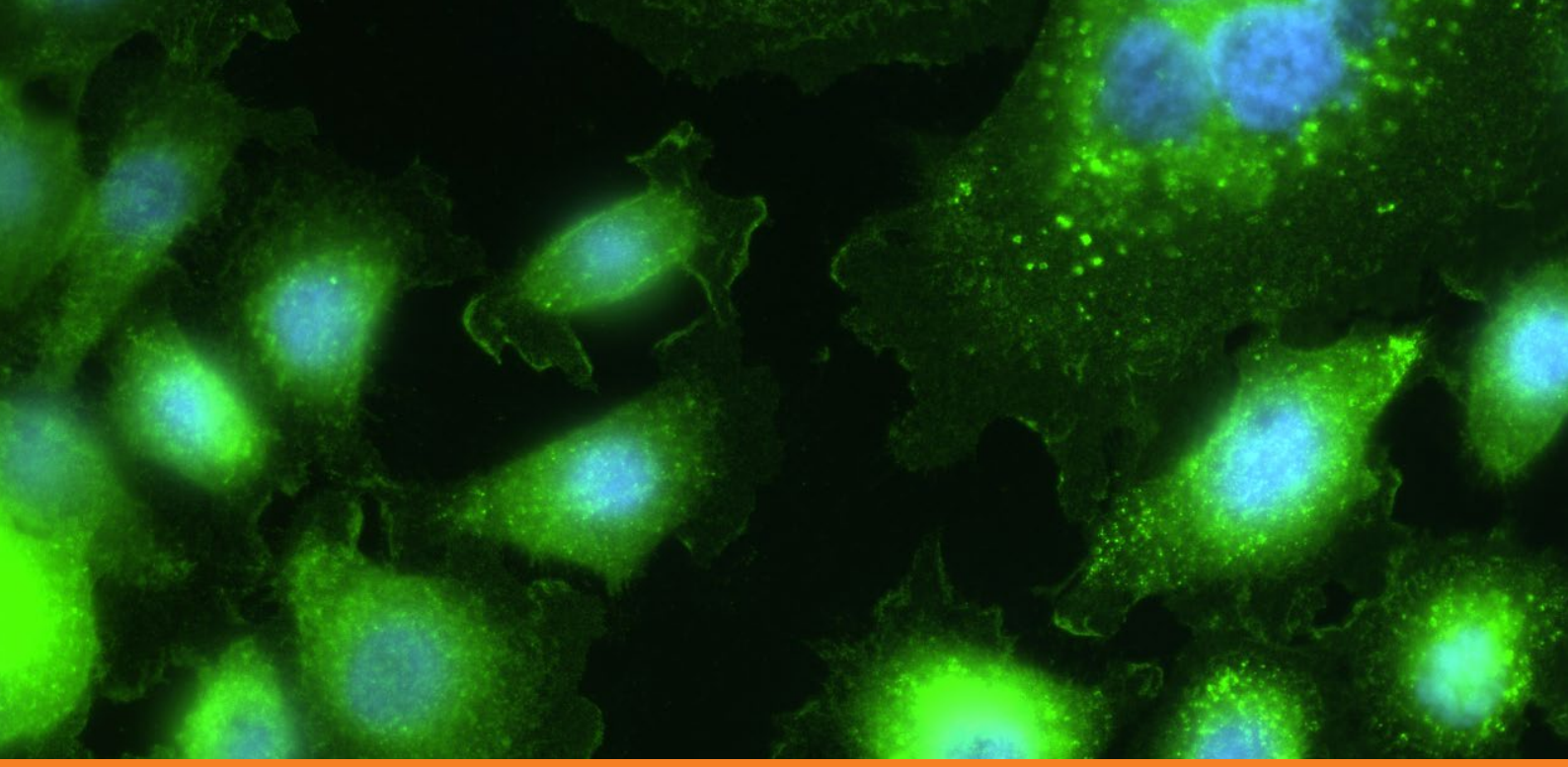


2013 Annual Report

CAST
CANCER • STEM CELL
INNOVATION CENTER

Established by the Research Council of Norway

sfi Centre for Research-based Innovation

Oslo University Hospital

UiO : University of Oslo

Introduction

SFI-CAST has been established by the Research Council of Norway to use the stem cell tool kit to better understand cancer, and to develop new therapeutic tools based on stem cell pathways.

In the seven years of the existence of the research centre, SFI-CAST researchers and their industry partners have established new analytical tools, identified novel therapeutic compounds that address the Wnt/ -catenin stemcell pathway, explored therapeutic benefits of stem cell specific miRNA, established innovative animal models, studied epitope specific photo-internalization and advanced concepts for immunotherapy based on stemcellness in cancer. The achieved results should be a valuable asset for the next steps on the path towards future personalized medicine.

Stefan Krauss
Director

We would like to thank the Research Council of Norway, the Oslo University Hospital and the University of Oslo for generous support. We want to thank the academic researchers and industry partners for their dedication and commitment. We would also like to express our gratitude to Inven2, the technology transfer office that has been supportive to the implementation of our commercialization strategy.

Ola Myklebost
Co-director

Finally, we would like to state that the ongoing research is not only about innovation and scientific or commercial progress; it is about saving lives. Cancer is a cruel, often un-curable disease that causes very severe suffering. In this context we feel privileged to be able to contribute to the development of novel potential therapeutic strategies at the cutting edge of science and technology.

Cover image: E-cadherin staining (green) on pancreas carcinoma cells BxPC-3 with a targeted deletion of the gene encoding CTNNB1 (β-catenin). DAPI staining (blue) of the cell nucleus. Photo by Petter A. Olsen.

Table of contents

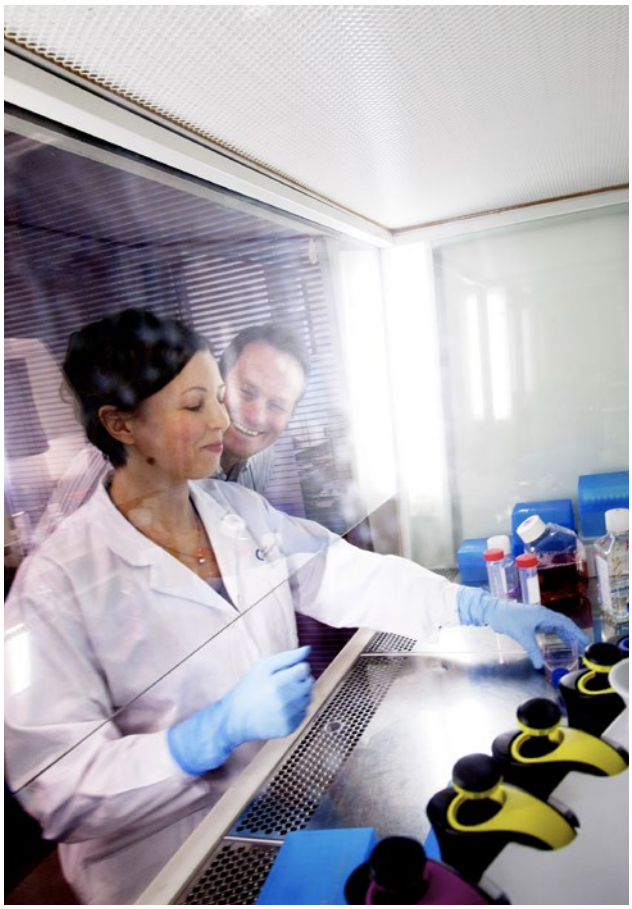
Summary

During the last decade, cancer research has gained substantial knowledge by applying a multidisciplinary understanding of tumour formation, progression and dynamics, as well as a precise analysis on individual differences between and within tumours at single cell resolution.

It is now becoming increasingly evident that cancer cells comprise a heterogeneous cell population with dynamic sub-populations of cells showing different biological profiles that affect cell proliferation, invasiveness and metastatic potential. The temporal and spatial dynamics of heterogeneity appears to be guided by a multitude of mechanisms, including autocrine and paracrine signals. The possibility to target these signals, combined with personalized tumour profiling has given new perspectives for addressing tumours more efficiently.

SFI-CAST develops innovative small drugs based interventions that specifically address stem cell pathways, cancer vaccines that are based on stemcell parameters, and photo-internalization based on epitopes that are enriched in specific cancer cells.

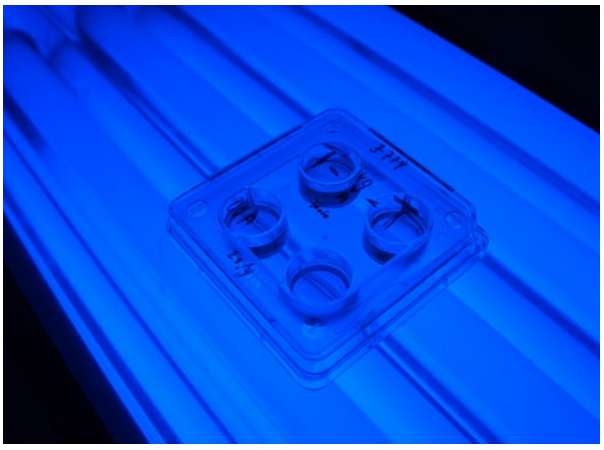
Pål K.Selbo working in the lab.



Ola Myklebost and Anastassia Serguienko working in the LAF-bench.

Vision/objectives

The SFI-CAST biomedical innovation centre works towards identifying new therapeutic intervention points in cancer.



PCI experiment (Photo: Arnfinn Christensen, Forskning.no)

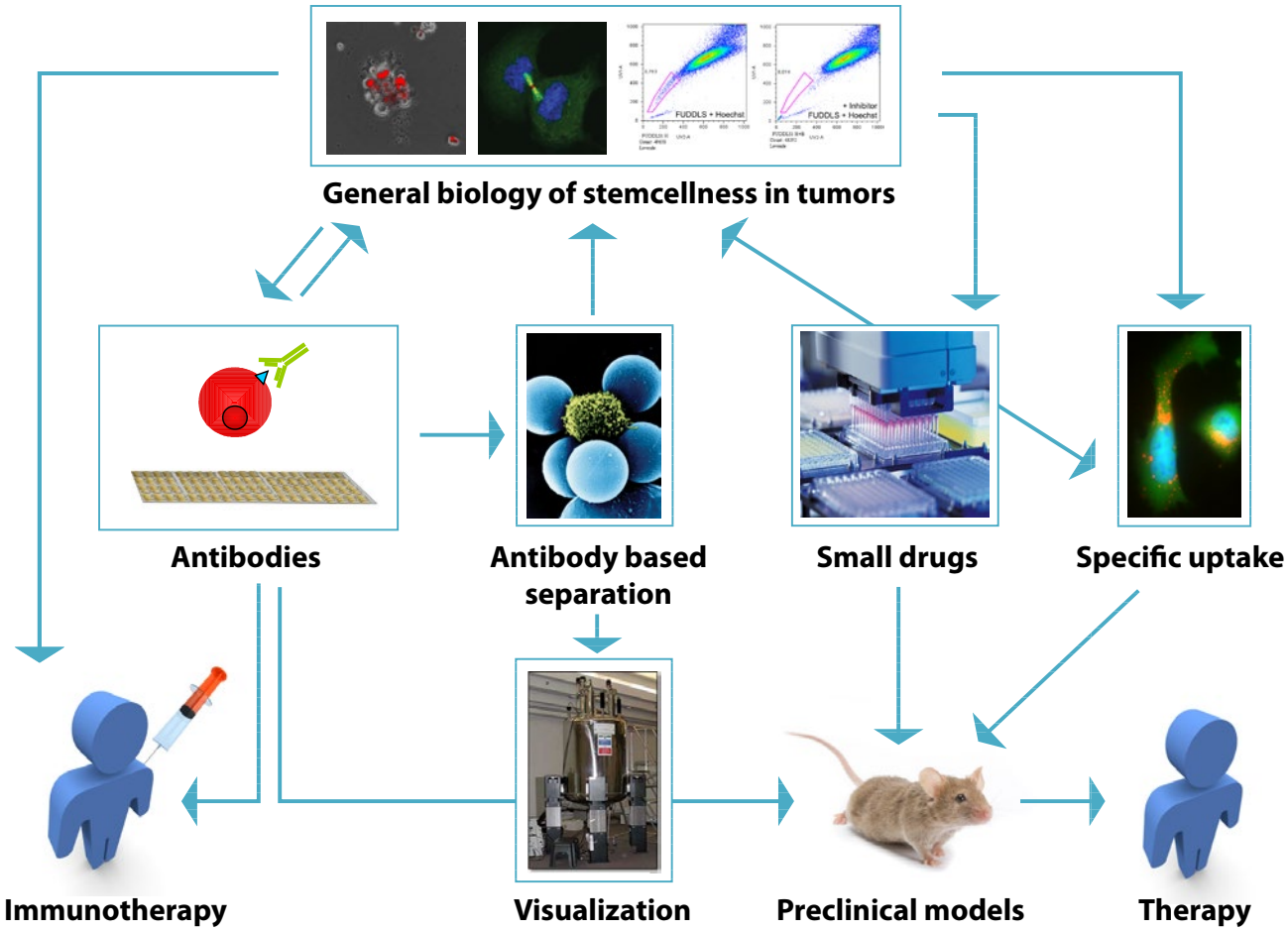
Cell culture work in the LAF bench

Jo Waaler working in the lab.

