III Cancer Research KI PI Retreat

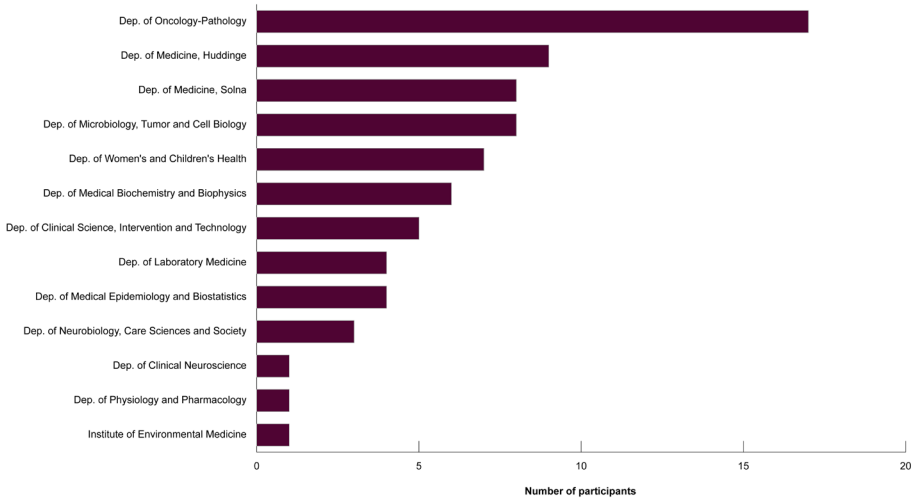
16-17 February, 2026

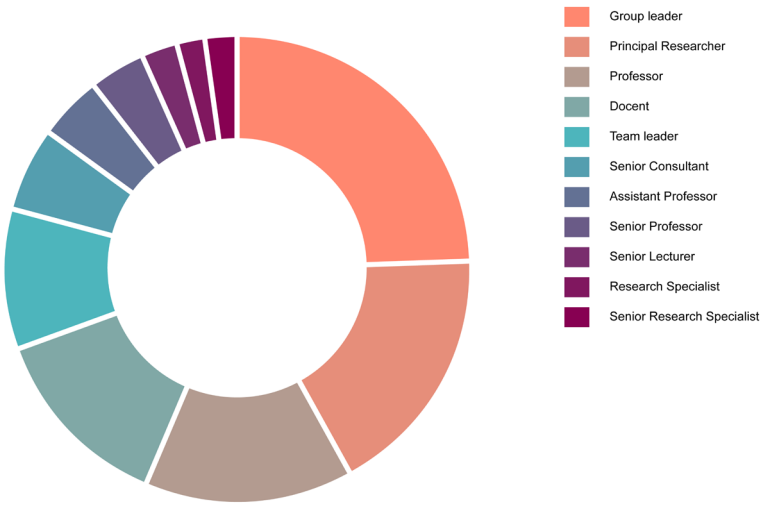
Sånga-Säby Conference Hotel

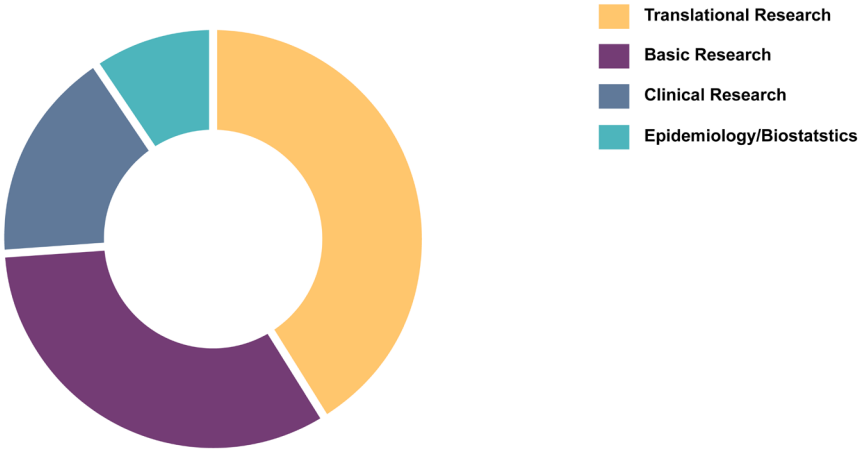
Welcome to the Cancer Research KI PI Retreat 2026

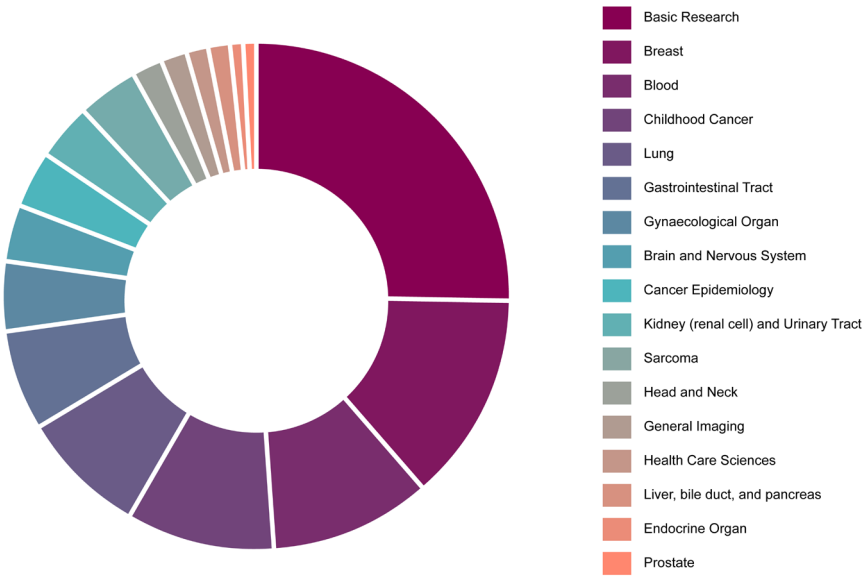
You are warmly welcome to a 2-day meeting with research presentations and networking opportunities, which is only open for PIs that head research groups at Karolinska Institutet within the field of cancer. The meeting will provide many possibilities for networking with other researchers within the cancer field, broadening your scientific horizons, and creating new possibilities for collaborations and funding initiatives. During the meeting, we will have oral presentations, elevator pitches, and sessions dedicated to important topics within cancer research.

We are happy to share that we will have 13 departments represented during the PI-retreat, from both Solna and Flemingsberg campuses, covering pre-clinical, translational, clinical and epidemiological research areas.









In this booklet you will find information about the attending researchers, including their research area, their needs for collaboration, a short description of their research, top publications and contact information. Using the search function in the PDF version of the abstract booklet you can easily find people and topics of interest to you. All retreat participants are listed in alphabetical order according to their last names.

This year, we will have four dedicated sessions which will address key strategic issues for the future of cancer research. You will find more information about the sessions and speakers details on the following pages.

Patient perspective and involvement in research

Patient and public involvement can benefit preclinical and clinical research, bringing new insights and perspectives, making the research more relevant to society, and promoting the use of findings in practice. During this session, Lise-lott Eriksson, Sophie Werkö and Andri Papakonstantinou will discuss the importance of patient perspective and involvement in research.

Lise-lott Eriksson is a Patient advocate active in Sweden and internationally since 2011, following a diagnosis of Essential Thrombocythemia (ET). She brings lived experience together with professional expertise in healthcare and research collaboration. Former physiotherapist with additional qualifications in healthcare science and business administration.

Founder and Chair of the Swedish blood cancer patient organisation Bloodcancerforum, established in 2023, focusing on policy development, patient access to innovative medicines, and meaningful patient involvement in research and clinical trials, as well as in drug development and Health Technology Assessment (HTA).

Former President and Board Member of Myeloma Patients Europe (MPE) and former Chair of the Swedish Blood Cancer Association. Currently patient representative in Cancer Research KI at Karolinska Institutet and member of the ESMO Patient Advocate Working Group, with a strong commitment to strengthening patient involvement as a core element of high-quality research.

Her take on the Patient perspective and involvement in research is: *“From my perspective as a patient advocate, patient involvement is not just about adding a patient voice at the end of a project, but about shaping research from the very beginning. When patients are meaningfully involved, research questions become more relevant, outcomes better reflect real-life needs, and the results are more likely to make a difference in patients’ everyday lives.*

Despite progress in recent years, patient involvement is still too often seen as optional rather than essential. When patient perspectives are missing, research may remain scientifically strong but risk being disconnected from the realities of living with disease. Strengthening patient involvement is therefore essential to ensure that research is relevant and meaningful from a patient perspective.”

Sophie Werkö has a PhD from the University of Stockholm. She has a longstanding engagement with HTA and started in HTA as Project Director at The Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU). She has over 15 years of experience leading, managing, and conducting evidence reviews in the field of HTA, translating research evidence, primarily for public policy decision makers and clinicians. This includes supervising, teaching and coordinating multidisciplinary research teams in conducting HTAs, including systematic evidence synthesis reports on clinical effectiveness, safety, cost-effectiveness and assessment of ethical and social aspects. She was part of the small team who developed SBU’s methodology for synthesis of studies with qualitative data collection and analysis and synthesis of patient-based evidence (PBE). For many years she led the work on Patient Involvement at SBU as well as the work by the Council for Knowledge-Based Policy’s working group on patient involvement, including participants from nine government agencies, which resulted in a common policy for patient engagement, approved in 2018. She is still very active in the work on Patient Involvement, both in Sweden and internationally.

Today she works as Director for International Relations at SBU and is currently representing Sweden in the EU Coordination Group under the EU HTA Regulation. She is Deputy editor for the International Journal of Technology Assessment (IJTAHC), member of the Editorial Board of Research Involvement and Engagement, and acts as reviewer and associate editor

in several scientific journals.

She became a patient representative in 2025, having been diagnosed with gynaecologic cancer in 2020 and recruited to a clinical trial the same year. She currently participates as a patient representative in Cancer Research KI Research Working Group and in the Scientific Committee for the Cancer Core Europe (CCE) Summer School.

Her take on the Patient perspective and involvement in research is: *"Patient involvement has historically been a neglected area for a long time, both in research and in practice. But over the last two decades, patient and public involvement (PPI) has become increasingly embedded as a concept in both research and in Health Technology Assessment (HTA). However, while patient involvement has become more common, it can still be seen as an optional extra, not always vital, or if missing, not seen as a fatal flaw in research or in HTA. Therefore, we must think about how we can strengthen patient involvement in research.*

The Patient involvement session on the importance of Patient involvement in research will include several perspectives. We'll start with the view from the patients, first from the patient organisations' perspective and then from the individual patient's perspective including comments of the value of research in this particular area. Then we'll move to a case example at KI and hear about patient involvement in a research project at KI."

Andri Papakonstantinou is a senior oncology consultant, head of the Unit of Breast Cancer, Endocrine tumors and Sarcoma oncology at the Karolinska Comprehensive Cancer Center and Leader of Cancer Research KI Outreach Working Group.

The gender perspective: inequalities in research

Gender inequality is still a long-standing problem in academia. Despite policy efforts at KI, national, and EU levels, gender inequalities persist in recruitment, promotion, leadership representation, and access to funding, thus shaping research priorities and, ultimately, patient outcomes. During this session, **Mia von Knorring**, Associate Professor in healthcare organization and program director for the FIELD program (Fellows in Gender Equal Career Development) and **Kristina Ullgren**, Equal Opportunities strategist & Coordinator at HR office at KI, will discuss:

- The current statistics on gender distribution and career progression at KI.
- Place these data in a broader national and global context.
- Highlight how gender inequality affects research careers, leadership, funding and, ultimately, patient outcomes.
- Share examples of successful strategies and concrete actions to promote gender equality and inclusive environments.

Infrastructure at KI and SciLifeLab: How to leverage what we have and build what we need

KI and SciLifeLab offer a wide range of service laboratories, competence centres and specialised equipment in areas such as imaging, biostatistics, biobanking, proteomics and genomics. This infrastructure is essential for moving cancer research forward and gives cancer researchers access to broad expertise and high-quality support. Therefore, it is important to understand what the infrastructure offers today and to help shape it's future so it continues to meet the needs of cancer research. During this session, **Karin Dahlman-Wright**, Chair of the KI board of infrastructure, and **Lars Holmgren**, Director of integration, SciLifeLab, will:

- Present the available infrastructure at KI and SciLifeLab.
- Describe how it can be used by researchers.
- Discuss the future of the infrastructure at KI and SciLifeLab.

Funding Landscape and Opportunities

Sweden's cancer research is strongly supported by **Barncancerfonden**, **Cancerfonden**, and **Radiumhemmets Forskningsfonder** - three major funders that provide stable, long-term support and enable collaboration between academia and healthcare. Barncancerfonden is the largest single funder of childhood cancer research in Sweden and supports both research and clinical studies to improve treatments and reduce side effects. Cancerfonden has supported Swedish cancer research for decades and made its largest investment so far in 2025, with over 1 billion SEK going to cancer research. Radiumhemmets Forskningsfonder focuses on patient-near cancer research, and in 2025 alone granted 102 million SEK, the largest distribution in the funds' 115-year history. During this session, **Mariette Nordzell**, Head of Unit, Research & Education from Barncancerfonden, **Annina Graan**, Head of Research Funding & **Joanna Bruzelius**, Research Funding Officer from Cancerfonden, and **Magdalena Nilsson**, Secretary General & **Mariann Eklund**, Economy Case Officer from Radiumhemmets Forskningsfonder will present:

- The long-term plans and scientific priorities for funding in cancer research.
- How the funding landscape will evolve in the coming years.
- The role and importance of patient involvement in funding calls.

We hope you have an enjoyable and fruitful retreat.

Welcome!

Dhifaf Sarhan and **Ninib Baryawno**
on behalf of the Organizing Committee

PRACTICAL INFORMATION

TRANSPORT & RETURN

Buses depart from Cityterminalen Monday, February 16th, at 8:30 (the extended terminal building at the Stockholm main railway station), entrance next to World Trade Center, Klarabergsviadukten. Check the monitors for a gate number for our buses “KI to Sånga”. The bus ride takes approximately one hour.

We return to the Stockholm City terminal on Tuesday afternoon, February 17th, approximately 17:00.

ARRIVAL AT SÅNGA-SÄBY

You will get a name badge when you arrive at the location of the meeting. We will be at SÖDRA Lecture Hall, located on the 2nd floor in the main building (see map). Please, wear the name badge visible throughout the conference. Coffee/tea and sandwiches are served prior to the conference that starts at 09:45. Our luggage will be stored temporarily until check-in time, which will be during the afternoon coffee break at 15:00. On the second day (Tuesday, February 17th), please check-out before the morning session at 8:30.

MEETING

The meeting will be held at SÖDRA lecture hall on floor 2, above reception, in the main building. The coffee breaks throughout the day and mingle will be held outside of the lecture hall (CAFE GUDRUN, see map). All presentations are given 10 min each. Please adhere to the allocated time! In addition, we hope that you will make the best possible use of breaks, free time, lunches and dinner, to connect and discuss possible joint interests with the other PIs attending the meeting!

MEALS - INTERNET - LEISURE

Breakfast, lunch and dinner will be served in the main building. Those of you who have informed us of special food requests please contact the serving staff in the restaurant. They have received the information beforehand.

Sånga-Säby's wireless net is free of charge. Log in: SangaGuest.

On the evening of 16th, the lake sauna and pool (overlooking Lake Mälaren) will be reserved exclusively for our group from 21:00–23:00. Drinks can be purchased at the sauna. Please, note that payment is by Swish only.

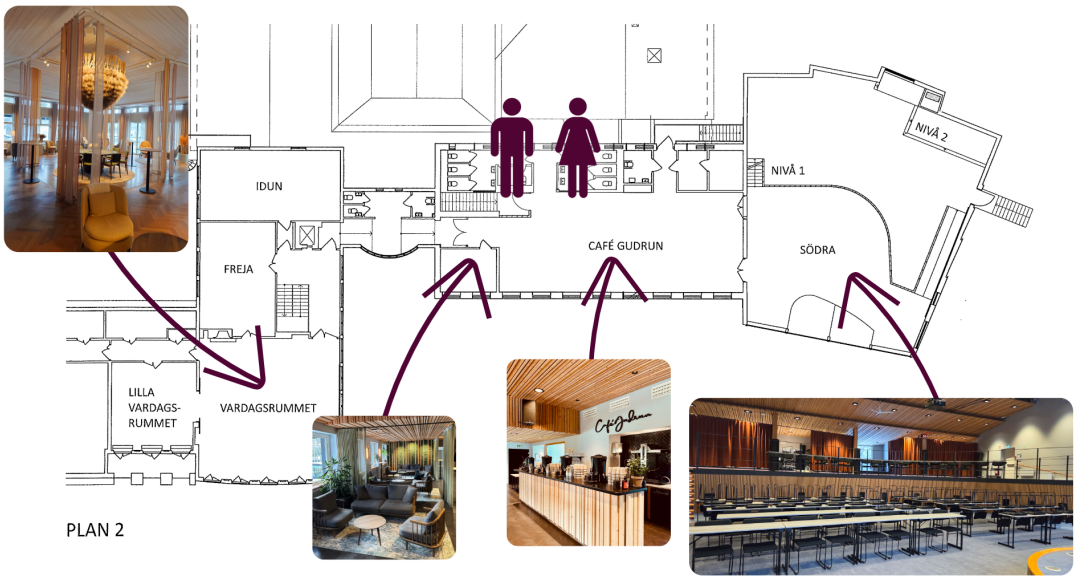
At the conference centre, you can also enjoy table tennis, shuffleboard, billiards, and boules in the lounge. The bar is open from 11:00 to 24:00 o'clock.

For more information about the hotel, please use this link.

PARKING

Parking is free, with plenty of spaces available. Accessible parking spaces are located directly in front of the main building. There are also 26 electric vehicle charging points on site.

We are looking forward to having you on board and we wish you a productive meeting and a pleasant stay!



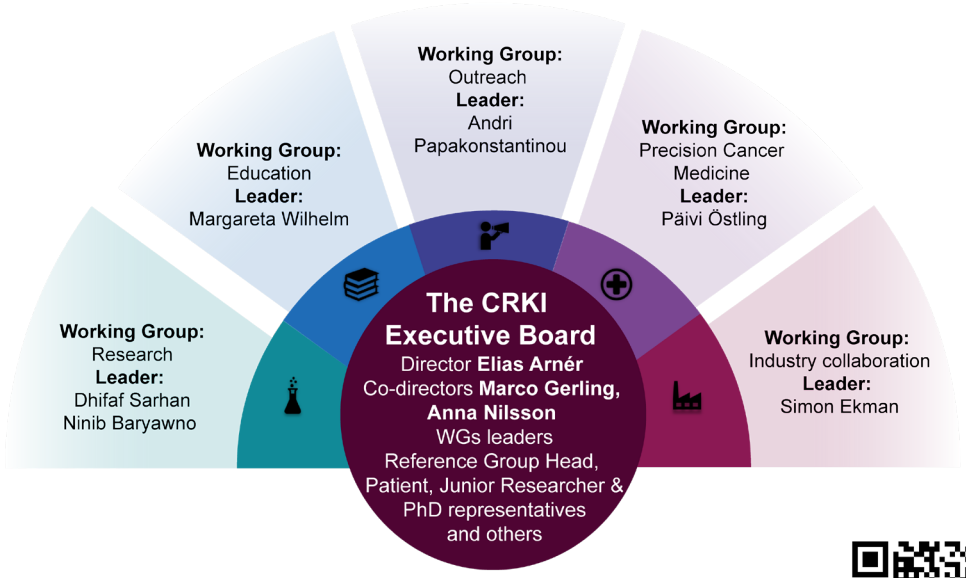
About Cancer Research KI

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 410 PIs in cancer research representing 21 departments



More information about the Executive Board is available online
Please scan the QR code or visit our website

About the Cancer Research KI PI Database

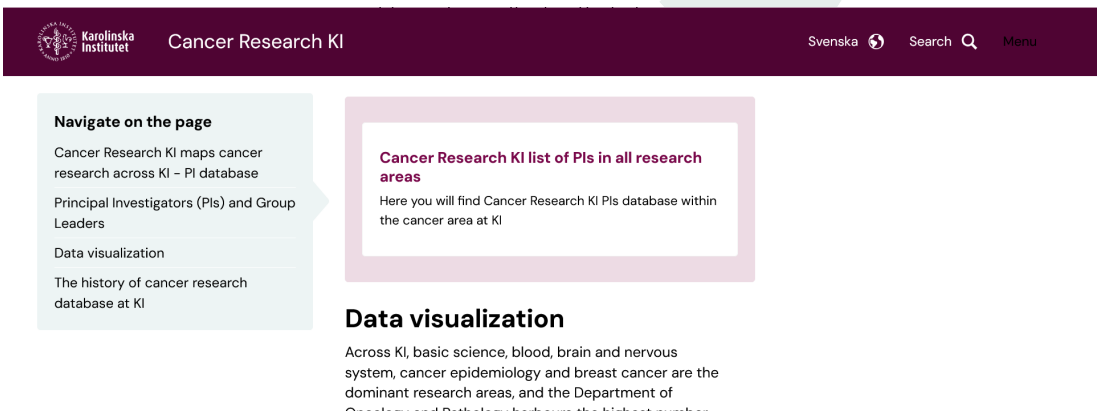
Cancer Research KI aims to map all principal investigators (PIs) and group leaders at KI to increase the visibility and facilitate internal, international, industrial collaborations.

A principal investigator (PI) at Cancer Research KI leads a research group, with personal responsibility for directing their research, managing their budget and their personnel. Specifically, every PI typically:

- Has their own funding in accounts controlled by them
- Supervises students and postdocs
- Teaches undergraduates and/or doctoral students and/or clinical trainees
- Publishes their own research, often as senior author
- Takes academic and/or clinical leadership responsibilities
- Upholds the highest standards of ethical behaviour

If you know a KI-based group leader/PI engaged in some cancer-related research and their name is not included in the database, then we would like to hear from you! Send us the name of the PI by email at cancerresearchki@ki.se and we will invite them to be part of Cancer Research KI database.

Visit the CRKI PI Database!



