MATRIX - Norwegian Centre for Clinical Cancer Research







Centre for Clinical Treatment Research MATRIX has an overall ambition to help patients with hard-to-treat cancers to live longer and with better quality of life

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MATRIX Co-Funders:

The Research Council of Norway The Norwegian Cancer Society



Centre for Clinical Treatment Research





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INTRODUCTION

Greetings from the Director

Dear friends, colleagues, and supporters of MATRIX, It is my pleasure to welcome you to the 2023 MATRIX Annual Report, our first year of full operations. This report covers the main activities from the past year and key features of what we do. Highlights from 2023 include the first industry research collaboration in MATRIX, the successful organization of the first Nordic Precision Cancer Medicine Symposium, the establishment of the MATRIX Scientific Advisory Board, strong participation in several large EU consortia, and initiation of a new master-level course, Introduction to Clinical Studies for Healthcare Personnel. Furthermore, funding to initiate the first MATRIX-designed clinical trial, MATRIX-RARE, has been secured, and several MATRIX-affiliated key players have been awarded prestigious prizes.

A key element in modern cancer treatment is the possibility of guiding patient treatment based on a detailed molecular characterization of each patient's disease - precision cancer medicine. Norway has, in recent years, built up an impressive precision cancer medicine ecosystem to be able to offer patients with advanced cancer systematic use of and equal access to molecular diagnostics and precision medicine via clinical trials, such as the national IMPRESS-Norway trial. The long-term goal of the initiative is to establish mechanisms to implement precision cancer medicine also within standard-of-care.

In Norway, extended molecular analyses are now provided by the national infrastructure for precision cancer diagnostics (InPreD), and this is reimbursed in the public healthcare system. Since the launch of InPreD and IMPRESS-Norway in April 2021, more than 1500 cancer patients with advanced disease have been included in the molecular profiling phase of IMPRESS-Norway, and around 27% of these are included in the treatment phase of the trial. MATRIX is the latest addition to the Norwegian precision cancer medicine ecosystem and collaborates closely with and will continue to build on the already existing initiatives, focusing among others on new diagnostics and therapy in earlier treatment lines. In addition, the centre has a strong focus on tailor-made, patient-centred treatments and prospective plans - also known as patient-centred care pathways.



MATRIX is a national research centre with an overall ambition to help patients with hard-to-treat cancers live longer with better guality of life. The scope of the centre is very broad, ranging from the development of next-generation diagnostics and treatment, development and implementation of new, digital cancer care tools as well as the clinical trial engine, a support function offering advice and hands-on support to academic investigators across Norway, who are planning or starting new clinical studies. A well-recognized obstacle to the implementation of precision cancer medicine is access to employees with state-of-the-art knowledge and expertise. Thus, there is a need to raise the competence of all types of study personnel nationwide. MATRIX is involved in training the next-generation study personnel, and we are pleased that the first master-level course launched in the fall of 2023, reached max capacity and had participants from all of Norway.



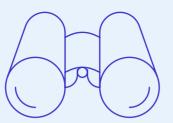
March 2024

We encourage researchers, industrial partners, patients and other interested parties to contact us to get more information and to discuss opportunities to shape the future of cancer treatment together.

Åslaug Helland Director, MATRIX

ABOUT

A Brief **Overview**



8

Years of Centre funding (2022-2030)

15 Hospitals across

>30

Research groups across Norway involved

The Norwegian Centre for Clinical Cancer Research, MATRIX, is a national research centre with an overall ambition to help patients with hard-to-treat cancers live longer, optimize their quality of life, and plan for a life with limited life expectancy by use of the concepts and competence of palliative care. MATRIX officially opened in August 2022 and has a broad range of activities, including the development of next-generation precision diagnostics and treatment as well as the development and implementation of new, digital patient-centred care pathways for improved shared decision-making, thus ensuring that the "patient's voice" is fully integrated into the entire course of treatment.

MATRIX collaborates closely with large ongoing national precision cancer medicine initiatives, national tumour groups, national initiatives in patient-centred care and the unique infrastructure for clinical trials, digital innovations for better patient care, care planning through a tight collaboration with a private ICT company - DNV Imatis. In total, Matrix is facilitating the development and implementation of next-generation cancer care. In addition, MATRIX has a broad network of international collaborators and is strongly involved in several large EU-funded projects within the areas of precision cancer medicine and patient-centred and palliative care.

The centre has partners and study sites across all health regions in Norway. Altogether, fifteen hospitals with cancer departments as well as the University of Oslo and Oslo Metropolitan University are partners in MATRIX.

MATRIX is one of four Centres for Clinical Treatment Research (FKB) in Norway. This funding scheme aims to establish and strengthen clinical research environments, and through outstanding research, the aim is to contribute to improved outcomes for Norwegian patients. The centres receive support for a total of eight years, and the primary research tasks for FKB centres are to perform clinical studies.

The Radium hospital, including the new proton centre, and the Researcher Building hosting the Institute for Cancer Research and the MATRIX management team Photo: HSØ







Patients planned into clinical trials

10

PhD and researcher positions funded directly by MATRIX

IMPACT

Clinical Cancer Research



AMBITIONS

Desired Outcomes



Improved diagnostics

MATRIX develops new diagnostic methods in molecular profiling (-omics), drug sensitivity screening, and immune system characterization, as well as artificial intelligence (AI) tools for analysis of images and clinical real-world data. The centre collaborates closely with the national infrastructure for precision diagnostics, InPreD. This ensures systematic and rapid testing of the clinical benefit of diagnostic tools in new clinical trials.



More clinical studies and precise treatment MATRIX develops and tests new treatment strategies in clinical trials. Trials in the Centre can include studies within precision cancer medicine and patient-centred care, including symptom and function improvements, cell therapy, and radiotherapy. Furthermore, MATRIX can design and offer studies in earlier treatment lines and can include e.g., drug combinations. Patients from all of Norway should have the opportunity to participate in these studies.



Patient follow-up and patient participation are central

There is a need for novel digital tools that ensure that the patient's needs and preferences are integrated into all treatment decisions. MATRIX will develop and implement systematic digital symptom assessment, digital patient-centred care pathways with evidence-based content that secures treatment and follow-up tailored to the individual patient. The Ministry of Health and Care Services has expressed a clear goal and wish that Norway should offer precision medicine to its citizens as part of an integrated line of treatment within the public healthcare system. The aim is to offer patients more precise and targeted diagnostics and treatment while avoiding treatment without effect, as well as to involve patients in shared decision-making processes.

MATRIX collaborates with and builds on already ongoing initiatives in Norway within precision cancer medicine and patient-centred care. Furthermore, MATRIX collaborates closely with the ongoing EU-funded consortium: "MyPath -The Digital Solution to Patient-centred Cancer Care" as well as with two large European precision medicine initiatives, PCM4EU and PRIME-ROSE. These two projects build on the success of national initiatives to expand access to precision cancer medicine to more patients across Europe and to address key challenges related to implementation. The overall aim of all the combined efforts is to make Norway world-leading in precision cancer research, treatment, and care.



MATRIX aims to

- Build competence and experience with next-generation diagnostics and treatment by conducting a number of clinical trials. Patients will be recruited at hospitals all over the country.
- Facilitate advanced clinical trials by establishing the Clinical Trial Engine for handling regulatory, logistical and clinical needs. The centre will also contribute to the training of study personnel.
- Establish a systematic pipeline for the development of new diagnostics, treatments and digital solutions, to be tested in clinical trials and implementation in the healthcare system.

WORK PACKAGES

Research



In 2022, the Cancer Registry of Norway registered more than 38 000 new cancer cases. Although most patients recover, cancer is still the number one cause of death in Norway, and more than 10,000 people die annually. There is still a need to improve diagnostics, detect disease at an earlier stage and develop new and more targeted treatment options, especially for hard-to-treat cancer subtypes. In addition to tumour-directed treatment, it is essential to focus on patient-centred care, acknowledging the patients' own report of symptoms and functioning, as more patients live longer with their disease and may experience late effects of the disease and the treatment after they are cured. Furthermore, to live with incurable cancer is very challenging for both patients and their families, and to involve them better in the planning of care is needed and may influence the right balance of anticancer therapy towards end of life.

A key element in modern cancer treatment is the possibility of guiding patient treatment based on a detailed molecular characterization of each patient's disease, also called precision cancer medicine. These individual molecular properties may explain why patients with the same type and stage of cancer may respond differently to the same treatment.

As a national research centre for clinical cancer treatment, MATRIX has an overarching goal of contributing to prolonging the lives of cancer patients as well as involving the patients actively in treatment decisions and thus improving their quality of life. Fifteen hospitals from all over the country and a number of research environments are involved in the centre. Based on our increased understanding of cancer, MATRIX aims to offer hard-to-treat cancer patients more precise and targeted diagnostics and anticancer treatment while avoiding ineffective treatment with potentially adverse effects on life quality. In addition, an innovation for patient-centred care, digital patient-centres care pathways, is in the process of being developed in close collaboration between clinicians, patients, patient representatives and DNV Imatis, a Scandinavian provider of software and information technology specially developed and adapted within the healthcare industry.

Research taking place in MATRIX is organized into five work packages, which together cover the broad scope of the centre:

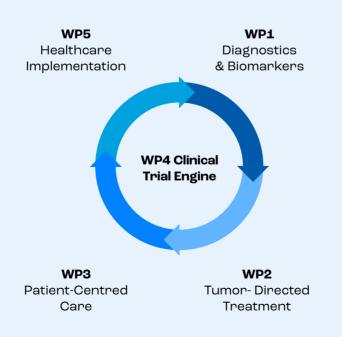


Photo: OUH. Lars Petter Devik



Next-Generation Cancer Diagnostics & Biomarkers

Research focus

There is a great potential to improve the benefit of therapy for individual cancer patients by better patient selection through increased biological characterization of their disease, as well as by design of unique synergistic combination therapies that could give cure or overcome treatment resistance. Furthermore, a driver for precision cancer medicine is the advancement of methods and technologies for advanced data analyses for systems biology, machine learning, and artificial intelligence (AI).