Dorna Misaghian working in the lab.

Research plan/strategy

The SFI-CAST biomedical innovation centre has a work program aimed at advancing basic research on stemcellness in tumours to novel therapeutic approaches. Together with our industrial partners, several interactive strategies are pursued. (i) Human therapeutic antibodies are identified and tested with industry partner Affitech Research AS. (ii) In collaboration with Odin Therapeutics AS, novel drugs are identified and tested that target the Wnt stemcell pathway. (iii) Specific antibodies are tested for improved therapeutic photo-internalization with industry partner PCI Biotech AS. (iv) Immunotherapy protocols are being explored and tested.



Scientific Highlights

PCI Biotech AS in collaboration with Ola Myklebost has shown that sarcoma cancer stem cells can be successfully targeted using CD133-specific PCI technology (Stratford et al., 2013). Together with the Stenmark group, **PCI Biotech** AS has also shown that photochemical internalization (PCI) of immunotoxins targeting CD133 is specific and potent at femtomolar levels in cells with cancer stem cell properties (Bostad et al., 2013).

In collaboration between **Affitech Research AS,** and the Stefan Krauss group, **PCI Biotech AS** has shown that an EpCAM-targeting monoclonal antibody linked to saporin is highly cytotoxic after photochemical internalization in breast, pancreas and colon cancer cell lines (Lund et al. in press).

ODIN Therapeutics AS has advanced a tankyrase specific inhibitor that has been developed together with the Krauss group and characterized by multiple members of the consortium to be licensed to Millipore/Merck.

The group of **Stefan Krauss** has further developed (Voronkov et al., 2013) and characterized the tankyrase inhibitor G007-LK in panels of cancer cells and *in vivo* mouse models (Lau et al., 2013). G007-LK currently serves as industry benchmark (highlighted by SciBX, a joint journal of Nature and Biocentury).

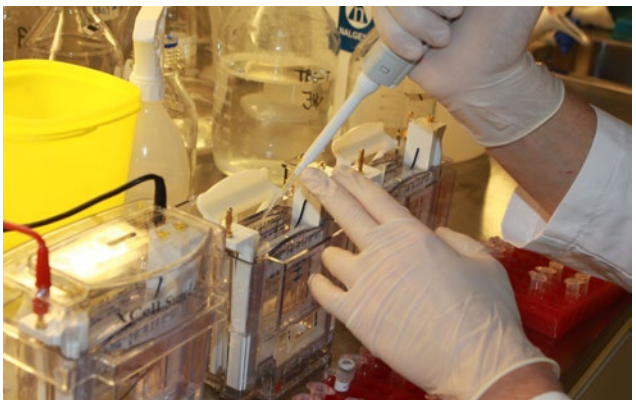
The group of **Ola Myklebost** has characterized the effect of a tankyrase specific inhibitor on osteosarcomas (Stratford et al., 2013). Furthermore, the group has evaluated potential efficacy of let-7 replacement therapy for liposarcoma *in vitro* and *in vivo* (Stratford et al., manuscript in prep) and has also investigated the role of HMGA2 and let-7 as regulators of tumour cell metabolism (Munthe et al, Serguienko et al, manuscripts in prep).

The group of **Harald Stenmark** has analyzed the effects of tankyrase inhibition on subcellular restructuring and protein turn over in colon cancer cells. The group has also characterized degenerative EGFR trafficking (Kostaras et al., 2013).

The group of **Therese Sørlie** has serially transplanted GLI1 induced mammary gland tumours in NOD/SCID mice and performed a thorough molecular characterization, identifying genetic alterations that appear early in the tumourigenic process. The group has established a multicolour transgenic reporter system enabling lineage tracing from Lgr5+ stem cells. This system is used to study tissue homeostasis of the small intestine upon treatment with a tankyrase specific inhibitor. Furthermore, together with the group of Mælandsmo it was shown that subtype-specific response to bevacizumab is reflected in the metabolome and transcriptome of breast cancer xenografts (Borgan et al., 2013).

The group of **Gunhild M. Mælandsmo** has generated experimental setups for studying the interplay between tumour and stroma (Bettum et al., 2014). The group has characterized primary breast cancer *in vivo* models (Lindholm et al., 2014) and established a link between S100A4 mediated signalling and EGFR. It is now tested whether the link can be explored in anti-metastatic therapy.

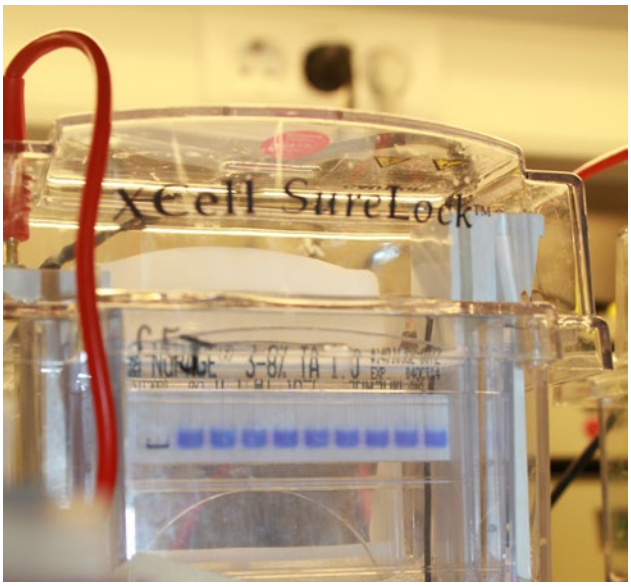
The group of **Iver A. Langmoen** has further characterized differences between glioblastoma and natural neural stem cell populations (Sandberg et al., 2013) and used the technique of growing glioblastoma cells as neurospheres for advancing an exploratory clinical immunotherapy trial (Vik-Mo et al., 2013).



Loading SDS-PAGE (Sodium dodecyl sulfate-Poly Acrylamide Gel Electrophoresis).

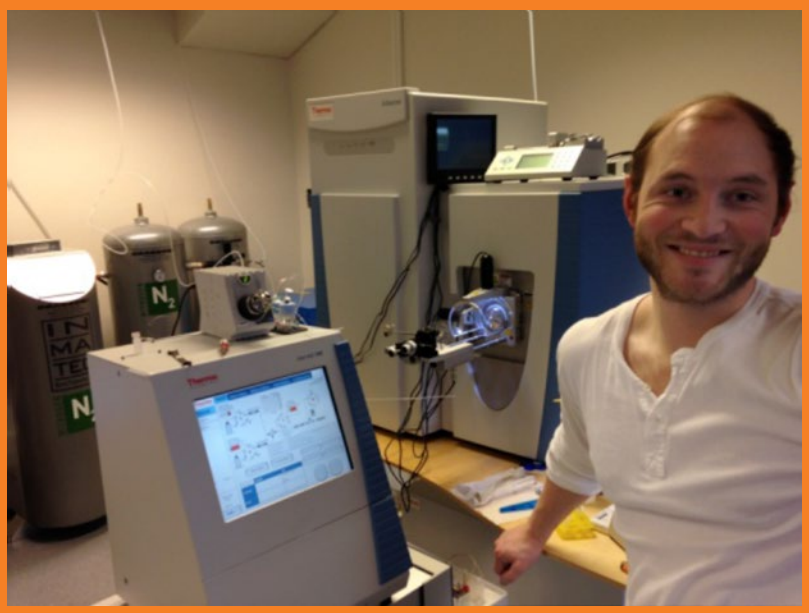
The group of **Rolf I. Skotheim** has identified novel fusion transcripts expressed in colorectal cancer, which involve the gene TCF7L2, encoding the WNT-effector TCF4 (Nome, Hoff et al., PLOS ONE in press). The group has published malignancy specific gene expression patterns in a stemness context, identified by transcriptome studies of embryonal carcinomas and embryonic stem cells (Alagaratnam et al., Stem Cells Dev., 2013).

The group of **Elsa Lundanes/ Steven Wilson** has further improved high sensitive metabolomics and proteomics platforms that can be linked to Wnt and Hh metabolism. The group has developed an ultra sensitive analytical platform for studying oxysterols (Røberg Larsen et al., in press). The group has also established a high performance proteomics system based on "sub-chip" dimensioned, open tubular liquid chromatography (LC) and mass spectrometry (MS) (Malerød et al., 2013; Røgeberg et al., 2013). The systems will allow sample analysis in small sub populations of cells in a tumour.



Running SDS-PAGE.

Jo Waaler is loading samples on SDS-PAGE.



PhD student Tore Vehus in front of the nanoLC-MS instrument.

Involved in the CAST-project from the Skotheim -group are, from left, Sigrid Marie Kraggerud, Anne Cathrine Bakken, Ragnhild A. Lothe, Rolf I. Skotheim, Andreas Hoff, and Sharmini Alagaratnam

Tor Espen Thorvaldsen and Nina Marie Pedersen from the Harald Stenmark-group

Organization

MANAGEMENT AND MEMBERS

SFI-CAST consists of 8 research groups; 7 groups at the Oslo University Hospital (OUS) and one group at the University of Oslo (UiO). There are three industry partners in the consortium. In 2013 the Centre's activities were located at the Norwegian Radium Hospital, Rikshospitalet, Ullevål University Hospital, at Domus Medica, at Oslo Research Park, and the department of Chemistry (University of Oslo) as well as in the different industries. In total SFI-CAST employs 80 scientific staff.

SFI-CAST is headed by Stefan Krauss (Director) and Ola Myklebost (Co-director). The administrative manager of SFI-CAST in 2013 was Piritta Nyberg.

The Centre has a project leadership group who meets on a regular basis. This group consists of the 8 principal investigators (PI) and representatives of industry partners of the consortium.

As SFI-CAST enters its last year of funding by the Research Council of Norway, core funding for 2014 will be focused on 6 research groups as a part of the transition plan.

ACADEMIC SFI-CAST MEMBERS

Stefan Krauss, Unit for Cell signalling, Dept. of Microbiology, Rikshospitalet, Oslo University Hospital

Iver A. Langmoen, Dept. of Neurosurgery, Ullevål University Hospital/Rikshospitalet, Oslo University Hospital

Elsa Lundanes/ Steven Wilson, Dept. of Chemistry, University of Oslo

Ola Myklebost, Dept. of Tumor Biology, Inst. for Cancer Research, the Norwegian Radium Hospital, Oslo University Hospital

Gunhild M. Mælandsmo, Dept. of Tumor Biology, Inst. for Cancer Research, the Norwegian Radium, Hospital Oslo University Hospital

Rolf I. Skotheim, Dept. of Cancer Prevention, Inst. for Cancer Research, the Norwegian Radium Hospital, Oslo University Hospital

Harald Stenmark, Dept. of Biochemistry, Inst. for Cancer Research, the Norwegian Radium Hospital, Oslo University Hospital

Therese Sørlie, Dept. of Genetics, Inst. for Cancer Research, the Norwegian Radium Hospital, Oslo University Hospital

INDUSTRY PARTNERS

Affitech Research AS
Gaustadalléen 21
N-0349 Oslo
Norway

ODIN Therapeutics AS
Gaustadalleén 21
N-0349 Oslo
Norway

PCI Biotech AS
Strandveien 55
N-1366 Lysaker
Norway

SCIENTIFIC ADVISORY BOARD

Thorarinn Gudjonsson
Biomedical Center
University of Iceland

Jens Peter von Kries
Institut für Molekulare Pharmakologie
Germany

Henrik Semb
Copenhagen University
Danish Stem Cell Center
Denmark

THE BOARD

Jonny Østensen, Oslo University Hospital/Inven2 (Chairman)

