





DIRECTOR'S COMMENTS

Dear all

On August 25, we had a very successful opening of the semester – with the Special Startup Seminar for Carina Strell, who received a TMS Starting Grant and is now transitioning from Uppsala University to continue her research and independent work as a group leader at CCBIO. Carina discussed some of her work, followed by presentations from Therese Sørlie and Solveig Hofvind. Congratulations again to Carina! You can read the full story inside and on the web.

Many congratulations also to other CCBIO members for their achievements: Line Bjørge, Emmet McCormack and Harsh Dongre for receiving two UiB Idé innovation grants; and to Ridhima Das and Silje Kjølle for having defended their PhD thesis work.

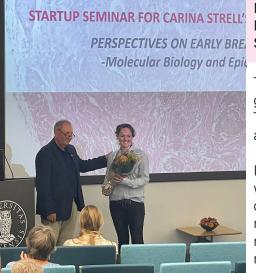
We also welcome Camilla Tvedt Ekanger to CCBIO and the Department of Clinical Medicine (Engelsen group), as a PhD candidate and also as coordinator of the CCBIO Seminars. Erling A. Høivik has been recruited to Wik's group to work on breast cancer in young patients. Agnete Engelsen and Carina Strell has been recruited to CCBIO as Associate Investigators (from June 1). Welcome to all of you!

You should also read about: calls for funding, upcoming events including CCBIO905 with keynote presentation by Klaus Pantel, ScanPath 2022, other events, published papers, and media appearances.

Best regards, Lars A. Akslen, Director

Capturing cancer complexity and clinical challenges

Offical welcome to Carina Strell



Flowers and smiles were in abundance when CCBIO, the Department of Clinical Medicine, the Medial Faculty and the Trond Mohn Foundation welcomed Carina Strell to the University of Bergen in a CCBIO Startup Seminar August 25.

The Trond Mohn Foundation awarded this year Carina Strell with a TMS starting grant for her project Understanding Early Breast Cancer Evolution in Space and Time (EvoMaps). Strell has a long-term collaboration with the Lars A. Akslen group at CCBIO, and her project is now starting up at CCBIO.

In her project, Strell aims to understand the biological mechanisms behind why some women experience recurrent and/or treatment resistant breast cancer while others do not. The hypothesis is that breast cancer progression and therapy response are not only dependent on the tumor cells alone, but also on the surrounding tissue microenvironment. The overall aim of this project is to uncover and map new mechanisms of early breast cancer evolution.

In the CCBIO Seminar, Strell gave the presentation Tumor-Stroma Interactions Driving Progression and Therapy-Resistance of DCIS, explaining how getting a better understanding of breast cancer evolution early on can improve treatment by identifying new therapeutical targets to overcome radio resistance and establishing new biomarkers to reduce the current overtreatment.

Two other speakers, Therese Sørlie and Solveig Hofvind, shed light on the importance of breast cancer research from different angles.

Read the full story here.



UiB Idé Innovation grant to CCBIO scientists

Congratulations to CCBIO scientists Line Bjørge, Emmet McCormack and Harsh Dongre for receiving UiB Idé innovation grants! Line and Emmet for the project *Precision surgery – developing intraoperative tumour-targeted fluorescence imaging*, and Harsh for the project *OFF-ON double functionalized nanodiamonds for targeted cancer treatment*.

The Precision Surgery project receives NOK 467 000, and aims to develop targeted

The Precision Surgery project receives NOK 467 000, and aims to develop targeted fluorescent contrast reagents for intraoperative molecular tumor visualization. The research group has developed the concept in mouse models, and results are promising. In order to further develop the method, PhD student and veterinarian Vibeke Fosse will use the contrast reagents in a treatment study of dogs with cancer that are to be treated with surgery. The study will focus on tolerability, pharmacokinetics and biodistribution of the contrast reagents, as well as clinical outcome parameters. The data generated will form the basis for a clinical treatment study with the contrast medium for patients with ovarian cancer.

Harsh Dongre receives NOK 483 000 for his project which is based on the principle of using double functionalized nanodiamonds (NDs): one functional arm specifically targeting cancer cells (search-and-find arm), and the other near-infrared (NIR) light activated arm killing them (cytotoxic arm). The next-gen NDs are activated specifically by NIR light with a tissue penetration depth of 10-20mm. This will give the opportunity to treat only the cancer cells, where you want and when you want. This would enable new ointments or mouthwash-based treatment for patients with skin, oral and vulvar cancer. The group has previously designed ND-conjugates with OFF-ON switch that could be activated with 450nm blue light. The efficacy and limited toxicity towards normal cells of these ND-conjugates was demonstrated both *in vitro* and *in vivo* models.



