BREAKOUT SESSIONS

XXIII Cancer Research KI Retreat

28-29 September, 2025

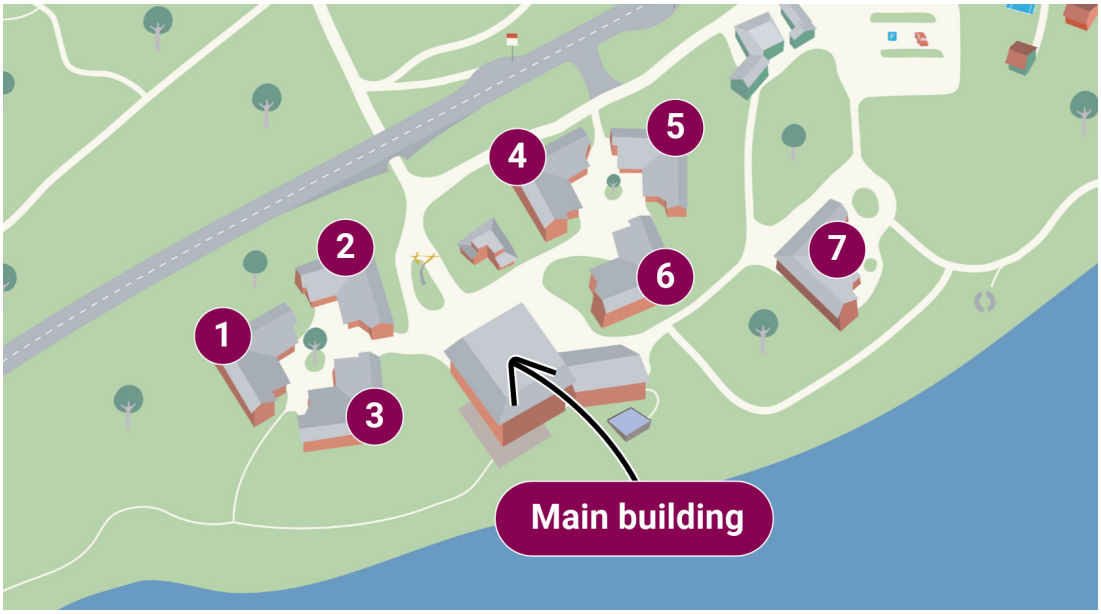
Djurönäset

BREAKOUT SESSIONS

Monday 28, 16:00 - 17:30

The sessions will take place simultaneously in various smaller rooms throughout the Djurönäset complex. Please **refer to the map below to find your way to the correct session**.

Keep in mind that **session capacity is limited**, and **you must attend the session you registered for**. If you have not registered for a session or experience any difficulty finding your room, please approach a member of the Cancer Research KI staff for assistance.



Breakout session 1: Patient Perspectives

Pancreatic Cancer
Marco Gerling, House 4 (Room 4A)

Childhood Cancer
Anna Nilsson, House 5 (Room 5A)

Breakout session 2: Scientific Presentations

Chair: **Dhifaf Sarhan**

House 7 (Conference Room 7A)

Breakout session 3: The AI Landscape at KI

Robert Svebeck, Development Officer, Department of Clinical Neuroscience, Karolinska Institutet

House 3 (Room 3A)

Breakout session 4: Meet the Scientist

Prof. Elaine Fuchs, House 1 (Coffee Lounge)

Dr. Joan Massagué, House 2 (Coffee Lounge)

Prof. Nicholas McGranahan, House 3 (Coffee Lounge)

MEET THE SCIENTIST

Elaine Fuchs

Rebecca C Lancefield Professor

Howard Hughes Medical Institute, The Rockefeller University, New York, USA

Location: House 1, Coffee Lounge

About Prof. Elaine Fuchs

Elaine Fuchs is renowned for her research in skin biology, its stem cells and associated disorders, including cancers and inflammation, and has published >380 manuscripts. She received her Ph.D. from Princeton, postdoctorate at MIT, and has been faculty at University of Chicago and now Rockefeller University, where she is an Investigator of the Howard Hughes Medical Institute. Her awards include the National Medal of Science, L'Oreal-UNESCO Award, International Society for Stem Cell Research Innovation Award, the Gairdner International Award and most recently the Franklin Medal. Fuchs holds membership in the National Academy of Sciences, National Academy of Medicine, American Philosophical Society, Pontifical Academy of Sciences, and the Royal Society.