The Cancer Research KI PI Retreat 2026

Organizing Committee

Dhifaf Sarhan

Ninib Baryawno

Hanna Brauner

Ourania Kostopoulou

Sophie Werkö

Keith Humphreys

Ioannis Zerdes

Twana Alkasalias

Stefina Milanova

Pablo Martí Andrés

Liselotte Bäckdahl

Booklet design: Pablo Martí Andrés

Photos: Sånga-Säby Conference Hotel

PROGRAM

Monday, February 16

08:30 Bus departs from Stockholm Cityterminalen

09:15 Arrival, coffee and registration

09:45 - 10:10 **Welcome**
Elias Arnér, Dhifaf Sarhan and Ninib Baryawno

Morning Session 1
Chair: **Nikolas Herold**

10:10 – 10:20 **Klas Wiman**, Department of Oncology-Pathology
Cancer precision medicine by targeting missense and nonsense mutant TP53

10:25 – 10:35 **Taras Kreslavsky**, Department of Medicine, Solna
Dissection of gamma-delta T cell antigen specificities in health and disease

10:40 – 10:50 **Antonino Cassotta,** Department of Medicine, Huddinge
Mapping myeloma-reactive T cells to develop novel adoptive cell therapies for multiple myeloma

10:55 – 11:05 **Xiaofei Li**, Department of Neurobiology, Care Sciences and Society
Targeting the Untargetable: A Novel Approach to Pediatric Ependymoma Therapy

11:10 – 11:40 **Coffee Break**

Morning Session 2
Chair: **Hanna Brauner**

11:40 – 11:50 **Alexios Matikas**, Department of Oncology-Pathology
Investigating the effect of (neo)adjuvant chemotherapy for early breast cancer: clinical and molecular correlations

11:55 – 12:05 **Marie Arsenian Henriksson**, Department of Microbiology, Tumor and Cell Biology
Metabolic reprogramming by MYC inhibition as precision medicine in clear cell renal carcinoma and childhood neuroblastoma

12:10 – 12:50 **Patient perspective and involvement in research**
Lise-lott Eriksson, Cancer Research KI Executive Board member, Founder and Chair of Blodcancerforum
Sophie Werkö, Patient representative, Cancer Research KI Research WG member, Director for International Relations at SBU
Andri Papakonstantinou, Department of Oncology-Pathology

12:50 – 13:00 **Group Photo**

13:00 – 14:00 **Lunch**

Afternoon Session 1
Chair: **Fredrik Wermeling**

14:00 – 14:10 **Carmen Gerlach**, Department of Medicine, Solna
From T cell subsets to axes of diversification – a novel conceptual framework for T cell diversification

14:15 – 14:25 **Tomas Sjöberg Bexelius**, Department of Women's and Children's Health
Molecular clock disruption and its consequence in childhood cancer, neuroblastoma

14:30 – 14:40 **Ana Teixeira,** Department of Physiology and Pharmacology
Mapping Her2 nanodomains in breast cancer cells

14:45 – 14:55 **Nikolas Herold,** Department of Women's and Children's Health
Deciphering drug-drug interactions in paediatric oncology

15:00 – 15:45 **Coffee Break and Check-in**

Afternoon Session 2
Chairs: **Dhifaf Sarhan** and **Ninib Baryawno**

15:45 – 16:45 **The gender perspective: inequalities in research**
Mia von Knorring, Associate Professor in healthcare organization and program director for the FIELD program (Fellows in Gender Equal Career Development), Department of Learning, Informatics, Management and Ethics
Kristina Ullgren, Equal Opportunities strategist & Coordinator, HR-office at KI

16:45 – 16:55 **Mikael Karlsson**, Department of Microbiology, Tumor and Cell Biology
Targeting immune cells in the tumor microenvironment to develop cure for cancer

17:00 – 17:10 **Fang Fang**, Institute of Environmental Medicine
Co-occurrence of cancer after mental disorders, phenotypic correlation, family coaggregation, genetic and environmental contribution

17:15 – 17:30 **Coffee Break**

Afternoon Session 3
Chair: **Ourania Kostopoulou**

17:30 – 17:40 **Elinor Nemlander**, Department of Neurobiology, Care Sciences and Society
The Stockholm Early Detection of Cancer Study (STEADY-CAN): expanding a population-based cohort to integrate sociodemographic and biomarker data for research on early cancer detection

17:45 – 17:55 **Tom Erkers**, Department of Oncology-Pathology
Functional Precision Medicine in Blood Cancers

18:00 – 18:10 **Hans Grönlund**, Department of Clinical Neuroscience
Bead-bound, personal neoantigens expand T cells from tumor regional lymph nodes (rLN) in colorectal cancer

18:15 – 18:30 **Patrik Blomquist**, KI Innovations
Venture building at KI

18:30 – 19:00 **Elevator Pitches**
Chair: **Twana Alkasalias**

Anita Göndör
Laszlo Szekely
Isabel Barragan
Karin Sundström
Erik Benson
Elias Arnér
Oscar Bedoya Reina
Hanna Brauner

19:00 – 20:00 **Mingle** (finger food available)

20:00 **Dinner**, followed by continued mingle

Tuesday, February 17

07:30 – 08:30 Breakfast and Check-out

Morning Session 1
Chair: **Ioannis Zerdes**

08:30 – 09:15 **Infrastructure at KI and SciLifeLab: How to Leverage What We Have and Build What We Need**
Karin Dahlman-Wright, Chair of the KI board of infrastructure
Lars Holmgren, Director of integration, SciLifeLab

09:15 – 09:25 **Susanne Gabrielsson**, Department of Medicine, Solna
Eliminating PD-L1 on dendritic cell extracellular vesicles for immunotherapy potentiates immune-mediated tumor rejection in mice

09:30 – 09:40 **Thomas Müller**, Department of Medicine, Huddinge
Tissue origin shapes human CD8+ T cell cytotoxicity

09:45 – 09:55 **Ingemar Ernberg**, Department of Microbiology, Tumor and Cell Biology
Rethinking cancer: unresolved enigmas in understanding the biology of nasopharyngal carcinoma (NPC)

10:00 – 10:30 **Coffe Break**

Morning session 2
Chair: **Brinton Seashore-Ludlow**

10:30 – 10:40 **Rainer Heuchel**, Department of Clinical Science, Intervention and Technology
Heterospheroid cell culture to identify new treatment options for pancreatic ductal adenocarcinoma

10:45 – 10:55 **Andreas Lennartsson**, Department of Medicine, Huddinge
Targeting Epigenetic and Transcriptional vulnerabilities in AML

11:00 – 11:10 **Mikael Benson**, Department of Clinical Science, Intervention and Technology
High-resolution computational models to prioritise early mechanisms, biomarkers and drug targets in malignant transformation

11:15 – 11:25 **Staffan Strömblad**, Department of Medicine, Huddinge
Mechanical regulation of cancer development and progression

11:30 – 12:30 **Lunch**

Afternoon Session 1
Chair: **Magdalena Paolino**

12:30 – 12:40 **Johan Hartman**, Department of Oncology-Pathology
Characterization of ER-low expressing breast cancers

12:45 – 12:55 **Helene Rundqvist**, Department of Laboratory Medicine
Exercise training reshapes the systemic immune environment in patients with metastatic breast cancer: results from the PREFERABLE-EFFECT multi-centre randomised-controlled trial

13:00 – 13:10 **Joakim Dillner**, Department of Clinical Science, Intervention and Technology
Center for Cervical Cancer Elimination: Advancing Strategies for HPV-Based Prevention

13:15 – 13:45 **Coffee Break**

13:45 – 15:15 **Funding Landscape and Opportunities**
Chairs: **Dhifaf Sarhan** and **Ninib Baryawno**

Mariette Nordzell, Head of Unit, Research & Education, *Barncancerfonden*
Annina Graan, Head of Research Funding & **Joanna Bruzelius**, Research Funding Officer, *Cancerfonden*
Magdalena Nilsson, Secretary General & **Mariann Eklund**, Economy Case Officer, *Radiumhemmets Forskningsfonder*

15:15 – 15:30 **Conclusion**

16:00 Bus departs to Stockholm Cityterminalen

ABSTRACTS

Twana Alkasalias

Assistant Professor

Division for Neonatology, Obstetrics, Gynaecology and Reproductive Health
Department of Women's and Children's Health
Solnavägen 9, 17165 Solna

0046 739558129

Cancer research areas:

Cancer initiation and prevention

Key research field interests:

Cancer initiation, 3D organoid models, Tumor microenvironment, Cancer prevention, Prophylactic treatments

Needs for collaboration:

- Proteomics
- Multi-omics and spatial biology data analysis

Selected publications:

1. Martin Widschwendter, Chiara Herzog, Mohammed Rasul, Nageswara Boggavarapu, Elisa Redl, Deborah Utjés, Angelique Flöter Rådestad, Kristina Gemzell- Danielsson, and Twana Alkasalias. (2026) Short-term hormonal modulation with mifepristone does not induce oncogenic changes in the endometrium of BRCA1/2 mutation carriers. Accepted in Commun. Med.
2. Redl E, Herzog C, Vavourakis C, Barrett J, Jones A, Evans I, Reisel D, Manchanda R, Bjørge L, Zikan M, Alkasalias T, Gemzell-Danielsson K, Dubeau L, MacDonald N, Jurkovic D, Pashayan N, Widschwendter M. (2026). The cervico-vaginal DNA methylation WID-qEC test: An epigenetic marker associated with ovarian cancer in the absence of endometrial and cervical cancer. Int J Cancer. Jan 29. doi: 10.1002/ijc.70354.
3. D. Utjés, N. R. Boggavarapu, M. Rasul, I. Koberg, A. Zulliger, S. Ponandai-Srinivasan, C. von Grothusen, P. G. Lalitkumar, K. Papaikonomou, Twana Alkasalias* and Gemzell K*. (2024). Transcriptomic profile of normal breast tissue post-mifepristone treatment: secondary outcomes of a randomized controlled trial. Int J Mol Sci. 2024 Jul 10;25(14):7590. doi: 10.3390/ijms25147590.

Human ex vivo models of early carcinogenesis to enable biomarker discovery and targeted cancer prevention

Cancer prevention for women at elevated inherited risk, particularly carriers of pathogenic BRCA mutations, remains an urgent yet challenging research priority. The complexity of early carcinogenesis, the limitations of current experimental systems, and the absence of e\ective non-surgical risk-reducing options underscore the need for physiologically relevant human models. Our research addresses this gap through a translational framework aimed at understanding and intercepting the earliest stages of breast, ovarian, and endometrial cancer development.

A central component of our work is the development of patient-derived ex vivo 3D organoid and mini-organ cultures that closely recreate human tissue architecture and microenvironment. These platforms allow us to model early oncogenic processes with a degree of fidelity that is not achievable in traditional cell lines or animal models. By incorporating epithelial and stromal elements, our systems enable the study of hormone-regulated cell state transitions and provide a versatile environment for testing preventive interventions.

Within this framework, we focus on delineating hormone-driven signaling pathways, particularly progesterone-mediated mechanisms implicated in BRCA-associated cancers. By integrating molecular, cellular, and functional analyses within our organoid systems, we aim to identify actionable nodes in early carcinogenesis that may serve as targets for non-invasive risk-reducing strategies.

In parallel, we pursue biomarker discovery for early detection and refined risk stratification, with the goal of strengthening predictive models for women at high genetic risk. Our translational approach further includes clinical prevention studies designed to bridge laboratory insights with real-world application.

Together, these e\orts aim to generate mechanistic understanding and clinically relevant tools that support earlier detection, personalized risk assessment, and the development of e\ective non-surgical cancer prevention strategies for high-risk women.

Elias Arnér

Professor
Division of Biochemistry
Department of Medical Biochemistry and Biophysics
Biomedicum, A9 quarter

0705569694

Cancer research areas:

Basic cancer biology

Key research field interests:

Redox pathways; Oxidative Stress; Antioxidant Defense; Intracellular Signaling

Needs for collaboration:

Happy to collaborate with groups having complementary expertise and shared interests. For a list of our current main collaborators, see https://ki.se/en/research/research-areas-centres-and-networks/research-groups/elias-arner-research-group#tab-collaborations

Selected publications:

1. Cheff, D.M., Huang, C., Scholzen, K.C., Gencheva, R., Ronzetti, M.H., Cheng, Q., Hall, M.D., Arnér, E.S.J. The ferroptosis inducing compounds RSL3 and ML162 are not direct inhibitors of GPX4 but of TXNRD1. Redox Biol. 62:102703 (2023)
2. Sabatier, P., Beusch, C.M., Gencheva, R., Cheng, Q., Zubarev, R., Arnér, E.S.J. Comprehensive chemical proteomics analyses reveal that the new TRi-1 and TRi-2 compounds are more specific thioredoxin reductase 1 inhibitors than auranofin. Redox Biol. 48:102184 (2021)
3. W. C. Stafford, X. Peng, M. H. Olofsson, X. Zhang, D. K. Luci, L. Lu, Q. Cheng, L. Trésaugues, T. S. Dexheimer, N. P. Coussens, M. Augsten, H.-S. M. Ahlzén, O. Orwar, A. Östman, S. Stone-Elander, D. J. Maloney, A. Jadhav, A. Simeonov, S. Linder, E. S. J. Arnér Irreversible inhibition of cytosolic thioredoxin reductase 1 as a mechanistic basis for anticancer therapy. Sci. Transl. Med. 10: eaaf7444 (2018)

Selenoproteins and redox biology in cancer - key pathways in control of signaling processes, cellular phenotypes and cell survival

Cellular reduction and oxidation (redox) processes are crucial in both physiological and pathological processes. Selenoproteins are particularly important in this context, which is a research field that we address with the following overriding questions:

- What specific roles do the selenoproteins thioredoxin reductase 1 (TrxR1, also named TXNRD1) and glutathione peroxidases 1 and 4 (GPX1 and GPX4) play in cancer, and how can drug targeting of these selenoproteins be utilized for the development of new and more efficient anticancer therapy protocols?
- How do redox modulated transcription factors underpin the effects of selenoprotein targeting, including Nrf2, NFkappaB, HIF and STAT3 in specific cell types, and what molecular mechanisms link these redox regulated signaling pathways to specific selenoproteins?

Our studies give important insights into the roles of TXNRD1 and GPX isoenzymes as targets for anticancer therapy, specifically aimed at better understanding the roles of these selenoprotein in redox signaling pathways, underpinning the potential development of new anticancer therapy protocols.

Marie Arsenian Henriksson

Professor

Tumor Biology
Department of Microbiology, Tumor and Cell Biology
Biomedicum B7, Solnavägen 9, 171 77 Stockholm

Cancer research areas:

Targeting MYC and Metabolism, Precision Medicine

Key research field interests:

Neural Childhood Cancer, clear cell Renal Carcinoma (ccRCC), Cervical Cancer, Metabolism, Neural Differentiation, MYC, Precision Medicine

Needs for collaboration:

We are open for collaborations in many different areas

Selected publications:

1. Dilraj Lama*, Thibault Vosselman, Cagla Sahin, Judit Liaño-Pons, Carmine P. Cerrato, Lennart Nilsson, Kaare Teilum, David P. Lane, Michael Landreh* & Marie Arsenian Henriksson*. A druggable conformational switch in the c-MYC transactivation domain. Nature Communications 15:1865 (2024).
2. Lourdes Sainero-Alcolado, Elisa Garde-Lapido, Marteinn Thor Snaebjörnsson,, Sarah Schoch, Irene Stevens, María Victoria Ruiz-Pérez, Christine Dyrager, Vicent Pelechano, Håkan Axelson, Almut Schulze, and Marie Arsenian-Henriksson*..Targeting MYC induces lipid droplet accumulation by upregulation of HILPDA in clear cell renal cell carcinoma. PNAS Vol. 121 No. 7 e2310479121 (2024).
3. Judit Liaño-Pons*, Elisa Garde-Lapido, Fenja L. Fahrig,, Merle Jäckering, Ye Yuan, Stina Andersson, Lea Schort, Maria Esteve, Sofie Mohlin, Oscar C Bedoya-Reina, and Marie Arsenian-Henriksson*. Combined targeting of PRDX6 and GSTP1 as a potential differentiation strategy for neuroblastoma treatment. PNAS Vol. 122 No. 25 e2427211122 (2025).

*Corresponding author

Metabolic reprogramming by MYC inhibition as precision medicine in clear cell renal carcinoma and childhood neuroblastoma

Metabolic reprogramming is critical during cancer development and maintenance of tumorigenesis. Many changes in tumor metabolism are driven by the MYC oncogene family. We have analyzed the importance of MYC-driven rewiring of lipid metabolism in two human solid cancers, childhood neuroblastoma (NB) and clear cell renal cell carcinoma (ccRCC), highlighting the importance of lipid metabolism in these malignancies.

Clear cell renal cell carcinoma (ccRCC) is characterized by accumulation of lipid droplets, organelles associated with therapy resistance and aggressiveness. Loss of the von Hippel-Lindau (VHL) tumor suppressor is found in almost all ccRCC cases resulting in the constitutive stabilization of HIF1/2-α. Moreover, MYC is amplified or overexpressed in 20% of the cases. We show that constitutive HIF expression combined with MYC inhibition in VHL negative ccRCC cells resulted in increased triglyceride content and potentiation of lipid droplet formation in a glutamine-dependent manner. Concurrent inhibition of MYC signaling and glutamine metabolism prevented lipid droplet accumulation and reduced tumor burden in mice. Importantly, we identified the hypoxia-inducible lipid droplet–associated protein (HILPDA) as the key driver for this process. Analysis of tissues from other renal cancer subtypes as well as healthy renal control samples identified HILPDA as a specific ccRCC biomarker.

Neuroblastoma (NB), an embryonal tumor of the sympathetic nervous system, is highly heterogenic, with cases that spontaneously regress to metastatic ones. The MYCN oncogene is amplified in 40% of the high-risk cases correlating with an undifferentiated phenotype and poor outcome. We previously demonstrated that MYCN-amplification induces reprogramming of metabolism with elevated fatty acid dependent respiration and high expression of enzymes from the antioxidant systems. We recently found that inhibition of peroxiredoxin 6 (PRDX6), a moonlighting enzyme involved in ROS scavenging and lipid metabolism, decreased MYC/MYCN levels, induced neural differentiation, and increased lipid droplet accumulation, crucial for neural cell differentiation. These effects were potentiated upon targeting PRDX6 in combination with Glutathione S-transferase Pi 1 (GSTP1), as well as combined silencing of both genes. Single-cell RNA-seq data from the developing murine adrenal gland revealed high PRDX6 and GSTP1 levels, suggesting key roles in maintaining redox homeostasis during development. MYCN-amplified tumors from high-risk NB patients have elevated expression of both PRDX6 and GSTP1 in association with undifferentiated tumors and poor prognosis.

Together, our results suggest that HILPDA inhibition affecting lipid metabolism in ccRCC as well as differentiation induction in NB by targeting PRDX6/GSTP1 are attractive approaches for novel therapeutic interventions for these MYC-driven cancers.

Isabel Barragan

Senior Researcher

Precision Cancer Medicine in Lung Cancer - Preclinical, Translational & Clinical Research
Department of Oncology-Pathology
Theme Cancer, J6:20, Visionsgatan 4 S-171 64 Solna

Cancer research areas:

In vitro diagnostic tests for personalised cancer immunotherapy

Key research field interests:

Epigenetics, metastasis, biomarkers, immunotherapy, SBRT, liquid biopsy, data integration, in silico modelling

Needs for collaboration:

Multicenter clinical studies, omics combinations, consortium calls for data integration, validation studies, international collaboration

Selected publications:

1. Combination of SABR With Anti-PD-1 in Oligoprogressive Non-Small Cell Lung Cancer and Melanoma: Results of a Prospective Multicenter Observational Study. Chicas-Sett R, Zafra J, Rodriguez-Abreu D, Castilla-Martinez J, Benitez G, Salas B, Hernandez S, Lloret M, Onieva JL, Barragan I*, Lara PC*. * Equal contribution. Int J Radiat Oncol Biol Phys. 2022 Nov 15;114(4):655-665. doi: 10.1016/j.ijrobp.2022.05.013. Epub 2022 May 18.
2. Epigenetic prediction of response to anti-PD-1 treatment in non-small-cell lung cancer: a multicentre, retrospective analysis. Duruisseaux M, Martínez-Cardús A, Calleja-Cervantes ME, Moran S, Castro de Moura M, Davalos V, Piñeyro D, Sanchez-Cespedes M, Girard N, Brevet M, Giroux-Leprieur E, Dumenil C, Pradotto M, Bironzo P, Capelletto E, Novello S, Cortot A, Copin MC, Karachaliou N, Gonzalez-Cao M, Peralta S, Montuenga LM, Gil-Bazo I, Baraibar I, Lozano MD, Varela M, Ruffinelli JC, Palmero R, Nadal E, Moran T, Perez L, Ramos I, Xiao Q, Fernandez AF, Fraga MF, Gut M, Gut I, Teixidó C, Vilariño N, Prat A, Reguart N, Benito A, Garrido P, Barragan I, Emile JF, Rosell R, Brambilla E, Esteller M. Lancet Respir Med. 2018 Oct;6(10):771-781.
3. Association of gut microbiota and immune gene expression with response to targeted therapy in BRAF mutated melanoma. Guardamagna M, Berciano-Guerrero MA, Lavado-Valenzuela R, Auclin É, Onieva-Zafra JL, Plaza-Andrades I, Oliver J, Garrido-Aranda A, Perez-Ruiz E, Álvarez M, Ocaña MC, Queipo-Ortuño MI, Barragán I*, Rueda-Dominguez A*. * Equal contribution. Sci Rep. 2025 Jul 14;15(1):25430.

Ninib Baryawno

Principal Investigator / Docent

Department of Women's and Children's Health

+46 76 589 77 40

Cancer research areas:

Childhood cancer and bone metastases

Key research field interests:

Bone metastases; Tumor microenvironment; Stem cells; Neuroblastoma; Stroma;Immune cells; Pre-clinical modeling

Selected publications:

1. Embaie BT, Sarkar H, Alchahin AM, Otte J, Olsen TK, Tümmler C, Kameneva P, Artemov AV, Akkuratova N, Adameyko I, Stukenborg JB, Wickström M, Kogner P, Johnsen JI, Mei S, Kharchenko PV, Baryawno N. Comparative Single-Cell Transcriptomics of Human Neuroblastoma and Preclinical Models Reveals Conservation of an Adrenergic Cell State. Cancer Research, 2025, doi: 10.1158/0008-5472.CAN-24-1507.
2. Olsen TK, Otte J, Mei S, Tesfai Embaie B, Kameneva P, Cheng H, Gao T, Zachariadis V, Tsea I, Björklund Å, Kryukov E, Hou Z, Johansson A, Sundström E, Martinsson T, Fransson S, Stenman J, Shirazi Fard S, Johnsen JI, Kogner P, Adameyko I, Enge M, Kharchenko PV and Baryawno N. Joint single-cell genetic and transcriptomic analysis reveal pre-malignant SCP-like subclones in human neuroblastoma. Molecular Cancer, 2024, 23:180. doi: 10.1186/s12943-024-02091-y.
3. Alchahin AM, Mei S, Tsea I, Hirz T, Kfoury Y, Dahl D, Wu CL, Subtelny AO, Wu S, Scadden DT, Shin JH, Saylor PJ, Sykes DB, Kharchenko PV, Baryawno N. A new transcriptional metastatic signature predicts survival in clear cell renal cell carcinoma. Nature Communications, 2022, 13:5747.

Decoding the metastatic cascade to the bone

Bone metastases are a major cause of cancer death, yet the mechanisms that allow rare tumor cells to seed, survive, and expand in bone remain essentially unknown, leaving patients with few curative options. Our lab asks three connected questions: (i) which tumor subclones are truly metastasis-competent, (ii) how bone marrow niches are remodeled to attract, arrest, and awaken disseminated cells, and (iii) which niche-dependent vulnerabilities can be exploited for therapy. Using barcoded patient-derived tumoroids, in vivo lineage tracing integrated with single-cell and spatial multi-omics, we are mapping the evolution from primary tumor to bone metastasis and functionally validate candidate drivers with CRISPR-based perturbations. Combining spatial transcriptomics, metabolomics, humanized mouse models and metastasis-on-a-chip systems we further aim to resolve ligand–receptor and metabolic circuits that govern homing, dormancy, and colonization in human bone marrow at cellular resolution. Finally, using in vivo CRISPR loss-of-function screens and preclinical drug testing we hope to define bone-specific dependencies with therapeutic potential. By integrating rare tissues from metastatic patients, cutting-edge technologies our lab in the short term to deliver in the long-term a mechanistic blueprint of the metastatic cascade to bone and nominate concrete therapeutic targets and biomarkers. In the long term, our ambition is to lay the foundation for therapies that prevent or eradicate bone metastases and significantly improve survival and quality of life for patients. Our work aims to move beyond our previous descriptive atlas work by directly linking human metastatic tissues to functional modeling, creating a platform that can be adapted to other cancers and metastatic organs.

Oscar Bedoya Reina

Researcher

Pediatric Oncology and Pediatric Surgery
Department of Women's and Children's Health
Widerströmska huset, hiss 1, plan 8 Tomtebodavägen 18A, 17177 Stockholm

Cancer research areas:

Computational Biology, Pediatric Cancer, Neuroblastoma

Key research field interests:

Neuroblastoma, single-cell sequencing, metastasis, adrenergic, mesenchymal-like

Needs for collaboration:

Always

Selected publications:

1. Radke K, Aaltonen K, Muciño-Olmos EA, Esfandyari J, Adamska A, Siaw JT, Adamic D, Lago C, Mañas A, Seger A, Hansson K, Rogova O, Lehn S, Mason DJ, O'Donovan DJ, Roberts I, Lock A, Brennan J, Pietras K, Davies EJ, Spégel P, Bedoya-Reina OC, Brown D, Thompson NT, Spadoni C, Bexell D. Repurposing statins and phenothiazines to treat chemoresistant neuroblastoma. EMBO Mol Med. 2025 Dec 23. doi: 10.1038/s44321-025-00349-6. Epub ahead of print. PMID: 41437160.
2. Yuan Y, Alzrigat M, Rodriguez-Garcia A, Wang X, Bexelius TS, Johnsen JI, Arsenian-Henriksson M, Liaño-Pons J, Bedoya-Reina OC. Target Genes of c-MYC and MYCN with Prognostic Power in Neuroblastoma Exhibit Different Expressions during Sympathoadrenal Development. Cancers (Basel). 2023 Sep 16;15(18):4599. doi: 10.3390/cancers15184599. PMID: 37760568; PMCID: PMC10527308.
3. Bedoya-Reina OC, Li W, Arceo M, Plescher M, Bullova P, Pui H, Kaucka M, Kharchenko P, Martinsson T, Holmberg J, Adameyko I, Deng Q, Larsson C, Juhlin CC, Kogner P, Schlisio S. Single-nuclei transcriptomes from human adrenal gland reveal distinct cellular identities of low and high-risk neuroblastoma tumors. Nat Commun. 2021 Sep 7;12(1):5309. doi: 10.1038/s41467-021-24870-7. PMID: 34493726; PMCID: PMC8423786.
4. Bedoya-Reina OC, Schlisio S. Chromaffin Cells with Sympathoblast Signature: Too Similar to Keep Apart? Cancer Cell. 2021 Feb 8;39(2):134-135. doi: 10.1016/j.ccell.2020.12.009. Epub 2020 Dec 31. PMID: 33385330.

From Primary Tumors to Metastases: A Single-Cell Perspective on High-Risk Neuroblastoma Evolution

Background: Neuroblastoma (NB) is a highly heterogeneous disease with a broad range of outcomes and prognoses. Understanding the cellular and molecular transitions from primary tumors to metastasis can support the design of targeted and less toxic therapeutic strategies. This study aimed to identify the cell of origin of metastasis in high-risk neuroblastoma and to reconstruct the molecular changes accompanying the progression from primary tumors to metastasis.

Aims: To address these objectives, we obtained and sequenced single cells from paired samples, including primary and metastatic tumors from three different patients.

Methods: Using Smart-Seq3, we sequenced approximately 9,000 live, high-quality cells sorted with specific markers. Quality control measures ensured reliable gene expression profiling. Data integration with batch correction was performed, followed by cluster annotation. Myeloid cell signatures were used as reference points for malignant cluster identification. Cells were clustered and analyzed based on transcriptional profiles.

Results: Our analysis revealed that different cell clusters exhibited varying degrees of similarity to the developing sympathoadrenal system, presenting adrenergic and mesenchymal-like signatures. Neuroendocrine cells most closely resembled noradrenergic neuroblastoma cells. The transcriptional profiles of metastatic cells indicated heterogeneous transitions, including dynamic NOR-to-MES shifts, which may contribute to metastasis. Signature scores and pseudotime reconstructions were used to track transcriptional changes over time.

Conclusions: This study provides a comprehensive view of the evolution of high-risk neuroblastoma cells from primary tumors to metastasis. The findings highlight the heterogeneity of neuroblastoma and the importance of adrenergic and mesenchymal-like transcriptional signatures in metastasis, offering valuable insights for future targeted therapies.

