





# CCBIOSE E LE COMP. CEDIO. NO. 6, VOL. 9, DEC 21, 2022

#### DIRECTOR'S COMMENTS

Dear all

In this last newsletter of 2022, we would like to congratulate several people: Oddbjørn Straume and Arne Östman for receiving grants from the Helse Vest Research Fund, and Carina Strell for receiving a Pionéer Grant from the Cancer Society of Norway. Congratulations also to Sushil Dhakal and Cecilie Askeland for having defended their PhD thesis work.

In particular, many congratulations to Dr. Bruce Zetter for his 50 years in cancer research! What an achievement. We all know the influence of "the Bruce factor" – thank you for being a motivator to so many of us!

Please read other stories and information about upcoming courses and other events. Our research advisor has listed several opportunities for future grants – take a close look.

You now have the opportunity to read even more about *Biomarkers of the Tumor Microenvironment*. Our new book on cancer biomarkers (second edition, upgraded to textbook format) was published earlier this fall and is available in electronic and paper versions. The book is, of course, highly recommended, with contributions from local colleagues and top international scientists. This textbook would be suitable for several of our courses.

Finally, thank you to all at CCBIO, administration and researchers, for all the hard work during 2022. Be careful and stay safe - Merry Christmas and warm wishes for 2023!

Best regards, Lars A. Akslen, Director

Capturing cancer complexity and clinical challenges

# Support to CCBIO project improving immunotherapy



November 26, the regional health authorities Helse Vest announced their funding for 2023, allocating 182 million NOK to 57 new projects, and renewed support to 160 fellows and projects. Among the new projects, CCBIO PI Oddbjørn Straume receives open project support for his project *Targeting AXL to improve immunotherapy: Deep clinical biomarker analysis for precision medicine.* The funding amounts to NOK 1.223.000 for the first year, and spans over three years.

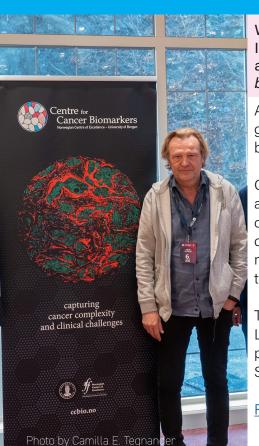
The primary objective of this project is to define a predictive biomarker signature for response to AXL targeting in combination with immunotherapy. The central hypothesis is that AXL-mediated immune suppression mechanisms drive immunotherapy failure and specific AXL-expressing cell constellations in the tumor microenvironment will predict response. The project rationale is that understanding of the molecular mechanisms underpinning AXL-mediated immunotherapy resistance will offer unique precision medicine-based opportunities.

The advent of immunotherapy dramatically improved the survival of many cancer patients. However, most patients still do not experience durable clinical response. This underscores the importance to identify predictive biomarkers. The Straume team translated their research on AXL-mediated immunotherapy resistance into a randomized Phase II clinical trial (NCT02872259) to evaluate AXL targeting to improve immunotherapy efficacy in melanoma. This clinical trial is now fully enrolled.

The expected outcome of this research is a new predicative biomarker signature for AXL targeting, and elucidation of the molecular mechanism underlying how AXL targeting improves immunotherapy in melanoma patients. This contribution is significant as it will elucidate new deep biomarker methodology and real time precision medicine approaches.

Read more here.

# Better biomarkers and drugs for ER+ breast cancer



We are happy to announce that CCBIO collaborator Arne Östman in our International Faculty also receives financial support from Helse Vest in their 2023 allocation. His project *Novel biomarkers and combination treatments for ER+breast cancer* receives NOK 1.500.000 in the first year.

Among breast cancers, the Estrogen Receptor-positive (ER+) is the most common group. Improved diagnostics and novel drugs have improved outcome. However, better biomarkers and drugs are needed for this large patient group.