Joan Massagué

Director

Sloan Kettering Institute, Memorial Sloan Kettering Cancer Center, New York, USA

Location: House 2, Coffee Lounge

About Dr. Joan Massagué

Joan Massagué (Barcelona, 1953), received a PhD degree in Pharmacy and Biochemistry from the University of Barcelona in 1978, postdoctoral training at Brown University (1979-1981), and a faculty appointment at the University of Massachusetts Medical School (1982-1989). He joined Memorial Sloan Kettering Cancer Center in 1989 as Chair, Cell Biology Program (1989–2003), Chair, Cancer Biology and Genetics Program (2003–2013), and Director, Sloan Kettering Institute (2014–), where he holds the Marie-Josée and Henry R. Kravis Chair. He was a HHMI Investigator from 1990 until he became HHMI Scientific Advisor in 2014. He was Adjunct Director (2004-2013) and Advisory Board Chair (2014–) of the Institute for Research in Biomedicine Barcelona.

Joan Massagué's scientific contributions have advanced our understanding of signaling pathways and transcriptional programs that maintain tissue integrity or promote cancer metastasis. He elucidated the TGF-β signal transduction pathway from membrane receptors to nuclear target genes. With his team, Massagué defined mechanisms by which TGF-β regulates cell proliferation, differentiation, immune reactivity, phenotypic plasticity, and survival. He explained how TGF-β turns from tumor suppressor to pro-metastatic signal during cancer progression. He went on to discover central principles and molecular mechanisms driving cancer cell dissemination, dormancy, immune evasion, and organ-specific metastasis. His work has opened new avenues for the prevention and treatment of cancer relapse.

Massagué is a member of the US National Academy of Sciences, National Academy of Medicine, American Academy of Arts and Sciences, European Molecular Biology Organization, and the Spanish Royal Academies of Medicine and of Pharmacy. He received the Prince of Asturias Prize, BBVA Frontiers Prize, Vilcek Prize, Pezcoller-AACR International Award, and Brupbacher Prize, among many other honors.

Nicholas McGranahan

Professor of Cancer Evolution

University College London, Cancer Institute, London, United Kingdom

Location: House 3, Coffee Lounge

About Prof. Nicholas McGranahan

Professor Nicholas McGranahan is a leading researcher in cancer evolutionary biology, applying evolutionary principles to understand how cancers develop, spread, and evade the immune system. Based at the UCL Cancer Institute, where he leads a research group focused on cancer evolution and genome instability and holds a position within the CRUK Lung Cancer Centre of Excellence, his work addresses a central question: if cancers evolve, can understanding the rules of that evolution help us predict - and ultimately better treat - them?

His research spans the natural history of lung cancer, from the genomic events that shape primary tumours to the evolutionary processes underlying metastasis and treatment resistance. He is a computational lead on the TRACERx study, one of the world's largest prospective longitudinal studies of tumour evolution, and co-leads analysis of the PEACE post-mortem study. Through this work, he has contributed important insights into intratumour heterogeneity, clonal neoantigens, genomic instability, and the evolving relationship between cancer and the immune system.

Professor McGranahan also develops computational approaches for reconstructing tumour evolution , allowing researchers to infer how individual cancers have changed over time and across metastatic sites and in response to the immune system. His work has been published in Nature, Science, and Cell and has contributed to the growing understanding of cancer evolution as both a fundamental biological process and a potential framework for improving cancer treatment.

