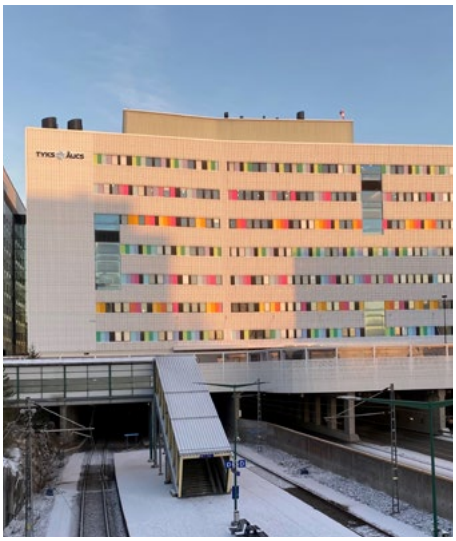
Tyks Cancer Centre Annual Report

2022

TYKS



OECI CANCER CENTRE

European Reference Network
for rare or low prevalence complex diseases

Network
Adult Cancers
(ERN EURACAN)

Member
Turku University Hospital — Finland

Content

Tyks Cancer Centre / Turku University Hospital Tyks

In November 2019 the Tyks Cancer Centre was approved as the Organization of European Cancer Institutes (OECI) Cancer Centre. Cancer Centre status confirms that Tyks meets all high quality standards of cancer care and research when compared and peer-reviewed with other cancer institutes in Europe. Tyks has been also a member of European Reference Network (ERN) and audited to European Cancer Network (Euracan) since 2016.

In 2022, Tyks has further developed the improvement proposals of the audit. The institutional cancer strategy has been adjusted and the same holds for research strategy in general. Dashboards for cancer care and management have been introduced. Palliative centre has established its function as a unit helping all palliative patients in the hospital.

The Tyks Cancer Centre is at the heart of all patient-centered cancer care and of the research cluster. Together with the network of the Western Finland Cancer Centre (FICAN West) – which includes the central hospitals of Pori (Satasairaala) and Vaasa and the Turku University Cancer Research Laboratories – it will be one of the leading centers of cancer care and science in Finland. The members of the Tyks Cancer Board (Clinical) represent all departments with operational responsibility for cancer care in this region.

We are committed to continuous development of personalized, precision medicine-based cancer care. An executive committee of the Tyks Cancer Board meets four times yearly. Its main task is to reinforce the collaboration related to decision-making, implementation of cancer care and cancer research across Tyks and the University of Turku. The members of this executive committee have been nominated by the CEO of Tyks and they represent the main heads of the departments involved in cancer treatment and research. The executive board operates in close collaboration with the Cancer Board (Clinical) and the Scientific Cancer Board which together cover all heads of departments and research directors involved in cancer treatment and research.

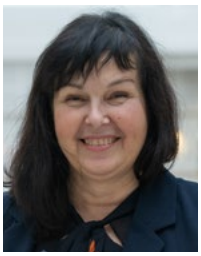
There have been many challenges concerning cancer care and clinical research during the year 2022. Covid pandemic has changed working conditions, updated digitalization in meetings, of which many can be arranged via Teams or Zoom. On the other hand, we had about 30% decrease in the amount of cancer diagnoses years 2020-21 probably due to patients scare to take part into the screening programs and difficulties in seeking care for diagnosis under covid epidemic, during the year 2022 we have taken all efforts to take care of these patients as soon as possible. Recent years have shown that there is increasing lack of health care professionals and our mission is to offer continuous education and see that this problem is taken very seriously, and professionals are offered all support they need in their demanding work.

In addition, the organisation of public healthcare, social welfare and rescue services will be reformed in Finland. The responsibility for organising these services will be transferred from municipalities to wellbeing services counties 1.1.2023. The key objective of the reform is to improve the availability and quality of basic public services throughout Finland.

Sirkku Jyrkkiö, MD, PhD, CEO of Tyks Hospital and Chair of the Executive Committee of Tyks Cancer Board

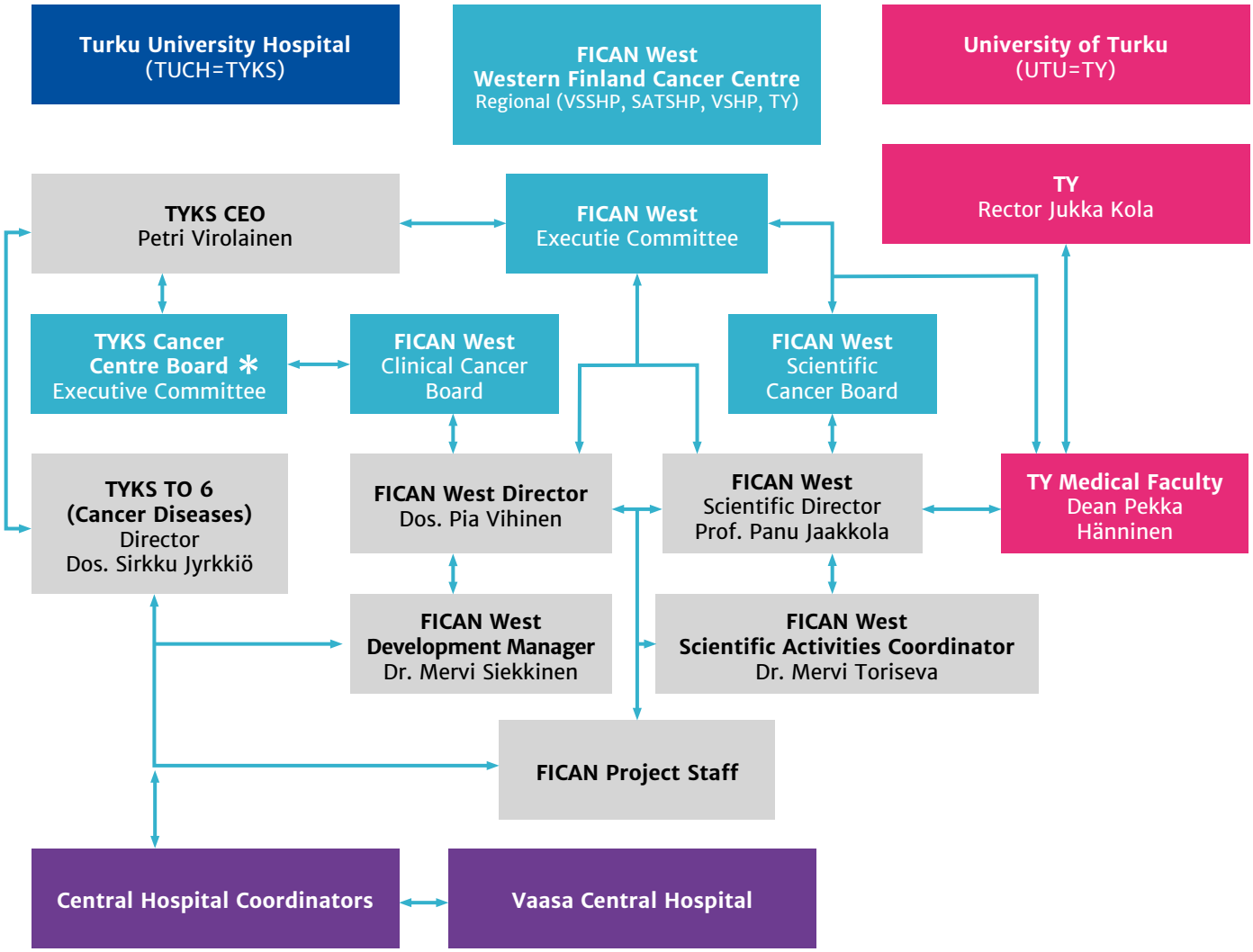
Panu Jaakkola, MD, PhD, Professor, Department of Oncology & Chief physician, Clinical trial unit

Pia Vihinen, MD, PhD, Chief physician, Director of FICAN West



Mervi Siekkinen, RTT, PhD, Development Manager of FICAN West

Organizational structure



*Tyks Cancer Centre Board (Executive)

Pia Vihinen, MD, Director, FICAN West
Sirkku Jyrkkiö, MD, CEO, TYKS (Chair)
Arto Rantala, MD, Director, Division of Digestive Surgery and Urology
Markku Kallajoki, prof, MD, Head, Department of Pathology
Panu Jaakkola, prof, MD PhD, Head of cancer trial unit FICAN West
Maija Itälä-Remes, prof, MD, Head, Department of Hematology
Ritva Kosklin, RN, Head Nurse, Division of Surgery and Oncology
Mervi Siekkinen, PhD, Development Manager, FICAN West (Secretary)

Clinical Cancer Board Members of TYKS, Satasairaala and Vaasa Central Hospital

Pia Vihinen, MD, PhD, Director, FICAN West (chair) Maria Gardberg, MD, PhD, Head, Department of Patology, TYKS
Sakari Hietanen, MD, PhD, Head, Department of Gynecologic Oncology, TYKS
Tuula Huumonen, Head Nurse, Department of Oncology, Satasairaala
Maija Itälä-Remes, prof, MD, PhD, Head, Department of Hematology, TYKS
Antti Jekunen, prof, MD, PhD, Head, Department of Oncology, Vaasa Central Hospital

Sirkku Jyrkkiö, MD, PhD, Director, Division of Surgery and Oncology, TYKS
Markku Kallajoki, prof, MD, PhD, Head, Department of Patology, TYKS
Marita Kilpeläinen, MD, PhD, Head, Department of Pulmonary Diseases, TYKS
Ritva Kosklin, Head Nurse, Division of Surgery and Oncology, TYKS
Jussi Liippo, MD, PhD Head, Department of Skin Diseases
Päivi Lähteenmäki, prof, MD, PhD, Head, Dep. of Pediatrics and Adolescent Hematology and Oncology, TYKS
Riitta Parkkola, prof, MD, PhD, Head, Department of Medical Imaging, TYKS
Kalevi Pulkkanen, MD, PhD, Head, Department of Oncology, Satasairaala
Arto Rantala, MD, PhD, Director, Division of Digestive Surgery and Urology, TYKS
Jaakko Rinne, prof, MD, PhD, Director, Division of Neurocentre, TYKS
Mervi Siekkinen, RTT, PhD, Development Manager, FICAN West
Tiia Sirkola, Head Nurse, Department of Oncology, Vaasa Central Hospital
Tero Soukka, MD, PhD, Head, Department of Oral and Maxillofacial Diseases, TYKS
Annika Ålgars, MD, PhD Head, Department of Oncology and Radiotherapy, TYKS
Esko Veräjänkorva, MD, PhD Head, Department of Plastic Surgery

Other operational experts of TYKS

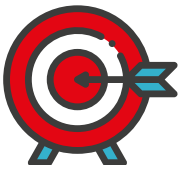
Vesa Anttila, MD, PhD, Head, Department of Cardiothoracic Surgery, TYKS
Peter Boström, MD, PhD, Head, Department of Urology, TYKS
Pauliina Hartiala, MD, PhD Department of Plastic Surgery, TYKS
Outi Hirvonen, MD, PhD, Head, Department of Palliative Care
Johanna Hynninen, MD, PhD Department of Gynecologic Oncology, TYKS
Heikki Irjala, prof, MD, PhD, Head, Department of Head and Neck Surgery, TYKS
Panu Jaakkola, prof, MD, PhD, FICAN West
Sari Johansson, Head Nurse Division of Neurocentre, TYKS
Gaber Komar, MD, PhD, Department of Medical Imaging, TYKS
Ilkka Koskivuo, MD, PhD, Head, Department of Plastic Surgery, TYKS
Veli-Matti Kähäri, prof, MD, PhD, Head, Department of Dermatology, TYKS
Anne Laapotti-Salo, Head Nurse, Division of Medicine (Hematology), TYKS
Heidi Laine, Head Nurse, Department of Cardiothoracic Surgery, TYKS
Maria Silvoniemi, MD, PhD Department of Pulmonary Diseases, TYKS
Aaro Turunen, MD, PhD Department of Oral and Maxillofacial Diseases, TYKS
Outi Tuominen, PhD, Head Nurse, Division of Pediatrics and Adolescent cancer, TYKS
Leila Varakas, Head Nurse, Division of Obstetrics and Gynecology, TYKS

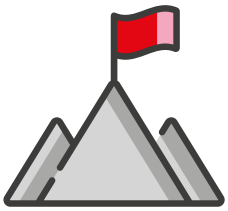
Scientific Cancer Board Members

Panu Jaakkola, prof, MD, PhD, UTU, TYKS, Department of Oncology, FICAN West, Scientific director, Chair of the board
Tero Aittokallio, prof, PhD, UTU, Statistics and Applied Mathematics
Peter Boström, MD, PhD, TYKS, Department of Urology
Klaus Elenius, prof, MD, PhD, UTU, Turku Bioscience, BioCity Turku, Director
Laura Elo, prof, PhD, UTU, Turku Bioscience
Pauliina Hartiala, MD, PhD, TYKS, Department of Plastic Surgery
Sakari Hietanen, MD, PhD, TYKS, Department of Gynecological Cancer
Maija Hollmén, PhD, UTU, MediCity Research Laboratories
Riikka Huovinen, MD, PhD, TYKS, Department of Oncology and Radiotherapy
Pekka Hänninen, prof, PhD, UTU, Faculty of Medicine, Dean
Maija Itälä-Remes, prof. MD, PhD, TYKS, Department of Hematology
Johanna Ivaska, prof. PhD, UTU, Turku Bioscience
Antti Jekunen, prof, MD, PhD, UTU, Vaasa Central Hospital, Department of Oncology and Radiotherapy
Jani Keyriläinen, PhD, TYKS, Department of Medical Physics
Ilpo Kinnunen, MD, PhD, TYKS, Department of Head and Neck Cancer Surgery
Veli-Matti Kähäri, prof, MD, PhD, UTU, TYKS, Department Dermatology
Riitta Lahesmaa, prof, MD, PhD, UTU, Turku Bioscience, Director
Päivi Lähteenmäki, prof, MD, PhD, TYKS, Department of Pediatrics and Adolescent Cancer and Karolinska Sjukhuset
Kim Pettersson, prof, PhD, UTU, Department of Life Technologies
Emilia Peuhu, PhD, UTU, Institute of Biomedicine
Matti Poutanen, prof, PhD, UTU, Institute of Biomedicine, Turku Center for Disease Modeling, Director
Kalevi Pulkkanen, MD, PhD, Satasairaala, Department of Oncology
Eeva Rainio, PhD, UTU, Faculty of Medicine, Head of faculty development
Paulina Salminen, prof, MD, PhD, UTU, TYKS, Department of Surgery
Johanna Schleutker, prof, PhD, UTU, Institute of Biomedicine and TYKS, Department of Genomics
Mervi Siekkinen, PhD, TYKS and FICAN West, Development manager
Maria Sundvall, MD, PhD, UTU, TYKS, Department of Oncology and Radiotherapy
Pekka Taimen, prof, MD, PhD, UTU, TYKS, Department of Pathology
Mervi Toriseva, PhD, UTU, Institute of Biomedicine, TYKS, FICAN West, secretary of the board
Pia Vihinen, MD, PhD, TYKS, Department of Oncology and Radiotherapy and FICAN West, Director
Jukka Westermarck, prof, MD, PhD, UTU, Turku Bioscience

Tyks Cancer Centre Strategy 2018-2022

The Tyks Cancer Centre Strategy 2018-2022 constitutes a strategic plan of the future, which will guarantee the population of the region high-quality and efficacious treatment of cancer, research and education in the context of a center of excellence to be.





VISION: The Tyks Cancer Centre is an internationally acknowledged quality center which produces evidence-based cancer treatment and high-level scientific research in a timely manner in an environment where the personnel has a high level of wellbeing.

MISSION: The Tyks Cancer Centre is the heart of the cancer care and research cluster together with the network of the Western Finland Cancer Centre (FICAN West), which includes the central hospitals in Pori and Vaasa and the Turku University Cancer Research Laboratories, it will be one of the leading centers in Finnish cancer care and research.

Assets and specialties of the Tyks Cancer Centre

- The Tyks Cancer Centre has all diagnostics and treatments available in Finland to be used to the benefit of cancer patients.
- Highly specialized development in personalized medicine and genomic diagnostics. The Auria Biobank and the clinical information unit provide a unique setting that makes it possible to combine information on tumor molecular biology with patient records, a combination that will provide real-world evidence data for daily practice and research. The hospital campus area harbors one of the leading PET centers in Europe and the Auria Biobank for collection, storage and advanced research on biological specimens.
- Multilingual, highly competent professionals. Cancer care is routinely provided in Finnish or Swedish.
- The leading stem cell transplantation unit in Finland.
- Basic cancer research and clinical research are combined and form the FICAN West Research network located in the same campus area. More than 100 cancer-oriented biotechnology companies at the same campus generate and develop research innovations from bench to bedside.
- Nursing science research is integrated into a program of the Tyks Cancer Centre called Psychosocial care and survivorship care of cancer patients.
- All facets of cancer care and research are easily reached within the campus area.

Tyks Cancer Centre: Key strategic measures 2018-2022

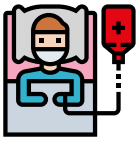
1. Strengthen the involvement of patients in their treatment.
2. Develop standardized and equal treatment facilities for all patients.
3. While supporting centralized treatment planning clinical cancer treatment is facilitated close to the home of the patient and in the vernacular of the patient. Increase work-sharing with central hospitals and the primary health service.
4. Support out-patient treatment.
5. Establish a palliative and supportive cancer care unit at Tyks.
6. Develop biological imaging and PET imaging of cancer with new tracers.
7. Strengthen the research network among FICAN West partners, start Phase I clinical trials and strengthen the involvement with the Nordic Network for Early Cancer Trials (NECT).
8. Increase the number of clinical trials in the most common cancer groups (breast cancer, prostate cancer, lung cancer) and improve patient accrual to trials.
9. Develop further the key cancer care areas of the FICAN: personalized medicine and supportive care.
10. Establish nationwide quality registers of cancer treatment and develop solutions for electronic follow-up and contact with patients.
11. Establish institutional governance for the Tyks Cancer Centre.
12. Increase the overall knowledge on cancer diseases and treatment facilities in Finland in collaboration with other FICAN partners.

Core activity data 2022

Diagnosed (new) patients
3 307 in 2021

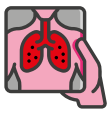
Radiotherapy patients 1 579

Molecular Tumour Board
patient cases 22

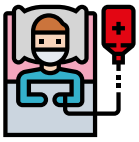


Chemotherapy patients 3 887

Radiotherapy treatments 1 605



Total number of medical imaging studies 16 204 (MRI, PET, PET-MRI, PET-CT, CT)



Chemotherapies 6 867

Ward care periods 6 373

Molecular pathological studies
6 946

Outpatient appointments
124 967

Ward care days 21 517

Relative survival

The Finnish Cancer Registry maintains the national registry of all the diagnosed cancer cases since 1953. It is also a statistical and epidemiological research institute that does active collaboration both nationally and internationally.

