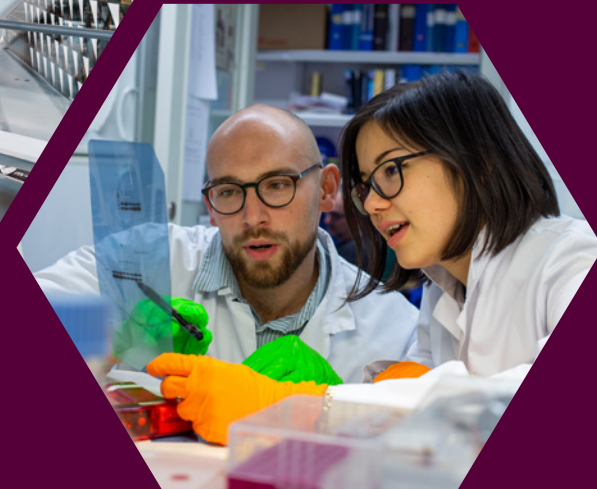


Welcome to the Department of Oncology-Pathology



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 an improved personalized therapy, and to drive drug discovery via innovative clinical trials. Further, we engage in education of next generation scientists and healthcare professionals in these areas. Our research teams are mainly located at the two research buildings, BioClinicum and Science for Life Laboratory (SciLifeLab), Solna, and at the hospital buildings including Pathology unit and New Karolinska University Hospital (NKS), Stockholm. In addition, few research groups form satellites in Södersjukhuset, Karolinska University Hospital in Huddinge and at Cancercentrum Karolinska, Solna.

SciLifeLab

Individual research groups are part of both the department of Oncology-Pathology and the SciLifeLab 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

Photos om frontpage: H. Flank, Erik Cronberg, E.H. Cheteh & S. Ceder



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.

At **SciLifeLab**, we develop novel technologies and high throughput platforms in the areas of proteomics, drug discovery and drug repurposing. We use these platforms for discovery of novel anti-cancer drugs and of biomarkers and towards function 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.

Bioclinicum

SciLifeLab

NKS and Pathology



Photos: H. Flank



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

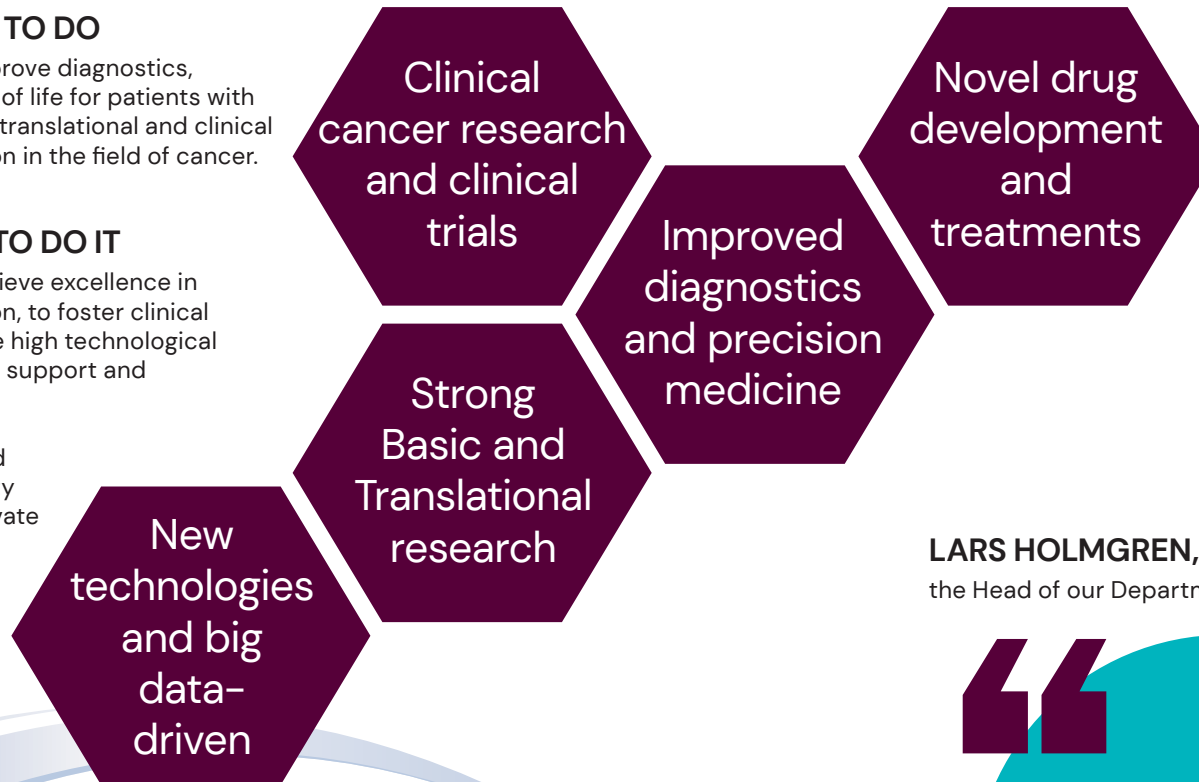
WHAT WE WANT TO DO

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 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."