Just one swab can be enough to detect endometrial cancer

A Simple Cervicovaginal Epigenetic Test for Screening and Rapid Triage of Women With Suspected Endometrial Cancer: Validation in Several Cohort and Case/Control Sets

Chian Herrag, PriC¹, Falima Marin, PriC¹, Millon Jones, St.¹, Ison Essait, Proc. March Lessait, Proc. Pric. Pric.

Line Bjørge is co-author of an article from the FORECEE project recently published in the Journal of Clinical Oncology. This has attracted much attention, and the results are encouraging, suggesting that a simple home swab test can lead to far fewer women having to undergo invasive diagnostic procedures, and reducing the time to diagnosis.

PURPOSE Endometrial cancer (EC) incidence has been rising over the past 10 years. Delays in diagnosis results are all processes of the past 10 years. Delays in diagnosis results are reliable to the past of the past 10 years. Delays in diagnosis results are reliable to the past of t

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was similar across menopulsal status, ago, and provided the for triage of women with symptoms stage.

CONCLUSION The WID-GEC is a noninvasive reliable test for triage of women with symptoms stage.

Because of the potential for self-collection, it could improve early diagnosis and reduce the relaince for in-per
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J Clin Oncol 90. © 2022 by American Society of Clinical Oncolog

INTRODUCTION

indometrial cancer (EC) is almong the turnor bytes wan be sharpest raining incidence over the past ID years. In horizontal bleeding, defined as any costimenopausa, the lead symptom. EC patient sunvival is strongly specified on stage at diagnosis, with delays in dispecial control of the strong of the strong grows and treatment resulting in significant adverse impacts on survival. The current visit delays in dispecial control of the strong suspected EC is transageral ultrasound (TVLIS) is lossed by hysterecoropy and endometral biopsy. Du time the CUVID-19 clockdown, referrals via the Z-read time the CUVID-19 clockdown, referrals via the Z-read time the CUVID-19 clockdown, referrals via the Z-read to the EVID-19 clockdown, referrals via the Z-read to the found to the control of the control o nited Kingdom, decreased by up to 0-15. In slay in EC diagnosis in England alone has I aggested to cause a loss of 6,305 life-years. A I lage modality that could rule out malignancies wi he need for initial specialist referral could im-

Current triage investigations. Assessment of suffer from several limitations. Assessment of metrial thickness using TVUS, the most fre used initial investigation, is only feasible in pc opausal women, and a cutoff of a 5 mm has sitivity of 96.2% and specificity of \$1.5%.1 women. the performance is poor and offers a se

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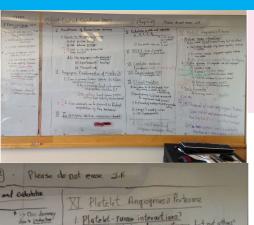
A trial on 1,288 women found the test detected all cases of cancer in the 63 patients who had it. And the false positive rate was lower than for traditional tests, meaning that fewer women might encounter cancer scares in error. The vaginal swab test was used on patients who experienced bleeding even though they had been through the menopause – a red flag symptom of the cancer.

Future prospective studies will confirm whether it could be used to replace ultrasound to triage women with suspected endometrial cancer, and further clarify its utility for screening in general and high-risk populations.

See the full article here: <u>A Simple Cervicovaginal Epigenetic Test for Screening and Rapid Triage of Women With Suspected Endometrial Cancer: Validation in Several Cohort and Case/Control Sets.</u>

See also international news articles in <u>The Eve Appeal</u> and in <u>The Sun</u>.

"Please do not erase" - the story of the Folkman whiteboard



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@ Removal of non-angiogenic (unter)

Photo by Scott Kirsner, Boston Globe.

A treasured whiteboard at Boston Children's Hospital in Boston has not been touched for 15 years. No one can erase what's on it because a sheet of plexiglass has been bolted over the board's surface. In the upper right corner, in basic black dry erase marker, it said, "Please do not erase J.F." J.F. was Judah Folkman, the hospital's former chief of surgery, and a pioneer in the field of cancer research. And on the board, you can see a very familiar CCBIO name.

