but measures have been taken to reduce the risk of unnecessary non-medical delays.

This highlights how systematic evaluation of complex cancer patient pathways may identify distinct areas of improvement and eventually lead to improved patient care.

Regional Meetings Lung Cancer

Frøydis Stornes

Regional courses for lung cancer patients

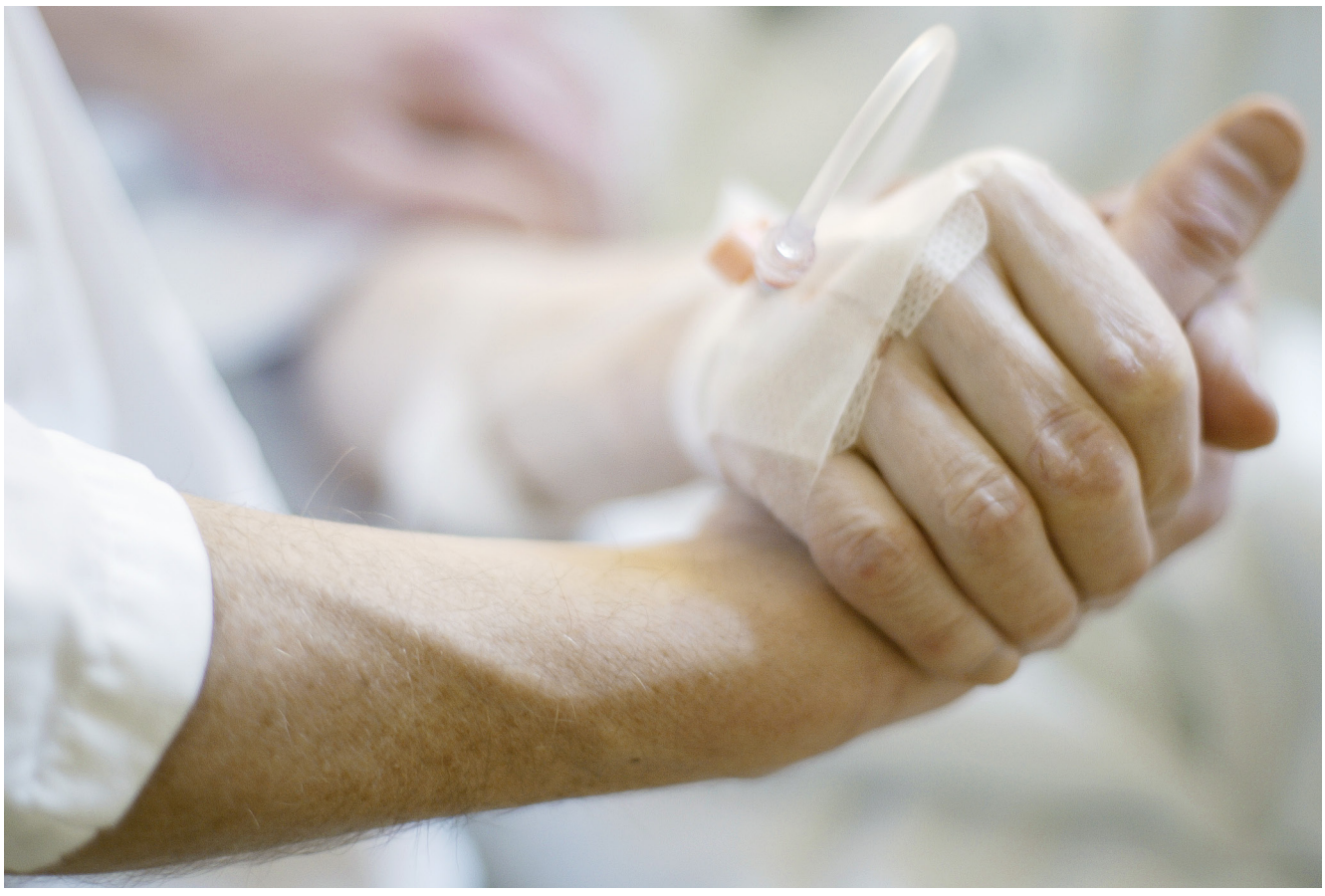
Investigation of suspected lung cancer is a complicated course and involves different specialists. There are often many surveys the patient has to go through. For some patients this involves examination or treatment in two hospitals. This has caused challenges with logistic as well as the flow between hospitals. As a result, more time has been used.

Therefore, Oslo University hospital CCC has organized a group consisting of representatives from all health trusts in HSØ. Currently, the group contains of pulmonologists, oncologists, surgeons and course coordinators. Furthermore, we plan to bring along pathologists and radiologist in the coming work.

Among the topics we have discussed, improved flow of information within hospitals is important for not wasting time. This applies to submission of clinical documentation as well as radiology. During this work we have gone through several patient courses and looked at bottlenecks within examination. Also, we have discussed which opportunities and ideas there are for further improvement.

In addition, we have gone through the practical use of coding within the standardized patient pathway. This is to ensure that the coding always is done correctly and in the same way. Our goal is to utilize the codes with their original intensions for the patient`s best.

As a result of these groups, we have organized a network that makes contact and flow easier for a better work for these patients.



#Check-day, Cervical Cancer Screening

Worldwide, cervical cancer is the fourth most common cancer in women. What sets this cancer apart from most other cancers is that cervical cancer can be prevented. Participation in the Cervical Cancer Screening Program will contribute to early detection of cervical dysplasia. Preventive measures such as cervical cancer screening and HPV vaccination will considerably reduce the incidence of cervical cancer.

- Thanks to HPV vaccination and the Cervical Cancer Screening Program, it is estimated that cervical cancer in Norway will almost be eradicated by 2039, says gynecologist Ane Gerda Zahl Eriksson, Department of Gynecological Cancer in Division of Cancer Medicine.

However, data from the national screening program shows that 30% of Norwegian women do not participate in the Cervical Cancer Screening Program, which means that 400,000 women in Norway do not use an important preventive service. During the pandemic, even fewer women took part in the national screening program. As a result, there has been a noticeable decrease in newly diagnosed cervical cancer cases in 2020, compared with previous years.

#Check-day

- In our department we do not usually perform routine cervical cytology, since women are already diagnosed with cervical cancer by the time they are referred to us, says Erik Rokkones, head of the Department of Gynecological Cancer.

The Department of Gynecological Cancer arranged a #Check-day during the Cervical Cancer Awareness month. The response to the event was substantial. More than 70 cervical samples were taken this day and many of the women who showed up had never had a cervical cytology before.

• In Norway, more than 350 women get cervical cancer every year.

• 70- 90 women die annually from the disease.

• The national Cervical Cancer Screening Program significantly reduces the incidence.

• The HPV vaccine helps to virtually eradicate it.

Developing a Key Cancer Data Dashboard

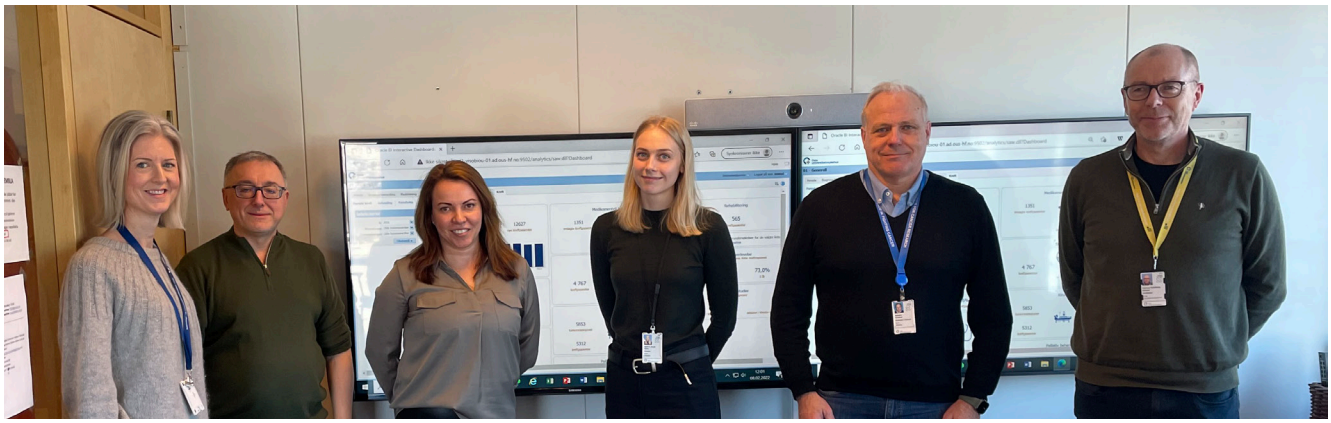
While the cancer patients' pathways cross the organizational boundaries, quality indicators are often confined to departments and divisions or specialization. To reflect the patient centered perspective of OUS CCC, in line with the existence of the CCC Board and Cancer pathway management groups, a project was formed in order to compile cancer patient data in one dashboard. Thus, the dashboard provides an opportunity to follow trends and better understand our activities.

The work group is composed of employees of the CCC Board secretary, Division of Cancer Medicine and the IT department. Importantly, clinicians have been involved throughout the process. In 2021 the prioritized process and outcome indicators were thoroughly defined and described.

Success factors

- Building on literature on experiences of developing dashboards, including content, technical solutions, design and use.
- Gaining knowledge of wanted quality indicators, as well as data quality, through conversations with future users.
- Composing a work group with complementary knowledge.
- Dedicating time to investigate each quality indicator thoroughly.
- Communicating the dashboard to users with written information as well as presentations introducing indicators and demonstrating use.