Photo: H. Flank

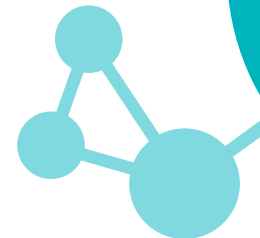
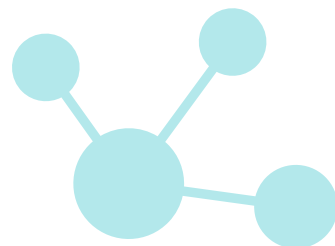
OUR NETWORKS ARE:



Cancer Research KI – network at Karolinska institutet
ki.se/en/cancerresearchki/cancer-research-ki



Cancer Core Europe – European Cancer Association
cancercoreeurope.eu/karolinska



Clinical cancer research

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 chemotherapy¹, 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.

1. Foukakis T, et al. Effect of tailored dose-dense chemotherapy vs standard 3-weekly adjuvant chemotherapy on recurrence-free survival among women with high-risk early breast cancer: A randomized clinical trial. *JAMA* 2016; 316: 1888-96.

2. Brandberg Y, et al. Long-term (up to 16 months) health-related quality of life after adjuvant tailored dose-dense chemotherapy vs. standard three-weekly chemotherapy in women with high-risk early breast cancer. *Breast Cancer Res Treat* 2020; 181: 87-96.

3. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Increasing the dose intensity of chemotherapy by more frequent administration or sequential scheduling: a patient-level meta-analysis of 37 298 women with early breast cancer in 26 randomised trials. *Lancet* 2019; 393:1440-52.

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.

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. *Oncolmmunology* 2020, VOL. 9, NO. 1, 1-11

THEO FOUKAKIS,

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



Our mission 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."



Novel Drug Discovery and Biomarkers

TARGETING THE DNA DAMAGE RESPONSE

Understanding the basic science of DNA repair is key to develop novel treatment concepts, targeting proteins with small molecules. We work in multidisciplinary teams to combine our groundbreaking and strong basic understanding of cancer biology with novel technologies and expertise in drug discovery to perform translational research and identify and develop novel treatments.

In 2005 the Helleday team demonstrated that targeting the enzyme PARP was a promising anti-cancer therapy for BRCA mutated cancer, harnessing a novel synthetic lethal concept for treatment of cancer. This treatment is now approved in BRCA mutated ovarian, breast, prostate, and pancreatic cancers and widely used in the oncology clinic. Since then, the team has developed inhibitors to oxidative DNA repair proteins MTH1 and OGG1, which are promising strategy for treatment of cancer and inflammation, evaluated in clinical trials. Recently, compounds that increase the repair by OGG1 have been characterized and a novel way of targeting the DNA damage response through cancer-specific metabolism.

1. Bryant H.E. et al. ... Helleday T. Specific killing of BRCA2-deficient tumours with inhibitors of poly(ADP-ribose) polymerase *Nature* 2005, 434, 913-7.
2. Gad H. et al. ... Helleday T. MTH1 inhibition eradicates cancer by preventing sanitation of the dNTP pool. *Nature*. 2014, 508(7495):215-21.
3. Visnes T. et al. ... Helleday T. Small-molecule inhibitor of OGG1 suppresses proinflammatory gene expression and inflammation. *Science* 2018, 16;362(6416):834-839.
4. Michel M. et al. ... Helleday T. Small molecule activation of OGG1 increases base excision repair by gaining a new enzymatic function. *Science* 2022, 376(6600):1471-1476.
5. Bonagas N. et al. ... Helleday T. Targeting MTHFD2 kills cancer via thymineless-induced replication stress. *Nature Cancer* 2022 3(2):156-172.

BIOMARKERS AND DRUG TARGETS IN THE TUMOR MICROENVIRONMENT

Cancer-associated fibroblasts (CAFs) is an important but poorly characterized cell type. The Östman group aims to better understand how CAFs contribute to tumor growth, and to exploit these cells as biomarkers and drug targets. Monika Ehnman's Team has a special focus on the understudied sarcoma micro-environment.