Cancer-associated fibroblasts is a poorly characterized cell type controlling tumor aggressiveness and response to treatment through communications with malignant cells and immune cells. This project tests the overall hypothesis that novel to-bedefined fibroblast subsets control ER+ breast cancer through interactions with malignant cells and immune cells, and thereby are potential biomarkers and drug targets.

The study will be performed through close collaborations with the group of Professor Lars A. Akslen, CCBIO/UiB and Swedish breast cancer experts. Additional key partners are the <u>drug screening</u> and the <u>digital image analyses facilities</u> at the SciLifeLab, Stockholm.

Read more here.

# Pioneer project increasing the efficacy of immunotherapy



The Norwegian Cancer Society has a new funding program, the Norwegian Cancer Society Pioneer Projects, which supports early-stage exploration of novel and innovative ideas with potential for breaking new grounds in cancer research. CCBIO Associate Investigator Carina Strell just got the news that she is awarded with funding from this program for her project "ImSignal – Mapping active immune signaling in the context of immunotherapy." This amounts to NOK 1.996.000 for the grant period 01.01.2023 to 31.12.2024.

Carina Strell is very happy to receive this grant. "There is certainly an urgent need to increase the efficacy of immunotherapy and optimize patient selection," she says.

"In this project, we hypothesize that information on the interactions of immune signaling pathways in diagnostic tissue samples is more powerful in predicting immunotherapy response than currently applied single marker analyses by immunohistochemistry. Therefore, we will develop a novel analytical tool in form of a highly multiplexed proximity ligation assay combined with protein-based cell-typing on the Hyperion Mass Imager at CCBIO.

This will allow us to spatially quantify immune cell subsets paralleled with a detailed map of cell and protein interactions reflecting pathway activation. The spatial pattern of immune signaling pathways will be evaluated in tissue samples of patients treated with immune check point inhibitors and associated with response and survival. This approach will help us to extend our knowledge on immune-regulatory signaling to the level of biomarker and drug targeting in the context of immunotherapy" she explains.

Read more here.



Carina was this year also <u>awarded with the TMS</u>
<u>Starting Grant</u> for another project: Understanding Early Breast Cancer Evolution in Space and Time (EvoMaps). Here above the TMS Starting Grant awardees for 2021 and 2022 are celebrated at the annual TMS meeting, December 2, 2022.

Photo on top by Ingvild Festervoll Melien, below by Camilla Krakstad

# 50 years in cancer research



Harvard Medical School and Boston Children's Hospital hosted November 4th a celebration in honor of Bruce Zetter, the Charles Nowiszewski Professor of Cancer Biology at Harvard Medical School and Boston Children's Hospital, Boston, MA, USA. Professor Zetter is very well known to CCBIO as part of our Scientific Advisory Board and through several talks and lectures in our joint INTPART activities.

The CCBIO Director Lars A. Akslen was invited to the event November 4th which included talks by many of our other <u>INTPART</u> partners from the Vascular Biology Program, such as Marsha A. Moses, Director of the Vascular Biology Program, Joyce Bischoff, Randy Watnick, Hong Chen, Michael Rogers and Diane Bielenberg.

"It was indeed great to be back in Boston and spend quality time with the *Folkman family*", says Professor Akslen.

"This was to honor and celebrate Bruce Zetter – a gifted scientist, educator and communicator – and his 50 years in cancer research! This is an extraordinary achievement. At the symposium, several world class scientists presented their most recent findings. As all of you know, Bruce has been a constant and loyal supporter of CCBIO through his role as member of our Scientific Advisory Board, as educator, – and as a mentor. Thank you Bruce – and congratulations to you and your family!"

# **Coming CCBIO courses**

The coming spring term, CCBIO will run the courses CCBIO907, course in cancer-related vascular biology March 20–31, and CCBIO908, Scientific Writing and Communication Seminar May 22–23. Save the dates! Both these courses are part of the INTPART collaboration *Bergen-Harvard Cancer Studies Phase 2: Continued Partnership for Responsible Education, Research and Innovation*, with lecturers from the Harvard community.