PATIENT PERSPECTIVES

Pancreatic Cancer

Chair: **Marco Gerling**

Location: House 4 (Room 4A)

About Marco Gerling

Marco Gerling is a physician-scientist and oncologist specializing in upper gastrointestinal cancers at Karolinska University Hospital, where he combines clinical practice with translational cancer research. As Group Leader at Karolinska Institutet, he investigates how cancer cells interact with and reshape healthy tissues as they invade organs such as the liver and pancreas and spread to distant sites. His research focuses on the dynamic interplay between malignant and non-malignant cells at the tumor interface, exploring how these interactions enable tumor growth, tissue remodeling, and metastatic dissemination.

A central aim of his work is to understand how tumors induce the atrophy and replacement of healthy organ tissue, and how these processes contribute to cancer progression. By uncovering the biological mechanisms that govern cancer cell-host interactions, his research seeks to identify novel predictive and prognostic biomarkers and reveal new opportunities for therapeutic intervention.

In addition to his research and clinical responsibilities, Gerling is actively involved in cancer research training and scientific leadership. He serves as Co-Director of Cancer Research KI and is a member of the steering board of the FoTO doctoral programme in Tumor Biology and Oncology, where he contributes to advancing translational cancer research and supporting the next generation of cancer scientists.

Childhood Cancer

Chair: **Anna Nilsson**

Location: House 5 (Room 5A)

About Anna Nilsson

Anna Nilsson is Professor at Karolinska Institutet and Senior Consultant in Pediatric Oncology and Head of Department at Karolinska University Hospital. She combines clinical leadership with research focused on the long-term function of the immune system in children treated for cancer. Her work seeks to understand how cancer therapies and immunomodulatory treatments affect the cells responsible for maintaining lasting immune protection.

A particular focus of her research is the biology of antibody-producing plasma cells and the supportive cellular environments that sustain them within the bone marrow. Children who receive chemotherapy often lose protective antibodies acquired through previous vaccinations, and revaccination does not always fully restore immunity against diseases such as measles and tetanus. Through both experimental and translational studies, Nilsson investigates the mechanisms underlying these effects and explores how different immunomodulatory treatments influence immune memory and antibody responses.

By advancing our understanding of long-term immune protection after cancer treatment, her research aims to improve the health and quality of life of childhood cancer survivors. Beyond her research and clinical work, she plays an active role in strengthening the cancer research community as Co-Director of Cancer Research KI, fostering collaboration across disciplines and supporting the translation of scientific discoveries into improved patient care.

SCIENTIFIC PRESENTATIONS

Scientific Presentations

Location: House 7 (Conference Room 7A)

Program

16:00 - 16:10 **Sara Abu Ajamieh**
"Advancing Precision Therapy for ALK-MYCN Amplified Neuroblastoma Using Patient-Derived Models"

16:15 - 16:25 **Andrä Brunner**
"A MYCN–FBXL12–FANCD2 axis maintains replication stress tolerance and defines therapeutic vulnerabilities in high-risk neuroblastoma"

16:30 - 16:40 **Ewa Kurzejamska**
"METTL5–RNA Polymerase I Drives Ribosome Biogenesis Fueling Endothelial Cell Plasticity and Angiogenesis"

16:45 - 16:55 **Ning Xu Landén**
"Radiotherapy-induced epigenetic memory impairs skin repair"

17:00 - 17:10 **Lionel Leck**
"In Vivo Evolutionary Selection Strategy for Tumour-Targeting DNA Nanostructures in Neuroblastoma"

17:15 - 17:25 **Celina Limbecker**
"The tumor–pancreas interface in pancreatic neuroendocrine tumors: linking vascular remodeling and peritumoral atrophy to modes of tumor invasion"

Sara Abu Ajamieh

PhD Student

Department of Women's and Children's Health

Time and location: 16:00, House 7

Advancing Precision Therapy for ALK-MYCN Amplified Neuroblastoma Using Patient-Derived Models

Neuroblastoma, the most common extracranial pediatric solid tumor, accounts for ~7% of childhood cancers. ALK amplification, frequently co-amplified with MYCN, occurs in ~4.5% of high-risk cases, and is associated with significantly inferior survival (28% vs. 51% in non-ALK-amplified high-risk disease), highlighting a critical unmet therapeutic need. However, resistance to ALK inhibition and the rarity and heterogeneity of ALK-driven disease continue to hinder clinical advances.