The group have identified novel pro-tumoral and anti-tumoral CAFs. Importantly, CAF composition of tumors shows large variation and associates with tumor aggressiveness and treatment response. One type of CAFs was found to predict radiotherapy response in breast cancer patients. Findings have been patented and are now being developed with a diagnostics company for validation and commercialization.

Most studies are collaborations with oncology and pathology experts as partners. Also, collaborations with SciLifeLab allow competitive and innovative tumor biology research and drug discovery efforts.

1. Pellinen T. et al. Fibroblast subsets in non-small cell lung cancer: associations with survival, mutations, and immune features. *J Natl Cancer Inst.* 2022, doi: 10.1093/jnci/djac178.
2. Strell C. et al. High PDGFRb Expression Predicts Resistance to Radiotherapy in DCIS within the SweDCIS Randomized Trial. *Clin Cancer Res.* 2021, 27(12): 3469-3477.
3. Strell C. et al. Impact of Epithelial-Stromal Interactions on Peritumoral Fibroblasts in Ductal Carcinoma in Situ. *J Natl Cancer Inst.* 2019, 111(9): 983-995.

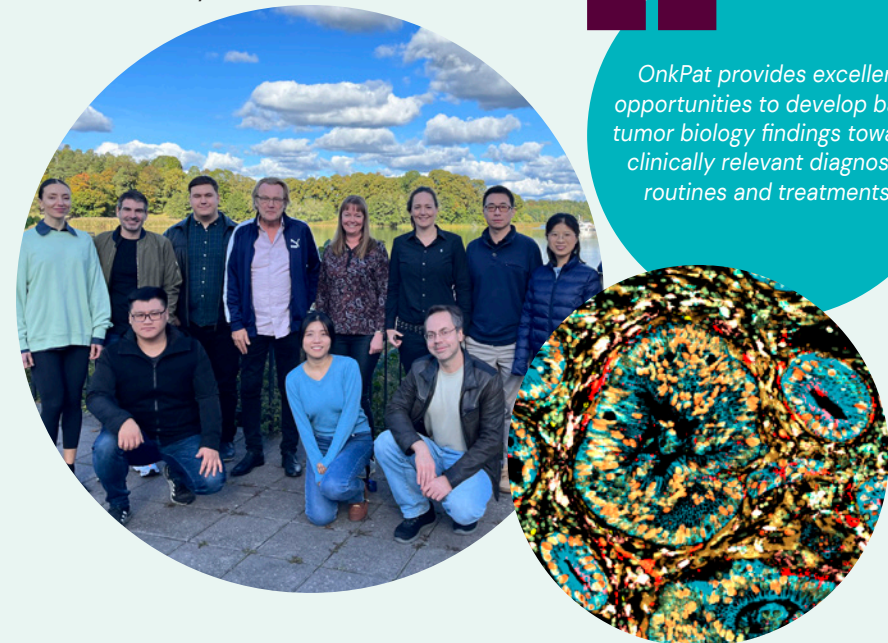
THOMAS HELLEDAY,
Professor, says:



Photos: H. Flank

“Multidisciplinary teams working together with scientists across the planet, both in academia and industry, is the key to our success”

ARNE ÖSTMAN,
Professor, says:

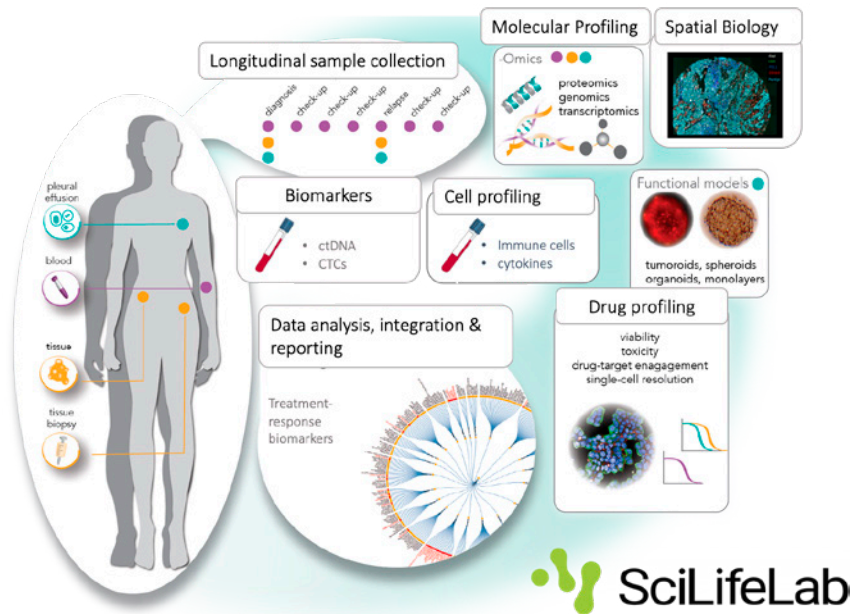


“OnkPat provides excellent opportunities to develop basic tumor biology findings towards clinically relevant diagnostic routines and treatments”