Research in WP1 is organized into two sub-projects

- WP1a utilizes and further develops available technologies in collaboration with <u>InPreD</u> (national infrastructure for precision diagnostics, cancer), leading to the implementation of next-generation diagnostics. Other omics, liquid biopsy assays as well as functional approaches such as cancer drug sensitivity screening and pharmacogenomic profiling, will be included.
- WP1b utilizes new imaging (MRI and PET) technologies and methodologies, such as multi-parametric scanning in collaboration with the <u>CRAI Unit</u> at OUH, to gain decisive insight into resistance factors. We expect that including clinico-pathological and / or molecular factors and analysis by learning algorithms (machine and deep learning) will aid the development of predictive / prognostic markers for treatment selection.

Major aims

- Establish advanced genomics for cancer diagnostics and standardize analysis to support clinical decisions on inclusion in trials
- Establish SOPs and transfer cancer drug sensitivity screening (CDSS) and CDSS-based testing to a diagnostic platform for patient stratification in clinical trials
- Develop a pipeline for circulating tumour DNA (ctDNA) sequencing for patient stratification in clinical trials
- Develop frameworks for efficient extraction of big radiological data from PACS to dedicated databases for deep learning-based model training
- Develop predictive models for assessment of treatment response
- Develop end-to-end pipelines for fully automated radio-genomic analysis for selected hard-to-treat cancers

"We aim to deliver new technologies that will facilitate the next generations of PCM trials using functional testing, imaging and modelling approaches",

Kjetil Taskén, WP1 leader

Work package leader Professor Kjetil Taskén, Oslo University Hospital Work package co-leader Professor Emiel Janssen, Stavanger University Hospital

Highlights in 2023

- A pilot for childhood cancer whole genome sequencing initiated, including prospective analyses and a paediatric molecular tumour board
- First industry research collaboration initiated with Oxford Nanopore; sequencer installed at the Institute for Cancer Research, OUH
- Cancer drug sensitivity screening established for chronic lymphocytic leukemia (CLL) with method paper published, and SOPs developed for colorectal cancer drug screening (COSENSE-1).
- Exemption from confidentiality to use existing health data in PACS for development and training of AI models without patient informed consent (Act on healthcare personnel, section 29 – "Dispensasjon fra taushetsplikt jfr § 29, Lov om helsepersonell").
- NeoMedSys, a framework for efficient extraction of big radiological data from PACS to dedicated database for deep learning-based model training, fully operational including web-interface for use of AI-models in research
- Methods for longitudinal tracking of brain tumour growth established as well as predictive models for treatment responses.

Lead WP1a Professor Hege Russnes, Oslo University Hospital **Lead WP1b** Kyrre E. Emblem, Oslo University Hospital

Goals for 2024

- Complete paediatric cancer prospective analyses and implement protocols into InPreD diagnostic pipeline.
- Reporting pipeline and interpretation tools for whole genome and whole transcriptome to be finalised for adult and paediatric patients.
- Cancer Drug Sensitivity Screening (CDSS) will be standardized and adaptated for patient stratification to trials in more cancers.
- Pipeline for ctDNA sequencing for patient stratification in clinical trials will be developed
- Al-based software solutions will be evaluated for deep learning on imaging data from different cancers and data sets for learning and validation assembled and annotated.

Photo: OUH. Thea Tønnesen



WP2 **Tumour-Directed** Treatment

Research focus

MATRIX supports and initiates trials focusing on hard-to-treat cancers, with participation and engagement in hospitals throughout Norway. Altogether, 15 hospitals are partners in MATRIX.

An overarching goal is to increase patient survival by using precision cancer medicine, and MATRIX therefore wants to move the precision cancer medicine approach forward in the lines of treatment. WP2 in particular collaborates with InPreD, the national infrastructure for precision diagnostics, the Centre for Advanced Cell & Gene Therapy (ACT) in addition to the pharma industry.

Next-generation diagnostics, including drug sensitivity screening, patient characteristics and symptomatology, imaging and omics-data, guide the use of precision cancer therapy with new and old drugs, alone and in combinations. The centre will facilitate the use of material and data across trials and connect clinical investigators with appropriate research groups and core facilities, allowing for use of cutting-edge-technology and expertise within immunology, genomics, proteomics, imaging and other areas. Interventions targeting mechanisms for tumour resistance and escape during therapy will be assessed.

In 2023, several investigator-initiated clinical studies were supported by MATRIX, enabling availability of more trials to Norwegian patients. Proposals are evaluated in the extended national management team. MATRIX-supported trials are described under the clinical trials section.



Work package leader Professor Åslaug Helland, Oslo University Hospital

Work package co-leader Professor Egil Blix, University Hospital North-Norway

Major aims

- Increase number of clinical studies available for patients with hard-to-treat cancers
- Increase number of patients included in clinical trials
- Increase number of national studies (multicentre trials)
- Include cell and gene therapy studies

Highlights in 2023

- Established a national management team, monthly meetings
- Twelve clinical trials discussed in the national management team
- Support allocated to six investigator-initiated trials
- National network for clinical trials established
- A PhD student recruited

Goals for 2024

- Initiate the MATRIX-RARE clinical study
- Expand MATRIX-RARE with more drugs available
- Support initiation of clinical studies

"We encourage investigators from across the country to participate in and initiate new clinical trials in collaboration with MATRIX",

Åslaug Helland, WP2 leader

WP3

Patientcentred Care

Work package leader Professor Stein Kaasa, Oslo University Hospital

Work package co-leader Associate Professor Jo-Åsmund Lund, Ålesund Hospital

Research focus

Patient-centred care focuses on the patient living with disease or life after treatment has ended and not exclusively on the specific cancer diagnosis. This aspect of cancer care applies to the entire treatment trajectory, from diagnostics, throughout treatment and beyond. The aim is to optimize and maintain quality of life, level of functioning and well-being in all phases of treatment, including survivorship care.

Patient-centred care needs to complement tumour-directed treatment in order to improve current cancer treatment. This is achieved by tailoring the treatment and care to the individual patient. Systematic information about the patient's symptoms, functions, needs, and preferences needs to be collected from the patient (Patient Reported Outcome Measures, PROMs). Although robust documentation from randomized trials show convincing patient-centred benefits of routine use of PROMs, this is still not part of routine clinical practice today.

WP3 in collaboration with <u>DNV Imatis</u> develops digital patient-centred care pathways (dPCCP) building on digital registrations of PROMs. Following iterative test-rounds and revisions, we plan to implement these pathways into routine clinical practice at centres participating in MATRIX. Four Norwegian hospitals are currently participating in the development and test phases: Ålesund Hospital, Helse Førde, Telemark Hospital and Oslo University Hospital.

Containing real-time and prior information from patients' digital self-reports, the dPCCPs will provide patients and healthcare providers with a plan for individualized symptom management and care. Rapid transfer of real-time data and online communication secure active patient involvement in decisions about their own care and treatment.

While WP3 operates on a national level, corresponding international solutions are being developed in the EU- funded project <u>MyPath</u>, also led by Stein Kaasa, OUH.

Major aims

- Develop digital patient-centred care pathways building on PROMs
- Revise the current version of Eir and other digital PROMs / PREMs to optimise the content for use in MATRIX clinical studies
- Perform iterative test rounds in mock patients and healthcare providers / clinicians to revise and adapt the patient-centred structure for optimal usability and performance
- Enhance screening and recruitment strategies to increase patient recruitment in clinical studies
- Monitor the effect of the abovementioned strategies

Highlights in 2023

- International expert groups established to develop the different pathways, starting with pain, nutrition, emotional distress and social function
- A prototype solution of the configured Eir tool ready for testing by patients and other stakeholders
- Prototyping of clinical work processes developed and tested. Feedback collected and revisions in process.
- Established a digital infrastructure for implementation of the MyPath digital solution into the digital platforms at the hospitals

Photo: OUH, Apeland & Lunke



 Involvements of patients and healthcare providers in designing the content and structure of the MyPath digital solutions

Goals for 2024:

- Presenting the first digital pathway prototype for on-site testing at all sites in Norway
- Finalize the content and structure of pain, nutrition, emotional distress and social function pathways
- Start the implementation of the digital tool – MyPath

"Custom-made digital patientcentred care pathways, implemented as an integrated part of routine cancer care and with an optimal use of healthcare providers, will improve the quality and efficiency of cancer care",

Stein Kaasa, WP3 leader

WP4 Clinical **Trial Engine**

Research focus

There are several hurdles in initiating and conducting clinical trials. This is in particular a challenge for academic investigators, and academic trials often suffer from delayed start-up and slow patient enrolment. MATRIX is addressing this issue by establishing a Clinical Trial Engine, a joint asset with hands-on support to investigators across the country.

The Clinical Trial Engine offers tailored services according to needs, which may vary. In addition to make the start-up of clinical trials more efficient, we aim to stimulate establishment of more decentralized studies and thus in the long term, build up expertise nationally and establish a wider network for clinical studies in Norway.

A well-recognized obstacle for implementation of precision cancer medicine is access to employees with state-of-the-art knowledge and expertise. Thus, there is a need to raise the competence of all types of study personnel (e.g. doctors, study nurses and project coordinators). WP4 in collaboration with OsloMet develop new master-level courses in clinical intervention studies. Furthermore, a program in collaboration with the Health Innovation School at UiO is in progress.