Year 2020 there were 3617 new cases of bowel cancer, 4885 new cases of breast cancer, and 5035 new cases of prostate cancer in Finland.

This table shows the data on relative survival of patients treated at the Hospital District of Southwest Finland area. Survival data originates from the Finnish Cancer Registry (www.cancerregistry.fi). Five-year patient survival (%) in patients diagnosed 2018-2020 for the five most common cancer diagnoses in Finland and for cutaneous melanoma by gender. The number of patients treated at the Hospital District of Southwest Finland area are also shown.

ICD-10	Tumor location	Gender	5-year survival Finland 2018–2020	5-year survival FICAN West 2018-2020	Patients (n) FICAN West 2020
C50	Breast	Female	91.40	90.75	826
C18-20	Colon		65.78	71.30	219
C54	Uterus		81.08	81.06	160
C33-34	Lung		13.64	21.84	171
C43	Melanoma		93.75	91.93	103
C65-68	Urinary tract		67.99	63.52	60
C61	Prostate	Male	94.09	93.42	919
C18-20	Colon		65.78	62.92	343
C33-34	Lung		13.64	12.50	310
C65-68	Urinary tract		74.85	75.99	183
C43	Melanoma		93.75	96.47	114

Quality system

Tyks Cancer Centre has been a member of Organization of European Cancer Institutes (OECI) Cancer Centre since 2016. Cancer Centre status received at 2019 confirmed that Tyks meets all high quality standards of cancer care and research when compared and peer-reviewed with other cancer institutes in Europe. Tyks has been also a member of European Reference Network (ERN) since 2016 and audited to European Cancer Network (Euracan).

Quality management means operative leadership, assessment and improvement aimed at reaching preset quality goals.

The goal of the quality management plan of TYKS at the Hospital District of Southwest Finland for 2022 is to support systematic and continuous development of quality and patient safety. The quality management plan is based on national legislation, organizational strategy, operative quality goals and on systematic assessment and continuous improvement of what is done.

In general, the SHQS quality program is used by all departments in the Tyks hospital that manage cancer patients. In addition, the work done within the Tyks laboratory functions (clinical chemistry, hematology, pathology and genetics) are accredited clinical laboratory activities (e.g., ISO1518). Medical imaging (clinical neurophysiology, clinical physiology, nuclear medicine, and – within PET – also production of radiopharmaceuticals) are accredited diagnostic functions (e.g., EN ISO / IEC 17025: 2017, FINAS). An external clinical audit of the use of medical radiation in the department of nuclear medicine, in the PET center and in radiotherapy (Labquality), has been carried out, as required by the Radiation Act.

Measures of quality of care and follow-up

Together with Tyks Information Service, with 2M-IT and with the Finnish Cancer Registry, FICAN West coordinates the development of cancer quality registries and a dashboard so that they support clinical work and the monitoring of the treatment effectiveness more effectively and facilitate scientific research. When a unified operative model is created, indicators of quality and follow-up must also be determined.

Quality registry

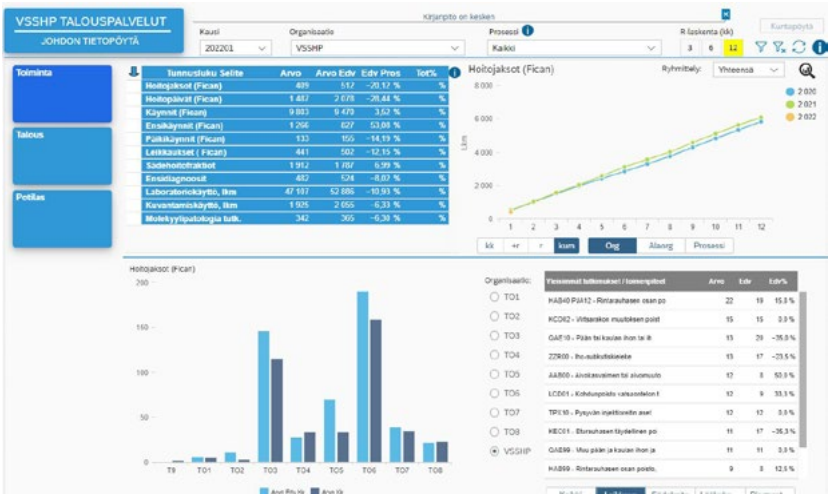
A central part of the quality register for cancer treatment and research is the national Finnish Cancer Registry. The Finnish Cancer Registry automatically receives information about new cases of cancer, histologically confirmed. The challenge is to create comprehensive clinical reports. The aim of the Cancer Registry is to expand the registry to allow for extensive clinical and epidemiological research.

The Hospital District of Southwest Finland has previously exposed the quality registry suppliers to competition, and BCB Medical has been selected. BCB Medical's quality registers are used in the university hospital, for example in orthopedics, colorectal surgery and urology. FICAN West works on a national level closely with other cancer centers, including the Finnish Cancer Registry, with the aim of improving coverage of the information of the entries of the Finnish Cancer Registry.

Quality registers, implemented in surgery, are expected to unify the way operative reports. Currently, systems are in place for collection of information on adverse events experienced by patients receiving oncological drugs and on disease follow-up (this is the case, e.g., in gynecology, hematology, lung diseases, pediatrics, oncology and urology). This has been made possible through modern technology which allows commercial companies or the Health village system to analyze data.

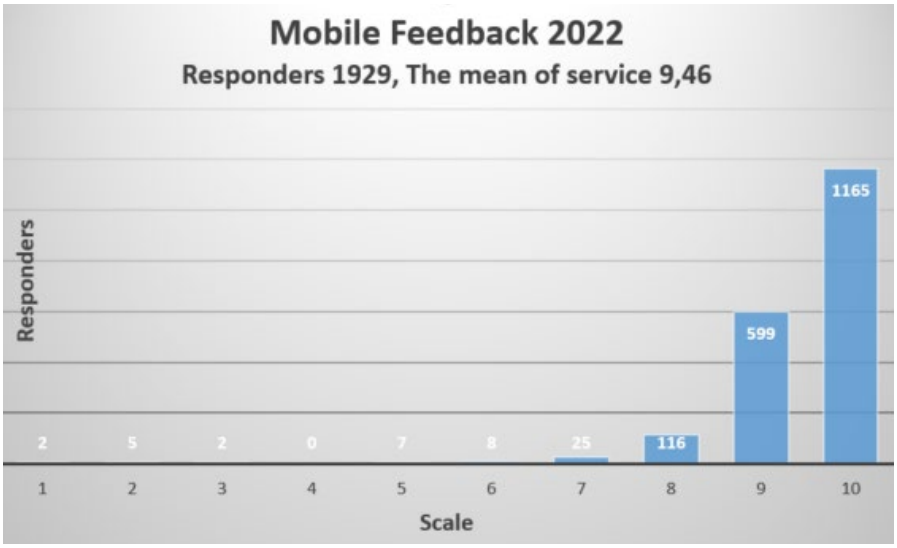
Dashboard

FICAN West has, in collaboration with the units of the Turku University Central Hospital that treat cancer patients, developed a dashboard for the administration. The dashboard covers a major section of the traditional parameters of daily administrative tasks and facilitates cancer treatment follow-up in the hospital.

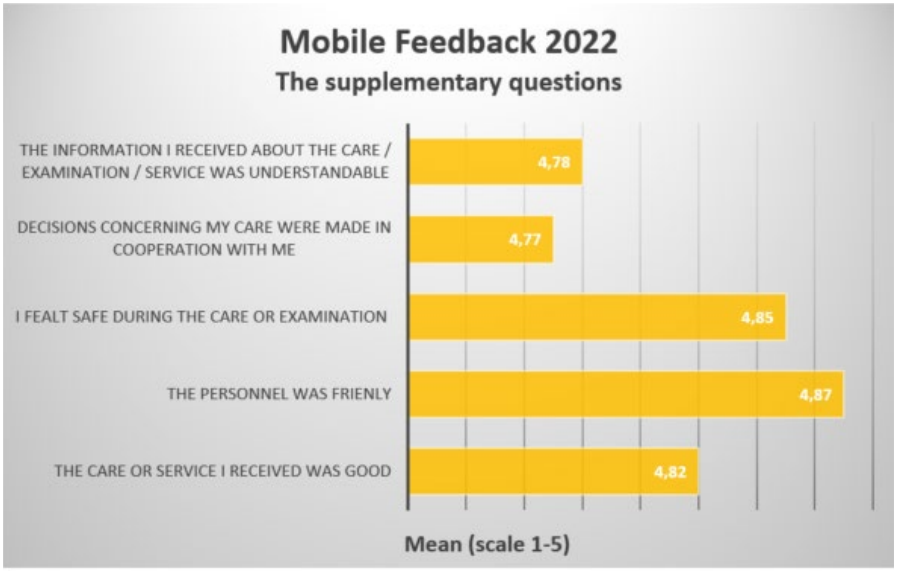


Patient satisfaction and mobile feedback 2022

We have measured patient satisfaction continuously. The patient satisfaction surveys (mobile feedback and feedback form) were open online to all cancer patients treated at Tyks. The main goal is to identify the need for future development. In 2022 the feedback was in line with the mobile feedback (the use of the feedback form was infrequent). During 2022, 1929 cancer patients from oncology unit answered. Overall, the cancer patients have provided very positively feedback, the mean satisfaction score has been 9.46 (on a scale from 1 to 10).



The scores provided by cancer patients have always been high. The lowest score was given to supplementary questions related to the item "Decisions concerning my care were made in cooperation with me" mean 4.77 points (on a scale from 1 to 5) and the highest score was given to the item "The personnel was friendly", mean 4,87 points (on a scale from 1 to 5). In addition to the 6 questions, the survey is open for comments.



The comments have, in general, been positive, e.g.:

The doctor was friendly and explained in a understandable way the current state of my illness and how the treatments will continue. Also in the outpatient clinic the nurse was friendly and made sure I was feeling well and understood the possible side effects of the medicine and their symptoms.

I learned a lot of new information about my illness, some of which I missed a bit, of course. But I was given a lot of material and phone numbers to help me clarify things that were not clear afterwards. The staff were patient and very empathetic throughout the whole treatment process.

Overall my journey during my breast cancer treatments has been safe because the professionalism and kindness of the doctors and nurses is so excellent.

The staff is expert and their empathetic attitude helps the patient in a mentally difficult situation. Roses and chocolates for them.

Some comments suggested improvement:

Treatment is entirely focused on the physical symptoms. The client is not treated as an individual and is not treated holistically. Constant turnover of doctors hampers continuity of care and reduces trust.

The doctor's appointment was almost 20 minutes late. As a result, my other treatments were also late. Fortunately, this does not happen often.

It is very hard to ask important questions in the appointment of the doctor. That is why would be good to get a call time about 2-3 days after the visit, so that I could ask more exact questions.

Patient Treatment

Standardization of patient care

The Tyks Cancer Centre follows ESMO, ASCO and national recommendations on the treatment of cancer.

To standardize and equalize the treatment in Finland, the national Finnish Cancer Centre (FICAN) has issued recommendations for treatment and follow-up of cancer patients. The first version of these recommendations has now been piloted by two associations for cancer specialists. Current national care recommendations (treatment guidelines) are available at terveysportti.fi intranet, which are limited to health care professionals (Current Care Guidelines). Our plan is to standardize all patient information and treatment instructions of the entire Hospital District of Southwest Finland. In addition, a standardization group for radiotherapy protocols was set up. These harmonized instructions are available for professionals at the proprietary intraweb of FICAN West (FICANintra).

For citizens, several cancer-related treatment instructions are available in the national web page www.terveyskyla.fi and www.terveysportti.fi. The web page www.hoito-ohjeet.fi, also containing information on treatments for patients and the general public, is maintained by FICAN West. The websites maintained by TYKS and www.ficanwest.fi for patients provide the following information:

- All recruiting clinical trials of the Cancer Centre.
- Updated information on waiting times for referral to the first treatment contact, to surgery, to chemotherapy and to radiotherapy for the most common cancer types.
- Cancer-specific patient pathways for most cancer illnesses. These pathways include information on the cancer and on how to support and improve patients' understanding on their illness, diagnosis and self-care.

New pathways are being updated continuously.

More flexible access to palliative radiation therapy for cancer patients with painful bone metastases

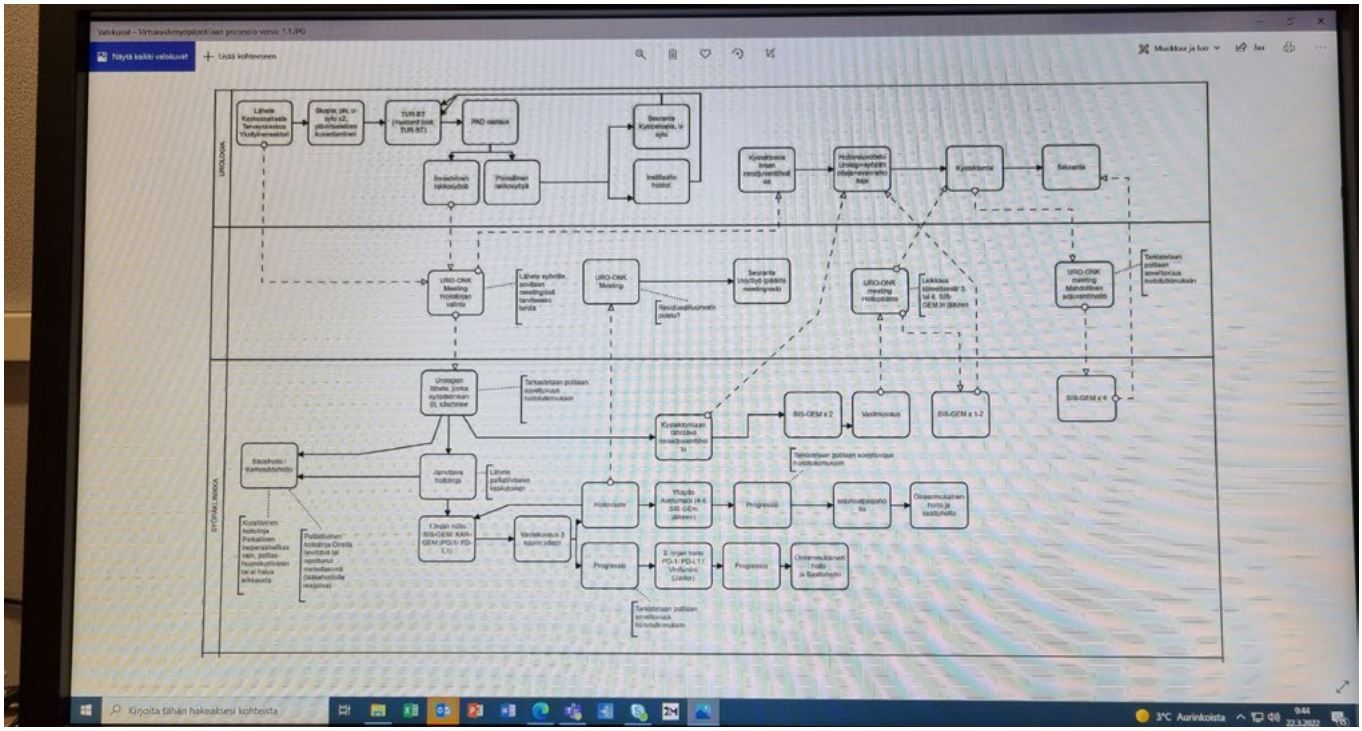
Some cancer patients get painful skeletal metastases which can be treated palliatively with radiation therapy. Patients needing palliation of painful bone metastases have had to queue for this treatment for quite some time, since they are in the same queue for radiotherapy as all other cancer patients. The most significant bottleneck is caused by the limited access to first visits to radiation oncologists. Because the start of radiation therapy is delayed, some of the planned radiation treatments of painful metastases are cancelled, interrupted or delayed further. The most common reason for cancellation or interruption of radiotherapy is worsening of the patient's general conditions, infection or death, i.e., the patient's condition becomes worse during the extended waiting time. The problems experienced by cancer patients, who are in pain while waiting for treatment and who have long waiting times for radiotherapy, only exacerbate symptoms and sufferings.

Since November, 2020, the oncology department at Tyks hospital has tested a new practice for radiation therapy: patients with painful skeletal metastases are provided expedited access to palliative radiotherapy. The goal of testing this new practice is to hasten the patient's access to simple palliative radiation therapy, to shorten the queue to radiotherapy and to increase the resources of physicians to provide services to those patients who can be treated curatively with radiotherapy.

Palliative radiotherapy to manage skeletal pain can now be instituted faster since the physicians at the oncology department and at the palliative center who have received the appropriate training have given the patients information about radiotherapy and its possible adverse events. This has made separate appointments to radiation oncologists unnecessary for some of the patients who only need palliative

radiotherapy for pain management. The radiation oncologist, who can call and give the patient additional information if needed, plans the radiation treatment, e.g., radiation dose and number of radiation fractions. In addition to oral information the patient receives written instructions before the radiotherapy sessions are started.

Our experience has been that cancer patients who need palliative radiotherapy to control skeletal pain have started this therapy about 11 days after the referral , which compares very favorable with a waiting time of up to 4 weeks before the new practice. During follow-up from NOV2020 to FEB2021 no radiotherapy session was cancelled or interrupted. The patients have been satisfied that they have gained access to the treatment quickly. At the same time, more appointments have become available for radiation oncologists. A scoring system was introduced during the project to evaluate the prognosis of the patient with the purpose to assess whether the patient is expected to benefit from the palliative radiotherapy or not. Since the results have been good, the new policy has been continued after the trial period. Our intention is to establish the new policy as a permanent practiceat the department of oncology at the Tyks hospital. Our goal is also to expand this practice to other clinics at the hospital in the future and thereby providing faster radiotherapy and pain relief for e.g. lung cancer, hematological cancer patients, as well.



Improving coordination of the treatment path for patients with urinary bladder cancer in the Tyks hospital

There have been some challenges in coordinating the treatment path of patients with urinary bladder cancer in the Tyks hospital. It has been unclear and confusing for patients and hospital staff how patients should move between the different units of the hospital. The urology and oncology clinics have collaborated to clarify the treatment path of this patient group. A multiprofessional working group was established with professionals and their supervisors (managers) involved in the treatment path of patients with urinary bladder cancer. The goal of the project was to improve the fluency of multiprofessional collaboration, to clarify how the treatment of bladder cancer patients should be coordinated in the Tyks hospital and to describe the management process of bladder cancer patients.