The developing of the Key Cancer Data Dashboard is by no means over. After launching the dashboard in early 2022, more quality indicators will be included and more data systems will be integrated.



Cancer Patients

Location	ICD-10	Number of cancer patients in OUS*			Number of new cancer patients in OUS*			Number of newly diagnosed cancer patients in OUS**		
		2019	2020	2021	2019	2020	2021	2019	2020	2021
All	All	32 313	31 941	32 050	12 487	11 944	12 102	4714	4566	4530
Breast	C50	4 743	4 676	4 951	1 721	1 617	1 879	588	564	633
Head and neck	C00 -C32	1 348	1 397	1 414	553	575	598	335	357	375
Myeloma	C90	493	492	511	169	159	160	33	44	41
Lymphoma	C81-C86, C88	1 925	1 711	1 568	594	521	470	241	199	201
Pancreas	C25	463	475	448	275	260	228	143	134	139
Colorectal	C18-C21	2 497	2 467	2 515	1 182	1 078	1 094	330	333	352
Bladder	C65-C67	1 106	1 135	1 103	275	295	228	144	163	130
Kidney	C64	479	455	453	185	251	321	103	79	84
Prostate	C61	4 554	4 651	4 528	1 523	1 525	1 482	636	613	592
Penis	C60	156	172	180	46	55	52	31	33	35
Testis	C62	1 425	1 382	1 279	205	183	197	67	78	70
Uterus	C54-C55	655	574	567	341	302	294	197	179	170
Ovary	C56	857	704	696	392	280	324	251	207	183
Cervix	C53	612	571	555	273	221	665	162	137	137
CNS	C71	784	802	855	281	290	319	153	149	162
Lung	C33-C34	1 896	1 941	1 985	1 157	1 165	1 190	385	341	322
Esophagus and stomach	C15-C16	655	723	788	389	368	389	172	174	200
Liver	C22	165	181	196	107	115	100	57	74	61
Sarcoma	C40-C41, C48-C49	1 054	1 001	968	411	339	285			
Thyroid gland	C73	851	887	861	190	229	237	106	142	129
Melanoma	C43	1 266	1 217	1 095	589	602	506	392	390	338
Bile ducts	C22,C24	148	131	135	112	94	94	70	58	57

** OUS' definition of cancer patients: Including all ICD-10 C-diagnoses excl. C44, incl. D32-33, D35.2-35.4, D42-3, D44.3-D44.5, D45-47 and Z08.

**ICD-10 codes related to patient pathways.

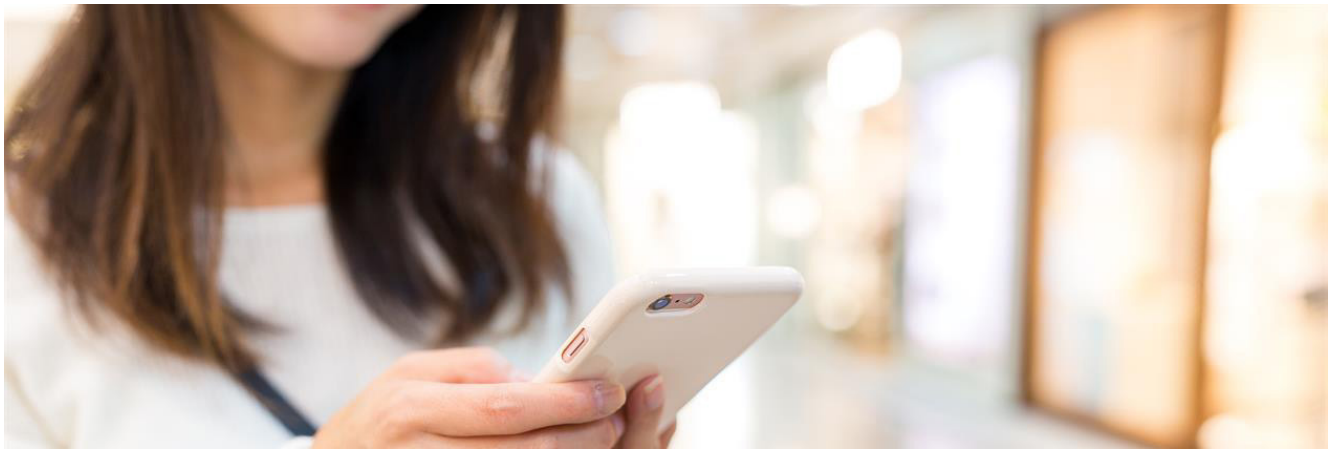
Patient Satisfaction

In 2021, 19 212 cancer patients replied to OUS' web-based survey. Results show overall high satisfaction scores (>90%). In addition, 7438 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.

	Cancer	(OUS)
Did the clinicians speak to you in such a way that you understood them?	97 %	(95 %)
Do you have confidence in the skills of the clinicians?	98 %	(95 %)
Do you have confidence in the skills of the other staff?	97 %	(94 %)
Did you receive sufficient information about your diagnosis / your ailments?	92 %	(87 %)
Did you experience that the treatment was adapted to your situation?	95 %	(91 %)
Were you sufficiently* involved in decisions concerning the treatment?	76 %	(74 %)
Did you experience that the institutions' work was well organized?	92 %	(88 %)
Did you have the impression that the institutions' equipment was in good condition?	94 %	(91 %)
All in all, was the assistance and treatment you received in the institution satisfactory?	96 %	(92 %)
Do you believe that you were given the wrong medical treatment (as far as you can judge)?	97 % **	(94 %)
Did you have to wait to receive help from the institution?	93 % **	(83 %)
All in all, what benefit have you had from the treatment in the institution?	92 %	(85 %)

*The word sufficiently was added in September 2021.

** Percentage represents negative responses.



Relative Survival

There has been a considerable improvement in relative survival within several diagnoses during the last five-year period. This is due to both medical development and changes in the task division between OUS and community hospitals. Diagnoses with a >10 percent point increase from the previous period are shown in the table below.

The data for relative survival is from the Cancer Registry (See Cancer in Norway for definition of relative survival).

Relative survival (%) estimated for two five-year periods for patients treated at OUS (operation or radiotherapy), with the associated 95% confidence intervals (CI).

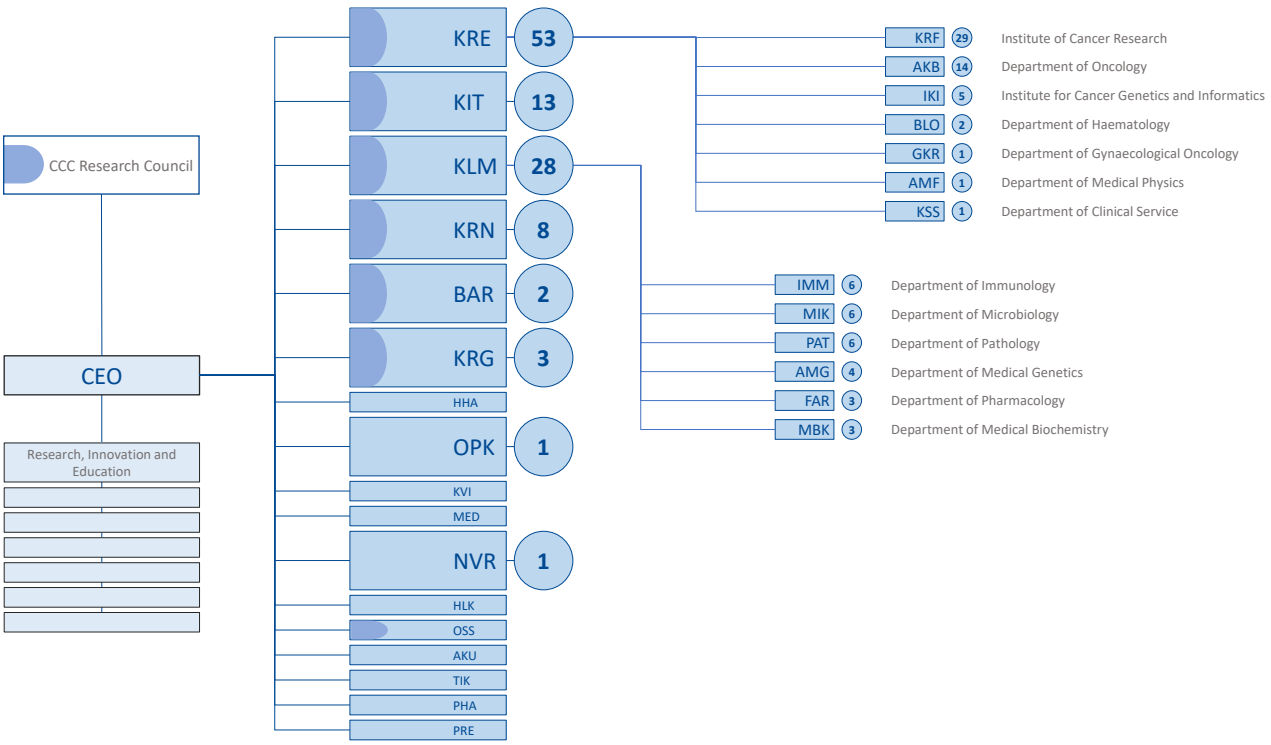
Gender	ICD-10	Location	Years from diagnosis	2007–2011			2017–2021			Difference in % points
				%	CI	N	%	CI	N	
All	All	All	3	69,7	(69,0–70,4)	28603	77,6	(77,0–78,2)	30724	7,9
			5	65,2	(64,4–66,0)		73,1	(72,4–73,8)		7,9
	C15	Esophagus	3	21,5	(17,2–26,8)	361	36,9	(32,7–41,7)	535	15,4
			5	16,5	(12,5–21,8)		29,6	(25,4–34,4)		13,1
	C16	Stomach	3	40,6	(33,8–48,7)	273	54,8	(49,2–61,1)	343	14,2
			5	29,1	(22,2–38,1)		47,3	(41,4–54,2)		18,2
	C22	Liver	3	52,3	(41,9–65,2)	161	61,9	(55,1–69,7)	239	9,6
			5	48,7	(38,0–62,3)		56,3	(49,3–64,4)		7,6
	C25	Pancreas	3	24,2	(19,4–30,2)	366	44,1	(39,4–49,4)	476	19,9
			5	19,3	(14,9–24,9)		35,6	(30,8–41,1)		16,3
	C33-34	Lung	3	28	(26,3–29,8)	3530	48	(46,4–49,7)	4259	20
			5	22	(20,3–23,7)		38,8	(37,1–40,6)		16,8
	C43	Melanoma	3	59,1	(56,1–62,2)	1291	82,6	(80,6–84,8)	1977	23,5
			5	54,4	(51,2–57,9)		78,7	(76,0–81,5)		24,3
	C81	Hodgkin lymphoma	3	83,2	(70,5–98,1)	163	94,7	(90,5–99,2)	127	11,5
			5	82,9	(70,1–98,0)		93,5	(88,6–98,7)		10,6
	C90	Myeloma	3	40,8	(34,2–48,6)	279	56	(48,2–65,0)	200	15,2
			5	27,9	(21,9–35,5)		42,7	(34,9–52,1)		14,8
Female	C56, 57.0-4, C48.2	Ovary	3	64,1	(60,2–68,2)	896	73,5	(70,0–77,1)	893	9,4
			5	51,7	(47,5–56,4)		61,7	(57,8–65,9)		10
Male	C61	Prostate	3	79,7	(77,7–81,7)	5514	93,5	(92,4–94,6)	5070	13,8
			5	78,5	(76,3–80,7)		93,1	(91,8–94,4)		14,6