Major aims

- More effective initiation and conduct of clinical trials
- Establish a structure for decentralised clinical trials
- Establish formal education / training for clinical trial personnel

Highlights in 2023

• A procedure for selecting trials to be supported by the MATRIX Clinical Trial Engine established and routines for multi-centre trials developed

Work package leader

Kyte, Oslo University

Hospital & OsloMet

Professor Jon Amund

Work package co-leader

Bjørnar Gilje, Stavanger University Hospital

- A Professor hired at OsloMet (20% position)
- Together with OsloMet prepared, established and completed teaching of a first master-level course in clinical research for health personnel

Goals for 2024

- · Provide low-threshold advice to trials prepared by MATRIX-institutions
- · Support trials selected by the MATRIX national management team
- Increase competence within the MATRIX **Clinical Trial Engine**
- Further develop and conduct the master-level course in clinical research for health personnel, together with OsloMet
- Work with OsloMet to prepare additional master-level education within clinical research

"We encourage investigators to contact the Clinical Trial Engine and to build know-how among their study personnel through master courses at OsloMet",

Jon Amund Kyte, WP4 leader

WP5

Healthcare Implementation

Research focus

The rising cancer incidence, and more people living with cancer and other complex conditions, has made the Norwegian Health Care Authorities request an increase in efficiency. Resource optimization in future cancer care calls for efficient ways of care delivery at all levels and implementation of new evidence into daily practice. Thus, existing and cutting-edge clinical research results must guide the evidence-based implementation in clinical care towards the goal of improved patient outcomes.

WP5 is together with WP3 aiming to improve the guality of patient-centred care, communication and logistics by implementing digital patient-centred care pathways (dPCCPs) that are developed and tested in WP3. We will use evidence-based implementation strategies to secure uptake in routine clinical care, not only as parts of designated clinical trials. Evaluation of success will follow the guidelines and theoretical frameworks for evaluation of complex interventions published by the Medical Research Council, including implementation theories, strategies, process and outcomes.

Major aims

- · Ensure commitment to WP5 activities at all involved sites
- Scoping at potential new sites as applicable
- Iterative test rounds of the dPCCP of pain, nutrition and emotional distress in synthetic patients and healthcare providers
- Publish a protocol for the implementation study
- Continue the integration, preparations with iterative test rounds among all end-users and ICT personnel
- ICT installations at all sites
- Start staggered implementation at the sites based on level of readiness

Work package leader Marianne Hjermstad, Oslo University Hospital

Work package co-leader Ørnulf Paulsen, Telemark Hospital



Highlights in 2023

- Anchoring the project at all four participating sites
- Scoping of the person-centred activities at the sites
- Testing of prototype dPCCP versions to inform further development
- Preparations for integration of ICT solutions into the hospital administrative systems (DIPS/ Helseplattformen)

Goals for 2024

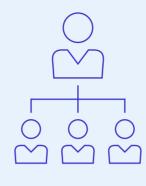
- Finalize protocol and ethics application for the implementation study
- Develop an overall clinical data management plan (d-PMP) for the flow, storage and handling of all collected data (gualitative, quantitative, clinical, process etc.)
- Implement the digital solution MyPath at the four participating sites
- Work jointly with WP3 on iterative gualitative and quantitative tests to revise the d-PMP and the dPCCP accordingly

"We work together with WP3 in the iterative test-rounds of the digital pathways, and provide timely data that are necessary for adjustments of the pathways"

Marianne Hjermstad, WP5 leader

ORGANIZATION

Centre Structure







Åslaug Helland

Stein Kaasa



Taskén



Jon Amund Kyte



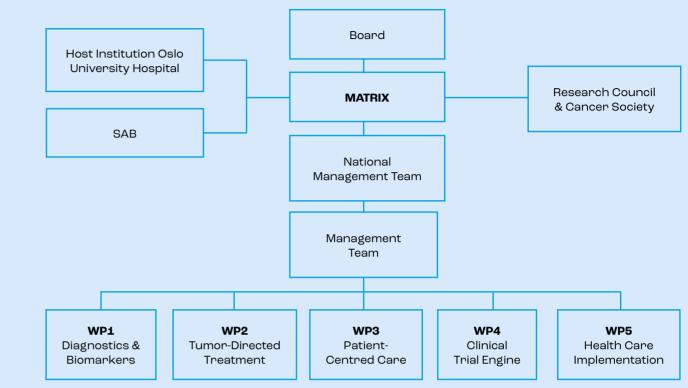
Elisa Bjørgo

MATRIX is funded by the Research Council of Norway and the Norwegian Cancer Society. The centre has partners and study sites across all health regions in Norway, and Oslo University Hospital (OUH) functions as host institution.

Centre Management Team

MATRIX is coordinated and managed from OUH. The Centre Management Team takes care of the day-to-day running of MATRIX and consists of:

- Director Åslaug Helland, MD, PhD, Professor, Research leader of Oslo University Hospital Comprehensive Cancer Centre & Head of IMPRESS-Norway
- Co-Director Stein Kaasa, MD, PhD, Professor, Head Department of Oncology, OUH
- Professor Kjetil Taskén, MD, PhD, Head of Institute for Cancer Research, OUH
- Jon Amund Kyte, MD, PhD, Head Department of Clinical Cancer Research, OUH
- Elisa Bjørgo, PhD, Administrative Manager



MATRIX Organizational Chart

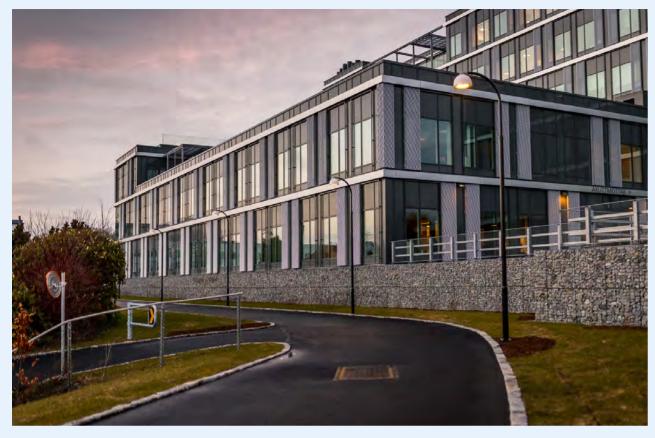
MATRIX Extended National Management Team

The Extended National Management Team coordinates activities in the five work packages and ensures national participation and engagement. The members of this team represent all health regions in Norway. Among the tasks of the national management team is assessment of trial proposals and approving initiation of new clinical trials within the centre.

The National Management Team currently consists of:

- Åslaug Helland, Oslo University Hospital
- Stein Kaasa, Oslo University Hospital
- Kjetil Taskén, Oslo University Hospital
- Jon Amund Kyte, Oslo University Hospital
- Hege G. Russnes, Oslo University Hospital
- Kyrre E. Emblem, Oslo University Hospital
- Marianne J. Hjermstad, Oslo University Hospital
- Egil Blix, University Hospital North-Norway
- Åsmund Flobak, St. Olav University Hospital
- Line Bjørge, Haukeland University Hospital
- Bjørnar Gilje, Stavanger University Hospital
- Emiel Janssen, Stavanger University Hospital
- Jo-Åsmund Lund, Ålesund Hospital
- Ørnulf Paulsen, Telemark Hospital

Photo: Helse Fonna



MATRIX Board

The Board is in collaboration with the Centre Management Team, responsible for the centre's overall coordination and progress. Furthermore, the Board must ensure that the interactions between the project management and collaboration partners work well.

The chair of the MATRIX Board is Sigbjørn Smeland, Head of the Division of Cancer Medicine at Oslo University Hospital. All consortium participants can appoint one member each to the Board. In addition, relevant patient organizations are also represented. Furthermore, the centre director and co-director participate in board meetings.

Scientific Advisory Board

The main mission of the MATRIX Scientific Advisory Board (SAB) is to offer academic and strategic advice as well as benchmark the performance of the centre internationally. The SAB consists of five internationally renowned

clinicians and researchers with expertise in precision medicine and cancer research and was appointed in 2023. The first start-up meeting took place in January 2024 and was a digital event where all MATRIX work package leaders and co-leaders were invited in addition to the Centre Management Team.

The following experts constitute the MATRIX SAB:

- Professor Ahmad H. Awada (Chair), Jules Bordet Cancer Institute, Brussels, Belgium
- Professor Irene Higginson, PhD, Kings College London, UK
- Professor Janne Lehtiö, PhD, Karolinska Institute, Sweden
- Professor Sonja Loges, MD, PhD, University Medical Center Mannheim / German Cancer Research Center (DKFZ), Heidelberg, Germany
- Peter Hall, PhD, Reader, Cancer Research UK Edinburgh Centre, The University of Edinburgh, UK

Consortium Participants

Helse

Helse

Vest

Midt-Norge

Helse

Sør-Øst

MATRIX consists of altogether seventeen consortium partners, including hospitals that represent all the health regions in Norway in addition to the University of Oslo and Oslo Metropolitan University.

Our national clinical network consists of fifteen hospitals with cancer departments that are all partners in MATRIX and are located all over the country. The participation of hospitals in all health regions will facilitate that Norwegian patients get the opportunity to participate in studies as close to their own homes as possible.

> Helse Nord

Helse Nord

- University Hospital of North Norway
- Nordland Hospital

Helse Midt-Norge

- St Olav University Hospital
- Levanger Hospital
- · Ålesund Hospital

Helse Vest

- Hospital
- Stavanger University Hospital
- Førde Hospital
- Haugesund Hospital



- Haukeland University

Helse Sør-Øst

- · Oslo University Hospital (Management & Coordination)
- Innlandet Hospital
- Østfold Hospital
- Telemark Hospital
- Vestfold Hospital
- · Sørlandet Hospital

Universities

- University of Oslo
- · OsloMet

CLINICAL NETWORK

Clinical Trials



Research Centres for Clinical Treatment (FKBs) are to carry out frontline research to improve treatment for Norwegian patients. One of MATRIX's primary research tasks is therefore to conduct clinical trials open for patients with hard-to-treat cancers. Our national clinical network consists of fifteen hospitals with cancer departments that represent all the health regions in Norway.

