DEPARTMENT OF ONCOLOGY-PATHOLOGY

We are a part of Karolinska Institutet, where we work with cancer research and offer educational programs at undergraduate, Master and doctoral levels. Uniting more than 30 research groups, the department’s broad focus on cancer combines basic, translational and clinical research, ranging from mechanisms of cancer development and biomarkers to development of new technologies for precision cancer medicine. Thus, our goals are, based on fundamental discoveries, to identify and implement cancer biomarkers supporting early diagnosis and improved personalized therapy, and to drive drug discovery via innovative clinical trials. Further, we engage in education of next generation scientist and healthcare professionals in these areas. Our research teams are mainly located at two research buildings, Bioclinicum and Science for Life Laboratories (SciLifeLab), Solna, and at hospital buildings including Pathology unit and New Karolinska Hospital (NKS), Stockholm. In addition, few research groups form satellites in Södersjukhuset, Karolinska hospital in Huddinge and at Cancercentrum Karolinska, Solna.

Science for Life laboratories
Individual research groups are part of both the department of Oncology-Pathology and the SciLifeLabs national infrastructure.

Bioclinicum
We are located on floors 5 and 6 with skyways connecting us to NKS, Karolinska Institutet campus Solna and Biomedicum.

Pathology and NKS
We combine our health care responsibilities with education at doctoral and postdoctoral levels, clinical research and clinical trials.

Photos: H. Flank
OUR RESEARCH AREAS

At **Bioclinicum**, we focus on basic molecular mechanisms that underlie cellular and physiological functions under normal conditions and during development and progression of cancer. Specifically, we study cell types and processes involved in cancer development and progression, including cancer cells and cancer initiating cells, cancer-associated stroma cells, such as fibroblasts, endothelial cells and angiogenesis, immune cells and inflammation, cell migration and metastasis. We conduct pre-clinical and translational studies to validate basic findings in in vivo models and in primary tumor tissues, and implement our discoveries in clinical trials.

**SciLifeLab**, we develop novel technologies and high throughput platforms in the areas of proteomics, drug discovery and drug development. We use these platforms for discovery of novel anti-cancer drugs and of biomarkers for precision medicine in cancer. We work in teams combining experts in engineering, chemistry and data science with oncologists, nurses and physicians as part of precision cancer medicine program across several different cancer types including leukemia, sarcoma, lung, breast, ovarian, and bladder cancer.

At **NKS and Pathology**, we conduct clinical research and clinical trials for better and early cancer diagnosis, and to discover novel predictive biomarkers for more efficient and personalized anti-cancer treatments. Combining our clinical expertise with research allows fast introduction of novel findings for the benefit of cancer patient. Our clinical studies result in discoveries of novel diagnostic and prognostic measurements and their implementation into clinical practice. Oncologists and pathologists develop and evaluate novel targeted therapies and collect tumor tissues and samples into Biobanks for both on-going and future translational research projects.
OUR GOALS AND STRENGTHS

WHAT WE WANT TO DO
Our MISSION is to improve diagnostics, treatment and quality of life for patients with cancer through basic, translational and clinical research and education in the field of cancer.

HOW WE WANT TO DO IT
Our GOALS are to achieve excellence in research and education, to foster clinical research and to create high technological platforms for research support and innovation.

Our VALUES are based on ethics, high diversity and equality. We cultivate openness, networking and collaborations to consolidate national and international forces to cure cancer.

OUR GOALS AND STRENGTHS

Clinical cancer research and clinical trials
Improved diagnostics and precision medicine
Novel drug development and treatments
New technologies and big data-driven research
Strong Basic and Translational research

OUR STRENGTHS

• Translating basic knowledge and discoveries into practice
• Improved and personalized cancer diagnostics
• Ex vivo drug screenings for precision medicine
• Immune and gene therapy
• Clinical trials validating novel drugs and drug combinations
• Novel treatment regimen for improved quality of life
• New drug development and therapies
• High quality courses and educational programs
• Nurturing junior scientists for future leadership

Lars Holmgren, the Head of our Department, says:

"We share skills, knowledge and resources through national and international networks, collaborations, conferences, courses and seminars and by building strong and advanced modern technological platforms."