Relative survival (%) estimated for Norway and regional catchment areas defined by patients' area of residence, with associated 95% confidence intervals. Five years from diagnosis, all genders. The estimates are predicated for 2017-2021.

ICD-10	Location	Norway		South East Region		Oslo	
		%	CI	%	CI	%	CI
All	All	76,8	(76,5–77,1)	76,8	(76,4–77,2)	78,2	(77,2–79,3)
C00-14	Oral cavity and pharynx	74,4	(72,4–76,4)	74	(71,4–76,8)	73,5	(67,1–80,6)
C15	Esophagus	24	(21,7–26,6)	22,8	(19,8–26,1)	18,8	(12,5–28,2)
C16	Stomach	31	(28,8–33,4)	28	(25,0–31,2)	26,5	(19,5–36,1)
C18	Colon	70,5	(69,4–71,5)	70,4	(69,0–71,8)	68,6	(64,7–72,7)
C19-20	Rectum	72,7	(71,3–74,1)	71,5	(69,6–73,4)	72	(67,0–77,4)
C22	Liver	25,2	(22,6–28,1)	26,1	(22,7–30,0)	32,1	(23,1–44,6)
C23-24	Gallbladder and biliary tract	26,1	(22,7–30,0)	22,7	(18,5–27,8)	29,5	(18,5–46,9)
C25	Pancreas	14,6	(13,4–15,9)	14,5	(12,9–16,3)	12,3	(8,6–17,5)
C33-34	Trachea and lung	29,3	(28,4–30,1)	28,5	(27,4–29,7)	29,4	(26,3–33,0)
C43	Melanoma	92,7	(91,8–93,6)	92,3	(91,1–93,5)	90,9	(87,8–94,2)
C40, C41	Osteosarcoma	66,8	(61,1–73,2)	69,2	(61,4–78,0)		
C64	Kidney	79,6	(78,0–81,2)	77,9	(75,7–80,1)	83	(77,2–89,2)
C67	Bladder	81,2	(79,8–82,6)	80,5	(78,6–82,5)	87	(82,2–92,2)
C70-72	CNS	66,7	(65,3–68,3)	68,1	(66,1–70,1)	68,5	(63,4–74,0)
C73	Thyroid gland	93,6	(92,0–95,1)	93,9	(91,8–96,0)	91,3	(86,5–96,4)
C81	Hodgkin lym-phoma	90,3	(87,8–92,9)	88,7	(85,3–92,2)	91,5	(83,7–100,2)
C82-86, C96	Non-Hodgkin lymphoma	78,9	(77,3–80,4)	78,3	(76,3–80,4)	81	(75,6–86,8)
C90	Myeloma	61,8	(59,3–64,4)	62,1	(58,7–65,7)	63,1	(55,1–72,2)
C91-95, excl.C91.1 and C92.1	Leukemia	49,8	(47,2–52,5)	49,1	(45,7–52,6)	54,9	(45,2–66,6)
C91.1	Chronic lympho-cytic leukemia	92,6	(90,2–95,0)	91,9	(88,8–95,2)	96,4	(88,2–105,3)


SIEMENS
220.0
-288.0
SOMATOM Force

CCC Research Groups



OUS CCC Research Activity 2021

Research is one of the main pillars in Oslo University Hospital Comprehensive Cancer Centre. In 2021, we had an evaluation by our Scientific Advisory Board, providing feedback on several aspects of our activities. Research within the OUS CCC is diverse and covers all major fields of cancer research. The year 2021 was a year with several accomplishments. Geir Hoff received the King's medal (Kongens fortjenstmedalje) for his work in research, clinical work and his efforts related to colorectal screening in Norway in April. Research groups at our CCC received substantial funding from the Cancer Society, the Regional Health Authorities and the Research Council of Norway, and several researchers published in highly ranked journals.

The national clinical precision medicine study IMPRESS-Norway was initiated in April, and the Infrastructure for Precision Diagnostics (InPreD) was established. Through this work, the aim is that Norwegian patients will have access to advanced diagnostics for studies in precision cancer medicine. In addition, we are very happy that the Centre for Advanced Cell Therapy is established. Cell and gene therapy are among the most dynamic research areas world-wide and can provide new therapies cancer patients.

Funding for a Research Centre for clinical cancer treatment was funded by the Norwegian Cancer Society and the Research Council of Norway. This centre is called MATRIX, and will have activities in diagnostics, clinical studies and quality of life and patient involvement.

In 2021 863 papers were published in peer reviewed journals of which 151 in journals with impact factor > 10. This is a significant increase since 2020.

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. Still, trying to expand this collaboration and ensure even more collaboration between different groups is a focus area for the coming years, also advised from our scientific advisory board.

In 2021, 956 patients have been included in clinical trials, representing a decrease from the 2020. This is due to some large investigator-initiated trials being finalised. Through several actions, we are working on increasing this number,- both the number of patients included in studies and the number of ongoing clinical studies.

Research in OUS CCC constitutes of all cancer-related research in all of OUS' 15 Divisions as well as the Cancer Registry. The following pages presents the divisions, departments and institutes contributing with significant research and excerpts from OUS CCC led research projects.

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

Division of Laboratory Medicine

The Division of Laboratory Medicine is localized in all hospital locations and includes seven departments; Dept. of Medical Genetics, Dept. of Microbiology, Dept. of Medical Biochemistry, Dept. of Immunology and Transfusion Medicine, Dept. of Pathology, Dept. of Pharmacology and Dept. of Forensic Medicine. The research activity is heterogeneous, and cancer research accounts for about 1/4, counted as cancer-related publications. The research at Dept. of Pathology is most cancer related (about 2/3 of the department's publications), followed by Dept. Medical Genetics (1/6) and Dept of Immunology. In total, about 100 full-time research years are invested in cancer research, resulting in 118 publications in 2021.

We are proud to host two new Strategic Areas at Oslo University Hospital 2022-2027 and both are associated to cancer research, and presented separately:

- "Spatial and multi-omics characterization of single cells to overcome treatment resistance in cancer" by PI Xavier Tekpli (Dept of Medical Genetics), co-PI Thomas Fleischer from KRE.
- "Preservation of fertility in cancer patients" by PI John Arne Dahl (Dept. Microbiology), co-PI Gareth Greggains from KVI and KRE.

