Karolinska Institutet | KAROLINSKA UNIVERSITY HOSPITAL

Karolinska Comprehensive Cancer Center

ABSTRACT BOOKLET

Photo: Erik Flyg

Karolinska Comprehensive Cancer Center Day

31st March 2025

POSTER 1

Novel Statistical Methods for Cancer Survivorship Research: Development, Implementation, and Application

PhD Student: ***Stefanie Antonilli***
Supervisors: Caroline E. Dietrich (KI), Therese M-L. Andersson (KI), Ingrid Glimelius (UU), Matthew Maurer (Mayo Clinic)

The growing global population of cancer survivors necessitates advancements in survivorship research. Developments in terms of biostatistical methods are required to meet the needs of this emerging research landscape. This PhD project aims to develop and implement user-friendly statistical methods while addressing clinically relevant questions in cancer survivorship. The planned studies are:

Study I. Development and Implementation of a Multiplicative Excess Hazards Model
I will develop and validate a multiplicative excess hazards model as a complement to the standard relative survival model (where cancer adds additively on the background mortality) for use in population-based cancer patient survival analysis. The model will be implemented in Stata and illustrated on a lymphoma patient dataset.

Study II. Risk of Thrombosis and Bleedings in Patients with Myeloproliferative Neoplasms
This study addresses the risks of bleeding and thrombosis in patients diagnosed with myeloproliferative neoplasms (MPNs), focusing on the entire patient pathway and disease trajectory to enhance understanding of these complications.

Study III. A Multistate Model with Additive Excess Hazards
Building on previous work for estimating additive and relative excess hazards using a control population, this study seeks to extend these newly developed methods to the multistate settings. Data on lymphoma patients will be used as a real-world example.

Study IV. Secondary Malignancies in Hodgkin Lymphoma Patients
Utilizing the methodology developed in Study III, the aim of this project is to quantify treatment-related risk of secondary malignancies among Hodgkin lymphoma patients, and contrast this to the cancer risk in the general population using a matched cohort design.

Jointly, the studies of this PhD project will significantly contribute to both methodological and clinical advancements in the field of cancer survivorship research.

POSTER 2

"Balancing Challenges and Personal Resources". Women's Experiences of Arm Impairment After Axillary Surgery for Breast Cancer

Matilda Appelgren[1,2], *Yvonne Wengström*[3,4], *Jana de Boniface*[1,2], *Helena Sackey*[1,5]

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Background
Arm morbidity after axillary surgery may affect the patient's daily life. However, there is limited knowledge regarding how patients face these consequences. A deeper understanding of patients' experiences of axillary surgery may improve patient information, care, and follow-up. Therefore, we conducted a qualitative study with the aim to investigate how breast cancer patients experience the consequences of axillary surgery.

Material and method
In total, six digital focus groups discussions were conducted, including 28 relapse-free female participants. All of whom had undergone sentinel lymph node biopsy with or without axillary dissection four years earlier. Data were analysed with qualitative content analysis and the theoretical framework, Sense of Coherence, was applied as an interpretative model.

Results
The analysis resulted in one theme and three related categories. The theme "Balancing challenges and personal resources" was a process that started at the time of diagnosis and was, for some, still ongoing. The three categories: "Sense-making", "Daily life", and "Driving force" reflects actions such as understanding arm symptoms, adjusting daily life, and the resources used to cope with the challenges. The majority of the participants experienced their new life situation as manageable, however, those with more pronounced arm impairments did not always feel that they had received adequate help, and their daily lives were negatively affected.

Conclusion
The return to everyday life is a process with varying degrees of challenges. For patients with persisting arm impairments, daily life is more challenging and has more limitations. Consequently, these patients should be identified and cared for, and further individualization of patient care and patient information is therefore of importance.

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POSTER 3

TEF-Health SE: Facilitation of AI innovation in Healthcare

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TEF-Health is a consortium launched in 2023, by the European Commission through Digital Europe program. Our consortium includes 9 countries and 52 partners, including Karolinska Institutet, which coordinates the Swedish node.

Our goal is to support AI developers to bring trustworthy AI to users more efficiently, and to contribute to the implementation of the AI Act. To achieve this, we are establishing reference sites across Europe open to all European health technology providers. Our focus is to support Small and Medium-sized Enterprises (SMEs) by testing and experimenting with their AI solutions. We anticipate them to need help on data generation, access to existing data such as electronic health care records and/or -omics data, data harmonization, cybersecurity testing to name a few of our services.

Currently we have gathered more than 300 services to support SMEs (displayed on our website: tefhealth.eu), organized by physical facilities, digital support, and consultancy, to help them through validation and certification of their latest AI technology. We also help to ensure compliance with relevant legal, ethical, quality, and interoperability standards, supporting SMEs throughout their healthcare implementation journey.

Furthermore, our TEF-Health team has launched a Center for AI Innovation at KI. We are now actively mapping clinical and research expertise in developing AI tools for healthcare. This strengthens our local network and helps us in our mission to bring safer and trustworthy AI solutions into routine care. Please let us know if you are interested in providing services from the Swedish node in supporting AI development in Europe.

POSTER 4

Severity of COVID-19 in individuals with chronic lymphocytic leukemia throughout the pandemic in Sweden: A nationwide multiple register cohort study conducted from 2020 to 2023

Lisa Blixt, *Pontus Hedberg, Sandra Eketorp Sylvan, Isabela Killander Möller, Hannes Lindahl, Fredrik Kahn, Åsa Nilsdotter-Augustinsson, Mats Fredrikson, Sofia Nyström, Richard Rosenquist Brandell, Peter Bergman, Christina Carlander, Soo Aleman, Anders Österborg, Lotta Hansson.*

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Individuals with chronic lymphocytic leukemia (CLL) face increased risk of severe COVID-19. This study from Sweden, a country with few mandatory restrictions at the onset of the pandemic, used 10 nationwide registers to compare risks of severe COVID-19 outcomes of PCR-verified SARS-CoV-2 infections through February 2023 in individuals with vs without CLL. From a population of 8,275,839 (6,653 CLL) individuals born 1930-2003, 2,088,163 first infections (1,289 CLL) were included. The 90-day all-cause mortality rate and adjusted relative risk (aRR [95% CI]) for individuals with CLL vs the general population was 24.8% (1.95 [1.58 2.41)) during Wild-type, 17.2% (2.38 [1.58-3.57)) during Alpha, 4.1% (0.71 [0.24-2.08]) during Delta, and 12.6% (1.49 [1.24-1.78]) during Omicron. Their mortality during Omicron was 0.6% (<65 years), 5.4% (65-74 years), and 19.7% (>75 years). Small molecule inhibitors (1.56 [1.03-2.37]) and corticosteroid usage (1.45 [1.04-2.02]) was associated with increased mortality.