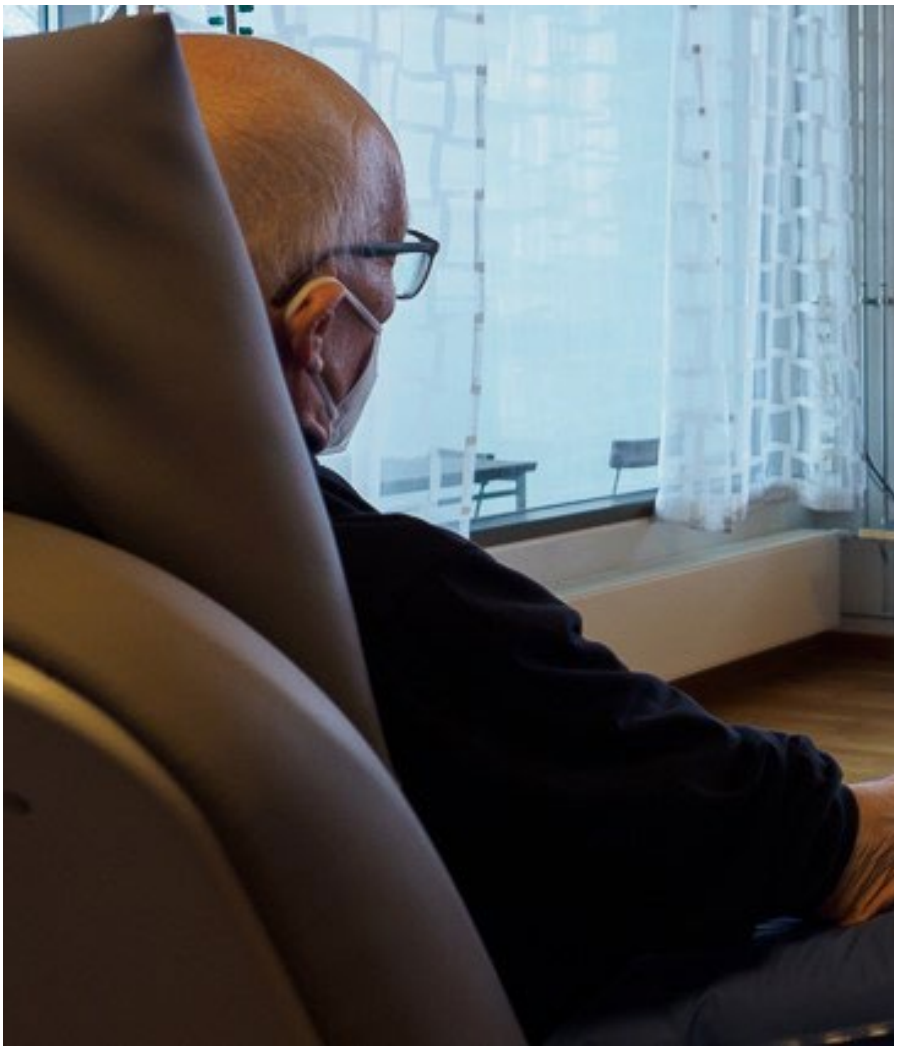
The working group of the project has held meetings regularly since the spring of 2019. The project has resulted in a description of the treatment path of patients with bladder cancer for medical professionals. The description states clearly where the responsibility for patient management resides along the entire treatment path. The process for multidisciplinary team meetings (MTD) for urological patients was also developed within the project. From now, nurses who are responsible for coordinating the treatment of these cancer patients will participate in the uro-oncological meetings for treatment planning and for coordination of the treatment path of individual patients.

The project has led to more fluent treatment coordination and clearer treatment paths. The project and multidisciplinary collaboration has continued. The future goal is to describe visually the treatment path of patients with cancer of the urinary bladder and to evaluate and follow how well treatment coordination works.

Piloting an oncogeriatric co-management model at the department of oncology

As the population ages, the number of elderly patients with cancer rises. Most cancer diagnoses are made in the population aged 65 and above. In this age group, also the prevalences of comorbidities, disabilities and the susceptibility to the adverse effects of chemotherapy are highest.

A pilot project of an oncogeriatric co-management model was started at the department of oncology in November 2022. The aim of the project is to recognize and evaluate frail and vulnerable older cancer patients, and – through comprehensive geriatric assessment (CGA) – to decrease the risk of adverse effects of chemotherapy and to increase the recognition of geriatric syndromes in these patients.

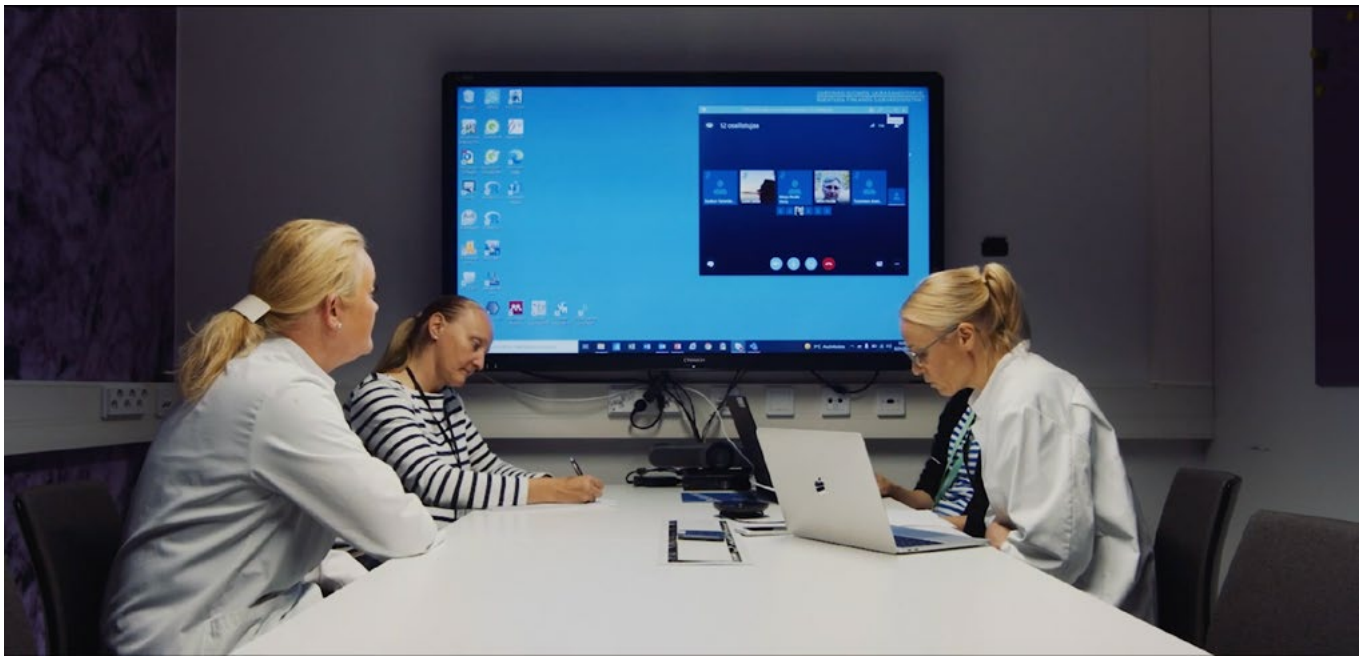


CGA is a multidisciplinary tool that covers evaluations of functional, psychological, cognitive, nutritional and social status of the patient, as well as evaluations of comorbidities and medications.

The treatment pathway consists of screening of patients aged ≥ 75 with a diagnosis of either gastrointestinal cancer or lymphoma. For screening, the G8 tool, specifically developed for older patients with cancer, is used. Patients with G8 ≤ 14 are referred for CGA. CGA is performed by a geriatrician and a nurse. The nurse assesses the different domains with selected tools at an appointment preceding the geriatrician's assessment. The results of the evaluation are assessed by an oncologist who makes the final treatment decision and treatment plan with the patient. All three appointments are held consecutively on the same day.

The experiences of the pilot have been encouraging and patients and their next of kin have been satisfied with the new treatment model. In the future, our goal is to establish an oncogeriatric treatment pathway as a permanent part of the routine practice at the department of oncology at Turku University Hospital.

FICAN West Molecular tumor board (MTB)



Molecular tumor boards (MTB) activity have been established in hospitals worldwide to facilitate the implementation of precision medicine. Since 2018 the multidisciplinary MTB team of FICAN West, consisting of cancer physicians, pathologists, clinical geneticists, clinical chemists and molecular biology experts, has met monthly to discuss individual patients who have undergone comprehensive genomic profiling in FICAN West. The work of the MTB has continued successfully in 2022.

Since 2021, two molecular pathologist have participated in the FICAN West MTB meetings. Molecular pathology combines traditional histopathological evaluation of tumors with a molecular based approach to find genomic targets for individualized treatment. Molecular pathologists interpret the comprehensive genomic profiling reports and present the functional effects of the detected genomic alterations to the tumor board. The clinicians and molecular pathologists work together to review the literature on treatment options based on these findings.

FICAN West MTB have an important role in two new studies with goal to further develop molecular tumor analyses and personalized cancer treatment at the Hospital District of Southwest Finland and FICAN West. FINPROVE is a nationwide Finnish Phase II study that aims to facilitate patients' access to targeted anti-cancer drugs by evaluating the efficacy of these drugs in treating advanced cancers with a known molecular profile. FINPROVE started to recruit patients in 2022 in FICAN West. The PROEXMET study aims to develop and set up local tumor sample collection, genetic analysis of clinical tumor samples and to screen patients for the FINPROVE study. It also aims to support and promote close research collaboration between clinical research and basic research and to facilitate cooperation between the Turku University Hospital, the University of Turku, the Åbo Akademi University and actors in the field of diagnostic technology. This cooperation has been founded in 2021–2022 and the PROEXMET study is expected to open in 2023.

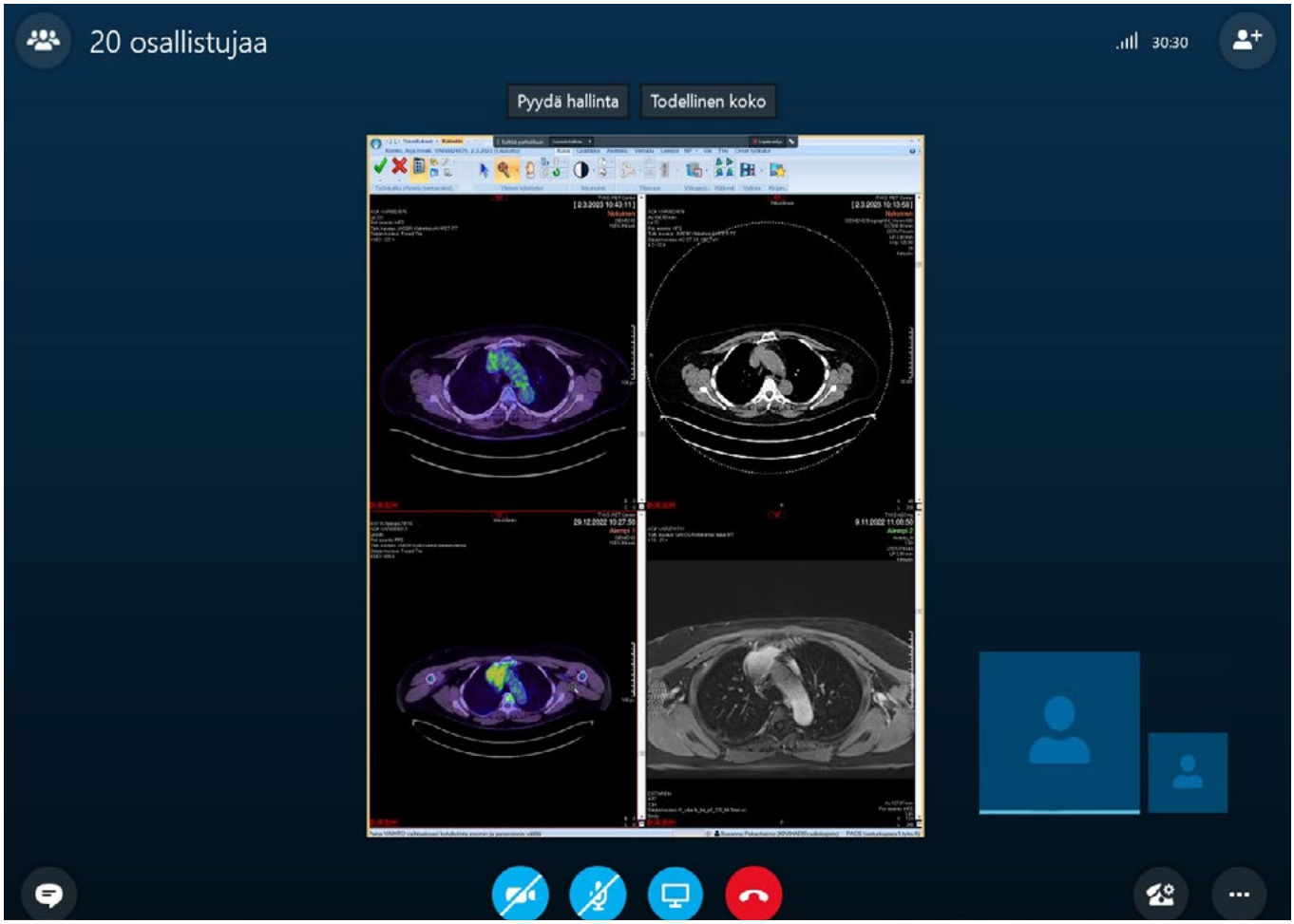
Educational event

An international workshop on comprehensive gene profiling, molecular tumor boards and artificial intelligence in the treatment of rare cancers organized by the FICAN West Cancer Center in cooperation with the European Reference Network

Genomic profiling is used increasingly in the diagnostics and treatment guidance of cancer. An international workshop focused on gene profiling of cancer, molecular tumor board activities for gene-guided cancer treatment and artificial intelligence was organized from September 29 to 30, 2022, at the Turku University Central Hospital in cooperation between the FICAN West Cancer Center, the Turku University Central Hospital and ERN (European Reference Network). The title of the workshop was comprehensive gene profiling, Molecular tumor board (mtb) and artificial intelligence in the diagnosis and treatment of patients with rare adult cancers. It was directed to clinicians involved in cancer treatment, specialists involved in cancer diagnostics, researchers and students. The speakers were top experts from the Nordic countries, the Netherlands and the United States. In addition, Finnish speakers and experts from the FICAN West Cancer Center played a significant role in implementing the workshop. The workshop was funded by ERN, which allowed 16 participants from all over Europe to participate. Both foreign and local participants presented challenging and rare cancer patient cases and got valuable comments from the MTB experts on patient cases. This type of training can be included as part of the studies required for medical specialization and for the Doctor of Philosophy degree. More than 120 people attended the two-day event.

The topics of the workshop are very current, considering the need for developing individual cancer treatment and gene profiling in different countries – locally and nationally. The workshop significantly increased the participants' awareness of the topics and boosted local, national and international cooperation. The feedback was very positive and participants called for similar events also in the future.

Multidisciplinary team (MDT) meetings at the Tyks Cancer Centre and FICAN West



In 2021, there were 20 regular clinical multidisciplinary team (MDT) meetings held in TYKS on different cancer types. 14 of these MDT meetings were weekly by skype. The MDT includes a surgeon, a pathologist, a radiologist, a medical oncologist, a radiotherapy oncologist and nurses from the surgical and oncological departments. Meetings on cancer of the head and neck, lung, brain, female genital tract and gastrointestinal tract cancers involved also a video conference connection with the central hospitals in Pori and Vaasa. The MDT makes recommendations on how the patient is to be treated, and these recommendations are registered in the patient records.

MDT meetings deal with specific tumor types of individual patients. Thus, every patient with breast cancer, colorectal cancer and testis cancer is discussed in an MDT after surgery. Patients suitable for neoadjuvant therapy, e.g., patients with gastric cancer and urothelial cancer, are brought to an MDT to ensure an uninterrupted treatment path for the patient from diagnosis to chemotherapy and surgery. The treatment of brain tumors, head neck cancers and lung cancers demand close collaboration between a radiologist, pathologist, surgeon and radiotherapy oncologist and patients with these tumor types are a natural and recurring topic at MDT meetings. Lymphoma patients who require high-intensity chemotherapy and stem cell transplantation rely on the collaboration between oncologists and hematologists which primarily convene at MDT meetings. Difficult cases and rare tumor types are typically discussed and decided upon at MDT meetings. Patients eligible for ongoing clinical trials are also often identified at MDT meetings.

Cancer Centre Client Board and Patient Involvement

The client board was established in 2019. Currently, the client board counts 29 members – patients and next-of-kins. They are of different age and the patients have (had) different cancers. Representatives of the Cancer Society of South-West Finland, the Satasairaala hospital and the Central hospital of Vaasa participated, as well. The members of the client board can give input on how to develop the work and services of FICAN West. The client board operates on a voluntary basis.

It has been the explicit wish of the board members to put improving rehabilitation of cancer patients into focus. The members have also had the opportunity to give input to the development of the function of the Tyks hospital by working together with the Tyks hospital and the Vakka-Suomi hospital.

In 2022 the development targets have been:

Cancer Center Client Board activity:

- Explore and contribute to developing the nutrition instructions on the web page hoito-ohjeet.fi: Maintaining good nutrition; Instructions how to solve problems of nutrition; and Intensive nutrition.

- A training session on nutrition was subsequently arranged for the Network of Cancer Nursing. The participants were informed of the evaluation of the nutritional guidance provided by the personnel to patients. The views expressed by an expert by experience were also presented.

- Further development targets are developing the layout, headlines, content and comprehensibility of the treatment paths for cancer patients on the Tyks.fi web page; and getting acquainted with the functions of the Cancer Society of South-West Finland.

Client Board of the TYKS Main hospital and the TYKS Vakka-Suomi hospital collaboration:

- Getting acquainted with the Tyks Lighthouse hospital.
- Testing the platform (entitled TaskuSote) maintained by the Tyks hospital for cancer patients for contacting relevant parties.

- Testing the visual appearance of the web pages of the wellbeing services county of Southwest Finland.

Collaboration partners:

- A member of the Tyks Cancer Center Client Board was nominated to the European Care Diseases (ERN /Euracan) Client Board.

- A member of the Tyks Cancer Center Client Board participated in a video on exercise produced by the Cancer Society of Finland

Promoting FICAN West clinical and supportive personnel and Cancer Society network

Patient organization co-operation

Tyks Cancer Center continued hosting remote physical exercise sessions for cancer patients in co-operation with the Cancer Society

In Finland, the Western Cancer Center region (FICAN West), the Turku University Central Hospital (Tyks) Cancer Center and the Cancer Society of Southwest Finland launched a project in early 2021 to provide cancer patients with exercise guidance through a remote, web-based platform. In the fall of 2021, a model was designed for how to best organize remote training sessions, which subsequently have been organized within the entire region of FICAN West. During 2022, co-operation among remote physical exercise sessions was further expanded by the Cancer Society of Finland. The goal was that all cancer patients in Finland have the opportunity to exercise safely at home via remote technology. The Cancer Society of Finland actively promoted remote exercise sessions on its social media channels. In this way, the regional cancer associations received information simultaneously and were able to share information through their own social media channels.