Erik Benson

Assistant Professor

Microbial pathogenesis / Scilifelab

Department of Microbiology, Tumor and Cell Biology
Tomtebodavägen 23B

Cancer research areas:

Drug delivery

Key research field interests:

DNA nanotechnology, Sequencing, Selection

Needs for collaboration:

Specialist bioinformatics, cell targeting, therapeutic oligonucleotides

Selected publications:

1. Petri, Alexander J., et al. “cONcat: Computational reconstruction of concatenated fragments from long Oxford Nanopore reads.” Plos one 20.7 (2025): e0321246.

Development of cell targeting DNA nanostructures by selection

In DNA nanotechnology synthetic DNA is designed so it assembles with high precision at the nanoscale. By adding proteins, chemical groups or drugs these structures can interact in specific ways with pathogens and cells for diagnostics and therapeutics. The fundamental challenge is that we often don't know what we should design to achieve our goal. We are developing an approach where we make large libraries of millions of DNA structures and use selection experiments to search for structures that specifically taken up by cell or tumor types. The hope is that we can turn the development of structures with specific properties from a design to a selection problem.

We have performed repeat selection in parallel in several cell types and use long read sequencing to characterize the populations of DNA structures that are taken up in different cell types. From this, we synthesize chosen DNA structures to validate their uptake in different cell types. We are also testing this approach to target neuroblastoma by producing DNA nanostructure libraries including GD2 targeting groups combined with repeated selection experiments in neuroblastoma cell lines. We are interested to know if this selection approach can be applied directly in vivo and have performed the first pilot experiments to validate that structures can be recovered and amplified from mouse tissues, including tumors.

Mikael Benson

Senior Researcher

Division of Ear, Nose and Throat Diseases
Department of Clinical Science, Intervention and Technology - CLINTEC
Tomtebodavägen 18

Cancer research areas:

High-resolution computational models of malignant transformation

Key research field interests:

High-resolution computational models of malignant transformation

Needs for collaboration:

Clinicians, pathologists, single cell and bioinformatics researchers

Selected publications:

1. Martin Smelik, Daniel Diaz-Roncero Gonzalez, Xiaojing An, Rakesh Heer, Lars Henningsohn, Xinxiu Li, Hui Wang, Yelin Zhao, Mikael Benson. Combining spatial transcriptomics, pseudotime and machine learning to find biomarkers for prostate cancer. Cancer Research 2025;85(13):2514-2526. doi: 10.1158/0008-5472.CAN-25-0269.)
2. Schäfer S, Smelik M, Sysoev O, Zhao Y, Eklund D, Lilja S, Gustafsson M, Heyn H, Julia A, Kovács IA, Loscalzo J, Marsal S, Zhang H, Li X, Gawel D, Wang H, Benson M. scDrugPrio: A framework for the analysis of single-cell transcriptomics to address multiple problems in precision medicine in immune-mediated inflammatory diseases. Genome Med 2024
3. Li X, Loscalzo J, Mahmud AKMF, Aly DM, Rzhetsky A, Zitnik M, Benson M. Digital twins as global learning health and disease models for preventive and personalized medicine. Genome Med. 2025 Feb 7;17(1):11. doi: 10.1186/s13073-025-01435-7

Hign-resolution computational models to prioritise early mechanisms, biomarkers and drug targets in malignant transformation

Early diagnosis and treatment are crucial for improving cancer prognosis. This is complicated by lack of biomarkers, which in turn depends on the complexity and heterogeneity of cancer development. Thousands of genes change their expression across multiple cell types. Those changes vary between patients with the same diagnosis, as well as between different stages and tumor locations in the same patient. The ideal biomarkers should be shared across patients with the same diagnosis, as well as between different stages. We hypothesized that pseudotime-based alignment of epithelial cells from spatial transcriptomics from different grades of prostate cancer (PCa) could be used to find such biomarkers. Our analyses of multi-omics data from blood, prostate and urine from almost 2000 patients showed that proteins encoded by the mRNAs most correlated with pseudotime had high AUCs for in urine (1). Limitations included that 1) epithelial cells only represent part of the complex multicellular networks in cancer; 2) the analyses did not include other diseases in the prostate, which may share mechanisms that confound the diagnostic accuracy of the biomarkers; 3) the biomarkers dont reflect individual variations that are important for personalized treatment. We therefore aim to expand the analyses by constructing multi-cellular network models (MCNMs) of different stages of malignant transformation to identify and prioritize mRNAs that encode proteins that have early driving roles in malignant transformation. The MCNMs are computational models that are constructed using scRNA-seq or spatial transcriptomics, based on predicted interactions between ligands and their receptors in sender/receiver cells (2). The principles were recently discussed in Nature Biotech (https://doi.org/10.1038/s41587-025-02847-x). We have previously shown that MCNMs can be analyzed to find individualized biomarkers and drug targets in inflammatory diseases (2). We are now developing MCNMs to find early driving mechanisms, biomarkers and drug targets in PCa and other malignancies (3).

Hanna Brauner

Associate Professor

Dermatology and Venereology
Department of Medicine, Solna
Center for Molecular Medicine (CMM), Visionsgatan 18, L8:03, 171 76 Solna

Cancer research areas:

Cutaneous lymphoma

Key research field interests:

Lymphoma, immunology, dermatology, tumor microenvironment, prognostic factors, co-morbidities, quality of life

Needs for collaboration:

Interest and knowledge of the tumor microenvironment of lymphoma. Expertise in complementary methods, including the generation of lymphoma cell lines and novel methods for the analysis of FFPE biopsies.

Selected publications:

1. Ivert LU, Ekberg S, Smedby KE, Brauner H. Increased mortality due to lymphoma and infections in patients with mycosis fungoides or Sézary syndrome: a Swedish nationwide population-based cohort study. Br J Dermatol. 2025 Sep 18;193(4):781-782. doi: 10.1093/bjd/ljaf233.
2. Nenonen J, Winther AH, Jonsson P, Ivert LU, Brauner H. Identification of subgroups of early-stage mycosis fungoides patients with increased itch and impaired quality of life. Front Oncol. 2025 Volume 15. doi: 10.3389/fonc.2025.1524353.
3. Scheffschick A, Nenonen J, Xiang M, Winther AH, Ehrström M, Wahren-Herlenius M, Eidsmo L, Brauner H. Skin infiltrating NK cells in cutaneous T-cell lymphoma are increased in number and display phenotypic alterations partially driven by the tumor. Front Immunol. 2023 Aug 25;14:1168684.

Cutaneous lymphoma – clinical and experimental studies

Lymphomas located to the skin are rare and less studied than other forms of lymphoma. A unique feature of this type of cancer is its accessibility which enables repetitive lymphoma biopsies throughout the course of the disease. Cutaneous lymphomas are often derived from different stages of T cell development (CTCL). The majority experience an indolent disease, but for some develop an aggressive form with high mortality. We aim to generate knowledge for increasing survival and health of CTCL patients, by combining epidemiologic and experimental studies. We will perform the first Swedish national register studies on prognostic factors, comorbidities and long-term effects of CTCL, utilizing the uniquely large and population-based cohort of approximately 1000 patients in the national lymphoma register. Experimentally we will determine if failed immune surveillance explain disease progression, in search for pathogenic mechanisms and biomarkers for aggressive disease. Lymphoma-infiltrating cytotoxic NK cells, CD8+ T cells and macrophages from early vs advanced stages of CTCL will be analyzed by functional phenotyping with flowcytometry, scRNA sequencing and spatial distribution analyzed by immunofluorescence and spatial proteomics. Lastly, the immune processes required for successful rejection of lymphoma will be investigated during treatment with curative intention.

Antonino Cassotta

Assistant Professor

Center for Hematology and Regenerative Medicine
Department of Medicine, Huddinge
NEO Medicinaren 25, HERM plan 7, Hälsovägen 7C, 14157 Huddinge/Stockholm

Cancer research areas:

Hematology, multiple myeloma, adaptive immunity, T cell immunotherapy, precision medicine

Key research field interests:

Antigen specificity of tumor-infiltrating T cells, specificity of regulatory T cells, clonal analysis of tumor-reactive T cells, discovery of tumor antigens, discovery of tumor-reactive T cell receptors, engineering of cytotoxic cell therapies, composition and evolution of TCR repertoire, immune evasion mechanisms

Needs for collaboration:

Further access to clinical samples

Selected publications:

1. Low, ..., Cassotta. Clonal analysis of immunodominance and cross-reactivity of the CD4 T cell response to SARS-CoV-2. Science. 2021; 372, 1336–1341.
2. Cassotta, et al. A single T cell epitope drives the neutralizing anti-drug antibody response to natalizumab in multiple sclerosis patients. Nature Medicine. 2019; 25, 1402–1407.
3. Cassotta, et al. Deciphering and predicting CD4+ T cell immunodominance of influenza virus hemagglutinin. Journal of Experimental Medicine. 2020; 217 (10): e20200206.

Jana de Boniface

Adjunct Professor

Jana de Boniface Research Group
Department of Medical Epidemiology and Biostatistics
Nobels väg 12A

Cancer research areas:

Breast cancer

Key research field interests:

Axillary surgery, exercise oncology, tumour immunology

Needs for collaboration:

Interested in the mechanisms of surgical trauma and immunosuppression in the context of cancer surgery

Selected publications:

1. de Boniface J, Filtenborg Tvedskov T, Rydén L, Szulkin R, Reimer T, Kühn T, Kontos M, Gentilini OD, Olofsson Bagge R, Sund M, Lundstedt D, Appelgren M, Ahlgren J, Norenstedt S, Celebioglu F, Scheel Andersen I, Hoyer U, Nyman PF, Vikhe Patil E, Wieslander E, Dahl Nissen H, Alkner S, Andersson Y, Vrou Offersen B, Bergkvist L, Frisell J, Christiansen P, and on behalf of the SENOMAC Trialists' Group. Omitting axillary dissection in breast cancer with sentinel node metastases. N Engl J Med 2024. 390:1163-1175. DOI: 10.1056/NEJMoa2313487
2. de Boniface J, Altena R, Haddad Ringborg C, Bolam KA, Wengström Y. Physical exercise during neoadjuvant chemotherapy for breast cancer as a mean to increase pathological complete response rates: trial protocol of the randomized Neo-ACT trial. PlosOne 2022. October 13. https://doi.org/10.1371/journal.pone.0274804
3. de Boniface J, Szulkin R, Johansson ALV. Major surgical postoperative complications and survival in breast cancer: Swedish population-based register study in 57152 women. British Journal of Surgery, 2022. 109: 977-983. doi: 10.1093/bjs/znac275 (this publication was awarded the BJS Prize in 2022).

Right-sizing of breast cancer surgery

Breast cancer surgery has previously been the only treatment available; today, with earlier detection and improved systemic treatment, surgery needs to re-invent itself and gauge its relevance for treatment and staging against its potential impact on morbidity and quality of life. I will present research aiming to right-size breast cancer surgery and discuss the challenges it encounters.

Joakim Dillner

Professor
Department of Clinical Science, Intervention and Technology - CLINTEC
Center for Cervical Cancer Elimination, F46, Karolinska University Hospital, Huddinge, 141 86 Stockholm
+46724682460

Cancer research areas:

Cancer Epidemiology; Cancer screening & prevention; Gynecological cancers

Key research field interests:

Cervical cancer, Human Papilloma virus prevention, Human Papilloma virus screening and vaccination

Needs for collaboration:

Searching for other PIs at KI who are also interested in cancer prevention

Selected publications:

1. Wang, J., Elfström, K.M., Dillner, J. Human papillomavirus-based cervical screening and long-term cervical cancer risk: a randomised health-care policy trial in Sweden. Lancet Public Health. 9. e886-e895. 2024. doi: 10.1016/S2468-2667(24)00218-4. PMID: 39486904.
2. Arroyo Mühr, L.S., Gini, A., Yilmaz, E., Hassan, S.S., Lagheden, C., Hultin, E., Garcia Serrano, A., Ure, A.E., Andersson, H., Merino, R., Elfström, K.M., Baussano, I., Dillner, J. Concomitant human papillomavirus (HPV) vaccination and screening for elimination of HPV and cervical cancer. Nat Commun. 15. 3679. 2024. doi: 10.1038/s41467-024-47909-x. PMID: 38693149; PMCID: PMC11063066.
3. Wang, J., Elfström, K.M., Lagheden, C., Eklund, C., Sundström, K., Sparén, P., Dillner, J. Impact of cervical screening by human papillomavirus genotype: Population-based estimations. PLoS Med. 20. e1004304. 2023. doi: 10.1371/journal.pmed.1004304. PMID: 37889928.

Center for Cervical Cancer Elimination: Advancing Strategies for HPV-Based Prevention

The Center for Cervical Cancer Elimination is dedicated to enhancing the scientific foundation for designing and evaluating optimal strategies to eliminate cervical cancer. Our work spans both basic and translational research on the Human Papillomavirus (HPV), the etiological agent of cervical cancer, with a strong focus on HPV-based prevention.

Key components of the center include:

- The International HPV Reference Center, which maintains and distributes validated reference clones of all known HPV types to support global research efforts.
- The Swedish National Quality Register for Cervical Cancer Prevention, which enables systematic evaluation and continuous improvement of national prevention strategies.

As part of Sweden's national campaign to eliminate cervical cancer by 2027, the center coordinates a dual approach of HPV vaccination and HPV screening among young women. Complementary initiatives target long-term non-attenders and offer catch-up screening for women over 70.

To further optimize prevention, we are developing an AI-driven, risk-based screening model to replace the current uniform screening protocol. This personalized approach aims to improve efficiency and outcomes across the population.

Tom Erkers

Senior Research Specialist

Functional Systems Oncology
Department of Oncology-Pathology
Scilifelab, Alpha 4, Tomtebodavägen 23a, 17165 Solna

Cancer research areas:

Precision Medicine

Key research field interests:

Functional precision medicine; leukemia and lymphoma; multiomics; alloimmunity; spatial proteomics

Needs for collaboration:

Clinical partners for fPM observational validation studies in blood cancers

Selected publications:

1. Delineating functional and molecular impact of ex vivo sample handling in precision medicine. Struyf N, Österroos A, Vesterlund M, Arnroth C, James T, Sunandar S, Mermelekas G, Bohlin A, Hamberg Levedahl K, Bengtzén S, Jafari R, Orre LM, Lehtiö J, Lehmann S, Östling P, Kallioniemi O, Seashore-Ludlow B, Erkers T. NPJ Precis Oncol. 2024 Feb 19;8(1):38. doi: 10.1038/s41698-024-00528-7.
2. High-parametric evaluation of human invariant natural killer T cells to delineate heterogeneity in allo- and autoimmunity. Erkers T, Xie BJ, Kenyon LJ, Smith B, Rieck M, Jensen KP, Ji X, Basina M, Strober S, Negrin RS, Maecker HT, Meyer EH. Blood. 2020 Mar 12;135(11):814-825. doi: 10.1182/blood.2019001903.

Functional Precision Medicine in Blood Cancers

We develop functional precision medicine by pairing rapid ex vivo drug testing of patient samples with multiomics and single cell analyses to reveal mechanisms of response and resistance and to generate tractable combination ideas. As one example, in FLT3-mutated acute myeloid leukemia we observed a progenitor like CD38+ CD45RA+ leukemic population that associated with resistance to the FLT3 inhibitor midostaurin. Resistant cells display disrupted membrane architecture and a shift in signaling from STAT5 to PI3K AKT, favoring survival over apoptosis. Ex vivo functional drug testing was consistent with clinical response to midostaurin and, together with the multiomic data, indicated the presence and relevance of this phenotype. Drug combination screening showed that cotargeting with SMAC mimetics restores apoptotic competence and selectively reduces the resistant population when combined with midostaurin. In contrast, venetoclax combinations preferentially affected CD34 high cells, underscoring distinct subpopulation vulnerabilities. Taken together, these findings suggest a biologically relevant mechanism underlying midostaurin resistance and illustrate how this functional precision medicine framework can expose subset specific vulnerabilities and nominate phenotype selective combinations for further mechanistic and preclinical evaluation.

Ingemar Ernberg

Senior Professor

Department of Microbiology, Tumor and Cell Biology
Biomedicum, Q8C, Karolinska Institutet, MTC, Fe 280, 17177 Stockholm

070 5467636

Cancer research areas:

Viral infections and Cancer, Invasion and Metastasis, Cell plasticity

Key research field interests:

Viral infections and Cancer, Invasion and Metastasis,Cell elasticity, P4 cancer Medicine, Nework Biology

Needs for collaboration:

Invasion and Metasatsis, Cell elasticity, Biological networks

Selected publications:

1. Masucci M, Karlsson C, Blomqvist L, Ernberg I. Bridging the Divide: A Review on the Implementation of Personalized Cancer Medicine. J Pers Med. 2024 May 24;14(6):561. doi: 10.3390/jpm14060561.PMID: 38929782
2. Masucci M, Del Villar Pérez J, Mazzocato P, Ernberg I, Brommels M.Implementing Personalized Cancer Medicine: Insights from a Qualitative Interview Study. J Pers Med. 2025 Apr 9;15(4):150. doi: 10.3390/jpm15040150.PMID: 40278329
3. Matskova L, Zheng S, Kashuba E, Ernberg I, Aspenström P.MTSS1: beyond the integration of actin and membrane dynamics.mCell Mol Life Sci. 2024 Dec 3;81(1):472. doi: 10.1007/s00018-024-05511-w.PMID: 39625546

Rethinking cancer: unresolved enigmas in understanding the biology of nasopharyngal carcinoma (NPC)

Among human cancers nasopharyngeal carcinoma (NPC) shows many particular features. The world wide epidemiology shows local high incidence areas in South East Asia, radiating out from the Southern Chinese provinces around the Pearl river, but also high incidences on Greenland and in North Africa, a stable higher incidence in males, an early onset of disease and close to 100% prevalence of latent Epstein-Barr virus (EBV) infection in the tumors in these endemic regions. Due to lack of consistent patterns of cancer-driving mutations and extensive DNA-methylation in the tumor cells NPC can be considered “an epigenetic” cancer.

Current treatment for advanced metastatic late NPC does not work well, with a 5-year survival below 50%. We are exploring the mechanisms of NPC metastasis with the ultimate aim to improve this situation.

We have shown that NPC has a metabolic profile involving lipid droplet (LD) accumulation and that this correlates to NPC migration and invasion. We also showed that MTSS1 (metastasis suppressor 1/missing in metastasis (MIM)), was downregulated in NPC metastasis, and that restoring its expression inhibited metastasis and LD accumulation. We are further exploring the link between MTSS1 inhibition of metastasis and lipid metabolism.

MTSS1 is expressed in most human tissues and has multiple functions. MTSS1 has attracted the most attention for its role as a tumor suppressor, being absent or expressed at reduced levels in advanced and metastasizing cancers of many types.

MTSS1 is emerging as a central player in cell biology with four well- documented biochemical functions: 1) it induces membrane protrusions (lamellipodia and filopodia) by a direct interaction between the I-BAR domain (Inverse- Bin/Amphiphysin/Rvs) 2) it modulates actin dynamics by slowing down actin nucleation and filament elongation via the WH2 domain; 3) it modulates the accumulation of F-actin at cell–cell borders or at filopodia via the I-BAR domain; and 4) it acts as a scaffolding protein, bringing together many accessory proteins, particularly in the context of cytoskeletal modulation and protein degradation.

We are studying how MTSS1 regulate metastasis of NPC and how this links to lipid metabolism.

Fang Fang

Professor

Unit of Integrative Epidemiology
Institute of Environmental Medicine
Nobels väg 13

Cancer research areas:

Cancer epidemiology

Key research field interests:

Co-morbidities between mental disorders and somatic conditions, including cancer and cardiovascular disease.

Needs for collaboration:

We would love to work with clinicians working on specific cancer types as well as experimental experts who might be able to help us disentangling underlying mechanisms for the link between specific mental disorders and cancer forms.

Selected publications:

1. Hu K, Barker MM, Herweijer E, Wang J, Feldman AL, Lu D, Valdimarsdóttir U, Sundström K, Fang F. The role of mental illness and neurodevelopmental conditions in human papillomavirus vaccination uptake within the Swedish school-based vaccination programme: a population-based cohort study. Lancet Public Health. 2024;9(9):e674-e683.
2. Liu Q, Yang F, László KD, Hu K, Feychting M, Wei D, Fall K, Valdimarsdottir U, Li J, Fang F. Increased risk of suicide attempt and death by suicide among spouses of cancer patients: a population-based cohort study in Denmark. JAMA Oncol. 2024;10(10):1323-1330. PMID: 39145973.
3. Hu K, Wang J, Sparén P, Herweijer E, Sjölander A, Adami HO, Valdimarsdóttir U, Sundström K, Fang F. Invasive cervical cancer, precancerous lesions, and cervical screening participation among women with mental illness in Sweden: a population-based observational study. Lancet Public Health. 2023 Apr;8(4):e266-e275. PMID: 36965981.

Oscar Fernandez-Capetillo

Professor

Genome Biology
Department of Medical Biochemistry and Biophysics
Scilifelab, Alpha 4, Solna

Cancer research areas:

Chemical screens; Genetic screens; mouse models; senescence; DNA damage

Key research field interests:

Discovery of novel cancer therapies; aging and age-related pathologies; mechanism of action; target ID; academic drug development

Needs for collaboration:

Always open to share

Selected publications:

1. Lopez-Pernas et al Biorxiv 2025
2. Sirozh et al Mol Cell 2024
3. Sanchez-Burgos et al EMBO Mol Med 2022

Drug-mediated kinase activation: A new type of cancer chemotherapy

The one-two-punch approach refers to the sequential administration of two different chemotherapies, the second of which targets cancer cells that resisted the initial treatment. To find such a second punch, we performed a chemical screen to find drugs that are preferentially toxic for cells with an activated DNA damage response (DDR). This screen identified the tyrosine kinase inhibitor GNF-7 as a top hit. Subsequent work revealed that GNF-7 is a potent senolytic, even when senescence is triggered by therapies that do not activate the DDR. Consistently, GNF-7 is highly efficacious to kill cancer cells previously treated with CDK4/6 inhibitors, including in patient-derived organoids and mouse xenografts. Surprisingly, the senolytic effect of GNF-7 is not mediated by the inhibition of a tyrosine kinase (TK), but rather by the activation of GCN2, an effect previously reported for other TK inhibitors and for which we now provide a molecular mechanism. Together, our study reports the discovery of a novel senolytic agent that strongly synergizes with CDK4/6 inhibitors and opens a new field of cancer chemotherapy based on the allosteric activation of stress kinases.

Anna Forsberg

Assistant Professor

Clinical Epidemiology
Department of Medicine, Solna
SCREESCO, Karolinska Universitetssjukhuset QA33,
Karolinska vägen 37A, S-171 76 Stockholm

Cancer research areas:

Prevention colorectal cancer

Key research field interests:

Colonoscopy quality; Colorectal cancer screening

Needs for collaboration:

Discussion microbiom studies

Selected publications:

1. Forsberg A, Westerberg M, Metcalfe C, Steele R, Blom J, Engstrand L, et al. Once-only colonoscopy or two rounds of faecal immunochemical testing 2 years apart for colorectal cancer screening (SCREESCO): preliminary report of a randomised controlled trial. Lancet Gastroenterol Hepatol. 2022;7(6):513-21.
2. Sekiguchi M, Westerberg M, Ekbom A, Hultcrantz R, Forsberg A. Endoscopist Characteristics and Polyp Detection in Colonoscopy: Cross-Sectional Analyses of Screening of Swedish Colons. Gastroenterology. 2023;164(2):293-5 e4.
3. Westerberg M, Eriksson J, Metcalfe C, Lowbeer C, Ekbom A, Steele R, et al. Colonoscopy findings after increasing two-stool faecal immunochemical test (FIT) cut-off: Cross-sectional analysis of the SCREESCO randomized trial. J Intern Med. 2024;296(2):187-199.

SCREEning of Swedish COlons (SCREESCO) - a national bowelcancer screening study

Colorectal cancer (CRC) is one of the leading causes of cancer-related morbidity and mortality. Prevention is achieved by removing premalignant polyps and through early detection, both of which reduce mortality. Colonoscopy is used as a primary screening method or as a follow-up to stool tests for blood. Randomized studies have shown that screening with FOBT (fecal occult blood test) or sigmoidoscopy reduces both incidence and mortality. For FIT (fecal immunochemical test), randomized controlled trials are lacking, and for colonoscopy, only observational data suggest effectiveness. Internationally, four RCTs are ongoing, including the Swedish SCREESCO study. To date, only NordICC has evaluated mortality as a primary endpoint, without significant difference between colonoscopy and control groups, though the study has been criticized for premature evaluation. More robust RCTs are therefore essential. The SCREESCO study (NCT02078804) was initiated in 2014 to compare two screening methods with a control group in a Swedish context. Eighteen regions participated. A total of 278,280 individuals (aged 60) were randomized into three arms:

1. Colonoscopy (31,140 participants)
2. FIT (60,300 participants)
3. Control without intervention (186,840 participants)

Participation was lower than expected in the colonoscopy group (35%), requiring adjustments to achieve statistical power. To date, 23 publications based on SCREESCO data have been released. Baseline analysis showed: Participation: 35% (colonoscopy), 56% (FIT); Complications: few, only two perforations among 16,555 colonoscopies; CRC cases: 49 in the colonoscopy group (1.6/1,000) vs. 121 in the FIT group (2.0/1,000); Advanced adenomas: 30/1,000 (colonoscopy) vs. 19/1,000 (FIT)

Results indicate that nationwide CRC screening is feasible and safe. Variation in endoscopists' detection rates suggests a need for quality improvement and certification. Nurse endoscopists demonstrated excellent quality and are essential for future screening programs. A cross-sectional study of the FIT population showed that raising the cut-off from 10 µg/g to 20–40 µg/g reduced the number of colonoscopies without compromising diagnostic accuracy for advanced neoplasia. Current Swedish thresholds are 40 µg/g for women and 80 µg/g for men, but findings support lowering the male threshold to 40 µg/g.