Stein Kvaløy, Oslo University Hospital

Kari Kværner, Oslo University Hospital

Henrik Schultz, University of Oslo

Michael Braunagel, Affitech Research AS

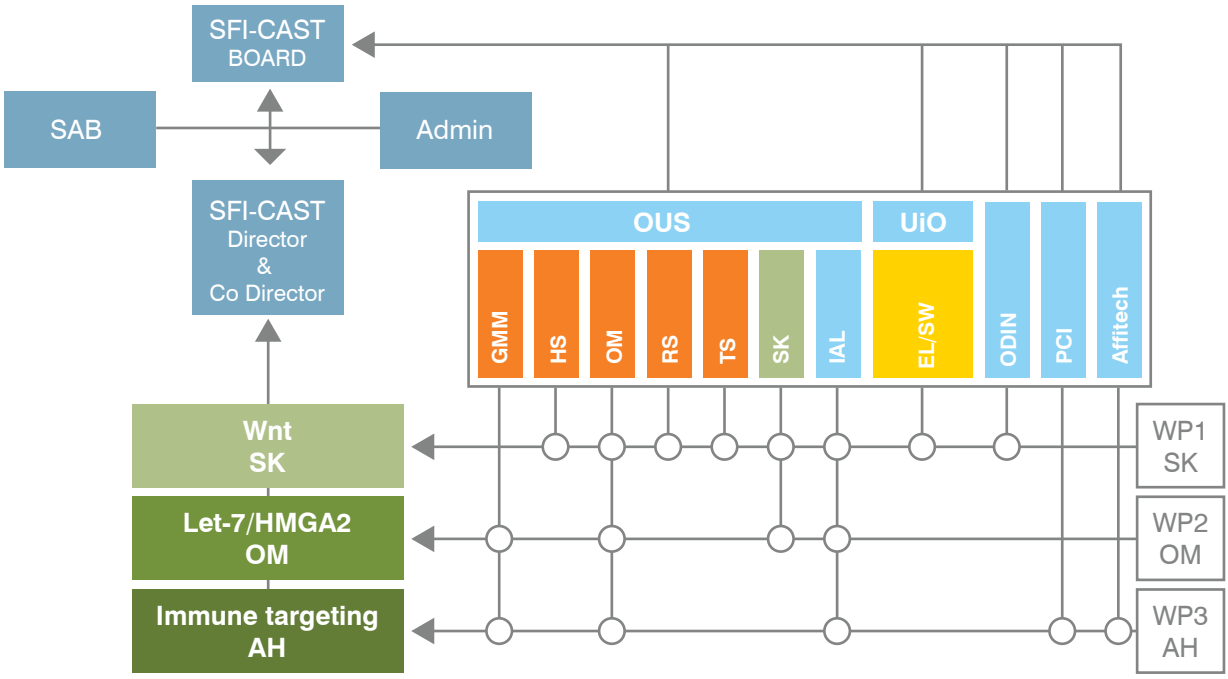
Olav Steinnes, ODIN Therapeutics AS

Anders Høgset, PCI Biotech AS

Øystein Rønning, Norwegian Research Council (Observer)

ORGANIZATION STRUCTURE

All partners (OUS, UiO and each industry partner) have a representative in the board. The project leadership group has the scientific responsibility and leader reports to the board. The organization on the working group level shows the competence, the collaboration and responsibilities.



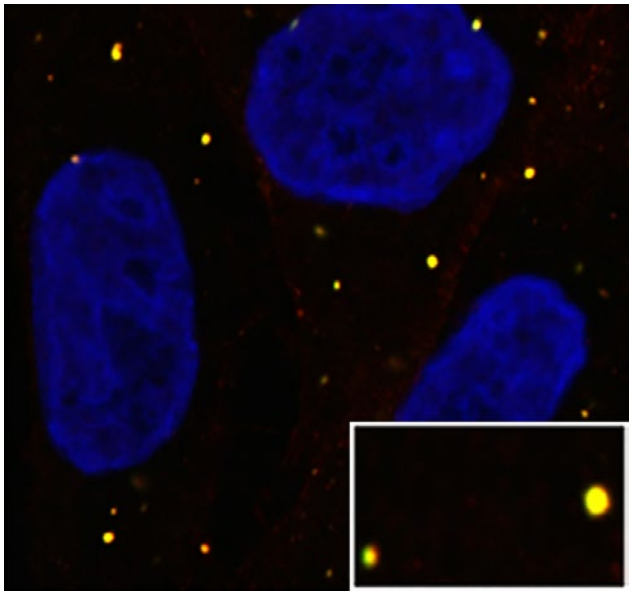
Abbreviations
OUS – Oslo Universitetssykehus (Oslo University Hospital)
UiO – Universitetet i Oslo (University of Oslo)
SAB - Scientific Advisory Board
GMM – Gunhild Mari Mælandsmo
HS – Harald Stenmark
OM – Ola Myklebost
RS – Rolf Skotheim
TS – Therese Sørlie
SK – Stefan Krauss
IAL – Iver Arne Langmoen
EL/SW – Elsa Lundanes/ Steven Wilson
AH – Anders Høgset
PCI – PCI Biotech AS
Affitech – Affitech Research AS
ODIN – ODIN Therapeutics AS
WP – Work Program

Partners

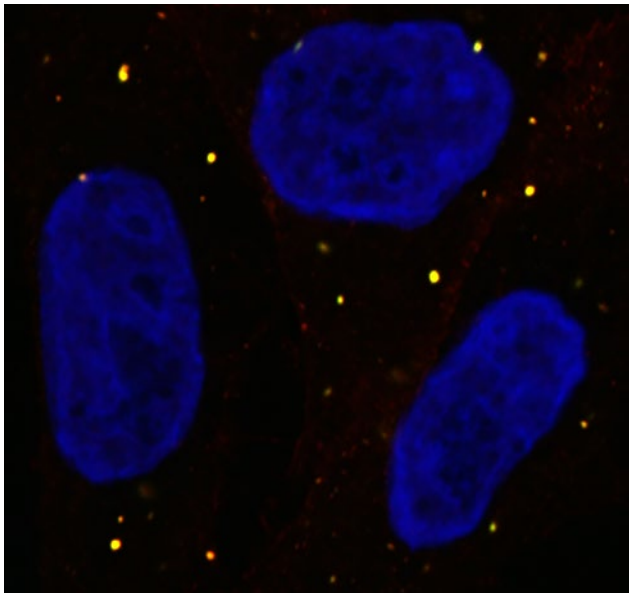
COOPERATION BETWEEN PARTNERS IN THE CENTRE

The SFI-CAST innovation centre is designed as an integrated structure where the academic partners are exchanging technology, materials and know how, while the industry partners can connect at any point they see potential for innovation.

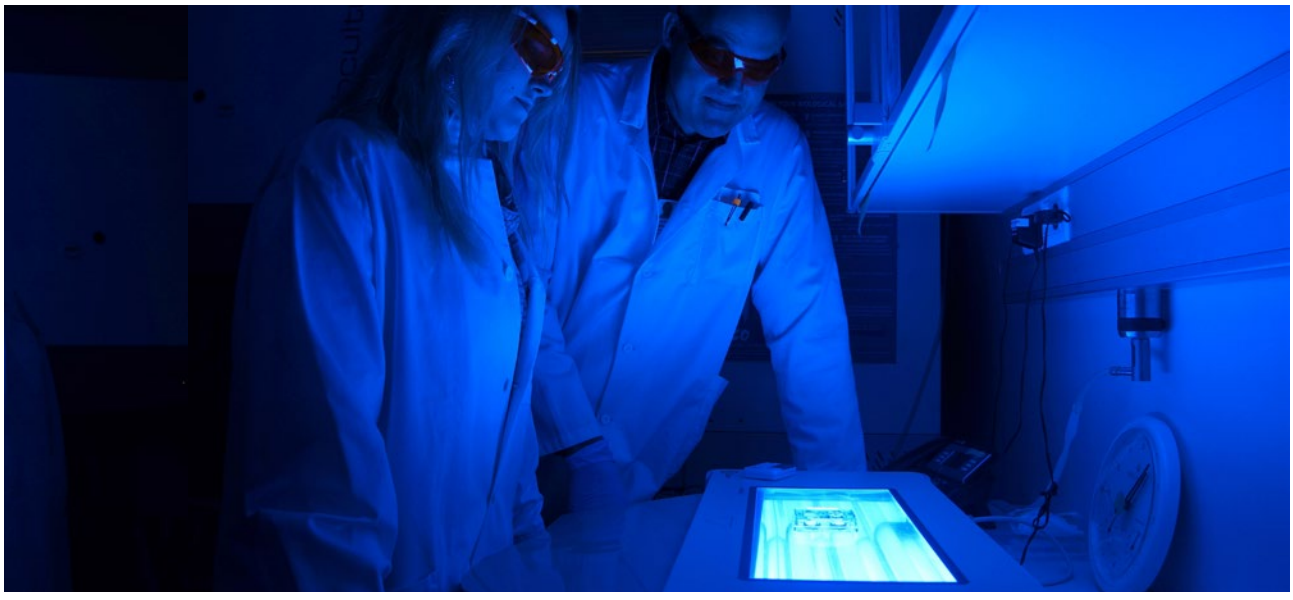
The collaborations between the academic partners and in selected areas with the industry include the SFI-CAST drug discovery platform, the immunotherapy platform and the photo internalization platform. Two annual retreats are held to track the progress of the partners. In addition, project work groups have been established that communicate on a daily/weekly basis.



Colocalization of Tankyrase and β-catenin (Photo: Tor Espen Thorvaldsen)



Total β-catenin (Photo: Tor Espen Thorvaldsen)



PCI experiment by Pål K. Selbo and Monica Bostad (Photo: Arnfinn Christensen, Forskning.no)

Industry Partners

www.affitech.com

AFFITECH RESEARCH AS

ABOUT THE COMPANY

Affitech Research AS, a privately owned biopharmaceutical company, is dedicated to the discovery and development of human antibody therapeutics in cancer and other diseases with unmet medical needs. The repeated use of antibodies as therapeutic agents to fight cancer requires antibodies that are non-immunogenic in humans. Affitech has therefore been focusing on the discovery and development of fully human antibodies, which we believe have the maximum potential for becoming ideal therapeutics for a variety of diseases combined with a lowered risk of immunogenicity.

SFI-CAST INTERACTION

In the frame of SFI-CAST, Affitech together with its academic partners and PCI Biotech AS and SFI-CAST academic partners is working towards characterizing antibodies targeting possible stem cell subpopulations that show increased chemotherapy resistance and increased metastatic potential.

STATUS 2013

The epithelial cell adhesion molecule (EpCAM) is expressed by a wide range of human carcinomas. Its recent identification on cancer stem cells has raised further interest in its use for tumour targeting and therapy. We characterized the therapeutic potential of a novel, fully human EpCAM-targeting mAb, 3-17I, and observed strong reactivity in human lung, colon, and breast tumour biopsies. We also show evidence for mAb-sequestration in endo-/lysosomes, suggesting internalization of 3-17I by receptor-mediated endocytosis. The ribosomal-inactivating toxin saporin was linked to 3-17I, creating the per se non-toxic immunotoxin 3-17I-saporin, a promising candidate for the drug delivery technology photochemical internalization. EpCAM-positive human cancer cell lines MCF7 (breast), BxPC-3 (pancreas), WiDr (colon), and the EpCAM-negative COLO320DM (colon), were treated with 3-17I-saporin in combination with the clinically relevant photosensitizer TPCS2a. Cell viability, proliferation and colony-forming capacity was strongly reduced in a light-dependent manner after PCI of 3-17I. Our results show that 3-17I is an excellent candidate for developing clinically relevant antibody-drug conjugates, using PCI for the treatment of localized tumours.

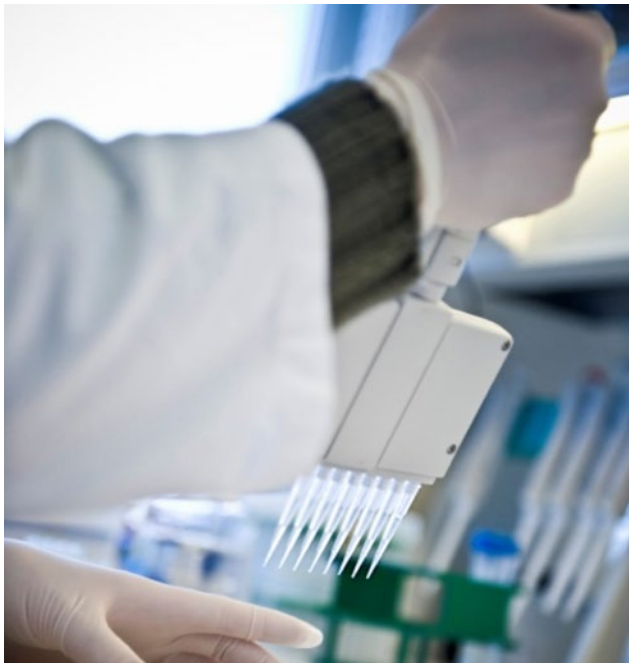


Photo: Affitech Research AS

Photo: Affitech Research AS

ODIN THERAPEUTICS AS

ABOUT THE COMPANY

ODIN Therapeutics AS is a spinoff company of the research in the Krauss-group laboratory. ODIN Therapeutics AS is fully owned by INVEN2, the technological transfer office of the Oslo University Hospital and the University of Oslo.