Cancer Research in KLM

- Publications: 118
- Collaborative projects within CCC: 35
- Researchers: 125 FTE

SELECTED RESEARCH HIGHLIGHTS

Collaborations

KRE

KLM

Spatial and multi-omics characterization of single cells to overcome treatment resistance in cancer

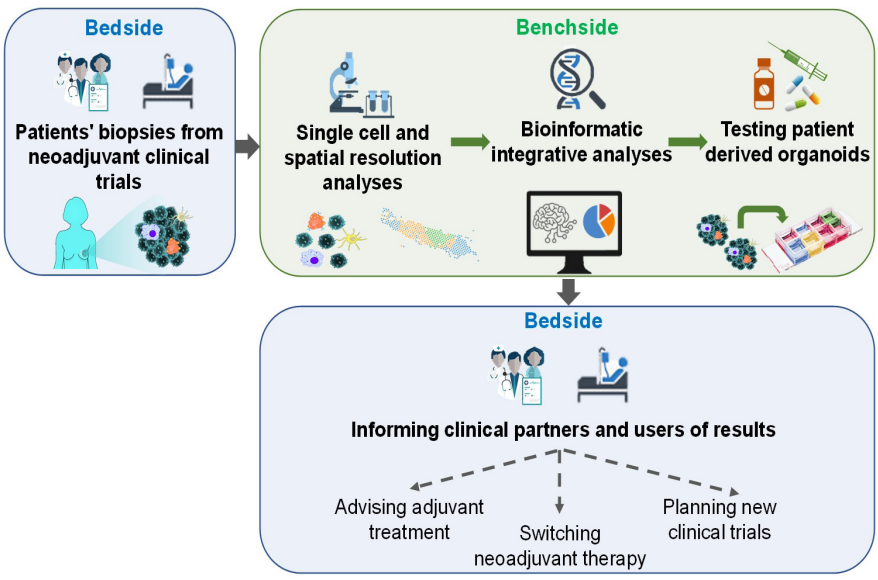
Resistance to treatment is the principal limitation for curing cancer patients. While macroscopically, breast cancer patient's response to treatment may look satisfactory, only few cells in a tumour may have acquired resistance and are sufficient to initiate relapse. In an April 2021 review in Cancer Discovery, single cell methods were perceived as 'leading a revolution in our ability to systematically dissect intratumour heterogeneity' (1). Our project aims at analysing single cell of breast tumours at different molecular levels (multi-omics) to identify in each cell the mechanisms involved in treatment resistance.

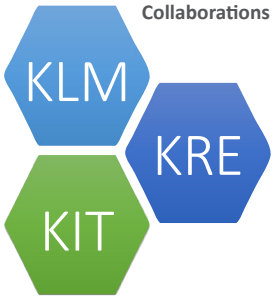
Moreover, we hypothesize that for cancer cells to become resistant to therapies, they need to receive signals and support from the surrounding cells in the tumor microenvironment. Cancer cells, immune cells, fibroblasts and endothelial cells interact and communicate to build local ecosystems. We will characterize such tumor ecosystems using spatial resolution methods and assess their role in treatment resistance. Spatially resolved transcriptomics is a relatively recent method which has been crowned Method of the Year by Nature Methods in 2020 (2).

To bring our results from single cell and spatial resolution analyses of breast tumors closer to clinical practice and personalized medicine, we culture patient-derived organoids. This gives us the possibility to test new treatment strategies for patient relapsing or resistant to therapies directly on their corresponding ex-vivo tumor organoids.

This project has been selected in 2022 as a strategic research area at Oslo University Hospital and will receive funding for six years. It is a strong collaboration and interaction between different divisions at Oslo University Hospital and Akershus University Hospital involving molecular biologists, oncologists, pathologists, mathematicians and bioinformaticians.

Xavier Tekpli





Preservation of fertility in cancer patients

Cancer treatment of young women can lead to side effects such as loss of fertility. Sterility due to chemotherapy can have a major impact on the quality of life of patients and their families. The development of advanced technology makes it possible to preserve fertility more and more often by freezing eggs, embryos or ovarian tissue. Improvements and variations in methods will affect the ability to preserve fertility. We will compare fertility in cancer patients who have received fertility-preserving treatment, up against standard treatment, and examine whether Norwegian patients have equal access to fertility-preserving treatment, measured against international standards. We have found that the epigenetic program (chemical labels in connection with DNA that helps to control the genes) has an important role in the maturation of egg cells and for embryonic development. This has been possible to detect since we have developed a world-leading method for examining epigenetic labels all the way down to the single cell level. By studying the epigenetic program in egg cells that undergo maturation, we will achieve an important measure to know whether egg cells mature correctly and completely. This will allow us to understand what goes wrong with the maturation of egg cells from frozen ovaries, and to develop improved methods that will provide better fertility-preserving treatment.

John Arne Dahl

The Cancer Registry of Norway

The Cancer Registry of Norway collects data and produce statistics on the incidence and prevalence of cancer in Norway. To conduct, promote, and provide a basis for research for new knowledge about the causes of cancer, diagnosis, natural course, and treatment effects is among core objectives of the Cancer Registry. Research activities are performed in Registry Department, Department of Registry informatics, all screening units and at the Research Department.

The Cancer Registry of Norway has about 20 researchers and an equivalent number of PhD students and Postdoctoral fellows with different professional background including epidemiology, medicine, statistics, informatics, molecular biology. In addition, the Cancer Registry advices the government and the general population about cancer preventive measures.

The strongest research area of the Registry is cancer epidemiology and statistics. The KRG provides cancer statistics and predictions for planning and quality control of cancer care in Norway. The KRG works closely with leading clinicians, cancer epidemiologists in Nordic countries, Europe and globally. The KRG also administers the cancer screening programs, and perform research within screening. This research focuses on more effective prevention strategies for equitable cancer prevention by improving communication, introducing novel technology, developing AI for mammographic and cervical cancer screening. A more recent focus is research within cancer molecular biology, in particular epidemiological studies conducted to inform cancer prevention strategies. The population-based biobanks and cohorts combined with epidemiological data from registries and health surveys provide a unique opportunity to identify biomarkers of cancer risk, early detection and treatment effects

Cancer Research in KRG

- Publications: 130
- Collaborative projects within CCC: 13
- Researchers: 24 FTE

SELECTED RESEARCH HIGHLIGHTS

The cancer screening programs

The cervical cancer program turned 25 years in 2021 and is moving into a new era, with the government granting funds for the CRN to work with the Directorate of Health to establish human papillomavirus (HPV) home testing. The anniversary was celebrated with a full day event, which included interesting talks from researchers and the minister of health.

We believe breast screening in Norway can be improved by offering personalized screening, so-called stratified screening. Such a screening program could offer screening to certain women more or less frequently than every other year based on their risk for developing breast cancer. Different risk factors are being studied, including mammographic density and new screening techniques such as tomosynthesis.

Collaborations

KRE

KRG

Research on occupational cancer risk-factors

It is well known that some of the chemical components in petroleum and its derivates can be carcinogenic. The CRN is therefore studying the incidence of cancer among Norwegian offshore workers and strive to understand whether there is a relationship between exposure from the working environment and cancer risk.

KIT

Division of Surgery, Inflammatory Diseases and Transplantation

The clinical patient care at the Division of Surgery, Inflammatory Diseases and Transplantation (KIT) is highly specialized and multidisciplinary, and has clinical and research activity at both Rikshospitalet, Ullevål, Aker and the Norwegian Radium Hospital. The division has five departments: Dept. of Gastrointestinal and Children Surgery, Dept. of Urology, Dept. of Transplantation, Dept, of Dermatology, and Dept. Rheumatology and Infectious Diseases. Surgery is a vital part of care for many patients with cancer. Our surgical departments provide a breadth of cancer care for gastrointestinal, hepatobiliary, pancreatic or urological malignancies. Each department is engaged in clinical research studies and basic science, and strives to better identify patients who can benefit from surgery, and to advance and implement new surgical techniques.

The research activity is organized into 25 different research groups, of which seven have a main focus on cancer research. The aim of these research groups is to conduct clinical and translational studies in surgical oncology. The groups also run register-based studies to evaluate and improve patient care. The research groups work in close collaboration with different research departments at the Institute of Cancer Research to integrate molecular and clinical studies.

Cancer Research in KIT

- Publications: 97
- Collaborative projects within CCC: 26
- Researchers: 25 FTE

SELECTED RESEARCH HIGHLIGHTS

The NORPACT trials – Neoadjuvant or downstaging chemotherapy in non-metastatic pancreatic cancer

Pancreatic cancer is expected to be the second-leading cause of cancer-related death by 2030. At time of diagnosis, 50 % present with metastatic disease. The best outcomes for patients with non-metastatic pancreatic cancer remain in those who have a successful surgical resection. However, only 15 % have resectable disease at time of diagnosis, whereas approximately 35 % of patients present with borderline resectable or locally advanced disease. Neoadjuvant therapy improves overall survival compared with a surgery-first approach in patients with borderline resectable pancreatic cancer. Evidence of higher quality is required to determine whether neoadjuvant therapy has potential benefits and improves survival for patients with resectable pancreatic cancer. Moreover, in a proportion of patients with locally advanced pancreatic cancer, the primary chemotherapy may result in downstaging to (borderline) resectable disease and offers the possibility of surgical resection if venous and/or arterial en-block resection and reconstruction can be performed.

The research group headed by professor Knut Jørgen Labori, Dept. of HPB Surgery has conducted two clinical trials from 2017-2022: Nordic Pancreatic Cancer Trial-1 (NORPACT-1) and Norwegian Pancreatic Cancer Trial-2 (NORPACT-2).

NORPACT-1 examines whether neoadjuvant chemotherapy improves survival in patients with primary resectable pancreatic cancer. NORPACT-1 is a Nordic multicenter study initiated and run from Oslo University Hospital, and started recruiting patients in March 2017 (Norway, Sweden, Denmark, Finland). The trial completed accrual of a total of 140 patients in April 2021. NORPACT-2 examines the effects of chemotherapy in borderline resectable and locally advanced pancreatic cancer in a population-based cohort, with a particular focus on the proportion of patients receiving curative pancreatic resection after neoadjuvant or downstaging chemotherapy. The study has recruited 250 patients at Oslo University Hospital from the South-Eastern Norway Regional Health Authority catchment area. Both studies have collected blood and tissue samples of the primary tumor for bolt on translational research (Professor Elin Kure, Institute of Cancer Research) and basic research (Professor Caroline Verbeke, Dept. of Pathology). The trials have received funding from The Norwegian Cancer Society (Kreftforeningen) and South-Eastern Regional Health Authority (Helse Sør-Øst).