Principal investigators from MATRIX partner institutions can contact the centre to register new trials or ask for support from the Clinical Trial Engine via <u>an electronic registration form</u>. Potential new trials connected to MATRIX must aim for patient benefit, either by offering precision cancer medicine, improved diagnostics or because it will extend the expected lifespan or improve the quality of life of cancer patients.

MATRIX trials allow for use of new drugs in earlier treatment lines, new diagnostics for treatment stratification and new study designs. The extended national management team have monthly meetings to assess trial proposals and approve initiation of new clinical trials within MATRIX. In the first 1.5 years of operations, the national management team has discussed 12 trials, and six clinical studies have been promised earmarked support based on registered needs and upon inclusion of patients. MATRIX-supported clinical trials

GAIN: Green Approach to Improve Nutritional support for cancer patients (NCT05544318)

Principal Investigators:

- Professor Christine Henriksen, RD, PhD, University of Oslo & Head Centre for Clinical Nutrition OUH/UiO
- Ingvild Paur, RD, PhD, Head Norwegian Advisory Unit on Disease-related Undernutrition, OUH

GAIN is an interventional study aiming to reduce the burden of malnutrition in cancer patients by implementing and evaluating an improved nutritional support, using digital monitoring and communication tools during the clinical pathway.

The effect of individualized, intensive nutrition support is evaluated in a randomized controlled trial. In addition, a cost-effectiveness analysis is planned. Altogether, more than 100 patients with lymphomas, gynecological, colorectal or lung cancer will be included in this trial.

So far, 47 patients have been included in this trial. MATRIX supports GAIN with funding for a study nurse to increase the inclusion rate of patients to this trial. Photo: OUH, Per M. Didriksen.



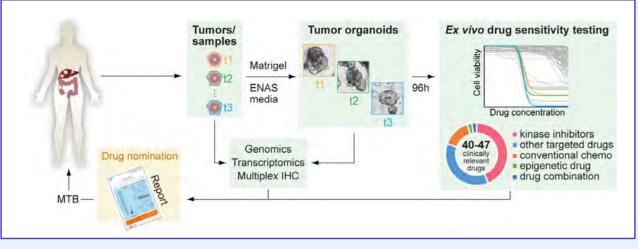


Illustration of the EVIDENT workflow

EVIDENT: *Ex vivo* drug sensitivity testing in metastatic colorectal cancer (EudraCT: 2020-003395-41)

Principal Investigators:

- Tormod Guren, MD, PhD, Oncologist, Oslo University Hospital (OUH)
- Professor Ragnhild A. Lothe, Head Dept. of Molecular Oncology, OUH

EVIDENT is an open-label, single arm interventional phase 2 study of *ex vivo* drug sensitivity testing in metastatic colorectal cancer at Oslo University Hospital. Based on a combination of cancer molecular profiling and drug sensitivity testing of personal *ex vivo* cancer models (tumour organoids), the trial expands the oncologic treatment repertoire and improves the selection of treatments to individual patients. Patient inclusion started in 2022 and will continue until the end of 2025.

A crucial aspect of this study is the experimental *ex vivo* diagnostics, involving culturing of cancer cells from tumour tissues under conditions fostering formation of 3D organoids that resemble the architecture of the patient's tumour. The organoids are subsequently exposed to many different drugs or drug combinations, providing robust read-outs of drug sensitivities. A combined pharmacogenomics profile of all tumour samples and organoids per patient is presented in a report to the molecular tumour board (MTB).

The MTB provides recommendations for *ex vivo*-guided treatment in the third line. EVIDENT has approval to intervene with 23 of the drugs in the screen, most of which are experimental treatments for metastatic colorectal cancer. Treatment nomination criteria include comparisons with a large reference of *ex vivo* drug sensitivities from an established living biobank of metastatic colorectal cancers. In addition, evaluation of multiple samples from each patient reduces the risk of nominating drugs with heterogeneous activities across lesions and tumour sub clones. This design puts EVIDENT at the international forefront of functional precision oncology research.

Since 2022, approximately 100 patient samples have been processed, with 70% showing growing organoids eligible for drug sensitivity screening (diagnostic phase of the trial). The first patient has now started treatment in the study based on the combined pharmacogenomics profile. MATRIX supports EVIDENT with a per-patient contribution for *ex vivo* diagnostics of up to 150 patients and for experimental treatment of up to 20 patients. STEAP1: CAR-T cell therapy targeting treatment refractory prostate cancer and Ewing Sarcoma

Principal Investigator:

 Professor Jon Amund Kyte, MD, PhD, Oncologist, Oslo University Hospital

Principle Investigator Kyte and his team have developed a specific CAR-T that targets the protein STEAP1. This protein is expressed in about 90% of all prostate cancers and subsets of other cancers, including non-small cell lung cancer, bladder cancer, Ewing sarcoma, breast cancer, pancreatic cancer, glioblastoma, and ovarian cancer. Moreover, STEAP1 is highly expressed in metastatic disease.

CAR-T cell therapy is approved against leukaemia, lymphoma, and myeloma, but CAR-T treatment against solid tumours is more challenging, and little documentation is still available.

The STEAP1 CAR-T study will be a phase 1/2 trial where the newly developed STEAP1 CAR-T will be used in patients with refractory Ewing sarcoma or prostate cancer. Ewing sarcoma is a rare form of cancer that often affects children and young adults (5-25 years) and is usually incurable after metastasis. Approximately 5-10 new cases are diagnosed in Norway each year. Prostate cancer is the most common cancer among males and among the most common causes of cancer-related death. Altogether, 30 patients are planned for the screening phase of the trial, whereas 20 patients can be included for treatment.

MATRIX supports the STEAP1 study provisionally with a per-patient contribution, provided that the GMP cell therapy product becomes approved.

SAMVAL: Integrating geriatric assessment and shared decision-making to optimize treatment choice in advanced lung cancer

Principal Investigator:

 Associate Professor Margrethe A. Schaufel, MD, PhD, Haukeland University Hospital

This trial is a phase IV implementation study looking at decision-making processes and patient outcomes in the treatment of advanced lung cancer. The aim is to improve the shared decision-making process. This multicentre study includes Haukeland University Hospital, Stavanger University Hospital, Helse Fonna and Helse Førde, and altogether, 40 patients with advanced lung cancer are planned included within the end of 2025.

So far, 23 patients have been included in the trial. MATRIX supports this trial with a per-patient contribution for inclusion of up to 40 patients.

COMIT-2: Combinatory Immunotherapy-2 (EudraCT: 2021-003266)

Principal Investigator:

 Vilde D. Haakensen, MD, PhD, Oncologist, Oslo University Hospital

Most patients with non-small cell lung cancer (NSCLC) who are treated with immune checkpoint inhibitors alone or in combination with chemotherapy, progress within the first year of treatment.

COMIT-2 is a phase 2 randomised open two-arm study to assess the tolerability and efficacy of immunotherapy combined with extensive radiotherapy for the treatment of stage IV NSCLC. Extensive radiotherapy is combined with immune checkpoint inhibitors alone or in combination with chemotherapy to increase response rates through immune activation, avoid hyper-progression by inducing local control and give the immune system time to develop cancer-specific immunity. The overall aim of the study is to develop a new personalized approach for immunotherapy treatment for patients with metastatic NSCLC to improve response rates and duration of response and potentially cure patients who are currently considered incurable.

In total, 30 patients without liver and brain metastases will be included in the trial by the end of 2028. In addition, patients with liver and brain metastases may be included. The trial includes patients from Oslo University Hospital, St Olavs Hospital and Innlandet Hospital.

By mid-February 2024, 13 patients had been included in this trial. MATRIX supports COMIT-2 with a per-patient contribution for patients included from 2024 and onwards.

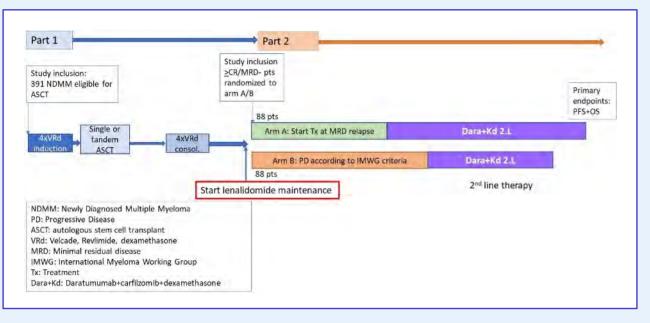


Illustration of the REMNANT workflow

REMNANT: The Relapse From MRD Negativity as Indication for Treatment (NCT04513639)

Principal Investigator:

 Fredrik Schjesvold, MD, PhD, Head Oslo Myeloma Center, Oslo University Hospital (OUH)

REMNANT is a national phase 2/3 trial for multiple myeloma patients. In addition, one hospital in Lithuania is participating in the study. The trial involves thirteen MATRIX partner hospitals, and 400 newly diagnosed myeloma patients are planned to be included in the trial over a four-year period (2020 – 2024). The study follows patients until they progress on second-line treatment, which means 10-12 years from enrolment in the trial.

Patients receive standard first-line treatment in the first part of the study (phase 2). Patients who show a deep response to treatment measured by the absence of minimal residual disease (MRD), subsequently move on to the part two (phase 3) of the study. These patients are randomized to receive relapse treatment according to current treatment guidelines for myeloma, or to receive treatment in the event of earlier and minor signs of recurrence (become MRD+). The aim of the study is to discover whether very early relapse treatment affects the long-term prognosis. Data from REMNANT may change international as well as national guidelines for when to start relapse treatment. No other study in the myeloma community are comparing starting relapse treatment early versus later.

More than 340 patients have so far been included in part one of the trial (phase 2), and 128 patients are enrolled in part two. Patients are included from altogether 13 Norwegian hospitals. MATRIX supports the inclusion of 50 patients in this study with a per-patient contribution to the MATRIX hospitals where the patients are treated.