To address this, we established and comprehensively characterized orthotopic patient-derived xenograft (PDX) models and matched 3D organoids from MYCN/ALK-amplified neuroblastoma. Molecular and phenotypic analyses across patient tumor, PDX tumors, and tumor-derived organoids demonstrated preservation of key tumor features, including small round blue cell morphology, an undifferentiated proliferative phenotype, and robust IHC positivity for N-MYC and ALK, as well as active downstream ALK signaling (p-AKT, p-ERK). Metastatic dissemination to the lung interstitium was also observed in a PDX model.

Functional drug screening revealed enhanced sensitivity of PDX-derived organoids to next-generation ALK inhibitors, with lorlatinib, neladalkib, and repotrectinib demonstrating superior potency compared to first-generation (R)-crizotinib and second-generation ensartinib. Together, these models closely recapitulate aggressive ALK-driven neuroblastoma and provide a robust translational platform for investigating resistance mechanisms and evaluating ALK-targeted therapeutic strategies. Our findings support the clinical development of next-generation ALK inhibitors to improve outcomes in this high-risk neuroblastoma patient subgroup.

Andrä Brunner

Research specialist

Department of Cell and Molecular Biology

Time and location: 16:15, House 7

A MYCN–FBXL12–FANCD2 axis maintains replication stress tolerance and defines therapeutic vulnerabilities in high-risk neuroblastoma

Neuroblastoma (NB) is the most common malignancy in infancy, with survival rates of ~50% for high-risk disease despite intensive multimodal therapy. Amplification of the MYCN oncogene drives aggressive disease and induces chronic replication stress (RS), yet the mechanisms that sustain tolerance to this stress in MYCN-driven tumours remain incompletely understood.

We previously demonstrated that the multimeric SCF–FBXL12 ubiquitin ligase supports RS tolerance in cancers by targeting CHK1-phosphorylated FANCD2 for proteasomal degradation, indicating that FBXL12 could be an attractive therapeutic target in RS–driven cancers. Here we show that FBXL12 expression is elevated in high-risk NB and predicts poor outcome independently of other clinical variables, with the strongest association in MYCN-amplified tumours.

Depletion of FBXL12 in MYCN-amplified NB cells stabilises FANCD2, elevates RS, and slows cell cycle progression, while improving survival in an NB xenograft model. Loss of FBXL12 increases DNA damage in S phase and impairs mitotic DNA synthesis (MiDAS), resulting in G1 phase lesions indicative of unresolved replication stress transmitted across cell cycles. Silencing of FANCD2 rescues these phenotypes, indicating that aberrant FANCD2 stabilisation underlies the compromised cell fitness upon FBXL12 depletion. Conversely, MYCN depletion attenuates DNA damage in S phase but not in G1, suggesting distinct roles for MYCN in RS induction and resolution.

Mechanistically, FANCD2 and MYCN co-localise at replication forks, and FANCD2 chromatin association declines upon MYCN depletion in an FBXL12-dependent manner, implicating MYCN in the regulation of FANCD2 fork residence. FBXL12 interacts with MYCN in NB cells, and MYCN shields FANCD2 from FBXL12-mediated degradation, sustaining fork protection under MYCN-driven RS. FBXL12 loss additionally increases MYCN protein stability, consistent with feedforward amplification of RS tolerance following FBXL12 loss. Transcriptomic analysis reveals upregulation of MYCN target gene signatures and ATR pathway activity in FBXL12-deficient cells, and drug sensitivity profiling demonstrates hypersensitivity to ATR and mTOR pathway inhibition as independent vulnerabilities.

