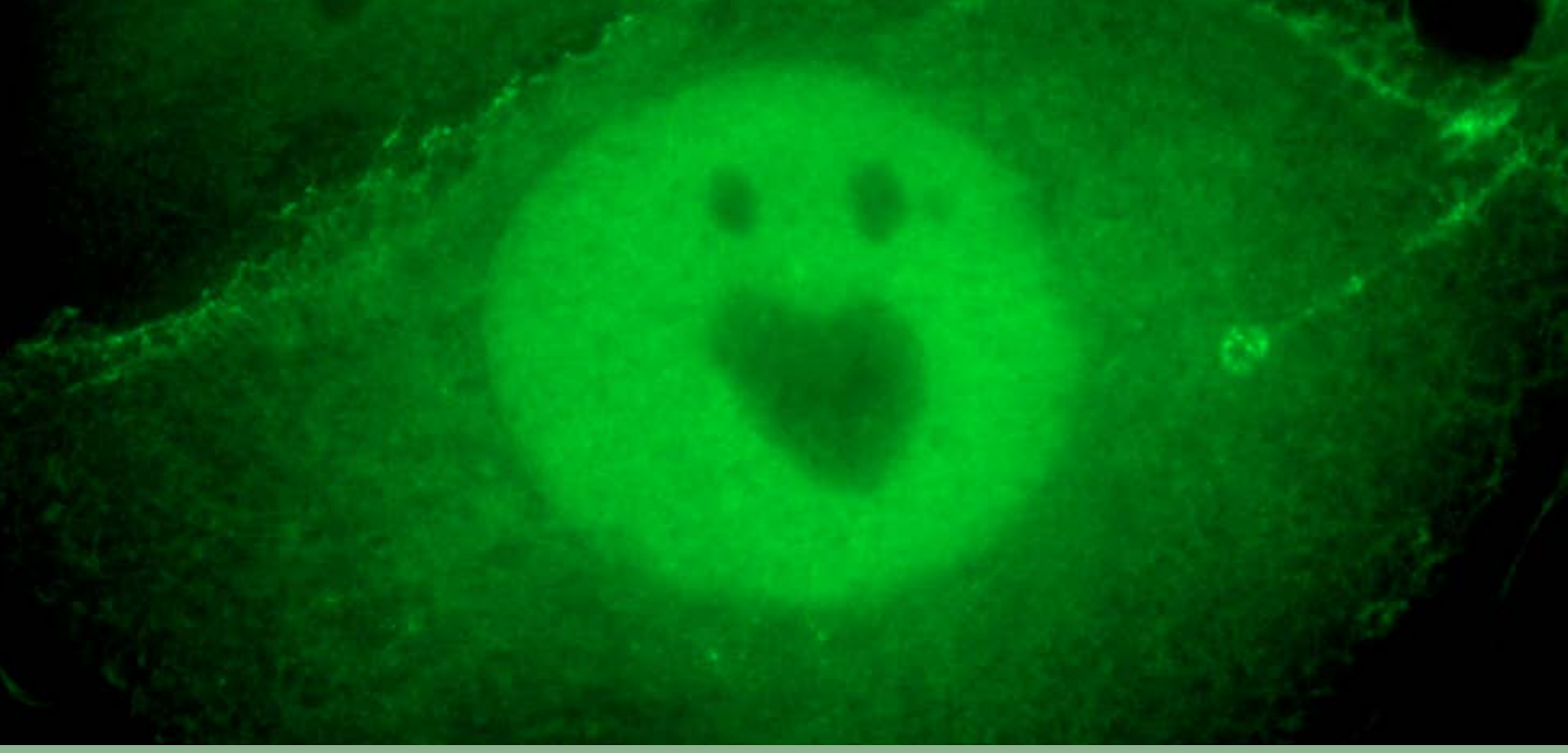


2011 Annual Report

CAST
CANCER • STEM CELL
INNOVATION CENTER

Established by the Research Council of Norway

sfi Centre for Research-based Innovation

Oslo University Hospital
Norwegian Radium Hospital

UiO : University of Oslo

Introduction

SFI-CAST has been established by the Research Council of Norway based on the unique strength of its concept and its strategic position at the crosslink between the internationally highly reputed Norwegian academic cancer research and an emerging cluster of innovative biotechnology industries.

Using the stem cell tool kit to understand cancer - the concept behind SFI-CAST - comprises a major advance in cancer research. After years of gradual improvements in treating cancer, it is now apparent that the concept of stemcellness in cancer provides a solid basis for major leaps in both diagnosis and treatment in the near future. It is fascinating to see how a novel scientific concept, as described in the initial centre application, turns into solid scientific evidence and subsequently forms the basis for product development with high innovative potential and commercial value.

In the 5 years of its existence, SFI-CAST researchers have established a portfolio of tools that comprise a solid basis for innovative industry development. Moreover, a platform of validated cancer cell lines is emerging that will serve as a standard for industrial SFI-CAST projects. Our lead drug discovery projects have gained maturity and several chemotypes are currently evaluated by industry partners. One spin off company based on SFI-CAST technology is emerging, and a second spin off is on the drawing board. Finally, a pioneering clinical trial based on an in house developed immunotherapy protocol is in progress.

We have no illusions: very substantial scientific and commercial challenges lie ahead of the centre. We face these challenges with confidence that the chosen strategy is correct.

We would like to thank the Research Council of Norway for its support in the SFI-CAST innovation centre, and 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 enthusiastically committed to the implementation of our commercialization strategy.

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 develop novel potential cures at the cutting edge of science and technology.

Stefan Krauss
Director

Ola Myklebost
Co-director

Cover front: *DMSO treated SW480 cell (colon cancer cell line) stained with β-catenin in green (Nina Therese Solberg).*
Cover back: *Super-resolution image of a cancer cell, with DNA in blue, endosomes in red and clathrin in green (Ellen Skarpen and Kay Schink).*

Table of contents

Summary

During the last decade, cancer research has gained substantial knowledge by applying a multidisciplinary developmental understanding of tumour formation and progression, as well as a precise analysis on individual differences in tumours with 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 including cell proliferation, invasiveness and metastatic potential. The temporal and spatial dynamics of heterogeneity appear to be directed by autocrine and paracrine short-and long range effects. Accordingly, evidence is mounting that drug efficacy can be strongly attenuated by the heterogeneous nature of tumour sub-populations, by interactions between those populations itself and the local environment, the immune system and systematic variations in long-range signalling.

The emergence of developmental and stem cell tools, combined with advanced validated high throughput analytical tools has dramatically enhanced our ability for addressing fundamental questions in oncology. We are now finally able to generate the necessary understanding for addressing and possibly predicting tumours spread, relapse and therapeutic efficacy in *ex vivo* systems as basic tools for drug discovery.

SFI-CAST is an integrated biomedical innovation centre that works towards the identification and characterization of stem cell parameters in tumours. SFI-CAST develops innovative approaches for finding small drugs and antibodies that address specifically stem cell issues in cancer.

Photo: Affitech Research AS

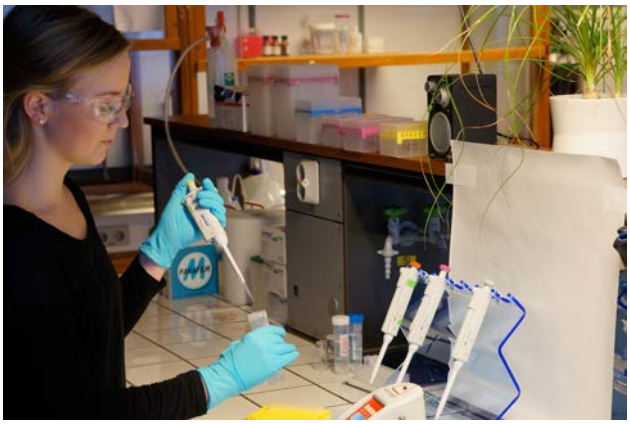
PhD-student Viola Lobert

Anne Cathrine Bakken and Andreas Midbøe Hoff

Vision/objectives

The SFI-CAST biomedical innovation centre works towards identifying new therapeutic intervention points in stemcell pathways and to test these in cancer. Based on validated intervention points, novel therapeutic reagents are developed. A main research focus of the research centre is on Wnt/β-catenin signalling.