Next, we analyzed the all-cause mortality in the capital (Stockholm), widely affected by SARS-CoV-2 at the onset of the pandemic. Mortality in individuals with CLL increased by 55% during the first 6 months of 2020 vs 2019 and age- and sex aRR by June 30 was 1.53 [1.09-2.15] for individuals with CLL (P=.02) and 1.29 [1.25-1.33] for the general population (P<.001). Collectively, a significantly increased risk of severe COVID-19 and death was observed among individuals with CLL in Sweden, particularly at the onset of the pandemic when few national protective measures were introduced, but also after Omicron emerged, emphasizing the need for a more pro-active pandemic strategy for CLL.

POSTER 6

Cardiovascular Disease Incidence Following Breast Cancer Treatment: A Comparative Study of BRCA1/2 Mutation Carriers and Sporadic Cases

Mehdi Dehghan Manshadi, PhD [b,f]; *Narges Manouchehri, PhD* [b,f]; *Annelie Liljegren, MD, PhD* [e,f]; *Laila Hubbert, MD, PhD* [a]; *Claudia Maes, MSc* [c]; *Johanna Rantala, MSc, PhD* [d]; *Narsis A.Kiani, PhD* [b,f]*; *Elham Hedayati, MD, PhD* [e,g]*

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Background: Cardiovascular disease (CVD) remains a leading cause of mortality among breast cancer (BC) survivors, primarily due to the cardiotoxic effects of oncological treatments, including chemotherapy and radiotherapy. Additionally, individuals with BRCA1/2 mutations may display an increased susceptibility to CVD after BC treatment, owing to impaired DNA repair mechanisms that can trigger a cascade of inflammatory responses. This study aims to determine whether female BRCA1/2 mutation carriers are at a higher risk of developing CVD following BC treatment compared to patients diagnosed with sporadic BC.

Methods: This study analysed female BC patients in the Stockholm-Gotland region of Sweden from 2008 to 2019. Data were collected from regional and national registries to evaluate pre-existing cardiovascular diseases, cardiovascular risk factors (CVRFs), cancer treatments, and demographic characteristics. The analysis concentrated on CVD events, assessing their incidence across various subgroups. The study design involved matching cohorts based on age, TNM classification, tumor laterality, and the presence of CVDs and CVRFs before the BC diagnosis. We used a regression-based approach to evaluate the effects of various conditions and treatments while accounting for potential confounding factors.

Results: After cohort matching, 171 BRCA-associated BC patients (out of 233) and 2,387 sporadic BC patients (out of 17,221) were selected for analysis. The median age at BC diagnosis for the studied cohort was 43.0 years (IQR: 37.0–54.0). BRCA-BC patients experienced their first CVD event post-BC diagnosis at a later median age (59.5 years, IQR: 45.8–66.5) compared to sporadic-BC patients (median: 50.0 years, IQR: 41.5–66.0). Following BC diagnosis, the prevalence of CVD increased in both groups, reaching 9.4% in BRCA-BC patients and 11.4%±2.7% in sporadic-BC patients. Considering a baseline

prevalence of 3.5% CVD events before BC diagnosis, sporadic-BC patients exhibited a slightly higher increase in CVD incidence.

Conclusions: Our initial findings indicate no significant difference in CVD outcomes between the BRCA and sporadic BC cohorts. Both groups experienced similar increases in cardiovascular events after treatment. This suggests that while genetic factors may influence CVD risk, the immediate impact of cardiotoxicity from cancer treatments could play a more dominant role in altering cardiovascular health among breast cancer survivors. This finding highlights the complex interplay between genetic factors and treatment-related risks in developing CVD post-cancer. Further research with long-term follow-ups and a larger BRCA sample size is necessary to uncover potential subtle differences that may not have been detected in this study.

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POSTER 7

Inactivating SAMHD1 by Targeting Allosteric Activation

Christopher Dirks, *Si Min Zhang and Sean G. Rudd*

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Objectives: SAMHD1 is a deoxynucleoside triphosphohydrolase (dNTPase) that regulates cellular dNTP levels and has recently been implicated as a resistance factor to nucleoside analogue antimetabolite chemotherapy. This makes SAMHD1 an attractive target for inhibitor development, but no cell-active compounds have been reported so far. In this project we therefore aim to improve our understanding of SAMHD1 biology, especially of its allosteric activation, oligomerisation and catalytic mechanisms. We aim to diversify the modes of inhibition towards SAMHD1 and provide a starting point to rationally develop allosterically targeting molecules.

Methods: We use mainly biochemical and biophysical methods to study modulators of SAMHD1 activity. This includes enzyme activity assays, a competitive binding assay to study allosteric site affinity and chemical crosslinking to study SAMHD1 oligomerisation.

Results: Antiviral guanine nucleotide analogues Acyclovir- and Ganciclovir-triphosphate can mimic the endogenous allosteric activator GTP by binding to its allosteric sites and inducing the formation of enzymatically competent homotetramers. However, depending on the analogue activator and dNTP substrate identity, the resulting catalytic activity can be drastically reduced.

Conclusions: By studying the modulation of SAMHD1 dNTPase activity via nucleotide analogues we identify new avenues of inhibiting this challenging target by trapping it in a stable, inactive tetramer. We thereby improve our understanding of the allosteric activation process and of SAMHD1's dNTPase activity in the context of its oligomerisation.

POSTER 8

Metacognitive therapy for cancer anxiety

*Helena Ilstedt[1], **Susanna Einarsson Berg**[1], Jeanette Winterling[1, 2]*

[1]Psychooncology Unit, Comprehensive Cancer Center, Karolinska University Hospital, Stockholm, Sweden
[2]Department for Neurology, Caring Science and Society, Section of Nursing, Karolinska Institute, Stockholm, Sweden

Background: Cancer survivors often experience psychological morbidity after treatment. Studies from U.K. have concluded that metacognitive therapy (MCT); a brief transdiagnostic psychological intervention, could be effective delivered to adult cancer survivors with psychological morbidity. MCT offers a promising approach but has not yet been used in a Swedish cancer rehabilitation context.

Methodology: We used an individually administrated, manual based and diagnose-specific MCT-treatment in fourteen individuals at a Psycho-oncology unit in Sweden. Each patient received between 7-10 sessions of MCT with a psychotherapist with a Master Class in Metacognitive therapy. Levels of anxiety, worry and metacognitive beliefs were assessed using GAD-7, PSWQ and GADS-R before and after treatment. A structured interview was administered after the completion of the treatment.

Impact on practice: Thirteen out of fourteen patients reported over cut off on PSWQ and ten out of fourteen patients reported severe anxiety on GAD-7 before treatment. After treatment all patients reported decreased anxiety. Ten out of fourteen reported under cut-off on PSWQ. Ten patients reported no anxiety and four mild anxiety on GAD-7 after treatment.

Discussion: MCT, a brief diagnostic-specific, psychological intervention can be delivered effectively to individuals with cancer anxiety with promising treatment effects. MCT was acceptable to patients and all patients completed all sessions. In the interviews they reported increased quality of life even in other areas of life outside fear of cancer.