OUR NETWORKS ARE:
Cancer Research KI – network at Karolinska Institutet
ki.se/en/cancerresearchki/cancer-research-ki
Cancer Core Europé – European Cancer Association
cancercoreeurope.eu/karolinska

Photo: H. Flank
SOME OF OUR DISCOVERIES AND ACHIEVEMENTS

THE PANTHER TRIAL AND BEYOND FOR HIGH-RISK BREAST CANCER

Cancer clinical trials are conducted at the Department in collaboration with the Karolinska University hospital. One aspect in these trials is the patients' health-related quality-of-life (HRQoL). It is a very important parameter as it is a combination of the treatment outcome and the patient's subjective experience of the disease and the treatment that helps to inform patients in the treatment decision. The Panther trial in women with high-risk early breast cancer showed a better event-free survival in a group receiving tailored dose-dense chemotherapy as compared to standard adjuvant chemotherapy2, but a lower HRQoL level during the treatment1. However, a long-term follow up revealed that HRQoL levels recovered once treatment was terminated2. A meta-analysis further showed that increasing the dose density of adjuvant chemotherapy was safe and resulted in fewer disease recurrences and fewer deaths from breast cancer3 and may therefore be more frequently used. For women offered this treatment it will be reassuring to know that although HRQoL decreases during the treatment, an improvement and recovery is expected after the treatment.


PHASE 1 TRIAL WITH TUMOR INFILTRATING LYMPHOCYTES AND DENDRITIC CELLS

Immunotherapy of cancer has achieved substantial progress, particularly when the Immune Checkpoint Inhibition, ICI, was introduced. This prolongs the survival of some patients with advanced melanoma. For those who fail, we are developing a new combination of two types of immuno-therapies. First, T-cells are extracted from the patient's tumor. These “Tumor Infiltrating Lymphocytes”, TILs, an important part of the body’s immune defense against cancer, are multiplied up to 50 billion cells and administered back to the patient in combination with Interleukin-2. What makes this study unique compared to other clinical TIL trials is that the patients are at the same time treated with several doses of a tumor vaccine consisting of dendritic cells, DC, which activate the immune system and give the injected TILs an extra boost. Of the four severely ill patients with malignant melanoma that failed to respond to any other treatment, three have responded with a complete or near complete remission while patients treated with TILs mono-therapy did not have the same favorable response. The method is a part of Karolinska University Hospital’s efforts in cell-based therapy, and Rolf Kiessling, head of the study, has applied to the Swedish Medical Products Agency for approval to test the method on other types of metastatic cancer.

1. Lövgren T, Wolodarski M, Wickström S et al., Complete and long-lasting clinical responses in immune checkpoint inhibitor-resistant, metastasized melanoma treated with adoptive T cell transfer combined with DC vaccination. Oncoimmunology 2020, VOL. 9, NO. 1, 1–11

THEO FOUKAKIS,
MD and a Team leader in J. Bergh group, says:

“...is that all women with breast cancer will be cured with minimal negative HRQoL effects from the treatment. We therefore continue our clinical research that includes novel therapeutic regimens and a careful follow-up of the combined disease and quality of life parameters to improve the clinical management of breast cancer.”

STINA WICKSTRÖM,
head of TIL production and immune monitoring, comments:

“Our clinical study has shown that Cell therapy with T-cells and DC vaccine has remarkable strong clinical effects on metastatic advanced malignant melanoma. We hope that the same approach will be efficient in other solid tumors, such as gynecological cancer. This demonstrates the strength of interdisciplinary collaborations between basic scientists and clinicians at Karolinska hospital in Solna and Huddinge.”