Photo: Linglong Huang

Precision Cancer Medicine Research

We are building a strong Precision Cancer Medicine (PCM) platform utilizing SciLifeLab technologies and in collaboration with Karolinska University Hospital. The combination of genomic and phenotype-level molecular profiling (multiomics) linked to drug efficacy profiling can improve how we match patients to potential treatments. The systematically generated data can also be applied to optimize drug discovery and development as well as help designing clinical trials for the cancer subtypes most likely to be responsive to the identified drugs or drug combinations.



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"



Photos: H. Flank



SOME OF OUR DISCOVERIES AND ACHIEVEMENTS

The way in science: future GROUP leaders

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."

1. Paulsson JO, et al., Whole-genome sequencing of synchronous thyroid carcinomas identifies aberrant DNA repair in thyroid cancer dedifferentiation. *J Pathol.* 2020 Feb;250(2):183-194.

2. Hysek M, et al., Clinical Routine TERT Promoter Mutational Screening of Follicular Thyroid Tumors of Uncertain Malignant Potential (FT-UMPs): A Useful Predictor of Metastatic Disease. *Cancers (Basel).* 2019 Sep 26;11(10):1443

3. Juhlin CC, et al., Parafibromin immunostainings of parathyroid tumors in clinical routine: a near-decade experience from a tertiary center. *Mod Pathol.* 2019 Jul;32(8):1082-1094.

HILDUR HELGADOTTIR

MD, PHD, TEAM LEADER IN J. HANSSON GROUP AT BIOCLINICUM

"I am an oncology consultant at Karolinska University Hospital and my research involves hereditary melanoma, melanoma epidemiology and treatments for metastatic melanoma and other skin cancers. The melanoma oncology field has been revolutionized by novel effective immuno- and targeted therapies. We have recently initiated a phase II trial with a goal to increase the efficacy of immune checkpoint inhibitors by adding high dose precision radiation to melanoma metastasis (the PROMMEL study). In my team we also want to discover factors that can predict treatment outcome and efficacy in different groups of melanoma patients. Thus, we showed that carriers of inherited CDKN2A mutations had inferior survival. However, we also demonstrated for the first time a high efficiency of immunotherapy in such melanoma patients suggesting them as good candidates for this treatment."

1. Spagnolo et al. Efficacy of BRAF and MEK Inhibition in Patients with BRAF-Mutant Advanced Melanoma and Germline CDKN2A Pathogenic Variants. *Cancers.* 2021, 18;13(10):2440.

2. Helgadóttir H et al. Multiple primary melanoma incidence trends over five decades, a nationwide population-based study. *J Natl Cancer Inst.* 2021, 113(3):318-328.

3. Helgadóttir H et al. Efficacy of novel immunotherapy regimens in metastatic melanoma patients with germline CDKN2A mutations. *J Med Genet.* 2020, 57(5):316-321, Epub 2018

4. Helgadóttir H et al. Germline CDKN2A Mutation Status and Survival in Familial Melanoma Cases. *J Natl Cancer Inst.* 2016, 108(11).

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."



HILDUR HELGADOTTIR,

MD, PhD, says:



My goal as a clinician and researcher, is to provide effective therapies to patients with melanoma and other skin cancers. In my team, we evaluate in clinical studies novel biomarkers for immune- and targeted therapy efficiency in metastatic melanoma"



Photos:
H. Flank
S. Zimmerman

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 GRADUATE 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.
- 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.

NICK TOBIN,

PhD, Principal Researcher and Director of Undergraduate Studies says:



Our department prides itself on providing the highest quality of education through the integration of expert basic and clinical researchers throughout our programs.

We consistently promote youth and see teaching as a means to support the long-term future of our researchers, whilst also attracting talented students who are interested in solving complex tumor biology and oncology questions"

SVETLANA BAJALICA LAGERCRANTZ,

M.D., PhD, Team Leader and 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 University Hospital and SciLifeLab 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.

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

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.




Breakfast
gatherings
Annual
Conference



Kick-off
International
Party
Seminars



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.



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.



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.

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 Rindsjö, erika.rindsjo@ki.se

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.