POSTER 10

Exploring the impact of physical exercise regimens on health-related quality of life following Oesophageal or gastric cancer surgery: a systematic review and meta-analysis of randomized controlled trials

Kenneth Färnqvist

Purpose: To assess the effectiveness and adverse events of postoperative physical exercise on health-related quality of life (HRQL) in patients who have undergone surgery for oesophageal or gastric cancer.

Methods: We conducted a systematic review and meta-analysis and reported it according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. Randomised controlled trials (RCT) that investigated HRQL factors following physical exercise interventions in patients undergoing oesophageal or gastric cancer surgery were included. Studies including participants who had undergone oesophagectomy or gastrectomy for cancer, of either sex and were 18 years or older were included. Participants with other cancers were excluded. Medline, Embase, CINAHL, Cochrane Library, PEDro, and trial registries were searched for studies from inception until February 2025. Results were synthesised using meta-analyses. Two independent reviewers assessed the risk of bias using the Cochrane risk of bias tool 2.0, and the grading of recommendations assessment, development and evaluation (GRADE) was used to evaluate the overall certainty of the evidence. PROSPERO ID CRD42022358493.

Results: Three studies enrolling 284 patients undergoing oesophagectomy were included, of which two were assessed at high risk of bias and one at some concerns. The global quality of life score from the European Organisation for Research and Rreatment of Cancer (EORTC) quality of life questionnaire Cancer QLQ-C30 was used to assess HRQL in all the included studies. The score ranges from 0 to 100, with higher scores indicating a better HRQL. Physical exercise therapy had no discernible impact on HRQL compared to the control group (mean difference 0.77 [95% CI -4.36, 5.90]. However, the quality of evidence was very low, which should be considered when interpreting the results as they can differ substantially from the true effects.

Conclusion: We found a significant lack of information about the effects of post-surgery physical exercise compared to standard care in patients who have undergone oesophagectomy or gastrectomy for cancer. Based on the current very low certainty evidence, the effectiveness on HRQL and the safety of postoperative physical exercise in patients treated with oesophagectomy for cancer is uncertain. We found no studies investigating gastric cancer and exercise.

POSTER 11

Feasibility of multimodal data generation for clinical trials

Rikard Fred[1], *Richard Rosenquist Brandell*[2], *Maria Creignou*[3], *Thoas Fioretos*[4], *Åsa Johansson*[5], *Janne Lehtiö*[6], *Naima Kayser Leozza*[1], *Anna Martling*[2], *Jeffrey Yachnin*[7] *and Päivi Östling*[1]

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The rapid development of technologies for molecular profiling paves the way for precision medicine approaches to match patients with effective treatment. We aim to increase access to SciLifeLab's technology platforms to support academic and industry-initiated clinical trials. Our goal is to identify mature technologies to be evaluated in observational studies and adopted in interventional biomarker-driven clinical trials. This means connecting SciLifeLab to clinical practice, key developments supporting cross-platform data, sample and analysis flows with timelines and quality complying with the needs of clinical trials are needed. We are currently funding five pilot projects through co-development to identify and improve sample and data flow within and between platforms to enable multimodal data generation for clinical trials. Currently, metadata is often collected project-by-project without established semantic standards, leading to fragmentation and hindering large-scale data-driven studies. Our goal is also to create a common data model for precision medicine to increase our readiness for handling multimodal precision medicine data.

POSTER 12

Centre for Imaging Research – CIR

Ida Friberger

CIR - the Centre for Imaging Research - is a joint venture of Karolinska University Hospital, Karolinska Institutet, and Region Stockholm, providing state-of-the-art imaging. The centre gathers a unique set of core facilities for structural, functional, and metabolic imaging, with a special focus on translational brain imaging. CIR serves academic, clinical, and industrial users with imaging facilities and services of the highest standard.

The centre is composed of eight core facilities: MR centre (MRI), KERIC, PET-MRI, National Core Facility for MEG (NatMEG), Brain Molecular Imaging Centre (BMIC), MedTechLabs, Autoradiography and Radiopharmacy facility. This unique setup offers cutting-edge structural, functional, and metabolic in vivo imaging of humans, non-human primates, and large and small animals. The imaging facilities are supported by an internationally acclaimed in-house Radiopharmacy with radionuclide production, radioligand development and a radioligand binding facility.

The Centre for Imaging Research is also involved in the European project for AI and Robotics in healthcare (TEF-Health). The Swedish representatives in the TEF project are CIR and SciLifeLab together with the Research Institute of Sweden (RISE). We are dedicated to creating an environment that enables AI developers, researchers, and industry to collaborate and overcome the challenges of integrating AI into healthcare. With funding from the EU, we can offer small- to medium-sized companies data management, validation, certification, testing and experimentation facilities at reduced prices. Henceforth, to facilitate medical research, improve patient outcomes and enhance healthcare delivery by ensuring safe, effective, and responsible use of AI in healthcare.

POSTER 13

Bead-bound, personal neoantigens expand T cells from regional lymph nodes in adoptive phase I/IIa clinical trial in colorectal cancer

Hans Grönlunf

Personalized Tumour-Trained Lymphocytes (pTTL) is a novel adoptive T cell therapy targeting tumor neoantigens in complex with the human HLA. The T cells are trained to recognize and remove tumor cells displaying proteins with subtle amino acid changes, which if unnoticed by the immune system, could propagate and become the initiation of cancer.

In personal T cell cancer immunotherapy, the EpiTCer® technology offers a novel and efficient approach to deliver, antigen-specific T cell activation and expansion. Paramagnetic beads are covered with six recombinant polypeptides, each containing six neoantigens. The bead size facilitates efficient phagocytosis, natural processing and cross-presentation to neoantigen-specific CD4 and CD8+ T cells by antigen presenting cells present in the RLN. The bead-RLN cell suspension is co-cultured for two weeks, beads then magnetically removed, and T cells given back to the patient. A first in human phase1/2a clinical trial in patients with stage IV colorectal cancer is ongoing.

The molecular and cellular phenotypic patterns of the 14-day cell expansion were compared at seven timepoints over the 14-day co-culture by multiomic approaches to follow the T cell fate analyzed using cutting edge Karolinska Institutet resident SME.