Primary research objectives moving forward:

1. Compare CRC incidence and colonoscopy-related complications between FIT, colonoscopy, and control groups. Under consideration for publication.
2. Identify risk factors for thromboembolic events post-colonoscopy.
3. Study individuals diagnosed with CRC after a negative colonoscopy.
4. Conduct health economic analyses.

Susanne Gabrielsson

Professor

Department
Immunology and Respiratory Medicine
Department of Medicine, Solna
Visionsgatan 18

+46707694127

Cancer research areas:

Melanoma; Urinary bladder cancer

Key research field interests:

Extracellular Vesicles; Biomarkers; Cancer vaccine

Needs for collaboration:

Patient material, Novel techniques

Selected publications:

1. Offens A, Teeuwen L, Gucluler Akpinar G, Steiner L, Kooijmans S, Mamand D, Weissinger H, Käll A, Eldh M, Wiklander OPB, El-Andaloussi S, Karlsson MCI, Vader P, Gabrielsson S. A fusion protein that targets antigen-loaded extracellular vesicles to B cells enhances antigen-specific T cell expansion. J Control Release. 2025 Mar 25;382:113665. PMID: 40147536.
2. Steiner L, Eldh M, Offens A, Veerman RE, Johansson M, Hemdan T, Netterling H, Huge Y, Abdul-Sattar Aljabery F, Alamdari F, Lidén O, Sherif A, Gabrielsson S. Protein profile in urinary extracellular vesicles is a marker of malignancy and correlates with muscle invasiveness in urinary bladder cancer. Cancer Lett. 2025 Jan 28;609:217352. PMID: 39586489.
3. Veerman, RE, Güclüler Akpinar G, Annemarijn Offens A, Steiner L, Larssen P, Lundqvist, A, Karlsson, MCI, Gabrielsson S. Antigen-Loaded Extracellular Vesicles Induce Responsiveness to Anti-PD-1 and Anti-PD-L1 Treatment in a Checkpoint Refractory Melanoma Model. Cancer Immunol. Res. 2022. 11:217-227. PMID: 36546872.

Carmen Gerlach

Group Leader, Principal Researcher

Rheumatology
Department of Medicine, Solna
Center for Molecular Medicine, CMM L8:03

Cancer research areas:

Immunotherapy; Tumor immunology basic research

Key research field interests:

CD8+ T cell responses to cancer and infections; T cell-based therapies

Needs for collaboration:

Interested

Selected publications:

1. Guidelines for T cell nomenclature - Nature Reviews Immunology 2025
2. The T cell subsetting challenge - Trends in Immunology 2025
3. Graded expression of the chemokine receptor CX3CR1 marks differentiation states of human and murine T cells and enables cross-species interpretation - Immunity 2023

From T cell subsets to axes of diversification – a novel conceptual framework for T cell diversification

CD8+ T cell responses to cancer and infections are highly diverse. Diversity is thought to arise from T cells differentiating into distinct subsets. While discrete subsets are apparent in limited-parameter analyses, high-dimensional profiling exposed an extensive continuum of T cell states. Segregation of continuous data into few discrete subsets, e.g. effector and memory subsets, may not reflect biological relevance and accounts for confusion in the literature, because while effector and memory subsets differ in differentiation, proliferation and activation state, these processes are not fully co-regulated, leaving T cells with hybrid properties inconsistently assigned to either subset. Here, we provide an alternative to T cell subsetting for measuring and explaining T cell heterogeneity. We hypothesized that orthogonal molecular programs drive T cell diversification in different dimensions, which we name axes of diversification. Focusing on acute infection, we profiled virus-specific CD8+ T cells at different timepoints after infection using CITEseq. Supporting the axes of diversification framework, we identified transcriptional patterns that reflect each T cell's differentiation state – on a graded scale from stem-like to cytotoxic – irrespective of the cell's activation and proliferation state. Likewise, we identified a transcriptional signature that reflects the cell's activation state, irrespective of differentiation and proliferation. Consequently, T cell differentiation, activation and proliferation are distinct axes of diversification, and a cell's 'position' along each axis serves as cell state measurement. To extend the usability of our signatures, we developed antibody panels that capture a T cell's activation and differentiation state irrespective of each other. We thereby provide a flow cytometry-based method to describe T cell heterogeneity without the need to force heterogeneous populations into idealized subsets. In addition, our activation signature enabled the distinction of pathogen-specific CD8+ T cells from bystander memory T cells during an ongoing infection. We are now investigating whether it also allows distinction of tumor-specific CD8+ T cells from bystander T cells in the tumor.

Hans Grönlund

Associate Professor

Neuro
Department of Clinical Neuroscience
CMM

+46704968786

Cancer research areas:

Cancer immunotherapy

Key research field interests:

Personal, precision, antigen-specific cancer immunotherapy

Needs for collaboration:

Novel nano/micro sized beads for cancer vaccination

Selected publications:

1. A neoantigen-microbead platform for personalized T cell cancer vaccination Long Jiang, et al doi: https://doi.org/10.1101/2025.11.21.689667
2. Generation of tumor-specific cytotoxic T cells from blood via in vitro expansion using autologous dendritic cells pulsed with neoantigen-coupled-microbeads. Kiessling A, et al Frontiers in Oncology 2022,31:866763

Bead-bound, personal neoantigens expand T cells from tumor regional lymph nodes (rLN) in colorectal cancer

Tumor-Trained Lymphocytes (pTTL) is a novel adoptive T cell-based therapy targeting personal neoantigens. Tumor-specific subtle amino acid substitutions in complex with patients HLA signal the T cells to recognize, propagate, activate and initiate the cancer removal. Cells from patients rLNs, including T cells and dendritic cells (DCs), are co-cultured for two weeks with 1 □m sized magnetic EpiTCer® beads. Each bead contains one of six unique, densely covalently linked, in all 36 neoantigens. Moreover, the beads are paramagnetic for robotic handling and removal from the cell suspension prior to cell transfer. The bead size is selected for efficient phagocytosis, natural protein processing and cross-presentation to CD4 and CD8+ T cells by neoantigen presentation via DCs. The precise technology presented here offers a novel and efficient approach to produce a great number of cancer-specific cytotoxic T cells. A first in human phase1/2a clinical trial in patients with stage IV colorectal cancer is ongoing. The poster will present molecular and cellular patterns of the 14 days cell expansion. Multiple multiomic techniques, such as ctDNA, FluoroSpot and TCR are used to follow the fate of the T cells from biopsy via GMP production to persistence vi vivo.

Anita Göndör

Associate Professor

Tema Cancer
Department of Oncology-Pathology
K7 Onkologi-Patologi, K7 Forskning Göndör, 171 77 Stockholm

+46737121603

Cancer research areas:

Gastrointestinal and breast tumors; principles escaping chemotherapy; reprogramming; new in situ technologies

Key research field interests:

Cancer evolution; epigenetics/genetics; chromatin structure; nuclear architecture; expression heterogeneities

Needs for collaboration:

Oncologists with access to tumor materials representing a spectrum of cancer evolution

Selected publications:

1. Zhao, H., Sifakis, E. G., Sumida, N., Millán-Ariño, L., Svensson, J. P., Chen, X., L. Ronnegren, A., Shahin Varnoosfaderani, F., Diettrich Mallet de Lima, C., Shi, C., Loseva, O., Yammine, S., Israelsson, M., Rathje, L., Németi, B., Fredlund, E., Helleday, T., Imreh, M. and Göndör, A*. PARP1- and CTCF-mediated contacts between active and repressed chromatin at the lamina promote oscillating transcription. Mol Cell, 2015 Sep 17; 59(6):984-97. PMID: 26321255
2. Scholz, B.S., Sumida, N., Diettrich Mallet de Lima, C., Chachoua, I., Martino, M., Tzelepis, I., Nikoshkov, A., Zhao, H., Mehmood, R., Sifakis, E.G., Bhartiya, D., Göndör, A.* and Ohlsson, R* WNT signaling and AHCTF1 promote oncogenic MYC expression through super-enhancer-mediated gene gating. Nature genetics, 2019, 51, 1723–1731, PMID: 31784729
3. Chachoua, I., Tzelepis, I., Dai, H., Lim, J.P., Lewandowska-Ronnegren, A., Casagrande, F., Wu, S., Vestlund, J., Diettrich Mallet de Lima, C., Bhartiya, D., Scholz, B., Martino, M., Mehmood, R. and Göndör, A.* Canonical WNT signaling-dependent gating of MYC requires a non-canonical CTCF function at a distal binding site Nature communications, 13, Article number: 204 (2022)

The CTCF-dependent spatial distribution of MYC is a regulator and biomarker of expression plasticity in cancer

Heterogeneous numbers of extra-chromosomal MYC (ecMYC) copies have frequently been linked to phenotypic plasticity driving cancer evolution. This correlation assumes the existence of a linear relationship between the number of ecMYC copies and their output at MYC protein levels and hence an escape from the negative autoregulatory feedback associated with MYC. We report here that MYC expression plasticity is highest in colorectal tumor cells harboring only 3-5 MYC ecMYC copies. This correlation, moreover, required their prominent distribution to the nuclear periphery in a manner anti-correlated by HSR MYC. We also show that such a feature exploits the autoregulatory feedback control to drive active but paused MYC copies to nuclear pores in HCT116 cells. This leads to facilitated nuclear export rates of MYC mRNAs, which is controlled by a single CTCF binding site within a distant super-enhancer, to increase the amplitude of MYC expression plasticity, as determined by heterogeneity metrics, such as coefficients of variation, Shannon entropy and population re-distributions. With subpopulations of colorectal tumor cells, characterized by both high proportions of peripheral ecMYC copies and low MYC expression identified as candidates for therapy resistance, we submit that the spatial distribution of MYC drives both tumor cell expansion and their adaptability.

Johan Hartman

Professor

Precision pathology and tumor heterogeneity
Department of Oncology-Pathology
Bioclinicum

+46739760242

Cancer research areas:

Breast cancer

Key research field interests:

AI, tumor heterogeneity, biomarkers

Needs for collaboration:

Yes

Selected publications:

1. Computational pathology annotation enhances the resolution and interpretation of breast cancer spatial transcriptomics data. Li T, Yang Q, Acs B, Sifakis E, Toosi H, Engblom C, Thrane K, Lin Q, Mold J, Sun W, Boyaci C, Steen S, Frisén J, Lagergren J, Lundeberg J, Chen X, Hartman J. NPJ Precision Oncology, In press.
2. Histological Grade Has Clinical Validity in Neoadjuvant-Treated Breast Cancer: A Multicenter Study. Steen S, Boissin C, Rantalainen M, Acs B, Hartman J. Mod Pathol. 2025 Jul 25;38(11)
3. Real-world overall survival and characteristics of patients with ER-zero and ER-low HER2- negative breast cancer treated as triple-negative breast cancer: a Swedish population-based cohort study. Acs B, Hartman J, Sönmez D, Lindman H, Johansson ALV, Fredriksson I. Lancet Reg Health Eur. 2024 Mar 19;40

Nikolas Herold

Group Leader, Associate Professor

Paediatric Oncology
Department of Women's and Children's Health
Tomtebodavägen 18a, plan 8

0812370210

Cancer research areas:

Sarcoma; Paediatric oncology; AML

Key research field interests:

Drug-drug interactions; Early clinical trials

Needs for collaboration:

Always open for new perspectives

Selected publications:

1. Lilienthal I, Tao S, Nilsson C, Leonard E, Zhang R, Sorteberg AL, Fredrikson L, Xagoraris I, Fard SS, Tsesmetzis N, Zachariadis V, Cai H, Sandhow L, Langebäck A, Bohlin A, Tamm KP, Bengtzén S, Schinazi RF, Lehmann S, Kim B, Rassidakis GZ, Qian H, Jädersten M, Herold N. Addition of hydroxyurea (hydroxycarbamide) enhances the efficacy of ludarabine/cytarabine-based salvage regimens against acute myeloid leukaemia. Br J Haematol. 2025 Sep 27. doi: 10.1111/bjh.70180.
2. Morsy MHA, Lilienthal I, Lord M, Merrien M, Wasik AM, Amador V, Sureda-Gómez M, Johansson HJ, Lehtiö J, García-Torre B, Martin-Subero JI, Tsesmetzis N, Tao S, Schinazi RF, Kim B, Sorteberg AL, Wickström M, Sheppard D, Rassidakis GZ, Taylor IA, Christensson B, Campo E, Herold N*, Sander B*.SOX11 is a novel binding partner and endogenous inhibitor of SAMHD1 ara-CTPase activity in mantle cell lymphoma. Blood. 2024 Jan 18:blood.2023022241. *shared last authorship
3. Herold N*#, Rudd SG*, Ljungblad L, Sanjiv K, Myrberg IH, Paulin CB, Heshmati Y, Hagenkort A, Kutzner J, Page BD, Calderón-Montaño JM, Loseva O, Jemth AS, Bulli L, Axelsson H, Tesi B, Valerie NC, Höglund A, Bladh J, Wiita E, Sundin M, Uhlin M, Rassidakis G, Heyman M, Tamm KP, Warpman-Berglund U, Walfridsson J, Lehmann S, Grandér D, Lundbäck T, Kogner P, Henter JI, Helleday T, Schaller T#. Targeting SAMHD1 with the Vpx protein to improve cytarabine therapy for hematological malignancies. Nat Med. 2017 Feb;23(2):256-263. doi: 10.1038/nm.4265. * equal contribution; # corresponding author

Deciphering drug-drug interactions in paediatric oncology

Empirical implementation of combination chemotherapy has transformed many paediatric and adult cancers from universally fatal to curable. Nevertheless, treatment failure resulting in refractory disease or relapse remains common in aggressive diseases such as acute myeloid leukemia (AML) and osteosarcoma. While these combination regimens are highly effective in some patients, others relapse or die despite receiving identical therapy. We try to decipher the molecular determinants of synergy between chemotherapeutic drugs. We hypothesize that successful treatment depends on synergistic drug interactions and that resistance is mediated by specific, currently unknown factors. To test this, we focus on clinically relevant drug combinations in leukaemia and sarcomas. Our strategy combines genome-wide screens to identify resistance factors, mass spectrometry-based assays to detect drug-target interactions, and systematic synergy analysis using Zero Interaction Potency (ZIP) models correlated to differential gene expression in whole transcriptomes. Candidate genes are validated in cell lines, patient-derived samples, and animal models, and linked to clinical outcomes through large-scale genomic datasets. Finally, phenotypic small-molecule screens will be used to identify compounds that restore synergy in resistant models. By integrating clinical insight with functional genomics and proteomics, we want to convert empirical combination chemotherapy into a precision-guided approach, ultimately improving survival for patients with high-risk cancers.

Rainer Heuchel

Principal Investigator

Surgery and Oncology
Department of Clinical Science, Intervention and Technology - CLINTEC
ANA Futura, Alfred Nobels Allé 8 Huddinge Sweden

0737860830

Cancer research areas:

Pancreatic cancer

Key research field interests:

Cancer-stoma cell crosstalk; Drug resistance

Needs for collaboration:

Drug target investigation

Selected publications:

1. The Crosstalk Analysis between mPSCs and Panc1 Cells Identifies CCN1 as a Positive Regulator of Gemcitabine Sensitivity in Pancreatic Cancer Cells. Gündel B, Liu X, Pfützenreuter A, Engelsberger V, Weiskirchen R, Löhr JM, Heuchel R. Int J Mol Sci. 2024 Aug 29;25(17):9369. PMID: 39273316
2. Liu X, Gündel B, Li X, Liu J, Wright A, Löhr M, Arvidsson G, Heuchel R: 3D heterospecies spheroids of pancreatic stroma and cancer cells demonstrate key phenotypes of pancreatic ductal adenocarcinoma. Transl Oncol 2021, 14(7):101107. PMID: 33201660
3. Norberg KJ, Liu X, Fernandez Moro C, Strell C, Nania S, Blumel M, Balboni A, Bozoky B, Heuchel RL, Löhr JM: A novel pancreatic tumour and stellate cell 3D co-culture spheroid model. BMC Cancer 2020, 20(1):475. PMID: 32460715

Heterospheroid cell culture to identify new treatment options for pancreatic ductal adenocarcinoma

Our research focus is on understanding the cancer-stromal cell interaction in pancreatic ductal adenocarcinoma. To this end we have developed a 3D heterospheroid model including human pancreatic cancer cells and mouse pancreatic stellate cells (CAFs) allowing the direct investigation of their crosstalk by expression profiling without any prior manipulation such as single cell preparation. We have adapted this model (then human/human) for high throughput drug screening in collaboration with the Chemical Biology Consortium Sweden (CBCS) and developed an imaging application as an optical reporter assay for viability as well as phenotypical shift determination (CAF-like □ cancer cell-like spheroid morphology). A major aim of the drug screen was to identify drugs that have a negative impact on cancer cells, while having little or no effect cancer associated fibroblasts (CAFs = stroma). We identified an indoleamine 2,3-dioxygenase (IDO) inhibitor which fulfils these criteria. IDO has been implicated in pathological immunosuppression in several diseases including cancer.

Mats Heyman

Associate Professor

Paediatric Oncology and Paediatric Surgery
Department of Women's and Children's Health
Widerströmska huset, Tomtebodavägen 18a

076-0502326

Cancer research areas:

Acute lymphoblastic leukaemia; Childhood cancer

Key research field interests:

Clinical trials; Leukaemia therapy toxicity

Needs for collaboration:

Translational researchers in acute leukaemia

Selected publications:

1. Conter V, Valsecchi MG, De Lorenzo P, Gandemer V, Heyman M, Saha V, Diaz P, Li CK, Attarbaschi A, Escherich G, Stary J, Schrappe M, Pieters R, Cario G, Biondi A. No clear benefit of preventive cranial radiotherapy in childhood Philadelphia-positive acute lymphoblastic leukemia: a retrospective analysis of the EsPhALL2010 study. Haematologica. 2024 Jul 18. doi: 10.3324/haematol.2024.285253. Online ahead of print. PMID: 39021218
2. Moorman AV, Enshaei A, Murdy D, Joy M, Boer JM, den Boer ML, Pieters R, de Haas V, Horstmann MA, Escherich G, Johansson B, Marquart HV, Schmiegelow K, Hancock J, Moppett J, Heyman M. Integration of genetics and MRD to define low risk patients with B-cell precursor acute lymphoblastic leukaemia with intermediate MRD levels at the end of induction. Leukemia. 2024 Sep;38(9):2023-2026. PMID: 38965371
3. Taalas TL, Oskarsson T, Heyman M, Lund B, Lepik K, Vaitkevičiene G, Jonsson OG, Eriksson J, Toft N, Griškevičius L, Hallbook H, Palk K, Wartiovaara-Kautto U, Quist-Paulsen P, Noren-Nystrom U, Vettenranta K, Abrahamsson J, Schmiegelow K, Lahteenmaki PM. Impact of age and sex on survival outcomes in patients aged 1-45 years with acute lymphoblastic leukemia treated according to the stratification used in the NOPHO ALL2008 trial. Haematologica. 2025 Aug 1;110(8):1723-1735. PMID: 39973352

ALLTogether1 - A large clinical trial for Acute Lymphoblastic Leukaemia in Children and Young Adults conducted in 15 European Countries

The aims of the project are to improve survival and quality of survival for children and young adults with ALL.

Background: ALL in young people has excellent outcomes with >90% survival in children and about 75% in young adults. Nevertheless, patients still die of disease and, importantly, a relatively large group are over-treated. All patients risk treatment-related death and some suffer long-term side-effects. To show improvement with such good survival, large patient-populations are needed

Workplan: Treating physicians from the Nordic and Baltic countries (NOPHO), UK (UKALL), Netherlands (DCOG), Germany (COALL), Belgium (BSPHO), Ireland (PHOAI), Portugal (PGLP) France (SFCE) and Spain (SEHOP) have designed a common treatment-protocol for children and young adults with ALL. It addresses over-treatment by two randomisations to treatment-reduction and two randomizations test either Inotuzumab or modified maintenance to reduce relapse-risk. Patients with ABL-class fusions receive Tyrosine-kinase inhibitors and patients with Down syndrome receive Blinatumomab instead of chemotherapy elements.

Preliminary Results: ALLTogether1 is recruiting since 2020 (recruited patients until 17 Dec 2025: 4383), has low treatment-related mortality and with short follow-up good survival (with a median follow-up of 714 days, 3328 patients (0-45 years) included until the end of 2024 had a 2-year EFS of 93,8% (+/- SE 0,5%) and OS of 96,5% (+/- SE 0,3%). Methods: ALLTogether1 defines a backbone of diagnostics, stratifying therapy and risk-adapted therapy onto which experimental interventions of which some are randomised are added in a modular fashion.

The study constitutes standard of care for 25% of children with cancer. It may identify less toxic, but equally efficacious therapy for sub-groups of patients. Innovative therapy may further reduce relapses and subsequent death of ALL. The study will promote further treatment- and translational research and is in itself an important platform for basic, translational and treatment-oriented research in ALL.

Keith Humphreys

Professor

Department
Department of Medical Epidemiology and Biostatistics
Nobels väg 12A

Cancer research areas:

Breast cancer

Key research field interests:

Biostatistics, breast cancer, epidemiology, screening

Needs for collaboration:

Clinical expertise

Selected publications:

1. Strandberg R, Czene K, Hall P, Humphreys K. (2023) Novel predictions of breast cancer risk in mammography screening cohorts. Statistics in Medicine. 42: 3816-3837.
2. Strandberg R, Abrahamsson L, Isheden G, Humphreys K. (2023) Tumour Growth Models of Breast Cancer for Evaluating Early Detection – a Summary and a Simulation Study. Cancers. 15, 912.
3. Isheden G, Grassman F, Czene K, Humphreys K. (2021) Lymph node metastases in breast cancer: investigating associations with tumour characteristics, molecular subtypes and polygenic risk score using a continuous growth model. Int. J. Cancer. 149: 1348-1357.

Statistical models for breast cancer screening data – studies of aggressive breast cancer and screening performance

We develop and use biologically motivated statistical models of tumour progression to study the incidence and mortality and epidemiology of breast cancer. We also use these models to predict the risk of breast cancer, in particular aggressive breast cancer. The models are estimated using data from detailed population-based studies of breast cancer and breast cancer screening, combining longitudinal register, questionnaire, image and molecular data. We try to shed light on the roles of different factors in screening and symptomatic detection of breast cancer, and in tumour onset, growth and spread. The information we create can hopefully be useful for planning and evaluating new approaches to (secondary) prevention of breast cancer. Our risk prediction models rigorously incorporate screening information. We also use the models for studying effects of endocrine treatment.

Rozbeh Jafari

Docent

Cancer Proteomics
Department of Oncology-Pathology
SciLifeLab, Tomtebodavägen 23, 171 65 Solna

Cancer research areas:

Pediatric leukemia; Cancer signaling mechanisms; Targeted cancer therapy; Translational oncology

Key research field interests:

Multi-omic analysis of leukemias; Precision therapy of leukemias; Functional and chemical proteomics; Data-driven life science; Biomarker discovery and resistance mechanisms

Needs for collaboration:

Collaboration interests include access to primary ALL samples, advanced FACS/ immunophenotyping, PDX and in vivo leukemia models, functional genomics, and translational leukemia research. Drug design and development.

Selected publications:

1. Leo IR, et al. Integrative multi-omics and drug response profiling of childhood acute lymphoblastic leukemia cell lines. Nature Communications 13, 1691 (2022).
2. Cheung LC, et al. Preclinical efficacy of azacitidine and venetoclax for infant KMT2A-rearranged acute lymphoblastic leukemia reveals a new therapeutic strategy. Leukemia, (2022).
3. Kurzawa N, et al. Deep thermal profiling for detection of functional proteoform groups. Nat Chem Biol 19, 962-971 (2023).
4. Leo I, et al. Functional proteoform group deconvolution reveals a broader spectrum of ibrutinib offtargets. Nature Communications 16, 1948 (2025).

Harnessing developmental negative selection as a therapeutic strategy in ALL

MEF2D-rearranged B-cell precursor acute lymphoblastic leukemia (MEF2Dr-ALL) is a high-risk pediatric subtype characterized by frequent relapse and lack of targeted therapies. MEF2D fusion proteins enforce developmental arrest and create a strong dependency on pre-B cell receptor (pre-BCR)–associated signaling. In normal B-cell development, excessive pre-BCR/PKC/ERK signaling activates a negative-selection checkpoint that eliminates aberrant cells. Here, we explore whether this developmental safeguard can be therapeutically reactivated to selectively kill leukemia. Using integrated functional assays, time-resolved proteomics/phosphoproteomics, and thermal proteome profiling, we show that the clinical-stage PKC modulator bryostatin-1 (bryo-1) selectively induces apoptosis in MEF2Dr-ALL models. Bryo-1 rapidly activates PKC and drives sustained ERK signaling, followed by dismantling of the pre-BCR signaling apparatus, cell-cycle arrest, increased B-lineage maturation, and intrinsic apoptosis. Pharmacological MEK inhibition rescues cell viability, supporting ERK-dependent, on-target cytotoxicity consistent with forced negative selection. To enhance translational relevance, we established ex vivo cultures of MEF2Dr patient-derived xenograft (PDX) models (4/6 successfully expanded). In an initial PDX model, bryo-1 markedly reduced leukemic viability, which was fully reversed by MEK inhibition. Ongoing work integrates proteomic biomarker discovery with a genome-wide CRISPR/Cas9 knockout screen to identify genetic determinants of sensitivity and resistance. Together, these findings introduce developmental checkpoint activation, rather than pathway inhibition, as a distinct therapeutic paradigm in acute lymphoblastic leukemia, and provide a framework for biomarker-guided translation in MEF2Dr-ALL. We welcome collaborations to expand clinical sample access, PDX validation, and functional interrogation of negative-selection–based leukemia precision therapies.