#### CCBIO907, course in cancer-related vascular biology

CCBIO907 is a 6 ECTS credit course covering topics ranging from an introduction to tumor and vascular biology via basic physiology of blood and lymphatic vessels and tumor perfusion, molecular signaling in vascular biology and therapeutic approaches, to related biomarkers from discovery to clinical application, the immune-angiogenic interactions and anti-angiogenic treatment in clinical practice. Participants attending this course will benefit from the knowledge of researchers who have been in the frontline of vascular biology research for decades and are experienced lecturers at Harvard Medical School. Confirmed lecturers are <u>Diane R. Bielenberg</u>, <u>Michael S. Rogers</u>, <u>Steven Swendeman</u>, <u>Randolph Watnick</u>, <u>Ed Smith</u>, and <u>Dipak Panigrahy</u>.

When: March 20-31, 2023.

**Program:** Will soon be posted <u>here</u>. See last time's program <u>here</u>. You might also be interested in reading an <u>earlier news article</u> about the course.

Where: Auditorium at campus Haukeland University Hospital, Bergen. In person.

**Academic responsible**: Agnete Engelsen and Lars A. Akslen.

#### **Option of 3 registration links:**

- I. With ECTS, already UiB student: register at <u>Studentweb</u>. Deadline is February 1, 2023. Opens December 12. Must attend all sessions + exam.
- 2. With ECTS, not a UiB student: register at <u>Søknadsweb</u>. Same deadline as above. Must attend all sessions + exam.
- 3. No ECTS: A separate link will be available <a href="here">here</a>. Choose the lectures you want. No need for group assignments or exam.

More information: at this website.







#### **CCBIO908, Scientific Writing & Communication**

A new season with this popular course! The 2 ECTS course aims to provide theoretical knowledge about various elements of scientific writing, give practical experience on text editing, and the tools to improve your scientific texts.

Learn how to:

- Organize ideas, results and messages in a scientific paper
- Improve titles and abstracts
- Present a clear problem statement
- Use punctuation, grammar and numbering in a scientific text
- Write an informative and convincing cover letter

The course will also present and discuss what is good research communication.

When: May 22–23, 2023.

**Program:** Not yet available. See last time's program here.

Where: Auditorium at campus Haukeland University Hospital, Bergen. In person.

Academic responsible: Elisabeth Wik.

#### **Option of 3 registration links:**

- 1. With ECTS, already UiB student: register at <u>Studentweb</u>. Deadline is February 1, 2023. Opens December 12. Must attend all sessions + exam.
- 2. With ECTS, not a UiB student: register at <u>Søknadsweb</u>. Same deadline as above. Must attend all sessions + exam.
- 3. No ECTS: A separate link will be available <a href="here">here</a>. Choose the lectures you want. No need for group assignments or exam.

More information: at this website.

## Recent doctoral defenses



Sushil Dhakal defended Friday December 16 his doctoral dissertation "AXL targeting to enhance tumor Type 1 interferon response and potentiate chemo-immunotherapy" at the UiB. Supervisors were Jim Lorens and Niels Aarsæther.

The group has previously shown that the AXL receptor can contribute to tumors becoming resistant to various forms of cancer treatment. In this work, the hypothesis is that AXL receptors limit the effect of immunotherapy by blocking the interferon response, an important process that normally helps the body to effectively fight the viral infection. AXL is known to regulate the interferon response in viral infections including coronavirus. Activation of the interferon response has now been shown to be vital for effective cancer immunotherapy.

In his thesis, Dhakal investigates how the AXL receptor inhibits the interferon response in tumor cells. The work uncovers how cell signals from AXL block the tumor cell activation of interferon and the anti-tumor immune response. Dhakal demonstrates that the efficacy of immunotherapy in a mouse model is strongly strengthened in combination with an AXL-inhibiting drug. Overall, the results show a new treatment principle that shows potential to improve the efficacy of immunotherapy for cancer patients.