POSTER 14

PCM Program

Päivi Östling, Claes Karlsson, Ingemar Ernberg

The Personalised Cancer Medicine (PCM) Program at Karolinska Institutet has been at the facilitating precision oncology initiatives at Karolinska and internationally for over a decade. The mission has been to integrate personalised medicine into clinical cancer care. With strategic funding from Radiumhemmets forskningsfonder, the program has focused on fostering a multidisciplinary collaborations between preclinical and clinical researchers and supports critical infrastructure development. Key ongoing projects include the Basket-of-Basket (BoB) trial, the Molecular Tumor Board Portal, and initiatives involving liquid biopsies, data-rich clinical trials (DART), and comprehensive research databases such as MCTM and ORRACLE. As part of the Cancer Research Karolinska Institutet Working Group 4 the PCM Program has been key promotes team science, supports the implementation of broad-panel sequencing and multi-omics through projects like iPCM and PhenoPCM. Further efforts include the support in development of the Cancer Core Europe Virtual Data Center (VDC), and projects related to integration of patient-reported outcomes, Symptomics. Recent efforts concern AI-driven support for clinical and research initiatives. Moreover the PCM Prgoram has also been conducting organzational research on PCM implementation in collaboration with the medical management centre at LIME, KI. With the full spectrum of these initiatives the aim has been to help bridge cancer research and clinical practice, advancing personalised cancer medicine for patient benefit in the Stockholm region and beyond.

POSTER 15

Fighting cancer with the 1-2-punch approach by identifying drug combinations that improve current cancer therapies

Wout Magits[1,2], *Gema López*[4], *Matilde Murga*[4], *Samuele Fisicaro*[1,2], *Oneka Perea Ariznabarreta*[1,2], *Wareed Ahmed*[3], *Maria Häggblad*[1,2], *Louise Lidemalm*[1,2], ***Daniela Hühn***[1,2], *Oskar Fernández-Capetillo*[1,2,4]

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Resistance to therapy has been estimated to contribute to treatment failure in up to 90% of cancer patients and remains one of the fundamental challenges in cancer. Drug tolerant and senescent cells accumulate as a consequence of many cancer therapies and are thought to contribute to therapy resistance. Accordingly, “to develop ways to overcome cancer’s resistance to therapy” was one of the 10 recommendations made from the Blue Ribbon Panel associated to the Cancer Moonshot initiative of the National Cancer Institute. In this regard, one specific idea is to find combinations that can eliminate the cancer cells that resist the initial treatment. This is the basis of the so-called “one-two-punch” strategy for cancer therapy, which aims to maximize the efficacy of the initial treatment and thereby reduce tumor relapse.

To advance this concept, we have developed a high-throughput phenotypic drug screening platform to identify novel one-two punch strategies across various cancer types and in combination with approved therapies. This innovative approach us to discover novel senolytics - drugs that specifically target senescent cells. These senolytics have shown remarkable potential in enhancing the anticancer effects of senescence-promoting drugs, such as the CDK4/6 inhibitor Palbociclib. We are expanding our research by testing the efficacy of our candidate compounds in combination with other therapeutics across multiple cancer cell lines, with a particular focus on breast and lung cancers.

By addressing the critical issue of therapy resistance, we aim to contribute significantly to the advancement of cancer treatment and potentially increase survival rates for patients.

POSTER 16

Metacognitive therapy for cancer anxiety

Helena Ilstedt[1], *Susanna Einarsson Berg*[1], *Jeanette Winterling*[1, 2]

[1]*Psychooncology Unit, Comprehensive Cancer Center, Karolinska University Hospital, Stockholm, Sweden*
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POSTER 17

Meeting psychological consequences after cancer diagnosis for AYA's with a person – centered approach through "Team Young"

Helena Ilstedt[1], *Tina Sundholm*[1], *Emelie Nilsson*[1], *Kajsa Asklöf*[3], *Jennie Falender*[1], *Christoffer Malmström*[1], *Alva Petri*[3], *Hanna Refsgaard*[3], *Anna Möllerstrand*[4], *Siri Kautsky*[5], *Maria Olsson*[3], *Anna Jervaeus*[2], *Jeanette Winterling*[1, 2]

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Background: Adolescents and young adults (AYAs) with cancer experience unique challenges facing a serious illness in the beginning of their lives. When offered, they often decline psychological support why the project myCode aims at creating a person-centered care model meeting the needs of AYAs, aged 16-30, newly diagnosed with cancer, by increasing the awareness of, and encourage them to accept psychological support.

Methodology: A co-design approach is applied where AYAs with a cancer experience are involved throughout the project. A "Team Young" has been created, consisting of youth coordinators and therapists, meeting all AYAs newly diagnosed with cancer. The aim is to connect with the AYA by listening to their story and find out about current psychosocial support through social network mapping. AYAs are then informed about available support: 1) support program Promoting Resilience in Stress Management (PRISM) 2) peer-to-peer support or 3) individual counselling. Evaluation is done by interviews with participating AYAs. Team Young was launched in October 2023. The goal is to include all AYAs at the two comprehensive cancer centers in Sweden involved in myCode.

Impact on practice: Approximately 25 AYAs have met with Team Young. Most of them have chosen to accept support and seem to appreciate the support.

Discussion: It seems that AYAs who meet Team Young raise their awareness of available support and those who not already receive support are willing to accept any of the presented support options.

POSTER 19

Samskapande genom patientnätverk Karolinska Comprehensive Cancer Center

Ann-Britt Johansson *och Louise Svanström*

Sammanfattning

Patientnätverket stärker patientinvolveringen.

Patientnätverket samlar representanter från olika områden inom Karolinska CCC för att använda patienters erfarenheter och perspektiv i utvecklingen av cancervården.

Genom att fokusera på strategiska frågor bidrar nätverket till en mer personcentrerad och jämlik vård för alla diagnoser inom Karolinska CCC där patienters röster blir en självklar del av framtidens cancervård

Bakgrund

Sedan 2023 har Karolinska CCC haft en patientrepresentant i sin styrgrupp, Boards of Directors (BoD). Genom att lyfta patienters och närståendes perspektiv på högsta ledningsnivå skapas möjligheter för aktivt partnerskap. På initiativ av patientrepresentanten etablerades 2024 ett dedikerat patientnätverk.

Målsättning

Att kontinuerligt förbättra vårdkvaliteten och stärka upplevelsen för alla patienter inom Karolinska CCC. Genom att tillvarata erfarenhetsbaserad kunskap och insikter formas cancervården efter patienternas och närståendes behov.

Syfte och beskrivning av nätverket

Patientnätverket är en plattform för utbyte av erfarenheter och kunskap med syfte att stärka patienters och närståendes roll i utvecklingen av cancervården. Nätverket integrerar sina erfarenheter i hela vårdkedjan – från prevention och tidig upptäckt till behandling, rehabilitering och uppföljning samt forskning och deltagande i kliniska studier.

Deltagare och uppdrag

Patientnätverket består av 27 representanter från Tema Cancer, Barnonkologi och Barnhematologi, Neurocentrum (Patientflöde Hjärntumörer), Medicinsk Diagnostik Karolinska (MDK) samt Cancer Research KI (Karolinska Institutet).

Nätverket utser representanter till centrala funktioner, som det strategiska patient- och närståenderådet inom Tema Cancer samt BoD. Representanterna väljs för en tvåårsperiod, med möjlighet till ett omval.

Samarbeten med andra forum

För att undvika parallella processer, exempelvis inom utbildning, samarbetar nätverket med det Strategiska rådet för Karolinska Universitetssjukhuset. Patientnätverkets närvaro i rådet säkerställer ett effektivt samarbete och ett helhetsperspektiv med fokus på cancerfrågor.