ClinicalTrials.gov Identifier: NCT02919787
ClinicalTrials.gov Identifier: NCT04423731

Nordic Pancreatic Cancer Trial – 1 NORPACT-1

Upfront surgery vs neoadjuvant chemotherapy (FOLFIRINOX) in resectable pancreatic cancer

Study design

Randomized clinical trial
2017-2021

140 patients,
resectable pancreatic cancer

Nordic, multicentre
12 centers in Norway,
Sweden, Denmark and Finland

Flowchart

1.Neoadjuvant 2.Upfront surgery

Endoscopy

FOLFIRINOX x 4

Surgery

Adjuvant chemotherapy

FOLFIRINOX x 8-12

Endpoints

Primary:
- overall survival 18 months (diff. 50 % vs 70 %)

Secondary:
- overall survival
- disease free survival
- safety/feasibility
- completion rates
- histopathology
- quality of life
- health economics
- translational research

Norwegian Pancreatic Cancer Trial – 2 NORPACT-2

Neoadjuvant or downstaging chemotherapy in borderline and locally advanced pancreatic cancer

Study design

Prospective, observational study (2018-2020)

Unselected, population based cohort (BRPC and LAPC)

Oslo, single centre
Catchment area 3.1 mill.

Flowchart

Endoscopy/(ERCP/PTC)

Chemotherapy 2-4 months

Surgery

Palliative chemotherapy/ Radiotherapy/ Best supportive care

Adjuvant chemotherapy

Endpoints

Primary:
- resection rate

Secondary:
- overall survival
- disease free survival
- safety/feasibility
- completion rates
- histopathology
- health economics
- quality of life
- translational research

The TESLA studies: Transplantation for non-operable bile duct cancers

Malignancy of the biliary tree (cholangiocarcinoma, CCA) is a rare cancer with an annual incidence around 150 cases in Norway. Cholangiocarcinoma can be subdivided into distal, perihilar, and intrahepatic according to their anatomical location. Despite improvements in multidisciplinary management, patients with CCA have a poor outcome and only 20 % of patients are eligible for surgical resection, with 5-year overall survival of less than 10 % for all patients. The only potentially curative treatment option is surgical resection with complete excision of tumor with negative margins. The majority of patients are ineligible for surgical resection because of tumor location, size, multifocality, or underlying liver disease with a median survival of less than 12 months following diagnosis, while 5-year survival following attempted radical surgical resection ranges from 25-45%. Non-surgical approaches, including systemic chemotherapy, local ablative therapies, and radiation, are also suboptimal, with only marginal improvement of CCA survival.

Liver transplantation is an established method of treatment for acute and chronic liver failure. One and five-year survival after liver transplantation is approximately 90% and 80%, respectively.

Certain malignancies are eligible for liver transplantation today, including hepatocellular carcinoma, hepatoblastoma, and hemangioendothelioma. The International Registry of Hepatic Tumors in Liver Transplantation show that survival of HCC patients after transplantation is above 70% and 60% at 1 and 5 years, respectively.

We hypothesize that highly selected patients with early disease may benefit from liver transplantation and achieve a 5-year survival of 80%. The research project headed by associate professor Sheraz Yaqub, Dept. of HPB Surgery and professor Pål Dag Line, Dept. of Transplantation Medicine have been designed as two prospective explorative studies, named TESLA-1 and TESLA-2, investigating liver transplantation in non-resectable intrahepatic cholangiocarcinoma and non-resectable hilar cholangiocarcinoma, respectively. The main objectives are to obtain long overall survival, good health-related Quality of Life, and identify pre-transplant clinical findings that can define a subgroup of patients with a 5-year survival of at least 50% or even cure from the disease. Both trials are recruiting patients from all over Norway.

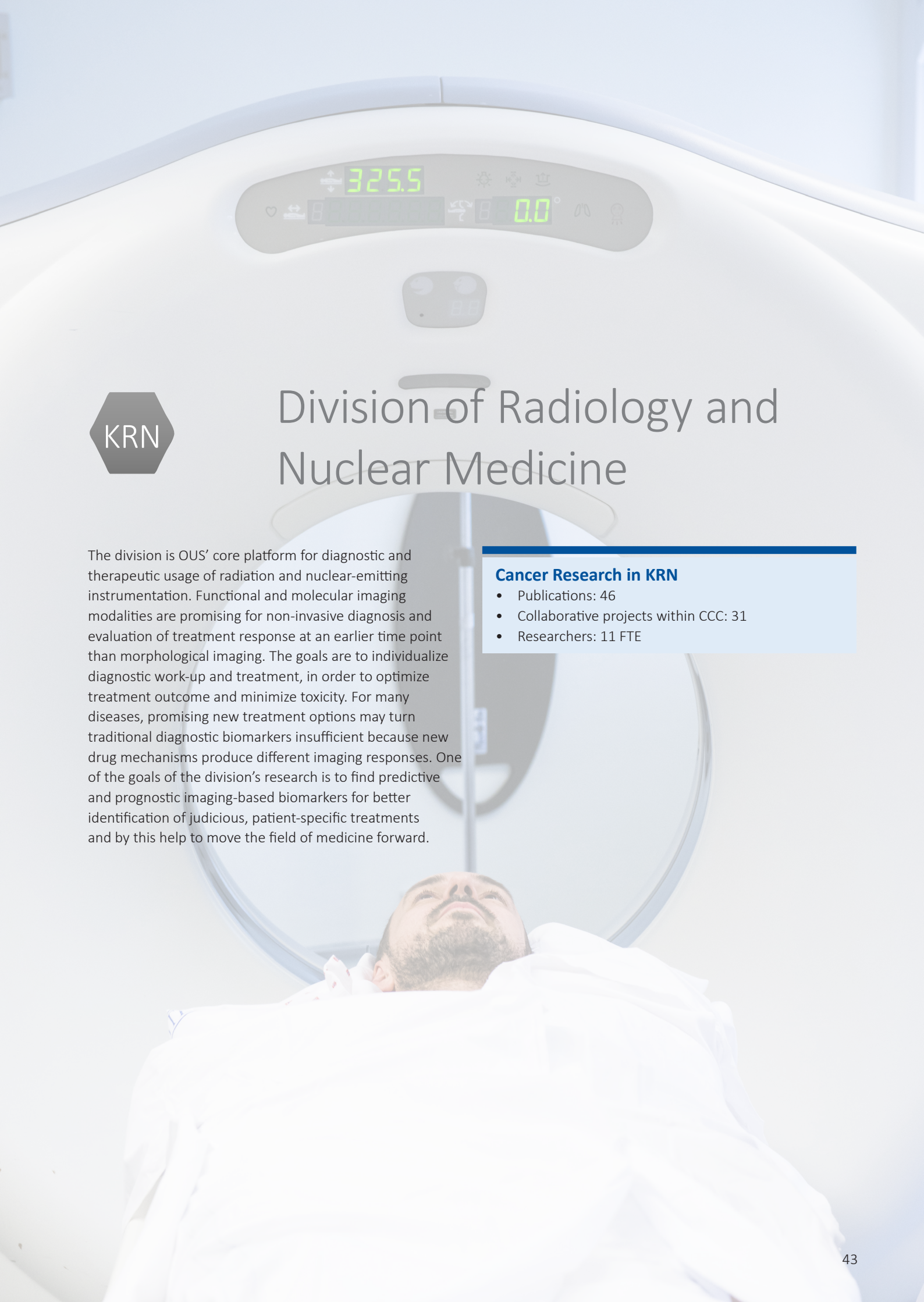
ClinicalTrials.gov Identifier: NCT04556214
ClinicalTrials.gov Identifier: NCT04993131

TESLA1
Liver Transplantation for Intrahepatic Cholangiocarsinoma

TESLA2
Liver Transplantation for Perihilar Cholangiocarsinoma

PÅL DAG LINE

SHERAZ YAQUB



KRN

Division of Radiology and Nuclear Medicine

The division is OUS' core platform for diagnostic and therapeutic usage of radiation and nuclear-emitting instrumentation. Functional and molecular imaging modalities are promising for non-invasive diagnosis and evaluation of treatment response at an earlier time point than morphological imaging. The goals are to individualize diagnostic work-up and treatment, in order to optimize treatment outcome and minimize toxicity. For many diseases, promising new treatment options may turn traditional diagnostic biomarkers insufficient because new drug mechanisms produce different imaging responses. One of the goals of the division's research is to find predictive and prognostic imaging-based biomarkers for better identification of judicious, patient-specific treatments and by this help to move the field of medicine forward.