Photo: Stockbyte

Photo: OUH, Lars Petter Devik



MATRIX-initiated clinical trials

MATRIX-RARE: Precision cancer medicine in hard-to-treat rare cancers - repurposing drugs in earlier lines of treatment (NCT06119789)

MATRIX-RARE is a clinical study where patients with some rare, hard-to-treat cancer types will be offered precision cancer medicine therapy in earlier treatment lines. This is the first study originating from the centre after the inauguration in 2022.

MATRIX-RARE is a prospective, non-randomized clinical trial evaluating the efficacy of commercially available anti-cancer drugs prescribed for patients with advanced cancer who have been diagnosed with potentially actionable alterations by molecular diagnostics. The trial is a nationwide study, and all partner hospitals in the centre will be invited to participate. The study will use a combined umbrella and basket design and a Simon two-stage model of expanding cohorts to follow up potentially effective combinations of biomarkers and drugs on specific indications. MATRIX-RARE will use knowledge from IMPRESS-Norway and focus on subgroups of patients with rare, hard-to-treat cancers who benefit from precision cancer treatment. The national IMPRESS-Norway trial has, since April 2021, included more than 1500 cancer patients with advanced disease, and an enrichment of rare cancers is observed (approximately half of all the patients in IMPRESS-Norway have rare cancers). Several hard-to-treat cancers are rare cancers. and few clinical studies are currently available for these patients. However, from IMPRESS-Norway, we now know that a larger proportion of these tumours (approx. 23%) have genetic changes that match targeted drugs approved for other indications and that 42% of these patients benefit from treatment that matches the molecular biomarker in their tumours.

In contrast to the IMPRESS-Norway trial, the MATRIX-RARE study will initiate treatment before progression on all other therapies. Initially, the study will include anaplastic thyroid cancer, salivary gland carcinoma, glioblastoma multiforme, cholangiocarcinoma, and small intestine cancers. The study has already entered into an agreement with a pharmaceutical company regarding access to drugs and will, according to plan, open for patient inclusion in 2024.

NEWS & EVENTS

Highlights 2023

King Olav V's Cancer Research Prize

MATRIX Director Åslaug Helland in May 2023 received the prestigious King Olav V's Cancer Research Prize for her excellent molecular and clinical research, particularly on lung cancer diagnosis and treatment and for her efforts to introduce precision oncology for all types of cancer in Norway. The prize, one million NOK, was presented by HM King Harald V in a ceremony in Oslo.

King Olav V's Cancer Research Prize has since 1992 been awarded annually to a cancer researcher or a research group that has contributed to promoting the quality and the extent of Norwegian cancer research.



From left: Secretary General of the Norwegian Cancer Society Ingrid Stenstadvold Ross, HM King Harald V, prize winner Åslaug Helland and chair of the Cancer Society Board Geir Riise. Photo: Jorunn Valle Nilsen, The Norwegian Cancer Society.



From left: Ingvild Kjerkol, Ole Alexander Opdalshei and Åslaug Helland Photo: Jorunn Valle Nilsen, The Norwegian Cancer Society.

When the winner of the 2023 award was revealed, Secretary General of the Norwegian Cancer Society Ingrid Stenstadvold Ross said:

"We are deeply grateful for all the hours Åslaug invests in developing cancer treatment and helping Norwegian cancer patients. We look forward to following also her future work".



Election to the Norwegian Academy of Science and Letters

MATRIX Director Åslaug Helland was elected to the prestigious <u>Norwegian Academy of Science</u> and <u>Letters</u> and received her diploma during a ceremony at the Academy's annual meeting in May 2023. Altogether, four new members were welcomed to the Academy's Natural Sciences Division in 2023, and Åslaug Helland joined the Medical Sciences group.

> "This is a major recognition of Helland's scientific work and her efforts to translate findings to clinical trials, offering additional lines of treatment,"

said Kjetil Taskén, Head of Institute for Cancer Research, Oslo University Hospital and Vice President and Head of the Natural Sciences Division of the Academy when the new members were announced.



Presentation of new DNVA members, from the left: Francois Benard (UiO), Åslaug Helland (OUH) and Odd S. Hopperstad (NTNU).

Prize winner Kjetil Taskén. Photo: UiO, Jarli & Jordan

University of Oslo Innovation Prize

Kjetil Taskén, Head of the Institute for Cancer Research, OUH, in September 2023 received the UiO Innovation Prize for his instrumental work in building up precision cancer medicine in Norway. In 2018, Norwegian cancer patients did not have public access to advanced molecular cancer diagnostics with treatment options that use a precision medicine approach. Kjetil Taskén led the work investigating what had to be implemented to introduce precision medicine in Norway. This work led to the establishment of a complete national ecosystem with a public national cancer diagnosis initiative (InPreD), a national clinical trial (IMPRESS-Norway), and a public-private partnership, CONNECT. The way this has been resolved in Norway has generated considerable international interest.



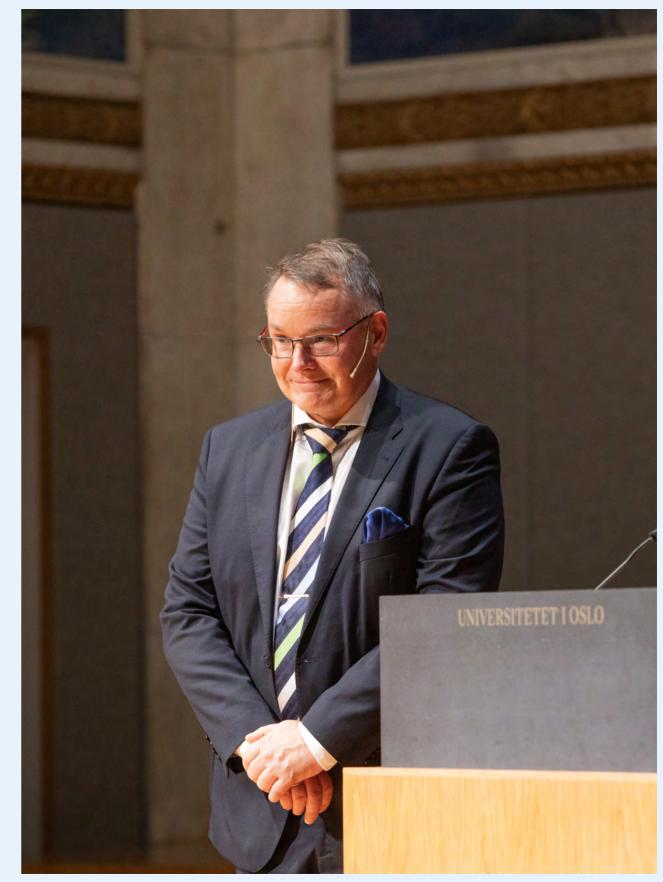
Kjetil Taskén received the innovation award during UiO's annual celebration. From left: Pro-rector UiO Åsa Gornitzka, Kjetil Taskén and UiO Rector Svein Stølen. Photo: UiO, Jarli & Jordan.



Photo: UiO, Jarli & Jordan

"We are highlighting UiO's very best researchers, communicators and teachers through these awards. This year's award winners show that long-term, targeted and hard work contributes to increased competence and knowledge which benefits all of us",

UiO rector Svein Stølen said when announcing the 2023 prize winners.



Acta Oncologica Nordic Precision Cancer Medicine Symposium

The first ACTA Oncologica <u>Nordic Precision Cancer Medicine</u> <u>Symposium</u> took place in Oslo on 17-19 September, and 260 people participated. In total, health personnel and academic researchers from 20 countries joined the conference. The industry was also widely represented by national and international delegates from eleven companies.

Precision Medicine is changing oncology through advanced molecular precision diagnostics, innovative clinical trials, and an increasing number of targeted drugs and treatment options. Over two days, 20 world-leading speakers from Australia, the USA, and Europe shared their knowledge and held exciting and inspiring talks on various aspects of precision cancer medicine.

MATRIX, together with Oslo University Hospital, organized the event, and the first Nordic Precision Cancer Medicine Symposium was made possible through good collaboration and support from <u>ACTA Oncologica</u>. The organizers plan to make this a regular event every second year.



Poster winner Astrid Medhus, OUH, receives her poster prize.



Panel debate about DRUP-like clinical trials. From the left: Kjetil Taskén, Loic Verlingue (MOSTPlus, France), Åslaug Helland (IMPRESS-Norway), Maeve Lowery (PROGRESS, Ireland), Julio Oliveira (POP, Portugal), Hans Gelderblom (DRUP, The Netherlands), Matthew Krebs (DETERMINE, UK), Kristoffer S. Rohrberg (ProTarget, Denmark), Katriina Jalkanen (FINPROVE, Finland) and Edvard Abel (FOCUSE, Sweden).

Initiation of MyPath-MATRIX at four Norwegian hospitals

MATRIX, in collaboration with DNV Imatis, is developing digital patient-centred pathways), and the aim is to implement these in the healthcare system. MATRIX operates on a national level (MyPath-MATRIX), but collaborates closely with the EU-funded project MyPath, developing similar solutions in the European arena.

Four hospitals are involved in the MyPath-MATRIX project: Ålesund Hospital, Helse Førde, Telemark Hospital and Oslo University Hospital. In 2023, MATRIX deputy director Stein Kaasa and his team visited all four sites to anchor the project within the hospital management, on the IT side and among the staff who will test and later adopt the newly developed solution.

In September, the team visited Førde, and the program included both a meeting for staff at the Cancer Department at the hospital, a meeting with the Helse Førde management and representatives from ICT Helse Vest and the Research & Innovation department, as well as more informal discussions with local representatives about practical solutions. Finally, focus group interviews of clinicians at Helse Førde were performed.



The MyPath-MATRIX visit in Førde ended with a radio interview at NRK Vestland. From left: MATRIX co-director Stein Kaasa and My-Path project coordinator in Førde Kristin Vassbotn Guldhav.

