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Centre for Cancer Biomarkers
Norwegian Centre of Excellence – University of Bergen

Norwegian Centre of Excellence
The Research Council of Norway

"CAPTURING CANCER COMPLEXITY AND CLINICAL CHALLENGES"

CCBIO Newsletter

EDITOR: eli.vidhammer@uib.no

DIRECTOR'S COMMENTS

Dear all

Although we still have to use adaptive formats and new ways of working, we have gotten off to a good start in 2021. In this first issue of the CCBIO Newsletter this year, you can read about the courses planned for the spring: CCBIO908, CCBIO903 and BMED904. I have previously urged the younger members of CCBIO, in particular all the incoming PhD students and postdocs, to register for these courses (deadline February 1st). It is however still possible to get in touch if some of you lost the opportunity (see below). The courses are all unique and tailored to the profile and visions of our center. Thank you to all involved.

The 9th CCBIO Annual Symposium is soon coming up. It is still in the making, but at least we will use the online format, with a possibility to attend Solstrand for the local CCBIO family. The decision on this is yet to be made.

Two CCBIO PhD candidates have recently and successfully defended their theses in health economics. Please read more below. Congratulations so much to Kelly and Beatriz!

Our research school is now actively collaborating with Neuro-SysMed (FKB Center) in the set-up of their own research school. So far, we have three common courses: Clinical Trials in Cancer and Neurological Diseases; Health Innovation; Patient and Public Involvement in Medical and Health Research. These are planned for the fall term. We are happy to share our experiences with Neuro-SysMed, and we look forward to the continuation of this strategic alliance. Read the full story below.

We recently launched the CCBIO Masterclass Program which is a closed seminar series (running in 2021) for 10 selected candidates. Topics important for career development will be discussed. This program is coordinated by research advisor Yamila Cleuren. Hopefully, we will be able to run another cycle during 2022.

We would like to welcome on board two new members of the CCBIO family, Manuel Carrasco and Vladan Milosevic. Thank you for deciding to join our teams.

Finally, please read about new publications, media appearances, and funding opportunities.

Best regards, Lars A. Akslen, Director

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

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
- Inge Jonassen

Strategic Advice
- Rolf Reed

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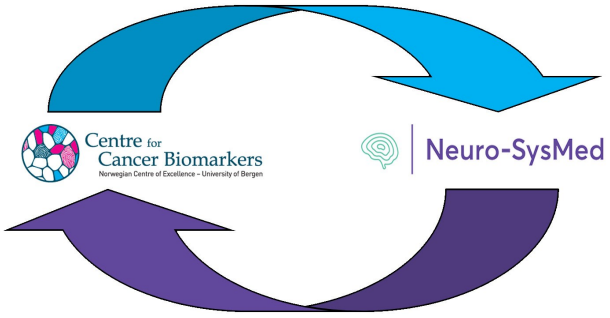
RESEARCH SCHOOL COLLABORATION BETWEEN CENTERS OF EXCELLENCE

CCBIO initiated its research school – CCBIO Research School for Cancer Studies (RSCS) – very early on, and the RSCS has since the startup in 2014 undergone a steady progress and expansion of the course portfolio. Now that CCBIO's parent department the Department of Clinical Medicine has been assigned an FKB center (Centre for Clinical Treatment Research) – Neuro-SysMed – CCBIO is happy to be able to share experiences and establish a new potential for synergy effects and mutually prosperous interactions.



Where CCBIO focuses its research on new cancer biomarkers and targeted cancer therapy, Neuro-SysMed is concerned with neurological diseases such as multiple sclerosis, dementia, Parkinson's disease and ALS. The focus areas of the two centers might be going in different directions, but there is still a potential for biological and clinical intersections. Young researchers are required to learn about research infrastructures, methods, legislation and other topics – common for all medical research fields.

"We are happy to contribute with our experiences, both from the initial establishment of the CCBIO RSCS by Lars A. Akslen and Anne Christine Johannessen, and from the ongoing progress throughout the research school period," says leader of the CCBIO RSCS, Elisabeth Wik. "We see a potential for various collaborations between our research schools," she continues. "PhD candidates are encouraged to acquire skills in generic topics within medical research, which are well suited for collaborative courses. Joint courses on common methods will be relevant, in addition to research school activities that focus on career planning for young researchers," she explains.