Identifierade områden för samskapande

- Rekrytera fler patientrepresentanter
- Identifiera behov av kompetensutveckling och utbildning för att stärka patientinvolveringen, både för vårdprofessionen och patientrepresentanter
- Att förstå vad som är viktigt för patienten kring kontinuitet i vården och använda insikterna för att förbättra vårdprocesser
- Implementera kunskap om fysisk aktivitet vid cancerbehandling

POSTER 20

Prediction model of fatal bleeding after SBRT of ultra-centrally located lung tumors

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Purpose

Stereotactic body radiotherapy (SBRT) for centrally located lung tumors close to the bronchial tree has resulted in high rates of fatal toxicities, especially grade 5 bronchopulmonary bleedings (1-4). However, SBRT may be the only potentially curative treatment option for these patients, and some fatal bleeding events are also caused by tumor growth. The purpose of this study was to find the dose-volume histogram (DVH) parameter of the bronchi that best predicts grade 5 bleeding after SBRT of centrally located lung tumors and include that parameter in a predictive model of grade 5 bleeding.

Materials and Methods

The patient material consisted of 230 patients treated with SBRT of 7Gy x 8, prescribed with inhomogeneous dose distribution to the PTV-encompassing isodose, for 238 tumors located within 2 cm from the tracheobronchial tree. Median follow-up time was 34 months (2-114 months). Twenty-one (9%) patients died of grade 5 bronchopulmonary bleeding 3-96 months after treatment.

A maximum likelihood optimization of a Cox-based univariable and bivariable normal-tissue complication probability (NTCP) model was performed, including the bronchial DVH (for the left main bronchus or the joint structure of the right main and intermediate bronchi, depending on which of these received the highest dose) and bronchial compression observed at planning CT:

$$NTCP(D,X,t)=1-e(-H0(t)\cdot e(\beta 1\cdot D+\beta 2\cdot X))$$

H0(t) = baseline cumulative hazard function at time *t*
βi = natural log of hazard ratio of each independent variable
D = DVH parameter value
X = bronchial compression (binary)

Three alternative DVH parameters were considered:

- Dose to a certain volume (Dv), optimizing volume v
- Equivalent Uniform Dose (EUD), optimizing the volume-effect parameter n
- Volume receiving a certain dose (Vd), optimizing dose d

The performance of each model was evaluated with Harrell's C-statistics correcting for optimism. The models were internally validated with bootstrap. Bronchial doses were recalculated into equivalent dose in 2 Gy fractions (EQD2) with α/β value 3 Gy.

Results

The bivariable outcome modelling resulted in the DVH parameters of D0.31cc, EUD with n=0.0238, and V82Gy,EQD2 as best predicting grade 5 bronchopulmonary bleeding, see Table 1. The first two models indicate that the dose to a small volume of the main and intermediate bronchi is the important DVH parameter for predicting grade 5 bleeding. These two models had an optimism-corrected C-statistic of 0.78 and 0.77, respectively, while the third model had a value of 0.80. However, the V82Gy,EQD2 model had a broader confidence interval.

The NTCP model for grade 5 bleeding at 1, 2, 3, 4, and 5 years after treatment including D0.31cc for the main and intermediate bronchi and bronchial compression is shown in Figure 1. The risk is strongly dependent on the presence of bronchial compression, which for the 2-year prediction is equivalent to a dose increase of 107 Gy.

Conclusion

Dose to a small volume of the main and intermediate bronchi and bronchial compression are important predictors for grade 5 bleeding. For patients with ultra-central lung tumors, this provides some guidance on how to limit the risk of fatal toxicity.

Table 1: *DVH parameter values, optimized parameters, and hazard ratios (HR) for the fitted univariable and bivariable models.*

Univariable models	**D_v model**	**EUD model**	**V_d model**
Optimized parameter	v = 0.35cc	n = 0.0747	d = 82 Gy (EQD2)
DVH parameter mean (IQR)	67.8 (30.6-92.9)	68.7 (33.9-93.5)	0.57 (0.00-0.65)
HR DVH parameter	1.02 (1.01-1.02)	1.02 (1.01-1.03)	1.83 (1.30-2.37)
HR bronchial compression	6.52 (1.95-17.26)		
Bivariable model	**D_v model**	**EUD model**	**V_d model**
Optimized parameter	v = 0.31cc	n = 0.0238	d = 82 Gy (EQD2)
DVH parameter mean (IQR)	69.2 (31.8-94.1)	84.6 (42.4-114.5)	0.57 (0.00-0.65)
HR DVH parameter	1.01 (1.00-1.02)	1.01 (1.00-1.02)	1.64 (1.05-2.39)
HR bronchial compression	3.58 (0.85-12.5)	3.95 (1.08-13.3)	3.96 (1.01-15.6)

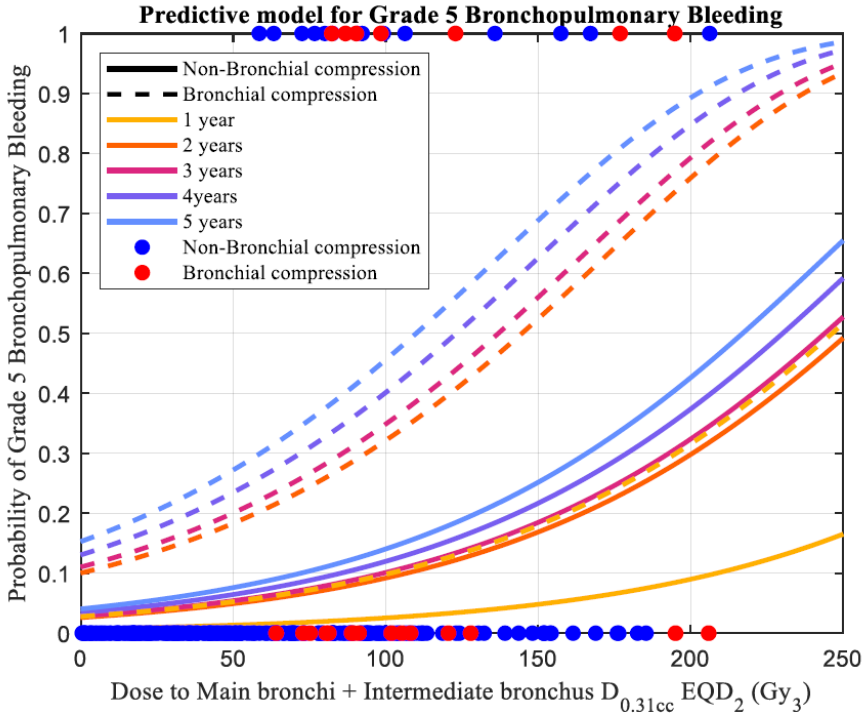

Figure 1. *Cox-based NTCP model for grade 5 bleeding at 1, 2, 3, 4, and 5 years after SBRT treatment including $D_{0.31cc}$ for the main and intermediate bronchi and bronchial compression. Solid lines are without bronchial compression and dashed lines are with bronchial.*