Anna Jervaeus

Lektor, Docent

Division of Nursing
Department of Neurobiology, Care Sciences and Society
Alfred Nobels alle 23

+46 70 264 2039

Cancer research areas:

Cancer prevention; psycho-oncology

Key research field interests:

Health care sciences, patient reported outcomes, mixed research methods, psychometrics

Needs for collaboration:

Research partners, funding collaboration

Selected publications:

1. Fritzell K, Hedberg B, Woudstra A, Forsberg A, Sventelius M, Kottorp A, Jervaeus A (2023). Making the BEST decision-the BESTa project Development, implementation and evaluation of a digital Decision Aid in Swedish cancer screening programmes- a description of a research project PLoS One, 18(12), e0294332. PMID: 38085710, DOI: 10.1371/journal.pone.0294332
2. Ödling M, Jervaeus A, Wengström Y, Rosenberg A.R, Yi-Frazier J.P, Winterling J (2024). Adaptation and feasibility of the Swedish Promoting Resilience in Stress Management intervention targeting adolescents and young adults newly diagnosed with cancer. Journal of Psychosocial Oncology, 1-17 (online ahead of print). PMID: 39466132, DOI: 10.1080/07347332.2024.2419663
3. Fritzell K, Wangmar J, Hedberg B, Woudstra A, Forsberg A, Kottorp A, Franklin K.A, Jervaeus A (2025). Making the BEST decision-the BESTa project: Description of the design and alpha phases as part of the development of a digital Decision Aid for cancer screening in Sweden. Journal of Cancer Education, (online ahead of print). PMID: 40285812, DOI: 10.1007/s13187-025-02633-y

My research focus: cancer prevention and individuals living with a cancer experience

I have, since the beginning of the nationwide Screening of Swedish Colons (SCREESCO) study in 2014, taken a central and active role in that project. Individuals were randomized to colonoscopy or faecal immunochemical test (FIT) aiming to investigate how colorectal cancer (CRC) screening impact incidence and mortality in CRC. These studies have formed the basis for the continuation of working with cancer screening and developing a web-based decision aid (DA) for individuals invited to cancer screening. For the work with the DA we have formed a steering group with individuals with different backgrounds (including lay people), research experiences and an international outlook. I received a three-year (2023-2025) Fellowship Prevention from The Swedish Cancer Society, SEK 3 774 000 for the project with the DA. With the fellowship I have led the project and taken the overall responsibility for the whole research process and the DA is now in the form of a web page.

I am involved in and lead the research project: Promoting Resilience In Stress Management (PRISM). PRISM is an evidenced-based psychosocial program designed to reduce stress and build resilience. PRISM is being integrated into standard care within “Team Young”, a program that provides individualized support and access to psychosocial resources. The project is part of a larger development project (MINKOD/ MYCODE) driven by the Centre for innovation at Karolinska University Hospital and the patient organization Ung Cancer. Partners are the Sahlgrenska University Hospital, Regional Cancer Centre in Stockholm-Gotland and West, and the Centre for Person-Cantered Care at University of Gothenburg. The aim is to improve the lives of teenagers and young people living with cancer by investigating how the health care sector can be more dynamic in creating new forms of meeting and support. The name MINKOD stands for my solution to influence my life as a patient, based on my needs and with technology that supports me. We have one doctoral student employed and one post-doc working with a process evaluation of the implementation of PRISM. The doctoral student focuses both on young persons with cancer and young persons from the general population (as a reference sample to the PRISM cohort) We collaborate with the founders of PRISM, in Seattle, US.

I am also a collaborator in two EU-projects regarding young people with cancer: PredictAYA aims to improve the understanding and prediction of late effects- especially reproductive toxicity- in adolescents and young adults (AYAs) treated for cancer.

PanCare4AYA will develop an international clinical guideline for screening and follow-up of late effects of Adolescent and Young Adult (AYA) cancer, which will be implemented via a novel person-centred screening program (AYA Cancer Survivor Screen). The project will improve the health and quality of life of survivors across Europe through better Survivorship Care.

John Johnsen

Associate Professor

Pediatric Oncology and Pediatric Surgery
Department of Women's and Children's Health
Tomtebodavägen 18A

0706640643

Cancer research areas:

Pediatric cancer, neuro-oncology, translational research

Key research field interests:

Preclinical in vivo models, drug screening, evolutional biology

Needs for collaboration:

Zebrafish modelling, fish pathology, comparative bioinformatic

Selected publications:

1. Milosevic J, Fransson S, Svensson J, Otte J, Olsen TK, Sveinbjornsson B, Hertwig F, Bartenhagen C, Abel F, Reinsbach SE, Djos A, Javanmardi N, Shi Y, Hehir-Kwa JY, Mensenkamp A, Tytgat GA, Holmberg J, Molenaar JJ, Jongmans M, Fischer M, Baryawno N, Gisselsson D, Martinsson T, Kogner P*, Johnsen J*I. Gain of chromosome 17 is an early genetic abnormality in neuroblastoma with PPM1D emerging as a strong candidate oncogene driving tumor progression. Cancer Lett. 2025 Aug 10;625:217769. doi: 10.1016/j.canlet.2025.217769. Epub 2025 May 2. PMID: 40320038. *Shared last authorship.
2. Olsen TK, Otte J, Mei S, Embaie BT, Kameneva P, Cheng H, Gao T, Zachariadis V, Tsea I, Björklund Å, Kryukov E, Hou Z, Johansson A, Sundström E, Martinsson T, Fransson S, Stenman J, Fard SS, Johnsen JI, Kogner P, Adameyko I, Enge M, Kharchenko PV, Baryawno N. Joint single-cell genetic and transcriptomic analysis reveal pre-malignant SCP-like subclones in human neuroblastoma. Mol Cancer. 2024 Aug 31;23(1):180. doi: 10.1186/s12943-024-02091-y. PMID: 39217332; PMCID: PMC11365129.
3. Verhoeven BM, Mei S, Olsen TK, Gustafsson KU, Valind A, Lindström A, Gisselsson Nord D, Fard SS, Kogner P, Karchenko PV Johnsen JI*, Baryawno N*. The immune cell atlas of human neuroblastoma. Cell Rep Med. 2022 Jun 21;3(6):100657. doi: 10.1016/j.xcrm.2022.100657. *Shared last authorship.

Decoding and targeting mechanisms of neuroblastoma evolution

The overall goal for the research group is to reveal the heterogeneities, plasticity, molecular landscapes and cellular interactions of malignant and corresponding non-malignant cells in neuroblastoma (NB) to identify the cellular origin, mechanisms of drug resistance and druggable targets that can be transferred into clinical trials and new treatment options. NB is a neural crest-derived tumor of the peripheral nervous system showing heterogeneous clinical behavior manifested through numerous segmental chromosomal aberrations in which gene amplification of MYCN, deletion of chromosome (Chr)1p or 11q and segmental gain of Chr17q are associated with poor prognosis. Among these, gain of Chr17 is the most frequent genetic alteration observed in 80% of the patients. We apply multi-omic analyses and preclinical in vivo models to identify molecular vulnerabilities in NB tumor cells and surrounding microenvironment. Spatial-omics together with evolutionary trajectories to dichotomize the accumulation of chromosomal instabilities in NB show that gain of Chr17 is an early genetic abnormality in NB development and linked to the accumulation of additional chromosomal aberrations and poor prognosis. Increased segmental gains of Chr17q are observed during clonal evolution, relapse disease, metastasis and treatment resistance. We show that the p53-inducible Ser/Thr phosphatase, PPM1D, located on chr17q22.3, which acts as a negative regulator of p53, is activated by frequent segmental 17q-gain, gene-fusion or gain-of-function somatic and germline mutations in NB and that PPM1D overexpression strongly correlates to poor patient survival. We have shown that PPM1D is a de novo oncogene developing tumors when overexpressed in zebrafish and mice, including NB. We also show that NB are strictly dependent on high expression of PPM1D for survival and that genetically or pharmacological inhibition of PPM1D suppress the growth of NB mouse xenografts. The importance of Chr17q gain and candidate genes on Chr17q in NB are currently investigated using zebrafish, HESC and iPS-derived neural crest cells in different phases of maturation as model systems.

Mikael Karlsson

Professor

Division of Virology and Immunology
Department of Microbiology, Tumor and Cell Biology
Biomedicum C7

Cancer research areas:

Immunotherapy for cancer

Key research field interests:

Immunology; Inflammation; Clinical translation

Needs for collaboration:

Interested in collaborations to study our target cells and molecules in clinical cohorts

Selected publications:

1. Lamorte S. Quevedo R, Jin R, Neufeld L, Liu K, Ciudad T.M, Lukhele S Bruce J, Mishra S, Zhang X, Kamil Saeed Z, Berman H, Philpott D, Girardin S, Harding S, Munn D, Mak T.W, Karlsson M.C.I, Brooks D and McGaha T. 2025. Lymph node macrophages drive immune tolerance and resistance to cancer therapy by induction of the immune-regulatory cytokine IL-33. Cancer Cell (accepted for publication)
2. Eisinger S, Sarhan D, Boura V.F, Ibarlucea-Benitez I, Tyystjärvi S, Oliynyk G, Arsenian-Henriksson, Lane D, Wikström S.L, Kiessling R, Virgilio T, Gonzalez S.F, Kazcynska D, Kanatani S, Daskalaki E, Wheelock C.E, Sedimbi S, Chambers B.J, Ravetch J.V and Karlsson M.C.I. 2020 Targeting a scavenger receptor on tumor-associated macrophages activates tumor cell killing by NK cells. Proc. Natl. Acad. Sci. 15;117(50):32005
3. Georgoudaki A.M, Prokopec K, Boura V.F, Hellqvist E, Sohn S, Östling J, Dahan, R, Harris R, Rantalainen M, Klevebring D, Sund M, Egyhazi Brage S, Fuxe J, Rolny C, Li F, Ravetch J.V.R, and Karlsson M.C.I. 2016 Reprograming tumor associated macrophages by antibody targeting inhibits cancer progression and metastasis. Cell Rep. 31;15(9):2000

Targeting immune cells in the tumor microenvironment to develop cure for cancer

It has been known for over one hundred years that the immune system has the capacity to recognize and kill tumor cells. However, it is only recently that immunotherapy has started to become effective and is taking its place alongside surgery, radiotherapy and chemotherapy as a fourth option for treatment of many cancers. The reason immunotherapy has taken so long to come into its own is that tumor antigens are for the most part “self” and therefore are not easily recognized by the immune system owing to inherited tolerance mechanisms. In addition, tumors evolve mechanisms for evading immune recognition and acquire the ability to actively suppress immune cell activation. It is thus only recently that checkpoint inhibitors targeting CTLA-4 and PD-1 were shown to release the breaks on the immune system, resulting in enhanced T cell activation against tumors. Although T-cell directed therapy has opened new avenues for treatment, many patients do not respond to checkpoint therapy and some types of cancer such as pancreatic cancer are harder to treat, and clinical trials have been disappointing. Tumor-associated macrophages (TAMs) are a major hurdle, blocking the efficiency of immunotherapy as they stop cytotoxic T cells and NK cells from killing tumor cells. It has also been shown that TAMs promote metastases formation. We have discovered that antibodies (anti-MARCO) targeting a pattern-recognition receptor of the scavenger receptor (SR) family expressed by TAMs, can be used to modify TAM polarization. This resulted in enhanced anti-tumor responses in mice and prevention of metastases. Thus we propose to target TAMs, neutrophils and B cells as a novel approach for immunotherapy. The central hypothesis is that the activation of key inflammatory pathways or deletion of specific subpopulations using appropriate antibodies will disturb and remodel the immunosuppressive environment within a tumor and thus increase the efficacy of immunotherapy. If successful, our project will lead to a paradigm shift in our approach to treat cancer and turn “cold” tumors into “hot” and treatable.

Ourania Kostopoulou

Docent

Cell-based immune therapy for cancer
Department of Oncology-Pathology
Bioclinicum J6:20, Solnavägen 30, 17164, Solna
+46762120329

Cancer research areas:

Childhood cancer

Key research field interests:

Neuroblastoma; Medulloblastoma; Therapy resistance; Protein synthesis

Needs for collaboration:

Patient material; Support on bioinformatic analysis; Machine learning expertise

Selected publications:

1. Lukoseviciute M, Birgersson M, Ceriani P, Wilhelm M, Kostopoulou ON. Dual PI3K/AKT and CDK4/6 inhibition reveals selective sensitivity in a SHH-Medulloblastoma stem cell model. Molecular oncology, in press 2026.
2. Lukoseviciute M, Need E, Birgersson M, Dalianis T, Kostopoulou ON. Enhancing targeted therapy by combining PI3K and AKT inhibitors with or without cisplatin or vincristine in medulloblastoma cell lines in vitro. Biomedicine and Pharmacotherapy, 180, 117500, 2024
3. Lukoseviciute M, Need E, Holzhauser S, Dalianis T, Kostopoulou ON. Combined targeted therapy with PI3K and CDK4/6, or FGFR inhibitors show synergistic effects in a neuroblastoma spheroid culture model. Biomedicine and Pharmacotherapy, 177, 116993, 2024.

Studies on combined targeted therapies on neuroblastoma and medulloblastoma

Medulloblastoma (MB) and Neuroblastoma (NB) are tumors of the central and peripheral nervous systems, respectively. MB primarily affects children and adults under 40 years old, while most but not all NBs are diagnosed in children. Despite initially effective therapies, high-risk NB and metastatic MB often develop resistance, leading to fatal outcomes, with survivors, especially those with MB, facing significant long-term side effects. Therefore, there is an urgent need for improved treatments. To overcome therapy resistance in MB and NB by systematically identifying and precisely targeting multiple key pathways based on the unique molecular profiles of these tumors.

Our group's main focus is to: 1) identify optimal combinations of novel drugs (Phosphatidylinositol 3-kinase (PI3K), fibroblast growth factor receptor (FGFR), Cyclin-dependent kinase (CDK) 4/6, and other novel inhibitors with/without cytostatics) on monolayer (2D) /spheroid (3D) cultures (the latter to better mimic the in vivo situation) in correlation to tumor molecular profile; 2) follow subclonal evolution after optimally selected combination treatments using barcoded NB/MB cell lines and identify gene expression alterations in resistant clones by single cell RNA sequencing; 3) validate the best in vitro drug combinations in vivo in zebrafish and mouse models.

Recent data have shown that combinations of PI3K-FGFR and PI3K-CDK4/6 inhibitors demonstrated synergistic effects in 2D NB/MB lines, allowing for reduced drug doses compared to single treatments. Preliminary results from 3D NB cultures are promising and align with the findings from the 2D models.

Therefore, this project aims to accelerate the development of optimized combination therapies for NB/MB, addressing resistance to conventional treatments and improving both patient survival and quality of life through more effective, lower-dose treatments.

My team is also working in close collaboration with Tina Dalianis group which is focused on targeted therapy in head and neck cancer.

Taras Kreslavskiy

Principal Researcher

Division of Immunology and Respiratory Medicine
Department of Medicine, Solna
CMM L8:05, Karolinska Universitetssjukhuset

Cancer research areas:

Gamma delta T cells in cancer

Key research field interests:

We have two main directions of research: I) mechanisms of cell fate decisions in humoral immune responses underlying the formation of immunological memory and II) specificity, development, and function of innate-like lymphocytes (in particular - gamma delta T cells, in general and in cancer setting).

Needs for collaboration:

We would be interested in collaborations on understanding gamma delta T cell antigen pecificities in human cancers

Selected publications:

1. You, Y., J. Dunst, K. Ye, P. Sandoz, A. Reinhardt, I. Sandrock, N. R. Comet, R. D. Sarkar, E. Yang, E. Duprez, J. Agudo, B. D. Brown, P. J. Utz, W. Kastenmüller, C. Gerlach, I. Prinz, B. Önfelt and T. Kreslavsky (2024). Direct presentation of inflammation-associated self-antigens by thymic innate-like T cells induces elimination of autoreactive CD8 thymocytes. Nature Immunology, 25(8):1367-1382 PMID: 38992254
2. Rauschmeier R., Reinhardt A., Gustafsson C., Glaros V., Artemov A.V., Dunst J., Taneja R., Adameyko I., Månsson R., Busslinger M.#, and T. Kreslavsky#. (2022) Bhlhe40 function in activated B and TFH cells restrains the GC reaction and prevents lymphomagenesis. (# - corresponding authors), Journal of Experimental Medicine, 219(2):e20211406. PMID: 34919144.
3. Glaros V., R. Rauschmeier, A.V. Artemov, A. Reinhardt, S. Ols, A. Emmanouilidi, C. Mirabello, Å.K. Björklund, L. Perez, N.P. King, D. Angeletti, K. Loré, I. Adameyko, M. Busslinger, and T. Kreslavsky. (2021) Limited access to antigen drives the generation of early B cell memory while restraining the plasmablast response. Immunity, 54(9):2005-2023.e10. PMID: 34525339

Dissection of gamma-delta T cell antigen specificities in health and disease

All three classes of lymphocytes that constitute the adaptive immune system of jawed vertebrates – B cells, alpha-beta (ab)T cells, and gamma-delta (gd)T cells – can be found in tumors. While the rules of antigen recognition by B cells and abT cells are well-understood, the nature of antigens for gdT cells remains largely elusive, which greatly limits our understanding of the functions of these cells. Multiple lines of evidence suggest that differentiation of many effector gdT cell subsets is driven by recognition of “endogenous antigens” by their gdT cell receptors (gdTCRs). While in most cases the molecular nature of such endogenous antigens remains enigmatic, a few known examples include molecules induced by stressed and transformed cells. It remains largely unknown whether gd tumor-infiltrating lymphocytes (gdTILs) recognize such antigens or operate through TCR-independent innate mechanisms.

To start dissecting antigen receptor specificities of gdT cells, we established a pipeline for assessing gdTCR reactivities. This involves expression of TCRs of interest in TCR signaling reporter cells, identification of TCR/ligand expressing cell pairs in co-culture experiments, and cDNA library screens for ligand identification. We first applied this approach to mouse gdTCRs cells at steady state. These experiments showed that a large fraction of mouse gdT cells recognize a diverse set of unknown endogenous antigens and allowed us to identify several of these gdTCR ligands. Unexpectedly, this included a proinflammatory cytokine receptor chain IL17RA that drove differentiation of ~10% of mouse gdT cells through an unusual superantigen-like interaction with their gdTCRs.

We next sought to apply this pipeline to understand antigen receptor specificity of human gdTILs. As gdT cells are particularly important early in ontogeny and function in an MHC-independent fashion, we focused our efforts on neuroblastoma (NB) – the deadliest pediatric cancer that frequently downregulates MHC I expression. Our scRNA/TCR-seq analysis of gdTILs identified expanded clones in 6 out of 6 NB patients in which TCR sequences were obtained for at least 50 gdTILs. Some of these clones exhibited cytotoxic signature, suggesting the possible participation in the anti-tumor response. Expression of 22 such TCRs in reporter cells allowed us to identify 7 TCRs that exhibited reactivity to NB cell lines. Taken together, these results indicate that clonally expanded NB-infiltrating gdT cells recognize yet-to-be-identified molecules expressed by NB cells.

Bennie Lemmens

Assistant Professor

Genome Biology
Department of Medical Biochemistry and Biophysics
SciLifeLab, Tomtebodavägen 23A, Floor A4

Cancer research areas:

Fundamental cancer cell biology and genetics

Key research field interests:

Genome Stability; DNA replication; Cell division; Drug responses; Advanced Microscopy

Needs for collaboration:

Retinoblastoma protein (RB) model systems

Selected publications:

1. Temporal control of human DNA replication licensing by CDK4/6-RB signalling and chemical genetics. Sosenko Piscitello A, Nilsson AS, Hawgood M, Sayyid AH, Dionellis VS, Giglio G, Urién B, Bajgain P, Ntallis SG, Bartek J, Halazonetis TD, Lemmens B Nat Commun 2025 Sep
2. Spatial mapping of DNA synthesis reveals dynamics and geometry of human replication nanostructures. Hawgood M, Urién B, Agostinho A, Thiagarajan P, Giglio G, Yang Y, Zhang X, Quijada G, Fonseca M, Bartek J, Blom H, Lemmens B EMBO J 2025 Oct

How does the CDK4/6-RB axis control DNA replication licensing and associated p53-dependent cell fates?

CDK4/6 inhibitors have become a mainstay in breast cancer therapy, targeting the RB pathway to block cell-cycle progression in metastatic tumors. Yet, the tumor-suppressive functions of RB are incompletely understood, and drug resistance to targeted therapies remains a major challenge in the clinic. Our recent preclinical work reveals that the CDK4/6–RB signaling axis not only governs cell-cycle entry but also controls DNA replication licensing, a process ensuring that each segment of the genome is duplicated once per cell cycle. We find that CDK4/6 activity promotes origin licensing in human cells by antagonizing all three RB family members: RB, RBL1, and RBL2. Therapeutic CDK4/6 inhibitors cause a defect in MCM and ORC6 loading, which, when maintained, triggers mitosis with unreplicated DNA in p53-deficient backgrounds. To monitor DNA replication dynamics in space and time and dissect the molecular mechanisms controlling replication licensing, we have developed advanced genetic models, conditional protein degradation systems, time-resolved EdU sequencing methods, and super-resolution microscopy assays. I look forward to discussing our latest findings with the CRKI community and together explore how we can convert these fundamental insights into potent RB- and p53-selective cancer therapies.

Andreas Lennartsson

Associate Professor, Docent

HERM
Department of Medicine, Huddinge
Hälsovägen 7C, 14145 Huddinge

Cancer research areas:

Acute Myeloid Leukemia

Key research field interests:

Epigenetics, transcriptomics

Needs for collaboration:

Metabolism

Selected publications:

1. Disease specific epigenetic deregulation of enhancers, transposons and polycomb targets in acute promyelocytic leukemia. Xiangfu Zhong*, Lina Cordeddu Angelica Gamboa-Cedeno, Sofia Bengtzén, Karl Ekwall, Andreas Lennartsson*, Sören Lehmann*, Genome Med. 2025 Oct 30;17(1):135. doi: 10.1186/s13073-025-01565-y, *Equal contribution
2. Targeting Dysegulated Epigenetic and Transcription Factor Networks in KMT2A-Rearranged AML Using iPSC Models, Anna Palau, Jonas Thier, Aonghus Naughton, Andrew Tae-Jun Kwon, David Cabrerizo Granados, Sophia Hofmann, Bogumił Kaczkowski, Xiangfu Zhong, Sören Lehmann, Erik Arner, Vanessa Lundin*, Andreas Lennartsson*, Blood Neoplasia, accepted in print *Equal contribution
3. Perturbed epigenetic transcriptional regulation in AML with IDH mutations causes increased susceptibility to NK cells Anna Palau, Filip Segerberg, Michael Lidschreiber, Katja Lidschreiber, Aonghus J. Naughton, Maria Needhamsen, Lisa Anna Jung, Maja Jagodic, Patrick Cramer, Sören Lehmann*, Mattias Carlsten*, Andreas Lennartsson*, Leukemia, 2023 Jul 26 doi: 10.1038/s41375-023-01972-3, *Equal contribution

Targeting Epigenetic and Transcriptional vulnerabilities in AML

Epigenetic dysregulation driven by various mechanisms is a major contributor to the development of acute myeloid leukemia (AML). We have identified several novel therapeutic approaches to target epigenetic and transcriptional deregulation in AML. Using induced pluripotent stem cells (iPSCs) derived from an AML patient, we demonstrate that inhibition of the Polycomb repressive complex 2 (PRC2) partially restores the AML phenotype in cases harboring KMT2A chromosomal rearrangements. KMT2A-rearranged AML is associated with a poor prognosis, and our findings may offer a novel therapeutic avenue for this AML subtype.

Mutations in isocitrate dehydrogenase (IDH) are present in approximately 20% of AML patients. Mutant IDH enzymes produce an oncometabolite that inhibits DNA demethylation. Genome-wide DNA methylation and RNA-seq analyses from a large AML patient cohort revealed that the HLA class I cluster is also hypermethylated and transcriptionally repressed. This repression increases susceptibility to NK cell–mediated cytotoxicity, suggesting that AML with IDH mutations may be particularly suitable for NK cell–based immunotherapy.

To further dissect the epigenomic and transcriptional variation in AML, we mapped the genome-wide landscape of eight histone modifications. In addition, we performed 5′-based RNA sequencing in both bulk (Cap Analysis of Gene Expression, CAGE; n = 88) and single-cell (n = 16) AML samples. Both approaches capture transcripts at transcription start sites, enabling the identification of transcribed cis-regulatory elements (tCREs), including promoters and enhancers. Based on bulk tCRE profiles, we classified four molecular subtypes characterized by distinct cellular compositions, clinical outcomes, and associations with specific somatic mutations. To explore cell type–specific effects of these mutations, we compared tCRE profiles of cells carrying mutant versus wild-type alleles using single-cell data. Integrating this information with deconvolution of bulk data, we identified differentially active tCREs across multiple cell types for the ten most frequent somatic mutations. Finally, to pinpoint key regulatory factors within these modules, we analyzed transcriptional regulatory network centrality. Centrality scores significantly reflected AML impact and were strongly associated with drug response. Overall, this study elucidates tCRE-driven regulatory mechanisms that are often overlooked by conventional gene-centric RNA-seq analyses, providing new insights into the transcriptional architecture of cytogenetically normal AML (CN-AML).