Working in the laboratory.

SFI-CAST INTERACTION

ODIN Therapeutics AS collaborates with SFI-CAST on chemical analoguing with the aim of advancing the specific tankyrase inhibitor series JW74 to achieve good PK/PD in humans. Furthermore, it is collaborating on identifying parameters for patient inclusion/exclusion initially in the colon cancer area.

Status 2013

Tankyrases 1 and 2 (TNKS1/2) are promising pharmacological biotargets with possible applications for the development of novel anticancer therapeutics. A focused structure-activity relationship study was conducted based on the tankyrase inhibitor JW74 leading to (G007-LK), a potent, "rule of 5" compliant and a metabolically stable TNKS1/2 inhibitor. G007-LK displays high selectivity toward tankyrases 1 and 2 and an excellent pharmacokinetic profile in mice. G007-LK and inhibits *in vivo* tumour growth in a subset of APC-mutant CRC xenograft models. In the xenograft model most sensitive to tankyrase inhibitor, COLO-320DM, G007-LK inhibits cell-cycle progression, reduces colony formation, and induces differentiation, suggesting that β-catenin-dependent maintenance of an undifferentiated state may be blocked by tankyrase inhibition.

www.pcibiotech.no

PCI BIOTECH AS

ABOUT THE COMPANY

PCI Biotech AS is an oncology-focused company developing products for localized cancer treatment. The products are based on PCI Biotech's patented drug delivery technology, photochemical internalization (PCI), which can strongly enhance the effect of anticancer drugs by targeted, light-directed drug delivery into cancer cells. PCI Biotech's lead candidate is the photosensitizer Amphinex® developed for treatment of head & neck cancer (currently in Phase II) and bile duct cancer (currently in Phase I/II). A second high priority is to develop PCI for boosting vaccination protocols.

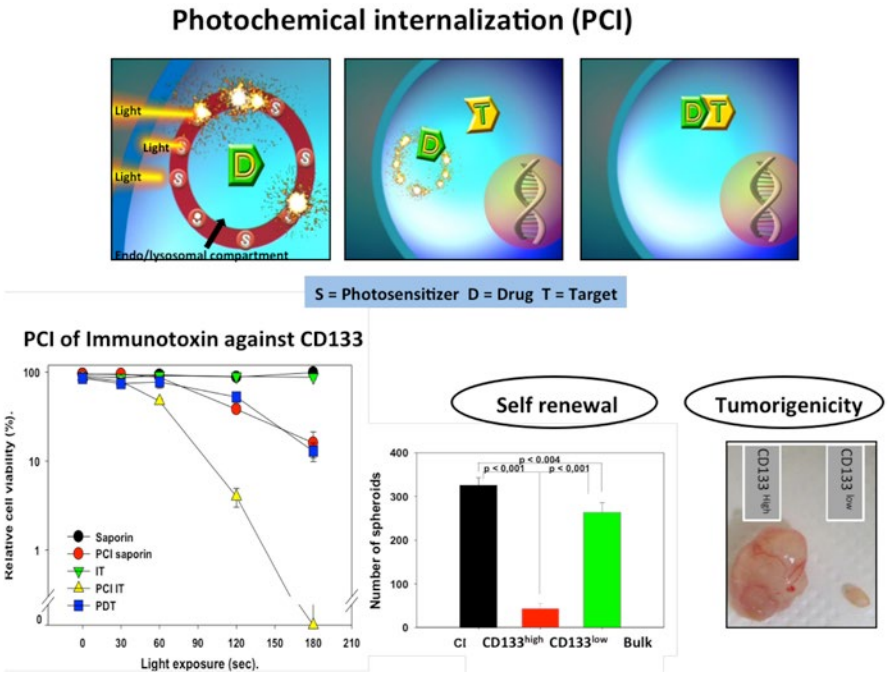
SFI-CAST INTERACTION

PCI Biotech has ongoing projects together with several SFI-CAST partners including the academic groups of Myklebost, Mælandsmo, Sørlie and Krauss on the targeting of stem cell markers in different cancers including sarcoma, carcinoma of breast, colon and pancreas. We also have collaboration with the industry partner Affitech Research AS on the PCI-based targeting of EpCAM.

STATUS 2013

PCI Biotech's patented photosensitizer Amphinex® in combination with cancer stem cell targeting toxins and light was demonstrated to be a highly efficient and selective method to eradicate CD133-expressing colon and pancreas cancer cells in addition to sarcoma cells. The PCI-induced purging of CD133-overexpressing sarcoma cells resulted in a significant reduction of tumour initiation of surviving cancer cells transplanted in immunodeficient mice (NOD SCID gamma null). The works were published in internationally recognized journals (Journal of Controlled Release and Biochim.Biophys.Acta) in 2013.

An open-label, multi-centre Phase I/II study in up to 45 patients to assess the safety and efficacy of Amphinex induced PCI of gemcitabine, followed by systemic cisplatin/gemcitabine in patients with inoperable bile duct cancer was initiated.



*PCI is a drug delivery technology based on the photochemical induced oxidation and rupture of endocytic vesicles, resulting in an endolysosomal release of the entrapped drugs of interest, which may react with its intracellular target (**upper panels**).*

*As a proof-of-concept, Bostad et al., demonstrate for the first time that PCI can be used to deliver therapeutics that target CSCs. PCI of a CD133-targeting immunotoxin was shown to be highly efficient down to femtomolar levels in cells of colorectal and pancreatic cancer origin (**lower left panel**).*

*The tumour-initiating capacity of the CD133high compared to the CD133^{low} population were also assessed revealing that tumour-initiation and aggressive growth in athymic nude Foxn1nu mice was obtained with only 10 (ten) CD133^{high} cells opposed to CD133^{low} cells (**lower right panel**).*

Research Groups/Academic Partners

STEFAN KRAUSS - GROUP STEM CELL SIGNALLING

AIM

The goal of the group within SFI CAST is to gain understanding on stemcellness in cancer, and to use this knowledge for developing therapeutic agents. The main focus is on Wnt/β-catenin signalling

STATUS

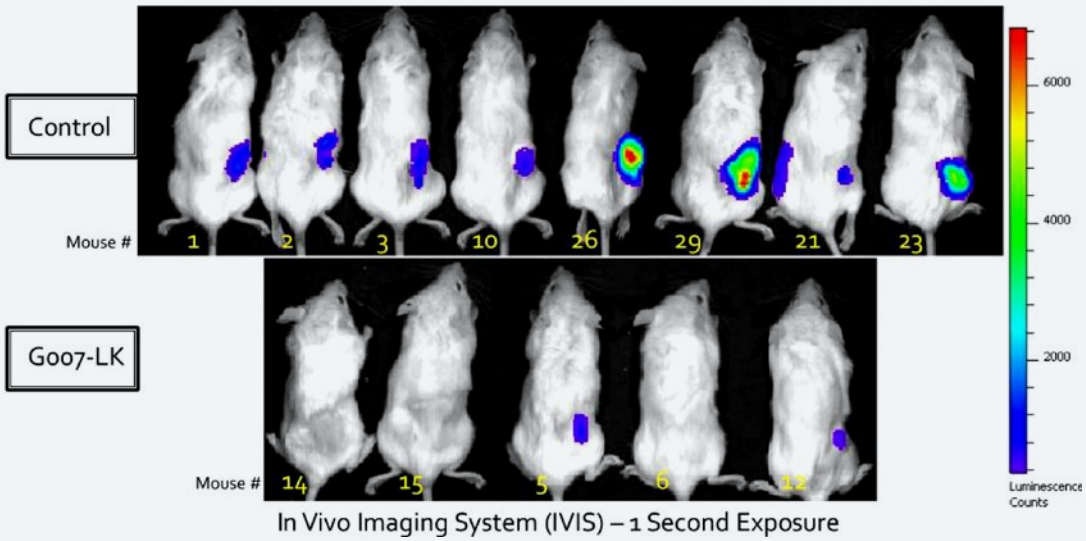
To attenuate Wnt/β-catenin signalling in tumours, we have developed a potent and specific small-molecule tankyrase inhibitor, G007-LK, that reduce Wnt/β-catenin signalling by preventing poly(ADP-ribosyl)ation-dependent AXIN degradation, thereby promoting β-catenin destabilization. Using two independent tumour cell panels we analyzed the efficacy of G007-LK on 660 tumour cell lines and identified a number of sensitive tumours. The basis for sensitivity to tankyrase inhibition is currently being analyzed in selected tumour cell lines. In addition we are looking through siRNA and chemical screens for enabling and disenabling factors. It was previously unknown whether the level of AXIN protein stabilization by tankyrase inhibition is sufficient to impact tumour growth in the absence of normal APC activity. Compound G007-LK displays favourable pharmacokinetic properties and inhibits *in vivo* tumour growth in a subset of APC-mutant CRC (Colorectal Cancer) xenograft models.

INNOVATIVE POTENTIAL

The tankyrase inhibitors have been patented and licensed. The siRNA and chemical screens may identify further relevant biotargets and chemotypes.

COLLABORATIONS WITHIN THE CENTER

We actively collaborate with E. Lundanes/S. Wilson group on analytical tools, with O. Myklebost, T. Sørlie, I.A. Langmoen and G.M. Mælandsmo-groups on tankyrase inhibitors in various tumour models and with H. Stenmark on subcellular alterations upon tankyrase inhibition. We have collaboration with PCI Biotech AS and Affitech Research AS on targeting sub populations of cells in cancer.



Mouse CRC (Colorectal Cancer) xenograft study using G007-LK

IVER A. LANGMOEN - GROUP MALIGNANT BRAIN TUMOURS

AIM

The main focus of the group within the frame of SFI-CAST is on cultivation and characterization of cancer stem cells in primary cultures from brain tumours and identification of new therapeutic targets in glioblastoma.

STATUS

Both normal and tumour stem cells show a high proliferation rate when cultured. Normal and tumour stem cells show a similar pattern of differentiation into neuronal and glial directions, although differentiated cells from the tumour are clearly morphologically abnormal and differentiate at increased kinetics. We have performed a number of experiments studying the effect of *in vitro* culturing on the tumour stem cells ability to form tumours, differentiate and induced changes in genotype end expresome. We have also explored the cellular organization of neuro- and tumourspheres, looking at the cellular heterogeneity of such spheres.

We have used microarray technology to compare the global gene expression in human adult neural stem cells and brain tumour stem cells in order to identify possible targets for treatment and to better understand the biology of the cell populations that escapes current treatment to cause recurrences. This comparison showed a significant up-regulation in tumour stem cells of genes connected to regulation of focal adhesion, actin cytoskeleton, axon guidance as well as the Wnt-signalling pathway.

The roles of the possible targets in the Wnt pathway are investigated using Wnt inhibitors. In particular, we have investigated a set of 20 genes that were highly up-regulated in GBM tumour cultures using micro-array data. Currently, the genes' roles in glioma are investigated using shRNA-knockdown based technology and its effect on proliferation, apoptosis and sphere-forming capacity.

We have established a translational clinical study for targeting autologous tumour stem cells by dendritic cell therapy, "Phase I/ II trial of vaccine therapy with hTERT, surviving and tumour stem cell derived mRNA transfected dendritic cells in patients receiving standard therapy for glioblastoma" (NCT00846456). Autologous CSC cultures were established from ten out of eleven tumours. Seven patients were able to be weaned from corticosteroids to receive DC immunotherapy. An immune response induced by vaccination was identified in all seven patients. No patients developed adverse autoimmune events or other side effects. Compared to matched controls, progression-free survival was 2.9 times longer in vaccinated patients (median 694 vs. 236 days, p = 0.0018, log-rank test).

INNOVATIVE POTENTIAL

FACS (facilitated cell sorting and cytometry) studies on cellular sub-groups within tumours combined with identification of new surface markers for both adult human neural stem cells and tumour stem cells will identify new therapeutic targets in restorative medicine and oncology. Further development on individualized therapies based on autologous cell cultures combined with immunotherapy is a main innovative aim for the group.

COLLABORATIONS WITHIN THE CENTRE

We actively collaborate with S. Krauss and Gunnar Kvalheim.

ELSA LUNDANES/ STEVEN WILSON - GROUP ANALYTICAL CHEMISTRY

AIM

We develop analytical tools for analysis of proteins and small molecules, mostly based on liquid chromatography and mass spectrometry, with emphasis on sensitivity, resolution and automation.

STATUS

Validated, very sensitive analytical platform for studying levels of (Hedgehog agonizing) oxysterols.

Establishment and routine application of high performance proteomics system based on "sub-chip" dimensioned, open tubular liquid chromatography (LC) and mass spectrometry (MS).

Development of on-line "sub-chip" enzymatic reactor on-line coupled with LC-MS for fast proteomics.