Hanne Håberg Mørk, master student from NTNU



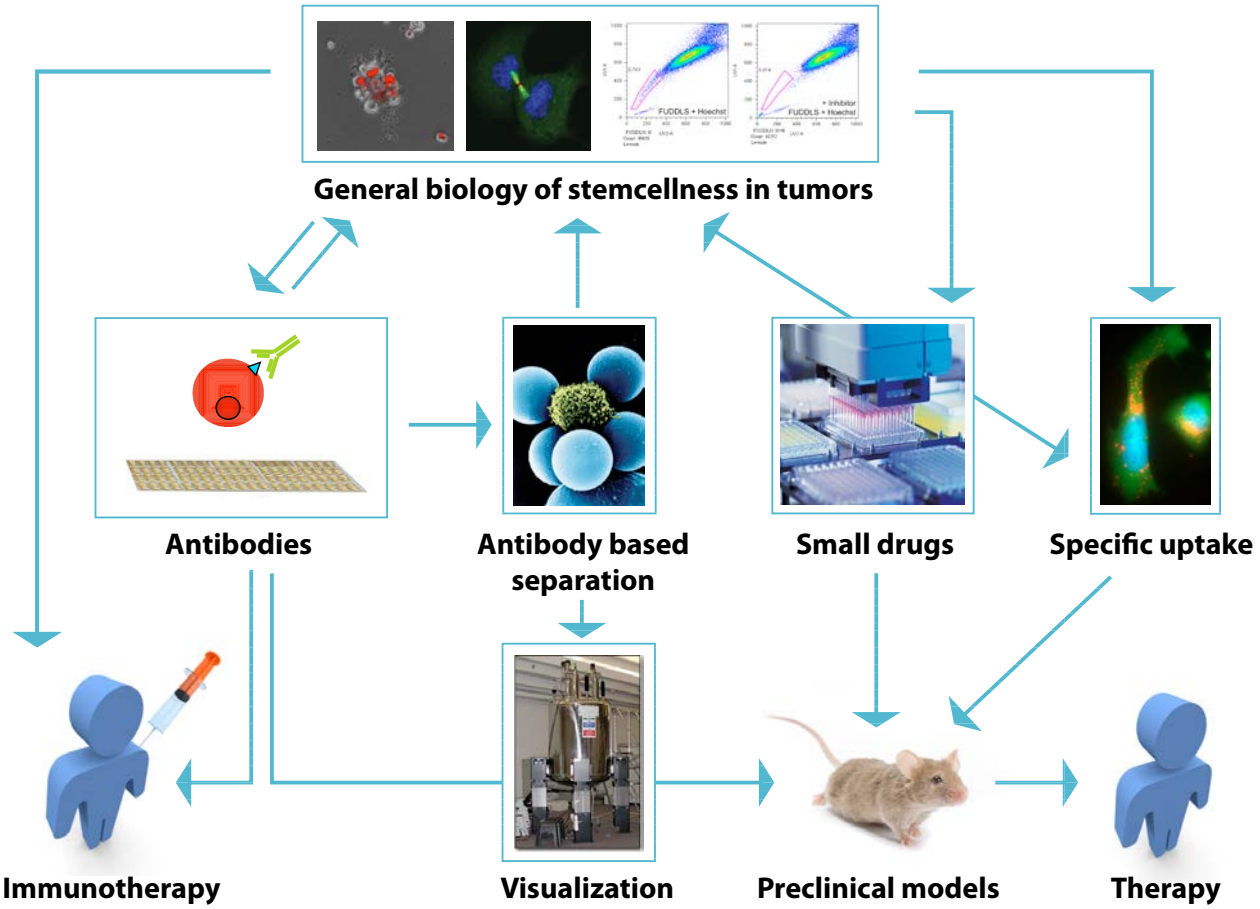
Working in the lab

Sharmini Alagaratnam

Research plan/strategy

The SFI-CAST biomedical innovation centre has a work program aimed at advancing basic research on stemcellness in cancer and tumour stem cells to experimental clinical trials. Based on the outcome of this effort, several interactive biotechnology pipelines are fed. (i) Human therapeutic antibodies against drug resistant sub-populations of cells in a tumour are explored with industry partner Affitech AS. (ii) Stem cell pathways are used for differential high throughput screens for novel drugs. (iii) Ways to find improved immunotherapy protocols and targets are being explored and tested. (iv) Specific protocols are tested for improved therapeutic photo-internalisation with industry partner PCI Biotech ASA.

A major focus of the centre is translational research. Partners at the Norwegian Radium Hospital have been responsible for more than 25 phase I/II clinical trials of cancer vaccines and immune-gene therapy, and will cooperate with clinicians involved in the project. This ensures a swift start of the translational aspect as well as providing clinical material for the individual work programs.



Scientific Activities and Results

Scientific Highlights

In 2011, 40 peer reviewed cancer related articles were published by CAST members. Several articles were published in high impact journals. Numerous articles were co-authored by several members of the CAST consortium.

A comparative study of the structural organization of spheres derived from the adult human subventricular zone and glioblastoma biopsies was carried out by Vik-Mo et al... and Langmoen and published in Exp Cell Res (2011 Apr 15;317(7):1049-59. Epub 2011 Jan 1).

It was shown that the MDM2 antagonist Nutlin-3a potentiates anti tumour activity of cytotoxic drugs in sarcoma cell lines by Ohnstad et al... and Myklebost. The work was published in BMC Cancer (2011 May 30;11:211:1-11. doi: 10.1186/1471-2407-11-211).

Cargo-dependent degradation of ESCRT-I as a feedback mechanism to modulate endosomal sorting was described by Malerød et al...and Stenmark. The work was published in the journal Traffic (2011 Sep;12(9):1211-26. doi: 10.1111/j.1600-0854.2011.01220.x. Epub 2011 Jun 13).

Cell polarity and migration: emerging role for the endosomal sorting machinery was reviewed by Lobert and Stenmark and published in the journal Physiology (2011 Jun;26(3):171-80).

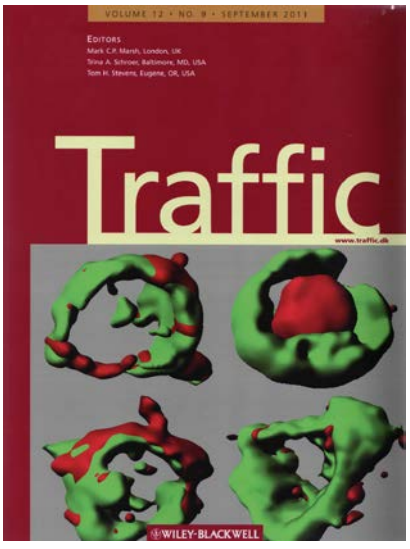
SPG20, encoding a regulator of cytokinesis, was identified as a novel biomarker for early detection of colorectal cancer was reported by Lind et al... and Lothe and published in Oncogene (2011 Sep 15;30(37):3967-78. doi: 10.1038/onc.2011.109. Epub 2011 Apr 18).

A genome wide single cell analysis of chemotherapy resistant metastatic cells was carried out for gastroesophageal adenocarcinoma and published by Hjortland et al... and Howig including Myklebost as co-author. The work was published in BMC Cancer (2011 Oct 20;11:455).

Osteopontin was described as an important downstream effector of S100A4-mediated invasion and metastasis by Berge et al... and Mælandsmo and published in Int J Cancer. (2011 Aug 15;129(4):780-90. doi: 10.1002/ijc.25735. Epub 2011 Mar 11).

Novel synthetic antagonists of canonical Wnt signalling were identified. The work was published by Waaler et al.... and Krauss in Cancer Research (2011 Jan 1;71(1):197-205).

A novel synthetic smoothened antagonist was identified by Strand et al...and Krauss and published in PLoS One (2011;6(6):e19904. Epub 2011 Jun 15).



Front page of"Traffic" where the CAST article "Cargo-dependent degradation of ESCRT-I as a feedback mechanism to modulate endosomal sorting", Malerød L et.al. is highlighted.

Innovative Highlights

Two small molecular tankyrase inhibitors were further advanced with the aim of developing a therapeutic intervention for reducing Wnt/β-catenin signalling in solid tumours (patent pending). One of the chemotypes has reached clinical candidate status (Krauss-group).

Links between Wnt inhibition, snRNA and differentiation were identified by Myklebost-group, and possible therapeutic implications have been investigated.