The whiteboard, located in a conference room on the 12th floor of a Children's research building, captures what Folkman considered central questions related to the field of angiogenesis research. (An example: Does the BRCA-1 gene regulate angiogenesis in human breast cancer?) When a question was answered by published research, Folkman would add new scientific mysteries to the board. The date on top says 2007.

Marsha Moses, director of the Vascular Biology Program at Children's Hospital, and a collaborator of Folkman's, said the whiteboard could be viewed as "his notebook." Why do some tumors shift from benign to fast-growing and deadly? Are there diagnostic tests we could develop to understand when that will happen? Are there ways to prevent them from making that switch, or reverse the switch once it is triggered?

There are a few names scrawled on the board, tying particular questions and topics to people Folkman was collaborating with — or had proposed collaborating with. Lars A. Akslen is one of them.

Read the full story in the Boston Globe.

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Recent doctoral defenses



Ridhima Das defended Thursday June 16, 2022 her doctoral dissertation "Novel Methods and Sources for Regeneration of Oral Mucosa" at the University of Bergen.

Ridhima did her PhD work at the Department of Clinical Science and CCBIO, with main supervisor Professor Daniela Elena Costea and co-supervisors Professor Anne Christine Johannessen, Professor Mihaela-Roxana Cimpan and Researcher Salwa Suliman.

The aim of the project has been to explore the possibility of producing oral mucosa in the laboratory, among other things using so-called 'induced pluripotent stem cells - iPSCs'. Ridhima used stem cells both in cell culture and in animal models to develop oral mucosa. This gives hope that in the future such methods can be used clinically to replace lost tissue during surgery.

See the press release (in Norwegian).



Silje Kjølle defended Tuesday August 30, 2022 her doctoral dissertation "Tumor microenvironment in breast cancer progression. A mass spectrometry-based proteomics study for biomarker discovery and validation" at the University of Bergen.

Silje did her work at the Department of Clinical Medicine and CCBIO, with main supervisor Professor Lars A. Akslen and co-supervisors PhD Kenneth Finne and PhD Heidrun Vethe.

Her PhD project focused on the stress response to low oxygen availability (hypoxia), separated proteins in the microenvironment, and associations to cancer tumors with a poor prognosis. The doctoral work has identified differences in the microenvironment between different types of breast cancers, and demonstrated groups of proteins (signatures) that can identify more aggressive tumors.

See the the press release (in Norwegian).

New faces



Not so much new faces this time as Erling has been in the CCBIO family for several years, and Camilla also for a while, but they are in new roles.

Erling A. Høivik (PhD, molecular biologist) is joining the BCY-B group of Elisabeth Wik, from mid September. He has previously been working within the CCBIO umbrella in the Bergen Gynecological Research Group, with main topic on characterizing metastasizing endometrial cancer. Erling will now expand his focus on female cancers, and we look forward to his contributions on breast cancer of the young.

Camilla Tvedt Ekanger completed her master's degree in biomedicine at the University of Bergen in Jim Lorens' group, in 2021. Se is now a PhD candidate at CCBIO with Agnete Engelsen as main supervisor. During her master, she established and characterized adult stem-cell derived lung organoids, which are complex 3D multicellular structures recapitulating the tissue features in situ. Her current project is to continue developing and characterizing organoid and explant models of normal lung tissue and non-small cell lung cancer (NSCLC) tissues. The aim is to utilize these models to profile early epithelial cell-immune cell interactions initiated by PAMP release during infection and DAMP release from immunogenic cancer cell death. This knowledge is important to optimize efficient immune cell infiltration and activation in both contexts. Furthermore, the patient-derived NSCLC models serve as a valuable tool to investigate non-genetic mechanisms of drug resistance, toxic side effects, and therapeutic efficacy.

Camilla has also recently taken on the responsibility as **coordinator of the CCBIO Seminars**, so be sure to open her CCBIO Seminar invitations on email!

Geneva Summer School alumna

PhD Candidate Camilla Tvedt Ekanger spent a week of her summer in Geneva, attending a science communication course at the Geneva University Summer School.

The course, <u>Science Communication in the Post-COVID19 Era</u>, goes through topics such as the lessons learned from the COVID-19 pandemic, how to be a better storyteller, how to build an online community to foster science education, how to navigate fake news and social media's role in fake news, and the importance of communicating risk efficiently. Camilla highly recommends attending this course.