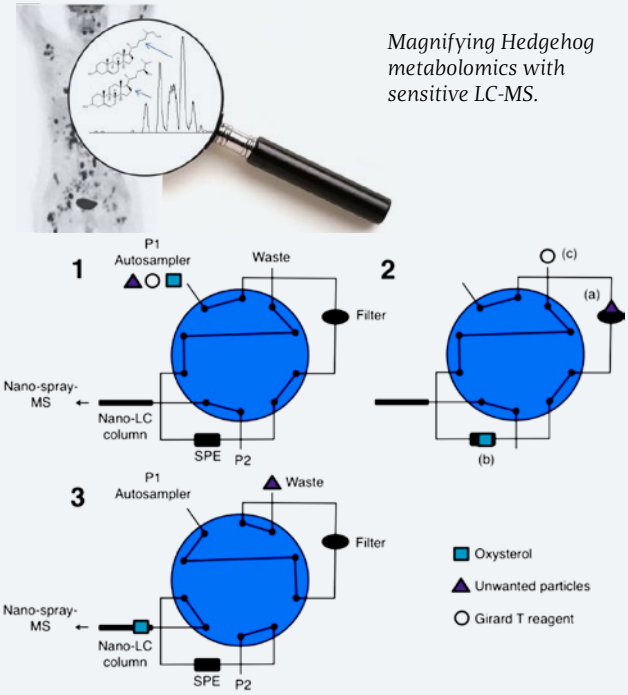
Platform for analysis of glycopeptides based on high resolving LC-MS.

INNOVATIVE POTENTIAL

Main innovations of 2013 have been related to advances in open tubular microfluidics; Use of such columns in "sub-chip" dimensions (20 ffim and lower) is a gateway to enhancement in sensitivity, speed, reproducibility and performance. Lundanes et al. have reached the point where such columns can be used for on-line protein preparation (i.e. splitting proteins into peptides, that are more MS/search data base-compatible) and chromatographic separation. Such systems have promise for accumulating significant amounts of data in short time (1-2 hours), with possible benefits as a diagnostic tool in e.g. evaluating presence/levels/mutations of Wnt and Hh pathway related proteins.

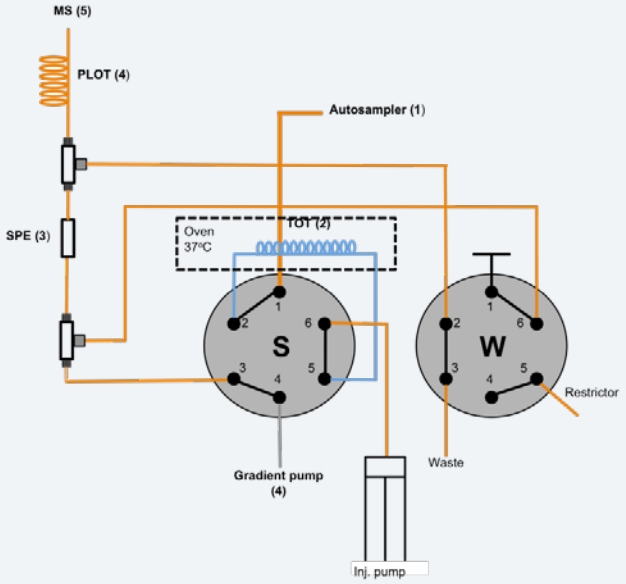
COLLABORATIONS WITHIN THE CENTRE

We are pro-active in cooperation with other CAST members, especially the Krauss-group, and co-publish regularly.



Magnifying Hedgehog metabolomics with sensitive LC-MS.

AFFL-SPE-nano LC system for sensitive, highly automated sterolomics.



Automated enzymatic digestion, peptide trapping and liquid chromatography using open tubular columns (5-10 µm inner diameter). The design is compatible with valves and plumbings of commercial nano LC systems. TOT = trypsin and lys C open tubular column (20 µm).

OLA MYKLEBOST - GROUP MESENCHYMAL PROGRAMMING

AIM

The main aim of our CAST-related work is to evaluate whether affecting the stemness/differentiation axis can be a useful therapeutic strategy for aggressive cancers of mesenchymal phenotype

STATUS

We have shown that tankyrase inhibition of osteosarcoma cells induce apoptosis, delay cell cycle progression and also importantly induce differentiation. Interestingly we have found that tankyrase inhibition also leads to increased let-7 microRNA expression and this effect may be responsible for the induction of differentiation. It is well known that let-7 is a tumour suppressor and an inducer of differentiation. Let-7 expression is lost or reduced in a range of cancers and let-7 replacement therapy has shown great potential. As a separate project, the role of let-7 in sarcoma is being studied using a number of liposarcoma (LPS) cell lines. We have found that let-7 inhibits proliferation and colony formation. Interestingly, let-7 does not affect migratory capacity but completely abolishes invasive potential of LPS cells. We are currently preparing to test the efficacy of let-7 replacement therapy *in vivo* using mouse xenograft models. The efficiency of PCI to stimulate and localize treatment with miRNA mimics will also be investigated in collaboration with PCIB.
To investigate the molecular pathways regulated by let-7 or its target gene HMGA2, we have performed global mRNA and protein analysis of aggressive breast cancer cells treated with either let-7 or HMGA2 siRNA. We have also confirmed functional effects on the metabolism of these cells based on changes observed in the transcriptome and proteome analysis.

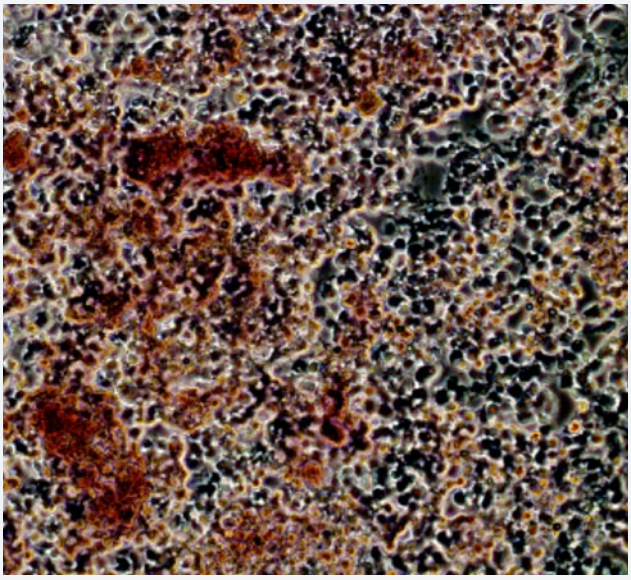
INNOVATIVE POTENTIAL

Therapeutic strategies based on Let-7 and miR34 will be evaluated in collaboration with Mirna Therapeutics (Austin, Texas).

The potential for PCI to augment treatment of tumours with miRNA mimics may contribute to the innovation of PCI Biotech.

COLLABORATIONS WITHIN THE CENTRE

We actively collaborate with S. Krauss and PCI Biotech AS.



SaOS2 cells treated with a combination of tankyrase inhibitor JW74 and osteogenic differentiation mix. The Alazarin Red Stainings marks the calcium-deposits specific for differentiated cells.

GUNHILD M. MÆLANDSMO - GROUP TUMOUR HETEROGENEITY

AIM

Identification of how the molecular and functional properties of various cancer cells are affected by micro environmental factors. We aim to reveal the peculiarities in the crosstalk between cancer cells and the microenvironment in various metastatic sites and consequence of such crosstalk for metastases development and drug-responses.

STATUS

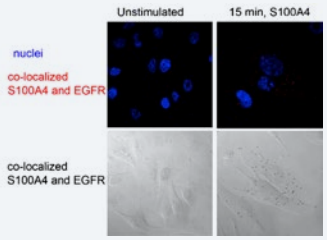
Intra-tumour heterogeneity and cellular plasticity studies
All cancer cells do not follow the "classical" CSC model. Acquisition of CSC characteristics is probably a dynamic process and many cancer cells can switch into transient CSC-like phenotype given appropriate signals from the microenvironment. Epithelial to mesenchymal transition (EMT) is one of the processes where epithelial cells are transformed to acquire more stem cell like features. We have been studying the regulation of phenotype-switching i.e. generation of stem-like subpopulations in response to microenvironmental stimuli, especially effects of stimulation with the metastasis promoting factor S100A4. We have developed *in vitro* and *in vivo* models allowing investigation of tumour-microenvironment interaction and its role on the phenotype and functional properties of cancer cells (see figure below). We have also been investigating whether S100A4 acts as a stabilizer of the mesenchymal phenotype, thereby contributing to both EMT and the inverse process MET. It is well known that matrix metalloproteinases (MMPs) can induce EMT in mammary epithelial cells, and furthermore that S100A4 induce expression of MMPs. We have characterized extracellular S100A4-mediated signalling programs responsible for induction of MMPs and found that S100A4 mediated MMP induction involve activation and internalization of EGFR and activation of ERK. We have also found that the presence of S100A4 in the microenvironment of epithelial cells change the downstream effects of EGF. In a heterogeneous tumour mass not all tumour cells respond in the same way to the external stimuli. Subclones of tumour cells might therefore have different degrees of phenotypic properties protecting them from the effects of the applied treatment. To characterize such differences, we analyzed the proteome of primary tumour cell subpopulations with differential *in vivo* tumourigenic activity. To unravel the general value in the identified molecular patterns, two ortothopically growing patient derivedxenograftsmodels(PDX)wereincludedinthisstudy. We have furthermore generated a PDX model from basal-like breast cancer with *in vivo* resistance to Paclitaxel treatment. The transcriptomic and genomic pattern of the developing resistant model has been analysed, and compared to the non-resistant mother tumour. The PDX models have also been used for testing the effect of Wnt-inhibitors and CSGP4-targeted PCI therapy.

INNOVATIVE POTENTIAL

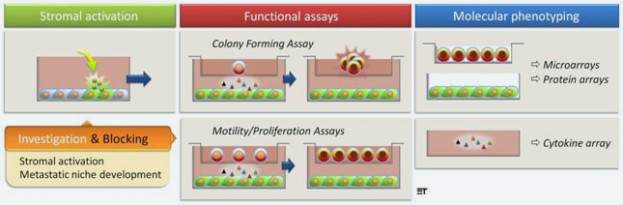
By better understanding of intra-tumoural heterogeneity and how subpopulations respond, escape from, and get resistant to treatment, more optimized combinations of targeted therapy may be revealed. S100A4 is a pro-metastatic protein in breast cancer and a marker for mesenchymal cells. The involvement of S100A4 in modulating the EGFR mediated responses to EGF is of great interest and might suggest broader applications of small molecule EGFR-inhibitors. Increased understanding of the tumour-microenvironment interactions might reveal novel targets for therapeutic intervention.

COLLABORATIONS WITHIN THE CENTER

We actively collaborate with T. Sørlie, S. Krauss and PCI Biotech AS.



Confocal images of duolink proximity ligation assay showing co-localization of s100a4 and EGFR inside mammary epithelial cells. Red dots (black in the b/w images below) indicate co-localization of the two proteins.



Illustrative summary of the experimental setup of stromal cell/tumour cell co-cultures. Direct contact- and soluble factor mediated effects on tumour cells, are measured in functional assays. The stromal cell layer was pre-activated by soluble factors. Multilevel molecular profiling of separate co-culture components has been performed.

ROLF I. SKOTHEIM - GROUP
STEM CELL BIOMARKERS

STEM CELL BIOMARKERS AND MUTATIONS IN COMPONENTS OF THE WNT SIGNALLING PATHWAY

AIM

We aim to identify molecules which can be used as cancer biomarkers in a stemness context. Throughout the CAST period, we have focused on the pluripotent cancer cells developing from testicular germ cells. Specifically, we compare mRNA profiles of embryonal carcinomas and embryonic stem cells to identify genes with malignancy specific expression, genes which are relevant for development into cancer stem cell biomarkers and drug targets. We also aim to identify mutations of the WNT proteome in colorectal cancer, and characterize their implications on tumour stem cells.

STATUS

Detailed transcriptome studies of panels of both embryonal carcinoma (EC) and phenotypically similar, but non-malignant, embryonic stem (ES) cell lines. Genome technologies such as exon microarrays and whole-transcriptome RNA-sequencing have been used to identify genes with malignancy specific expression or transcript structures. From the top-most differentially expressed genes and individual exons between EC and ES cells, we have now validated several genes and transcripts. We did in 2013 publish parts of this work in Stem Cells and Development (Alagaratnam et al., 2013).