Cancer Research in KRN

- Publications: 46
- Collaborative projects within CCC: 31
- Researchers: 11 FTE

SELECTED RESEARCH HIGHLIGHT

Collaborations

KIT KRE KRG

Targeted Radionuclide Therapy (TRT) for metastatic cancer

Target-seeking “missiles” with explosive charge: find and kill cancer cells

Radiation therapy is the most common type of cancer treatment. Radiation is delivered from a machine for the treatment of localized tumors. Unfortunately, it cannot be used to treat widespread cancer that remains a major unmet clinical challenge, and metastatic recurrence is the main cause of mortality of cancer patients. The recent advancements in nuclear and molecular biology technologies allow the development of novel systemic radiopharmaceuticals, that either accumulates by physiological mechanisms or binds preferentially to cancer cells, for cancer diagnosis (molecular imaging) and therapy. Most radiopharmaceuticals contain a radionuclide and a cancer cell-targeting molecule, such as monoclonal antibody or small molecule (Figure 1A). Systemic targeted radionuclide therapy (TRT) is based on a personalised patient selection using nuclear medicine imaging techniques to assess the presence of a biologic target (Figure 1B). TRT is a rapidly developing treatment modality in oncology.

Each cancer is requiring different and specific radiopharmaceutical, destroying mostly cancer cells, but not healthy cells. Our goal is to optimize TRT using novel radiopharmaceuticals developed in Norway. The exact mechanisms of action, side effects and safety of these radiopharmaceuticals need to be understood and will be at the center stage of our research.

The long-term goal is to prolong survival, as well as improve quality of life in these patients. To achieve this, radio- and tumour-biological aspects of the disease and the treatment must be understood based on preclinical studies from the interdisciplinary team who will have access to the most advanced core facilities, imaging scanners, technology platforms and associated expertise. The project also stimulate transfer of research outputs and interactions between researchers, clinicians and industry. As a result of this new patentable discoveries are expected. Our solution is personalization of TRT through optimization of theranostics (diagnosis and therapy).

This project focus on the clinical need, identification of relevant molecular targets, optimization and preclinical testing of novel radiopharmaceuticals, technologies and therapeutic strategies for high precision delivery of ionizing radiation to tumour cells. Additionally, TRT is studied alone (single or multiple injections) and in combination with other treatment modalities due to non-overlapping mechanisms of action.

Main objectives:

1. Development and characterization of novel radiopharmaceuticals for advanced prostate, multiple myeloma, neuroendocrine tumours, osteosarcoma, glioblastoma, ovarian, colorectal, breast cancers, etc. (Figure 1A). Different target agents are under testing.
2. Proof of principal- Preclinical validation of radiopharmaceuticals (cellular uptake, viability, tumour targeting, therapeutic efficacy, toxicity, single injection, multiple injections, the target receptor expression level before and after TRT;
3. Mechanisms of action of TRT (DNA and membrane damage, intercellular communication, senescence, autophagy, bystander and immunogenic effects);
4. Imaging and dosimetry (Figure 1B) using best-in-class tools;
5. Combination of TRT with other therapies (hormone therapy, immunotherapy, chemotherapy, different inhibitors, proton therapy, etc.);
6. Translational and clinical issues.

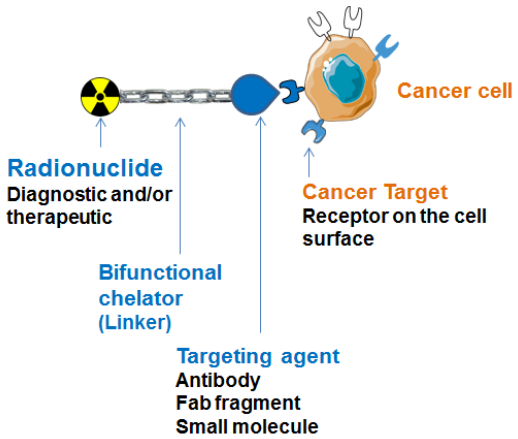


Figure 1A. Radiopharmaceuticals consist of a radionuclide, targeting moiety and linker.

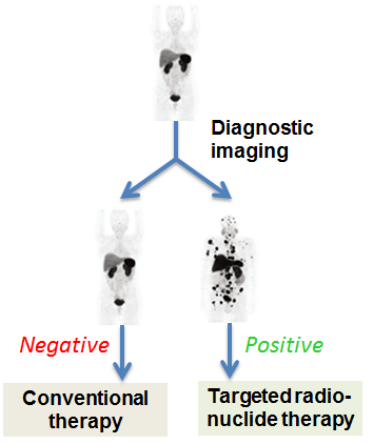


Figure 1B. Diagnostic imaging is used to detect the presence of a molecular target and select patients for personalized treatment of cancer.

BAR

Division of Paediatric and Adolescent Medicine

Childhood Cancer Research at Oslo University Hospital (OUH) is closely integrated with clinical work and activity. The research activity is formally organized through two OUH research groups, INTERPRET and TRANSLATE. The INTERPRET research groups focuses on clinical aspects of childhood cancer (late effects, health services, palliative and supportive treatment), while the TRANSLATE research group focuses on the more translational research aspects of childhood cancer (preclinical cellular, molecular, genetic and immunological aspects of cancer with emphasis on translational targeted therapy potential). The pediatric cancer research activity is further supported by infrastructures such as the National Childhood Cancer Biobank (NCCB) and the center for Innovative Therapies for Children (ITCC), both located at the Pediatric Research Unit at OUS. The NCCB (https://ous-research.no/barnekreftbiobank/) has been collecting biological material from all consenting newly diagnosed childhood cancer patients at OUH since 2017, and nationally from 2019, with an over 95% inclusion rate. The main aim of the ITCC center is to develop novel therapies for pediatric cancers in cooperation with regulatory bodies and pharmaceutical enterprises through conducting early phase clinical trials in children and adolescents. In addition, approximately 40% of children diagnosed with childhood cancer are included in clinical treatment trials within international pediatric CNS, solid tumor and liquid cancer collaborations, where clinical and molecular data is collected and research is performed in the larger international consortia.

Cancer Research in BAR

- Publications: 54
- Collaborative projects within CCC: 30
- Researchers: 10 FTE

KRE

Division of Cancer Medicine

The Division of Cancer Medicine (KRE) contribute in the teaching of medical students and conduct research, dissemination and innovation. KRE has five departments: Oncology, Gynaecological Cancer, Haematology, Clinical Service, and Medical Physics. The Division also hosts two research institutes: Cancer Research and Cancer Genetics and Informatics. A Norwegian Research Centre of Excellence – Centre for Cancer Cell Reprogramming (CanCell) is affiliated with The Division of Cancer Medicine. The Division has its main activity at Radiumhospitalet, but also operates at Rikshospitalet, Ullevål and Aker Hospitals.

The research is organised into 55 research groups. About 30 doctoral degrees are awarded annually in the clinic. The research activities include clinical, translational and explanatory research, and a clinical trial unit. A number of regional core research facilities are run in the clinic:

Bioinformatics, confocal microscopy, electron microscopy, flow cytometry, proteomics, microarray and sequencing, genotyping, comparative medicine, and animal MRI.

The Division is co-located with, and a member of, the innovation cluster Oslo Cancer Cluster, and students from Ullern High School do practice at the Institute of Cancer Research. The division is also host to Oslo University Hospital Comprehensive Cancer Centre (OUS-CCC).

Cancer Research in KRE

- Publications: 467
- Collaborative projects within CCC: 320
- Researchers: 452 FTE

Department of Oncology

The department is headed by Prof Stein Kaasa and has a regional responsibility for the oncological cancer care in Health South-East with a population of 2,950,000 people, and a local hospital responsibility for five districts in Oslo with a population of 220,000. This responsibility includes clinical activities, teaching / training, research and professional development. We offer radiation therapy, and treatment with chemotherapy, hormone therapy, immunotherapy and other new, targeted drugs in addition to thyroid / parathyroid surgery and most of the breast surgery. The department also has its own palliative unit. We treat most cancers. The treatment is carried out in close collaboration with other departments at Oslo University Hospital and with the other hospitals in the region.

The cancer treatment department consists of 18 sections and three staff units. There are varying numbers of chief physicians in each section, but in addition to the section chief physician, all sections also have one who is responsible for research and one for the relevant tumor groups. In addition to clinical activity, the department has significant tasks related to education and training, research and professional development. There are about 80 clinical studies that are ongoing at the department, and the department has 5 professorships. We are involved in the education of medical students throughout the program. The number of annual scientific publications is about 140

Cancer Research in AKB

- Publications: 140
- Collaborative projects within CCC: 107
- Researchers: 40 FTE

Department of Haematology

The Department of Haematology (BLO) examines and treats patients with all types of blood disorders. Our aim is to deliver good patient care, research at a high international level and teaching within the specialist area of blood diseases. The department has research activities in most areas where the department has a treatment offer. The department's role in the CCC covers diseases in cancer in blood system, including leukaemia and myeloma. Three research groups conduct cancer research at the department.

The department is also host for Oslo Myeloma Center, which is the largest center for clinical myeloma research in the Nordics. It collaborates with basal and translational research groups, especially with the KG Jebsen center for B cell malignancies at our hospital, with projects in drug-sensitivity screening, pathophysiology and immune therapy. In addition, they have a myeloma registry with both prospective and retrospective data.

Cancer Research in BLO

- Publications: 26
- Collaborative projects within CCC: 22
- Researchers: 11 FTE

Institute of Cancer Research

The Institute has internationally strong research groups within biochemistry, cell and tumor biology, genetics, radiation biology, immunology and cancer prevention. For more than 30 years there has been a close interaction between researchers at the Institute and cancer surgeons, oncologists and pathologists. This emphasis on translational science has resulted in numerous clinical protocols based on in-house research, and the Institute is a key partner in the Comprehensive Cancer Center, organizationally under the Division of Cancer Medicine at Oslo University Hospital. Institute Director is Prof Kjetil Taskén.