These findings define a MYCN–FBXL12–FANCD2 axis that sustains RS tolerance in high-risk NB. Its disruption functionally converts FANCD2 into a source of mitotic vulnerability and exposes therapeutically actionable dependencies on ATR and mTOR signalling.

Ewa Kurzejamska

Assistant Professor

Department of Laboratory Medicine

Time and location: 16:30, House 7

METTL5–RNA Polymerase I Drives Ribosome Biogenesis Fueling Endothelial Cell Plasticity and Angiogenesis

Ribosome biogenesis is classically viewed as a process supporting growth; however, its role in endothelial plasticity remains poorly understood.

Here, we identify a ribosome biogenesis program that specifies angiogenic endothelial tip cells and drives vascular sprouting. Tip cell formation is marked by elevated RNA polymerase I (Pol I) activity and selective engagement of the 18S rRNA m6A methyltransferase METTL5. We uncover a METTL5–Pol I complex that coordinates rRNA biogenesis with tip cell gene expression and angiogenic behavior, revealing a catalysis-independent function.

Targeting this pathway with Pol I inhibitors or endothelial-specific METTL5 deletion suppresses angiogenesis across in vitro, zebrafish, and mouse cancer models, reducing tumor growth and metastasis.

Together, these findings establish ribosome biogenesis as a functional driver of endothelial fate and highlight a therapeutically targetable mechanism in pathological angiogenesis.

Ning Xu Landén

Senior Lecturer / Associate Professor

Department of Medicine, Solna

Time and location: 16:45, House 7

Radiotherapy-induced epigenetic memory impairs skin repair

Radiotherapy is essential for cancer treatment, yet many survivors develop chronic skin fragility and poor wound repair months to years after exposure. Our study aimed to define how radiotherapy creates long-lasting regenerative failure in human skin and to identify targetable regulators of this process. We profiled paired irradiated and non-irradiated skin from breast cancer patients using ex vivo wound healing models, primary cell assays, DNA methylation profiling, and single-cell multi-omics integrating RNA-seq, ATAC-seq, and Nano-CUT&Tag. Key mechanisms were functionally validated in a murine radiation-wound healing model. Irradiated skin displayed an aging-like state with delayed wound closure, defective keratinocyte migration and proliferation, and impaired fibroblast function. In fibroblasts, chromatin accessibility profiling identified a primed thrombospondin 1 (THBS1) regulatory state, causing excessive THBS1 induction after injury; THBS1 inhibition improved ex vivo wound repair of previously irradiated human skin. In the epidermis, forkhead box M1 (FOXM1) was persistently reduced in proliferative basal keratinocytes. DNA methylation profiling revealed HCFC1 promoter hypermethylation, reduced HCFC1 expression, and diminished HCFC1 binding at the FOXM1 promoter, leading to sustained FOXM1 repression. Silencing HCFC1 or FOXM1 recapitulated irradiation-induced defects, whereas FOXM1 overexpression restored keratinocyte proliferation and accelerated wound closure. Single-cell multi-omics further revealed radiation-associated inflammation, cell-cycle suppression, and senescence-like states, with AP-1 linked to increased chromatin accessibility and KLF-family factors linked to reduced accessibility. Together, these findings reveal that radiotherapy imprints a durable epigenetic scar in human skin, locking regenerative cells into dysfunctional states and exposing new therapeutic opportunities to restore tissue repair.

Lionel Leck

SciLifeLab PULSE Fellow

Department of Oncology-Pathology, KI; Department of Microbiology, Tumor and Cell Biology, KI; SciLifeLab

Time and location: 17:00, House 7

In Vivo Evolutionary Selection Strategy for Tumour-Targeting DNA Nanostructures in Neuroblastoma

Background: Neuroblastoma (NB) is the most common extracranial solid tumour in children, with high-risk disease associated with poor survival. Current treatments rely on intensive multimodal therapy that often causes significant off-target toxicity. Although nucleic acid therapeutics offer strong gene-silencing potential, clinical translation is limited by poor tumour delivery and liver accumulation.