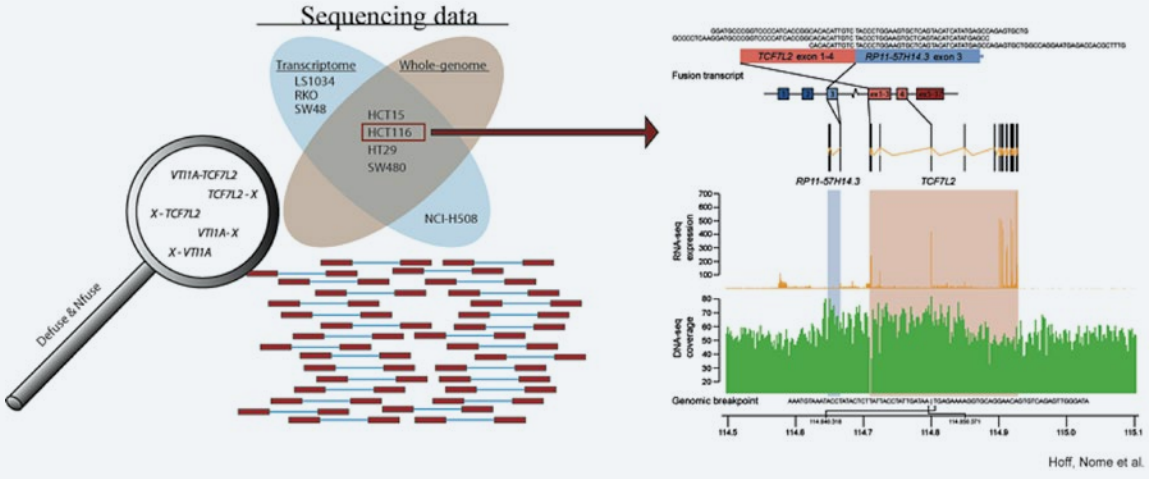
The gene *TCF7L2*, encoding the WNT-effector TCF4, has been identified as partner of a fusion gene in colorectal cancer. We have performed whole-transcriptome sequencing of colorectal cancer, and found a novel fusion partner to *TCF7L2*. Further, from characterization of a clinical colorectal cancer biobank, we found that chimeric RNA molecules involving *TCF7L2* are more frequently expressed than previously anticipated, although at low levels. The relevance for the tumourigenesis of these low-level fusion transcripts is yet to be determined.

INNOVATIVE POTENTIAL

Molecules which are specific to cancer cells with stemness properties can be used both as cancer biomarkers and as targets for therapy. Relevant patent applications are filed, and we work with the hospital's TTO, Inven2, for collaborations with aim of commercialization.

COLLABORATIONS WITHIN THE CENTER

We have collaboration with the Stenmark group on functional cell biology studies, and with the Myklebost group on cancer genomics.



The gene TCF7L2 encodes a transcription factor which is an effector of the stemness related WNT-signalling, a pathway which is commonly altered in colorectal cancers. The Skotheim group have used deep sequencing of RNA and DNA from colorectal cancers, and identified several novel fusion transcripts involving TCF7L2.

HARALD STENMARK - GROUP
INTRACELLULAR TRAFFICKING AND SIGNALLING

AIM

To understand the mode of action of tankyrase inhibitors with high subcellular resolution

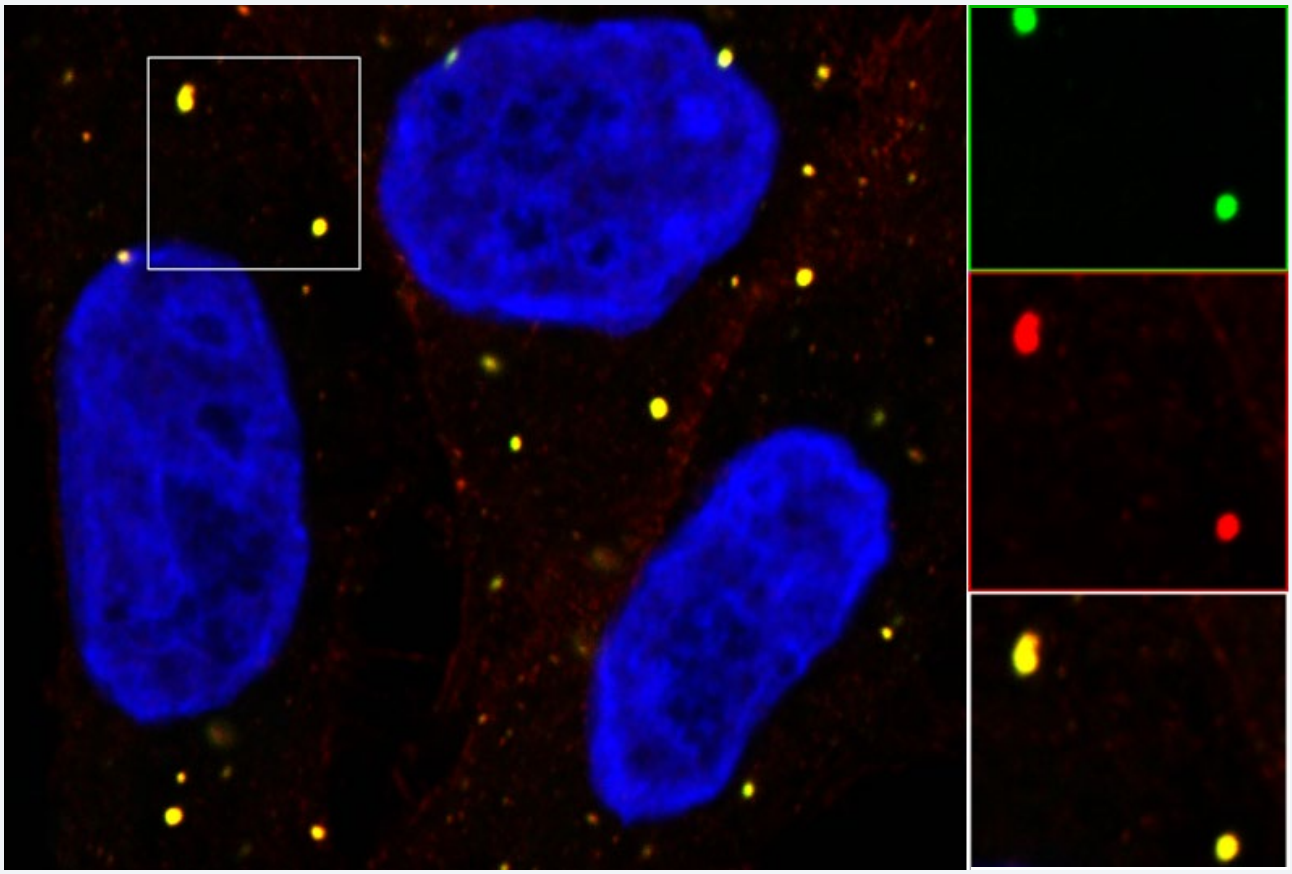
STATUS

We have generated a stable SW480 cell line expressing at low level of GFP-tankyrase. By live-cell microscopy we have analysed the kinetics of formation of "aggregates" of destruction complexes upon inhibitor treatment, and the resolution of these after removal of the inhibitor. Using the same cell line we have also used an affinity purification approach (GFP-trap) to isolate protein complexes associated with GFP-tankyrase in the absence and presence of inhibitor. This analysis has resulted in a number of very interesting hits, whose interaction with Tankyrase we are currently validating.

Our working hypothesis is that β-catenin is degraded in response to tankyrase inhibition by both proteasomes and autophagosomes. Using specific inhibition of these two pathways, we have tested this hypothesis. Our preliminary results indicate that β-catenin is mainly degraded by proteasomes after inhibitor treatment.

COLLABORATIONS WITHIN THE CENTER

We collaborate with S. Krauss-group, T. Sørlie-group and R. Skotheim-group.



Stably GFPTNKS1 expressing SW480 cells incubated with tankyrase inhibitor (G007-LK) for 24 hours. β-catenin (red) colocalizes with GFPTNKS1 (green) in tankyrase inhibitor-induced protein clusters.

THERESE SØRLIE - GROUP
WNT AND Hh SIGNALLING IN BREAST CANCER DEVELOPMENT

AIM

Our group focuses on the interplay between Hedgehog and Wnt signalling pathway and LGR5-dependent signalling on mammary cancer stem cells and tumour development. An important part of our work is to establish transgenic models to study the effect of various types of drugs.

STATUS

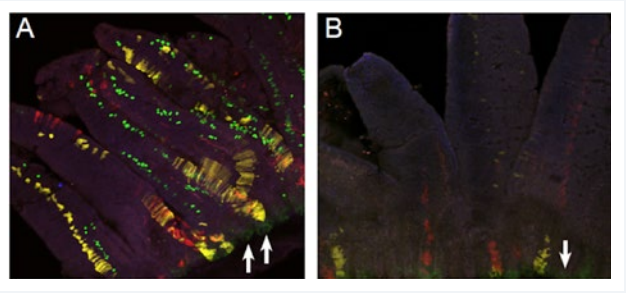
Wnt signalling is important for mammary gland development and is implicated in mammary oncogenesis. LGR5 is a downstream target of Wnt; it marks stem cells with an active Hh pathway in the intestine and skin and recently, Lgr5+ were cells found to be sufficient and essential for mammary gland organogenesis. To address the role of the Hh and Wnt pathways in mammary tumour development, we have established chemically and genetically inducible mouse mammary gland tumour models; more specifically, mice that express the Hh pathway effectors GLI1 or LGR5 in the mammary epithelium. We have serially transplanted GLI1 induced mammary gland tumours for 10 generations and are characterizing the tumours using gene expression, sequencing and copy number analysis. To this end, we have identified several different mutations, some of which appear early in the tumourigenic process, suggesting these might be important for further tumour development and growth. Both Lgr5+ and Lgr5- cells show tumourigenic capacity. Moreover, we have established an *in vivo* model system based on the R26R-confetti strain which enables lineage tracing. We are using this system to study the effect on normal Lgr5+ stem cells of the small intestine upon treatment with the tankyrase inhibitor G007-LK. The results so far suggest that the drug is well tolerated by the mice and the treatment results in reduced lineage tracing from Lgr5+ intestinal stem cells without affecting homeostasis of the small intestine.

INNOVATIVE POTENTIAL

Preclinical studies are essential for testing the efficacy and safety of drugs to be used in humans. The models we have established provide useful tools for such testing of both existing drugs and novel compounds identified in the cancer biomarker projects.

COLLABORATIONS WITHIN THE CENTRE

We collaborate with G. Mælandsmo, S. Krauss, H. Stenmark, and PCI Biotech AS.



G007-LK treatment reduced lineage tracing from Lgr5+ stem cells in the small intestine. Lineage tracing was induced from Lgr5 positive stem cells residing in the bottom of the small intestinal crypts. These cells are labelled with cytoplasmic green fluorescent protein, as indicated with arrows. The linage traced cells in the upper part of the crypts and villi are labelled stochastically with either green (nuclear), yellow (cytoplasmic), red (cytoplasmic) or cyan (membrane) fluorescent protein. The mice were treated with vehicle ***(A)*** *or G007-LK tankyrase inhibitor* ***(B)*** *for 7 days prior to sampling of small intestinal tissue and confocal microscopy imaging.*

Recruitment

DOCTORAL DEGREES

Martin Frank Strand, *Modulating the Hedgehog pathway*, 18th of January 2013, supervised by Stefan Krauss (University of Oslo).

Heidi Maria Namløs, *Studies of genome-wide patterns of gene expression and methylation in osteosarcoma*, 15th of May 2013, supervised by Ola Myklebost (University of Oslo).

Hege Oma Ohnstad, *Novel therapeutic strategies in sarcoma*, 21st of May 2013, supervised by Ola Myklebost (University of Oslo).

Jo Waaler, *Development of specific tankyrase inhibitors for attenuating canonical Wnt/β-catenin signaling*, 8th of November. 2013, supervised by Ondrej Machon and Stefan Krauss (University of Oslo).

Ida Grotterød, *Signal Transduction Induced by S100A4; Activation of NF-kB and Epidermal Growth Factor Receptor*, 10th October 2013, supervised by Gunhild M. Mælandsmo (University of Oslo).

Magnus Røgeberg, *Monolithic and porous layer open tubular nano columns for peptide and protein separation in liquid chromatography – mass spectrometry*, 13th of December 2013, supervised by Elsa Lundanes (University of Oslo).

Mrinal Joel, *Characterization of stem cell-enriched glioblastoma cells in vitro and in xenotypic tissue environments.* 10th December 2013, supervised by Iver Langmoen (University of Oslo).

Evita Maria Lindholm, *Antiangiogenic treatment in breast cancer - identifying responders and mechanisms driving resistance.* 07th June 2013, supervised by Olav Engebråten (University of Oslo).

MASTER DEGREES

Cecilie Aass. *Chromatography and mass spectrometry of phosphatidylinositol phosphates*, 1st of February 2013, supervised by Elsa Lundanes.