The Institute is engaged in both basic and translational cancer research involving experimental research on model organisms from various evolutionary levels as well as human material from all types of cells and tissues. The co-localisation with a large cancer hospital fulfils the premises for advanced medical research across sciences, a necessity towards the goals of individualised diagnostics and treatment for cancer patients.

Cancer Research in KRF

- Publications: 242 (50 IF>10)
- Collaborative projects within CCC: 430 total, 87 collab
- Researchers: 343 FTE

CanCell – Centre of Cancer Cell Reprogramming

CanCell is a Centre of Excellence initiated 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 around 100 MNOK (10M€) 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. Even though the covid-19 pandemic hit the world hard in 2021, CanCell's research has continued to advance our knowledge on the basic cellular and molecular mechanisms of cancer. The centre's scientists published 35 articles in 2021 in international journals of high esteem, including papers in top journals such as Nature and Cell. Three of CanCell's young scientists defended their PhD theses in 2021, and 8 MSc degrees were obtained. CanCell's MSc/PhD course, "Molecular Cancer Medicine", was implemented with good participation and strong efforts by CanCell's junior scientists as teachers.

Cancer Research in CanCell SFF

- Publications: 35
- Collaborative projects within CCC: 22
- Researchers: 87 FTE

Institute of Cancer Genetics and Informatics

The Institute for Cancer Genetics and Informatics performs research in biomedicine and informatics to develop and establish new methods for diagnosis and prognostication and applies these methods to large clinical series in collaboration with the clinical departments and Department of Pathology at Oslo University Hospital. Successful trials are then made applicable and offered as routine clinical practice, preferably established and performed by us.

In recent years, we have focused on new technologies, often referred to as artificial intelligence (AI). We continue establishing new knowledge in the laboratory and then taking it to the clinic. This strategy requires an interdisciplinary approach, and close integration between scientists, technologists and clinicians. Our basic research strategy is to focus on nucleomics, our innovation strategy is focused on microscopy based image analysis, and our overall goal is to enable better cancer treatment through new methods for improved diagnosis and prognosis of cancer. The IKI is headed by Prof Håvard Danielsen.

Cancer Research in IKI

- Publications: 22
- Collaborative projects within CCC: 19
- Researchers: 39 FTE

K.G. Jebsen Centre for B-cell malignancies

K.G. Jebsen Centre for B-cell cancer started in 2018. The research at the centre focuses on knowledge about blood cancer, lymphoma and bone marrow cancer. The centre conducts interdisciplinary research in immunotherapy and personalized treatment, so-called precision medicine. The centre aims to identify new biomarkers and to develop and test new therapies for patients with leukaemia (B-ALL and CLL), lymphoma and multiple myeloma, and is headed by Professor Ludvig Munthe (KLM), assisted by Associate Professor June Helen Myklebust (KRE). In 2021 the Centre received additional allocation of 9 million NOK from the Kristian Gerhard Jebsen Foundation, increasing the duration of the centre until 2024. The extension enables continuation of important research on immunotherapy and precision medicine.

One of the centre's strengths is that it has brought together laboratory researchers and clinicians from various medical field. The centre has completed or operates more than 80 clinical trials, and over 30 of these are now recruiting patients. The goal is to be able to offer patients with B-cell cancer better treatment. The centre's researchers are testing new treatments, including new combinations of cytotoxic drugs, new monoclonal antibodies against cancer cells and developing new forms of immunotherapy. They have also developed analyses that test the effect of new cancer drugs on patients' cancer cells. The results can be used in personalized treatment and these analyses make it possible to identify high-risk patients who need more intensive treatment. A further focus in the centre is studies of the microenvironment in the cancer cell tissue to find new therapeutic points of attack.

In 2021, researchers at the centre published 57 articles including 49 original articles. Many were published in top ranked journal such as N Engl J Med, Lancet Oncol, and Cancer Cell. The research output has led to five DOFIs, two international patents and three patent applications on new therapeutic drugs.

Cancer Research

- Publications: 57
- Collaborative projects within CCC: 26
- Researchers: 41

Centre for B-cell malignancies

New immunotherapy for cancer based on the mechanism of transplant rejection

Muhammed Ali and Eirini Giannakopoulou in Johanna Olweus' research group joined by a team of scientists from University of Oslo/Oslo University Hospital (OUS) and Karolinska Institutet (KI) developed a new type of immunotherapy for cancer. The new treatment makes the patient's immune cells "believe" that cancer is a transplanted organ that should be rejected. The immune cells then attack and fight the cancer cells, thereby curing the cancer. This is made possible thanks to a new technology, developed by the research group, and genetic modification of the immune cells. The scientists have demonstrated the efficacy of the new treatment on patient leukemia cells in cell cultures and in mouse models, and are planning a clinical trial in patients with acute leukemia.

First authors M. Ali and E. Giannakopoulou with project leader J. Olweus

When an organ is transplanted from a donor to a patient, the patient must receive life-long immunosuppressive medication to avoid rejection of the organ. If medication is stopped, the patient's T cells, will reject the transplanted organ in a short time. Cancer can occasionally develop in the transplanted organ, but stopping immunosuppression in such cases usually suffices to "reject" the cancer, even if it has metastasized outside of the organ. The same mechanism that is responsible for transplant rejection, seems capable of curing cancer. If T cells could be devised to attack only one type of cell instead of a whole organ containing a large number of different cell types, this could provide a basis for development of a new type of immunotherapy. By exploiting the technology that Ali took part in developing in the group, he was able to identify TCRs recognizing an enzyme that is present at high levels in the nucleus of leukemia cancer cells. The results were published in Nature Biotechnology on 6 December 2021, proving the concept of Olewus' ERC grant "Outsource": to utilize the mechanism of transplant rejection to identify self-reactive, therapeutic TCRs from healthy donors.

Novel gene expression-based classification of metastatic colorectal cancer published in Genome Medicine

The multidisciplinary team of the K.G.Jebsen Colorectal Cancer Research Centre publishes a novel gene expression-based classification of metastatic colorectal cancer. PhD student S. Hossein Moosavi in Anita Sveen's project group at the Dept. of Molecular Oncology at the Institute for Cancer Research is 1st author of this paper published in Genome Medicine. This is the first large study of multi-metastatic gene expression profiling of colorectal cancer liver metastases, and the new metastasis-oriented subtyping framework showed prognostic relevance in the context of tumor heterogeneity.

The five biologically distinct liver metastasis subtypes (LMS1-5) originated from different progenitor cell types, and a subtype expressing biological features of cancer aggressiveness was also an independent predictor of a poor patient survival. The aim of a recent innovation project with the TTO Inven2 is to develop the subtypes into a framework for biology-guided treatment of metastatic colorectal cancers.

S. Hossein Moosavi, 1st author

	LMS1	LMS2-4	LMS5
	Epithelial-like		Mesenchymal-like
Prevalence:	13-18%	55-59%	24-32%
Genetic:	*KRAS* and *TP53* mut	*TP53* mut	
Progenitor:	Secretory cells	LGR5+ cells, enterocytes	Qiescent stem cells
Phenotype:	MSI-like	Transit amplifying	Immune and stromal infiltration
Clinical:	Worse survival		Synchronous metastasis
Heterogeneity:	+	+++	++

Liver metastatic subtypes

Improving Risk stratification of Ductal Carcinoma In Situ (DCIS)

Breast cancer recently surpassed lung cancer as the most commonly diagnosed cancer in the world. Pre-invasive breast cancer, or DCIS, once an uncommon diagnosis, accounts today for about 20% of newly diagnosed breast cancers. Many of these will not progress to invasive cancer, but due to the uncertainty about the risk potential and the optimal way to manage these patients, most are treated with surgery followed by radiation therapy.

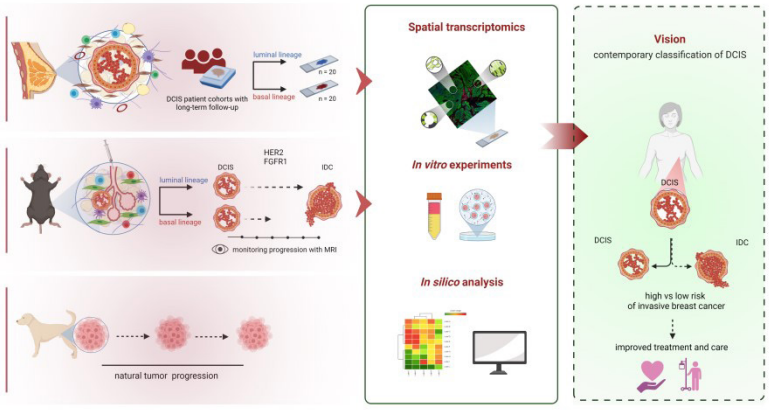
The group headed by Therese Sørlie at Dep. of Cancer Genetics, Institute for Cancer Research, is investigating how breast cancer develops along the two main lineage-specific paths, which largely correspond to the luminal epithelial and the basal or myoepithelial cell differentiation pathways. The cellular microenvironment plays an important role in the transition from in situ lesions to infiltrating carcinomas and the group is using spatial profiling technologies to study carcinoma cells, fibroblasts and immune cells and their interactions. They are also using mouse intraductal tumor models to be able to study tumor initiation and progression from the earliest mammary tumor stages in a relevant model system. Data collection through these experimental approaches will allow for exploration of similarities and differences in tumor characteristics between human DCIS and murine mammary tumors.