See the press release (in Norwegian).

Cecilie Askeland defended Friday December 9 her doctoral dissertation "Biomarkers of aggressive breast cancer with emphasis on tumor-stroma crosstalk" at the UiB. Supervisors were Lars A. Akslen, Elisabeth Wik and Ingunn Stefansson.

In her doctoral work, Askeland investigated selected biomarkers linked to characteristics of tumor cells and the immune microenvironment in breast cancer, with main focus on stathmin, a protein that helps to regulate the cells' cytoskeleton. Stathmin is important for several cell functions, including cell division.

High expression of stathmin in tumor cells was associated with more aggressive basaloid and BRCA1 mutated breast cancer, with inhibited immune response and reduced patient survival. An increased amount of immune cells was linked to unfavorable characteristics, vessel neoplasia and aggressive types of breast cancer. At the same time, a high incidence of lymphocytes expressing stathmin was associated with increased survival among women with triple negative breast cancer. Imaging mass cytometry showed that the expression level of stathmin in lymphocytes varied between different subtypes of T-lymphocytes. The lymphocytes' expression of stathmin also appeared to influence their location in the cancerous tissue.

The study has provided increased knowledge about the interaction between tumor cells and their microenvironment and can contribute to more personalized follow-up and treatment of breast cancer patients.

See the press release (Norwegian).



## **New edition of CCBIO book**

Book from CCBIO
Second Edition, 2022

Lars A. Ascler
Eurodojah S. Watnick
Chitres

Biomarkers
of the Tumor
Microenvironment

Second Editor

Second Edition, 2022

Lars A. Ascler
Eurodojah S. Watnick
Chitres

Second Editor

Second Ed

Springer Publishing recently upgraded the CCBIO book "Biomarkers of the Tumor Microenvironment" by editors Akslen and Watnick, to a textbook.

As is said in the foreword: Professor Lars A. Akslen and Professor Randolph S. Watnick have succeeded in the formidable task of assembling an extensively revisited book on the tumor microenvironment. This new edition deals with the most important aspects of the tumor microenvironment, providing an in-depth analysis of the interactions that take place between normal and malignant cell types. This new edition provides a rather exhaustive scrutiny of the phenotypes and organizations of components of the vascular systems, decoding the roles enacted by stromal fbroblasts, infammatory cells, and immune cells and offers noteworthy insight into innervation within the tumor microenvironment. This book also provides in-depth insight into the clinical relevance of strategically important signaling systems. The advent of new technologies is also discussed, with a topical refection on how these technologies are being engineered for the discovery of new biomarkers toward the optimization of clinical trials.

Access the book at Springer Link.

# 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 <a href="External funding opportunities">External funding opportunities</a>.

Note the NorCRIN inormation meeting January 5 in Bergen, "European Research Infrastructures – how can you benefit." The UiB and Helse Bergen are members of four European research infrastructures in the field of translational medicine: BBMRI, ELIXIR, EATRIS, and ECRIN. Researchers are invited to learn more about each research infrastructure and how they can help you with a focus on services that support funding applications. The national coordinators of each research infrastructure are available for 1:1 meeting where you can ask specific questions regarding your project or get more information. Here is the registration page and agenda.

#### **Horizon Europe**

Don't know where to start? Have a look at the upcoming workshop organized by FIA:

- How to write competitive proposals for the ERC Consolidator and Advanced Grants | Støtte til eksternfinansierte prosjekter (BOA) | UiB
- ERC 2023

<u>Consolidator Grant</u>: Deadline February 2, 2023 <u>Advanced Grant</u>: Deadline May 23, 2023

- Missions in Horizon Europe Conquering cancer
   Next deadline is in Spring 2023.
- Erasmus+: Project establishment support (PESstøtte) for the development of applications under the centralized initiatives in Erasmus+. More information here.

#### **Research Council of Norway**

There will be no FRIPRO call in the February 2023 call, but we expect it to be announced before the summer 2023 with funding allocated for start in 2024.