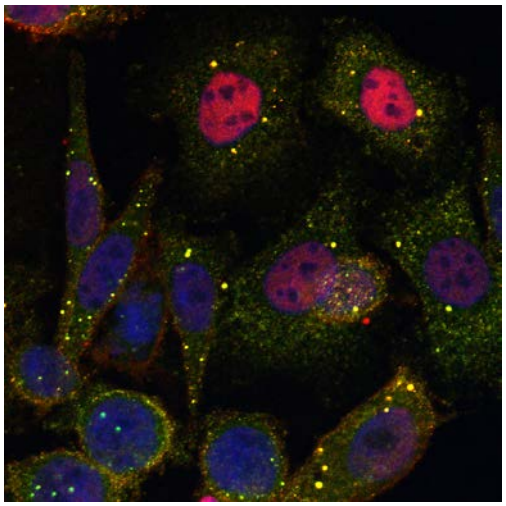
Based on development of biomarkers suitable for early detection of colorectal cancer in the groups of Lothe and Skotheim, Inven2, on behalf of Oslo University Hospital, has recently signed a licence agreement with Oxford Gene Technology http://www.inven2.com/en/oxford-gene-technology]. In addition, the same groups have filed patent applications on two genetic signatures, named ColoGuideEx and ColoGuidePro, with prognostic value in different stages of colorectal cancer. This project is further supported by Innovation funding from the Health Region of South-Eastern Norway.

A clinical immune vaccination trial on Glioblastoma was advanced. The clinical phase I trial targeting cancer stem cells in glioblastoma patients has recruited 18 of 20 patients. The preliminary results show the feasibility of producing autologous tumour stem cells for clinical intervention. We have through mRNA loaded dendritic cells been able to induce an immune response in most patients. This intervention we so far consider safe as no major adverse events have been identified. Also, the possible effect of the immunotherapy on progression free survival seems promising (Langmoen-group).

Substantial improvement of automated sample preparation/chromatography with in-house developed AFFL-SPE-LC (patent applied) and development of high speed LC-MS for high resolution proteomics using silica based monolithic LC columns at high temperature was achieved by Lundanes-group.

Disulfonated tetraphenyl chlorine (TPCS2a), a novel photosensitizer developed for clinical utilization of photochemical internalization was published by PCI Biotech.

PCI Biotech has successfully completed a clinical phase I/II study with Amphinex in combination with the well-established cytotoxic agent bleomycin.



SW480 cells stained with anti-axin and anti-b-catenin upon JW270 treatment (Nina Marie Pedersen)

CAST Core Facilities

The SFI-CAST animal and cell sorting core facility was established thanks to a grant from Radium Hospital and was serviced by four technical employees through 2011. The facility provides advanced cell and animal technology, like high-speed flow-cytometry assisted cell sorting, and cell isolation, propagation, and analysis, as well as a NOD/SCID colony for establishment of xenografts and *in vivo* experiments. In addition to advanced flow sorting equipment (Aria, BD), the core also has also acquired an automatic colony counter (GelCount, Oxford Optronix), a time-lapse equipment (Incucyte, Essenbio) and a gentleMACS tissue Dissociator (Milteny Biotec).

The main goal of the cell culture platform is to establish a collection of CSC model systems for cancer types that are frequent and for which there is a lack of good therapies. The CSC model lines will be characterized for stem cell characteristics like expression of stem cell-specific cell surface markers, aldehyde dehydrogenase activity, the capacity to exclude drugs, and their proliferative capacity by label retention. Stem-cells will be evaluated by the ability to grow anchorage-independent as colonies in 3D cultures.

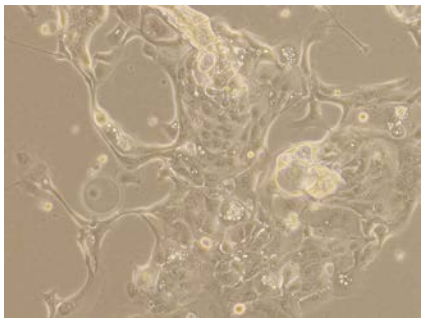
In 2011 we have focused on stem cell models from pancreatic adenocarcinoma. First, we generated 8 xenografts from patient material from surgical removal of primary tumours, which can be serially passaged in NOD/SCID gamma-null mice. In collaboration with the experienced pancreatic pathologist that provided the patient material from Ullevål, we have confirmed that the generated xenografts have high similarity to original patient tumour material, and that *in vivo* propagation of the tumours maintains their structural integrity.

We have successfully established long-term *in vitro* cultures from four of these xenografts. The generated cell lines harbour tumourigenic cells, shown by their ability to regenerate tumours *in vivo*, after injection of as few as 10 000 cells in NOD/SCID mice. These cell lines have been thoroughly characterized for expression of cell surface markers and stem cell characteristics over time in *in vitro* cultures.

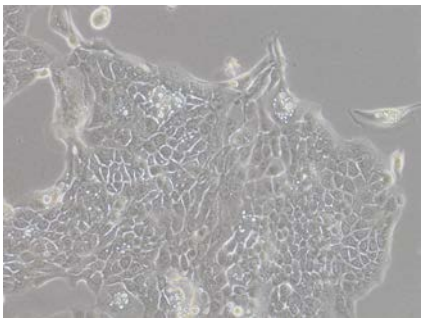
These pancreatic xenograft and cell models are CAST proprietary and available for all CAST members. In particular, these models could be employed to evaluate PCI labelled EpCam antibodies as the expression of EpCam is high in all the cell lines. In addition, they could also be used to test potential pancreatic drugs.

Personnel 2011

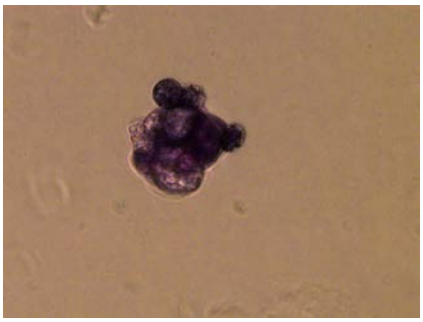
Anna Berit Wennerström, Menaka Sathermugathevan (Cell technicians), Petros Gebregziabher (Animal technician), Nomdo A.C. Westerdaal (Flow sorting technician), Else Munthe (Project leader, Postdoc). MS and EM were supported by industry contributions.



Cell line



Pancreatic Cell Line



ppa

Organisation

Management and members

The partners of SFI-CAST have in 2011 consisted of nine research groups and two industry partners. A third industry partner is expected to be granted SFI-CAST membership in January 2012. Seven research groups are located at Oslo University Hospital and two groups at the University of Oslo. In 2011 research activities were carried out at the Norwegian Radium Hospital, the Oslo Research Park, the Ullevål Oslo University Hospital, Domus Medica and the Department of Chemistry (University of Oslo), as well as in the different industries. In total 60 researchers are associated with, or employed by SFI-CAST.

SFI-CAST is headed by Stefan Krauss (director) and Ola Myklebost (assistant director). The administrative manager in 2011 was Bie Ekblad.

The centre has a project leadership group who meets on a regular basis. The group consists of the eight primary investigators (PI) and representatives of industry partners of the consortium.

The board is responsible for ensuring that SFI-CAST is developed in accordance with the current research plan.

Academic SFI-CAST members

Elsa Lundanes/Tyge Greibrokk, Department of Chemistry, University of Oslo

Gunhild M. Mælandsmo, Department of Tumour Biology, Oslo University Hospital, the Norwegian Radium Hospital

Harald Stenmark, Department of Biochemistry, Institute for Cancer Research, Oslo University Hospital, the Norwegian Radium Hospital

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

Joel Glover, Department of Physiology, Institute of Basic Medical Sciences, University of Oslo

Ragnhild A. Lothe, Department of Cancer Prevention, Oslo University Hospital, the Norwegian Radium Hospital

Ola Myklebost, Department of Tumour Biology, Oslo University Hospital, the Norwegian Radium Hospital

Stefan Krauss, Unit for Cell Signalling, Oslo University Hospital, Rikshospitalet

Therese Sørlie, Department of Genetics, Oslo University Hospital, the Norwegian Radium Hospital

Industry Partners

Affitech AS
PCI Biotech Holding ASA
ODIN Therapeutics AS (pending)

The Board

In 2011 the board members were

Jonny Østensen, Inven2 (Chairman)