The goal of the remote exercise sessions was to encourage cancer patients to pursue physical activity and to exercise in a versatile fashion during and after cancer treatments and to help them get peer support. The purpose was to encourage cancer patients – by participating through a distance learning platform – to attain and maintain the level of exercise recommended by international experts. The types of exercise were versatile muscle strength training and exercises to maintain and improve mobility, balance and movement control. Endurance training may be well carried out by the participant without any need for external help.

Professional exercise and rehabilitation instructors and a non-professional peers directed the exercises. Each training event had a duration between 20 and 45 minutes. On Mondays muscle strength training was on the program, every second Tuesday lymphatic exercises, on Wednesdays the FasciaMethod, on Thursdays relaxation and on Fridays exercise in Swedish.

Information desk of the Cancer Society of Southwest Finland

An information desk of the Cancer Society is situated on the first floor of the Tyks T hospital, in the vicinity of the departments that manage cancer patients. The office provides information on matters like information courses arranged by the Cancer Society of Southwest Finland, the availability of peer support and the availability of medical professionals.

The information desk has been managed by professionals and volunteers from the Cancer Society of Southwest Finland who are there to respond to questions on rehabilitation in general, on the activities of the Society for young adults and about prostate cancer. A nurse of the Society has been available on Wednesdays from 9 to 12 AM and an expert on family work of the Society on Thursdays from 12 to 2 PM. The expert provides information specifically on services directed to families and on activities for adults. Volunteers from the volunteer group ETUSET, which handles questions related to prostate cancer, have been available on Tuesdays from 9 to 12 AM.

At times when nobody is available at the information desk, it is possible for clients and patients to get information via TV screens and brochures and to take home information leaflets on the activities of the Cancer Society.

Educational events

Cancer Nursing Network afternoons

The network organizes networking events, training sessions and workshops and distributes science-based information electronically. Operations are constantly being developed to respond to the needs of the healthcare staff. Organizationally,

the Cancer Nursing Network involves collaboration among three hospitals: the Tyks hospital and the central hospital of Pori and Vaasa.

The goal for 2022 was to organize two training events in cancer nursing. The first of these events was cancelled because of a nurse strike. The other event was carried out as planned early in the fall. The training event included topics like nutrition of cancer patients and discussions on how to improve networking among clinical professionals in cancer patient management.

The training afternoon was very popular and were attended by 50 professionals from tertiary care, the cancer society and primary care. According to the feedback from this afternoon training session corresponded very well to what the expectations were and provided the audience with new information and new ways to look at cancer nursing. The network of cancer nursing is active, and a future goal is to organize trainings and other events for the network.

Supporting the family of adult cancer patients seminar

Family members of persons who fall ill with cancer may become anxious and depressed. They are concerned about how the illness may affect family relations, their financial situation and how the perceived responsibility for managing the needs of the family and its economy are affected. In 2019, FICAN West launched a development project to focus more on the patient's family and family needs. The goal of the project was to improve the wellbeing of the family of the adult cancer patient and to make better use of multiprofessional collaboration and client orientation in the context of cancer patient management.

In 2022, the project focused on increasing and securing the knowhow of the cancer nursing personnel. Two training events were carried out. The topic of the first one was "broaching the subject of family". Several speakers discussed how best to take the family of cancer patients – from babe to oldster – into consideration. There were 115 participants, some by remote access. The participants were professionals engaged in treating and nursing cancer patients and also persons interested in the subject. The participants were of various clinical backgrounds and came from all over Finland. Much positive feedback was given. The discussion on broaching the family of cancer patients was lively, indeed. Taking the family into consideration when treating cancer patients was felt to be important and similar training events were called for in the future.

The topic of the second training event involving family centers (=child guidance and family counseling centers) in supporting adult cancer patients. There were presentations on the work done by the family centers within the entire FICAN West region and on how the activities maintained by the family centers could be used to support rehabilitation of families of adult cancer patients. The event was attended by more than 30 cancer treatment professionals with a variety of backgrounds. The discussion was lively. The responses by cancer treatment professionals after the event found that the update on the work done by the family centers contained much new and valuable information. Integrating the supportive function of the family centers into the treatment path of cancer patients was felt to be important. Intensified collaboration with the family centers was on the wish list of the participants.

The project has resulted in an operational family model that should be implemented in all health care units where cancer patients are treated. A goal was also set on intensifying collaboration between primary health care and the third sector with the aim to improve the support for cancer patient families.

Work and Cancer webinar

FICAN West and the Association of Cancer Patients in Finland arranged a webinar entitled "Cancer and working life". The target groups were health care professionals, students and other interested parties working in cancer care. The goal was to increase and secure the knowhow of the participants about the challenges of working life faced by cancer patients and to evaluate the patients' need for support in matters like rehabilitation and assessment of working ability. What is the best way to support and collaborate with professionals working in occupational health care? What support do the patient organizations have to offer? The meeting was organized in the form of a webinar.

The meeting was opened by the director of FICAN West, Pia Vihinen, adjunct professor. Emma Andersson, who is an expert from the Association of Cancer Patients in Finland gave a presentation entitled "Observations of the 'cancer and working life equation'". This was followed by a presentation by Satu Rantala, expert by experience, who spoke under the title "Returning to working life with a cancer diagnosis". The participants came from the units that treat cancer patients in the Tyks hospital.

Highlights in psychosocial and rehabilitation support projects

Development of psychosocial training

The program for developing psychosocial rehabilitation support and the scientific program of the FICAN West constitute an effort to respond to the psychosocial needs of cancer patients and to support the needs of them and their families. The program was prepared in 2021 by WG (professors of the Department of Nursing Science and Psychiatry at the University of Turku, by multidisciplinary experts on cancer treatment and psychiatry at the Tyks, Satasairaala and Vaasa Central hospitals, by representatives of the Turku University of Applied Sciences and by representatives of the Cancer Associations in western Finland).

The priorities of the program are: well-working psycho-oncological services, methods to support patient care, sufficient professional know-how, education, assessment, development and research.

In early 2022, the concerned head nurses of the Tyks hospital convened to discuss the present state of support and the degree of interest in implementing concrete actions in all cancer care departments of the hospital. The key action selected was development of psychosocial training.
The vision of the training model, called "Psychosocial support for seriously ill persons", is that the personnel have the capability and know-how to provide individualized psychosocial support to persons who have a cancer diagnosis and their near of kin. The intention being to secure sufficient know-how hybrid kickoff meeting was held on 2MAY2022. The goal was set on integrating training of psychosocial support into a unified national career-path model in collaboration with hospitals, vocational training institutions and the university, initially within the Health Campus Turku region.

The second meeting of took place in the fall of 2022. The participants of TYKS (hospital management), Turku University (nursing department), Turku University of Applied Sciences and FICAN West provided an update on the training situation and the career-path model as they stand today both on a national level and on regional levels. There is, as yet, no training entity com-

patible with a career-path model. It was decided that during 2023 a continuing education entity will be planned and it will follow a systematic career path, after basic training, and ultimately leading to the job description of expert/specialist. The next meeting will focus on models to describe competencies.

Low-threshold nurse consultations pilot to increase psychosocial support to cancer patients

The aim of the pilot of a new type of nurse reception 2021-22 at the Cancer Clinic and Palliative Care Center is to provide low-threshold psychosocial support for adults with cancer. Firstly, three cancer clinic nurses received training to have additional competence of psychosocial support. Secondly, the once a week low-threshold psychosocial support reception was build up.

In the reception process, the individual encounter of the patient and the understanding of the changed life situation are essential. The purpose of the reception is to:

- Assess the comprehensive mental, social and spiritual situation of the patient and nearbyothers.
- Support the patient's daily survival.
- Promote the patient's mental and social survival at different stages of the disease.
- Provide information and guidance on the right services.

During 2022 low-threshold nurse consultation appointments have been established in the oncology clinic and palliative center. This activity has expanded and currently each unit within the cancer clinic and palliative center has at least one nurse employed for providing this service to cancer patients. Information about this service has reached well out to professionals who treat cancer patients and the service is used by patients who need psychosocial support.

In 2022 increasing and securing the psychosocial knowhow of nurses was in focus. Education of nurses was intensified and job rotation was promoted. One of the nurses embarked on studies in brief psychotherapy and another one began job rotation by moving over to adult psychiatry. In the future, additional nurses will be trained to help patients who need access to psychosocial support with a low threshold.

The functionality of low-threshold nurse consultations will be evaluated. The goal is also to introduce a systematic way to evaluate the need for psychosocial support of cancer patients and to use this information as an integral part of patient management by the nurses who provide these consultations.

Visit by the Survivalship care plan WG to the rehabilitation centre in Lund

The project Survivalship care plan was launched in the Tyks hospital in OCT2022 by a visit to the oncological rehabilitation center of the Lund hospital. The goal of the project is to create an organized model for rehabilitation planning, where a cancer patient maintains and supports his/her functional capacity and working ability with the support of a professional instructor from the very start of the patient's treatment period. The main thing is to support the patient's own activity and participation and to modify the patient's surroundings so that it supports rehabilitation. The project group learned about the "Mina Planer" ideology (My Plans) and about multiprofessional collaboration which is directed toward the patient not only surviving but living ("Att leva – inte bara överleva"). The same ways of working might be implemented in the Tyks hospital. The visit was part of a more comprehensive project financed by the Ministry of Social Affairs and Health and run by the FICAN West (1JAN2023–30APR2023). It was initiated by FICAN Mid. The project leader is Annika Auranen, adjunct professor.

Highlights of digital development projects

Digital pathway to support cancer patient information needs

The patients of the TYKS Hospital cancer clinic have since 2019 been offered an electronic service channel, a digital treatment path built on the Health village platform. By using the electronic service channel the patient can contact the hospital personnel and vice versa. The service channel contains information on cancer, rehabilitation, support services and coping with cancer.

The nursing personnel may use the electronic service channel for individualizing patient education. The service channel may also be used by the patient for reporting symptoms. An example: the symptoms and wellbeing of patients on immuno-oncological treatments are followed up during treatments through weekly symptom surveys entered into the system by the patient. The goal is that the patients and the personnel of Tyks will found the digital service channel easy to use and helpful and uniform between different cancer types.

In 2022, the use of the digital treatment path for cancer patients increased further. FICAN West and the different clinics treating cancer patients collaborated in an effort to check and unify the instructional content of the urology, gastroenterology and gynecology paths. The digital treatment path for prostate cancer patients was worked on within a sperate project of the urology clinic and the contents of the path improved. This work was concluded in 2022. Construction of the treatment path for gynecological cancer patients was started within a project run by the gynecology clinic. Piloting of the treatment path is being planned.

In 2022, a pilot project was launched alongside the cancer patient treatment path: an electronic service with which the patient herself can book appointments with the breast cancer nurse. The pilot

was launched in the oncology clinic in late 2022. During the pilot the usability of the system will be surveyed by patient inquiries and feed back will be collected regarding its functionality.

In 2022, a multiprofessional team started to plan a pilot project to follow up the quality of life of cancer patients. This pilot is planned to start in 2023 and it will assess and follow up systematically the quality of life of cancer patients. The functionality of the digital treatment path as a follow-up tool will also be assessed.

National FICAN (Finnish Cancer Centre) unification of digital treatment pathways

There is variability all over Finland as to how well cancer patients can contact their treatment organization electronically. Unification of digital treatment paths was initiated on a national level in 2022 and this work has, as proposed by the FICAN Expert forum, been coordinated by FICAN West. The responsible coordinators from all national cancer centers are members of the FICAN Digital treatment path forum and they come from the following centers: FICAN East, FICAN Mid, FICAN North, FICAN South and FICAN West. The purpose of the coordinating meetings is to develop the recommendations presented in the FICAN Digital treatment path in collaboration within FICAN. This is done in line with a strategic policy that has been agreed on (e.g., quality register scores and surveys are used). The current state of affairs was examined in the kick off meeting of the forum and it was found that several digital programs in use. They operate on different platforms and their content varies. Proprietary and commercial programs are used, as well as programs of the Health Village. The responsible physicians / coordinators / developers of the digital treatment paths, who all are members of the forum, work as mentors to each other, and it was hoped that a national digital treatment path model for FICAN is created to form the basis for a unified treatment path.

At the second meeting, measures taken to unify the content and to create a common platform were analyzed. A subgroup was nominated to bring forth a proposal for the third meeting of the forum on how to further develop and improve the instruction on rehabilitation. The goal is to identify an impartial platform for distribution of self-care instructions. It would then be possible to use the same instructions throughout without the need for a therapy relationship between the cancer patient and a professional. The platform would also be the source of an information reserve of uniform training materials for continuous education purposes, e.g. the Health Village.

Improving the digital competencies of healthcare and social welfare professionals

Digitalization is changing the world, our working methods and the work content. In addition to technical competence, healthcare and social welfare professionals will have to master several other digitalization-related skills in the future. To maintain the skills and ensure competence, sufficient and appropriate training must be provided. Competence mapping, organizational support and career development models support the long-term development of competence.

A report of the nursing staffs' digital competence base for training planning was the outcome of a thesis project carried out in collaboration between FICAN West and Turku University of Applied Sciences. The aim of the project was to improve the digital capabilities of nursing staff treating cancer patients in the Turku University Hospital. The purpose was to describe the baseline of digital competence, the need for improved proficiency and to develop a training plan. Service design methods and action research principles were applied to collect user-orientated information. Three separate workshops brought together 14 professionals to discuss digitalization and to create new ideas to improve competence.

The report describes the basis for how to improve digital competence and training planning within the organization. Some practical tools for competence mapping and for modelling career development were developed. The report can be used as a tool to facilitate personnel recruitment, to support development discussion, for planning of training programs and as a reference for mentoring.

Research

Tyks Cancer Centre and FICAN West Research Cluster

Cancer research at FICAN West encompasses the University hospital at Turku (Tyks), the Central Hospital of Pori (Satasairaala), the Central Hospital of Vaasa and the cancer research at the University of Turku. The aim of FICAN West is to bring together and support basic and clinical cancer research.

Both academic laboratory research as well as investigator-initiated and industry-based clinical trials are run at FICAN West. The FICAN West cancer centre research laboratory is located at Medisiina D building since 2018, and it is dedicated for basic cancer research of approximately 10 research groups and 50 laboratory researchers. In total, FICAN West cancer research network includes about 30 research groups and 150 scientists working full-time in translational and basic research in the campus area. On the hospital side over hundred physicians are dedicated to the treatment of cancer patients and about half of them are actively involved in clinical trials. and about half of them are actively involved in clinical trials.

The estimated annual research budget in 2022 for TYKS Cancer Centre clinical research was ca. 2.7 mil. €, where the portion of Finnish state research funding was 0.5 mil €. For translational and basic research, the estimated annual research budget in 2022 was ca. 10.1 mil. €. For translational and basic research, 38% of the funding is provided by national public organizations and 62% by national private sources, EU, other international sources and by commercial co-operation organizations. In 2022 about 200 cancer associated articles were published in international peer review journals by the clinical divisions and translational and basic research in FICAN West.

Clinical trials are pursued at several hospital divisions. The clinical cancer trial unit (FICAN West CTU) runs studies for the Departments of oncology and radiotherapy, gynecologic oncology and lung cancer as well as urology. The division employs five full-time study nurses and two study coordinators. The stem cell transplantation unit employs 2 full-time study nurses and department of urology one study nurse. The clinical trial division has trial dedicated physician (medical oncologist) allocated for clinical trials. A number of physicians across the departments as well as central hospitals in Pori and Vaasa take part in the trials as principal or subinvestigators. Clinical trials that are recruiting are listed on the website (www.ficanwest.fi). The Tyks Cancer Centre is a member of the Nordic Network for Early Clinical Trials (NECT). We have research collaboration with the Department of Nursing Science at University of Turku which is highly ranked. FICAN West research activity and strategy are discussed in the common boards of the Tyks Cancer Centre and of FICAN West. The Scientific Cancer Board includes senior members from all cancer related Tyks divisions, and Pori and Vaasa Central Hospitals, as well as scientists pursuing cancer research at diverse departments of the University of Turku. The science and research strategy of the Tyks Cancer Centre and FICAN West is described below.

Western Finland Cancer Centre (FICAN West): science and research strategy 2019-2022

The strategy for 2019-2022 is a part of the strategic planning of the future of the entire FICAN West. It is aimed at securing effective and high-quality treatment, research and training in the field of oncology for the population in the catchment area.

Vision

FICAN West and its Scientific Cancer Board coordinate the cancer research in the FICAN West region and guarantee uninterrupted funding of high-quality cancer research. They secure rapid and effective adaptation of scientific research results into practice and innovations. FICAN West also unifies and develops collaboration in the field of education.

Values

FICAN West operates by the following values:

- Values of the science and research strategy of the Turku University Hospital (TYKS): ethical, critical, patient/client centered and clinically and socially efficient.
- Strategic values of the University of Turku: ethical, critical, creative, open-minded and societal.
- Strategic values of the FICAN West: patient oriented, equal admission to treatment and high-quality care, innovative and capable personnel, high-quality scientific research and comprehensive, innovative and international collaboration networks.

Strategic goals

The strategic goals of the FICAN West Cancer Centre overlap with those of the research activities of the working environment.

1) High-quality scientific research

- supports the strongholds of the working environment: 1) drug development and diagnostics, 2) bioimaging, 3) research into the molecular biology, genetics and immunology of cancer and 4) clinical drug and stem cell trials
- has established functional structures and sufficient material and human resources
- funding is secured and has an established financial strategy which covers the topics and areas needing financing – public financing, foundations, international funding and research collaboration agreements
- has access to vast patient registry data and biobank material
- guaranteed by up-to-date assessment and follow-up of clinical research

2) Improving research effectivity through networking

- functions as the central coordinating unit and integrates cancer research within the FICAN West research environment
- guarantees that research collaboration with the projects undertaken by the Health Campus of Turku functions smoothly and effectively across administrative borders and between universities, faculties and hospital districts
- guarantees that the infrastructure related to cancer research (e.g., Auria Biobank and the Turku Clinical Research Center) functions well
- guarantees smooth cooperation with the functions of the biotechnology business cluster within the region
- takes place with companies only through the FICAN research center (one-stop-shop principle)
- guarantees continuity of research through training, clinical scientists' positions and recruitment

3) Promoting application of new information

- Promotes, within its working environment, the transfer of information on cancer research outcomes from basic research to the clinic by communicating and by arranging joint meetings
- manages the introduction of new procedures and quality assessments in the domains of cancer prevention, diagnostics, treatment and rehabilitation, new drug treatments, new diagnostic methods, psychosocial support and patient instruction
- strengthens the knowhow of the personnel and promotes a research-oriented atmosphere
- guarantees patient involvement and adherence to research and development projects

4) Promoting innovation

- supports collaboration with the Health Campus of Turku and with its innovation ecosystem platforms

- is strengthened by collaboration with companies and relies on the thematic entity of drug development and diagnostics within the University of Turku

5) Making a national and international impact

- on the national level, this is done through collaboration within the entire FICAN (national and regional cancer centers)
- collaboration is pursued with cancer organizations and patient organizations
- acts as a member of the European cancer network OECI (Organization of European Cancer Institutes), the European reference network on rare adult cancers (ERN EURACAN) and the European reference network on pediatric oncology (ERN PAEDCAN)
- extensive activity (e.g., memberships and specialist assignments) within national and international research teams and teams working to improve and develop cancer treatment

6) Promoting assessment of research effectiveness

- the research strategy is assessed as a part of the overriding science and research strategy, center-of-excellence-strategy and accreditation by the OECI

7) Dissemination of research information

- consists of national and international activity and is part of the overriding strategy of the FICAN
- is presented in plain language for stakeholders and interest groups

Key indicators 2022

202
Total number of journal publications produced across divisions and basic research.

30
Number of cancer research groups in basic and translational research

9
Academic projects funded by EU

32
Number of publications with impact factor (IF) > 10

€ 12.9 million
Estimate of total research budget

2
Academic projects with other international funding

9
Number or publications with IF> 20

57
Academic projects with national private funding

16
Published PhDs

102
Number of clinical drug trials

41
Academic projects with national public funding

9
Disclosures of invention

299
Number of all clinical studies

Promoting FICAN West Research Network

The environment for pursuing advanced cancer research is excellent. With more than one hundred biotechnology companies, with the first biobank in Finland (Auria), with the nationally leading center of nursing science and with profiling research projects of the Academy of Finland, cancer research is targeted for success.