PHASE 1 TRIAL WITH TUMOR INFILTRATING LYMPHOCYTES AND DENDRITIC CELLS

Immunotherapy of cancer has achieved substantial progress, particularly when the Immune Checkpoint Inhibition, ICI, was introduced. This prolongs the survival of some patients with advanced melanoma. For those who fail, we are developing a new combination of two types of immuno-therapies. First, T-cells are extracted from the patient's tumor. These “Tumor Infiltrating Lymphocytes”, TILs, an important part of the body’s immune defense against cancer, are multiplied up to 50 billion cells and administered back to the patient in combination with Interleukin-2. What makes this study unique compared to other clinical TIL trials is that the patients are at the same time treated with several doses of a tumor vaccine consisting of dendritic cells, DC, which activate the immune system and give the injected TILs an extra boost. Of the four severely ill patients with malignant melanoma that failed to respond to any other treatment, three have responded with a complete or near complete remission while patients treated with TILs mono-therapy did not have the same favorable response. The method is a part of Karolinska University Hospital’s efforts in cell-based therapy, and Rolf Kiessling, head of the study, has applied to the Swedish Medical Products Agency for approval to test the method on other types of metastatic cancer.

1. Lövgren T, Wolodarski M, Wickström S et al., Complete and long-lasting clinical responses in immune checkpoint inhibitor-resistant, metastasized melanoma treated with adoptive T cell transfer combined with DC vaccination. Oncoimmunology 2020, VOL. 9, NO. 1, 1–11
NOVEL DRUG DISCOVERIES:
FROM BENCH TO BEDSIDE

TARGETING MTH1
BY KARONUDIB

Developing novel therapies requires not only a unique idea, but also medicinal chemistry, pharmacology and pharmacokinetic expertise. We work in multidisciplinary teams to combine our groundbreaking and strong basic understanding of cancer pathology with novel technologies and expertise in drug discovery to perform translational research and identify and develop novel anti-cancer treatments.

In 2014 the Helleday team demonstrated that targeting the enzyme MTH1 (NUDT1) was a promising potential anti-cancer therapy with very limited general toxicity. Three years later, we had developed a clinical candidate, Karonudib (Karolinska NUDT1 inhibitor), designed clinical trial protocol and obtained approvals from Medical Product Agency and Ethical Committee to initiate clinical trials. Presently two phase I trials are on-going at Karolinska University Hospital, MASTIFF and MAATEO, with the primary goal to investigate safety and tolerability of Karonudib in patients with advanced solid malignancies or hematological cancers.

TARGETING MUTANT P53
BY APR-246

The TP53 tumor suppressor gene is mutated in around 50% of all human tumors. Can we exploit mutant p53 as a therapeutic target in cancer? We in Wiman group have developed a novel therapeutic strategy based on pharmacological reactivation of mutant p53. We identified and subsequently developed a clinical candidate, APR-246. The compound is converted to the Michael acceptor, MQ, promotes p53 refolding and also causes oxidative stress, resulting in robust cancer cell death.

We founded the company Aprea Therapeutics in 2003 with the aim of taking APR-246 to clinical trials. A first-in-man phase I clinical study was initiated 2009. Currently APR-246 is tested in a phase III clinical trial in combination with azacitidine (AZA) in patients with TP53-mutant MDS (myelodysplastic syndrome). APR-246 has received Fast Track and Breakthrough Therapy designation from the FDA (www.aprea.com).

2. Warpman Berglund et al., Validation and Development of MTH1 Inhibitors for Treatment of Cancer, Ann Oncol 2016, 12:2275-2283
We are building a strong Precision cancer medicine (PCM) platform in collaboration with SciLifeLab, KTH, Uppsala University and Karolinska University Hospital. The combination of molecular profiling and drug resistance testing can help to individualize care of patients, but can also be applied to optimize drug discovery and development as well as help design clinical trials to the most promising drugs in the cancer subtypes most likely to be responsive.

**Päivi Östling**, co-PI of O. Kallioniemi group at SciLifeLab, says:

“We have established an efficient network and tight coordination between clinical and scientific teams, and put in place the technical solutions to screen the tumor cells from patients for sensitivity to a broad range of drugs and drug combinations. This is tricky but very rewarding when in the future the patients can benefit from the fine-tuned personalized treatment.”
Educating and supporting young scientists for a continuous future strong translational cancer research is an important goal for the department. Ambitious researchers that become Team leaders within a research group get the support before taking the next step to an independent group leader.