Three joint PhD courses will be launched in the fall term of 2021:

- Clinical Trials in Cancer and Neurological Diseases
- Patient and Public Involvement in Medical and Health Research
- Health Innovation

Read the full article here.

SAVE THE DATES FOR THE CCBIO ANNUAL SYMPOSIUM

We have the great pleasure of inviting you to the 9th CCBIO Annual Symposium, **May 19-20, 2021**! The format is yet to be finally decided, whether we will run it fully digital, or as a hybrid, with local attendants and speakers at Solstrand with live streaming and international audience and speakers through a digital platform. Either way—save the date!

The Annual Symposium will this year be a flexible format allowing for top notch keynote presentations online, several interactive panel discussions, and as many credit-giving presentations from young researchers as there would normally be posters on-site. This will all take place regardless of whether we will arrange the symposium online only or as a combination of online talks and local on-site participation at Solstrand.

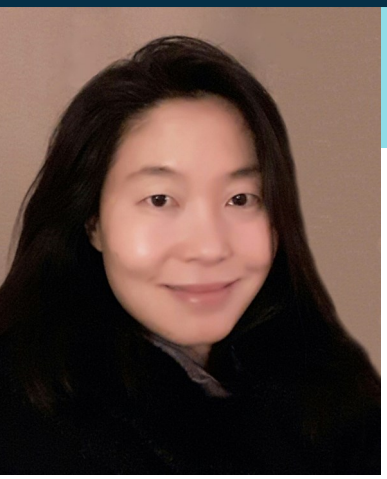
The symposium is open for all, so please feel free to pass on this information.

CCBIO normally hosts a Satellite Symposium which takes place the day before the Annual Symposium, also at Solstrand. This year, speakers and topics of the Satellite Symposium will be joint with the Annual Symposium.

Registration: not yet available. Announcement will come when available. Stay tuned on this page.

CCBIO'S FIRST COMPLETED PhDs IN HEALTH ECONOMY

We are happy to present CCBIO's first ever completed PhDs in health economy; Kelly Seo from the London School of Hygiene and Tropical Medicine (LSHTM), and Ana Beatriz Mateus D'Avó Luís from the Department of Economics, University of Bergen.



Kelly Seo completed her PhD in November, 2020. Her thesis title is "Economic evaluations of companion cancer biomarkers for targeted therapies", supervised by Professor John Cairns and Dr. Alec Miners at London School of Hygiene and Tropical Medicine (LSHTM).

Kelly's PhD work aimed to investigate the current and good practices of assessing the value for money of co-dependent technologies such as biomarker-guided therapies, companion diagnostics for targeted therapies in cancer. It reviewed methodological/ modeling approaches and biomarker characteristics considered in existing economic evaluations and conducted a cost-effectiveness analysis on a case study of a novel biomarker (HSP27 expression). These studies contributed to the development of possible solutions for incorporating the characteristics of companion biomarker tests and a practical guide to modeling companion biomarker tests. Kelly found that the use of companion biomarkers could save some costs, however the saving was not large enough to make targeted therapies cost-effective, and the cost-effectiveness of biomarker-guided therapies was more likely to be driven by the characteristics of corresponding drugs rather than those of companion cancer biomarkers. The thesis also highlighted current challenges and issues to be overcome to reach a consensus on methods and data requirements for economic evaluations of companion biomarker tests.

The study findings suggest that there is no consistency when it comes to modeling approaches in the health economic assessment of companion biomarkers as part of economic evaluations of corresponding therapies. It is recommended to fully capture the clinical and economic value of biomarker testing along the entire care pathway when conducting economic evaluations of biomarker-guided therapies.