Karen Marie Ulshagen, University of Oslo

Stein Kvaløy, Oslo University Hospital, the Norwegian Radium Hospital

Kari Kværner, Oslo University Hospital

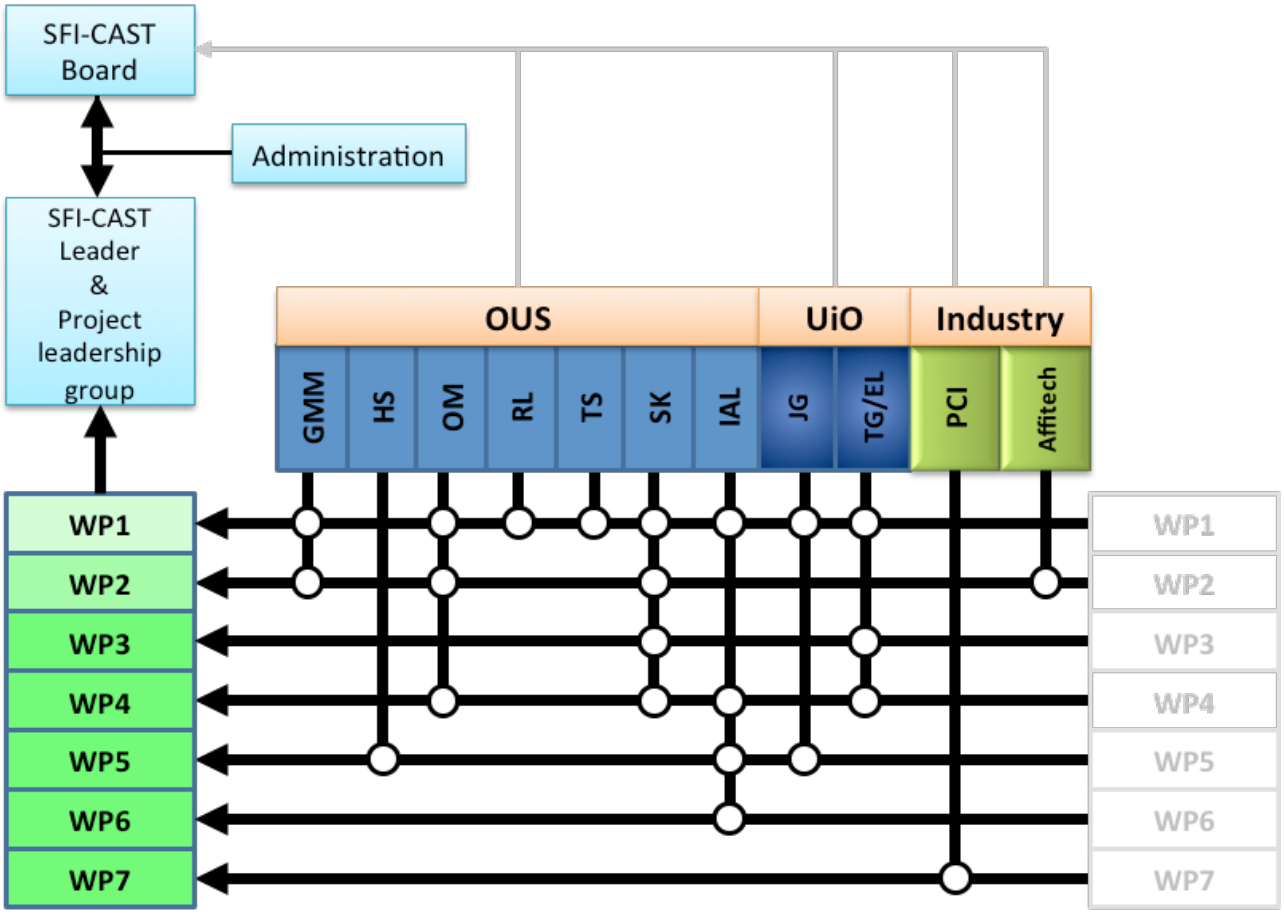
Michael Braunagel, Affitech AS

Anders Høgset, PCI Biotech Holding ASA

Øystein Rønning, Norwegian Research Council (Observer)

Organisation 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 competences, the collaboration and responsibilities.

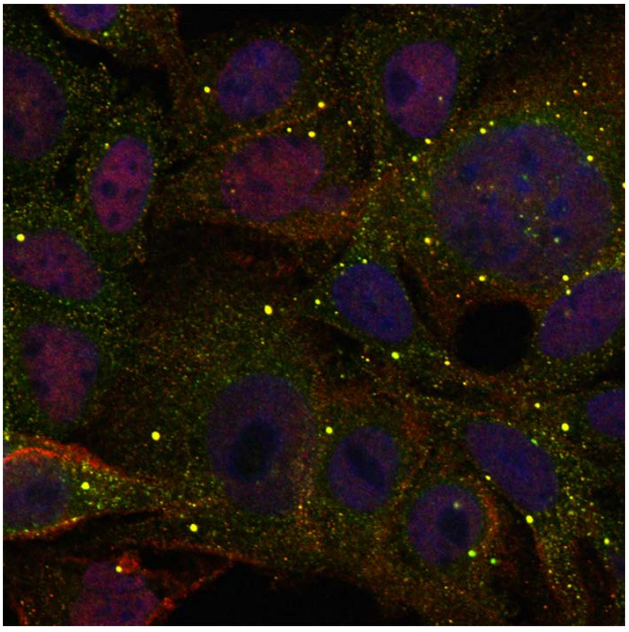


Abbreviations
OUS – Oslo Universitetssykehus (Oslo University Hospital)
UiO – Universitetet i Oslo (University of Oslo)
GMM - Gunhild Mari Mælandsmo group
HS - Harald Stenmark group
OM - Ola Myklebost group
RL - Ragnhild A. Lothe group
SK - Stefan Krauss group
IAL - Iver Arne Langmoen group
JG - Joel Glover group
TG/EL - Tyge Greibrokk/Elsa Lundanes group
PCI - PCI Biotech Holding ASA
Affitech - Affitech Research AS
WP - Work Program

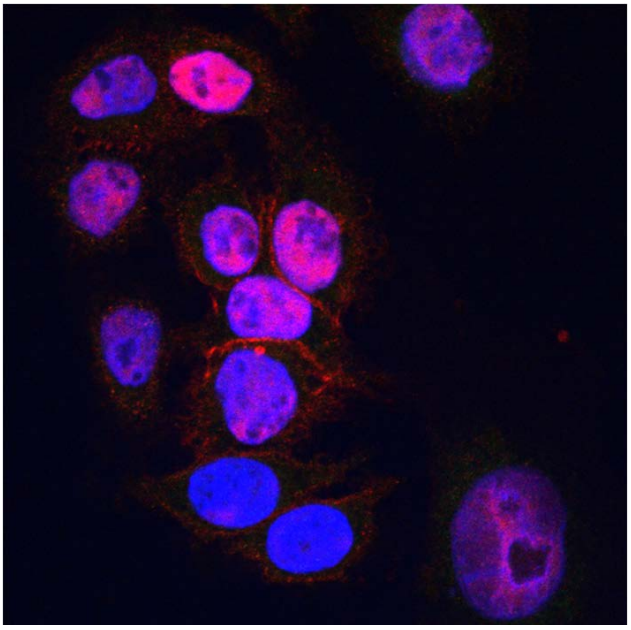
Partners

Cooperation between the centre's partners

All centre activities are centred on integrated work programs. All academic groups in the centre and the industry partners are involved in studying aspects of the Wnt/β-catenin stem cell signalling and its inhibition by a proprietary series of small drug in various tumour models. Several groups, including O. Myklebost, G. Mælandsmo and T. Sørlie work on elucidating the link small nuclear RNA and stem cell signalling in cancer. Furthermore, links between S100A4 and stem cell signalling in tumours are established. Collaborations between the industry partners and between industry partners and academic partners are ongoing on a proprietary therapeutic antibody.



SW480 cells stained with anti-axin and anti-β-catenin upon JW270 treatment (Nina Marie Pedersen).



SW480 cells stained with anti-axin and anti-β-catenin, Control cells (Nina Marie Pedersen).

STEFAN KRAUSS-GROUP
STEM CELL SIGNALLING

Aim

The main goal of the group within SFI-CAST is to gain understanding on stemcellness in cancer, and to use this knowledge for developing antagonists to the stem cell pathway.