ESMO Conference in Madrid

The annual ESMO congress in 2023 took place in Madrid on October 20-24. Many clinicians and researchers across Norway attended this event, including from MATRIX. The European Society for Medical Oncology (ESMO) has more than 34 000 members across 170 countries, and the annual conference is an excellent arena to learn more about news and developments within cancer care, from prevention and diagnosis to new drugs and treatment options as well as palliative care and patient follow-up. ESMO is also an important arena to connect with the industry and meet their global representatives, and it is a great opportunity to present one's own research either at poster sessions or if given the chance, to give an oral presentation.

ESMO represents an excellent opportunity to promote the entire precision cancer medicine ecosystem in Norway, including MATRIX, to industry partners in order to recruit more drugs to IMPRESS-Norway or other trials and discuss new collaboration opportunities. The MATRIX management team had around 20 fruitful meetings with global representatives from more than 10 companies during the conference. In addition, MATRIX attended the business event organized by NorTrials and Innovation Norway at the Embassy of Norway in Spain, where representatives from the international healthcare industry and the Norwegian healthcare services were present.

Three MATRIX work package leaders (Åslaug Helland, Stein Kaasa and Marianne Hjermstad) gave oral presentations at ESMO. In addition, MATRIX-affiliated researchers presented several posters.



Opening lecture at ESMO 2023. Photo: OUH

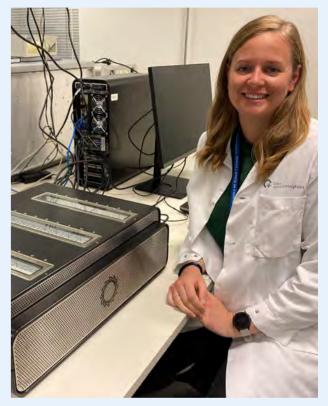
First industry collaboration – Oxford Nanopore

MATRIX's first official industry research

collaboration explores the clinical value of Oxford Nanopore's DNA and RNA sequencing technology in precision cancer medicine and was announced in November 2023.

The collaboration will initially focus on tumours of the central nervous system and be conducted at Oslo University Hospital (OUH) under the direction of Professor and senior physician Hege Russnes, who also leads the national precision diagnostics in cancer program (InPreD), in close collaboration with neuropathologist Pitt Niehusmann. This project focuses on DNA methylation-based classification in the central nervous system (CNS) tumours, detection of somatic and pathogenic copy number variants and tumour heterogeneity of gene expression, mutations and fusions at a single cell level.

The project will use Oxford Nanopore's PromethION 24 device. Nanopore sequencing provides scalable platforms, and this technology could potentially be deployed across the different hospitals in Norway, ensuring that sequencing is performed close to the patients and that clinical reports can be returned quickly.



Special engineer Inger Riise Bergheim has together with Daniel Nebdal and the Nanopore team installed the Nanopore instrument at Oslo University Hospital. Photo: OUH.

Researcher of the Year for 2023 at ICR

Sigrid Skånland, project leader at the Institute for Cancer Research (ICR) at Oslo University Hospital and researcher in functional precision cancer medicine in MATRIX, end of 2023 received the ICR Researcher of the Year award at the institute. The award prize of 100,000 NOK is funded by the Radium Hospital Foundation. Sigrid Skånland received the prize for her efforts to develop and implement precision medicine for patients with blood cancer.



Sigrid Skånland - Researcher of the year at Institute for Cancer Research.



Professor Johanna Olweus (to the right) on behalf of the leadership team at the ICR announced and handed over the prize to Sigrid Skånland.

Opening of new master course

Oslo Metropolitan University (OsloMet) has in collaboration with MATRIX developed a new master-level course: Introduction to clinical studies for healthcare personnel (MAVIT5800). The first course opened in October with invited guests from The Ministry of Health and Care Services, the Norwegian Cancer Society, the Research Council of Norway and Oslo University Hospital. The interest for this course has been overwhelming, and the first course was fully signed up, with a waiting list. Students from all health regions in Norway participated in this digital course.



"If clinical research is to become an integral part of patient treatment, we must have the right professionals who have the skills to contribute to the implementation of clinical studies. This masterlevel course will provide you with formal competence as a research assistant or study nurse. This is putting the national action plan for clinical studies into practice!"



Dean Gro Jamtvedt at the Faculty of Health Sciences, OsloMet, opened the new master-level course in October 2023.

At the opening of the course, the organizers and students received greetings from the Minister of Health and Care services, Ingvild Kjerkol:

NEWS & EVENTS

International Collaboration



The MATRIX work package leaders and many MATRIX-affiliated researchers have well-established international networks and are all part of larger international consortia connected to their research. In 2023, MATRIX-affiliated researchers and Oslo University Hospital have in particular been heavily involved in three large EU-funded projects.

MγPath

MyPath: The digital solution to patientcentred cancer care (2022 – 2027)

MyPath, funded for five years over the EU's Horizon Europe program, is coordinated by MATRIX co-director Stein Kaasa and includes 15 partners from research, clinics, SMEs and NGOs to jointly develop and implement novel patient-centred care pathways, patient-reported outcome measures (PROMs), patient-reported experience measures (PREMs) and treatment decision support incorporated in a user-friendly digital solution. The project, funded with 6.5 million Euro, aims to integrate the MyPath solution in routine cancer care in nine cancer centres in Europe to prove its effectiveness and sustainability. MATRIX is tightly connected to this project and is developing similar solutions in Norway to implement these in the Norwegian healthcare system. Currently, four Norwegian hospitals are involved in the development and testing phases of the MyPath-MATRIX solutions.

MyPath 2023 highlights involving MATRIXaffiliated researchers include:

- Initiation of the MyPath implementation science seminar series (February)
- Second MyPath General Assembly in Valencia, Spain (June).
- First MyPath focus group workshop held in Brussel with 14 ESMO Designated Centres. OUH co-organizers of the event (September).
- MyPath European Parliament launch event where MATRIX deputy Director Stein Kaasa presented the project, solutions under development and the need for more systematic patient-centred care (October).





PCM4EU project meeting in Holmenkollen, Oslo, September 2023.

PCM4EU

PCM4EU: Personalised Cancer Medicine for all EU Citizens (2023-2024)

PCM4EU, funded for two years over the EU4Health program, is coordinated by Leiden University Medical Centre (LUMC), The Netherlands and includes 17 partners from altogether 15 European countries. The PCM4EU project, funded with 3 million Euro, is set up to facilitate the use of precision cancer medicine diagnostics and pragmatic trials across Europe, and it builds on the family of DRUP-like clinical trials. The aim is to widen access to molecular diagnostics and precision cancer medicine within regions and countries in the EU.

MATRIX-affiliated researchers play essential roles in the project and have three work package co-leaders:

- WP2 Molecular diagnostics & Tumour Boards: Hege G. Russnes (OUH)
- WP3 Implementation of DRUP-like clinical trials: Åslaug Helland (OUH)
- WP4 Implementation & Dissemination: Kjetil Taskén (OUH)

PCM4EU 2023 highlights involving MATRIX-affiliated researchers include:

- Project kick-off meeting in Leiden, The Netherlands (January)
- PCM4EU @Melanoma Patient Network Europe Workshop in Brussel gave an opportunity to interact directly with a European patient organization as well as with patient and physician communities. Kjetil Taskén invited as speaker (April).
- Hybrid course "Advantages and limitations of precision oncology in clinical practice" in Warsaw, Poland. Åslaug Helland invited as speaker (June).
- The PCM4EU podcast series providing training material about different aspects of precision cancer medicine. MATRIX-affiliated researchers interviewed for several episodes.
- 2nd PCM4EU project meeting organized in Oslo (September)
- White paper "Guidance on personalised diagnostics" finalized (In Press). This was a deliverable in WP2, co-lead by Hege G. Russnes (OUH).



PRIME-ROSE: Combining Expertise Across Borders to Promote Precision Cancer Medicine in Europe (2023-2028)

PRIME-ROSE, funded for five years by the EU Cancer Mission, is coordinated by Kjetil Taskén, OUH, and currently consists of 24 partners from altogether 18 European countries. The project was launched in July 2023 and is funded with 6 million Euro. The PRIME-ROSE vision is access to affordable precision cancer medicine that prolongs life at the best quality possible for all cancer patients. Whereas PCM4EU focuses on the deployment of novel PCM diagnostic tools, PRIME-ROSE is treatment-oriented. The PRIME-ROSE kick-off event took place at Institute for Cancer Research, OUH, in September. Photo: Per Marius Didriksen, OUH.