- Deadline Feb 8, 2023: Researcher Project for Scientific Renewal (Thematic Priority Call) (forskningsradet.no)
   Health: 60MNOK for project within "women's health" (text may change until Dec 14th)
- For a full overview: <u>Current calls for proposals</u> apply for funding (forskningsradet.no)

#### **UiB**

- Stays abroad for PhDs and postdocs at the Medical Faculty: next deadline is in March. <u>More info here.</u>
- Fond og legater: UiB is building a new database and application system. Therefore the deadline is delayed to *January 2023*. System will open Jan 2nd, and deadline will be before end of January (exact date TBC).

#### **UiO**

The Anders Jahre Awards for Medical Research

Nominate candidates for two medical prizes: I. The Anders Jahre Medical Prize for outstanding scientific

activity or results within Nordic medicine. The prize amounts to NOK 1 000 000 (approximately € 95 000).

II. The Anders Jahre Medical Prize to young medical investigators within the Nordic countries. The candidate must be below the age of 40 by June 15, 2023. The prize amounts to NOK 400 000 (approximately € 38 000).

All professors of medicine serving in a Nordic country are invited to nominate potential awardees. The nominations must be received before February 1, 2023. See info here.

#### 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.

**DAM Foundation**: Research program opens Nov 15, with a deadline Feb 15 2023.

**Trond Mohn Foundation** – <u>Trustworthy AI</u>: Deadline 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**

For more info and advice on grants and applications, contact our Research Advisor at CCBIO, Yamila Torres Cleuren (Yamila.cleuren@uib.no).



# **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.



- January 26, CCBIO Seminar with Bjørn Tore Gjertsen
- February 2, 2023, CCBIO Junior Scientist Symposium
- February 20-21 (not a CCBIO event but we wish to highligt it nevertheless), Converging on the person, Emerging technologies for the common good, Pontificial Academy for Life, Vatican City, Rome. Speaker for the opening lecture is CCBIO PI Roger Strand. You can participate in the workshop online.









- May 8-10, 2023 for next year's CCBIO Annual Symposium, also this time at Solstrand Hotel, outside of Bergen.
- May 22-23, 2023 for CCBIO908, the Scientific Writing and Communication Seminar 2023. We are repeating the success from earlier years, in the CCBIO/ Harvard INTPART collaboration. Open for all.
- May 25, CCBIO Seminar
- June 8, 2023, CCBIO Junior Scientist Symposium
- June 15, CCBIO Seminar





# Other relevant coming events

Events from collaboration partners and other relevant events.

- Gikk du glipp av webinaret Tverrfaglig brystkreftbehandling onkologisk, kirurgisk og patologisk? Du kan fremdeles se opptak av det ved å melde deg på via <u>denne lenken</u>.
- Did you miss the webinar: Treatment approaches for elderly/unfit patients with AML in the Nordic countries? You can still make it! The webinar can be viewed when you want on this link.
- January 5, NorCRIN Info meeting: European Research Infrastructures how can they benefit you? Improve your chances with funding opportunities. Bergen.
  - January 26, <u>Cancer Crosslinks 2023</u>, Oslo Cancer Cluster, Oslo. Join this milestone 15th Edition and hear from a distinguished panel of experts as they address progress CANCER CROSSLINKS in precision treatment and cancer immunotherapy. This meeting promotes interaction between researchers and

clinicians to enhance translational and clinical research and encourage new collaborations. <u>Program</u> is now available.



- February 13, Norway Life Science 2023, Livsvitenskapskonferansen. UiO, Oslo and some events digitally.
- March 20-22, March 28-30, <u>Bio-Europe Spring</u>, 3 days in-person (Basel, Switzerland), 3 days virtually.
- June 2-6, ASCO Annual Meeting 2023, Chicago and online.
- June 8-11 EHA2023 Hybrid Congress, Frankfurt, Germany and online on the Congress platform, and virtual days from June 14-16, 2023.
- Oncology, Istanbul.