**CHRISTOFER JUHLIN**  
MD, PhD, TEAM LEADER IN C. LARSSON GROUP AT BIOCLINICUM  

“I am an attending endocrine pathologist at the Karolinska University Hospital responsible for diagnosing patients with tumors in endocrine (hormone-producing) organs, such as the thyroid, parathyroid and adrenal glands. Besides my clinical duties, I am also a research team leader at OncPat. My team recently discovered that mutations of the TERT promoter are not only significantly associated with malignant thyroid tumors but can also predict the transition from histologically “benign” tumors to malignant tumors, and therefore this biomarker was rapidly introduced into clinical setting for the right diagnosis and treatment algorithms for this patient category.”

**NINA GUSTAFSSON**  
PhD, TEAM LEADER IN T. HELLEDAY GROUP AT SCI Lifelabs  

“I went to Stockholm University, where I majored in Molecular Biology. After that I continued with PhD studies in Medical Science at KI followed by postdoctoral studies in Computational Medicine, Cancer Metabolism and Chemical Biology. In 2018 we discovered that the glycolytic enzyme PFKFB3 also functions as an essential regulator of DNA repair and genomic stability. This unexpected discovery resulted in a patent, and I could form, with support from the Swedish Childhood Cancer Foundation, my research team in 2019, and I hope in the future to start my own independent group.

We will further unravel how PFKFB3 network contributes to DNA repair and provide novel and ground-breaking biological insights into the largely unexplored connection between the DNA damage response and cancer metabolism beyond nucleotide metabolism.”

**Christofer Juhlin, MD, PhD, says:**

"In my research, I am striving to uncover novel genetic mechanisms in endocrine tumors which could aid in our daily work as surgical pathologists with the end goal to modernize endocrine pathology and implement comprehensive, genome-wide analyses of these tumors into clinical practice."

**Nina Gustafsson, PhD, says:**

"Most anti-cancer therapies exert their toxicity by introducing DNA damage. These cytotoxic effects can be greatly potentiated by simultaneously targeting DNA repair mechanisms. This is our strategy for developing novel anti-cancer therapies."

**The Way in Science: Future Group Leaders**


We are proud of the high-quality learning environment the Department offers. We have expert preclinical as well as clinical teachers who can demonstrate the links between basic and clinical research and clinical reality. They keep updating the learning materials they present, and they strive to help students be active learners.”

Mimmi Shoshan, Director of Undergraduate Studies, says:

“We teach Cancer Biology and Oncology

We at The Department of Oncology-Pathology are enthusiastic teachers! Our main goal is to give the most comprehensive and state-of-the-art knowledge on mechanisms of cancer development, on cancer diagnostics and treatment as well as technical developments in these fields.

**UNDERGRADUATE EDUCATION**

- Courses in Tumor Biology, Medical and Molecular Oncology, advanced and palliative treatment, and Pathology and Forensic medicine. Target groups: KI students in Medicine and Biomedicine and Master students at KI
- Commissioned courses in Tumor Biology-related subjects. Target groups: health care providers, pharmaceutical research companies.

**GRADUATE EDUCATION**

- Courses in Oncology, Tumor Biology, Tumor immunology, Molecular Methods, Omics, Bioinformatics. Target group: M. Sc., PhD students with full-time research at KI
- National research school (NatiOn) in clinical and translational cancer research. Target group: M.D. PhD students with a clinical or translational project in cancer research field, M.D. and future clinical researchers in the cancer field.
- Courses for physicians in specialist training.

We at The Department of Oncology-Pathology are enthusiastic teachers! Our main goal is to give the most comprehensive and state-of-the-art knowledge on mechanisms of cancer development, on cancer diagnostics and treatment as well as technical developments in these fields.

**UNDERGRADUATE EDUCATION**

- Courses in Tumor Biology, Medical and Molecular Oncology, advanced and palliative treatment, and Pathology and Forensic medicine. Target groups: KI students in Medicine and Biomedicine and Master students at KI
- Commissioned courses in Tumor Biology-related subjects. Target groups: health care providers, pharmaceutical research companies.