Here, we developed an in vivo evolutionary selection strategy to identify short ssDNA nanostructures (200-300 nt) from a computationally designed library that preferentially home to NB tumours. Structures contain diverse folding architectures. Constructs were conjugated to GD2, a clinically relevant NB surface marker. This agnostic system enables in vivo enrichment of tumour-binding nanostructures without prior knowledge of tumour-specific markers. The goal is to establish a modular delivery platform to enhance internalisation and tumour killing.

Methods: A diverse ssDNA nanostructure library (~200-300 nt) underwent five rounds of in vivo selection in SK-N-BE(2) NB xenograft mice. Each round involved tail-vein injection, one-hour circulation, tumour harvest, gDNA extraction, streptavidin pull-down purification, AMPure clean-up, PCR amplification, and nanostructure refolding prior to reinjection. Five empty-selection controls without mouse injection were included to assess PCR bias. Organ biodistribution was assessed using liver and spleen samples from R1 and R5 mice. Additional controls were included for background assessment. All samples underwent multiplexed nanopore sequencing.

Results: Following the first selection round (R1), DNA nanostructures were successfully recovered from tumour-derived gDNA and sequenced. Compared with the crude library, R1 showed a tighter read-length distribution with reduced long-tail noise above 400 nt, indicating improved construct integrity after in vivo circulation. Several fragment populations (17-18 nt) appeared enriched from crude to R1, suggesting early structural selection preferences. Approximately 85% of expected constructs were recovered, while ~15% aligned to the human genome, supporting in vivo stability and tumour recovery. Downstream analyses will apply a three-layer filtering strategy incorporating empty-selection controls, organ biodistribution, and background controls.

Conclusions and Future Directions: These findings establish a robust platform for in vivo selection of tumour-targeting DNA nanostructures. Top candidates will be evaluated as delivery ligands for nucleic acid therapeutics by combining tumour-binding nanostructures with gene-targeting payloads. Future studies will explore radiolabelled ligand conjugation for tumour-specific killing and plasma cytokine profiling to assess DNA library-associated toxicity. This work complements ongoing antisense oligonucleotide (ASO) development within the Karlsson Lab and AstraZeneca collaboration, supporting safer and more effective NB-targeted therapies.

Celina Limbecker

Affiliated to research / Medical doctor

Department of Clinical Science, Intervention and Technology - CLINTEC

Time and location: 17:15, House 7

The tumor–pancreas interface in pancreatic neuroendocrine tumors: linking vascular remodeling and peritumoral atrophy to modes of tumor invasion

Background: Tumor-cell infiltration into the host tissue is a marker of aggressiveness. Yet not all tumors grow invasively but instead are surrounded by a fibrotic capsule that separates the tumor from the adjacent parenchyma. Pancreatic neuroendocrine tumors (panNETs) provide a bona fide example of this phenomenon.

PanNETs arise from the endocrine cells of the pancreas and represent the second most common primary pancreatic malignancy. The growth patterns of these tumors range from encapsulation to aggressive invasion of tumor cells into the pancreas. Previous studies on panNET growth patterns have linked a high degree of encapsulation to a more indolent clinical behavior. Yet, it remains unclear which mechanisms drive panNET encapsulation and invasion, respectively.

Little is known about how panNET growth shapes the adjacent pancreas. We hypothesized that tumor-associated remodeling of the peritumoral pancreas may play a crucial role in capsule formation, and that the state of the peritumoral pancreas differs between areas of encapsulation and invasion.

Methods: This ongoing study aims to characterize the panNET–pancreas interface to understand the key mechanisms involved in encapsulation and invasion. Using a detailed manual histopathological annotation approach, we analyzed 49 consecutive panNETs resected at Karolinska University Hospital between 2010 and 2015. Across 238 whole-slide images comprising 62,674 individual annotations, we mapped the tumor invasion front, distinguishing areas of encapsulation from areas of invasion. In the peritumoral pancreas, we assessed the morphology of the vasculature and the degree of pancreatic atrophy.