FICAN West collaboration with Turku Cancer Research Society

FICAN West has been partnering with Turku Cancer Research Society (TCRS) since 2018 to arrange scientific program for academic and clinical cancer researchers as monthly Cancer Research Seminars Series. Due to the COVID-19 pandemic, the first two seminars in 2022 were still arranged in virtual only. Since April 2022, it has been possible to participate the seminars either on-line or in the lecture hall.

During the year 2022, TCRS and FICAN West jointly arranged 6 monthly seminars. The seminars have traditionally had one local presentation on translational or clinical research and one on basic research. This year, four of the seminars had special program instead: an international guest speaker from Beatson Institute, Cancer Research UK, talks by the two Young Principal investigators that were awarded by TCRS in the previous year, sharing lessons from the visit to IFOM Institute in Milan about translation of basic science findings to clinical use and the discussion, and the joint FICAN seminar organized by FICAN West. The number of participants was good, ranging from 50 to more than 100 attendees. The Spring Seminar Event "New Cutting-Edge Methods in Cancer Research" was organized as a hybrid event on May 3rd 2022 gathering altogether 134 participants. In this event, presentations were given by local scientists from the methodological point of view. For instance, cyclic IF and imaging mass cytometry and other spatial single cell tissue analytics available were introduced.

The Christmas Seminar Event was arranged on December 13th 2022 with about 70 participants on-site only. Once again, the traditional Christmas Event was a success with both social activities and fascinating presentations, including historical perspectives and development of pathology, modern methods to cancer diagnostics, and targeting non-coding RNAs and other novel key molecular players to prevent and treat bone metastasis.

The PhD Thesis of the Year Award was given to MD Mikael Anttinen for his thesis "Novel imaging and image-guided therapy of prostate cancer". Anttinen demonstrated that a novel MRI-guided transurethral ultrasound ablation (TULSA) method is effective in prostate cancer focal therapy and that prostate-specific membrane antigen positron emission tomography-computed tomography (PSMA PET-CT) is a sensitive method for detecting metastatic disease and the extent of local disease before and after TULSA treatment. The work was supervised by Adjunct Professor Peter J. Boström, Professor Roberto Blanco Sequeiros and Associate Professor Pekka Taimen, Departments of Urology, Diagnostic Radiology and Pathology, respectively, Turku University Hospital.

The feedback about Cancer Research Seminar Series has been exclusively and continuously positive.

The winner of the PhD Thesis of the Year Award Dr. Mikael Anttinen got greetings from TCRS Chairman Maria Sundvall.

New mentoring program to support cancer research network

FICAN West has started a new mentoring program to develop the cancer centre activities and to promote local cancer research. The mentoring program is aimed at all FICAN West cancer researchers at different career stages and working in either clinical, translational or basic research. Participation provides a possibility to strengthen individual-level expertise, bring in new perspectives for one's research and expand one's social and professional network. The focus of the current mentoring program is to bring together as pairs professionals from the clinics and from academic research with a similar level of professional background.

Mentoring is a voluntary activity where working experts share their experiences and support each other in thinking about working life and professional development. Mentoring is often considered as an activity between a mentor and an actor, where the mentor provides his/her experience and skills to support the actor. In the FICAN West mentoring program, we use peer mentoring, which is based on an equal interaction relationship, where the mentor pair shares knowledge and experiences from work reciprocally. The goal of this transdisciplinary peer mentoring is to support learning and strengthen well-being at work, and also to support new research ideas and practices and to make different work cultures familiar.

The application call to participate in the current mentoring program was opened in December 2022. The program is carried out at FICAN West for the first time. The mentoring program that will be tested at FICAN West environment is planned to become a permanent operating model to develop the network's collaborative culture. The construction and development of the mentoring program is part of a project "Transdisciplinary mentoring as a mechanism in the development of networked research collaboration", which was launched in October 2022 and is implemented in cooperation with the Turku School of Economics, University of Turku, and the Hospital District of Southwest Finland. The project lasts two years and is financed by The Finnish Work Environment Fund.

FICANWest
LÄNTINEN SYÖPÄKESKUS | VÄSTRA CANCERCENTRET
WESTERN FINLAND CANCER CENTRE

UNIVERSITY OF TURKU
Turku School of Economics

Työsuojelurahasto
Arbetarskyddsfonden
The Finnish Work Environment Fund

Joint FICAN Seminar Series

One of the main goals in the science and research strategy of FICAN West is improving research effectivity through networking. This includes supporting collaborations across institutional and administrative borders as well as giving an input to the scientific training. In spring 2022, FICAN West and the other four regional FICAN units started together a joint FICAN seminar series. The seminar series provides an easy-access chance to hear well established scientists' presentations across Finland. The information about the seminars is communicated in all regional FICAN units coordinatedly. This seminar series is arranged completely on-line in Microsoft Teams -platform which is easily accessed also in the hospital environment. Each regional FICAN takes turns hosting the seminars and has an opportunity to give a presentation. Since May 2022, three of the five regional FICAN units have hosted a seminar, the presentations being given by FICAN Professors Matti Nykter, University of Tampere and FICAN Mid, and Juha Klefström, University of Helsinki and FICAN South, and by Finnish Cancer Institute Professor Johanna Ivaska, University of Turku, FICAN West. The presentations can be either from clinical or translational and basic science background but they always show a strong contact surface for patient care or diagnostics. The number of participants has so far ranged between 100-160 attendees. The seminar series will continue next year by the presentations from FICAN East and North, and the next round is in course of preparation.

Highlights in basic and translational research activities

Cancer Cell Growth Regulation

Most recurring cancer-associated mutations exhibit a high degree of tissue specificity. Yet, the cancer cell phenotype is similar across all cancers, characterized by unrestricted growth of cells that invade neighboring healthy tissue. One explanation for this phenomenon is that diverse types of upstream oncogenes that contribute to major forms of human cancer, converge to activate a set of common downstream growth regulatory processes. This redundancy in the upstream signaling represents a major challenge for cancer therapy because it enables the cells to bypass the drug target, restoring the malignant phenotype. Underlying hypothesis in our research is that the shared downstream effectors of growth regulatory pathways consist of a wide range of presently unknown therapeutic opportunities that less likely to be escaped by collateral pathway activation.

We study these essential outcomes of cancer cell signaling by utilizing a range of proteomics, single-cell omics, and genome editing techniques. Current projects focus on the regulation of rRNA synthesis, proteogenomic and spatially resolved analyses of head and neck cancers, targeted therapy resistance in melanoma, and acid-labile phosphorylation. Our projects also involve method development in Turku Proteomics facility where the group is located.

https://bioscience.fi/research/cancer-proteomics/profile/

https://bioscience.fi/services/services/

Principal Investigator:
Otto Kauko, MD, PhD, Head of Turku Proteomics Facility and group leader in Turku Bioscience Centre

Publications:

Pihlajamaa P, Kauko O, Sahu B, Kivioja T, Taipale J. A competitive precision CRISPR method to identify the fitness effects of transcription factor binding sites. Nat Biotechnol. 2022. https://doi.org/10.1038/s41587-022-01444-6

Kauko O, Imanishi SY, Kulesskiy E, Yetukuri L, Laajala TD, Sharma M, Pavic K, Aakula A, Rupp C, Jumppanen M, Haapaniemi P, Ruan L, Yadav B, Suni V, Varila T, Corthals GL, Reimand J, Wennerberg K, Aittokallio T, Westermarck J. Phosphoproteome and drug-response effects mediated by the three protein phosphatase 2A inhibitor proteins CIP2A, SET, and PME-1. J Biol Chem. 295:4194-4211. 2020.

Kauko O, O'Connor CM, Kulesskiy E, Sangodkar J, Aakula A, Izadmehr S, Yetukuri L, Yadav B, Padzik A, Laajala TD, Haapaniemi P, Momeny M, Varila T, Ohlmeyer M, Aittokallio T, Wennerberg K, Narla G, Westermarck J. PP2A inhibition is a druggable MEK inhibitor resistance mechanism in KRAS-mutant lung cancer cells. Sci Transl Med. 2018;10(450).

Biology and epidemiology of the cancer syndrome neurofibromatosis 1

Mutations of NF1 gene cause the multi organ syndrome neurofibromatosis 1 (NF1) with a birth incidence of about 1:2000. NF1 is also the most common cancer syndrome, and can also be classified as a Rasopathy. Our research penetrates to the question how a single mutation in the NF1 gene can cause the development of tumor masses, skeletal disfigurement, speech defects, and tumors of the optic pathway. We have established the Finnish neurofibromatosis cohort which is total population based and comprehensive. This has enabled the recognition of novel cancer associations in NF1 stratified by type, age, and sex. A finding that breast cancer is common in women with NF1 under the age of 40 has had impact on surveillance for breast cancer among women with NF1 in EU and USA. NF1-related breast cancer shows overrepresentation of unfavourable prognostic factors.

Principal investigator:
Professor Juha Peltonen,
Cancer research Unit / Institute of Biomedine, University of Turku & FICAN West

Funding:
Cancer Foundation Finland

Publications:

Uusitalo E, Rantanen M, Kallionpää RA, Pöyhönen M, Leppävirta J, Ylä-Outinen H, Riccardi VM, Pukkala E, Pitkäniemi J, Peltonen S, and Peltonen J: Distinctive cancer associations in patients with Neurofibromatosis 1. J Clin Oncol. 34:1978-1986, 2016

Uusitalo E, Kallionpää RA, Kurki S, Rantanen M, Pitkäniemi J, Kronqvist P, Härkönen P, Huovinen R, Carpen O, Pöyhönen M, Peltonen S and Peltonen J: Breast Cancer in Neurofibromatosis Type 1 (NF1): Overrepresentation of Unfavorable Prognostic Factors Br J Cancer 116:211-217, 2017

Evans DGR, Kallionpää RA, Clementi M, Trevisson E, Mautner V, Howell SJ, Lewis L, Zehou O, Peltonen S, Brunello A, Harkness EF, Wolkenstein P, Peltonen J: Risk of contralateral breast cancer and survival in neurofibromatosis 1: A five country cohort study. Genet Med. 22:398-406, 2020

High-dimensional immune profiling of cancer tissues equals immunotherapy development

Cancer is a leading cause of death worldwide. The 2018 Nobel prize breakthrough in medicine showed that antibody-mediated blockade of the immune homeostasis regulators induces a potent antitumor immune response in metastatic melanoma and many other solid cancers, giving birth to immune checkpoint therapies (ICT). Despite achieving fantastic 52% overall responses in metastatic melanoma, a large fraction of patients is still refractory to ICT.

MIORG is an immuno-oncology research group with the ultimate goal of improving patients' cancer immunity to achieve better responses to ICT.

The group's research strategy is based on a "reverse translational" approach. This means that the research starts in the patient's biopsy, where the group uncover new biomarkers associated with ICT resistance for a comprehensive understanding of the cellular and molecular mechanisms associated with poor outcomes to anti-PD1/PD-L1 and antiCTLA4 therapies.

These biomarkers can become new prognostication tools and targets for new adjuvant immunotherapies, also developed within the groups premises.

Novel biomarkers are evaluated functionally using well-established in vivo and ex vivo immune assays. Selected targets are then used for rational development of combinatory approaches to unleash responses to ICT.

The group recently described a mechanism by which cancer cells induce faults in antigen processing and priming of effector T lymphocytes. Using state-of-the-art tools, such as mass cytometry and NanoString GeoMX spatial analysis for full transcriptomic analysis and interrogation of more than 50 immune proteins in patients biopsies, the group aims to expand the understand of this mechanism of resistance by building rational unprecedented models for ICT prognostication.

Blocking these faults using specific inhibitory monoclonal antibodies, the group aims to restore the generation and tumor infiltration of

CD8+ T cells to improve ICT clinical benefit.

The group's research is mostly funded by external funding (Academy of Finland Research Grant and InFlames) and local funding (Sigrid Juselius, JAES Foundation and Lounais-Suomen Syöpäyhdistys).

Our international team consists of two scientists, three PhD student and one Master student.

The group also brings international collaboration to Finland, including clinical partners from the University of Liverpool (UK) and Columbia University (US).

https://miorg.fi/

Principal investigator:
Adj. Professor Carlos Rogerio Figueiredo, Ph.D.

Publications:
Matareed M, Maranou E, et al (2023). Novel prognostication biomarker adipophilin reveals a metabolic shift in uveal melanoma and new therapeutic opportunities. ***Journal of Pathology***. 2023 Feb 24. DOI: 10.1002/path.6076

Wang MM, et al (2021). Applying Single-Cell Technology in Uveal Melanomas: Current Trends and Perspectives for Improving Uveal Melanoma Metastasis Surveillance and Tumor Profiling. ***Frontiers in Molecular Biosciences*** ;7:611584.

Figueiredo CR, et al. (2020). Loss of BAP1 expression is associated with an immunosuppressive microenvironment in uveal melanoma, with implications for immunotherapy development. ***Journal of Pathology***. Apr;250(4):420-439.

Selected abstracts of doctoral theses

Risk factors and biomarkers for metastatic cutaneous squamous cell carcinoma

Jaakko Knuutila,
disputation 2022-11-25

The incidence of cutaneous squamous cell carcinoma (cSCC) continues to increase. Although proportion of cSCCs metastasize and cause mortality, sufficient means to identify the metastasis-prone tumors are not available.

Metastatic cSCCs from the area served by Turku University Hospital were identified and characterized. The rate of metastasis in the study region was 2.3%. Metastasis occurred rapidly. Invasion depth, tumor diameter, age, location on lower lip or forehead and usage of isosorbide mono-/dinitrate and aspirin were associated with the risk of metastasis.

With multiplexed immunohistochemistry, it was demonstrated that elevation of fibroblast activating protein (FAP) and platelet-derived growth factor receptor-β (PDGFRβ) is associated with metastasis. High expression of stromal PDGFRβ and periostin were associated with worse prognosis. CAF107 (PDGFRα-/PDGFRβ+/FAP+) subset was associated with invasion and metastasis, and predicted poor prognosis of cSCC.

A deep learning algorithm was harnessed to distinguish primary tumors that metastasize rapidly from non-metastatic cSCCs with slide level area under the receiver operating characteristic curve (AUROC) of 0.747 on whole slide images representing primary cSCCs. A risk factor model, that utilized prediction by AI, was created and provided staging systems and comparative risk factor models surpassing classification and prognostivity.

Results indicate that CAF-markers and AI could provide clinical tools for the metastasis risk assessment.

Original Publications:

1. Knuutila JS, Riihilä P, Kurki S, Nissinen L, Kähäri VM. Risk factors and prognosis for metastatic cutaneous squamous cell carcinoma: a cohort study. Acta Derm Venereol. 2020; 100(16): adv00266.

2. Knuutila JS, Riihilä P, Nissinen L, Kallionpää R, Pellinen T, Kähäri VM. Cancer-associated fibroblast activation predicts progression, metastasis and prognosis of cutaneous squamous cell carcinoma. (Submitted manuscript)

3. Knuutila JS, Riihilä P, Karlsson A, Tukiainen M, Talve L, Nissinen L, Kähäri VM. Identification of metastatic primary cutaneous squamous cell carcinoma utilizing artificial intelligence analysis of whole slide images. Sci Rep. 2022; 12(1): 9876.

Supervisors: Professor Veli-Matti Kähäri, Department of Dermatology and Venereology, University of Turku;
Docent Pilvi Riihilä, Department of Dermatology and Venereology, University of Turku;
Docent Liisa Nissinen, Department of Dermatology and Venereology, University of Turku

Opponent: Professor Ilkka Harvima, Department of Dermatology, University of Eastern Finland, Kuopio, Finland

Novel Prognostic Factors for Advanced Melanoma and Localized Renal Cell Carcinoma

Kalle Mattila,
disputation 2022-1-28

Prognostic factors are required to tailor optimal cancer treatment and follow-up based on tumor and patient characteristics. In this thesis, prognostic factors were studied in melanoma and renal cell carcinoma (RCC) patients.

Before modern treatment options, 146 metastatic melanoma patients had received BOLD-IFN chemotherapy at Turku University Hospital in 1991-2010. The median overall survival (OS) was only 8.9 (7.5–10.4) months and the 5-year survival rate 13%. Long-term survivors were found among patients without visceral metastases (5-year survival rate 28%).

The Finnish Melanoma Group conducted a nationwide trial, where 38 metastatic melanoma patients were treated with temozolomide, lomustine, vincristine, and interferon-alpha ± vemurafenib. Elevated LDH was associated with short OS unlike asymptomatic brain metastases. Higher plasma circulating tumor DNA levels were inversely associated with OS. Patients with persistent detectable ctDNA during treatment had poorest prognosis.

Over 30% of patients will develop disease recurrence after surgery for localized RCC. Tumor size, tumor grade, and microvascular invasion were sufficient for the accurate prediction of metastasis-free survival in 196 localized RCC patients. The ”three-feature prediction model” was validated in an external cohort of 714 patients. It retained similar accuracy as the well-established Leibovich model (C-index 0.836 vs. 0.848, p=0.106) and had even better prognostic value for long-term prediction.

Original Publications:

1. Mattila K, Raanta P, Lahtela V, Pyrhonen S, Koskivuo I, Vihinen P. Long-term survival of stage IV melanoma patients treated with BOLD combination chemotherapy and intermediate-dose subcutaneous interferon-alpha. Anticancer Res. 2018;38:6393-6397.