**GRADUATE EDUCATION**

- Courses in Oncology, Tumor Biology, Tumor immunology, Molecular Methods, Omics, Bioinformatics. Target group: M. Sc., PhD students with full-time research at KI
- National research school (NatiOn) in clinical and translational cancer research. Target group: M.D. PhD students with a clinical or translational project in cancer research field, M.D. and future clinical researchers in the cancer field.
- Courses for physicians in specialist training.

**NATIONAL RESEARCH SCHOOL (NATION) IN CLINICAL AND TRANSLATIONAL CANCER RESEARCH**

The program offers a tailored package of courses primarily in molecular oncology and research methods for MDs clinically active in the cancer field. During a total of 20 weeks divided into blocks during three years, a solid and advanced foundation for clinical cancer research is provided. Completion of this program meets the requirements of KI and most other Swedish medical universities for tuition in doctoral (Ph.D.) studies.

Svetlana Bajalica Lagercrantz, Chairman of NATION, says:

“We created this school more than 10 years ago as a unique package of courses to provide the mandatory research education for medical doctors who want to combine clinical work and doctoral studies. With today’s rapid advances in molecular oncology, doctors need to learn more about research tools in order to actively participate in and lead clinical trials and studies. Only research can radically improve cancer treatment based on novel discoveries and drug development, leading to a more personalized treatment of each cancer patient!”
WORKING AT DEPARTMENT OF ONCOLOGY-PATHOLOGY

As a part of KI, we strive for the highest level of research combined with educational activities. At Bioclinicum, we are conveniently located between Karolinska hospital and SciLifeLabs to foster our close connection with the clinic and our urge to use state-of-art technologies. Some of the regular events that drive our people together through scientific exchange are the weekly seminars, our annual conference, and not to forget the popular monthly breakfast gatherings in the relaxed environment. Our members come from different countries and an annual International party brings us together and invites to taste the homemade food from all the corners of the world. Our goal is that everybody is equally treated and have opportunities to pursue their ambitions in research and personal growth.

Breakfast gatherings
Annual Conference

The monthly “breakfast gatherings” bring out the news from the Department Chair and brief individual presentations with the latest breakthrough research.

Kick-off
International Party
Seminars

Once a year the Department gathers at a Kick-off: a 1-day retreat full with scientific presentations from the groups followed by a delicious dinner. Coffee combined with poster presentations and fruitful discussions inspires collaborations.

International Party. As we are more than 30 nationalities united at the Department, we gather every year to taste the best food from all the corners of the world followed by games and dancing.

Our Annual Conference of the Department, “Frontiers in Cancer Research and Therapy”, is being held for 17 years. We invite speakers from Sweden and abroad. The prizes are distributed for the best poster at the conference, the best Teacher and the best Scientific Paper of the year as well as the Dan Grandér prize for the best PhD thesis of the year in the field of cancer.

Seminars. Friday seminars with both Swedish and international speakers are organized weekly, as well as PhD students’ seminars that are included in PhD education at KI. TRAP (Translational Research Activity Program) seminars held monthly are specifically devoted to clinical and translational research.
Karolinska Institutet is one of the world’s leading medical universities. Our vision is to advance knowledge about life and strive towards better health for all. Karolinska Institutet accounts for the single largest share of all academic medical research conducted in Sweden and offers the country’s broadest range of education in medicine and health sciences. The Nobel Assembly at Karolinska Institutet selects the Nobel laureates in Physiology or Medicine.

CONTACT

Have questions or interested to learn more about our research and activities? Contact the Head of the Department, Prof. Lars Holmgren, lars.holmgren@ki.se

Want to get more information about the structure and function of our department or about financial questions? Contact the Head of our Administration, Maria Von Witting, maria.von.witting@ki.se

For donations, use KI’s SWISH 123 202 32 08 or the bank account 5310-6217 and write K7 (the code of our Department) and the name of the group leader whose research you want to support. Questions? Contact maria.von.witting@ki.se

Want to enquire about the possibilities to do internship or Master at our Department, look for ads at KI home page or contact the group leaders directly. For questions about PhD education at Department of Oncology-Pathology, contact our Director of doctoral education Associate Professor Andreas Lundqvist, andreas.lundqvist@ki.se or Administrator Erika Rindsjo, erika.rindsjo@ki.se