Kelly used clinical data from CCBIO in her work, and collaborated with Lars A. Akslen, Oddbjørn Straume, Cornelia Schuster, Roger Strand, and Jan Erik Askildsen at the University of Bergen side. She is now moved on to a postdoc position at Imperial College London as a research associate in health economics for NIHR In-Vitro Diagnostics Co-operative at the Faculty of Medicine, Department of Surgery and Cancer.

See also the paper HSP27 Expression as a Novel Predictive Biomarker for Bevacizumab: is it Cost Effective? Seo MK, Straume O, Akslen LA, Cairns J. Pharmacoecon Open. 2020 Sep;4(3):529-539.

Ana Beatriz Mateus D'Avó Luís completed her PhD in February, 2021. Her thesis title is "Essays on Economic Incentives and Implications of Biomarker Tests, an introductory chapter and three research papers on specific economic aspects of personalized medicine". Main supervisor has been Professor Tommy Staahl Gabrielsen, and co-supervisor has been Associate Professor Julie Riise.

The approach is empirical in the first paper and theoretical in the second and third papers. In the introductory chapter, Ana gives an account of the factors that have contributed to the slower-than-expected growth of the use of biomarker tests in clinical practice to predict drug response. There have been challenges at the scientific, regulatory, and economic levels, but there have also been some successes. The goal of this dissertation as a whole is to clarify the implications of some of these challenges and successes for the development and use of biomarker tests. In this chapter, Ana discusses how the research questions relate to the personalized medicine literature and summarizes each of the three papers.

The first paper seeks to determine the importance of the scientific complexity and predictive capability of biomarker tests. In particular, it studies how the introduction in the Norwegian health system of biomarker tests that guide cancer therapy by predicting drug response has affected the health of cancer patients.

The second paper investigates the impact of policies to encourage drug producers to collaborate in the development of biomarker tests to predict drug response.

The third paper considers two drug manufacturers that face the decision of whether to use a biomarker test to select clinical trial participants and a health authority that chooses which drug to approve for the market.

See the press release in Norwegian here.

The thesis is available here in the Bergen Open Research Archive.

CCBIO COURSES IN THE SPRING TERM

This spring term, we will run the CCBIO Research School courses CCBIO908, CCBIO903 and BMED904. CCBIO908 will be on digital platform only, CCBIO903 requires on-site participation, and BMED904 will be run as a combination. Registration for ECTS participation was February 1st, so students who missed this, will have to send a request to the course coordinators. CCBIO908 and BMED904 are also available for non–ECTS participation.

CCBIO908—Scientific Writing and Communication Seminar


Illustration: colourbox.com

April 12-15 2021 (4 half days, from ca. 11.00). **Online format (Zoom).**

This 2 ECTS course is part of the CCBIO/INTPART program, where students' education and exchange is promoted through collaboration between CCBIO and the Boston based Harvard Medical School and Harvard Kennedy School.

Lecturers:

Christine Møller, an experienced lecturer in medical and scientific writing with many years of experience as assistant editor of APMIS.
Randy Watnick, assistant professor at the Vascular Biology Program, Harvard Medical School.
Media Advisor Marion Solheim will be adding a lecture on science presentation.

We will look into topics such as Organizing your ideas and improving your manuscript, Clear writing, The Art of Scientific Story Telling, The problem statement, Titles and Abstracts, Punctuation, Making a manuscript memorable, Writing a convincing cover letter, and How to avoid death by PowerPoint.

There is something to learn for all of us! Senior staff is also very welcome. ECTS-providing participation is now fully booked, but you can still join the lectures for professional update. In that case, you register through this link. Note that the link will be closed without further notice when fully booked.

Elisabeth Wik is coordinating the INTPART program. Course coordinator is vandana.ardawatia@uib.no, and academic responsible Yamila Torres Cleuren. **More info**: at this page.

CCBIO903 Cancer research: Ethical, economic and social aspects

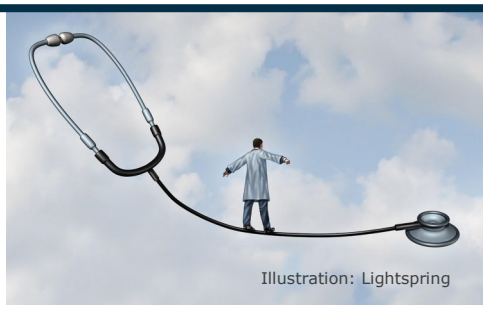


Illustration: Lightspring

Course week 1: May 31 to June 4, 2021, and course week 2: September 6-10, 2021.