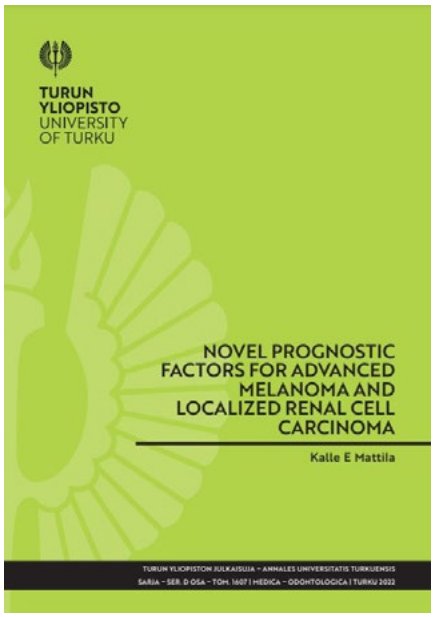
2. Mattila KE, Vihinen P, Ramadan S, et al. Combination chemotherapy with temozolomide, lomustine, vincristine and interferon-alpha (TOL-IFN) plus vemurafenib or TOL-IFN as first-line treatment for patients with advanced melanoma. Acta Oncol. 2020;59:310-314.

3. Mattila KE, Mäkelä S, Kytölä S, Andersson E, Vihinen P, Ramadan S, Skyttä T, Tiainen L, Vuoristo MS, Tyynelä-Korhonen K, Koivunen J, Kohtamäki L, Aittomäki K, Hernberg M. Circulating tumor DNA is a prognostic biomarker in metastatic melanoma patients treated with chemoimmunotherapy and BRAF inhibitor. Acta Oncol. 2022;61:1263-1267.

4. Mattila KE, Laajala TD, Tornberg SV, et al. A three-feature prediction model for metastasis-free survival after surgery of localized clear cell renal cell carcinoma. Sci Rep. 2021;11:8650-9.

Supervisors: Professor Panu Jaakkola, Department of Oncology and Radiotherapy, University of Turku and Turku University Hospital, Finland;
Docent Pia Vihinen, FICAN West Cancer Centre, University of Turku and Turku University Hospital, Finland;
Professor Heikki Minn, Department of Oncology and Radiotherapy, University of Turku and Turku University Hospital, Finland

Opponent: Docent Lars Ny, Department of Oncology, Institute of Clinical Sciences Sahlgrenska Academy at the University of Gothenburg and Sahlgrenska University Hospital, Sweden



Mathematical modelling and survival prediction in cancer

Anni Halkola,
disputation 2022-12-02

Cancer is one of the main causes of death opening a vast need for research. Survival and treatment benefits can be predicted with mathematical modelling and regression analysis. In this dissertation, various modelling approaches were used to predict cancer behavior, treatment outcomes and patient survival.

An ordinary differential equation model was developed to investigate changes in cancer cell density. Immunotherapy was included, since the immune response is a crucial part of cancer development. An adaptive treatment resulted in lower cancer burden and less time in treatment. In addition, combination treatments generally resulted in smaller cancer burden than monotherapies.

A metapopulation model was developed with the focus on angiogenesis and cancer cell emigration. In general, angiogenesis contribution was desired quality for cancer cells in absence of anti-angiogenic treatment. With the treatment, angiogenesis diminished, however the risk of treatment resistance increased.

Two regression methods were developed for survival prediction. A greedy budget-constrained Cox regression (Greedy Cox) utilizes L2-penalty and considers the cost of parameters. Optimal Subset CArdinality Regression (OSCAR) method utilizes L0-pseudonorm penalty to provide sparse models. The methods were validated on prostate cancer data and a comparable level of prediction accuracy was already reached with a few parameters.

The dissertation provides a comprehensive research of novel tools for predicting cancer behavior and patient survival. Important hallmarks of cancer development, such as immune response and angiogenic switch have been included with corresponding treatments that have potential to change the traditional treatment regimens.

Original Publications:

1. Anni S. Halkola, Kalle Parvinen, Henna Kasanen, Satu Mustjoki, Tero Aittokallio. Modelling of killer T-cell and cancer cell subpopulation dynamics under immuno- and chemotherapies. Journal of Theoretical Biology, 2020; 488: 110136.

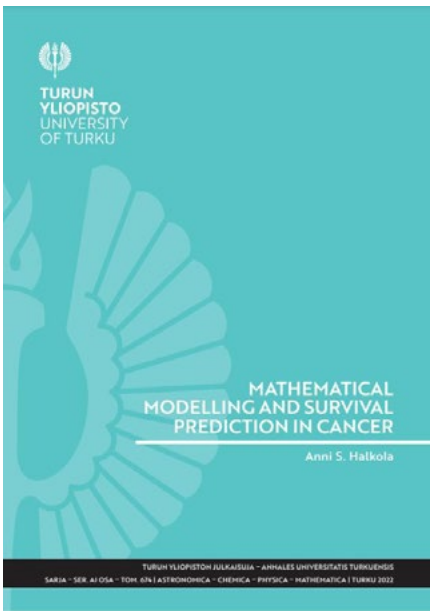
2. Anni S. Halkola, Tero Aittokallio, Kalle Parvinen. Tumor microenvironment as a metapopulation model: The effects of angiogenesis, emigration and treatment modalities. Journal of Theoretical Biology, 2022; 545: 111147.

3. Mika Murtojärvi, Anni S. Halkola, Antti Airola, Teemu D. Laajala, Tuomas Mirtti, Tero Aittokallio, Tapio Pahikkala. Cost-effective survival prediction for patients with advanced prostate cancer using clinical trial and real-world hospital registry datasets. International Journal of Medical Informatics, 2020; 133: 104014.

4. Anni S. Halkola, Kaisa Joki, Tuomas Mirtti, Marko M. Mäkelä, Tero Aittokallio, Teemu D. Laajala. OSCAR: Optimal subset cardinality regression using the L0-pseudonorm with applications to prognostic modelling of prostate cancer. Submitted for publication.

Supervisors: Associate Professor Kalle Parvinen, Department of Mathematics and Statistics, University of Turku, Turku, Finland and Advancing Systems Analysis Program, International Institute for Applied Systems Analysis (IIASA), Laxenburg, Austria;
Professor Tero Aittokallio, Institute for Molecular Medicine Finland (FIMM), University of Helsinki,Helsinki, Finland and Institute for Cancer Research, Oslo University Hospital, Oslo, Norway and Oslo Centre for Biostatistics and Epidemiology (OCBE), University of Oslo, Oslo, Norway

Opponent: Professor Joel S. Brown, Moffitt cancer center, Tampa, FL, USA and University of Illinois, Chicago, USA



Machine Learning and Computational Methods to Identify Molecular and Clinical Markers for Complex Diseases – Case Studies in Cancer and Obesity

Fatemeh Seyednasrollah, disputation 2021-02-04

In her doctoral dissertation, Fatemeh Seyednasrollah developed mathematical tools to improve treatment decision making for complex diseases, with case studies in cancer and obesity. The proposed predictive methods are utilized to predict disease onset and prognosis, as well as to identify beneficial therapy at individual patient level. Often, clinical decision making relies on assessment of the disease sub-type and prognosis, which can be a difficult task without robust predictive methods. These predictive methods determine "which and how" a set of pre-defined bio-clinical markers can be utilized to assist in choosing the most appropriate therapeutic strategies.

In the case of renal cell carcinoma, tumors are known to be heterogenous with distinct histological sub-types. This dissertation proposes a data-driven risk stratification method to identify prognostic biological markers for clear cell renal cell carcinoma using patients' gene expression profiles. In addition to making a prognosis assessment, some of the proposed novel biomarkers have the potential to serve as drug target candidates. Together, these findings represent for a first time an approach to determine the prevalence of gamma-secretase cleavage among RTKs. Moreover, this study presents novel methods for identifying still largely unknown RTK cleavage associated signaling. The results of this thesis can provide new insights into the regulation of RTK functions and can be used to develop new strategies for treating cancers.

This dissertation also addresses the challenging question of predicting the efficacy of chemotherapy in metastatic prostate cancer. In clinical practice, not every patient with advanced prostate cancer would benefit from chemotherapy and instead, 10-20 percent of patients may experience undesirable adverse events and deterioration of survival time and life quality. As a solution, we proposed an ensemble-based predictive model to assist clinicians to choose correct candidates for further chemotherapy treatments utilizing baseline clinical characteristics.

Original Publications:

1. Seyednasrollah, F., Laiho, A. & Elo, L. L. Comparison of software packages for detecting differential expression in RNA-seq studies. Brief. Bioinform. 16, 59–70 (2015).

2. Seyednasrollah, F., Rantanen, K., Jaakkola, P. & Elo, L. L. ROTS: reproducible RNA-seq biomarker detector—prognostic markers for clear cell renal cell cancer. Nucleic Acids Res. gkv806 (2015).

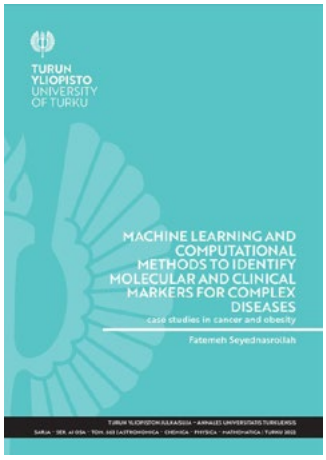
3. Seyednasrollah, F., Koestler, C. D., Wang T., Piccolo, S. R., Vega, R., Greiner, R., Fuchs, C., Gofer, E., Kumar, L., Wolfinger, R. D., Kanigel, Winner K., Bare, C., Neto E. C., Yu, T., Shen, L., Abdallah, K., Norman, T., Stolovitzky, G., Soule, H. R., Sweeney, C. J., Ryan, C. J., Scher, H. I., Sartor, O., Elo, L. L., Zhou, F. L., Guinney, J., Costello, J. C., and Prostate Cancer DREAM Challenge Community A DREAM Challenge to Build Prediction Models for Short-Term Discontinuation of Docetaxel in Metastatic Castration-Resistant Prostate Cancer. JCO Clin. Cancer Inform. 1–15 (2017).

4. Seyednasrollah, F., Mahmoudian, M., Rautakorpi, L., Hirvonen, O., Laitinen, T., Jyrkkio, S., Elo, L. L. How Reliable are Trial-based Prognostic Models in Real-world Patients with Metastatic Castration-resistant Prostate Cancer? Eur. Urol. 71, 838–840 (2017).

5. Seyednasrollah, F., Makela, J., Pitkanen, N., Juonala, M., Hutri-Kahonen, N., Lehtimaki, T., Viikari, J., Kelly, T., Li, C., Bazzano, L., Elo, L. L., Raitakari, O. T. Prediction of Adulthood Obesity Using Genetic and Childhood Clinical Risk Factors in the Cardiovascular Risk in Young Finns Study. Circ. Cardiovasc. Genet. 10, e001554 (2017).

Supervisors: Professor Laura L. Elo, Turku Bioscience Centre, University of Turku and Åbo Akademi, Turku, Finland;
Professor Marko M. Mäkelä, Department of Mathematics and Statistics, University of Turku, Turku, Finland

Opponent: Professor Ewa Szczurek, Institute of Informatics, University of Warsaw, Warsaw, Poland



Highlights in clinical research activities

Clinical cancer trial unit

Strong patient recruitment and intake of new cancer trials continued at the clinical cancer trial unit (FICAN West CTU) during 2022. Over 20 new trials were started and recruitment of new patients proceeded as expected. In 2022 the clinical trial unit had 63 recruiting trials of which 53 were drug trials. Of the 102 trials, 72 were sponsored commercial trials and the rest academic researcher-initiated trials. About 30 were actively recruiting trials and the rest were in follow-up phase. Two phase 1 trials continued recruitment during 2022.

The clinical trial unit employed eight full time personnel; two study coordinators, four study nurses and in total one trial dedicated investigator on top of approximately 10 part-time PIs and subinvestigators. The unit is headed by professor Panu Jaakkola. All personnel were funded by the income from sponsored clinical trials. The estimated turnover, excluding drugs, was over one million euros. There have been marked savings in cancer drug costs for the hospital. It is worth mentioning that just the immuno-oncological drugs given in clinical trials during 2017-2020 have been estimated to be worth of 1,5 million euros.

Director of FICAN West CTU:
Prof. Panu Jaakkola, MD, PhD

Turku Urology Research Unit

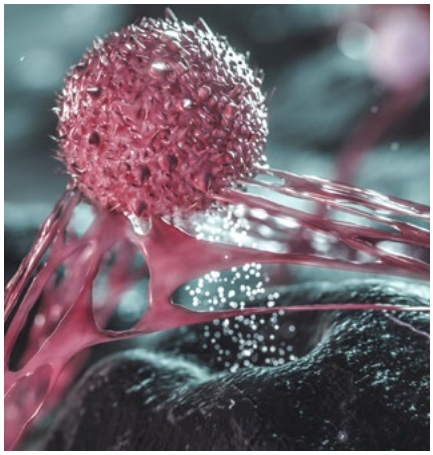
The Urology research team has long-standing track-record of clinical, translational and basic research especially within uro-oncology focusing especially on prostate and bladder cancer. The team has significant research activity on both pharma-sponsored and academic trials. Dr. Boström is the PI in several national prospective randomized trials.

Within the field of prostate cancer, the clinical research has lately focused on medical imaging, e.g. the use of MRI in the detection of prostate cancer and the use of PSMA-PET in primary staging of high-risk prostate cancer as well as TULSA (transurethral ultrasound ablation of prostate) as a novel ablation for localized prostate cancer. In bladder cancer research focus has been mainly on BCG therapy of non-muscle invasive cancer and markers and quality parameters of muscle-invasive cancer treated with radical surgery.

Next to the clinical studies, the urology research team is running multiple translational and basic science projects. The basis for these studies is the high-volume University clinical unit, which is responsible for the entire prostate cancer diagnosis and treatment in the south-west Finland and it serves as a tertiary care referral center for the west-coast of Finland. The prostate cancer surgeries have been carried out with robotic surgery since 2010.

The Urology clinical research team consists of academic urologists, clinical and translational research coordinators and research nurses. The team is supported by a data manager/biostatistician.manager/biostatistician.

Principal investigator:
Peter Boström, MD, PhD



Clinical Hematology Research Unit

Clinical hematology research group is committed to performing innovative research in hematological diseases, including hematological cancers like acute and chronic leukemias and multiple myeloma. Our research group also conducts clinical trials in patients receiving allogeneic stem cell transplantations. We participate actively both in international and national patient-oriented research, including interventional clinical trials. The immediate aim is to constantly develop treatments and apply new findings to the treatment of our patients. Participation in clinical trials also ensures that our patients are able to receive the most advanced forms of hematological treatment.

Our research group comprises of physicians, all of whom carry out research projects and trials along with the routine clinical work. Furthermore, many of our physicians acted as sub-investigators. In addition, our research group consist of two full-time study nurses and a part-time research coordinator.

In 2022, we had 12 clinical trials ongoing. Clinical trials with sponsored study drugs bring remarkable cost-savings to the hospital. External funding, mainly by the income of sponsored clinical trials has also enabled us to employ one of the study nurses and a research coordinator.

The hematology research group is located in the T-hospital. Our stem cell transplantation unit, a part of the Western Cancer Centre (FICAN West), has been nominated as a Centre of Excellence in the Hospital District of Southwest Finland since 2019. This is a proof of our high-level research as one of the leading criteria for granting the Centre of Excellence status is active and qualified research work.

Principal investigator:
Professor Maija Itälä-Remes, MD, Chief Physician and Head of Hematology section

CAR-T CELL THERAPY RESEARCH

CAR-T therapy has revolutionized cancer research and treatment. CAR-T therapy is a whole new form of adoptive cancer therapy, which provides patients with a new and effective treatment option for hematological cancers. Using this new treatment option, we are able to treat certain blood cancers in patients who have not responded to other treatments. CAR-T treatment has proven to be a very effective form of treatment, especially in B-cell-derived non-Hodgin's lymphomas, B-cell acute lymphocytic leukemia and myeloma. However, CAR-T therapy is currently being studied in almost all hematological cancers and also in many solid tumors.

CAR-T cells are the patient's own T-lymphocyte cells, which are collected from the blood with an apheresis machine and then genetically modified in a laboratory so that they better recognize and kill cancer cells. The modified T-cells (CAR-T) will be reinfused into the patient.

In 2022 we started our first CAR-T clinical trial: CARTITUDE-5. A standard treatment for newly diagnosed multiple myeloma includes the drugs bortezomib, lenalidomide, and dexamethasone (abbreviated VRd) followed by lenalidomide and dexamethasone (Rd). This trial is comparing the safety and efficacy of VRd followed by an investigational CAR-T cell therapy versus VRd and Rd in participants with newly diagnosed multiple myeloma.

The investigational medication is an investigational autologous chimeric antigen receptor T cell (CAR-T) therapy called JNJ-68284528 (also known as ciltacabtagene autoleucel or "cilta-cel"). It's a CAR-T therapy made from patient's own T cells, to recognize and kill patient's cancerous multiple myeloma cells. Participants in this study will be randomly assigned to receive VRd followed by either Rd or a single dose of cilta-cel.

By the end of 2022, we have recruited three patients into this trial and patient recruitment will continue in 2023. We are very pleased to be able to offer this novel treatment option to our patients.

Dr. Juha Ranti, Principal investigator of CARTITUDE-5 trial

Health and quality of life in patients with early age onset cancer

There are several ongoing projects in the department of paediatric and adolescent haematology/oncology which aim at recognising and alleviating the adverse effects of cancer and its treatment. Another research focus is genetic background of malignancies and sequelae of their treatment.

Milli-C (Microbiota and later life of childhood cancer patients) is still recruiting, and evaluates the association between immune reconstitution and metabolic adverse effects (e.g., obesity) and changes in the gut microbiota. Project is led by Anu Huurre and Liisa Järvelä.

A local project, called Digital tools in detecting late effects in adult childhood cancer survivors (LERACA), has started at our late-effects clinic, and first two publications based on the use of datalakes have been finalized. One of these publications is describing the possibilities of using text-mining in prediction of need for psychosocial support at the end of cancer treatment.

A Nordic project on the late effects of high-risk acute lymphoblastic leukaemia survivors, the HALLON-study, has started recruitment in 2022 together with another late-effect study (ALLStar) that examines low and intermediate risk ALL-patients. Project leaders for high-risk study are professor Arja Harila-Saari from Uppsala University and Päivi Lähteenmäki from University of Turku.

Palliative care is also one main topic of our research group, and here the principal investigator is MD, PhD Marika Grönroos.

A new project PeCCAPs concentrates at first on the ethics of germline testing in childhood cancer patients. Principal investigator for this project is MD, PhD Laura Korhonen.

iCAN-PEDI (Functional Precision Medicine For Pediatric Solid Tumors) is a project led by docent Minna Koskenvuo in Turku and Vilja Pietiäinen in Helsinki. The project aims to improve the selection of right treatment for a right patient by studying how a patient's tumor

cells respond to the drugs, and what are the molecular alterations resulting in cancer. New analytical methods are developed to improve diagnosis and treatment of patients with pediatric solid cancers. For next term, the aim is to further utilize ther findings by directing the patients to clinical trials based on the molecular and functional profiling, and by establishing novel clinical trials. Further aim is to expand the study as a longitudinal follow-up study for childhood cancer survivors, to enable their healthier adulthood.