Xiaofei Li

Assistant Professor

Neurogeriatrics
Department of Neurobiology, Care Sciences and Society
Solnavägen 30

0703167775

Cancer research areas:

CNS tumor, childhood cancer

Key research field interests:

Cancer stem cells, organoids, single-cell and spatial omics

Needs for collaboration:

Gene editing, scCRISPR screening

Selected publications:

1. Li X; Andrusivova Z; Czarnewski P; Langseth CM; Andersson A; Liu Y; Gyllborg D; Braun E; Larsson L; Hu L; Alekseenko Z; Lee H; Avenel C; Kallner HK; Akesson E; Adameyko I; Nilsson M; Linnarsson S; Lundeberg J; Sundstrom E. Profiling spatiotemporal gene expression of the developing human spinal cord and implications for ependymoma origin. NATURE NEUROSCIENCE. 2023;26(5):891-901.

Sten Linnarsson

Professor

Molecular Neurobiology
Department of Medical Biochemistry and Biophysics
Solnavägen 9

+46703993206

Cancer research areas:

Brain cancer

Key research field interests:

Brain cancer, single-cell transcriptomics, spatial transcriptomics, lipid nanoparticles, DNA therapy, ATMP, gene therapy

Needs for collaboration:

Expertise in translation of advances therapies, development of therapeutic DNA vectors, immuno-oncology

Selected publications:

1. Futile wound healing drives mesenchymal-like cell phenotypes in human glioblastoma Alejandro Mossi Albiach, Jokubas Janusauskas, Jesper Kjaer Jacobsen, Ivana Kapustová, Razieh Karamzadeh, Egle Kvedaraite, Lijuan Hu, Marina C. M. Franck, Camiel Mannens, Simone Codeluppi, Johannes B. Munting, Lars E. Borm, Alia Shamikh, Peter Lönnerberg, Kimberly A. Siletti, Oscar Persson, Sten Linnarsson bioRxiv 2023.09.01.555882; doi: https://doi.org/10.1101/2023.09.01.555882
2. Siletti K, Hodge R, Mossi Albiach A, Lee KW, Ding SL, Hu L, Lönnerberg P, Bakken T, Casper T, Clark M, Dee N, Gloe J, Hirschstein D, Shapovalova NV, Keene CD, Nyhus J, Tung H, Yanny AM, Arenas E, Lein ES, Linnarsson S. Transcriptomic diversity of cell types across the adult human brain. Science 382(6667):eadd7046. 2023
3. Braun E, Danan-Gotthold M, Borm LE, Lee KW, Vinsland E, Lönnerberg P, Hu L, Li X, He X, Andrusivová Ž, Lundeberg J, Barker RA, Arenas E, Sundström E, Linnarsson S. Comprehensive cell atlas of the first-trimester developing human brain. Science 382(6667):eadf1226. 2023

Towards DNA immunotherapy for glioblastoma

Glioblastoma affects about 350 persons annually in Sweden. Treatment options are non-targeted (surgery, radiotherapy, chemotherapy) and ineffective, leading to a median survival of only about 12 months, essentially unchanged for decades. Targeted molecular therapies have failed, despite hundreds of trials, and so have initial trials of checkpoint inhibitors and cancer vaccines. CAR T cells have shown some promise in a few individual patients in early trials, but most cases have been resistant or relapsed rapidly. Thus, new approaches are needed. We are developing a DNA immunotherapy based on the intratumoral reprogramming of tumor cells to antigen-presenting type 1 dendritic cells (cDC1s), pioneered by Filipe Pereira in Lund. To deliver DNA efficiently and specifically to glioblastoma tumor cells, we have developed peptide-decorated lipid nanoparticles targeting ubiquitous tumor receptors. To enhance reprogramming efficiency, we are optimizing the DNA vector with engineered DNA, RNA and protein features that maximize transcription, translation and reprogramming in the specific epigenetic context of human primary glioblastoma. I will discuss (1) key challenges in developing DNA-based therapy for brain cancer, (2) perspectives towards a maximally informative “window-of-opportunity” design of future phase I trials, (3) the ethics of such a trial design.

Sergio Martinez Høyer

Project Leader

Virology and Immunology
Department of Microbiology, Tumor and Cell Biology
Biomedicum C7, Solnavägen 9 171 65 Solna

Cancer research areas:

Hematology

Key research field interests:

Hematopoiesis, Type 2 inflammation, Innate lymphoid cells, clonal hematopoiesis, myeloid malignancies

Needs for collaboration:

Study type 2 inflammation in different cancer models

Selected publications:

1. Mathä L*, Krabbendam L*, Martinez Høyer S*, et al. Human CD127 negative ILC2s show immunological memory. J Exp Med. 2024;221(8):e20231827. doi:10.1084/jem.20231827. *Equal contribution.
2. Ma J, Urgard E, Runge S, Classon CH, Mathä L, Stark JM, Cheng L, Álvarez JA, von Zedtwitz S, Baleviciute A, Martinez Hoyer S, Li M, Gernand AM, Osbelt L, Bielecka AA, Lesker TR, Huang HJ, Vrtala S, Boon L, Beyaert R, Adner M, Martinez Gonzalez I, Strowig T, Du J, Nylén S, Rosshart SP, Coquet JM. Laboratory mice with a wild microbiota generate strong allergic immune responses. Sci Immunol. 2023 Sep 29;8(87):eadf7702. doi: 10.1126/sciimmunol.adf7702.
3. Martinez-Høyer S, Deng Y, Parker J, et al. Loss of lenalidomide-induced megakaryocytic differentiation leads to therapy resistance in del(5q) myelodysplastic syndrome. Nat Cell Biol. 2020;22(5):526-533. doi:10.1038/s41556-020-0497-9.

Alexios Matikas

Associate Professor, Team Leader, Senior Consultant

Translational Breast Cancer Research
Department of Oncology-Pathology
Gävlegatan 55

Cancer research areas:

Breast cancer

Key research field interests:

Clinical oncology, epidemiology, translational research/biomarker discovery, biostatistics methods

Needs for collaboration:

In vitro/functional studies for confirmation of findings from correlative multiomics analyses from clinical samples

Selected publications:

1. Offens A, Teeuwen L, Gucluler Akpinar G, Steiner L, Kooijmans S, Mamand D, Weissinger H, Käll A, Eldh M, Wiklander OPB, El-Andaloussi S, Karlsson MCI, Vader P, Gabrielsson S. A fusion protein that targets antigen-loaded extracellular vesicles to B cells enhances antigen-specific T cell expansion. J Control Release. 2025 Mar 25;382:113665. PMID: 40147536.
2. Steiner L, Eldh M, Offens A, Veerman RE, Johansson M, Hemdan T, Netterling H, Huge Y, Abdul-Sattar Aljabery F, Alamdari F, Lidén O, Sherif A, Gabrielsson S. Protein profile in urinary extracellular vesicles is a marker of malignancy and correlates with muscle invasiveness in urinary bladder cancer. Cancer Lett. 2025 Jan 28;609:217352. PMID: 39586489.
3. Veerman, RE, Güclüler Akpinar G, Annemarijn Offens A, Steiner L, Larssen P, Lundqvist, A, Karlsson, MCI, Gabrielsson S. Antigen-Loaded Extracellular Vesicles Induce Responsiveness to Anti-PD-1 and Anti-PD-L1 Treatment in a Checkpoint Refractory Melanoma Model. Cancer Immunol. Res. 2022. 11:217-227. PMID: 36546872.

Investigating the effect of (neo)adjuvant chemotherapy for early breast cancer: clinical and molecular correlations

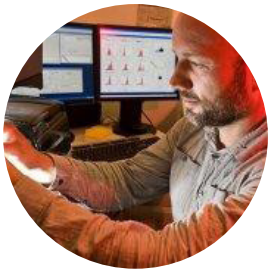
Neoadjuvant and adjuvant chemotherapy for early breast cancer improves patient survival, although not all patients respond and can thus be exposed to unnecessary side effects. The overarching goal is to understand the factors and mechanisms that govern response to treatment.

In the academic phase 3 trial PANTHER, dose dense and standard interval adjuvant chemotherapy were compared. Long-term follow-up is available, with the primary analysis recently published in JCO (Matikas et al 2024). RNA sequencing from >500 patients has been completed, digitized H&E images from >1000 patients are available, whereas multiplex fluorescent immunohistochemistry is underway. The goal is to identify predictive biomarkers for dose dense chemotherapy, a sparsely explored area in the breast cancer literature. In a preliminary analysis, we will present at San Antonio Breast Cancer Symposium one of the very first transcriptomic profiles that predict benefit to dose dense, but not to standard interval chemotherapy (Salgkamis, ... , Matikas. Abstract received a merit award). In another example of development of a predictive biomarker, using the neoadjuvant PREDIX LumB trial which compared preoperative palbociclib/endocrine therapy versus chemotherapy, we developed and externally validated CDKPredX, the very first predictive transcriptomic profile for CDK4/6 inhibitors (Matikas et al, under second round of review in Nature Communications).

At the same time, we explore neoadjuvant treatment for HER2-positive breast cancer in the academic randomized phase 2 trial ARIADNE which is ongoing in Sweden, Norway and Belgium and will soon open in Italy and Netherlands. In total, approximately 100 patients have been enrolled and 300 more will be included to receive either standard chemotherapy and dual HER2 blockade (TCHP) or the revolutionary antibody-drug conjugate trastuzumab deruxtecan, with further treatment individualization according to molecular subtyping. Within ARIADNE baseline, on-treatment and post-treatment biopsies are obtained and cores are both snap frozen for bulk whole exome and RNA seq and dissociated immediately for single-cell analyses.

The third focus of my research is based on registry data, where we have constructed and curated a dataset of primary breast cancer with linkage to multiple registries and completed missing data from patient charts to give answers to pertinent clinical questions. Using this dataset, during the past 15 months we have published four original articles in journals with IF >8 (senior author in three).

Jakob Michaelsson



Group Leader

CIM
Department of Medicine, Huddinge
Alfred Nobels allé 8, Huddinge

+46-763-142535

Cancer research areas:

Lung cancer; basic research

Key research field interests:

Immunology, NK cells

Needs for collaboration:

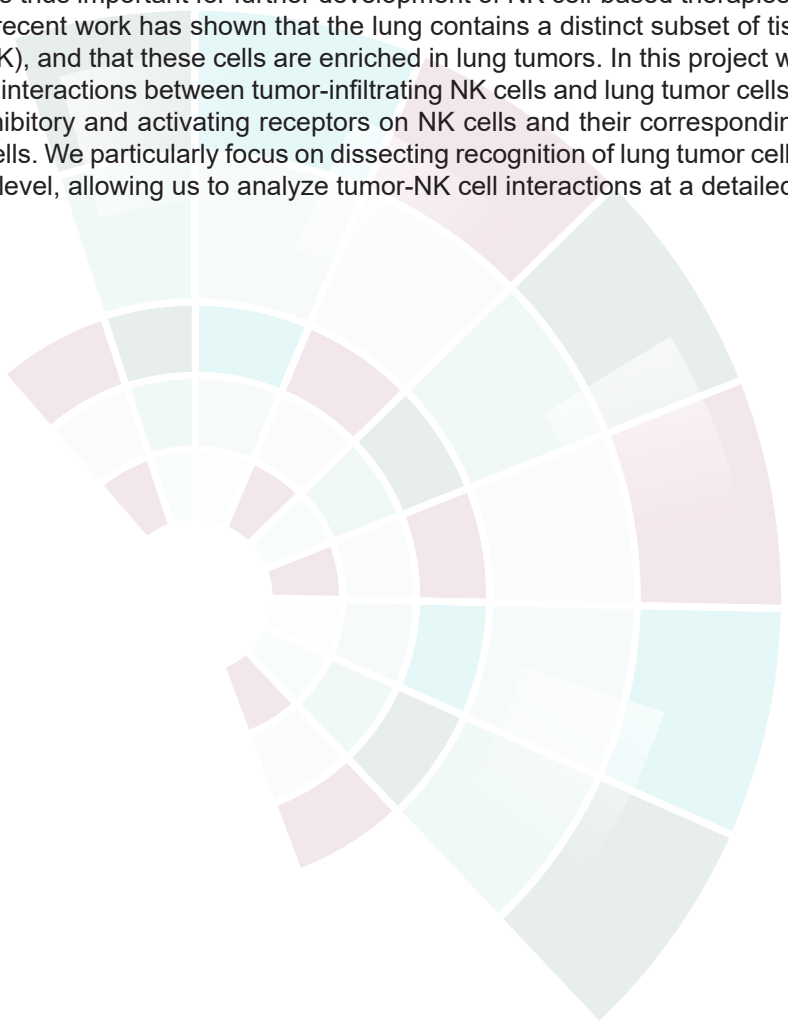
Access to fresh clinical material

Selected publications:

1. Expansions of adaptive-like NK cells with a tissue-resident phenotype in human lung and blood. Brownlie D, Scharenberg M, Mold JE, Hård J, Kekäläinen E, Buggert M, Nguyen S, Wilson JN, Al-Ameri M, Ljunggren HG, Marquardt N, Michaëlsson J. Proc Natl Acad Sci U S A. 2021, 118(11):e2016580118.
2. Unique transcriptional and protein-expression signature in human lung tissue-resident NK cells. Marquardt N, Kekäläinen E, Chen P, Lourda M, Wilson JN, Scharenberg M, Bergman P, Al-Ameri M, Hård J, Mold JE, Ljunggren HG, Michaëlsson J. Nat Commun. 2019, 10(1):3841.
3. Accumulation of tissue-resident natural killer cells, innate lymphoid cells, and CD8(+) T cells towards the center of human lung tumors. Brownlie D, von Kries A, Valenzano G, Wild N, Yilmaz E, Säfholm J, Al-Ameri M, Alici E, Ljunggren HG, Schliemann I, Aricak O, Haglund de Flon F, Michaëlsson J, Marquardt N. Oncoimmunology. 2023, 12(1):2233402.

Dissecting the functional regulation of lung tumor-infiltrating human NK Cells

NK cells are innate lymphocytes known to mediate cytotoxicity against tumor cells. Most of our knowledge regarding human NK cell function comes from studies of blood, and less is known about NK cells in tissues, including the lung. Elucidating the functional regulation of NK cells in lung tumors is thus important for further development of NK cell-based therapies against lung cancer. Our recent work has shown that the lung contains a distinct subset of tissue-resident NK cells (trNK), and that these cells are enriched in lung tumors. In this project we are aiming at dissecting interactions between tumor-infiltrating NK cells and lung tumor cells, in particular analysing inhibitory and activating receptors on NK cells and their corresponding ligands on lung tumor cells. We particularly focus on dissecting recognition of lung tumor cells by NK cells at the clonal level, allowing us to analyze tumor-NK cell interactions at a detailed level.



Thomas Müller

Assistant Professor

HERM
Department of Medicine, Huddinge
Medicinaren 25
Neo Blickagången 16, 141 52 Huddinge

Cancer research areas:

Biology of tumor-specific T cell responses; T cell engineering for immunotherapy

Key research field interests:

High-throughput identification of antigen-specific T cells; Characterization of T cell responses in solid tumors & circulation (tumor-specific & bystander responses) including cross-talk with other immune subsets; Tissue-homing and physiological adaptations to microenvironment; Synthetic immunity / T cell engineering / TCR-T cells

Needs for collaboration:

Immunopeptidomics / Prediction of tumor-specific epitopes; Machine Learning & Mathematical Modelling; Clinical partners (exchange & knowledge transfer, samples)

Selected publications:

1. Tissue origin and virus specificity shape human CD8+ T cell cytotoxicity; Science Immunology, DOI: 10.1126/sciimmunol.adq4881
2. Orthotopic replacement of T-cell receptor α- and β-chains with preservation of near-physiological T-cell function; Nature Biomedical Engineering, DOI: 10.1038/s41551-019-0409-0
3. Targeted T cell receptor gene editing provides predictable T cell product function for immunotherapy; Cell Reports Medicine, DOI: 10.1016/j.xcrm.2021.100374

Tissue origin shapes human CD8+ T cell cytotoxicity

CD8+ T cells are the immune system's premier cytotoxic effectors, yet how their killing machinery adapts across different tissue environments remains poorly understood – a critical gap given that tumor-infiltrating T cells must function within challenging microenvironments similar to the situation in normal tissues. Using a unique human organ donor cohort, we discovered that CD8+ T cell cytotoxicity is significantly remodeled based on tissue location, revealing previously unrecognized compartmentalization of immune function.

Circulating memory CD8+ T cells displayed peak expression of classical cytotoxic molecules – granulysin, perforin, and granzyme B – but these weapons were progressively downregulated as T cells took up residence in tissues, inversely correlating with classical tissue residency markers CD69 and CD103. Remarkably, other granzymes (A, H, K, M) showed distinct tissue-specific patterns indicating divergent function and regulation.

To understand the mechanisms driving this compartmentalization, we used an in vitro tonsil system that revealed TGF-β as a key environmental sculptor, creating discordant regulation between cytotoxic molecules and residency markers. However, IL-15 could override this programming, driving proliferation and restoring potent killing activity through perforin and granzyme B pathways, as confirmed by comprehensive CRISPR/Cas9 knockout experiments.

These findings refine our understanding of T cell biology, demonstrating that cytotoxic function is intricately tuned by local environmental cues rather than being a fixed cellular property. For cancer immunotherapy, this work suggests that tissue-resident T cells within tumors may require specific activation strategies distinct from circulating populations, potentially explaining variable therapeutic responses and opening new avenues for enhancing anti-tumor immunity through targeted manipulation of tissue-specific T cell programs.

Elinor Nemlander

PhD, Principal Investigator for STEADY-CAN

Division of Family Medicine and Primary Care
Department of Neurobiology, Care Sciences and Society
Alfred Nobels allé 23, A4 141 83 Huddinge

Cancer research areas:

Early detection and diagnosis; Primary care oncology; Cancer epidemiology; Real-world data; Implementation science; Health equity

Key research field interests:

Early cancer detection across cancer types; Diagnostic pathways and risk prediction in primary care; Implementation of new technologies for cancer diagnosis; Real-world data linkage and machine learning; Health services and equity in cancer care; Socio-demographic determinants of cancer diagnosis.

Needs for collaboration:

I am looking for collaborations with researchers interested in early cancer detection, diagnostic pathways, and risk prediction. In particular, I welcome partnerships with data scientists, biostatisticians, clinicians, health economists, and translational researchers who can contribute to modelling, biomarker integration, health economic evaluations, and equity analyses using the STEADY-CAN cohort. Collaborations around implementation and evaluation of new diagnostic technologies in primary care and population-based settings are also highly relevant.

Selected publications:

1. Nemlander E, Abedi E, Ljungman P, Hasselström J, Carlsson AC, Rosenblad A. The Stockholm early detection of cancer study (STEADY-CAN): rationale, design, data collection, and baseline characteristics for 2.7 million participants. Eur J Epidemiol. 2025 Jan;40(1):123-136. doi: 10.1007/s10654-024-01192-8. Epub 2025 Jan 5. PMID: 39755982; PMCID: PMC11799118.
2. Nemlander E, Schultz K, Nilsson G, Lapins J. New technology and working methods to improve healthcare for suspected malignant skin lesions: Implementation of teledermatoscopy in comprehensive healthcare. JEADV CLINICAL PRACTICE. 2024;3(5):1467-1477. DOI: 10.1002/jvc2.486
3. Nemlander E, Ewing M, Abedi E, Hasselstrom J, Sjovall A, Carlsson A, Rosenblad A. A machine learning tool for identifying non-metastatic colorectal cancer in primary care. EUROPEAN JOURNAL OF CANCER. 2023;182:100-106. PMID: 36758474, DOI: 10.1016/j.ejca.2023.01.011

The Stockholm Early Detection of Cancer Study (STEADY-CAN): expanding a population-based cohort to integrate sociodemographic and biomarker data for research on early cancer detection

Background: Early detection of cancer remains one of the greatest challenges in population health and primary care. To improve understanding of the early diagnostic phase, the Stockholm Early Detection of Cancer Study (STEADY-CAN) was established as a large, population-based cohort linking real-world healthcare data from multiple sources in the Stockholm region. The overarching aim is to identify clinical, laboratory, and healthcare utilization patterns associated with undiagnosed cancer and to develop risk prediction tools that can support general practitioners in timely cancer detection.

Methods: The STEADY-CAN cohort includes longitudinal data on 2,732,005 adults residing in or receiving healthcare in the Stockholm region during 2011–2021. Data sources comprise regional electronic health records (primary, outpatient, and inpatient care), laboratory data, prescribed drug registers, and the Swedish Cancer Registry, with historical linkage back to 1992 for previous cancer diagnoses. For individuals without prior cancer, 140,042 incident cancer cases (5.1%) were identified during 2012–2021, alongside 2,591,963 cancer-free controls (94.9%). For each cancer case, detailed data on tumour site, date of diagnosis, and TNM stage are available. Recent developments include linkage with Statistics Sweden (SCB) data on country of birth and educational level, as well as new ethical approval to incorporate faecal haemoglobin (f-Hb) test results from regional laboratories.

Results: The integration of sociodemographic and biomarker data substantially enhances the cohort's potential to address questions on diagnostic equity, risk stratification, and symptom–test combinations predictive of cancer. The dataset enables investigation of both specific cancer pathways (e.g. colorectal, lung, haematological) and cross-cancer indicators such as anaemia, test frequency, and healthcare contact patterns. The combination of large sample size, longitudinal follow-up, and linkage across registries provides exceptional opportunities for advanced epidemiological and machine-learning analyses.

Discussion and Conclusions: STEADY-CAN represents one of the largest regional healthcare-based cohorts for cancer detection research in Europe. Its continuous expansion to include new sociodemographic and biomarker data opens avenues for interprofessional and translational collaborations spanning primary care, oncology, epidemiology, and data science. The resource supports studies on both clinical and health equity aspects of cancer diagnosis and serves as a foundation for developing predictive tools and strategies to improve early detection in real-world clinical practice.

Magnus Nilsson

Professor

Surgery and Oncology
Department of Clinical Science, Intervention and Technology - CLINTEC
ME Övre buk, C1-77, Karolinska University Hospital Huddinge, 141 86 Stockholm

+46736402021

Cancer research areas:

Gastric cancer; oesophageal cancer

Key research field interests:

Gastro-oesophageal cancer; peritoneal metastases; tumour immune microenvironment; clinical trials; cell therapy

Needs for collaboration:

Expertise in PDX models of peritoneal tumours; innovative gastro-oesophageal and peritoneal tumour microenvironment analyses and bioinformatics

Selected publications:

1. Ericson J, Klevebro F, Sunde B, Szabo E, Halldestam I, Smedh U, Wallner B, Johansson J, Johnsen G, Aahlin EK, Johannessen HO, Hjortland GO, Lorentzen SS, Slott M, Schroder W, Rouvelas I, Nilsson M. Nutritional outcomes and impact of malnutrition in a randomised comparison between standard and prolonged time to surgery after neoadjuvant chemoradiotherapy for oesophageal cancer. European Journal of Surgical Oncology 2025. 51(9).
2. Nilsson K, Klevebro F, Sunde ,Rouvelas I, Lindblad M, Szabo E, Halldestam I, Smedh U, Wallner B, Johansson J, Johnsen G, Aahlin EK, Johannessen HO, Alexandersson von Döbeln G, Hjortland GO, Wang N, Shang Y, Borg D, Quaas A, Bartella I, Bruns C, Schröder W and Nilsson M. Oncological outcomes of standard versus prolonged time to surgery after neoadjuvant chemoradiotherapy for oesophageal cancer in the multicentre randomised controlled NeoRes II trial. Annals of Oncology 2023 Nov;34(11):1015-1024.
3. Smyth EC, Nilsson M, Grabsch HI, van Grieken NCT, Lordick F. Gastric Cancer Seminar. The Lancet 2020; 396(10251): 635-648. Review.

Clinical and translational studies on gastric and oesophageal cancer

The background of the group was initially clinical epidemiology and then gradually moved more into leading international academic clinical trials addressing neoadjuvant therapies and definitive (curative intent) chemoradiotherapy in oesophageal cancer. In the last years our focus has widened, and we have intensified biobanking and collaboration with basic science groups. Together we are doing multi-omics in blood, primary tumour, metastases and healthy mucosa from patients with oesophageal and gastric cancer. Recently we have particularly focused on gastric cancer (GC) with peritoneal metastases (PM), where our preliminary data suggest a severely immunodepleted tumour immune microenvironment (TIME). We have recently started an international phase III trial on intraperitoneally (IP) administered paclitaxel in GC PM patients, in which we will follow the peritoneal TIME longitudinally. We are exploring the possibility of developing IP immunotherapies, including cell therapies.

Magdalena Paolino

Principal Researcher

Cardiovascular Medicine
Department of Medicine, Solna
Bioclinicum, J8:20, Solnavägen 30, 171 64 Solna

0704204482

Cancer research areas:

Colorectal Cancer; Osteosarcoma; Immunotherapy

Key research field interests:

Immunotherapy; Metastasis; Preclinical cancer models; Gene-editing; Ubiquitination

Needs for collaboration:

I seek collaborations to access human sample cohorts; partner with experts in omics (transcriptomics, proteomics), bioinformatics, and high-throughput drug screening; and build long-term collaborations to advance preclinical findings toward therapeutic concepts.

Selected publications:

1. Zhang Z, Xie Y*, Yi Q, Liu J, Yang L, Wang R, Cai J, Li X, Feng X, Yao S, Pan Z, Paolino M*, Zhou Q*. PEAK1 maintains tight junctions in intestinal epithelial cells and resists colitis by inhibiting autophagy-mediated ZO-1 degradation. Nat. Commun., 2025, 16, 6777.
2. Li XY, Sun B, Qian HR, Ma JR, Paolino M*, Zhang ZY. A high-efficiency and versatile CRISPR/Cas9-mediated HDR-based biallelic editing system. J. Zhejiang Univ. Sci. B, 2022, 23;2 141-152.
3. Gavali S, Liu J, Li X, Paolino M*. Ubiquitination in T-Cell Activation and Checkpoint Inhibition: New Avenues for Targeted Cancer Immunotherapy. Int. J. Mol. Sci., 2021, 22;19.