CCBIO903 is a 5 ECTS course which focuses on ethical, economical and societal aspects of cancer and cancer research and aims to equip PhD candidates with tools for systematic reflection on their own and related research as well as methods for assessing the cost benefit of health measures and methods of treatment.

The course will address difficult questions:

- How can we deal with the uncertainties in the lab, while maintaining the quality of our science?
- Which drug is more suited to a patient?
- How can medical science contribute to debates on what is good for society?
- How can economic models help guide health care resource allocation?

Location will be announced (will be at the UiB campus). We will continuously monitor the Corona situation and consider adaptations. However, the course concept is highly interactive and process-oriented that precludes a fully digital teaching format.

John Cairns, Roger Strand and Anne Blanchard Bremer are academic responsible for the course. Administrative coordinator is Kjetil Utvik Harkestad. **More info**: at this page.

BMED904—Graduate course in Extracellular Matrix

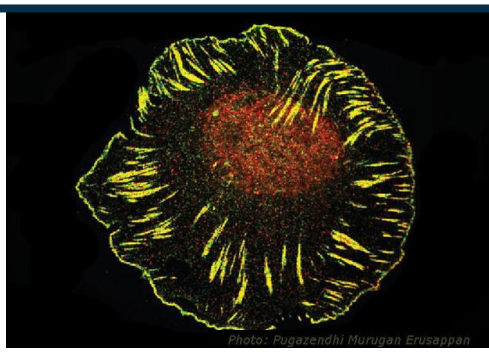


Photo: Pugazendhi Murugan Erusappan

June 07-11, 2021. Hybrid solution on-site/online.

This 3 ECTS course will cover various aspects of extracellular matrix (ECM) biology. A recurring theme will be the roles of the various ECM molecules and their functions in health and disease. Note, due to the uncertainty regarding the Covid-19 situation, the course is planned to combine face-to-face "seat time" for students attending in Bergen with online presentations of all lectures and lab demonstrations. The lectures are open to all interested.

Scientific program: See the preliminary program at this link.

If you want to follow the lectures of this course for **professional updates** and don't need the ECTS, please register here to get access. For the ECTS; please send a request to Margarethe Bittins.

Place: option of on location at the University of Bergen, Haukeland University Hospital, or through a live Zoom streaming online.

Academic responsible are Marion Kusche-Gullberg and Donald Gullberg.
Administrative coordinator is Margarethe Bittins. **More info**: at this page.

RELEVANT CALLS FOR FUNDING

Here is a list of current and relevant calls, so take a look and see if any of these are relevant for you.

- 4/3/2021: ERAPerMed (pre-proposals)
- 10/3/2021: Kreftforeningen (cancer prevention call, 1-4 years, 1-5 MNOK)
- 2/4/2021: Worldwide cancer research (1-3 years, 2.5 MNOK)
- 20/4/2021: ERC consolidator grant (2M €, 5 years) Consolidator Grants | ERC: European Research Council (europa.eu)
- 22/4/2021: Cancer Grand Challenges (EOI)
- 6/5/2021: KG Jebsen Center (main application)
- 12/5/2021: FKB center
- June 2021: Kreftforeningen open call (date to be announced)
- 10/6/2021: DAM stiftelse – research 2021 (phase 2)
- 17/6/2021: ERA PerMed (full proposals)
- 31/8/2021: ERC advanced grant (2.5M €, 5 years) Advanced Grants | ERC: European Research Council (europa.eu)

More info and advise on grants and applications:
contact CCBIO Research Advisor Yamila Torres Cleuren

NEW FACES

Manuel Carrasco is a new researcher in Lars A. Akslen's group. Manuel holds a degree in pharmacy by the University of Sevilla, an MS Degree in biotechnology by the University Pablo de Olavide, and a PhD from the Andalusian Molecular Biology and Regenerative Medicine Centre (CABIMER) on how transcriptional networks control pancreas embryonic formation and adult pancreatic function. He did his postdoctoral training in the Diabetes Center, Department of Clinical Science at UiB, where he investigated the cellular processes leading to pediatric endocrine diseases, such as diabetes and disorders of the ovaries and testes.