One science communication tip from the course:

Know your audience! Always be aware of who your audience is and imagine your audience in front of you when you write. This is especially important when you are writing the introduction.



Relevant calls for funding



Here is an overview of the upcoming deadlines for funding, relevant to our CCBIO students and researchers. For more details, please check the links below and find more at the Medical Faculty's page on <u>External funding opportunities</u>.

Horizon Europe

ERC 2023

Starting Grant: October 25th, 2022

Consolidator Grant: February 2nd, 2023

Advanced Grant: May 23rd, 2023

Synergy Grant: November 8th, 2022

Marie Sklodowska-Curie Actions (MSCA)

<u>Doctoral Networks</u>: November 15th, 2022

Missions in Horizon Europe - Conquering cancer

- We have been requesting input to shape the upcoming calls – this is key in making sure our interests are included. With your help, we will continue our efforts.
- Next upcoming deadline is September 2022, with more in Spring 2023.

Diku

 Erasmus+: project establishment support for the development of applications for centralized information in Erasmus+. More information here.

UiB

 Stays abroad for PhDs and postdocs at the Medical Faculty: next deadline October 1st. <u>More information</u> <u>here.</u>

Individual fellowships and personal grants

• EMBO: personal fellowships and career grants, open year-round. More information here.

Innovation grants from the Norwegian Research Council

 Qualification – Research Commercialisation from Publicly Funded Research – Commercialisation Project 2022. Open-ended, 3-12 months, 200-500 000 NOK.

 <u>Proof-of-Concept</u> – Research Commercialisation from Publicly Funded Research – Commercialisation Project 2022. Open-ended, 12-36 months, 1-5 MNOK.

Other Research Council calls

- on this link.

Trond Mohn Foundation – <u>Trustworthy Al</u>: January 10, 2023

- Step 1: Research projects: call for and select a limited number of research projects to be nominated to the TMS Trustworthy AI – call (maximum 18 MNOK)
- Step 2: Overarching coordination project: When the awarding projects has been decided by TMS, the UiB-Al steering group and the project Pls jointly, is invited to propose an overarching coordination project to facilitate common activities, common communication initiatives, and collaboration between the funded projects (maximum 2 MNOK)

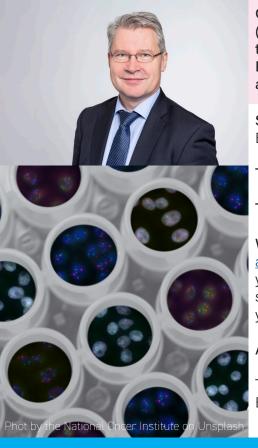
Research Advisor



advice For info more and applications. and on grants **CCBIO** contacť Research our Advisor Yamila Torres (Yamila.cleuren@uib.no).

Yamila can among other discuss relevant calls with you, guide your proposal design, review you proposals for national and international funding sources, from draft to submission stage, and provide information about and advice on implementation of cross-cutting issues into your project (gender perspective, user involvement, innovation, RRI, etc).

CCBIO Special Seminar with Professor Klaus Pantel



Over the past ten years, circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA) have received enormous attention as new biomarkers and subject of translational research. Join us in a Zoom webinar September 29 to hear Professor Pantel, considered as the father of the term liquid biopsy, give a talk on the application of CTCs and ctDNA in cancer research.

Speaker: <u>Professor Klaus Pantel</u>, Director of the Institute of Tumor Biology, Center for Experimental Medicine, UKE Hamburg, and part of the CCBIO International Faculty.

Title: "The promise of ctDNA and CTCs in the evaluation of cancer treatment efficacy"

Time: Thursday September 29, 2022 at 12.30 - 13.30.

Where: Digital event in Zoom, open to all, no pre-registration necessary. Use this access link as audience. Remember to write your name when logging in and not use your username or shortcode. Your sound and video will be turned off as default for security reasons, and host will unmute your sound and address you by your name if you raise your hand in the question round.

Abstract: Will be available on this webpage.

This Special Seminar is also part of the course CCBIO905, Methods in Cancer Biomarker Research, but opened up to a larger audience.

SCANPATH 2022 - Open for registration



SCANPATH – the Scandinavian Seminar on Translational Pathology – will this year be hosted by CCBIO at Solstrand Hotel & Bad close to Bergen, Norway, November 14-15, 2022, and is now open for registration!