Status

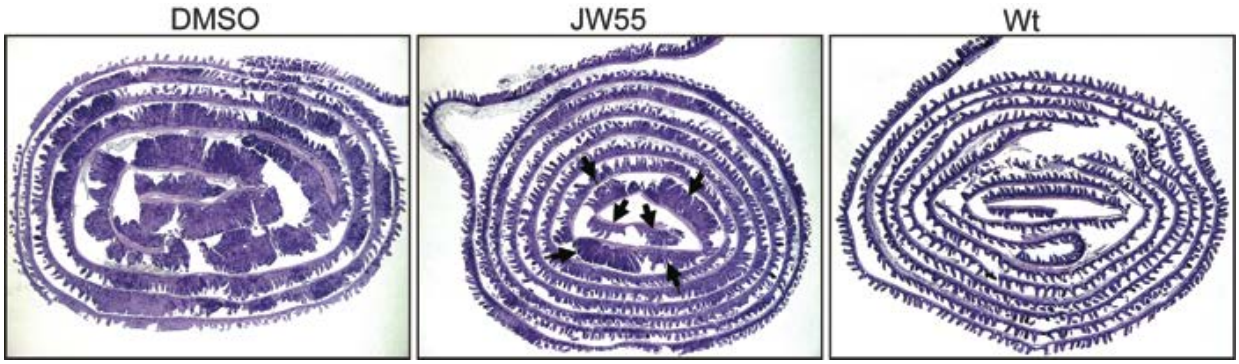
Wnt/β-catenin signalling is a functional network that regulates centrally stem cell properties in a cell and broad range of biological systems, including organ development and control of intracellular metabolism. Deregulated canonical Wnt signalling is a common denominator in a variety of tumours. About 90% of sporadic colon cancers show aberrant Wnt signalling, while all pancreatic adenocarcinomas exhibit alterations in Wnt/Notch signalling. Other major cancers with Wnt activating mutations include gastric, hepatocellular, ovarian, prostate, and non small cell lung cancers, as well as melanoma, breast cancer and cancers of the hematopoietic system. We and others have identified the adenosine binding pocket of tankyrase as an attractive biotarget to inhibit Wnt/β-catenin signalling. We have developed a series of highly specific tankyrase inhibitors that show efficacy *in vitro* and *in vivo* in mouse models. The inhibitors are now further developed with the aim of using the inhibitors as potential human therapeutics.

Innovative potential

The novel small drug tankyrase inhibitors that we develop could have significant therapeutic potential.

Collaborations within the centre

We actively collaborate with E. Lundanes/T. Greibrokk on analytical tools, with O. Myklebost and I. Langmoen on tankyrase inhibitors in various tumour models and with H. Stenmark on the DC complex. Work with T. Sørlie on animal models and with G. Mælandsmo on tumour models is planned.



JW55 treatment decreases development of adenomas in conditional Apc knockout mice. A, representative microscopy images showing H&E-stained sections of Swiss-rolls (the distal part of the ileum is centered) demonstrating an extensive decrease in adenoma development in the small intestine of JW55-treated (100 mg/kg) mice when compared to control mice (DMSO).

IVER LANGMOENS-GROUP
MALIGNANT BRAIN TUMOURS

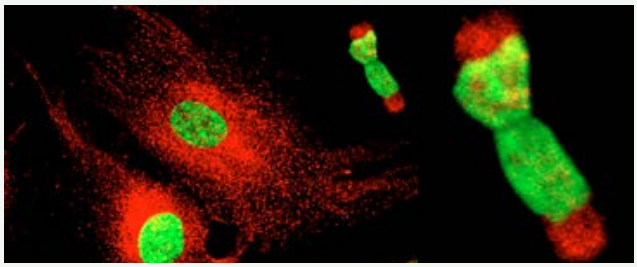
Aim

The main focus of the group in 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. Interestingly, the proliferation rate falls dramatically also in tumour stem cells when they are induced to differentiate. Normal and tumour stem cells show a similar pattern of differentiation, i.e. in neuronal and glial directions, although differentiated cells from the tumour were clearly abnormal morphologically and differentiation in itself progressed much faster. We performed a number of experiments studying the effect that *in vitro* culture of tumour stem cells has on the cells' ability to form tumours, to differentiate and to undergo genotypic and expressional changes. We have also explored the cellular organization of neuro- and tumour spheres, looking at the cellular heterogeneity of such spheres. By sorting tumour cells based on surface antigens, we hope to establish methods for better identification of the progenitor population.

We used microarray technology to compare the global gene expression in normal stem cells and tumour stem cells, in order to identify possible targets for treatment and to better understand the biology of the cell population that escapes current treatment and causes recurrences. The results of this comparison study show 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. Putative target genes have been confirmed at the protein level using immunohistochemistry and Western blot. This work is currently submitted for publication. The roles of the possible targets in the Wnt pathway are investigated using Wnt inhibitors. In particular, we 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. Preliminary results look very promising with publications in preparation.



Expression of NAA30 in GMB-T0595 and normal cells

Based on the preclinical data we have established a clinical protocol. This protocol is designed to harness the patients' own immunity. The inclusion of patients into the "Phase I/II trial of vaccine therapy with hTERT, survivin and tumour stem cell derived mRNA-transfected dendritic cells in patients receiving standard therapy for glioblastoma" started in February 2009. So far 18 patients have been included in the study. This clinical trial is backed up from the collaboration through the Cancer Stem Cell Innovation Centre (SFI CAST) and is collaboration with the Neurosurgical department, Dept. for Clinical cancer Research, Dept. for Cell Therapy, and Dept. for Immunology, Inst. for Cancer Research, the Norwegian Radium Hospital and the Oncological department at Oslo University Hospital.

Innovative potential

We advance FACs (facilitated cell sorting and cytometry) to carry out specific measurements of cell sub-group behaviour within cell populations and allows for elaborate assessment of experimental parameters. The ability for distinction of many wavelengths of fluorophore as well as the development of sophisticated antibody-fluorophore conjugates means that data relating to cell cycle, division rate, phenotype and even transitory signalling pathway activation can be assessed within control and experimental cell populations.

Collaborations within the centre

We actively collaborate with J. Glover and S. Krauss.

RAGNHILD A. LOTHES-GROUP
STEM CELL BIOMARKERS

Aim

We aim to gain insight into the role of stem cells in the development and progression of cancer, and in particular for 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.

Status

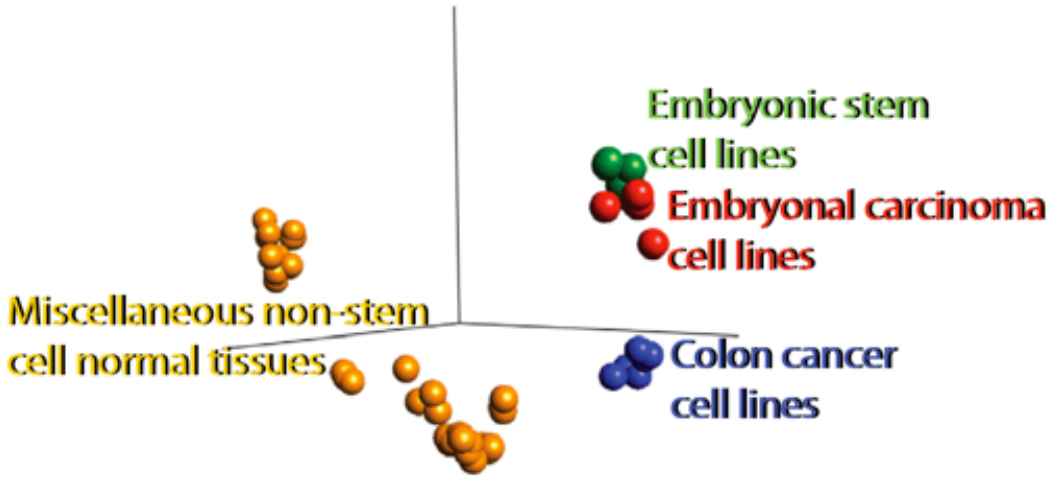
We have carried out detailed transcriptome studies of panels of both embryonal carcinoma (EC) and phenotypically similar, but non-malignant, embryonic stem (ES) cell lines. Genome technologies such as exon microarrays and whole-transcriptome RNA-sequencing have been used to identify genes with malignancy 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 that we are in progress of defining their role in cancer.

Innovative potential

Molecules which are specific to cancer cells with stemness properties can be used both as cancer biomarkers and as targets for therapy.

Collaborations within the centre

We collaborate predominantly with H. Stenmark.