## **Publications**

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

- Othman J, Meggendorfer M, Tiacci E, Thiede C, Schlenk RF, Dillon R, Stasik S, Venanzi A, Bertoli S, Delabesse É, Dumas PY, Pigneux A, Bidet A, Gilkes AF, Thomas I, Voso MT, Rambaldi A, Brunetti L, Perriello VM, Andresen V, Gjertsen BT, Martelli MP, Récher C, Serve H, Müller-Tidow C, Baldus CD, Haferlach T, Russell NH, Falini B. Overlapping features of therapyrelated and de novoNPM1-mutated AML. Blood. 2022 Dec 12:blood.2022018108. doi: 10.1182/blood.2022018108. Online ahead of print. PMID: 36508705
- Berg HF, Engerud H, Myrvold M, Lien HE, Hjelmeland ME, Halle MK, Woie K, Hoivik EA, Haldorsen IS, Vintermyr O, Trovik J, Krakstad C. Mismatch repair markers in preoperative and operative endometrial cancer samples; expression concordance and prognostic value. Br J Cancer. 2022 Dec 8. doi: 10.1038/s41416-022-02063-3. Online ahead of print. PMID: 36482191
- Kang J, Cairns J. Exploring uncertainty and use of realworld data in the National Institute for Health and Care

- Excellence single technology appraisals of targeted cancer therapy. BMC Cancer. 2022 Dec 5;22(1):1268. doi: 10.1186/s12885-022-10350-8. PMID: 36471259
- Sofiyeva N, Krakstad C, Halle MK, O'Mara TA, Romundstad P, Hveem K, Vatten L, Lønning PE, Gansmo LB, Knappskog S. APOBEC3A/B deletion polymorphism and endometrial cancer risk. Cancer Med. 2022 Nov 16. doi: 10.1002/cam4.5448. Online ahead of print. PMID: 36394079
- Aamdal E, Skovlund E, Jacobsen KD, Straume O, Kersten C, Herlofsen O, Karlsen J, Hussain I, Amundsen A, Dalhaug A, Nyakas M, Hagene KT, Holmsen K, Aamdal S, Kaasa S, Guren TK, Kyte JA. Health-related quality of life in patients with advanced melanoma treated with ipilimumab: prognostic implications and changes during treatment. ESMO Open. 2022 Oct;7(5):100588. doi: 10.1016/j.esmoop.2022.100588. Epub 2022 Sep 16. PMID: 36116420

# **Recent CCBIO in the media**

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

- 13.12.22, HealthTalk, "Pasienter med akutt myelogen leukemi kan leve lenger med ny behandlingsform", Bjørn Tore Gjertsen.
- 12.11.22, Khrono, "Til vanleg forskar han på brystkreft. Men onsdag kveld er det oboen som er i fokus", Manuel Carrasco.
- 09.11.22, NRK, "Forskere forbauset: Kvinne (36) overlever aggressiv kreft gang etter gang", CCBIO Hyperion photo used.
- 04.11.22. Dagbladet, "Fikk skrekkbeskjed: Trodde det var covid", Bjørn Tore Gjertsen.
- 02.11.22, Kreftforeningen.no, "186 millioner til livsviktig forskning", Jim Lorens.
- 31.10.22, Health Talk, "Hun utvikler miniversjoner av bukhinnen for å bedre forstå hvordan eggstokkreft utvikler seg og kan behandles", Christiane Helgestad Gjerde.
- 29.10.22, Health Talk, "Fant ulik immunrespons hos pasienter med eggstokkreft som ble behandlet med to immunterapier", Luka Tandaric.
- 27.10.22, Health Talk, "ESGO 2022: PARP hemmere er det største medisinske gjennombruddet de siste 30 årene nå kommer også immunterapi", Line Bjørge.

#### **Programs and Research Teams**

#### **Mechanisms of Tumor Micro**environment 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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