SCANPATH is an annual network meeting for Scandinavian tumor pathologists and pre-clinical scientists with an interest in the prospects of next generation tissue profiling. The aim is to stimulate tissue-based studies of tumor mechanisms and biomarker mapping. This initiative has been a success since the startup in 2016, and SCANPATH is now a well established annual forum. The meeting is open for all with an interest in morphology oriented research.

Similar to previous years, like last time in Lund in 2021, the seminar will include inspirational speakers representing different research groups attending the meeting.

We will have one poster session where participants can present their work, and ample time for informal interaction. Please let us know if would like to present a poster (deadline for submitting poster abstract is October 15).

Time: November 14-15, 2022, 09:00-18:00 the 1st day, and 09:00-16:00 the 2nd day.

Place: Bergen, Norway at Solstrand Hotel & Bad.

Practical information: See practical information on this PDF link.

Registration: We first open up for external participants, <u>registration through this link</u>, and from **September 23** also for local participants. Deadline is *October 1*.

Fee: The subsidized participation fee is 3000 NOK/300 Euro per person and covers lodging and meals November 14-15.

Program: will be available at this website.

Coming CCBIO events



Make sure to save the dates in your calendar, and register when applicable. You can see all planned CCBIO events in the CCBIO web calendar.



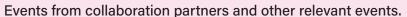
- September 27-29, CCBIO905 course, Methods in Cancer Biomarker Research
- September 29, CCBIO Special Seminar with Professor Klaus Pantel, in Zoom
- October 6, CCBIO Junior Scientist Symposium
- October 27, CCBIO Seminar
- November 14-15, SCANPATH, the Scandinavian Seminar on Translational Pathology, will this year be hosted by CCBIO in Bergen (Solstrand Hotel)
- November 24, CCBIO Seminar
- Nov. 30 Dec. 2., CCBIONeur910 course Patient and Public Involvement in Medical and Health Research.
- December 8, CCBIO Junior Scientist Symposium
- December 15, CCBIO Seminar

Note date for next year's CCBIO Annual Symposium: May 8-10, 2023, also this time at Solstrand Hotel, outside of Bergen.





Other relevant coming events



- September 26, <u>Life Science Data Management: Planning workshop</u>. Generate a data management plan for a Life Science research project that will meet the requirements of Norwegian institutions. Centre for Digital Life, online event.
- September 27, Mind the Bridge the Narrow Road to Scaling. In this event, Abelia and FIN The Association for Innovation Companies will focus on what it takes to go from 0 to a billion dollars in health tech. Co-hosted by Oslo Cancer Cluster.
- September 28-29, Nordic Life Science Days, Malmø, Sweden (Postponed from April 20-21)
- September 30, Reality Check: Are You US Investor-Ready? Oslo Cancer Cluster, digital meeting
- September 28-30, Norwegian Bioinformatics Days 2022, Sundvolden Hotel. Event co-organized by the Centre for Digital Life Norway
- October 14, <u>CONNECT Seminar: Inclusion of clinical opinions in economic evaluations: From theory to practice</u>, Kreftforeningens Vitensenter, with opportunity to join digitally.
- October 20-21, <u>Digital Life 2022</u>, Trondheim. The annual conference for the Centre for Digital Life Norway
- October 24, 2nd meeting in the CONNECT Clinical Trials Meeting Series: Akademiske/utprøverinitierte studier og forskning Hvordan lykkes med det på sykehusene hva kreves? Hvordan «tenker» industri mht støtte til uavhengig forskning hvordan navigere i strategier og ulike industriprosesser? Digital Oslo Cancer Cluster meeting.
- November 9-11, <u>NEUROSYSM930 Applied bioinformatics and data analysis in medical research</u>, Bergen
- December 8, Oslo Cancer Cluster December Gathering & Introduction of New Members 2022, Oslo.
- See also the BBB-seminars for the fall term.



Publications

You can find the CCBIO publications on this pubmed link. See the most recent 5 below.