Guro Tveit. *Isolation and identification of N-glycoproteins in pancreatic cancer cells by hydrazide chemistry and liquid chromatography tandem mass spectrometry*,14th of February, supervised by Elsa Lundanes.

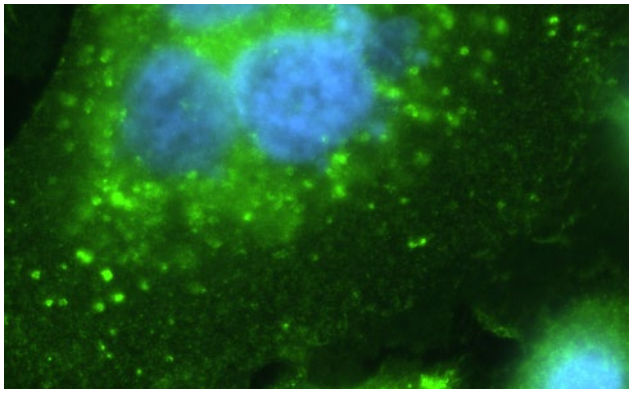
Jagdip Kaur, M.pharm. *Eradication of stem-like cancer cells by photochemical internalization (PCI) of immunotoxins targeting CSPG4 and CD271 in malignant melanoma and breast cancer*, May 2013, supervised by Pål K. Selbo.

Marianne Kausberg, M.pharm. *Photochemical internalization of immunotoxins targeting the cancer stem cell markers CD44 and CD90 in carcinoma and sarcoma*, May 2013, supervised by Pål K. Selbo.

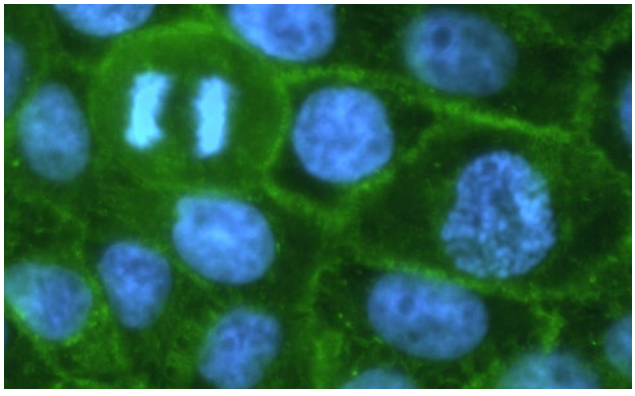
Vibeke Wethe Rognlien, *The role of the metastasis promoting protein S100A4 during EMT in mammary gland epithelial cells"*, 21st of May, 2013, Oslo and Akershus University College of Applied Science, supervised by Kristin Andersen.

Siri Olsen. *Evaluation of the hydrazide enrichment method for N-linked glycoproteins in cancer cells by nano liquid chromatography mass spectrometry*, 13th of June 2013, supervised by Elsa Lundanes.

Lene Grutle. *Monolithic precolumns and porous layer open tubular columns for separation of peptides and digested proteins*, 28th of June 2013, supervised by Elsa Lundanes.



E-cadherin staining (green) on pancreas carcinoma cells BxPC-3 with a targeted deletion of the gene encoding CTNNB1 (β-catenin). *DAPI staining (blue) of the cell nucleus. Photo by Petter A. Olsen.*



E-cadherin staining (green) on wild type pancreas carcinoma cells BxPC-3 (β-catenin *gene is not deleted).*
DAPI staining (blue) of the cell nucleus. Photo by Petter A. Olsen.

Awards

EXCELLENT RESEARCHER AWARD

Oslo University Hospital is every year awarding researchers within the hospital for outstanding research. The Excellent Researcher Award for 2013 went to Harald Stenmark.

Harald Stenmark

RIMINGTON PRIZE

In November 2013 Pål K. Selbo (PCI Biotech/ Department of Radiation Biology, OUS) received the Claude Rimington Commemorative Prize.

Norwegian Society for Photobiology and Photomedicine (NOFFOF) awards the Rimington Prize to distinguished researchers in the field of photobiology and photomedicine. One of the criteria to earn the prize is to act as an ambassasador for photobiology, a role Pål K. Selbo has fulfilled excellently. During the ceremony Selbo gave his Rimington-speech; "Shining light on the dark side of cancer: Photochemical internalization of cancer stem cell-targeting therapeutics".

Pål K. Selbo and Prof. Hanne Hjorth Tønnesen, leader of the prize committee.

Professor Claude Rimington (1902-1993) was a British biochemist who devoted his work to the study of porphyrines and the photosensitization of farm animals.

M.J.E. GOLAY AWARD

At the 37th International Symposium on Capillary Chromatography in Palm Springs May 14-16, Tyge Greibrokk was awarded the M.J.E. Golay Award for his "pioneering work in the development of capillary chromatography". The awardee was presented by the chairman of the Award Committee, Professor M. V. Novotny from Indiana University.

Tyge Greibrokk with the M.J.E. Golay Award for his "pioneering work in the development of capillary chromatography".

International cooperation

INTERNATIONAL NETWORKS

European Network for Oxysterol Research (ENOR); Steven Wilson and PhD student Hanne Røberg-Larsen are active members.

Euro PDX consortium. The EurOPDX Consortium is an initiative of translational and clinical researchers from 14 cancer centers and universities across nine European countries, with the common goal of creating a network of clinically relevant models of human cancer, and in particular patient-derived xenograft (PDX) models. It is headed by Sergio Roman-Roman, Institute Curie, Paris, France (http://mct.aacrjournals.org/content/12/11_Supplement/A8.short?rss=1).

INTERNATIONAL COLLABORATIONS

Jens von Kries, Berlin Leibnitz Institute, Germany. Academic: siRNA and compound screening.

TC Scientific, Alberta, Canada. Industry: Chemical synthesis.

Genentech Inc., San Francisco, USA. Industry: Compound validation.

Nai-Wen Chi, University of San Diego, USA. Academic: Biochemistry of TNSK inhibition.

Lari Lehtiö, Univeristy of Oulu, Finland. Academic: Crystallography.

Ondrej Machon, University of Prague, Czech Republic. Academic: Animal models for CRC.

Mani Sendurai, MD Anderson Cancer Center, USA. Academic: The role of HMGA2 and Let-7 miRNA in EMT and cancer.

Andy Bader, MiRNA Terapeutic, USA. Industry: The role of Let-7 miRNAs and mir-34 in sarcoma and breast cancer.

David Thomas, PeterMacCallum Cancer Center, Australia. Academic: Function of liposarcoma stem cells.

Peter W. Andrews, Centre for Stem Cell Biology and the Department of Biomedical Science, University of Sheffield, Sheffield, UK, Academic: Pluripotency phenotypes and genomics of embryonal carcinomas.

Rune Toftgård, Karolinska Institute, Stockholm, Sweden. Academic: on development of breast cancer using transgenic mouse models.

Raoul Kuiper, Laboratory for morphologic phenotype analysis, Karolinska University Hospital, Stockholm, Sweden. Academic: on comparative pathology.

Ole W. Petersen, Dep. of Cellular and Molecular Medicine, University of Copenhagen, Denmark. Academic: on intra-tumour heterogeneity and tumour markers.

Peter James, Lund University, Sweden. Academic: on proteomic characterization of cells from xenograft tumour models representing different tumour subtypes.

Elisabetta Marangoni, Curie Institute, Paris, France. Academic: on studies of orthotopic breast cancer xenografts and exchange of orthotopic breast cancer models of luminal and basal-like breast cancer.

Paul Cotton, Curie Institute, Paris, France. Academic: Exchange of orthotopic breast cancer models of luminal and basal-like breast cancer.

Soldano Ferrone, Mass General Hospital/Harvard Medical School, USA. Academic: Targeting of CSPG4 in triple negative breast cancer and malignant melanoma.

Michael Rosenblum, MD Anderson Cancer Center, USA. Academic: Construction of CSC-targeting therapeutics.

Thorarinn Gudjonsson, Biomedical Centre, University of Iceland, Reykjavik, Iceland. Academic: Collaborate on the role of S100A4 in EMT and stemness of mammary epithelial cells, and the role of S100A4 signalling through EGFR.

Bernhard Kuster Technische Universität München, Germany. Academic: related to phosphoanalysis of cell samples using in-house developed nano-LC chromatographic columns. Through 2013 we have sent prepared columns and analyzed samples on our system.

National cooperation

NATIONAL COOPERATION

Norwegian Stem Cell Center – Mesenchymal Stem cells. Academic: mesenchymale stem cells.

Tone Frost Bathen, Dept. of Circulation and Medical Imaging, NTNU. Academic: MR spectroscopy of breast tumours.

Olav Engebråten, Dep. of Tumor Biology and Oncology, Oslo University Hospital. Academic: Tumour heterogeneity and the use of transgenic mouse models for studying breast cancer development and response to treatment.

Partner in OSBREAC and K.G. Jebsen Center for Breast Cancer Research: Headed by Rolf Kåresen, (OSBREAC – Oslo Breast Cancer Research Consortium), and Anne-Lise Børresen-Dale (K.G. Jebsen Center for Breast Cancer Research). Academic: breast cancer research.

Analytical chemistry at School of Pharmacy, University of Oslo within the platform Bioanalytics@UiO. Academic: Collaboration in development of analytical chemistry technology.

Communication and dissemination activities

MEDIA COVERAGE

NEWSPAPERS/RESEARCH MAGAZINES

Sci-Bx (Science Business Exchange)
Analysis: Cover Story Cancer, *SciBX* 6(15); doi:10.1038/scibx.2013.353, Published online 18th of April 2013, *Targeting tankyrase*, by Lev Osherovich, Senior Writer.
Researchers from SFI CAST Innovation Center at the Oslo University Hospital and the University of Oslo, led by Prof. S. Krauss, in cooperation with Roche's Genentech Inc. Unit, have developed several selective inhibitors of tankyrases TNKS and TNKS2. **http://www.nature.com/scibx/journal/v6/n15/full/scibx.2013.353.html**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Analysis: Cover Story - Cancer
SciBX 6(15); doi:10.1038/scibx.2013.353
Published online April 18 2013
Targeting tankyrase
by Lev Osherovich, Senior Writer
Researchers from the University of Oslo and Roche's Genentech Inc. unit have developed several selective inhibitors of tankyrases TNKS and TNKS2, two druggable targets in the otherwise hard-to-hit WNT pathway. The lead compound has been licensed to Odin for colorectal cancer.
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Aftenposten, *Mange frykter at oppblomstringen av nye bedrifter innen avansert kreftmedisin i Norge vil stoppe opp.* Mister gode hoder til oljebransjen. Interview with, among others, O. Myklebost.

VG, *6 nye våpen mot kreft. Norske forskere om den nye kreftbekjempelsen,* Interview with, among others G. M. Mælandsmo regarding the project "MetAction – Actionable targets in cancer metastasis. From bed to bench to byte to bedside", 5th of April 2013

VG, *Blodprøve oppdager kreft,* artikkel om sirkulerende svultsDNA. Comments by O. Myklebost, November 2013.

Apollon 4 2013, *Beregner seg frem til ny kreftbehandling,* O. Myklebost, Interview about the Norwegian Research Council projects; Personalised cancer medicine. http://www.apollon.uio.no/artikler/2013/4_kreft_myklebost.html

INTERNET

Forskningsrådet.no, *Tester skreddersydd kreftbehandling*, Featuring: G.M. Mælandsmo, Flatmark, Ree, Børresen-Dale, 1st of March 2013. Writer: Elin Fugelsnes. http://www.forskningsradet.no/no/Nyheter/Tester_skreddersydd_kreftbehandling/1253984175483?lang=no

Forskning.no, *Kreftceller kler seg ut som stamceller*, S. Krauss, 3rd of Mach 2013, http://www.forskning.no/artikler/2013/februar/349867

Forskning.no, *Tester skreddersydd kreftbehandling*, G. M. Mælandsmo, 8th of March 2013, http://www.forskning.no/artikler/2013/januar/344200

Forskning.no, *Kartlegger kreftgenene*, O. Myklebost, 11th of May 2013, Interview about the Norwegian Research Council projects; Personalised cancer medicine.
http://www.forskning.no/artikler/2013/mai/356227

Forskning.no, *Vil bekjempe kreft med lys*, P.K. Selbo/PCI-Biotech, 13th of May 2013
http://www.forskning.no/artikler/2013/mai/356576
(same in **NRK.viten**).


Vil bekjempe kreft med lys
En intens lysstråle slipper giftstoffene løs i slumrende kreftstamceller.
Arnfinn Christensen
Journalist
Mandag 13. mai 2013
kl. 05:00
Monica Bostad og Pål Selbo studerer kreftceller i petriskåler på Senter for forskningsdrevet innovasjon ved Radiumhospitalet. (Foto: Arnfinn Christensen, forskning.no.)