Results: A high proportion of invasion along the tumor–pancreas interface correlated positively with the Ki-67 index ($p = 0.041$). Predominantly encapsulated panNETs trended toward improved recurrence-free survival ($p = 0.054$).

The morphology of the peritumoral pancreas differed markedly between predominantly encapsulated and predominantly invasive panNETs.

Encapsulation correlated with severe atrophy of the peritumoral pancreas ($p = 0.002$) and a high density of peritumoral vessels ($p < 0.001$). Peritumoral atrophy and vessel density were independently correlated ($p = 0.043$). Conversely, predominantly invasive panNETs were surrounded by less atrophic pancreas and displayed the lowest density of peritumoral vessels.

Discussion: Based on these findings, we propose a model of panNET encapsulation in which vascular and atrophic remodeling of the surrounding pancreas contribute to capsule formation. A high density of peritumoral vessels may reflect tumor-associated remodeling of the host

vasculature, potentially redirecting blood flow toward the tumor and promoting pancreatic atrophy. The fibrotic capsule may represent an advanced stage of this atrophic remodeling.

Future work will test this morphology-based model mechanistically and explore whether capsule formation can be promoted in areas of invasive tumor growth.

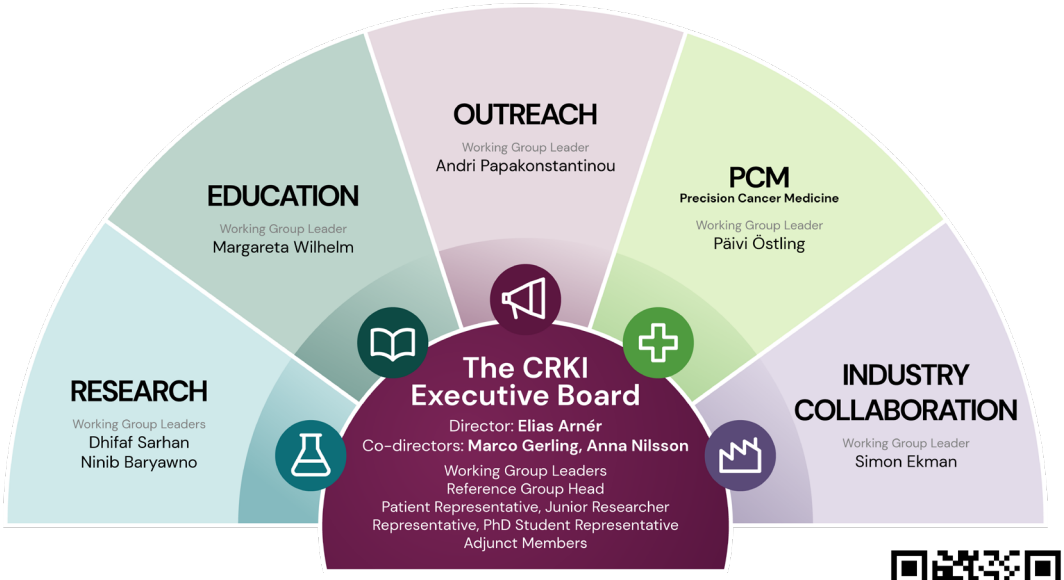
About Cancer Research KI

Our Mission:

To support the generation of new scientific discoveries that can be rapidly translated into clinical practice for the benefit of patients and society.

- An umbrella organization for cancer research at Karolinska Institutet
- A Strategic Research Program in Cancer since 2009 (formerly StratCan)
- An initiative that provides various types of support for all cancer researchers at KI
- A hub for communicating cancer research at KI to the general public

Over 400 PIs in cancer research representing 21 departments



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Please scan the QR code to access the website

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Our website is regularly updated with the latest news and events from Cancer Research KI

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