At CCBIO, Manuel will work with organoids as a model system for microenvironmental interactions in breast cancer, combining his scientific experience as a developmental biologist with his background as a pharmacist to better understand the mutual interactions between the nervous system, cancer treatments and tumor microenvironment in breast cancer.

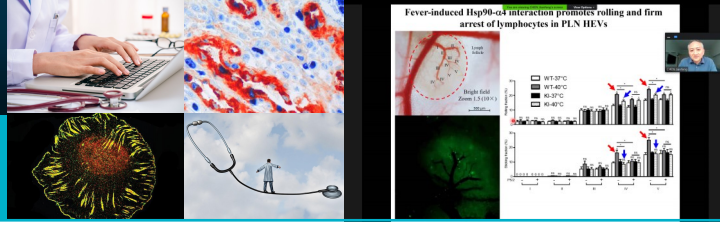
Vladan Milosevic is primarily affiliated to Arne Östman's group, and is also a researcher in Lars A. Akslen's group from February this year, in a collaborative project. Vladan is an MD holding a PhD in molecular medicine from the University of Turin, Italy, where he investigated the potential role of malignant pleural mesothelioma stem cells in the development of the chemoresistant and immune-resistant phenotype of this highly aggressive tumor. In his postdoc period at the University of Regensburg, Germany, Vladan worked 2 years with a project on minimal residual disease in breast cancer
patients and the role of disseminated cancer cells in the onset of metastasis.

At CCBIO, Vladan will be working on a project which aims to identify novel biomarkers and therapeutic targets of aggressive breast cancer through high-multiplex profiling of the tumor microenvironment using the Hyperion imaging mass cytometry platform.

We look forward to exciting work from both Manuel and Vladan!

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.



- March 25, CCBIO Seminar with speaker Randy Watnick. Title: "Identification of a novel paracrine acting stimulator of tumor growth and progression via modulation of Tsp-1 in the tumor microenvironment." Chair: Lars A. Akslen. Digital event (Zoom webinar).
- April 12-15, CCBIO908 – Scientific Writing and Communication Seminar. Digital event.
- April 29, CCBIO Seminar with speaker Ian Mills. Title: "Non-oncogene addiction and stress response signaling." Chair: Karl-Henning Kalland. Digital event (Zoom webinar).
- May 19-20, CCBIO Annual Symposium, Solstrand/online
- May 27, CCBIO Seminar, speaker to be announced. Digital event (Zoom webinar).
- May 31-June 4 + September 6-10, CCBIO903 – Cancer research: Ethical, economic and social aspects, on campus
- June 7-11, BMED904 – Graduate Course in Extracellular Matrix, on campus + digital platform
- June 10, CCBIO Seminar with speaker Andrew Leask. Chair: Donald Gullberg. Digital event.
- June 17, CCBIO Junior Scientist Symposium, (on campus if possible, digital platform otherwise)

OTHER COMING EVENTS



- March 10-12, Science, Technology, and Society: RRI Course, Centre for Digital Life Norway, Selbusjøen.
- March 18 and 25, Know-how webinar on regulatory affairs: Basic principles medical devices, Centre for Digital Life Norway. Digital event.
- March 22-25, BIO-Europe Spring Digital 2021, digital event.
- March 26, Intelligent systems for disease risk prediction, Centre for Digital Life Norway. Digital seminar.
- April 15 and 22, Know-how webinar on IPR in digital biotech. IPR biotech and software – basic laws and regulations. For researchers who are developing digital biotechnology solutions. Centre for Digital Life Norway. Digital event.
- April 20-23, Nordic Life Science Days 2021, digital event.
- May 3-7, Biotechgate Digital Partnering, digital event.
- May 10-12, From Systems Medicine towards Digital Health, the 8th Conference on Systems Biology of Mammalian Cells, Heidelberg, Germany.
- May 12, Oslo Cancer Cluster's 2021 Norwegian Constitution Day Networking Breakfast.
- June 9-11, 5th conference of Digital Life Norway Research School, Malangen Resort (Tromsø).
- June 14-18, BIO International Convention Digital.