Atypical Ubiquitination in Cancer: Mechanisms, Preclinical Mouse Models, and Translational Opportunities

Overview:

My laboratory uncovers and characterizes novel pathophysiological roles of ubiquitination, focusing on atypical ubiquitin chains (e.g., ubiquitin chains linked by lysine K6, K27, K29, or K33) and the deubiquitinating enzymes that regulate them. Although ubiquitination is central to cellular and cancer biology, the roles of atypical linkages remain largely unexplored. We address this gap through an integrated platform combining genetic and molecular perturbations in cell lines, primary and 3D ex vivo cultures, preclinical mouse models, and human cohorts to ensure translational relevance.

Projects:

To study colorectal cancer (CRC), we use conditional and transgenic mutant mice, as well as genetically engineered and metastasis-prone CRC models carrying combinations of Apc, Trp53, and Kras mutations. These are coupled with 3D intestinal organoids and RNA-seq to dissect stem cell regulation, tumor initiation, and progression. Our work demonstrates that atypical ubiquitin chains are essential in the intestinal stem cell niche, controlling tumor burden and metastatic spread.

Most recently, we uncovered a significant role for atypical ubiquitination in osteosarcoma (OS), an aggressive pediatric malignancy with limited molecular understanding and few therapeutic options. Using loss-of-function approaches, we are mapping ubiquitin-dependent pathways that shape OS tumor growth, lung metastasis, and responses to immunotherapy and chemotherapy. In close collaboration with the KI Sarcoma Task Force, we aim to translate these findings into improved patient stratification and molecularly informed interventions, and to initiate drug screening efforts to identify candidate inhibitors.

We also have preliminary projects in neuroblastoma, where modulation of atypical ubiquitin chains efficiently controls tumor growth in vitro and in vivo. Additionally, we are investigating how atypical ubiquitin signaling in neutrophils regulates melanoma metastasis.

Approach:

We employ virus-mediated gene editing (stable/ inducible, knockdown shRNA/overexpression) and loss-of-function conditional mutant mice to dissect gene function in vivo. Our experimental platform spans 3D organoids, specialized primary cultures, and a broad spectrum of preclinical cancer in vivo models, including metastasis-prone colorectal cancer, melanoma, and pediatric cancer models. For mechanistic insights, we apply RNA sequencing, complemented by flow cytometry, histology, and diverse molecular assays. To ensure clinical relevance, we explore human cohorts and maintain close collaborations with clinicians.

Vision:

By decoding the pathophysiological roles of atypical ubiquitination in cancer biology, we aim to close critical knowledge gaps in the ubiquitin field while addressing therapeutic challenges to enable novel precision interventions for patients.

Sylvain Peuget

Group Leader

Tumor Biology
Department of Microbiology, Tumor and Cell Biology
Biomedicum C8, Solnavägen 9, 171 65 Solna

Cancer research areas:

Cancer Microbiology, Basic cancer research, Gastrointestinal tract cancer

Key research field interests:

p53, tumor suppression, inflammation, microbiota, oncogenic bacteria

Needs for collaboration:

We always welcome clinical collaborators that can provide patient data and material to complement our own expertise at the molecular level. Specifically, we would be interested in patient material and/or RNA seq data from colorectal tumors and matched metastases for our current project.

Selected publications:

1. Translating p53-based therapies for cancer into the clinic. Peuget S, Zhou X, Selivanova G. Nat Rev Cancer. 2024 Mar;24(3):192-215. PMID: 38287107
2. Enterobacteria impair host p53 tumor suppressor activity through mRNA destabilization. Aschtgen MS, Fragkoulis K, Sanz G, Normark S, Selivanova G, Henriques-Normark B, Peuget S. Oncogene. 2022 Apr;41(15):2173-2186. PMID: 35197571
3. Pifithrin-α alters p53 post-translational modifications pattern and differentially inhibits p53 target genes. Zhu J, Singh M, Selivanova G, Peuget S. Sci Rep. 2020 Jan 23;10(1):1049. PMID: 31974452

Mechanisms of p53 dysregulation by oncogenic bacteria in cancer

Our lab aims to investigate the molecular interplay linking microbiota and cancer, with a focus on the regulation of the key tumor suppressor protein p53 by bacteria. Over the last decade, dysregulation of the microbiome has been recognized as an enabling characteristic of cancer. Moreover, growing evidence highlights that microbiota dysregulation can significantly influence various stages of cancer, from initiation to therapeutic response. However, the precise molecular mechanisms by which bacteria contribute to tumorigenesis are still largely unknown.

To address this gap, our lab investigates how certain bacteria modulate the p53 pathway and its consequence for carcinogenic processes. Notably, we examine how cancer-associated bacteria can disrupt p53 function either through inflammatory response or by secreting p53-targeting toxins. For instance, we have shown that inflammation induced by Klebsiella pneumoniae, a putative oncogenic bacterium, can impair p53 tumor suppressive function under genotoxic and oncogenic stress, effectively lowering the barrier against cancer progression in absence of p53 mutation and impacting response to chemotherapy.

Additionally, we are identifying and characterizing specific bacterial systems responsible for p53 inhibition and analyzing their contribution to tumorigenic processes, both in vitro and in animal studies in mice. Ultimately, our research aims to identify novel molecular targets that account for microbiota-cancer interactions, either from the host or the microbiota, paving the way for innovative cancer therapies.

Helene Rundqvist

Senior Researcher

Division of Clinical Physiology
Department of Laboratory Medicine
Alfred Nobels Alle 8, Ana Futura

0046704838830

Cancer research areas:

Breast cancer; Melanoma; RCTs, pre-clinical models

Key research field interests:

Exercise interventions; metabolism; TME; hypoxia biology; immunology

Needs for collaboration:

Working on immuno-oncology, immune cell metabolism, or plasma biomarkers for immunotherapy response? Feel free to reach out—I'd be happy to discuss more.

Selected publications:

1. Stromberg A, Mandic M, Wadsworth B, Proschinger S, Alam S, Eriksson L, Barbieri L, Rullman E, Rundqvist H. Functional characterisation of CD8+ T cells mobilised with acute supramaximal high-intensity interval exercise: implications for immune surveillance. CLINICAL & TRANSLATIONAL IMMUNOLOGY. 2025;14(6):e70037.
2. Hiensch A, Depenbusch J, Schmidt M, Monninkhof E, Pelaez M, Clauss D, Gunasekara N, Zimmer P, Belloso J, Trevaskis M, Rundqvist H, Wiskemann J, Mueller J, Sweegers M, Fremd C, Altena R, Gorecki M, Bijlsma R, van Leeuwen-Snoeks L, ten Bokkel Huinink D, Sonke G, Lahuerta A, Mann G, Francis P, Richardson G, Malter W, van der Wall E, Aaronson N, Senkus E, Urruticoechea A, Zopf E, Bloch W, Stuiver M, Wengstrom Y, Steindorf K, May A. Supervised, structured and individualized exercise in metastatic breast cancer: a randomized controlled trial. NATURE MEDICINE. 2024;30(10):2957-2966.
3. Rundqvist H, Velica P, Barbieri L, Gameiro P, Bargiela D, Gojkovic M, Mijwel S, Reitzner S, Wulliman D, Ahlstedt E, Ule J, Ostman A, Johnson R. Cytotoxic T-cells mediate exercise-induced reductions in tumor growth. ELIFE. 2020;9:e59996.

Exercise training reshapes the systemic immune environment in patients with metastatic breast cancer: results from the PREFERABLE-EFFECT multi-centre randomised-controlled trial

Background: Exercise training supports physical functioning, alleviates treatment-related side effects, and improves neoadjuvant treatment response in patients with breast cancer (BC), potentially through mechanisms linked to altered systemic- and antitumor immunity. The multinational PREFERABLE-EFFECT RCT (NCT04120298) demonstrated beneficial effects of a 9-month supervised exercise program on fatigue and quality of life among 357 patients with metastatic BC (mBC). In this study, the impact of the PREFERABLE-EFFECT exercise intervention on systemic inflammation and lymphocyte subsets (secondary outcome) was investigated and associated with patient reported fatigue.

Methods: Blood samples were collected at baseline, 3 months and 6 months into the intervention. PBMCs were analysed with multicolour (17 markers) flow cytometry. Plasma samples were analysed for circulating proteins on the Olink immuno-oncology platform. A Ridge logistic-regression based fatigue classifier was used to identify physiological and proteomic markers associated with baseline fatigue assessed using the EORTC QLQ-C30 questionnaire.

Results: Consistent trends toward a higher proportion CD8+T and CD56dim and a lower proportion of CD4+T cells were found in the exercise group and flowSOM cluster analyses revealed increases in circulating subsets of CD8+T-, gdT- and NK-cells compared to controls. Significant reductions in inflammatory mediators, including IL-6, CSF-1, CCL3, CD8A and the progression marker PTN were found in the exercise group. TWEAK and CASP-8, both related to apoptosis, were increased 6 months into the intervention. The exercise responsive proteins CSF-1, IL-6, TWEAK and PTN contributed to clinically relevant fatigue stratification.

Conclusion: Our results demonstrate that the PREFERABLE-EFFECT intervention proportionally enriched specific immune cell subsets with cytotoxic potential and attenuated chronic inflammation. Multiple exercise responsive proteins were also linked to improvements in fatigue, thereby advancing the mechanistic understanding of exercise effects in patients with mBC.

Johan Sandberg

Professor

CIM
Department of Medicine, Huddinge
CIM, ANA Futura, Alfred Nobels Allé 8, 14152 Huddinge

0707930885

Cancer research areas:

Lung

Key research field interests:

Human T cell immunology

Needs for collaboration:

Patient sample access

Selected publications:

1. Boulouis, C., Mouchtaridi, E., Muller, T. R., Mak, J. Y. M, Fairlie, D. P., Bergman, P., Michaelsson, J., Halfvarson, J., Mjösberg, J., Buggert, M. and Sandberg, J. K. (2025) Human MAIT cell response profiles biased towards IL-17 and IL-10 are effector states directed by the cytokine milieu. Proc. Natl. Acad. Sci. USA. 122: e2414230122
2. Parrot, T., Healy, K., Boulouis, C., Sobkowiak, M., Leeansyah, E., Aleman, S., Bertoletti, A., Sällberg Chen, M. and Sandberg, J. K. (2021) Expansion of donor-unrestricted MAIT cells with enhanced cytolytic function suitable for TCR-redirection. JCI Insight. 6: e140074.
3. Kammann, T., Cai, C., Sekine, T., Mouchtaridi, E., Boulouis, C., Nilsén, V., Rivera Ballesteros, O., Müller, T. R., Gao, Y., Raineri, E. J. M., Akhirunnesa, M., Adamo, S., Constantz, C., Niessl, J., Weigel, W., Kokkinou, E., Stamper, C., Marchalot, A., Bassett, J., Ferreira, S., Rødahl, I., Wild, N., Brownlie, D., Tibbitt, C., Mak, J. Y. W., Fairlie, D. P., Leeansyah, E., Michaelsson, J., Marquardt, N., Mjösberg, J., Jorns, C., Buggert, M. and Sandberg, J. K. (2024) MAIT cell heterogeneity across paired human tissues reveals specialization of distinct regulatory and enhanced effector phenotypes. Science Immunology. 9: eadn2362.

Unconventional innate-like MAIT cells in cancer

Mucosa-associated invariant T (MAIT) cells are a large subset of unconventional, innate-like T cells that are highly abundant in barrier tissues and peripheral blood. The MAIT cell T cell receptor recognizes microbial riboflavin metabolites from a wide range of microbes presented by the highly evolutionarily conserved and non-polymorphic MHC class I-like MR1 molecules. MAIT cells thus represent a highly conserved arm of cell-mediated antimicrobial immunity. Furthermore, emerging evidence indicates that MAIT cells also play important roles in antiviral and antitumor immunity via rapid innate activation even in situations where MR1-presented antigen may not be present. Nevertheless, many aspects of MAIT cell immunobiology and role in human disease remain unexplored. In relation to cancer our goals are four-fold: First, we unravel the functional diversity of human MAIT cell subsets. Second, we investigate the role and residency of these MAIT cell subsets in human liver, intestinal and lung tissue. Third, we investigate the ability of MAIT cells to infiltrate lung and liver tumors and assess their function in the tumor tissue. Fourth, we explore ways to harness MAIT cells as a platform for immunotherapy. We hope that these investigations will significantly enhance our understanding of the role innate-like MAIT cells play in human tissues, in the setting of cancer, and help design approaches to utilize MAIT cells in tumor immunotherapy.

Dhifaf Sarhan

Associate Professor / Senior Lecturer

Pathology
Department of Laboratory Medicine
ANA Futura, 8th floor

0704487830

Cancer research areas:

Tumor immunology; Cancer immunotherapy; Tumor microenvironment; Precision oncology

Key research field interests:

Adaptive and memory-like NK cells; Innate immune memory; Myeloid cell–mediated immune suppression; Sex-immune dimorphism in cancer; Spatial immunology; Translational immunotherapy; NK cell–based therapeutic strategies

Needs for collaboration:

- Clinical–translational collaborations with oncology, surgery, and pathology
- Access to well-annotated patient cohorts and longitudinal clinical samples
- Active collaboration with patient representatives to inform research priorities, study design, and translational relevance
- Spatial biology, single-cell and multi-omics integration
- Computational biology and AI-based prediction algorithms for tumor-derived peptide discovery
- Systems immunology and immune-tumor interaction modeling
- Immunotherapy and early-phase clinical trial development
- Cross-CRKI collaborations on sex-specific cancer biology and precision immunotherapy

Selected publications:

1. Sun Y et al., Sarhan D. Adaptive NK Cells Exhibit Tumor-Specific Immune Memory and Cytotoxicity in Ovarian Cancer. Cancer Immunology Research, 2025.
2. He F et al., Sarhan D. FPR2 shapes an immune-excluded pancreatic tumor microenvironment and drives T-cell exhaustion in a sex-dependent manner. Cancer Research, 2023.
3. La Fleur L et al., Sarhan D. Targeting MARCO and IL-37R on immunosuppressive macrophages in lung cancer blocks regulatory T cells and supports cytotoxic lymphocyte function. Cancer Research, 2020.

Tackling Cancer from Two Directions: Empowering Adaptive NK Cells while Reprogramming the Tumor Microenvironment

Tumor progression and resistance to immunotherapy are driven by complex interactions between malignant cells and the tumor microenvironment (TME). My research focuses on defining how innate immune cells, particularly natural killer (NK) cells and myeloid populations, are regulated within the TME, and how these interactions can be therapeutically exploited to restore durable anti-tumor immunity.

A central axis of our work is the biology of adaptive NK (aNK) cells, a memory-like NK cell subset capable of antigen-specific responses and resistance to tumor-induced immune suppression. We have demonstrated that aNK cells can acquire tumor-specific immune memory, recognize non-canonical tumor-derived peptides presented by HLA-E, and maintain cytotoxic activity in highly suppressive tumor environments. These findings challenge the classical view of NK cells as short-lived innate effectors and open new opportunities for NK-based precision immunotherapy.

In parallel, we investigate how immunosuppressive macrophages and myeloid-derived suppressor cells actively restrain cytotoxic lymphocytes in solid tumors, including pancreatic and ovarian cancer, and how targeted reprogramming of these populations can reinvigorate anti-tumor immune responses. More recently, our work has uncovered pronounced sex-specific differences in immune regulation within the TME, identifying macrophage-driven pathways that contribute to sex-biased immune suppression and therapeutic response.

By integrating spatial biology, single-cell and bulk multi-omics, and functional immunology, our research aims to define context- and sex-informed immunotherapeutic strategies with direct translational relevance.

Brinton Seashore-Ludlow

Senior Research Specialist

Functional Precision Medicine
Department of Oncology-Pathology
Tomtebodavägen 23, 17165 Solna, Sweden

Cancer research areas:

Ovarian cancer

Key research field interests:

Drug screening, advanced disease models

Needs for collaboration:

Multi omics integration

Selected publications:

1. MOLECULAR ONCOLOGY. 2025;19(9):2574-2593. Systematic profiling of cancer-fibroblast interactions reveals drug combinations in ovarian cancer. Gudoityte G; Sharma O; Leuenberger L; Wallin E; Fernebro J; Ostling P; Bergstroem R; Lindberg J; Joneborg U; Kallioniemi O; Seashore-Ludlow B
2. COMMUNICATIONS BIOLOGY. 2025;8(1):303. Evaluating feature extraction in ovarian cancer cell line co-cultures using deep neural networks. Sharma O; Gudoityte G; Minozada R; Kallioniemi OP; Turkki R; Paavolainen L; Seashore-Ludlow B
3. NPJ PRECISION ONCOLOGY. 2023;7(1):111. The drug efficacy testing in 3D cultures platform identifies effective drugs for ovarian cancer patients. Akerlund E; Gudoityte G; Moussaud-Lamodiere E; Lind O; Bwanika HC; Lehti K; Salehi S; Carlson J; Wallin E; Fernebro J; Ostling P; Kallioniemi O; Joneborg U; Seashore-Ludlow B

Functional precision medicine approaches to gynecological cancers

Traditional in vitro disease models often fail to predict how drugs will perform in patients—both in terms of efficacy and safety—limiting their value for guiding treatment decisions or advancing new clinical candidates. Our research program addresses this gap by developing next-generation methods to study drug sensitivity and resistance in physiologically relevant, patient-proximal systems.

We have established high-content screening pipelines for short-term ex vivo drug testing and are now expanding these platforms to dissect how specific components of the tumor microenvironment shape drug responses. While our primary focus is gynecological cancers—particularly high-grade serous ovarian cancer—we are also extending our ex vivomethodologies to pediatric cancers to meet critical unmet clinical needs.

Our long-term vision is to build a robust framework for functional precision medicine, enabling treatment strategies that are tailored to the biology of each individual patient, as well as functional study of disease.

Galina Selivanova

Senior Professor

Tumor Biology
Department of Microbiology, Tumor and Cell Biology
Biomedicum B7

0852486302

Cancer research areas:

p53; molecular biology of cancer; breast cancer; cancer immunesurveillance

Key research field interests:

p53, regulation of anti-cancer immune response by p53, reactivation of the p53 tumor suppression function by small molecules or base editing

Needs for collaboration:

Breast cancer clinical samples; mouse models

Selected publications:

1. Zhou X, Singh M, Sanz Santos G, Guerlavais V, Carvajal LA, Aivado M, Zhan Y, Oliveira MMS, Westerberg LS, Annis DA, Johnsen JI, Selivanova G. (2021) Pharmacologic Activation of p53 Triggers Viral Mimicry Response Thereby Abolishing Tumor Immune Evasion and Promoting Antitumor Immunity. Cancer Discovery, Vol 11 (12) 3090-3105.
2. Zhou, X; Santos, GS; Zhan, Y; Oliveira, MMS; Rezaei, S; Singh, M; Peuget, S; Westerberg, LS; Johnsen, JI; Selivanova, G.(2022) Mutant p53 gain of function mediates cancer immune escape that is counteracted by APR-246. British Journal of Cancer, 2022, 127(11):2060-2071.
3. Peuget, S; Zhou, X; Selivanova, G (2024) Translating p53-based therapies for cancer into the clinic . Nature Reviews Cancer Vol 24(3),p192-215.

Abstract

p53 as a major tumor suppressor which inactivation is required for tumor development. This inspires the idea of p53 reactivation to combat cancer. The mutant p53-reactivating compound PRIMA1MET/APR-246 which we discovered has been tested in several clinical trials. With the advent of immune anti-cancer therapy it becomes imperative to understand how immune checkpoints are affected by novel target-specific drugs.

In this project we will capitalize on our recent discovery that p53 can boost anticancer immune response via trigerring interferon (IFN) pathway. We aim to find out whether and how mutant p53 is involved in the regulation of IFNs, thereby promoting inflamed tumor microenvironment. We will identify the molecular mechanisms of the newly discovered gain-of-function mutant p53 properties affecting immune cancer surveillance in vitro, ex vivo, in vivo and in patient samples using modern molecular biology and highthroughput approaches. We will find out whether restoration of mutant p53 function by APR-246 or correction of A to G point mutations in p53 by base editing can boost the IFN response, regulate immune checkpoints, promote immune cell infiltration and synergize with immune checkpoint therapy using mouse models.

Our results might help to promote clinical trials of p53-targeting therapies and to stratify patient cohorts, allowing personalized cancer medicines for the benefit of patients.

Tomas Sjöberg Bexelius

MD, PhD

Barnonkologi
Department of Women's and Children's Health
C33:12, Eurgeniavägen 23

Cancer research areas:

Paediatric cancer; neuroblastoma; medulloblastoma; drug development; circadian clock

Key research field interests:

Consequenses of biological rhythm disruption in embryonal malignant tumours; biomarker development; targeted therapy; neurotrophins

Needs for collaboration:

Translating preclinical research to phase I/II trials; MYC driven malignancies, and circadian clock disruption

Selected publications:

1. Deland L, Keane S, Olsson Bontell T, Sjöberg Bexelius T, Gudinaviciene I, De La Cuesta E, De Luca F, Nilsson JA, Carén H, Mörse H, Abel F. A pilocytic astrocytoma with novel ATG16L1::NTRK2 fusion responsive to larotrectinib: a case report with genomic and functional analysis. Oncologist. 2025 Mar 10;30(3):oyae254. doi: 10.1093/oncolo/oyae254. PMID: 39326005; PMCID: PMC11954494.
2. Sainero-Alcolado L, Sjöberg Bexelius T, Santopolo G, Yuan Y, Liaño-Pons J, Arsenian-Henriksson M. Defining neuroblastoma: From origin to precision medicine. Neuro Oncol. 2024 Dec 5;26(12):2174-2192. doi: 10.1093/neuonc/noae152. Erratum in: Neuro Oncol. 2024 Dec 5;26(12):2398. doi: 10.1093/neuonc/noae218. PMID: 39101440; PMCID: PMC11630532.
3. Yuan Y, Alzrigat M, Rodriguez-Garcia A, Wang X, Bexelius TS, Johnsen JI, Arsenian-Henriksson M, Liaño-Pons J, Bedoya-Reina OC. Target Genes of c-MYC and MYCN with Prognostic Power in Neuroblastoma Exhibit Different Expressions during Sympathoadrenal Development. Cancers (Basel). 2023 Sep 16;15(18):4599. doi: 10.3390/cancers15184599. PMID: 37760568; PMCID: PMC10527308.

Circadian Clock Disruption as a Prognostic Factor and Regulator of Metabolism in Neuroblastoma

Background: Neuroblastoma, the most common cancer in infants, accounts for 10–15% of childhood cancer deaths. High-risk disease, often characterized by MYCN amplification* faces relapse rates exceeding 50%. The mammalian circadian clock, which regulates physiological processes in a 24-hour cycle, is disrupted by MYCN amplification, and its restoration has shown tumor-suppressive effects in preclinical models.

Aims: This study sought to quantify circadian clock disruption in neuroblastoma using a novel metric, the Clock Correlation Distance (CCD), correlate CCD with clinical outcomes, and explore the prognostic value of 12 core clock genes and their link to metabolic reprogramming.

Methods: A retrospective analysis was performed on two large neuroblastoma cohorts (SEQC: n=498; KOCAK: n=649). The CCD was calculated by comparing the co-expression of 12 clock genes to a synchronized mouse reference. Statistical methods included Mann-Whitney, Kruskal-Wallis, and Kaplan-Meier survival analyses.

Key Findings: A higher CCD (greater disruption) was significantly associated with indicators of poor prognosis, including MYCN-amplified tumors, high-risk groups, Stage 4 disease, and deceased patients. Analysis of individual clock genes revealed specific prognostic markers: high expression of ARNTL and CRY2$ correlated with better survival, while high expression of CRY1 and PER2 correlated with worse survival. Tumors without MYCN amplification showed higher overall clock gene expression. Furthermore, disrupted circadian rhythm correlated with significant metabolic reprogramming, including increased oxidative phosphorylation (OXPHOS) and decreased fatty acid synthesis and glycolysis.

Conclusion: Circadian clock disruption, quantifiable by CCD, is a robust biomarker of malignancy and poor prognosis in neuroblastoma. The findings demonstrate that clock dysregulation is intrinsically linked to unfavorable metabolic shifts, providing a strong rationale for developing circadian-based therapeutics to restore clock function and potentially target MYCN-driven disease.

Staffan Strömblad

Professor

ICCA
Department of Medicine, Huddinge
Neo

+46704484612

Cancer research areas:

Cancer Cell Biology

Key research field interests:

Cell-matrix interactions, mechanotransduction, cellular signaling, cellular senescence, cancer development, cancer progression

Needs for collaboration:

Spatial bioinformatics to analyze tissue niches

Selected publications:

1. Hu, J., Gong, X. & Strömblad, S. Local Rac-GTP nadirs and peaks restrict cell protrusions and retractions. Sci Adv. 8, eabl3667 (2022).
2. Hu, J., Serra-Picamal X., Bakker, G-J., Van Troys, M., Winograd-Katz, Ege, S.N., Gong X., Didan, Y., Grosheva, I., Polansky, O., Bakkali, K., Van Hamme, E., van Erp, M., Vullings, M., Felix Weiss, F., Clucas, J., Dowbaj, A.M., Sahai, E., Ampe, C., Geiger, B., Peter Friedl, P., Bottai, M., & Strömblad, S. Multi-site assessment of reproducibility in high-content cell migration imaging data. Mol Systems Biol. e11490 (2023).
3. Göransson, S., Olofsson, H., Yan, F., Johansson, H., Vogiatzakis, C., Liang, S., Masvidal, L., Hajj, GNM., Martins Bellato, H., Hartman, J., Larsson, O., Lehtiö, J. & Strömblad, S. Mechanical control of breast cancer malignancy by promotion of mevalonate pathway enzyme synthesis. Matrix biology, 140, 1-15 (2025).
4. Yan, F. Göransson, S., Olofsson, H.,Vogiatzakis, C., Acharekar, A., & Strömblad, S. Matrix stiffness-induced IKBKE signaling drives a malignant breast cancer cell phenotype. Cell Communication and Signaling 23, 269 (2025).