The PRIME-ROSE consortium will:

- Enable cross-border data sharing
- Build synthetic randomized trials
- Design and conduct pragmatic clinical trials
- Provide the necessary data for implementation
- Involve patients in a consistent and meaningful manner
- Focus on multi-stakeholder collaboration
- Share knowledge and provide education and training

PRIME-ROSE 2023 highlights involving MATRIX-affiliated researchers include

- Kick-off meeting in Oslo (September)
- PRIME-ROSE hang-out networking event during the ESMO conference in Madrid (October)
- Editorial by Kjetil Taskén on the European initiatives PCM4EU and PRIME-ROSE published in HealthcareTech Outlook (December)
- 1st Community Advisory Board workshop on health-related Quality of Life (hrQoL) in Oslo (January 2024)

CENTRE

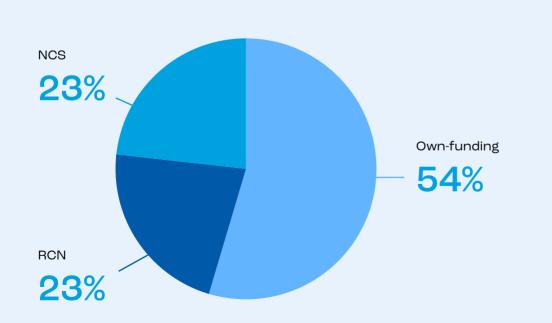
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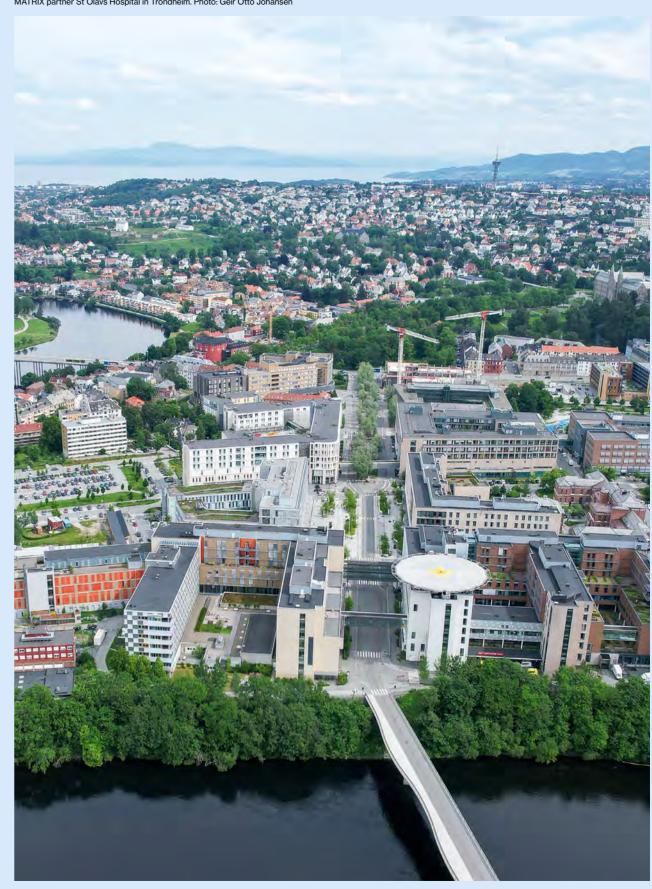


MATRIX receives core funding from the Research Council of Norway (RCN) and the Norwegian Cancer Society (NCS). The Centre has been awarded 128 million NOK under the funding scheme for Centres for Clinical Treatment Research (FKB). This funding is granted over an eight-year period (2022 - 2030), pending a successful midterm evaluation after the first five years. A prerequisite for the awarded funding as a Centres for Clinical Treatment Research is an own contribution of at least 50%. MATRIX has budgeted with an own-funding of 54% over the entire Centre period.

In 2023, MATRIX spent in total 38.5 MNOK, including own funding. Of the 17 partners in the Centre, eight partners had costs related to the project in 2023: Oslo University Hospital (OUH) spent 31.9 MNOK, the University of Oslo spent 3.14 MNOK, Stavanger University Hospital spent 1.37 MNOK, St. Olav Hospital spent 0.8 MNOK, Ålesund Hospital spent 0.56 MNOK, Telemark Hospital spent 0.42 MNOK, the University Hospital North-Norway spent 0.2 MNOK and OsloMet spent 0.11 MNOK.

Core Funding





MATRIX activities 2023

MATRIX 2023 cost distribution on the different work packages (cost in MNOK).

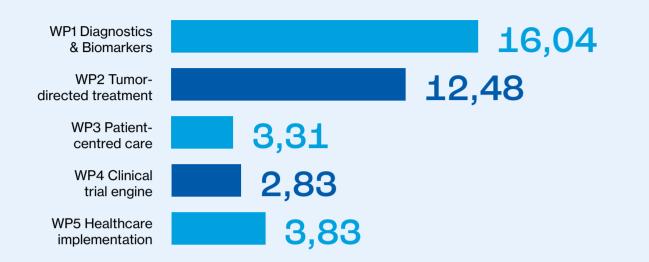


Photo: OUH, Lars Petter Devik

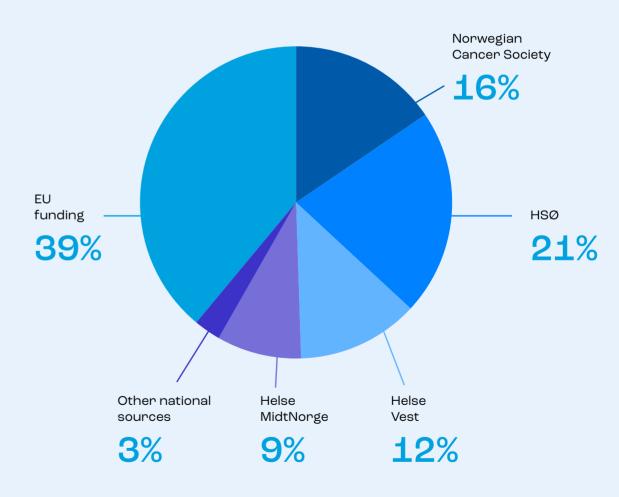


External funding

There is a clear expectation that research environments in MATRIX are able to attract additional funding from both national and international sources. In 2023, around 51 MNOK in the form of national and international grants to research groups affiliated with MATRIX, has been secured as additional external funding. National external funding includes 8 MNOK from the Norwegian

External funding secured 2023

External funding for MATRIX-affiliated projects secured in 2023



Cancer Society, 11 MNOK from the South-Eastern Norway Regional Health Authority, 6.4 MNOK from the West Norway Regional Health Authority and 4.5 MNOK from the Central Norway Regional Health Authority for projects that will be running in the coming years. In addition, MATRIX-affiliated researchers are currently heavily involved in three EU projects. In addition to MyPath and PCM4EU, OUH secured approx. 20 MNOK from the PRIME-ROSE project in 2023 (to be spent over 5 years).

Publications

Andersen AN, Brodersen AM, Ayuda-Duran P, Piechaczyk L, Tadele DS, Baken L, Fredriksen J, Stoksflod M, Lenartova A, Fløisand Y, Skånland SS, Enserink JM (2023) Clinical Forecasting of Acute Myeloid Leukemia Using *Ex Vivo* Drug Sensitivity Profiling. Cell Reports Methods, 2023 3 (12), 100654, DOI 10.1016/j. crmeth.2023.100654

Ayuda-Duran P, Hermansen JU, Giliberto M, Yin Y, Hanes R, Gordon S, Kuusanmäki H, Brodersen AM, Andersen AN, Taskén K, Wennerberg K, Enserink J, Skånland SS (2023) **Standardized assays to monitor drug sensitivity in hematologic cancers.** Cell Death Discov, 9 (1), 435, DOI <u>10.1038/</u> s41420-023-01722-5

Bakke KM, Meltzer S, Grøvik E, Negård A, Holmedal SH, Mikalsen LTG, Færden AE, Lyckander LG, Julbø FMI, Bjørnerud A, Gjesdal KI, Ree AH, Redalen KR (2023) Imaging the tumour microenvironment in rectal cancer: Decline in tumour blood flow during radiotherapy predicts good outcome Phys Imaging Radiat Oncol, 25, 100417, DOI <u>10.1016/j.</u> phro.2023.100417 Børø S, Thoresen S, Boge Brant S, Helland Å (2023) Initial investigation of using Norwegian health data for the purpose of external comparator arms - an example for non-small cell lung cancer Acta Oncol, 62 (12), 1642-1648, DOI 080/0284186X,2023,2264484

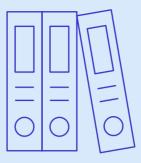
Datta M, Chatterjee S, Perez EM, Gritsch S, Roberge S, Duguette M, Chen IX, Naxerova K, Kumar AS, Ghosh M, Emblem KE, Ng MR, Ho WW, Kumar P, Krishnan S, Dong X, Speranza MC, Neagu MR, Iorgulescu JB, Huang RY, Youssef G, Reardon DA, Sharpe AH, Freeman GJ, Suvà ML et al. (2023) Losartan controls immune checkpoint blocker-induced edema and improves survival in glioblastoma mouse models Proc Natl Acad Sci U S A, 120 (6), e2219199120, DOI 10.1073/ pnas.2219199120

Flobak Å, Zobolas J, Vazquez M, Steigedal T, Thommesen L, Grislingås A, Niederdorfer B, Folkesson E, Kuiper M (2023) Fine tuning a logical model of cancer cells to predict drug synergies: combining manual curation and automated parameterization. Front. Syst. Biol., Vol 3, DOI <u>10.3389/</u> fsysb.2023.1252961 García-Díaz N, Wei Q, Taskén K (2023) Small molecule inhibitors targeting regulatory T cells for cancer treatment-Eur J of Immunol, e2350448 (in press), DOI <u>10.1002/</u> eji.202350448

Hangel G, Schmitz-Abecassis B, Sollmann N, Pinto J, Arzanforoosh F, Barkhof F, Booth T, Calvo-Imirizaldu M, Cassia G, Chmelik M, Clement P, Ercan E, Fernández-Seara MA, Furtner J, Fuster-Garcia E, Grech-Sollars M, Guven NT, Hatay GH, Karami G, Keil VC, Kim M, Koekkoek JAF, Kukran S, Mancini L, Nechifor RE et al. (2023) Advanced MR Techniques for Preoperative Glioma Characterization: Part

J Magn Reson Imaging, 57 (6), 1676-1695, DOI <u>10.1002/</u> jmri.28663

Heck KA, Lindholm HT, Niederdorfer B, Tsirvouli E, Kuiper M, Flobak Å, Lægreid A, Thommesen L (2023) Characterisation of Colorectal Cancer Cell Lines through Proteomic Profiling of Their Extracellular Vesicles. Proteomes, 11(1):3, DOI: <u>10.3390/</u> proteomes11010003



Hermansen JU, Yin Y, Urban A, Myklebust CV, Karlsen L, Melvold K, Tveita AA, Taskén K, Munthe LA, Tjønnfjord GE, Skånland SS (2023) A tumor microenvironment model of chronic lymphocyticleukemia enables drug sensitivity testing to guide precision medicine. Cell Death Discov, 9 (1), 125, DOI: <u>10.1038/</u> s41420-023-01426-w