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POSTER 21

Survival mechanism of pancreatic tumor bacteria and their ability to metabolize chemotherapy drugs

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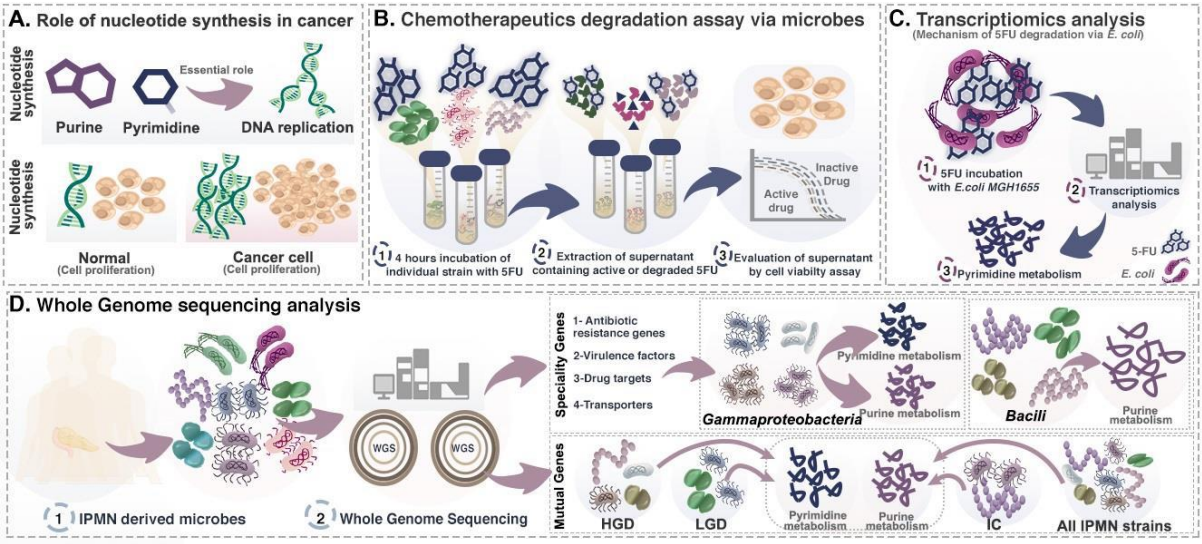

Background: Microbes are impacted by the environment where they reside, and this includes tumor microbes which reside in tumor microenvironment (TME). Nucleotide biosynthesize plays a major role in TME via nucleotide precursor through synthesizes of purine and pyrimidine molecules. Our previous study identified pancreas tumor-associated strains isolated from intraductal papillary mucinous neoplasms (IPMNs) of distinctive pathology grades. Here, we report phenotypic and genotypic characteristics of these tumor-derived isolates and their ability to metabolize chemotherapeutics.

Methods: In this study, phenotypic characterization and antimicrobial effect of chemotherapy drugs (fluorouracil and gemcitabine) was determined through half maximal inhibitory concentration for IPMN strains. We studied the impact of chemotherapeutics on whether IPMN

derived strain can metabolize them or not and verify drug's efficacy through different pancreatic cancer cell lines. Furthermore, Whole Genome Sequencing (WGS) was performed to study the genomic alterations for the Gammaproteobacteria and Bacilli strains.

Results: Our results indicate that most of IPMN-derived strains were sensitive to gemcitabine and resistant to fluorouracil. However, we also observe that these stains were also able to degrade both gemcitabine and fluorouracil, which we verified through pancreatic cancer cell lines. Sequencing analysis of bacterial profiling reveals that among the IPMN bacteria isolates, Gammaproteobacteria were two-fold functionally enriched compared to Bacilli strains and differed significantly in enrichment of nucleotide metabolism in specialized genes mapped with antibiotic resistance genes, drug targets, virulence factors, and transporters.

Conclusion: Our comprehensive phenotypic and genotypic characterization reveals that IPMN strains enriched nucleotide metabolism encoded pyrimidine and purine metabolism pathways in IPMN grades to survive in precancerous environment which might be enriched as a counter mechanism against nucleotide biosynthesis. It has been verified that Escherichia coli enriched pyrimidine metabolism to degrade fluorouracil through transcriptomics analysis. We speculate that as IPMN stains are pre-enriched in nucleotide metabolism that might be the reason why IPMN strains metabolized chemotherapeutics drugs.

POSTER 22

Drug sensitivity-testing of lung cancer patient-derived cells ex vivo for optimal and personalised treatment in the clinic

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Tumors of the lung and pleura, including primary pleural mesothelioma and metastatic lung cancer are aggressive tumors with great morphological heterogeneity and very poor prognosis. The first sign of cancer spread to the pleura is an accumulation of a pleural fluid, which contains variable number of malignant cells. Currently, only about 40% of tumors respond to treatments: approximately 60% of patients undergo toxic treatment despite the benefits being, at the best, uncertain.

A recently developed approach on ovarian cancer established a scalable functional precision medicine platform which allows to assess the response of patient cells to drugs and drug combinations are quantified with live-cell imaging. In collaboration with SciLifeLab, Stockholm, we applied this protocol to the isolated tumor cells from patient-derived pleural effusions and cultured in 3D, followed by ex vivo treatment of the cells with clinically relevant drugs. Interestingly, the highest drug concentrations did not correlate with the highest overall response for several samples. Moreover, most patients' cells exhibited a greater response to combination treatments. Preliminary results have shown a positive relationship by plotting Drug Sensitivity Score to the Progression-Free Survival of the selected patients. This protocol provides results within 10 days after sample collection, making it a potential candidate for integration into clinical workflows. Our work highlights the potential of the ex vivo testing to transform personalized oncology care.

POSTER 23

Human skin mesenchymal stem cells provide a unique niche for acute myeloid leukemia-initiating stem cells

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Acute myeloid leukemia (AML) is aggressive blood cancer and often accompanied with extramedullary infiltrations in other organs including skin and brain. Leukemic cell infiltration in skin signifies a poorer prognosis in patients with AML. However, it is not clear how the AML cells are maintained in the skin. We have recently in a mouse model demonstrated the AML cells in skin are highly enriched with AML leukemia-initiating stem cells (LSCs) and better protected by skin mesenchymal stem cells (MSCs) to during chemotherapy (Sandhow et al., J. Exp. Med, 2023). However, it remains unexplored whether human skin MSCs exert the same functional impact.