- Sommerfelt H, Sandvik LF, Bachmann IM, Brekke RL, Svendsen HL, Guttormsen AB, Aziz S, Dillekås H, Straume O. Toxic epidermal necrolysis after immune checkpoint inhibition, case report, and review of the literature. Acta Oncol. 2022 Sep 8:1-5. doi: 10.1080/0284186X.2022.2119099. Online ahead of print. PMID: 36073292
- Martínez-Nieto GA, Teppo HR, Petrelius N, Izzi V, Devarajan R, Petäistö T, Liu H, Kim KS, Karppinen SM, Ruotsalainen H, Koivunen J, Mäki JM, Walker GC, Pihlajaniemi T, Gullberg D, Heljasvaara R. Upregulated integrin all in the stroma of cutaneous squamous cell carcinoma promotes skin carcinogenesis. Front Oncol. 2022 Aug 8;12:981009. doi: 10.3389/fonc.2022.981009. eCollection 2022. PMID: 36003785
- Herzog C, Marín F, Jones A, Evans I, Reisel D, Redl E, Schreiberhuber L, Paytubi S, Pelegrina B, Carmona Á, Peremiquel-Trillas P, Frias-Gomez J, Pineda M, Brunet J, Ponce J, Matias-Guiu X, de Sanjosé S, Alemany L,

- Olaitan A, Wong M, Jurkovic D, Crosbie EJ, Rosenthal AN, Bjørge L, Zikan M, Dostalek L, Cibula D, Sundström K, Dillner J, Costas L, Widschwendter M. A Simple Cervicovaginal Epigenetic Test for Screening and Rapid Triage of Women With Suspected Endometrial Cancer: Validation in Several Cohort and Case/Control Sets. J Clin Oncol. 2022 Aug 24:JCO2200266. doi: 10.1200/ JCO.22.00266. Online ahead of print. PMID: 36001862
- Ingebriktsen LM, Finne K, Akslen LA, Wik E. A novel age-related gene expression signature associates with proliferation and disease progression in breast cancer. Br J Cancer. 2022 Aug 23. doi: 10.1038/s41416-022-01953-w. Online ahead of print. PMID: 35995935
- Larrieu CM, Storevik S, Guyon J, Pagano Zottola AC, Bouchez CL, Derieppe MA, Tan TZ, Miletic H, Lorens J, Tronstad KJ, Daubon T, Røsland GV. Refining the Role of Pyruvate Dehydrogenase Kinases in Glioblastoma Development. Cancers (Basel). 2022 Aug 2;14(15):3769. doi: 10.3390/cancers14153769. PMID: 35954433

Recent CCBIO in the media

Recent media appearances by CCBIO PIs and group members. For all media hits, see CCBIO's web pages.

- 01.09.22, HealthTalk, "ESMO-studie: En del av pasientene med eggstokkreft som fikk olaparib ble kurert", Line Bjørge.
- 01.08.22. Dagens Medisin, "Det er tillatt å være saklig, Kristiansen", Eirik Joakim Tranvåg, Ole Frithjof Norheim.
- 28.07.22, Boston Globe, "'Please do not erase': A treasured whiteboard at Boston Children's Hospital has not been touched for 15 years", Lars A. Akslen.
- 07.07.22, Vi.no, "Paracetamol kan påvirke kreftbehandling negativt", Oddbjørn Straume.
- 07.07.22, Dagens Medisin, "Beslutningsforum følger føringer som er satt", Eirik Joakim Tranvåg.
- 06.07.22, Bergens Tidende, "Paracet kan svekke effekten av immunterapi hos kreftpasienter: Jeg ble litt overrasket og skremt", Oddbjørn Straume.
- 05.07.22, Dagens Medisin, "Studie reiser spørsmål om paracetamol og immunterapi", Oddbjørn Straume.
- 01.07.22, UiB Nyheter, "Beslutningsforum betaler meir for å behandle alvorlege tilstandar", Eirik Joakim Tranvåg.
- 29.06.22, EurekAlert!, "New study using confidential drug prices demonstrate how disease severity impact drug coverage decisions", Eirik Joakim Tranvåg.
- 29.06.22, På Høyden, "Høg kvalitet på innovasjonsidear", Harsh Dongre, Line Bjørge.

Programs and Research Teams

Mechanisms of Tumor Microenvironment Interactions:

- Donald Gullberg Karl-Henning Kalland Emmet McCormack

Exploration and Validation of Cancer Biomarkers:

- Lars A. Akslen Jim Lorens
- Camilla Krakstad
- Daniela Costea
- Elisabeth Wik Carina Strell
- Agnete Engelsen

Clinical Applications and Trial Studies:

- Bjørn Tore Gjertsen
- Oddbjørn Straume Line Bjørge

Health Ethics, Prioritization and Economics: Roger Strand John Cairns Ole Frithjof Norheim

Additional resources:

Bioinformatics and Big Data

IngeJonassen

Strategic Advice Rolf Reed

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