Overall features of the gene expression profiles, as seen from principal components analysis, demonstrate the close relatedness between EC and ES cells.

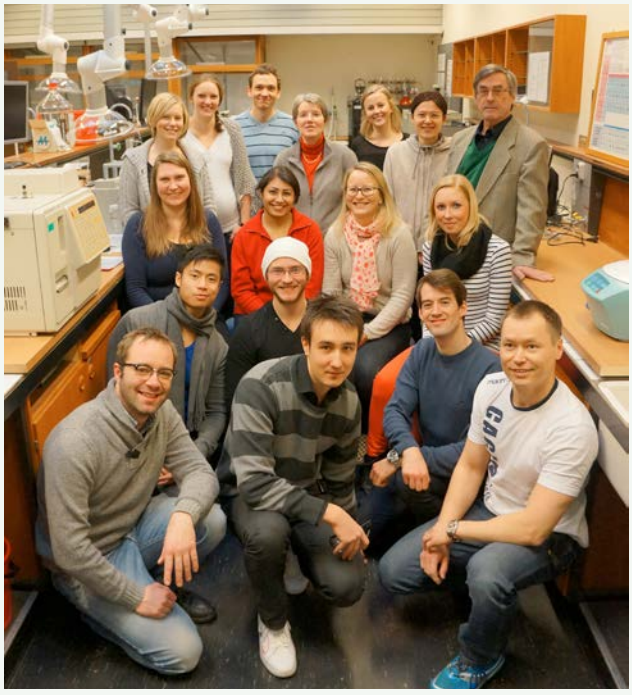
ELSA LUNDANES AND TYGE GREIBROKK-GROUP ANALYTICAL CHEMISTRY

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

The Lundanes group has developed analytical tools for sensitive determination of potential cancer biomarkers such as oxysterols. In addition, an ambitious effort is being put in to developing a label-free method for drug target discovery ("drug deconvolution"). The group expects the method, which may significantly aid drug discovery, to be completed in 2012. The Lundanes groups is pro-active in cooperation with other CAST members, especially the Krauss group, and co-publish regularly. Recently, members of the Lundanes group have engaged in cooperation with CAST industry partner Affitech AS, in a co-effort to develop and apply novel technology for the analysis of glycoproteins.



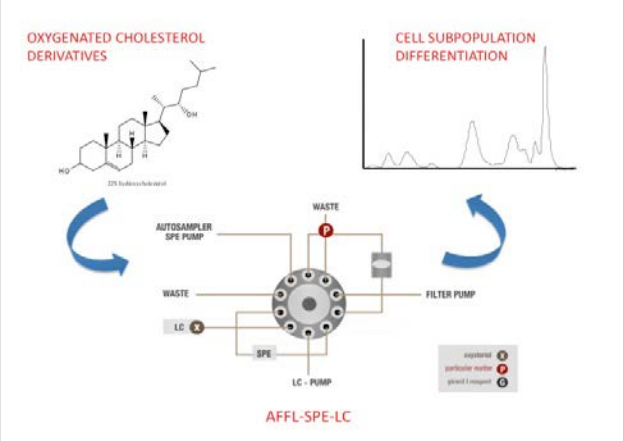
The research group of Elsa Lundanes and Tyge Greibrokk at Inst. for Chemistry

Innovative potential

The Lundanes group has prioritized patenting, and is in discussions with external industry partners regarding commercialization of analytical methods.

Collaborations within the centre

We actively collaborate with S. Krauss on analytical methods for small molecules, metabolites and proteins. We also collaborate with industry partner Affitech AS.



The Lundanes group develops novel technology able to study complex cellular processes with minimal amounts of sample.

OLA MYKLEBOST-GROUP
MESENCHYMAL PROGRAMMING

Aim

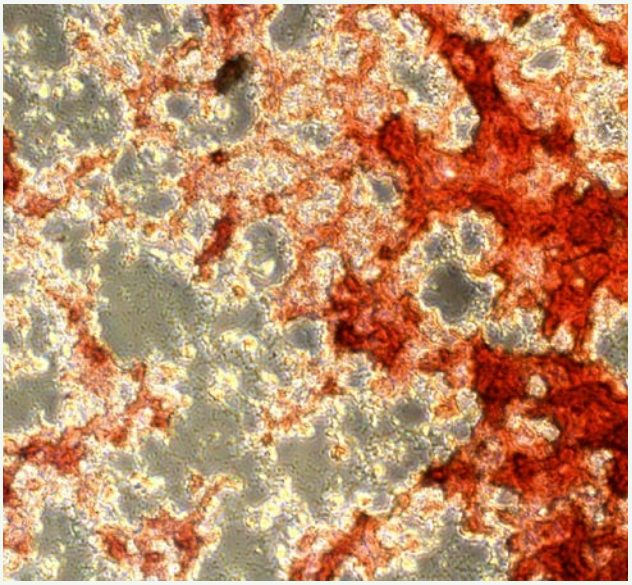
The Myklebost group is focused on the biology of mesenchymal cancers, also known as sarcomas, and is investigating the regulation and properties of stemness and differentiation in these tumours. The studies are extended to breast cancers of the mesenchymal phenotype.

Status

The microRNA let-7 is considered a tumour suppressor and a regulator of stemness and differentiation, and is normally highly expressed in well differentiated tissues. The expression of let-7 is frequently lost in cancer. Interestingly, HMGA2 is expressed early in development, but is abruptly downregulated following expression of let-7, thus HMGA2 and let-7 are conversely expressed. HMGA2, which is an architectural transcription factor, is amplified and rearranged in sarcomas, and frequently upregulated in a variety of epithelial-derived cancers, such as breast, ovarian, pancreatic and lung cancer. Using a model system consisting of a human breast epithelial cell lines and the mesenchymal counterpart (which have undergone epithelial to mesenchymal transition (EMT)); we have found that HMGA2 is preferentially expressed in the more aggressive mesenchymal-like breast cells. Furthermore, continued expression of HMGA2 in these mesenchymal-like cells is essential for survival of these cells. We are currently investigating the exact role of HMGA2 and let-7 in this EMT model system, with focus on the mechanism regulating cell proliferation.

The Wnt pathway is frequently upregulated in osteosarcoma and Wnt inhibition may therefore have therapeutic potential in these cells. We are currently testing the effects of specific tankyrase inhibitors developed by the Krauss group in our osteosarcoma cell lines, with focus on proliferation, apoptosis, differentiation, colony formation and invasive capacity.

Using a liposarcoma xenograft model system we have shown that cancer stem-like cells are strongly enriched by cell sorting based on Aldefluor in combination with CD133. The Aldefluor^{high} CD133^{high} subpopulation generates tumours more efficiently *in vivo* and colonies more efficiently *in vitro*. In collaboration with PCI Biotech we have successfully targeted the CD133 positive population, thus eliminating the cancer stem-like cells, in this model system, using *in vitro* PCI technology.



Osteogenic differentiation in osteosarcoma cells induced by the tankyrase specific inhibitor OD270

Innovative potential

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

Collaborations within the centre

We actively collaborate with S. Krauss, J. Glover and PCI Biotech AS as well as with Affitech AS.

GUNHILD MÆLANDSMO-GROUP
TUMOUR HETEROGENEITY

Aim

A central aim of the group has been to optimize methods for single cell preparation from tumour tissue, isolation of various cell populations from the heterogeneous tumour mass and cultivation of the cells for maintenance and further evaluation of stemness characteristics and differentiation capability.

Status

In the breast cancer project we now utilize several models representative for basal-like and luminal-like breast cancer grown orthotopically in nude mice. We have isolated and characterized tumour cell populations from two such models. Subpopulations from the luminal like tumour had the highest tumour initiating potential and more detailed analysis revealed population heterogeneity with respect to several cell surface markers Re-injected pure subpopulations defined by chosen markers, indicated differences *in vivo* tumourigenicity as well as regenerative capacity. In collaboration with T. Sørlie whole genome expression analysis has been performed, and some interesting pathway differences have been found. Studies of the proteome and epigenetic differences have been initiated.