To investigate this, we first have utilized a co-culture of human AML cells with human skin MSCs isolated and expanded from healthy donors, followed by RNA sequencing and metabolic assays. RNA sequencing revealed that human skin MSCs also expressed key hematopoietic stem cell regulatory genes including *THPO, SCF, CXCL12* and *LAMA4*, with even higher levels of *THPO* and *KITLG* than their bone marrow (BM) counterparts ($p<0.0001$ and $p<0.05$, respectively). In line with this, our co-culture experiments indicated that skin MSCs displayed a superior protective effect on human AML cell line THP-1 than their BM cell counterparts during cytarabine (Ara-C) treatment. There were more residual chemo-resistant AML cells following Ara-C treatment, reflected in the higher number of CD36+ AML cells in cocultures with skin MSCs, compared to that with BM MSCs ($p=0.0065$). Further functional assays showed increased numbers of residual cobblestone area-forming cells ($p=0.0298$) and colony-forming units ($p=0.038$) in the co-culture with skin MSCs, relative to that with BM MSCs, confirming the superior protective function of skin MSCs for AML LSCs.

Mechanistically, the protective function of human skin MSCs might be related to their resistance to AML remodeling as our RNA-sequencing revealed that human skin MSCs displayed much less molecular alterations than BM MSCs after being exposed to THP1 AML cells for 72 hours (221 vs 1761 altered genes with adjusted p values <0.05). Speculatively, such a resistance could in turn contribute to maintaining AML cells in quiescence status, thereby protecting AML cells from Ara-C treatment. This hypothesis was supported by increased fraction of AML cells in G0 in co-culture with skin MSCs. In addition, gene set enrichment analysis showed upregulated genes associated with fatty acid metabolisms and ribosome in skin MSCs, indicating a potential superior metabolic support of skin MSCs for AML cells. Consistent with this, single cell metabolism assay, called SCENITH showed higher capacity of fatty acid and amino acid oxidation in the AML cells co-cultured with human skin

MSCs compared to that with BM MSCs during Ara-C treatment (p=0.0167), suggesting that skin MSCs might protect AML cells via better metabolic support.

Taken together, our preliminary data indicate human skin MSCs may provide a unique protective niche for AML cells, particularly during Ara-C treatment. More work is required to elucidate the underlying mechanisms.

POSTER 25

Differential impacts of *Lama4* expression in bone marrow niche on chronic myeloid leukemia initiation and progression

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Objectives

The current challenge for treating chronic myeloid leukemia (CML) is to eradicate CML-initiating stem cells (LSCs). This has led to CML persistence and relapse afer treatment discontinuation. Evidence suggests that bone marrow (BM) niche plays a critical role in maintaining and protecting the LSCs. However, the molecular mechanisms remain poorly defined, limiting opportunities to identify new treatment options targeting the LSCs. We have recently shown that *LAMA4,* a functional chain for several laminin isoforms, is downregulated in BM mesenchymal stem cells (MSCs) of newly diagnosed patients with CML (Dolinska, Cai, Månsson et al., Blood, 2023) and mice with acute myeloid leukemia (AML). Importantly, deletion of *Lama4* in the microenvironment accelerated AML progression and relapse in mice (Cai and Kondo et al., Blood, 2022). Nevertheless, the functional impact of LAMA4 on CML progression remains unclear.

Methods

We here have explored the significance of *Lama4* expression in the niche on CML development by using inducible *SCL-tTA×TRE-BCR::ABL1* (*BCR::ABL1*) CML mice crossed with *Lama4*$^{-/-}$ mice. The potential changes in CML development kinetics and the fates of hematopoietic stem and progenitor cells in the *BCR::ABL1×Lama4*$^{-/-}$ double transgenic mice was assessed by multi-color fluorescent-activated cell sorting (FACS) and droplet digital PCR after inducing CML by tetracycline withdrawal.

Results

Contrary to what we observed in AML mice, we have observed prolonged CML onset (p=0.009) and survival (p=0.04) in the *BCR::ABL1×Lama4*$^{-/-}$ mice compared to that in *BCR::ABL1×Lama4*$^{+/+}$ mice after CML induction by tetracycline withdrawal. This was accompanied with the delayed increase of *BCR::ABL1*$^{+}$ cell fraction and (CD11B^{+}GR1high) cells (p=0.02) in the blood of *BCR::ABL1×Lama4*$^{-/-}$ mice. Further, FACS analysis showed a reduced number of granulocyte-macrophage progenitors (p=0.047), megakaryocyte progenitors (p=0.036), and hematopoietic stem cells (LIN^{-}SCA1^{+}KIT^{+}CD150^{+}, p=0.02) in the *BCR::ABL1×Lama4*$^{-/-}$ mouse spleen at 6 weeks after tetracycline withdrawal. These data suggest a regulatory role of *Lama4*$^{-/-}$ niche in controlling CML development. Interestingly, such a functional impact became less dramatic in *Lama4*$^{-/-}$ mice carrying double allele of *BCR::ABL1* which is linked to a more aggressive phenotype. However, CML progression appeared to be accelerated in sublethally irradiated *Lama4*$^{-/-}$ host mice after being

transplanted with BM cells from mice with symptomatic CML, indicating a permissive role of *Lama4* deficient niche on CML progression.

Conclusion

Out data suggest possible opposing roles of *Lama4* expression in the niche during CML development under steady state and after transplantation of activated CML cells. It is likely that *Lama4* deficiency provides an unfit niche for *BCR::ABL1*-expressing cells at the initial phase of CML development, however, once CML is established with high *BCR::ABL1* burden, the niche became more permissive. Nevertheless, the mechanisms need to be further studied.

POSTER 27

Progesterone Receptor Modulator: Novel Avenues in Breast Cancer Prevention

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Women with BRCA1 or BRCA2 gene mutation have an increased risk of developing breast and ovarian cancers. Apart from the direct effect on DNA repair mechanisms, BRCA mutations via non-cell autonomous factors, including progesterone, drive cancer initiation. Our multidisciplinary combined clinical and basic research project aims at developing cancer-preventative strategies via evaluating the potential of using progesterone receptor modulators (PRM) like mifepristone. Two groups of premenopausal women are recruited for this study; The first comprises women undergoing surgery for benign breast reduction mammoplasty. The second consists of women carrying BRCA1 or BRCA2 mutations who are undergoing risk-reducing mastectomy. To investigate and validate our hypothesis, we've developed an advanced high-throughput 3D-organoid culture model using freshly isolated breast tissues. Our findings reveal that PRM effectively reduces the proliferation and growth of cancer precursor cells, encompassing luminal progenitor and basal cells, among both individuals with BRCA mutations and those without. Concurrently, it encourages the differentiation and enrichment of mature luminal cells. Intriguingly, the impact of PRM diminishes as breast cells replicate and age over time. Moreover, we've observed that PRM induces apoptosis in breast cells in a dose-dependent manner. These insights underscore the substantial role of PRM in mitigating the risk of cancer initiation and progression, demonstrating its significance for both normal and BRCA mutation carrier women.