Two central growth factor receptors, the Human Epidermal growth factor Receptor 2 (HER2), and Fibroblast Growth Factor Receptor 1 (FGFR1), have essential functions in breast cancer when aberrantly expressed. The HER2 protein when expressed at high levels lead to more aggressive breast cancers and is also a therapeutic target for such tumors, whereas its role in DCIS and specifically in the transition from DCIS to invasive carcinomas is unclear. FGFR1 is overexpressed in a substantial number of hormone receptor positive breast cancers and has a role in endocrine resistance, but how FGFR1 is involved in DCIS and the early progression stages is yet unknown. Sørlie and her team is specifically focusing on these two receptors in their studies of progression of the different breast cancer subtypes.

Identifying and implementing more precise molecular prognostic markers for DCIS would greatly advance patient management and would reduce treatment burden for women with low-risk disease and refine the treatment for those with risk of progression. The group's vision is that their research will give insights that can be used to develop risk predictive signatures for clinical use.

Sørlie has received funding from The Norwegian Cancer Society (Kreftforeningen) and the Pink Ribbon Campaign, and South-Eastern Regional Health Authority (Helse Sør-Øst). In addition, they are part of a project led from NMBU that has received funding from the Research Council's joint funding initiative "Fellesløftet", which will explore the potential of using dogs as models for human breast cancer. The project will specifically study multiple breast malignancies in dogs that give a unique opportunity to study tumor cell evolution which is not possible in human breast cancer.

Therese Sørlie



Studies of breast cancer initiation through in silico, in vitro and in vivo experimental approaches to arrive at improved classification of DCIS

Novel biomarker for Antibody Drug Conjugate

Dr Olav Engebråten and Anette Weyergang from the Institute for Cancer Research are 1st and last authors on the manuscript.

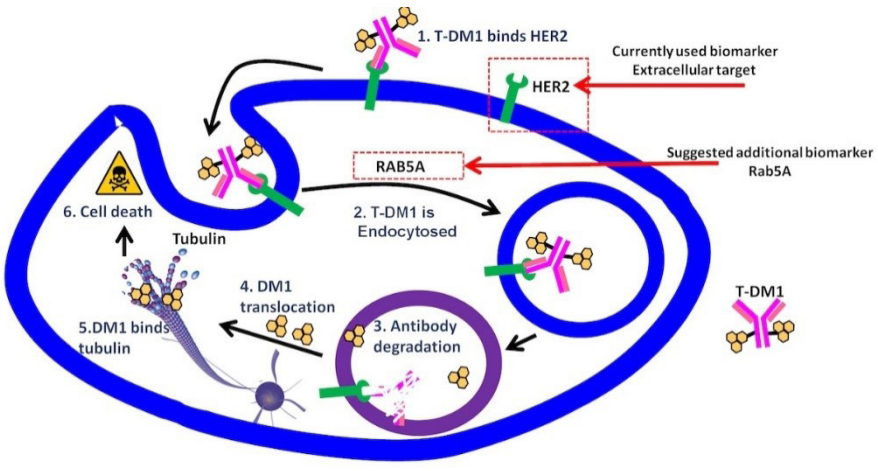
The current use of precision medicine improves specificity of cancer treatment, but not in all patients. Better predictive markers for clinical response are therefore warranted.

The study «RAB5A expression is a predictive biomarker for trastuzumab emtansine in breast cancer», led by Dr Anette Weyergang, is the first demonstrating that proteins involved in intracellular transport can be utilized as biomarkers for ADC treatment. The manuscript has been published in Nature Communications.

The study is focused on antibody drug conjugates (ADCs), an up and coming drug class within cancer therapeutics. In this study the authors first showed a high correlation between Rab5A, a protein involved in endocytosis, and T-DM1, an HER2 targeted ADC in a cell line panel. The result was validated in a clinical cohort from the I-SPY2 study in collaboration with Laura Esserman and her research team at UCSF, and finally verified in an independent clinical cohort from the Kamilla study at OUS.

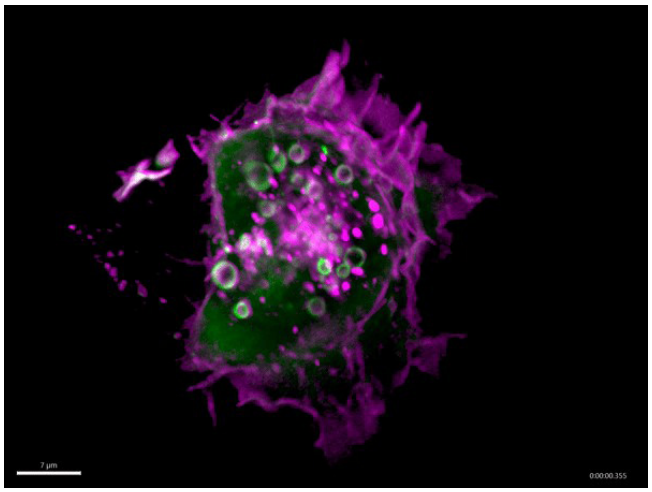
Overall, the results of this study imply that current and future ADC treatment will benefit from the incorporation of biomarkers reflecting uptake and intracellular transport.

The project is admitted to the SPARK innovation program.



Phafin2, new regulator of macropinocytosis, an important mechanism for nutrient acquisition by cancer cells

3D movie (image captured) of a cancer cell forming macropinosomes. The video was taken on a new advanced light sheet microscope that was recently constructed in the Stenmark lab. Magenta outlines the cell membrane, green shows the localization of the protein Phafin2 during macropinocytosis.



In a recent article in Nature Communications, project group leader Kay Oliver Schink and his coworkers in Harald Stenmark's group at the Institute for Cancer Research and the Centre for Cancer Cell Reprogramming (CanCell) identify a new mechanism how the protein Phafin2 can regulate a process called "macropinocytosis".

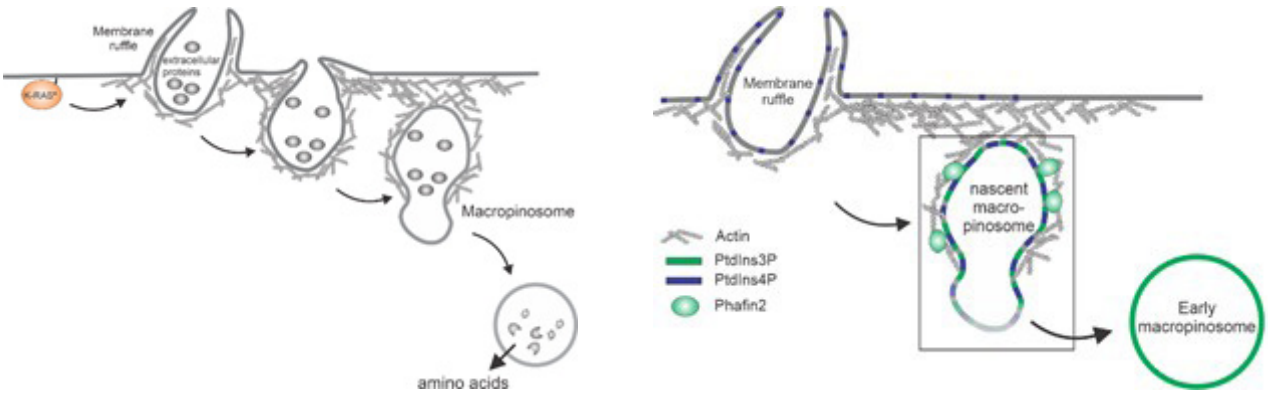
Macropinocytosis – also called "cellular drinking"- has recently gained much attention as a potential target for cancer treatment, as cancer cells use this process to gain additional nutrients to fuel their growth. Aggressive cancer types, such as pancreatic cancer, exploit macropinocytosis as a mechanism to take up additional nutrients.

The fast growth of these cancers requires lots of energy and amino acids, which often become scarce within a tumor. To be able to grow quickly, these cells drink – by using macropinocytosis – the protein-rich extracellular fluids, which are then digested. The resulting amino acids are then used by the cancer cells to fuel their growth.

Schink and his co-workers have identified a new regulator of this process, the protein Phafin2. They find that Phafin2 is involved in very early events of macropinocytosis, directly after the macropinosome is formed at the surface of the cell. During this process, Phafin2 interacts with the actin cytoskeleton and allows the newly formed macropinosome to remove actin from its surface to fully enter the cell. Cells lacking Phafin2 show defects in macropinocytosis.

During their studies, the authors found that many cancer types show amplifications of Phafin2, which suggest that this gives cancer cells a growth advantage. To test this hypothesis, they used CRISPR/Cas9 to knock out Phafin2 in pancreatic cancer cells. The Phafin2 knockout cells are not able to use macropinocytosis and show impaired growth when nutrients are scarce.

As many of the highly aggressive RAS-transformed cancers – especially KRAS-transformed pancreatic cancers - show high levels of macropinocytosis, this process is an attractive target for cancer therapy, as disrupting the amino acid supply routes would slow cancer cell growth. Moreover, nanoparticles and other large drug conjugates are preferably taken up via macropinocytosis and identifying cancer cells with high or low levels of macropinocytosis could guide targeted therapy.



(a) Cancer cells can exploit macropinocytosis to take up extracellular proteins which can then serve as additional amino acid source to fuel cancer growth. (b) The protein Phafin2 regulates macropinocytosis by removing the actin cytoskeleton from forming vesicles.

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