PUBLICATIONS

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

- Hemsing AL, Gjertsen BT, Spetalen S, Helgeland L, Reikvam H. Favorable outcome of a patient with an unclassifiable myelodysplastic syndrome/myeloproliferative neoplasm treated with allogeneic hematopoietic stem cell transplantation. SAGE Open Med Case Rep. 2021 Jan 22;9:2050313X20988413. doi: 10.1177/2050313X20988413. eCollection 2021.

- Kreitman RJ, Dearden C, Zinzani PL, Delgado J, Robak T, le Coutre PD, Gjertsen BT, Troussard X, Roboz GJ, KarlinL, Gladstone DE, Kuptsova-Clarkson N, Liu S, Patel P, Rotolo F, Mitry E, Pastan I, Giles F; Study 1053 investingators. Moxetumomab pasudotox in heavily pre-treated patients with relapsed/refractory hairy cell leukemia (HCL): long-term follow-up from the pivotal trial. J Hematol Oncol. 2021 Feb 24;14(1):35. doi: 10.1186/s13045-020-01004-y.

- Børretzen A, Gravdal K, Haukaas SA, Mannelqvist M, Beisland C, Akslen LA, Halvorsen OJ. The epithelial-mesenchymal transition regulators Twist, Slug, and Snail are associated with aggressive tumour features and poor outcome in prostate cancer patients. J Pathol Clin Res. 2021 Feb 19. doi: 10.1002/cjp2.202. Online ahead of print.

- Krüger K, Silwal-Pandit L, Wik E, Straume O, Stefansson IM, Borgen E, Garred Ø, Naume B, Engebraaten O, Akslen LA. Baseline microvessel density predicts response to neoadjuvant bevacizumab treatment of locally advanced breast cancer. Sci Rep. 2021 Feb 9;11(1):3388. doi: 10.1038/s41598-021-81914-0.

- Jacob H, Dybvik JA, Ytre-Hauge S, Fasmer KE, Hoivik EA, Trovik J, Krakstad C, Haldorsen IS. An MRI-Based Radiomic Prognostic Index Predicts Poor Outcome and Specific Genetic Alterations in Endometrial Cancer. J Clin Med. 2021 Feb 2;10(3):538. doi: 10.3390/jcm10030538.

RECENT CCBIO IN THE MEDIA

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

17.02.21, På Høyden, "UiB må fortsatt satse på fremragende sentre", Inge Jonassen.

07.02.21, ABC Nyheter, "Kreftceller kan gå i dvale og unngå cellegift. Nå vet forskere mer om hvordan de skal vekke og drepe dem", Lars A. Akslen

04.02.21, Deutsche Welle, "Cancer research: Could drugs already on the market provide a cure?", Karl-Henning Kalland

01.02.21, Forskning.no, "Kreftceller kan gå i dvale og unngå cellegift. Nå vet forskere mer om hvordan de skal vekke og drepe dem", Lars A. Akslen

07.01,21, VG, "Ny metode mot føflekk-kreft", Lars A. Akslen.

29.12.20, Bergens Tidende, "Gode resultater for bergensk kreftvaksine", Karl-Henning Kalland.

21.12.20, Fremtiden, "Fylkeslegen med tilsynssak mot laserklinikk: – Vi følger alle regler", Oddbjørn Straume.

12.12.20, Khrono, "På tide å sette av fem prosent av prosjektmidlene til datahåndtering?", Inge Jonassen.

08.12.20, Dagens Medisin, "Norskutviklet behandling med effekt i kombinasjon med cellegift", Bjørn Tore Gjertsen.

06.12.20, Dagens Medisin, "Forsker på mulig immunterapi for minimal restsykdom", Bjørn Tore Gjertsen.