Hirschler L, Sollmann N, Schmitz-Abecassis B, Pinto J, Arzanforoosh F, Barkhof F, Booth T. Calvo-Imirizaldu M. Cassia G, Chmelik M, Clement P, Ercan E, Fernández-Seara MA, Furtner J, Fuster-Garcia E, Grech-Sollars M, Guven NT, Hatay GH, Karami G, Keil VC, Kim M, Koekkoek JAF, Kukran S, Mancini L, Nechifor RE et al. (2023) Advanced MR **Techniques for Preoperative** Glioma Characterization: Part 1 J Magn Reson Imaging, 57 (6), 1655-1675, DOI 10.1002/ imri.28662

Horndalsveen H, Alver TN, Dalsgaard AM, Rogg LV, Helbekkmo N, Grønberg BH, Halvorsen TO, Ramberg C, Haakensen VD, Öjlert ÅK, Bjaanes MM, Helland Å (2023) Atezolizumab and stereotactic body radiotherapy in patients with advanced non-small cell lung cancer: safety, clinical activity and ctDNA responses – the ComIT-1 trial Mol Oncol, 17(3): 487–498, DOI: <u>10.1002/1878-0261.13330</u>

Le Tourneau, C., André, F., Helland, Å., Mileshkin, L., Minnaard, W., Schiel, A., Taskén, K., Thomas, D.M., Veronese, M.L., Duran-Pacheco, G., Leyens, L., Rufibach, K., Thomas, M., Krämer, A. (2023) Modified study designs to expand treatment options in personalised oncology: A multi-stakeholder view. Eur J Cancer, 194, 113278, DOI <u>10.1016/j.ejca.2023.113278</u>

Nilssen Y, Solberg S, Brustugun OT, Møller B, Sundset A, Wahl SGF, Helland Å (2023) Tracheal cancer: a rare and deadly but potentially curable disease that also affects younger people Eur J Cardiothorac Surg, 64 (1), DOI <u>10.1093/ejcts/ezad244</u>

Osadebey M, Liu Q, Fuster-Garcia E, Emblem KE (2023) Interpreting deep learning models for glioma survival classification using visualization and textual explanations BMC Med Inform Decis Mak, 23 (1), 225, DOI <u>10.1186/</u> <u>\$12911-023-02320-2</u> Ottesen JA, Yi D, Tong E, Iv M, Latysheva A, Saxhaug C, Jacobsen KD, Helland Å, Emblem KE, Rubin DL, Bjørnerud A, Zaharchuk G, Grøvik E (2023) **2.5D** and **3D** segmentation of brain metastases with deep learning on multinational MRI data Front Neuroinform, 18:16:1056068, DOI: <u>10.3389/</u> fninf.2022.1056068

Sakshaug BC, Folkesson E, Haukaas TH, Visnes T, Flobak Å (2023) **Systematic review: predictive value of organoids in colorectal cancer.** Scientific Reports, 13(1):18124, DOI: <u>10.1038/</u> s41598-023-45297-8

Svensson SF, Halldórsson S, Latysheva A, Fuster-Garcia E, Hjørnevik T, Fraser-Green J, Birkeland Bugge RA, Grinband J, Holm S, Sinkus R, Vik-Mo EO, Emblem KE (2023) MR elastography identifies regions of extracellular matrix reorganization associated with shorter survival in glioblastoma patients Neurooncol Adv, 5 (1), vdad021, DOI 10.1093/noajnl/vdad021

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Dissemination Activities 2023



The MATRIX website has information available in both Norwegian and English. News and other updates are shared both there and via social media channels (X and LinkedIn) regularly.

Researchers affiliated to MATRIX give frequent presentations at both national and international conferences and participate in panel debates, podcasts and other forums to discuss and disseminate new research findings, precision cancer medicine initiatives both in Norway and Europe as well as information about clinical trials. Furthermore, media show an interest in MATRIXrelated research and several press items were published in 2023.

A selection of 2023 press items include

- <u>Åslaug Helland valgt inn i vitenskapsakademi:</u>
 <u>En anerkjennelse</u>, Health Talk 23.02.2023
- Har fått 66 millioner kroner fra EU
 dette skal PRIME-ROSE-prosjektet jobbe
 med, Health Talk 24.04.2023
- Kreften hadde spredt seg overalt i kroppen. Men Kari Grønås ble ikke gitt opp av legen sin, Aftenposten 26.04.2023
- Kong Harald hedret Helland, Kreftforeningen 02.05.2023
- <u>Kjetil Tasken får Innovasjonsprisen fra</u> <u>Universitetet i Oslo</u>, Health Talk 08.05.2023

- <u>Setter personen, ikke pasienten i sentrum,</u> Kreftforeningen 11.05.2023
- Dette superteamet skal løse våre største kreftutfordringer, Forskning.no 06.06.2023
- MyPath-MATRIX i Førde: Intervju NRK Radio, Sogn og Fjordane 13.09.2023
- <u>OUS-forskere leder EU-prosjekt på pasient-</u> <u>fokusert behandling - presenterte fremgan-</u> <u>gen på ESMO</u>, Health Talk 21.10.2023
- <u>8 millioner kroner til forskning fra OUS på</u> <u>persontilpasset immunterapi mot brystk-</u> <u>reft</u>, Health Talk 13.11.2023
- Kunstig intelligens: Kan ha svaret på vår tids største helsetrusler, Norske Tilstander, TV2: Episode 30 – Kunstig Intelligens og helseutfordninger 16.11.2023
- <u>Årets forsker 2023 vil skreddersy behan-</u> <u>dling for blodkreft-pasienter</u>, Health Talk 06.12.2023



Kjetil Tasken får Innovasjonsprisen fra Universitetet i Oslo

Kong Harald hedret Helland

Stadig flere pasienter overlever lungekreft. Det skyldes ikke mins innsatsen til Åslaug Helland (56), årets mottaker av Kreftforening





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8 millioner kroner til forskning fra OUS på persontilpasset immunterapi mot brystkreft

Økt livskvalitet



OUS-forskere leder EU-prosjekt på pasientfokusert behandling - presenterte fremgangen på ESMO

lungekreft. Men samtidig ga hun håp. Det var studier på gang.



olusjon? Det var tema i ukens episode av

Løder av Langelzefiltoveningen Karl Grønla röser krefilege Adnug Helland og berniet Jeam. - Hun ser ingen hindre, står på for pasiernese sine, letter øtter ittveler og är ørientert, sier hun. Fons Diego Musice Zamora



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Har fått 66 millioner kroner fra EU - dette skal PRIME-ROSE-prosjektet jobbe med

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New MATRIX staff

MATRIX consists of research environments at 17 partner institutions across Norway, and the affiliated research groups were already operative before the centre opened. In particular, PhD students and postdocs affiliated with MATRIX groups (funded elsewhere) and involved in clinical trials, are already included in MATRIX activities and such involvement is planned throughout the project period. In addition, thirteen positions are directly funded by MATRIX throughout the project period to make sure specific tasks can be fulfilled.

In 2023 the following have joined MATRIX

Sigrid Skånland

Sigrid Skånland joined MATRIX January 2023 and is hired as a researcher in functional precision cancer medicine at OUH. Sigrid has a PhD from the University of Oslo, followed by an EMBO fellowship at the Goethe University School of Medicine in Frankfurt, Germany. In recent years, she has been a project leader at OUH, focusing on the development of functional precision medicine for hematologic malignancies.

Alen Brkic

Alen Brkic joined MATRIX and OUH in January 2023 as a postdoctoral researcher connected to work packages 3 and 5. Alen is a medical doctor, has a master degree in public health, and defended his PhD in Medicine and Health Sciences at NTNU in 2023.

Qian Wei

Qian Wei joined MATRIX at OUH February 2023 as a researcher in precision immune-oncology at OUH. Qian has a PhD from the University Academy of Sciences in China followed by postdoc positions at the University of Oslo and OUH. She has a strong background in tumour molecular biology and immunology.



Martin Røvang

Martin Røvang joined MATRIX at OUH in March 2023 as a software developer / researcher and has joined the team working on developing new imaging (MRI and PET) technologies and methodologies in WP1. Martin has a master degree in deep learning and has solid experience in machine learning and medical imaging.

Jon Amund Kyte

Jon Amund Kyte joined the Faculty of Health Sciences at OsloMet as a Professor (20% position) in August 2023. This position, funded by MATRIX, is linked to the areas of clinical trials and master level teaching.

Katarina Puco

Katarina Puco joined MATRIX as a PhD fellow at OUH in September 2023. Katarina is an oncologist, and she will combine the 50% PhD position with her 50% position as a study doctor in IMPRESS-Norway.

Ingrid Aune Bergstrøm

Ingrid Aune Bergstrøm joined MATRIX as a PhD fellow at St Olavs Hospital in November 2023. Ingrid is a medical doctor and has now joined a functional precision medicine project in Åsmund Flobak's research group in Trondheim.

Almaz Nigatu Tesfahun

Almaz Nigatu Tesfahun joined MATRIX as a researcher at Stavanger University Hospital in January 2024. Almaz is a molecular biologist and has a PhD in DNA damages and repair mechanisms from the University of Stavanger. For the past three years, she has worked with NGS within diagnostics.

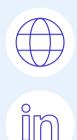
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- Åslaug Helland, Director
- Stein Kaasa, Co-Director
- Kjetil Taskén, Head Institute for Cancer Research
- · Jon Amund Kyte, Head Section for **Experimental Cancer Treatment**
- Elisa Bjørgo, Administrative Manager •

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Nordland Hospital, Bodø Astrid Dalhaug



Helse Nord-Trøndelag - Levanger Hospital

Helse Møre & Romsdal – Ålesund Hospital

Haukeland University Hospital, Bergen

Helse Fonna – Haugesund Hospital

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Helse Vest

HELSE FØRDE





Helse Midt-Norge

HELSE NORD-TRØNDELAG

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