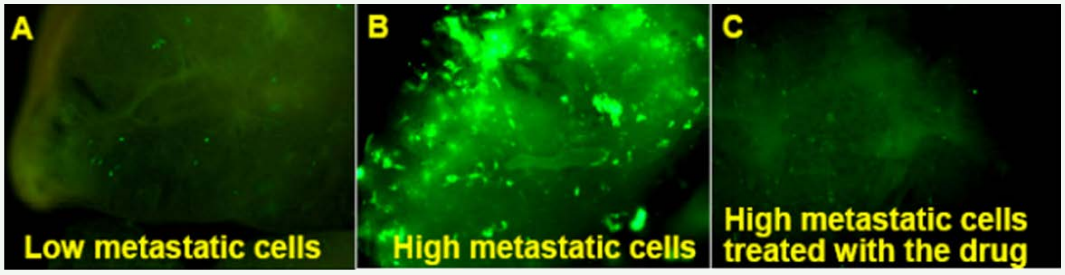
In the Melanoma project, our recent publication suggests that melanoma does not harbour a small stable cell subpopulation that could be distinguished by specific CSC-related markers. Rather, our data suggests that a large fraction of melanoma cells from heterogeneous subpopulations have CSC-like properties; alternatively, that most of the cells can transiently adopt a CSC-like identity. The latter has been linked to a phenomenon called "phenotype-switching", which seems to be regulated by the signals from tumour microenvironment (TME). Therefore, we are focusing now on how TME factors affect melanoma cells phenotypes and functions related to metastasis and drug-response. In another subproject we are investigating the molecular and functional characteristics of melanoma cells isolated from different sites of metastases i.e. different microenvironments. In parallel, we are studying how the microenvironment is modulated by the developing metastases in order to identify TMAE alterations that could be linked to metastatic growth.

Innovative potential

The ultimate goal is to identify how the molecular and functional properties of melanoma cells are affected by the microenvironment factors. Further, to reveal the peculiarities in the crosstalk between melanoma cells and the microenvironment in various metastatic sites and the consequence of such crosstalk for metastases development and drug-response. Increased understanding of the tumour-microenvironment interactions might reveal novel targets for therapeutic intervention.

Collaborations within the centre

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



Ex vivo clonogenic growth of low (A) and high (B, C) metastatic melanoma cells in puma without (A, B) or with (C) the Brafv600e inhibitor Vemurafenib. The images illustrate the inhibotory effect on metastatic colony formation in lung tissue. Melanome cells were labelled with green fluorescent protein, and intensley green areas represent tumour colonies.

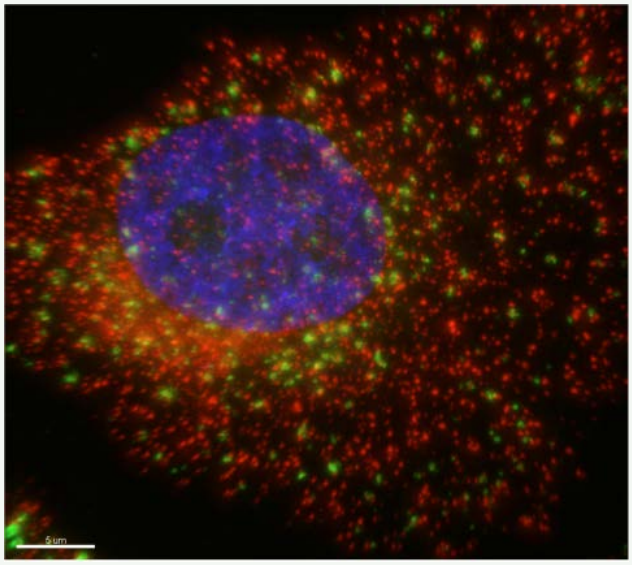
HARALD STENMARK-GROUP
INTRACELLULAR TRAFFICKING AND SIGNALLING

Aim

The aim of this group's research is to understand how intracellular membrane trafficking serves to regulate stem cell signalling, in particular signalling in the Wnt pathway.

Status

The group works on a molecular dissection of the Wnt signalling pathway, with focus on components of the endocytic pathway. Recent evidence suggests that endosomal sequestration of inhibitory factors is a key event in Wnt signalling, and the group will explore this further as a possible target for therapy.



Super-resolution image of a cancer cell, with DNA in blue, endosomes in red and clathrin in green. Image courtesy of Ellen Skarpen and Kay Schink.

Innovative potential

This research has innovative potential to point out new avenues for therapeutic targeting of Wnt signalling – one of the key signalling pathways in cancer stem cells.

Collaborations within the centre

Within CAST, the group collaborates closely with the group of S. Krauss in pharmacological targeting of the Wnt pathway, and with the group of R. A. Lothe/R. Skotheim in identification of tumourigenic hits on the Wnt pathway.

THERESE SØRLIES-GROUP
BREAST CANCER HETEROGENEITY

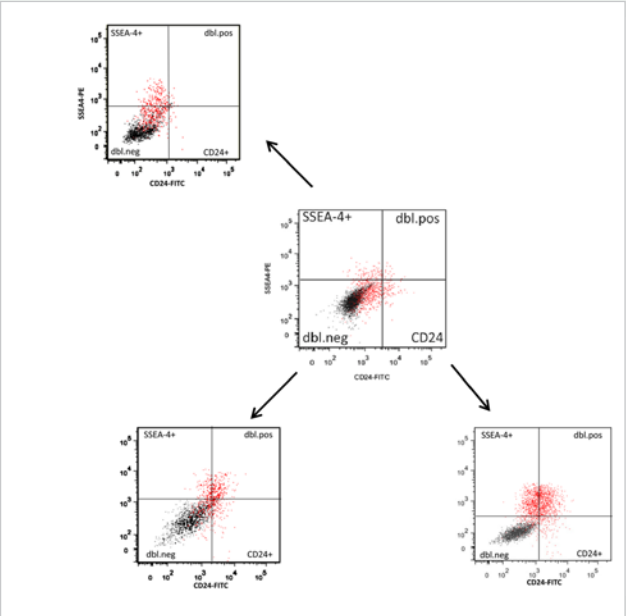
Aim

In the frame of CAST, our group focuses on intra-tumour heterogeneity and the role of different sub-populations of cells for progression of breast cancer.

Status

Breast cancer is a collection of diseases demonstrating heterogeneity at the molecular, histopathological and clinical level. Several subpopulations of cells exist within tumours which are different with respect to differentiation status and ability to drive tumour growth. We are studying breast cancer heterogeneity by using both cell lines and orthotopically growing xenograft models. By use of sets of specific surface markers and FACS sorting, we have identified, isolated and characterized cells that are different with respect to invasiveness and tumourigenicity, *in vitro* as well as *in vivo*. These have been further characterized by gene expression profiling and signatures and candidate single markers with potential clinical implication have been identified.

From the characterization of tumour cell subpopulations using microarrays and mass spectrometry (underway), we expect to identify markers for the more aggressive tumour cells. These could potentially be used for further separation of the cell populations and as candidates for small molecule targeting.



Flow cytometry analysis of a luminal breast cancer xenograft model using CD24 and SSEA-4.

Innovative potential

We will establish conditional transgenic mouse models in combination with reporter gene and linage tracing mouse strains to study expression patterns of specific proteins and cells of origin of tumour formation. These will be ideal for testing of targeting drug candidates.

Collaborations within the centre

We collaborate with the Mælandsmo group on the breast cancer project.

JOEL GLOVERS-GROUP IMAGING

Aim

In vivo imaging for following the fate of tumour cells and potential tumour stem cells in animal models. Develop labelling and imaging protocols that facilitate non-invasive *in vivo* cell tracking at the highest possible spatial resolution.

Status

Magnetic resonance imaging (MRI)-based tracking is increasingly attracting attention as a means of better understanding stem cell dynamics in vivo. Intracellular labelling with micrometer-sized particles of iron oxide (MPIOs) provides a practical MRI-based approach due to superior detectability relative to smaller iron oxide particles. However, insufficient information is available about the general utility across cell types and the effects on cell vitality of MPIO labelling of human stem cells. We labelled 6 human cell types from different sources: mesenchymal stem cells derived from bone marrow (MSCs), mesenchymal stem cells derived from adipose tissue (ASCs), presumptive adult neural stem cells (ad-NSCs), foetal neural progenitor cells (f-NPCs), a glioma cell line (U87) and glioblastoma tumour stem cells (GSCs), with two different sizes of MPIOs (0.9 and 2.84 ffim). Labelling and uptake efficiencies were highly variable among cell types. Several parameters of general cell function were tested *in vitro*. Only minor differences were found between labelled and unlabeled cells with respect to proliferation rate, mitotic duration, random motility and capacity for differentiation to specific phenotypes. *In vivo* behaviour was tested in chicken embryos and severe combined immunodeficient (SCID) mice. Post-mortem histology showed that labelled cells survived and could integrate into various tissues. MRI-based tracking over several weeks in the SCID mice showed that labelled GSCs and f-NPCs injected into the brain exhibited translocations similar to those seen for unlabeled cells and as expected from migratory behaviour described in previous studies. The results support MPIO-based cell tracking as a generally useful tool for studies of human stem cell dynamics *in vivo*.