Forskning.no, *Beregner seg frem til ny kreftbehandling*, O. Myklebost, 11th of November 2013, Interview about the Norwegian Research Council projects; Personal cancer medicine. http://www.forskning.no/artikler/2013/november/371982

VG-nett, *Blodprøve oppdager kreft*, O. Myklebost and L. Meza-Zapeda, 24th of november 2013, http://www.vg.no/helse/artikkel.php?artid=10133266


VG FORBRUKER

Blodprøve oppdager kreft

Myklebust og Leonardo Meza-Zapeda på Radiumhospitalet. Foto: NYEBILDER.NO

Dagensmedisin.no, *Helseprioriteringene blir enda mer krevende*, O. Myklebost, 3rd December 2013, http://www.dagensmedisin.no/nyheter/--helseprioriteringene-blir-enda-mer-krevende/

Cosmos, No.51, 2013, *Hope from within*, http://www.cosmosmagazine.com/issue/issue-51-big-data/, IA. Langmoen.

Cancerstemcell.no, SFI-CAST homepage on Internet www.cancerstemcell.no is used for continuous publishing and covering of news and events in SFI-CAST.

BOOKS

KREFTER: *Åtte fortellinger*, Ola Henmo & Paul Aadnestad. Portrett av O. Myklebost Kreftforeningen, Gyldendal 2013.

Appendix

PERSONNEL

PRINCIPAL INVESTIGATORS

Stefan Krauss
Ola Myklebost
Elsa Lundanes
Gunhild Mari Mælandsmo
Harald Stenmark
Iver Arne Langmoen
Rolf I. Skotheim
Therese Sørlie
Anders Høgset

ADMINISTRATIVE MANAGER

Piritta Nyberg
Line Mygland

SENIOR SCIENTISTS

Einar O. Vik-Mo
Leonardo Meza-Zepeda
Lina Prasmickaite
Petter Angell Olsen
Pål K. Selbo
Ragnhild A. Lothe
Steven Ray Wilson

POSTDOCTORAL RESEARCHERS

Andrey Voronkov
Biljana Stangeland
Else Munthe
Ellen Tenstad
Eva Wessel Stratford
Gisle Berge
Iwona Grad
Jennifer L. Dembinski
Jens Henrik Norum
Kristin Andersen
Martin F. Strand
Nina Marie Pedersen
Nina Therese Solberg
Sharmini Alagaratnam
Viola Lobert

PHD STUDENTS

Anastassia Serguienko
Andreas M. Hoff
Awais Mughal Ahmad
Cecilie Sandberg
Elin Johnsen
Evita Maria Lindholm
Hanne K. Hustoft
Hanne Røberg-Larsen
Hege Oma Ohnstad
Heidi Maria Namløs
Ida Grotterød
Ingrid Johanne Bettum
Jo Waaler
Kaja Lund
Magnus Røgeberg
Marius Strømbo Eng
Monica Bostad
Mrinal Joel
Nirma Skrbo
Tor Espen Thorvaldsen
Tore Vehus

MASTER STUDENTS

Caroline Vesterdal
Cecilie Aass
Guro Tveit
Hong Diem Nguyen
Jagdip Kaur
Kirsten Strømme
Kristoffer Arnesen
Lars Folven
Lene Grutle
Marianne Kausberg
Marie Elise Engkvist
Ole Kristian Brandtzæg
Rena Record
Siri Olsen
Vibeke Wethe Rognlien

TECHNICAL PERSONNEL

Anna-Berit Wennerström
Anne Cathrine Bakken
Birthe Mikkelsen
Dorna Mishagian
Jeanette Daffinrud
Kobra Sultani
Menaka Sathermugathevan
Monika Gelazauskaite
Nomdo A.C. Westerdaal
Petros Gebregziabher
Russel Castro
Solveig Pettersen
Tove Øyjord
Victoria Edwards

Statement of Accounts

FUNDING AND COST

Funding

		Amount
The Research Council	The Norwegian Research Council	10 895
The Host Institution	Oslo University Hospital HF	10 503
Research Partners	University of Oslo	1 364
Enterprise partners	PCI Biotech AS	1 330
	Affitech Research AS	400
	Total	24 422

All figures in 1000 NOK

Costs

		Amount
The Host Institution	Oslo University Hospital HF	19 175
Research Partners	University of Oslo	2 760
Enterprise partners	PCI Biotech AS	1 387
	Affitech Research AS	400
	Odin Therapeutics AS	500
	IncuCyte System Package	200
Total		24 422

All figures in 1000 NOK

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P.A. Olsen, Implications of targeted genomic disruption of beta catenin in BxPC3 pancreatic adenocarcinoma cells, **Wnt Symposium 2013**, July 14 – 16, Heidelberg, Germany, **Poster**.

J. Waaler, The tankyrase-specific inhibitor JW74 affects cell cycle progression and induces apoptosis and differentiation in osteosarcoma cell lines, **Wnt Symposium 2013**, July 14 – 16 Heidelberg, Germany, **Poster**.

N. Solberg, P.A. Olsen, A. Urbanucci, K.Lund, I.G. Mills and **S. Krauss,** Epigenetic analysis of β-catenin deficiency in the pancreatic adenocarcinoma cell line BxPC-3, **Wnt Symposium 2013**, July 14 – 16, Heidelberg, Germany, **Poster**.

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BOOKS

KREFTER: Åtte fortellinger, Ola Henmo & Paul Aadnestad. Portrett av O. Myklebost Kreftforeningen, Gyldendal 2013.

CONTACT INFORMATION

ACADEMIC PARTNERS

Stefan Krauss – Centre Director
Unit for Cell Signalling
Dept. of Microbiology
Rikshospitalet
Oslo University Hospital
stefan.krauss@rr-research.no
+ 47 23 07 90 17

Ola Myklebost – Co-director
Dept. of Tumor Biology
Institute for Cancer Research
The Norwegian Radium Hospital
Oslo University Hospital
ola.myklebost@imbv.uio.no
+ 47 22 78 17 79

Iver A. Langmoen
Dept. of Neurosurgery
Ullevål University Hospital
Oslo University Hospital
iver.a.langmoem@rr-research.no
+ 47 23 01 54 62

Rolf I. Skotheim
Dept. of Cancer Prevention
Institute for Cancer Research
The Norwegian Radium Hospital
Oslo University Hospital
rolf.i.skotheim@rr-research.no
+ 47 22 78 17 27

Elsa Lundanes
Dept. of Chemistry
University of Oslo
elsa.lundanes@kjemi.uio.no
+ 47 22 85 55 53

Gunhild M. Mælandsmo
Dept. of Tumor Biology
Institute for Cancer Research
The Norwegian Radium Hospital
Oslo University Hospital
gunhildm@rr-research.no
+ 47 22 78 18 79

Harald Stenmark
Dept. of Biochemistry
Institute for Cancer Research
The Norwegian Radium Hospital
Oslo University Hospital
stenmark@ulrik.uio.no
+ 47 22 78 18 18

Therese Sørlie
Dept. of Genetics
Institute for Cancer Research
The Norwegian Radium Hospital
Oslo University Hospital
therese.sorlie@rr-research.no
+ 47 22 78 13 64

INDUSTRY PARTNERS

Affitech Research AS
Michael Braunagel
Oslo Research Park
Gaustadalléen 21
N-0349 Oslo, Norway
m.braunagel@affitech.com
+ 47 22 95 88 63

ODIN Therapeutics AS
Olav Steinnes, CFO
Oslo Research Park
N-0349 Oslo, Norway
olav.steinnes@odintherapeutics.com
+47 22 84 33 41

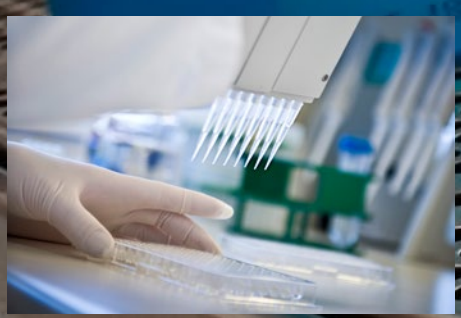
PCI Biotech AS
Anders Høgset, CSO
Hoffsveien 48
0377 Oslo, Norway
anders.hogset@pcibiotech.no
+ 47 23 25 40 03

SCIENTIFIC ADVISORY BOARD

Thorarinn Gudjonsson
Biomedical Center
University of Iceland
tgudjons@hi.is
+354 5254827

Henrik Semb
Copenhagen University
Danish Stem Cell Center
semb@sund.ku.dk
+ 45 23 30 20 52

Jens Peter von Kries
Institut für Molekulare
Pharmakologie
kries@fmp-berlin.de
+ 030 94 06 29 82



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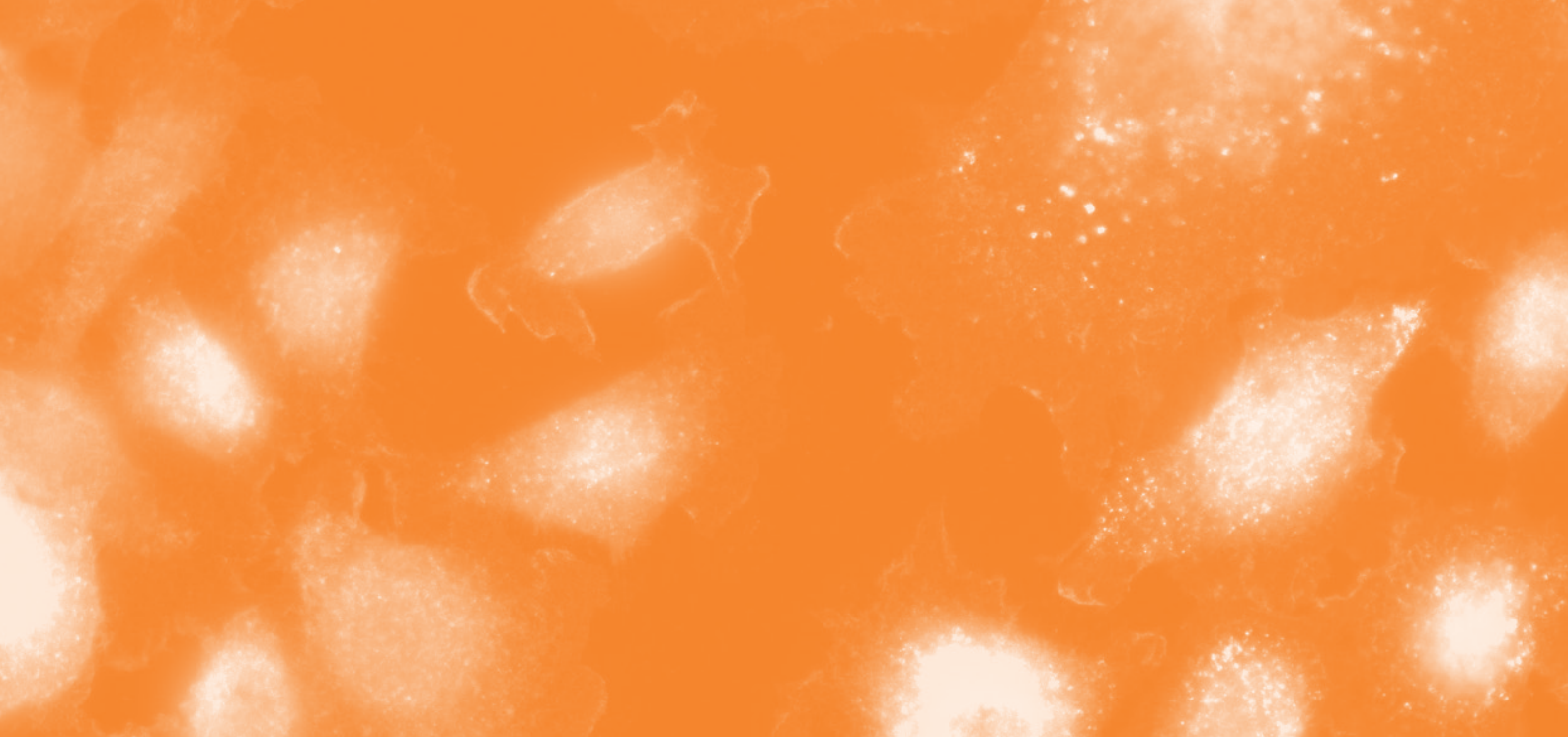

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SFI CAST

Oslo University Hospital HF, Rikshospitalet
Domus Medica II
Gaustadalleèn 34
0372 Oslo, Norway

Director
Prof. Stefan Krauss
stefan.krauss@rr-research.no
+47 23 07 90 17

Co-director
Prof. Ola Myklebost
ola.myklebost@imbv.uio.no
+47 22 78 17 79

Administrative Manager
Line Mygland
line.mygland@rr-research.no
+47 23 07 90 16

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