POSTER 28

The Swedish Childhood Tumor Biobank – A national omics and tissue research resource for pediatric cancers

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Background

In Sweden approximately 350 children are diagnosed with cancer each year. Today more than 85% of the patients will survive, even so, cancer is one of the major medical causes of childhood death. Moreover, the survivors often suffer from sequelae due to the treatment. Therefore, deeper biological knowledge regarding these malignancies is essential for improved survival and quality of life for affected children. The aim of the Swedish Childhood Tumor Biobank (Barntumörbanken, BTB) is to increase the understanding of pediatric solid tumors by providing infrastructure resources, biological samples and molecular/genomic data for research.

Methods

BTB has a multidisciplinary nation-wide collaboration with the six university hospitals that treat pediatric cancer patients. Fresh frozen tumors and blood samples are collected, and some additional specimen types including CSF, viable tumor cells, digital pathology slides, and parental blood. BTB registers, prepares and stores the biobank samples with linked patient information, as well as performs whole genome sequencing (WGS), whole transcriptome sequencing (WTS) and methylation array (MA) profiling. All according to established ethical permit and biobank agreements. The comprehensive genomic and molecular characterization is done at Science for Life Laboratory, were BTB in collaboration also develops bioinformatic pipelines. Moreover, internal variant databases and data portal structure for secure data/metadata organization, traceability and visualization are developed in BTB.

Results

More than 2400 cases are now registered in BTB and approximately 60 000 samples collected and/or prepared. Around 1600 cases have been genomically characterized where BTB manages the generated data, including for the Genomic Medicine Sweden Childhood Cancer (GMS Barncancer) study where BTB is partly co-coordinating this national clinical implementation project for WGS and WTS analysis in the routine pediatric cancer care. BTB samples and/or generated data, including from GMS Barncancer, have so far been shared to more than 20 different research projects after formal application processes for secondary use.

Sample and data access include medicolegal assessment followed by decision and specific agreements since sensitive material and information. BTB is moreover assisting several clinical studies with sample logistics, regulatory support and data analysis/interpretation.

Discussion/Conclusions

BTB is a research project and infrastructure that systematically collects biological specimens and informed consent from more than 90% of the Swedish pediatric patients with solid tumors, and produce and manage high quality data. The continuous usage of the samples and the omics data in approved studies and research projects will contribute to increased knowledge and likely have a positive impact on the future clinical care of children with cancer.

POSTER 29

Case-Mix Adjusted Benchmarking of Breast Cancer Mortality Rates Across Swedish University Hospitals

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Background
Accurately comparing hospital outcomes in breast cancer (BC) care is essential for identifying disparities, promoting best practices, and ensuring equitable care. Long-term survival is a key BC outcome but can be challenging to benchmark because it is influenced by multiple factors, including age, comorbidity, and tumor characteristics. Consequently, case-mix adjustment is necessary for fair comparisons. In our previous work (not yet published, but accepted for presentation at ESMO Breast), we developed case-mix models enabling hospital- and regional- comparisons of 5- and 10-year breast cancer–specific mortality (BCSM) rates. In current study we apply these models to assess case-mix–adjusted BCSM rates across Swedish university hospitals.

Methods
The case-mix model is based on 31,000 Swedish BC patients diagnosed between 2008 and 2014. We used Cox modeling, adjusting for age, comorbidities, educational level, and tumor-biological predictors of BCSM. Both the 5-year and 10-year models showed excellent discrimination (C-statistic > 0.80) and calibration. We incorporated university hospitals as dummy variables to estimate adjusted BCSM rates. Significant deviations were defined as HR <0.9 or >1.1 ($p<0.05$).

Results
Three university hospitals exhibited higher-than-expected 5-year BCSM rates, with two of these also showing elevated 10-year BCSM rates. Conversely, one university hospital demonstrated significantly lower-than-expected 5- and 10-year BCSM rates. To ensure fair interpretation, further validation and sensitivity analyses are underway before disclosing hospital-specific hazard ratios. Detailed results will be presented at the KCCC day.

Conclusions

This study represents the first case-mix adjusted analysis of BCSM rates across Swedish university hospitals. Our findings reveal substantial survival disparities, underscoring the need for continuous benchmarking to ensure high-quality, equitable BC care across Sweden. The models could be integrated into the Swedish Breast Cancer Register for real-world quality assessments and targeted improvements in BC care.

POSTER 30

How fibroblasts control malignant mesothelioma

Presented by: ***Oscar Wagner*** *(Master Student)*

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Mesothelioma is an aggressive cancer with poor prognosis, largely due to its complex tumor microenvironment (TME). Among the key components of the TME, cancer-associated fibroblasts (CAFs) play a crucial role in tumor progression, immune evasion, and therapy resistance. They remodel the extracellular matrix (ECM), secrete protumorigenic cytokines, and promote tumor cell survival and migration.

Recent work by Ries et al. (2023) identified Meso-CAFs as key drivers of pleural mesothelioma, influencing PM cells through ECM modifications. To explore their role in tumor invasion, we conducted live-cell imaging revealing variations in CAF migration speed, size, shape, and persistence. Preliminary data indicate distinct migratory behaviors among Meso-CAFs, with even greater differences observed in patients with shorter survival times. These findings highlight the potential of CAF-targeted therapies for pleural mesothelioma treatment.

POSTER 31

The impact of bacterial metabolites on colon cancer progression

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Background
Colorectal cancer, a leading cause of cancer-related mortality worldwide is closely associated with the gut microbiota, which plays a critical role in the tumor microenvironment. Gut microbes can directly or indirectly affect host cells, and disruption of the normal microbial community leads to dysbiosis, which can impact cancer progression. Recent studies have identified specific microbiome profiles associated with colorectal cancer. Currently, studies are examining the impact of metabolites produced by the gut microbiome on the progression of colorectal cancer.

Methods
To assess cell viability, cancer cell lines from colorectal cancer and several other cancer types as well as normal cells (immortalized skin fibroblasts and primary gingival fibroblasts) were infected or treated with 10% bacterial supernatants collected from several pathogens and their various strains or commensal bacteria. After 48h cell viability was measured using resazurin assay. Metabolic fractions were isolated by filtering bacterial supernatants using Amicon 3kDa cutoff filters.

Results
Colon cancer primary and metastatic cell lines surprisingly did not exhibit altered viability when infected with pathogens that have been associated with colorectal cancer. However, treatment with a specific microbial supernatant (hereafter referred to as "bacteria X" or "Bx" led to a significant decrease in the viability of SW480 and SW620 cells. By testing over 20 cancer cell lines from various origins, we found that this phenomenon occurred specifically in colon and medulloblastoma cell lines. Importantly, normal cells remained unaffected. Furthermore, supernatants from different Bx strains demonstrated differential killing potential, while commensal bacteria had no effect. Finally, using supernatant fractionation, we identified the active component responsible for the tumor-killing potential as a metabolite(s).

Conclusions
By discovering novel metabolic vulnerabilities, this study highlights the importance of microbial metabolites as a potential source of therapeutic anticancer agents and opens new perspectives in drug discovery.