Studies on immunosuppression, vaccinations and infections after non-SCT treatment of childhood cancer patients are led by MD, PhD Linnea Schuez-Havupalo.

PACS (Pregnancy associated cancer and survival) is a Nordic study on the short-term and long-term consequences of pregnancy-associated cancer in women and their offspring. The study runs in collaboration with scientists from Denmark, Sweden and Norway. PhD student in this project is MD Riikka Kuvaja.

Dr Lähteenmäki is the principal investigator of a Nordic study on the epidemiology, biology, treatment and survival of children with cancer and severe haematological diseases (NOPHO-CARE). This study is funded by the Swedish Childhood Cancer Foundation.

Project on "Immune reconstitution in children after allogeneic stem cell transplantation (SCT)" has started by docent Minna Koskenvuo in 2012 in Helsinki University Hospital: the first aim is to bring forth new knowledge of immune system regeneration following HSCT, with special focus on the susceptibility to viral reactivations along with the T cell reconstitution. The second aim is to gather data on the effects of reduced intensive conditioning on immune reconditioning and to compare it to the immune reconstitution after myeloablative conditioning. The third aim of the study is to perform detailed functionality tests on T-cells following HSCT. The fourth aim is to discover new connections between genetic predisposition and risk of HSCT complications, such as infection, viral reactivation, and graft versus host disease (GvHD).

Another SCT-related project by docent Koskenvuo is called: Monitoring the hemostasis following allogeneic HSCT. It focuses on changes in hemostasis and thrombin generation followed by HSCT. The detailed studies concerning the thrombin generation has been done in collaboration with professor Riitta Lassila, Helsinki University.

https://www.tyks.fi/tietoa-tyksista/tyksin-organisaatio/potilashoidon-toimi-ja-palvelualueet/lasten-ja-nuorten-10

Senior scientist:

Päivi Lähteenmäki, docent, MD, PhD,
Minna Koskvenvuo, docent, MD, PhD

Project leaders:

Anu Huurre, MD, PhD;
Liisa Järvelä, MD, PhD;
Marika Grönroos, MD, PhD,
Laura Korhonen, MD, PhD,
Linnea Schuez-Havupalo, MD, PhD

PhD-students:

Riikka Kuvaja, MD,
Tuomas Lähteenmäki Taalas, MD

Gynecologic cancer research

High-grade serous ovarian cancer (HGSOC) kills more than 44,000 women in Europe every year due to lack of effective and long-lasting therapeutic regimens. Although most patients respond initially well to surgery and chemotherapy, more than half experience relapse and develop resistance to chemotherapy. This leads to 5-year survival of only 43%. TUCH Gynecologic oncology unit has strong research background and high-quality prospective ongoing sample collection for translational research purposes. We also provide essential clinical expertise to the projects. To date, over 560 patients have been recruited. We collect tissue and ascites samples at surgery for tumor genome analyses, 3D organoid cultures and longitudinal blood samples before and during chemotherapy for ctDNA and biomarker analyses.

https://sites.utu.fi/ovariancancer/fi/

PERSONALIZED TREATMENTS FOR CHEMORESISTANT HGSOC

TYKS is a partner in Horizon 2020 granted consortium DECIDER (2021-2026) coordinated by the University of Helsinki (prof Sampsa Hautaniemi) and has partners in Denmark, Germany, Italy, Spain, and Sweden. Importantly, all patients participating DECIDER are recruited and treated in the TYKS/FICAN West area. The main goals are to develop diagnostic tools and treatments for HGSOC with the help of AI methods. The aim is to identify earlier those patients who do not respond well to the first-line treatments, and to find effective treatments to patients with a drug-resistant cancer. Treatment response is predicted using e.g. histopathological and genomic data from the patient. Genomic changes and aberrations in gene functions are used to find effective, personalized treatments. Using this information, doctors can more easily identify effective drugs for their patient. The tissue samples are analyzed by WGS, RNA seq, drug screenings are made with patient derived organoids and tumoroids.

Funding: EU

Principal investigator in TYKS:
Johanna Hynninen Adj prof, MD, PhD

FUNCTIONAL DNA REPAIR IN OVARIAN CANCER

Chemotherapy induces damage to the DNA of tumor cells. In most HGSOC patients, tumors eventually overcome chemotherapy-induced DNA damage, typically leading to resistance and fatal refractory disease. The overall goal is to develop optimal anti-cancer drugs/drug combinations and doses. We scrutinize the multi-faceted cellular response induced by DNA-damaging platinum agents (the current first-line therapy in ovarian cancer), by PARP inhibitors (emerging, clinically highly promising therapy) and by their combination. Ex vivo experiments will be conducted directly on clinical tumor tissue. These include performing state-of-the-art (and beyond, developed by the consortium) molecular measurements of drug transport and metabolism, DNA repair proficiency, bioenergetic pathways, mitochondrial function and PARP activity. By consolidating these read-outs with carefully recorded clinical information and with the mutational status affecting pharmacokinetics and tumor genes from the same patients into a systems-level model, we will deliver a predictor of which anti-cancer drugs are expected to provide maximal efficacy and minimal toxicity.

Funding: Academy of Finland, Cancer Foundation Finland

Principal investigator in TYKS:
Sakari Hietanen Adj prof, MD, PhD

HYPOXIA IN OVARIAN CANCER

Hypoxia is one of the most important drivers of chemoresistance. Tumor hypoxia can be evaluated preoperatively with PET and with the use a novel hypoxia-specific tracer, 18FEF5. The feasibility of 18F-EF5 PET/ CT-imaging in EOC patients with widespread carcinosis has not been established. The objectives of the OVANOX project is to identify and localize hypoxic sites in ovarian tumors with 18F-EF5 PET/ CT in a diagnostic and neoadjuvant setting and to characterize comprehensively the molecular pathways, aberrations and bioenergetic profile in targeted samples of hypoxic EOC tumors. Hypoxic tumor areas have so far been identified in EF5 PET/CT in 46 % of these patients.

Funding: VTR-funding, EU project Hercules

Principal investigator in TYKS:
Sakari Hietanen Adj prof, MD, PhD

CTDNA IN OVARIAN CANCER

In solid cancers, such as HGSOC, ctDNA (circulating tumor DNA) profiling is currently the only technique that permits longitudinal assessment of genomic alterations through-out treatment and follow-up. Our prospective patient cohort with longitudinal plasma sample collection is ideal to study early detection of chemoresistant patients and the usefulness of ctDNA in clinical decision making in disease relapse. We use ctDNA to study tumor evolution during treatment and search for druggable targets.

Funding: Sakari Alhopuro foundation, VTR-funding

Principal investigator in TYKS:
Johanna Hynninen Adj prof, MD, PhD

MOLECULAR CLASSIFICATION AND ACTIONABLE TARGET SEARCH IN ENDOMETRIAL CANCER

Endometrial cancer is the most common gynecologic cancer. Surgery is curative for most patients in early stage and favourable histology. Adjuvant radiation, chemotherapy or their combination is used to reduce recurrence in patients with histopathological features that have been associated with poor prognosis. Although universally applied, current risk assessment for potential adjuvant therapy has proven suboptimal.

The current prognosis for recurrent endometrial cancer is poor and adjuvant therapy is currently based mostly on conventional chemotherapy, radiation or hormone therapy. For this group of patients, actionable genetic alterations might reveal specific targets for more effective treatment.

Since the days of the TCGA results in 2013 next generation sequencing has greatly advanced allowing nowadays the use of formalin fixed material. FoundationOne by Foundation Medicine has been successfully used in our hospital for search for actionable mutations in different cancers of patients that cannot be offered an effective standard treatment. This analysis offers also the possibility to study endometrial cancer in archival material and classify the results according to the original TCGA classification. In addition, the results of this test provide mutation analysis on >300 genes related to cancer. Some of the found mutations may prove to be of critical importance for the tumor growth (driver mutation) and may be targeted in case of recurrence.

We have been studying a cohort of endometrial cancers gathered in Turku University Hospital during 2008-2021. Our main focus is to 1) search for molecular alterations which predict the recurrence in low-grade low-stage endometrioid cancers, 2) perform molecular classification of cancers, and to 3) search for potentially actionable mutations.

Funding: VTR-funding

Principal investigator in TYKS:
Sakari Hietanen Adj prof, MD, PhD

Clinical Research Activities at Vaasa Cancer Clinic

The Vaasa Cancer Clinic at Vaasa Central Hospital in the region FICAN West is the largest active cancer unit among central hospitals in the whole Finland. We have about 3,500 patients annually receiving active treatment at our department, of which 1 150 patients receive radiotherapy. Our clinical research unit was established in 2012 and has been actively involved in clinical research ever since. We have currently a capacity to accomplish 6-8 active clinical trials at the same time. Our research functions mainly through GCP-trained physicians and clinical trial nurses. We have our own hospital cell biologist, who has been critical in updating our gene analysis processes. Our research unit is an EMA listed study site.

In addition to clinical drug development trials, we have initiated a clinic wide project to improve existing cancer treatments. Our target is to develop better care including implementing new diagnostics and treatments for clinical practice, but also smoothen existing treatment processes. We are part of various studies using gene-targeted/driven therapies. We have experience in improving surveillance protocols and methods for patients undergoing active cancer treatment and of those who have had successful completion of treatment.

As our clinic is compact and dynamic, we are quick to explore pilot treatment processes and initiate research projects. We at the Vaasa Cancer Clinic were first in Finland to start selecting patients based on DPD enzyme defects before initiating fluoronucleoside-based treatments in both adjuvant and metastatic settings. We believe on openness and thus currently we write around ten scientific reports about our research annually. Now we are extending our activity towards own research protocols, e.g. stereotactic radiotherapy for treatment of oligometastases. The Vaasa Clinical Cancer Research Unit is also popular among students at University of Umeå for their diploma works. These ongoing projects include treatment results in melanoma, lung, breast cancers and involvement of socioeconomic factors in treatment decision making.

Principal Investigator:
Professor, Chief Physician Antti Jekunen, MD, PhD

Study Nurses:
Helena Ingo, Niina Salo

Clinical Cancer Research Activities at Satasairaala

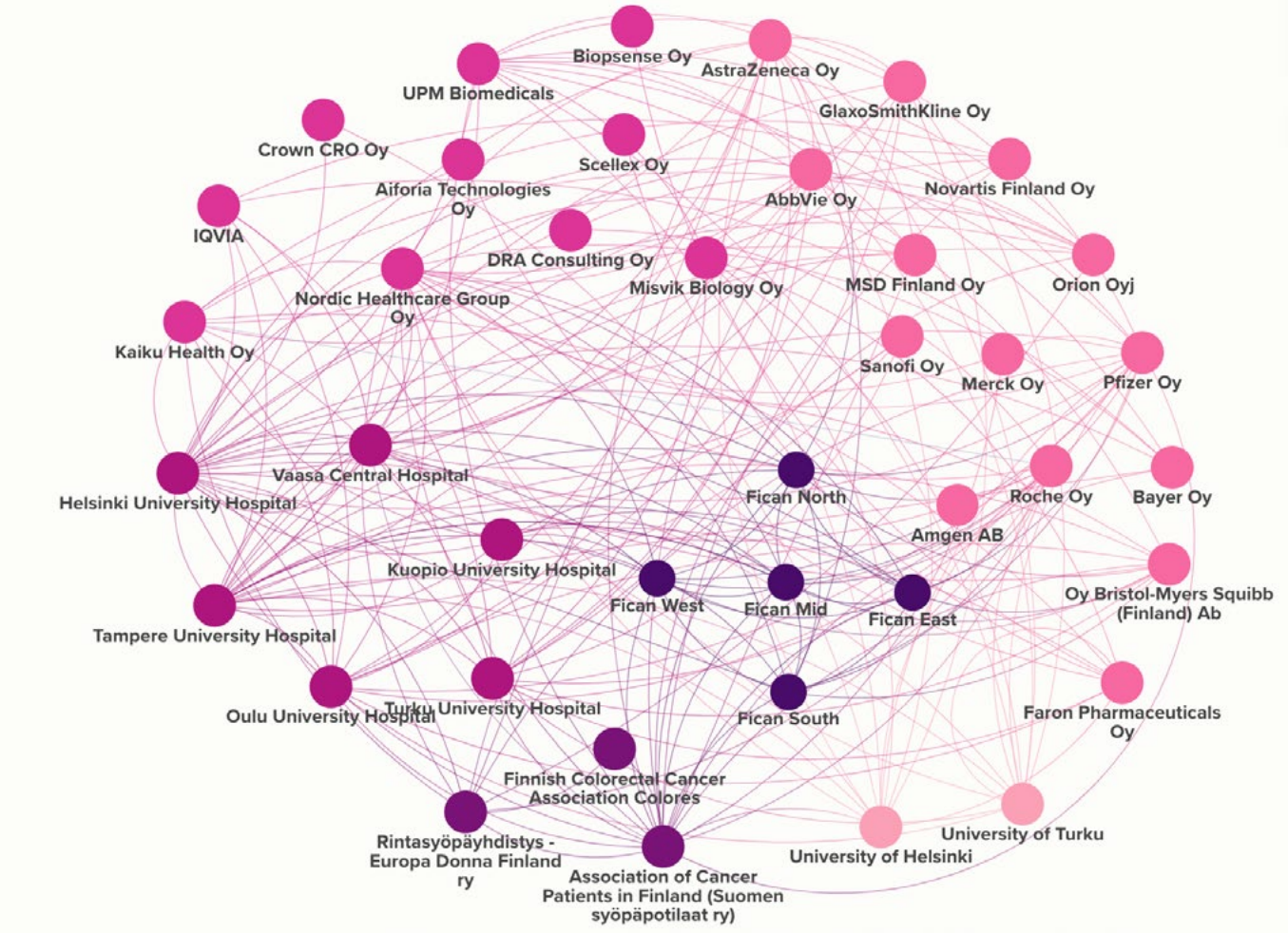
The clinical research group of the Cancer Unit at Satakunta Central Hospital (Satasairaala) in Pori is currently involved in clinical cancer trials as follows:

Breast cancer:
- adjuvant trial for hormone receptor positive and Her-2 negative tumors
- first line trial for hormone receptor positive and Her-2 negative tumors

Colon cancer
- first line trial for B-Raf mutation positive tumors

GIST
- adjuvant trial for 3 versus 5 years of imatinib

Principal Investigator:
Chief of Oncology Kalevi Pulkkanen, MD, PhD



FICAN West collaborates with Cancer IO research and innovation project

Cancer IO is a cancer immunotherapy focused collaborative research and innovation project that is a part of the Business Finland's Personalized Health Program. The Helsinki University coordinated project integrates immuno-oncology (IO) activities at the University of Helsinki and University of Turku, Turku University Hospital and three other university hospitals, Vaasa central hospital, Finnish small or medium enterprises, cancer patient organizations and the IO-investing pharmaceutical companies. Cancer IO collaborates with all FICAN Cancer Centers.

Cancer IO looks at immunotherapies from 360 degree perspective: three core themes focus on Society, Research and Health Care. FICAN West is involved in e.g. Cancer IO's RWD project and in preparation of Cancer IO's reports. The report, Cancer Clinical Trials – Preparedness in Finnish Hospitals was published in September 2021, and included Cancer IO's recommendations to increase clinical trial activity in Finland. Cancer IO's academic research is conducted in Klefström and Mustjoki laboratories at University of Helsinki and in Hollmén laboratory at University of Turku, FICAN West.

The Cancer IO ecosystem, bringing together nearly 40 key organisations in the Finnish IO field, enables extensive collaboration between hospitals, research organizations, companies, and patient organizations, improving patient care, increasing the visibility of Finnish innovations, and contributing to the implementation of the Health Sector's Growth Strategy.

The main activities of the Cancer IO Project were finished by the end of the year 2022. RWD Project continues during the spring 2023 because of the delays in the Findata process.

Cancer IO Director:
FICAN Research Professor Juha Klefström

www.cancerio.org

https://cancerio.org/en/cancer-clinical-trials-preparedness-in-finnish-hospitals/

https://cancerio.org/en/ecosystem/

Cancer IO
Translating Immuno-Oncology into Health Actions

Physics research in radiotherapy

Adj. Professor Jani Keyriläinen, PhD, Department of Medical Physics, Turku University Hospital

Four physics projects are based on a collaboration between local collaborators, national and international hospitals and institutes, national radiation safety authority, and manufacturers. One of the main objectives is to produce postgraduate degrees for the physics students, in particular for those targeting a vocational certified degree in medical physics. Currently, there are six physics postgraduate students working in the projects described in the following sections.

Dosimetry and dose calculation in radiotherapy

The capacity of radiation therapy (RT) is based on the dose response of cells, which describes the response of the biological object for the ionizing radiation. The dose response is characteristic for different types of cells, and the difference between the response of tumor cells and the response of normal cells is the base from which all the doses for clinical treatment are chosen. The clinical requirements on dose accuracy are based on evidence from dose response curves for tumor control probability (TCP) and for normal tissue complication probability (NTCP). The steepness of the given TCP or NTCP curve versus dose defines the change in response expected for a given change in delivered dose. Thus, uncertainties in delivered dose translate into either reductions in TCP from the optimized expected value or increases in NTCP from the optimized expected value, both of which worsen the clinical outcome.

Treatment with ionizing radiation using small photon fields has been an established practice in stereotactic RT for many years. At the same time, there has been an increasing availability of novel treatment units specifically designed for intensity-modulated RT or volumetric-modulated arc therapy treatments. These technical improvements implicitly encourage the use of small treatment field sizes on equipment originally designed and commissioned for treatments based on traditional, broad photon fields. An experimental determination of small field dosimetric data is challenging and the use of radiotherapy planning (RTP) systems and treatment units not designed nor commissioned for small fields can introduce significant errors in the delivery of treatments.

This project is designed to investigate and understand the physics and challenges behind the small photon fields in terms of measurement, calibration and calculation. The most suitable equipment, detector systems and methods for the determination of dosimetric parameters as well as quality assurance aspects relevant to the use of narrow collimated fields are reviewed. The overall objective is to improve the accuracy of RT for cancer patients. The factors that influence the accuracy of measurement and determination of absorbed dose distribution in a tissue equivalent phantom and the calculation accuracy of RTP system in the particular case of small and composite fields are studied. Topics are carefully conducted with extensive measurements by several types of radiation detectors and subsequently compared to the most accurate Monte Carlo simulations. The project is run by the physicists working at Tampere and Turku University Hospitals and at the Radiation & Nuclear Safety Authority (Helsinki, Finland).

Publications:

Saikkonen A, Ojala J, Keyriläinen J. Analytical Anisotropic Algorithm calculation in total body irradiation: a comparison with Monte Carlo calculation and dosimetry. J Cancer Sci Clin Ther. 5:532-547, 2021.

Niemelä J, Partanen M, Ojala J, Kapanen M, Keyriläinen J. Dose-area product ratio in external small-beam radiotherapy: beam shape, size and energy dependencies in clinical photon beams. Biomed Phys Eng Express. 7:035019, 2021.