Mechanical regulation of cancer development and progression

My group has long experience in studies of cell-matrix interactions in cancer. Our current focus is how the mechanical properties of the extracellular matrix (ECM) affects cancer development and progression. Increased stiffness is a physical hallmark of many solid cancers, including breast cancer, where the increased extracellular matrix stiffness contributes to aggressiveness and poor prognosis. We study, at the molecular level, how the mechanical properties of the ECM generate intracellular signaling in cancer cells and how these signals control cell proliferation and invasion in cancer development and progression.

We utilize in vitro and in vivo cancer models where we perturb the matrix stiffness to analyze the cellular responses and then perturb the molecular responses to stiffness to infer the mediating molecular mechanisms. We perform analysis of the ECM organization in tissues by circular polarized light imaging and combine this with multiplexed immunolabeling in mouse and human pre-cancerous and cancerous tissues to assess the relation between the matrix organization and the tumor lesion properties and componentry. We are currently setting up Stereo-seq spatial transcriptomics analysis of mouse lung cancer tissues to be overlayed with polarized light images to better understand the cellular response to ECM stiffness. For this, we are looking for collaborations for spatial bioinformatic analysis.

Karin Sundström

Principal Researcher

Center for Cervical Cancer Elimination
Department of Clinical Science, Intervention and Technology - CLINTEC
Forskargatan 56, Karolinska University Hospital Huddinge, S-141 86 Stockholm

Cancer research areas:

Gynecological cancer

Key research field interests:

Gynecological cancer (cervical, endometrial, ovarian). HPV-related diseases (benign lesions, dysplasias, cancers of multiple sites). HPV vaccination and HPV-based cervical screening.

Needs for collaboration:

Translational projects: Bringing promising biomarkers to bedside. I am both in epidemiology and clinical pathology and my main interest is to collaborate in bringing promising lab biomarkers to actual health practice.

Selected publications:

1. Yao Q, Wang J, Elfström KM, Strander B, Dillner J, Sundström K. Evaluation of primary HPV-based cervical screening among older women: Long-term follow-up of a randomized healthcare policy trial in Sweden. PLoS Med. 2024 Dec 19;21(12):e1004505.
2. Wang J, Salomonsson S, Sönmez D, Nordqvist Kleppe S, Feldman AL, Andersson MS, Bencina G, Fang F, Sundström K. Mental disorders and socioeconomic outcomes in women with cervical cancer, and their children and co-parents. J Natl Cancer Inst. 2025 Sep 1;117(9):1825-1835.
3. Barrett JE, Sundström K, Jones A, Evans I, Wang J, Herzog C, Dillner J, Widschwendter M. The WID-CIN test identifies women with, and at risk of, cervical intraepithelial neoplasia grade 3 and invasive cervical cancer. Genome Med. 2022 Oct 19;14(1):116.

Human papillomavirus testing as diagnostic support in cervical and anal cancer

HPV16 shows high infection isolate diversity between different women, but not within the same woman at different body sites. In other words, when we investigate infection in the same woman's body in multiple places, the virus should practically speaking be rather identical in sequence (Mirabello, 2017). Women with a history of cervical precancerous lesions (previously termed CIN3+, now approximately equivalent to HSIL) are at higher risk for anal cancer than the general population, and that increased risk persists for 25 years (Stier, 2017; Hernandez, 2005; Sand et al, 2016; Saleem et al, 2011; Edgren and Sparén 2007; Evans et al, 2003; Coffey et al. 2015). However, molecular-level research addressing the genetic sequence characteristics of anal HPV16 infection and associated dysplasia, particularly in conjunction with concurrent HSIL, is notably scarce.

Research questions

We will use the NKCx linked to the Cancer Registry, and/or local hospital pathology databases to identify all cases of Stockholm women diagnosed both with anal dysplasia or cancer (AIN3, or squamous cell carcinoma) and with cervical precancerous lesions or cancers. We will ascertain the HPV types present in formalin-fixed, paraffin-embedded tissue and/or liquid-based cytology (LBC) material from the anus and cervix, respectively. In all cases positive for HPV16 (estimated to be more than 90%), we will further categorize them into subtypes (A, B, C, D) and sublineages (A1, A2, A3, A4, B1, C1, D1, D2, D3, D4). In women who are HPV16-positive in both cervical and anal sites, we will determine if the viral isolate is identical or not.

Methods

100 microliters of stored LBC samples from the cervix and extracted FFPE material from the anus will be analyzed, respectively. HPV testing and HPV16 subtypes will be determined as described above. The SPSS software (version 29.0.0.0, SPSS, Inc., Chicago, IL, USA) will be used for data analyses. The cervical and anal dysplasia/cancer groups will be compared using paired design statistical tests including the Wilcoxon-signed rank test or pared t-test for continuous variables, and the McNemar's test for categorical data.

Significance

We hypothesize that women with a cervical HPV16 infection with conserved E7 gene carry the highest risk also for subsequent anal lesions, and so should dominate this material. This remains to be proven, but if correct, could support that women with cervical HPV16 infection of conserved status should be monitored for anal lesions as well, perhaps through the use of anal HPV-testing or cytology, which has been proposed as screening methods for anal lesions.

Laszlo Szekely

Professor

Patology
Department of Laboratory Medicine
Karolinska University Hospital, Huddinge, F49

Cancer research areas:

All types of live human solid and effusion tumors from biopsies or surgical resections.

Key research field interests:

Individualized cancer therapy; ex vivo live cell diagnostic.

Needs for collaboration:

Open for collaboration with surgeons, oncologists as well as basic researchers with interest about multiomics on primary cancer samples.

Selected publications:

1. Zhang, Yu, Xiaoyuan Wu, Ping He, Jieyu Wu, Xia Gu, Matyas Bendek, Rita Ötvös, and Laszlo Szekely. 2023. “The D ~ Sense Ex-Vivo Viability Assay Application in a Patient with Stage IV Lung Adenocarcinoma: A Case Report.” Journal of Medical Case Reports 17 (1): 1–9.
2. Razaghi, Ali, Attila Szakos, Marwa Alouda, Béla Bozóky, Mikael Björnstedt, and Laszlo Szekely. 2022. “Proteomic Analysis of Pleural Effusions from COVID-19 Deceased Patients: Enhanced Inflammatory Markers.” Diagnostics 12 (11).
3. Zhen Xin, Kristian Holgersson, Pengcheng Zhu, Hongtu Tan, Guangyan Shi, Laszlo Szekely, Tao Wu 2024 ” Silencing UBE2K inhibits the growth of glioma cells by inducing the autophagy-related apoptosis” Journal of Biochemical and Molecular Toxicology 38:e23758.

Leaving no stone unturned - testing all available anti-cancer medicines on primary ex vivo tumor samples to assist individualized therapy

We have developed an ex vivo drug sensitivity assay for primary human tumor cells that can test all available approved anti-cancer drugs (currently 180), a selection of experimental drugs (30) and a collection of standardized extracts of traditional medicines (30). The optimal starting material is ten million isolated live tumor cells although the assay can provide reliable readings with as few as 300 thousand cells. The assay takes 5 days and provide a ranking of predicted clinical efficiency in the relevant dose range. Tumor samples that are compatible with the assay are leukemias, lymphomas, tumor effusions, lymph node scrapings - samples that readily can be converted to cell suspension format. For all other solid tumors with abundant stroma we have adapted a non-enzymatic dissociation method using computer controlled mechanical tissue griding device. We are conducting clinical trials at multiple partner hospital to test a great variety of late stage cancers such as lung, colorectal, pancreatobiliary, kidney, liver, breast, ovary, endometrium, nasopharynx cancer as well as various sarcomas and mesotheliomas. Based on the drug sensitivity profile we also identify the molecular targets of cancer drug vulnerability. The technique is also used for systematic drug screening of varios chemical and natural product libraries.

Ana Teixeira

Principal Researcher

Nanomedicine and spatial biology
Department of Physiology and Pharmacology
Biomedicum, Quarter C5

Cancer research areas:

Breast cancer

Key research field interests:

Nanomedicine and diagnostics

Needs for collaboration:

Clinical collaborations

Selected publications:

1. Ambrosetti, E., Bernardinelli, G., Hoffecker, I., Hartmanis, L., Kiriako, G., De Marco, A., Sandberg, R., Högberg, B., and Teixeira, A.I. A DNA nanoassembly-based approach to map membrane protein nanoenvironments. Nature Nanotechnology. 2021;16, 85-95.
2. Fang, T., Alvelid, J., Ambrosetti, E., Testa, I., and Teixeira, A.I. Spatial regulation of T-cell signaling by programmed death-ligand-1 on wireframe DNA origami flat sheets. ACS Nano. 2021;15(2), 3441-3452.
3. Shaw, A.*, Lundin, V.*, Petrova, K., Fordos, F., Benson, E., Al-Amin, A., Herland, A., Blokzijl, A., Hogberg, B.*, and Teixeira, A.I.* Spatial control of membrane receptor function using ligand nano-callipers. Nature Methods. 2014; 11(8):841-6. *Equal contribution.

Mapping Her2 nanodomains in breast cancer cells

HER2 expression levels in breast cancer are used to stratify patients selected to receive HER2-targeted therapies. HER2 expression in breast cancer is currently assessed using immunohistochemistry to evaluate protein levels and/or by in situ hybridization (ISH) to detect gene amplification. However, recent advances in single-cell and spatial profiling technologies have revealed that HER2 expression in breast cancer is highly heterogeneous between and within tumors. Additionally, HER2 organizes into dynamic nanoclusters at the plasma membrane, where it engages in signaling via homo- and heterodimerization with other membrane receptors, especially with HER3. These nanoscale configurations are disrupted or modulated by HER2-targeted drugs, directly impacting therapeutic efficacy.

Current super-resolution imaging technologies are limited by low throughput and low sampling fractions, which is a limitation when aiming to capture the cellular heterogeneity in tumors. We developed NanoDeep, a DNA-nanoassembly based sequencing method to decipher the nanoscale organization of membrane proteins in cell populations. NanoDeep used DNA sequencing as a readout of how frequently specific proteins populate defined positions within the nanoenvironment of any protein of interest. We aim to develop NanoDeep to enable mapping of HER2 nanodomains to contribute to improving patient selection for HER2-targeted therapies and ultimately improve clinical outcomes in breast cancer.

Per Uhlén

Professor

Division of Molecular Neurobiology
Department of Medical Biochemistry and Biophysics
Biomedium, Solnavägen 9

0706642814

Cancer research areas:

Bladder cancer and breast cancer

Key research field interests:

Tumor microdomains, histopathology, 3D imaging, AI analysis, and PD-L1/PD-1 signaling

Needs for collaboration:

New collaborations are always interesting and stimulating

Selected publications:

1. Tanaka N, Kanatani S, Kaczynska D, Fukumoto K, Louhivuori L, Mizutani T, Kopper O, Kronqvist P, Robertson S, Lindh C, Kis L, Pronk R, Niwa N, Matsumoto K, Oya M, Miyakawa A, Falk A, Hartman J, Sahlgren C, Clevers H, Uhlén P “Three-dimensional single-cell imaging for the analysis of RNA and protein expression in intact tumour biopsies”. Nature Biomedical Engineering Sep;4(9):875-888 (2020).
2. Zhang S, Miyakawa A, Wickström M, Elfman L, Louhivuori L, Varas-Godoy M, Kemppainen K, Kanatani S, Kaczynska D, Dehnisch Ellström I, Dyberg C, Kronqvist P, Repo H, Mikoshiba K, Sahlgren C, Johnsen JI, Uhlén P “GIT1 Protects against Breast Cancer Growth through Negative Regulation of Notch”. Nature Communications Mar 22;13(1):1537 (2022).
3. Fukumoto K, Kanatani S, Jaremko G, West Z, Al Rayyes I, Niwa N, Axelsson TA, Tanaka N, Oya M, Miyakawa A, Brehmer M, Uhlén P “Three-Dimensional Imaging of Endoscopy Biopsies To Improve Diagnostic Yield and Accuracy of Upper Tract Urothelial Carcinoma Diagnosis”. Journal of Clinical Investigation - Insight Jul 22;9(14):e175751 (2024).

Advancing histopathology through volumetric 3D imaging

Life unfolds in three dimensions, and understanding tissue function and disease requires methods that preserve this spatial integrity. Three-dimensional (3D) imaging now enables visualization of molecular and structural features throughout entire, intact samples, revealing the full cellular and architectural complexity of organs. By combining tissue clearing, multiplex labeling, and volumetric microscopy, proteins and RNA can be spatially mapped simultaneously within whole specimens, providing a comprehensive view of biological systems.

We show that 3D imaging can more accurately distinguish muscle-invasive bladder cancer by characterizing the tumor vasculature, including vessel density and spatial organization, providing information not captured by conventional analyses. In triple-negative breast cancer, volumetric imaging detects small and spatially distinct cell populations that may be overlooked in traditional clinical assessments, offering new insights into tumor heterogeneity and microinvasion.

Unlike conventional approaches that examine only a fraction of a sample, 3D pathology allows quantitative analysis of every cell within its native environment. This holistic perspective uncovers spatial relationships, network dynamics, and rare pathological features that may be missed in traditional two-dimensional assessments or limited sampling, opening new possibilities for precision diagnosis and mechanistic understanding of disease.

Trung Nghia Vu

Principal Researcher

Computational Medicine and Bioinformatics
Department of Medical Epidemiology and Biostatistics
Nobels väg 12A, 17165 Solna

Cancer research areas:

Pharmacogenomics analysis; circular RNA; precision oncology; acute myeloid leukemia

Key research field interests:

Bioinformatics methods; Cancer research; Pharmacogenomics; Omics analysis

Needs for collaboration:

We are seeking collaborations for accessing omics & drug data, validating circular RNAs, and applying our developed methods to other diseases.

Selected publications:

1. Wang Q, Khatri P, Dinh HQ, Huang J, Pawitan Y, Vu TN. A cluster-based cell-type deconvolution of spatial transcriptomic data. Nucleic acids research 2025 53;14.
2. Trac QT, Pawitan Y, Mou T, Erkers T, Östling P, Bohlin A, Österroos A, Vesterlund M, Jafari R, Siavelis I, Bäckvall H, Kiviluoto S, Orre LM, Rantalainen M, Lehtiö J, Lehmann S, Kallioniemi O, Vu TN. Prediction model for drug response of acute myeloid leukemia patients. NPJ precision oncology 2023 7;1 32-.
3. Pan L, Dinh HQ, Pawitan Y, Vu TN. Isoform-level quantification for single-cell RNA sequencing. Bioinformatics (Oxford, England) 2022 38;5 1287-1294.

Statistical and bioinformatics methodologies for omics data analysis in precision oncology

Our research group focuses on advancing bioinformatics methodologies to improve cancer research and treatment. We develop statistical and computational tools for analysis of different types of high-throughput omics data, for example, gene and isoform quantification from RNA sequencing, metagenomics, abnormal RNA detection (gene fusions, circular RNAs), and deconvolution from spatial transcriptomics. In single-cell sequencing, we focus on analyzing scRNA-seq data, developing methods for differential expression analysis, isoform expression discovery, and mutation detection to explore deeper insights into cellular heterogeneity. Our cancer research emphasizes identifying driver alterations and subtype-specific biomarkers, particularly in acute myeloid leukemia (AML), as well as investigating mutant-allele expression. We also focus on pharmacogenomics, developing predictive models for drug responses in both monotherapy and combination therapies, with application in AML. By integrating multi-omics data and advanced computational models, our goal is to enhance personalized cancer therapy and contribute to more effective, data-driven medical treatments.

Fredrik Wermeling

Associate Professor/Docent, PI

Rheumatology
Department of Medicine, Solna
CMM:03, Visionsgatan 18, 171 64, Solna

Cancer research areas:

CRISPR screens; drug resistance

Key research field interests:

CRISPR screens; drug resistance

Selected publications:

1. CRISPR/Cas9-Induced DNA Damage Enriches for Mutations in a p53-Linked Interactome: Implications for CRISPR-Based Therapies. Jiang L, Ingelshed K, Shen Y, Boddul SV, Iyer VS, Kasza Z, Sedimbi S, Lane DP, Wermeling F. Cancer Res. 2022 Jan 1;82(1):36-45. doi: 10.1158/0008-5472.CAN-21-1692. Epub 2021 Nov 18. PMID: 34750099
2. Green Listed v2.0: A Web Application for Streamlined Design of Custom CRISPR Screens. Henkel E, Li Z, Uvehag D, Schmierer B, Henkel M, Wermeling F. CRISPR J. 2025 Jun;8(3):216-223. doi: 10.1089/crispr.2025.0023. Epub 2025 May 7. PMID: 40329823
3. Dnmt3a mutations limit normal and autoreactive Tfh differentiation [preprint]. Yunbing Shen, Zhaojun Li, Sanjaykumar Boddul, Zsolt Kasza, Alexander Espinosa, Lars Klareskog, Fredrik Wermeling. bioRxiv 2024.02.16.580463; doi: https://doi.org/10.1101/2024.02.16.580463

Oscar Wiklander

Assistant Professor

Biomolecular and Cellular Medicine (BCM)
Department of Laboratory Medicine
ANA Futura, Alfred Nobels Allé 8, 141 52 Huddinge

Cancer research areas:

Preclinical / translational. Solid tumors (extra interest in breast cancer).

Key research field interests:

Liquid biopsies. Targeted therapies. Extracellular vesicles. Nanoparticles. Solid tumors.

Needs for collaboration:

Expertise in different omics, interest in analysis of tumor associated exosomes/extracellular vesicles. Patient samples.

Selected publications:

1. Wiklander OPB, Mamand D, Mohammad D, Zheng W, Jawad Wiklander R, Sych T, Zickler A, Liang X, Sharma H, Lavado A, Bost J, Roudi S, Corso G, Lennaárd A, Abedi-Valugerdi M, Mäger I, Alici E, Sezgin E, Nordin J, Gupta D, Görgens A, EL Andaloussi S. Targeted Therapy by Antibody Displaying Extracellular Vesicles. Nature Biomedical Engineering (2024).
2. Lennaárd AJ, Mamand DR, Wiklander RJ, El Andaloussi S, Wiklander OPB. Optimised Electroporation for Loading of Extracellular Vesicles with Doxorubicin. Pharmaceutics (2021).
3. Wiklander OPB, R. B. Bostancioglu, J. A. Welsh, A. M. Zickler, F. Murke, G. Corso, U. Felldin, D. W. Hagey, B. Evertsson, X.-M. Liang, M. O. Gustafsson, D. K. Mohammad, C. Wiek, H. Hanenberg, M. Bremer, D. Gupta, M. Björnstedt, B. Giebel, J. Z. Nordin, J. C. Jones, S. EL Andaloussi, A. Görgens. Systematic Methodological Evaluation of a Multiplex Bead-Based Flow Cytometry Assay for Detection of Extracellular Vesicle Surface Signatures. Frontiers in Immunology (2018).

Extracellular vesicles-based liquid biopsy and targeted therapy in metastatic cancer

In oncology, precision medicine has gained tremendous attention in recent years with the hope to tailor treatments to specific disease driving alterations to improve treatment efficacy and reduce side effects. The need of improved diagnostic tools to identify these specific alterations has also spurred an intense development of various omics to pinpoint relevant biomarkers. Despite intense research, there is still a great need for improved tissue specific targeted drugs and improved diagnostics. The hypothesis is that cell secreted extracellular vesicles (EVs) could be utilized as therapeutic targetable vectors and as improved cancer biomarkers. EVs are nanoscale, membrane enclosed particles ubiquitously present in bodily fluids and tissues. Their ability to transport a plethora of different cargo, including protein, DNA, RNA, lipids and metabolites, through complex tissue microenvironments and deliver this to recipient cells makes them attractive candidates as diagnostic and therapeutic agents in a wide range of diseases, including cancer. The aim of my research focus is to engineer EVs as tailored targeted therapy and to explore circulating tumor EVs (tEVs), acting as a fingerprint of the cancer and its current status, as improved biomarkers for 1) early detection of relapsing cancer, 2) identification of molecular traits to aid cancer treatment choice, and 3) individualized dosing of targeted cancer drugs.

Cecilia Williams

Principal Investigator

GUT
Department of Medicine, Huddinge
SciLifeLab

Cancer research areas:

Colorectal cancer

Key research field interests:

Hormonal signaling, sex differences, immune microenvironment, microbiome, transcriptomics, nuclear receptors

Needs for collaboration:

Clinical expertise, wider nuclear receptor field

Selected publications:

1. Birgersson M, Holm M, Gallardo-Dodd CJ, Chen B, Stepanauskaitė L, Hases L, Kutter C, Archer A, Williams C. Intestinal estrogen receptor beta modulates the murine colon tumor immune microenvironment. Cancer Letters 622:217661 (2025)
2. Monteiro FL, Voskuil JLA, Williams C. YCharOS protocol for antibody validation. Nature Protocols 20(6):1389-1390 (2025)
3. Holm M, Stepanauskaitė L, Bäckström A, Birgersson M, Socciarelli F, Archer A, Stadler C, Williams C. Spatial profiling of the mouse colonic immune landscape associated with colitis and sex. Communications Biology 7(1):1595 (2024)

Estrogen impacts the colon immune microenvironment and anti-tumor immunity

Estrogen-only menopausal hormone therapy reduces colorectal tumor development. We have found that estrogen receptor beta (ERβ) in mouse colon tumor models suppresses cytokine signaling and tumor development. Recently, we demonstrated that the deletion of ERβ in colon epithelial cells prevents the recruitment of NK cells into colon tumors. To investigate how estrogen and ERβ regulate tissue immunity, we spatially profile the immune cell landscape (using COMET multiplex immunofluorescence, unsupervised clustering, and spatial image analysis of tissues (SPIAT) for interactions) and explore the correlation between transcriptome and microbiome using spatial metatranscriptomics. We observe clear sex differences in the colon immune landscape, and our combined data suggest that estrogenic activation of ERβ may counter an immunosuppressive tumor microenvironment.

Klas Wiman

Professor

Department of Oncology-Pathology
Akademiska Stråket 1, 171 64 Solna

0739866586

Cancer research areas:

Cancer biology; TP53; novel therapy

Key research field interests:

Tumor suppressor genes, TP53, cell death, drug discovery

Needs for collaboration:

Patient samples, bioinformatics, preclinical development, clinical trials

Selected publications:

1. Mice carrying nonsense mutant p53 develop spontaneous tumors with frequent metastasis. Strandgren C, Rondahl V, Heldin A, Öhlin S, Oppelt AS, Wiman KG. Cell Death Dis., accepted for publication; available at bioRxiv, doi: https://doi.org/10.1101/2025.03.12.642796.
2. Capturing unicorns: targeting cancers with TP53 mutations, RAS alterations beyond G12C, and MTAP loss - no target is out of the realm of possibility. Shah PA, Wiman KG, Cichowski K, Rodon Ahnert J. Am Soc Clin Oncol Educ Book. 2025 Jun;45(3):e473616.
3. Pharmacological reactivation of p53 in the era of precision anticancer medicine. Tuval A, Strandgren C, Heldin A, Palomar-Siles M, Wiman KG. Nature Rev Clin Oncol. 2024 Feb;21(2):106-120.

Cancer precision medicine by targeting missense and nonsense mutant TP53

TP53 is the most frequently mutated gene in cancer. Loss of normal p53 function allows evasion of p53-induced cell death in response to cellular stress, e.g. oncogenic stress. Reactivation of mutant p53 can trigger tumor cell death. A majority of TP53 mutations are missense mutations that disrupt p53 specific DNA binding and transactivation of target genes. Compounds that target missense mutant p53 have been identified and some have been tested in clinical trials. We are developing novel synergistic combination treatment with our molecule APR-246 and other agents, for example inhibitors of the cystine-glutamate antiporter xCT/SLC7A11 that alter cellular redox homeostasis. Judicious design of combinatorial treatment may allow efficient tumor elimination with minimal side effects in normal tissues. Our aim is a clinical study with a selected combination. Around 10% of TP53 mutations are nonsense mutations that give rise to truncated inactive p53 protein. R213X is the most common TP53 nonsense mutation and one of the 10 most common TP53 mutations overall. We previously found that the 5-FU metabolite 5-fluorouridine can induce translational readthrough of R213X nonsense mutant TP53 and apoptotic cell death. Our screening of chemical libraries led to the identification of several additional compounds with readthrough activity. To further explore translational readthrough as an anti-cancer therapeutic strategy, we have recently generated Trp53 R210X nonsense mutant knock-in mice (mouse Trp53 R210X corresponds to human TP53 R213X). Homozygous Trp53 R210X mice begin to present tumors at 2.5 months of age whereas heterozygous mice develop tumors from 9 months of age. Many tumors from the heterozygous mice show loss of heterozygosity (LOH). This unique mouse model will enable detailed in vivo studies of readthrough-inducing agents and serve as a platform for the development of novel readthrough-based cancer therapy. Since not only TP53 but also other tumor suppressor genes, e.g. APC, PTEN, RB1 and TET2, are often inactivated by nonsense mutations in tumors, pharmacological induction of translational readthrough is a promising novel therapeutic strategy with potentially broad applicability.

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