Partanen M, Niemelä J, Ojala J, Keyriläinen J, Kapanen M. Properties of IBA Razor Nano Chamber in small-field radiation therapy using 6 MV FF, 6 MV FFF, and 10 MV FFF photon beams. Acta Oncol. 60:1419-1424, 2021.

MRI-only in radiotherapy planning

Superior soft-tissue contrast obtainable in magnetic resonance imaging (MRI) compared with other clinical imaging methods enables more accurate definition and delineation of treatment target and organs at risk (OAR) volumes. Also, monitoring of treatment outcome and evaluation of treatment response can be accurate using MR images.

Current practice in the use of MR images for RTP is based on the co-registration of computed tomography (CT) and MR images. This enables the utilization of additional anatomical details provided by MRI, although the dose calculation is based on electron density information available by CT. The use of two different imaging modalities, however, requires additional work and raises costs. Moreover, the error associated with co-registration increases the uncertainty in treatment accuracy. For the aforementioned reasons, it would be ideal to create a practice which is based on a single imaging modality only.

The overall objective of this project is to improve the accuracy of target and OAR definition. The specific aim is to examine the effect of MRI's geometric distortion to dose calculation accuracy in MRI-only-based RTP. Significant distortions in MRI are possible, especially when larger field-of-views are used. A particular branch of examination is the magnitude of geometric distortions produced during diffusion-weighted MRI (DW-MRI). In rapid imaging sequences the gradient magnetic fields required in image encoding produce local eddy currents that cause permanent distortions to both geometry and image intensity. This complicates the definition of treatment volume, hence reducing the usability of DW-based imaging techniques for MRI-only RTP.

In the project, the possibilities of using the MRI for dose calculation are studied in pelvic, brain and head and neck cancers that could diminish the need for CT. On MR images, the tumor and other structures can be differentiated better than on CT images, but they do not contain the electron density information required for dose calculation. The MRI scanner located at the RT department of Turku University Hospital is equipped with a software, which is capable of producing so-called synthetic CT images based on MR image information. These images can be utilized directly in a clinical RTP system. This project is conducted by a close co-operation with other hospitals and the MRI manufacturer Philips Oy (Vantaa, Finland).

In addition to reduced radiation exposure for the patients due to the use of non-ionizing radiation, the methods reduce the number of hospital visits for patients and amount of work for the personnel. This may cause significant savings in time and costs. Clinical advantage for patients is the result of the improved target and OAR definition. In the long term, this may manifest itself as a reduction of complications caused by increased tumor control probability. Determining this would, however, require a large clinical material and a long follow-up period.

Publications:

Keyriläinen J, Sjöblom O, Turnbull-Smith S, Hovirinta T, Minn H. Clinical experience and cost evaluation of magnetic resonance imaging -only workflow in radiation therapy planning of prostate cancer. Phys Imag Radiat Oncol. 19:66-71, 2021.

Yu V, Keyriläinen J, Suilamo S, Beslimane I, Dresner A, Halkola A, Van der Heide UA, Tyagi N. A multi-institutional analysis of a general pelvis continuous Hounsfield unit synthetic CT software for radiotherapy. J Appl Clin Med Phys. 22:207-215, 2021.

Ranta I, Teuho J, Linden J, Klén R, Teräs M, Kapanen M, Keyriläinen J. Assessment of MRI-based attenuation correction for MRI-only radiotherapy treatment planning of the brain. Diagnostics. 10:299, 2020.

Kuisma A, Ranta I, Keyriläinen J, Suilamo S, Wright P, Pesola M, Warner L, Löyttyniemi E, Minn H. Validation of automated magnetic resonance image segmentation for radiation therapy planning in prostate cancer. Phys Imag Radiat Oncol. 13:14-20, 2020.

Depauw N, Keyriläinen J, Suilamo S, Warner L, Bzdusek K, Olsen C, Kooy H. MRI-based IMPT planning for prostate cancer. Radiother Oncol. 144:79-85, 2020.

Automated segmentation tools for radiotherapy using deep learning algorithms

Manual segmentation of the OARs per patient can take a long time even for an experienced clinician. Depending on the disease and its location, it can vary from a few minutes to an hour. By using accurate and robust automated segmentation algorithms, up to several hours of segmentation work can be automated, whilst the contributions of clinicians can be relieved for other important tasks, such as a doctor's practice.

The automated segmentation tool uses branches of machine learning called deep learning (DL). DL is a subfield of machine learning concerned with artificial neural networks, which are models inspired by the structure and function of the brain. DL models try to find good multiple level representations of the unknown input distribution in a hierarchical fashion, similarly as e.g. in the human visual cortex. These automatically learned abstract features allow the constructed multidimensional functions to produce an output from input without the features of human designed functions. In this project, the problem distribution is a medical imaging dataset and the target output to be learned by the artificial neural network are the segmented contours of regions of interest, such as target and OARs.

A tool capable of producing automatically segmented target and OAR structures on CT and MR images of various cancer sites, e.g. prostate, breast and brain, is studied, developed and validated. The overall objective of the work is to automate the entire process of target and OAR segmentation required for the RTP. Hundreds of anonymous CT and MR images with manually segmented target and OAR structures are retrospectively collected to be used as an input distribution for level-feature learning of the DL algorithm.

The retrieval and anonymization tasks of the patient images and corresponding segmentations from the image database can be automated by a database daemon script. This project is carried out in a close collaboration with other hospitals and MVision AI Oy (Helsinki, Finland) that is able to provide the development work and training for the DL-based workflow. Evaluation, validation and testing parts are put into an action by the clinicians and physicists. Traditional evaluation metrics, e.g. Dice coefficient, difference between the volumes and the 95% Hausdorff distance, are used to compare the outcome with the ground truths defined by clinicians. Obviously, the project also includes fitting the application into a clinical workflow in order to significantly lower the working hours spent for image segmentation.

Publications:

Kiljunen T, Akram S, Niemelä J, Löyttyniemi E, Seppälä J, Heikkilä J, Vuolukka K, Heikkilä V-P, Lehtiö K, Nikkinen J, Gershkevitsh E, Borkvel A, Adamson M, Zolotuhhin D, Kolk K, Pang EPP, Tuan JKL, Master Z, Chua MLK, Joensuu T, Kononen J, Myllykangas M, Riener M, Mokka M, Keyriläinen J. A deep learning -based automated CT segmentation of prostate cancer anatomy for radiation therapy planning - a retrospective multicenter study. Diagnostics. 10:959, 2020.

Biologically guided radiotherapy

The RT department collaborates with Turku PET Centre in combining anatomical, metabolic positron emission tomography (PET) and functional MRI with RT. Our interdisciplinary research include both dose painting by numbers based on the hypoxic agent EF5 and investigation of predictive factors for head and neck cancer patients, as well as acetate based dose escalation of intraprostatic lesions. The research conducted includes both long-term evaluation of treatment outcomes and development of future methods for RT delivery.

Publications:

Kuisma A, Wright P, Suilamo S, Seppälä J, Koivisto M, Lindholm P, Minn H. Long-term outcome of biologically guided dose-escalated radiotherapy of localized prostate cancer. Acta Oncol. Online ahead of print:1-7, 2021.

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Highlights in research infrastructure

Auria Biobank

The aim of biobanks is to promote health by providing a research infrastructure for biomedical research. Biobanks collect biological samples and related clinical data from patients who have given biobank consent to be used for research purposes. The donation of a sample to biobank is voluntary but highly valuable for biomedical research. The data generated in the biobank studies helps to understand diseases and supports the development of new personalized therapies. The results from biobank studies return to biobank adding value to the samples.

Auria Biobank is the oldest Finnish hospital biobank established in 2012 by University of Turku and the hospital districts of Southwest Finland, Satakunta and Vaasa. Auria is the operating biobank in the respective wellbeing services counties established from 2023. In 2022 the team at Auria Biobank, part of Turku University Hospital's Laboratory Division, has achieved ISO 20387:2020 accreditation. This makes Auria the first Nordic biobank to demonstrate quality to this international standard. The current scope of accreditation includes acquisition, handling and distribution of certain liquid samples.

Auria's samples are mainly collected as part of normal diagnostics or treatment. Over 1,5 million human biological FFPE tissue samples are stored at Auria Biobank. There is an ongoing collection of also other sample types such as plasma, serum, cerebrospinal fluid CSF and DNA. Genotype data is available for ca 37 000 samples. Approximately one fourth of Auria's samples are cancer tissue samples.

Clinical data collected as part of patient treatment in the hospital can be linked to the biobank samples. Based on e.g. genotype information and clinical parameters, Auria Biobank is able to recall defined groups of patients for clinical trials. Auria has extensive experience in serving both academic research as well as pharmaceutical and diagnostic industry. The abstracts of the >200 biobank studies are collected at Auria's web pages (www.auria.fi).

https://www.auria.fi/biopankki/
Perttu Terho, Acting Director
Merja Perälä, Project Manager

Turku Center for Disease Modeling

The TCDM is a research and research service organization of the Faculty of Medicine in the University of Turku. It is also a part of the Biocenter Finland "Model Organisms" network. TCDM provides state-of-the-art research facilities and expertise in studies involving experimental animals to support preclinical research for academic and industry purposes.

Rodent studies in vivo are an essential part of studies aiming for understanding mechanisms of tumor growth and treatment responses. TCDM offers expertise e.g. 1) to generate and study xenograft models in mice and rats, 2) to generate and maintenance genetically modified mouse models for cancer research, and 3) has expertise to perform chemically induced cancer models in mice. TCDM personnel are qualified to perform various surgical and pharmacological interventions in preclinical studies. The experimental studies in rodents are supported by several image-analyzing techniques allowing to follow tumor growth metabolism, including optical, PET and ultrasound imaging. Direct connections have been also built to facilities providing histological services and molecular pathology at the Institute of Biomedicine. TCDM holds a spectrum of slide scanners enabling the digital pathology services for experimental cancer models, and has recently established a platform for high resolution laser microdissection of histological section and cells. In activities carried out together with Auria Biobank and Turku Prostate Cancer Consortium, TCDM has established methods to generate patient-derived cell lines from various cancers and their benign counterparts, providing the potential to generate models for personalized models and e.g. for drug sensitivity testing carried out together with Misvik Biology.

https://www.tcdm.fi/
Matti Poutanen, Professor, Director of TCDM
Petra Sipilä, Adjunct Professor, Vice Director of TCDM

AURIA CLINICAL INFORMATICS
FINDATA PARTNER

Auria Clinical Informatics

Auria Clinical Informatics (ACI) supports scientific research, education and data-driven management based on the secondary use of patient records in specialized healthcare. ACI serves both basic academic research and industry-sponsored scientific studies and its services for researches include:

- Feasibility reports on data availability
- Study planning support
- Data extraction
- Statistical analyses
- Access to a secure data analytics platform

Cancer studies based on patient records often require tight collaboration between ACI and local clinicians. The suitability and coverage of the patient records data need to be evaluated from a technical and clinical perspective. For this purpose, ACI has created a wide network of oncologists, surgeons and pathologists treating cancer patients and doing cancer research at the Wellbeing services county of Southwest Finland.

In fact, ACI has supported ca. 100 cancer studies based on patient records in 2019-2022. In the future, we see the demand for patient records data growing for cancer research. A rising trend is to form control cohorts for clinical studies based on patient records.

For the TYKS Cancer Center, ACI has created and maintains statistics for times to treatment in selected cancer types for presentation on the public website of TYKS. In addition, ACI maintains a more detailed internal cancer treatment dashboard for the TYKS Cancer Center for data-driven management purposes.

https://www.auria.fi/tietopalvelu/en/

Arho Virkki, Chief Analytics Officer at the Wellbeing services county of Southwest Finland Head of Auria Clinical Informatics

Turku PET Centre

The Oncology research group assesses prospectively new hybrid imaging technologies and acquisition protocols with standard and new tracers at the Turku PET Center. The aim is to increase the clinical impact and diagnostic accuracy of PET imaging and PET-related research. Moreover, possibilities of new AI technologies with deep learning capabilities are being investigated for facilitating and improving diagnostic analysis of oncological PET images.

Innovations through translational research by local and international collaborators are being evaluated for immune cell interaction studies, for circulating tumor DNA and microenvironment in relation to molecular imaging which may guide immunotherapy, for biologically planned adaptive radiotherapy, and for particle therapy.

We are currently studying the development of chemotherapy resistance and hypoxia in ovarian cancer with PET imaging in clinical studies by developing artificial intelligence methods to identify effective treatment modalities. Hypoxia is one of the most important drivers of chemoresistance in cancers. Tumor hypoxia can be evaluated preoperatively with PET with the novel tracer EF5 (18F-[2-82-nitro-1-H-imidazol- 1-yt)-N-(2.2,3,3,3-pentafluoropropyl) acetamide]).

Prostate specific membrane antigen (PSMA) targeted PET/CT or PET/MRI represents a very promising imaging method for prostate cancer diagnosis, staging and treatment response evaluation. To improve the diagnostic accuracy in staging of high risk prostate cancer, we have multiple ongoing studies comparing the new novel imaging methods to conventional guideline imaging (Bone scintigraphy and CT) in primary staging of prostate cancer.

Fibroblast activation protein (FAP) is a very promising molecular target for imaging and therapy in cancer. 18F-labelled FAP inhibitors PET-CT/MRI research will be one of the major interests of our group in the near future in various types of cancers.

Theranostics refers to the use of molecular probes that have both diagnostic and therapeutic properties; these probes have a radionuclide attached, e.g., 177-Lu or Ac-225. We are also studying PSMA receptors and somatostatin receptors in phase I trials and in archival biobanked material for their potential as targets for alpha- and beta-emitting radionuclide therapy.

A recent grant from the Academy of Finland will support a prospective study on the effects of physical activity on the response to anticancer treatment. Additional funding is provided by the Finnish Cancer Organization, the Nordic Cancer Union, and European Union. Currently we are installing a total body PET/CT scanner, Siemens Vision

Quadra, which allows dynamic whole torso imaging in patients with cancer. This will further enhance our possibilities for cancer research.

https://turkupetcentre.fi/

Professor Juhani Knuuti, Director of Turku PET Centre.

Turku Clinical Research Center (TurkuCRC)

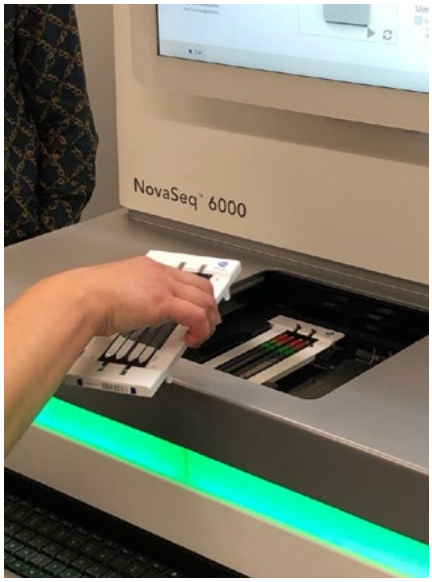
The goals of the research services of the hospital district are to reinforce the prerequisites of scientific research, to guarantee the quality of research, to ease the workload of the study groups by managing the administration of the research and to make co-operation with external stakeholders faster and more efficient. The research services.

- support the ethics committee
- process research contract issues
- administer state health research funding
- administer EU-projects

TurkuCRC and the University of Turku function as a guide and advisor for researchers and commissioners in the planning of research projects and in acquiring support services needed for by the research team and to follow that laws, acts, regulations and the GCP principles are duly followed. In addition, TurkuCRC provides monitoring services to investigator-initiated research projects and organizes education in the field of healthcare research to scientists and other research staff.

http://www.turkucrc.fi/

Päivi Rautava, professor, Director of TurkuCRC



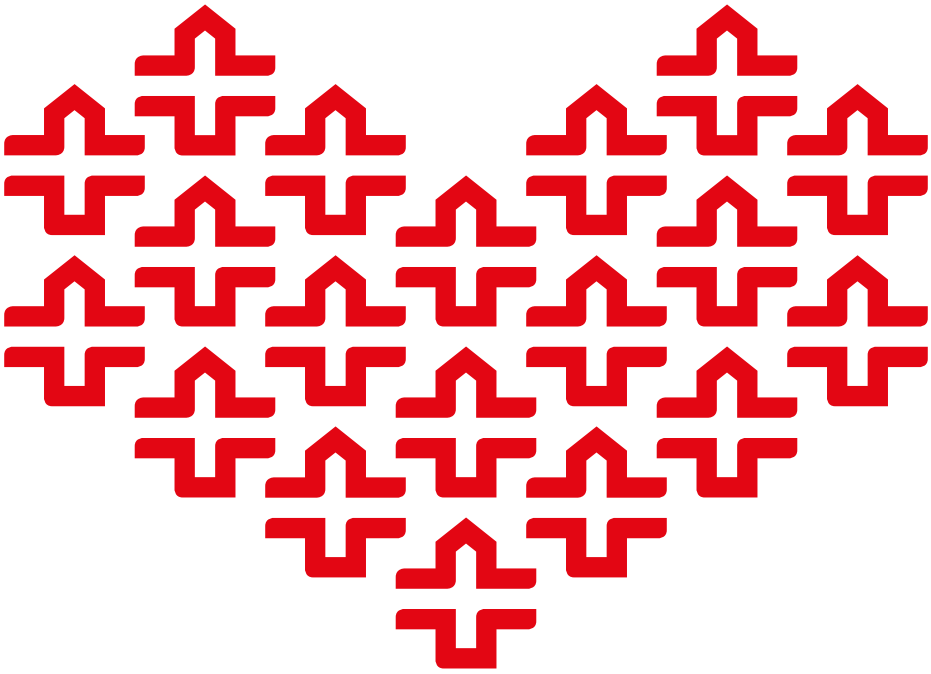
Finnish Functional Genomics Centre

Finnish Functional Genomics Centre (FFGC) is a national core facility for genomics services and a testing laboratory No. T351 accredited by FINAS Finnish Accreditation Service for production of sequence raw data for various further analyses from genomic DNA with next-generation sequencing (accreditation requirement SFS-EN ISO 17025:2017). FFGC operates at the Turku Bioscience Centre, which is a joint department of University of Turku and Åbo Akademi University and belongs to the national Biocenter Finland infrastructure network.

FFGC supports high level research by providing open access to the state-of-the art technologies and services with the latest methods available for genome analysis. Currently the most important services include next-generation sequencing based analysis of genomes, exomes, transcriptomes, epigenomes and metagenomes. The service users include academic and government's research units, health care units and organizations from private sector. FFGC continuously develops and improves the provided services in close collaboration with the key stakeholders, such as Molecular Tumor Board to develop services for cancer diagnostics, and in collaboration with the Genomics Unit of Turku University Hospital Laboratories provides services for exome and whole genome sequencing.

https://bioscience.fi/services/functional-genomics/services/

Minna Kyläniemi, PhD, Head of FFGC



Parannamme joka päivä

TYKS

OECI CANCER CENTRE