Innovative potential

We work towards evaluating the potential for developing specialized MPIOs for targeted delivery of drugs.

Collaborations within the centre

An active collaboration has been maintained with the groups of I. Langmoen and O. Myklebost.

www.affitech.com

AFFITECH RESEARCH AS

About the company

Affitech Research AS, a biopharmaceutical company listed on the Nasdaq OMX Copenhagen exchange, 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, autoimmune or infectious diseases, 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 is working towards the discovery of antibodies targeting possible stem cell subpopulations of pancreatic cancer cells that show increased chemotherapy resistance and increased metastatic potential. The project is funded by the Research Council of Norway through the Industrial PhD scheme.

Status 2011

Affitech's Russian partner IBC Generium has filed a Clinical Trial Application in Russia for testing of r84 in clinical trials. R84, an antibody developed by Affitech in collaboration with Peregrine Inc. The product candidate is a new patented human monoclonal antibody to human vascular endothelial growth factor (VEGF), and is being developed as a potential treatment of cancer. The anti-VEGF antibody will be evaluated in patients with various cancers and is a possible competitor to bevacizumab (Avastin® – Roche).

Also in 2011, Affitech's first anti-GPCR antibody program AT008, designed to block the binding of chemokine ligands to its cell surface receptor CCR4, entered preclinical pharmacology testing. The program includes several different antibodies with multiple potential mechanisms of action targeting hematological cancers and solid tumours, either directly, through metastatic lesions and/or regulatory T cells. It also has potential utility in some immunological diseases such as severe asthma. A lead candidate has now been identified.

Photo:
Affitech Research AS

www.pcibiotech.no

PCI BIOTECH HOLDING ASA

About the company

A New Concept in Localised Cancer Treatment

PCI Biotech® has developed a unique and patented photochemical drug delivery technology for use in cancer therapy and other diseases.

PCI (PhotoChemical Internalisation) is a technology for light-directed drug delivery by triggered endosomal release and was developed to introduce therapeutic molecules in a biologically active form specifically into diseased cells. This proprietary technology can provide local enhancement of a range of different drugs, including several cancer drugs currently in clinical use.

PCI Biotech is creating value via 2 axes; 1)develop the proprietary photosensitiser Amphinex® for use in combination with marketed cancer drugs and 2) develop PCI for use in other areas.

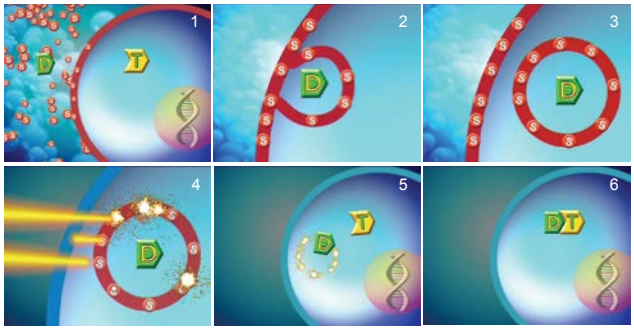
PCI Biotech has completed a clinical phase I/II study with Amphinex in combination with the well-established cytotoxic agent bleomycin (Blenoxane®) at University College Hospital in London. The study has primarily enrolled patients with Head & Neck cancer, a disease with local control issues that the PCI technology could potentially contribute to solve. Strong tumour response was observed in all patients, and a phase II study within Head & Neck cancer is planned to start in Q4 2011/Q1 2012.

SFI-CAST interaction

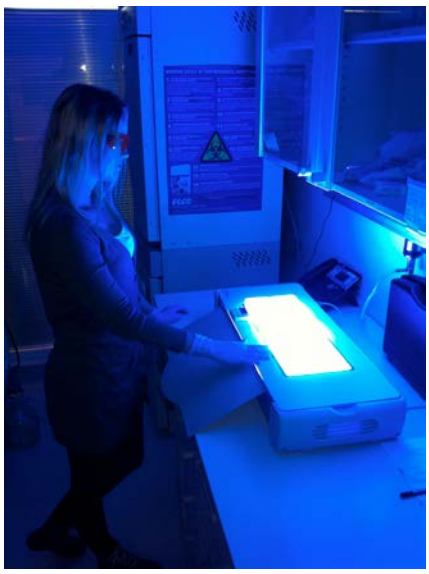
PCI biotech has together with several SFI-CAST partners (Myklebost, Mælandsmo, Stenmark and Krauss) initiated and obtained encouraging results after targeting of different cancer cells (sarcoma, carcinoma of breast, colon and pancreas) expressing relevant stem cell markers.

Goals for 2012

We aim to further document the concept of combining PCI with cancer stem cell targeting toxins *in vivo*.



Principle of the PCI technology; 1, Administration of photosensitizer (S) and drug (D). 2, D an S is taken up by endocytosis and 3, sequester in endo-lysosomal vesicles. 4, Light activation of (S) leads to formation of reactive oxygen species, which burst the membrane of the vesicles leading to 5, cytosolic release of the drug and 6, interaction with its biological target (T).



Monica Bostad, Ph.D. student in Pål K. Selbo's project group is performing an in vitro photochemical internalization (PCI) experiment. Blue light is used to trigger PCI-based delivery of a model toxin drug that is targeting a cancer stem cell marker.

Recruitment

Awards

- Hanne Røberg Larsen: Waters Innovation Award: "On-line filtration to improve robustness in automated solid phase extraction liquid chromatography" Group leader: Elsa Lundanes
- Hanne Røberg Larsen: GE Healthcare Award for Young Scientist. Group leader: Elsa Lundanes
- PCI Biotech won two prizes in DnB NOR's Innovation Prize Award 2011 September 6th. As well as receiving the "People's Choice Award", they also won the main prize. The price money is in total 1.1 MNOK.
- Harald Stenmark elected member of the European Academy of Cancer Sciences (EACS)

Hanne Røberg Larsen receives the GE Healthcare Award for Young Scientist

DnB NOR's Innovation Prize Award 2011 and People's Choice Award

Doctoral Degrees

- **Einar Osland Vik-Mo,** M**,** *Propagation and characterization of stem like cells from brain tumours - establishment of a clinical protocol for immunotherapeutic targeting of tumour stem cells in glioblastomas*, supervised by Iver A. Langmoen, Univ. of Oslo

- **Ying Jing**, F, *Identification of a distinct subpopulation of slow cycling tumour initiating cells in oesophagus cancer cell lines*, supervised by Stefan Krauss and Ondrej Machon, Univ. of Oslo (PhD in Republic of China)

- **Christoph R Müller** , M, *Novel approaches to the treatment of high-grade sarcoma.*, supervised by Gunnar Sæter and Ola Myklebost, Univ. of Oslo

Master Degrees

- **Hanne Røberg-Larsen**, *Determination of oxysterols in cancer stem cells using on-line automated filtration and filter-flush solid phase extraction liquid chromatography tandem mass spectrometry*, F, Elsa Lundanes and Tyge Greibrokk, Dept. of Chemistry, Univ. of Oslo.

- **Tale Barøy,** *Characterization of LSAMP, a novel candidate tumour suppressor gene in osteosarcomas*, F, supervised by Ola Myklebost, Dept. of Tumor Biology, OUS /Univ. of Oslo

- **Eivind Valen Egeland,** *Osteogenic differentiation of mesenchymal stem cells: identification of potential regulators*, M, supervised by Ola Myklebost, Dept. of Tumor Biology, OUS/ Univ. of Oslo

- **Andreas Hoff,** *Stem cell related and malignancy-specific transcripts*, M, supervised by Rolf I. Skotheim and Ragnhild A. Lothe, Dept. of Cancer Prevention, OUS/Univ. of Oslo

- **Hemaseh Bideli,** *Studier av TGFα og S100A4 mediert regulering av matriks metalloproteinase 3 i epitelceller fra mammakjertel.* Oslo and Akershus University College of Applied Sciences, Supervisor: Kristin Andersen,

- **Kotryna Vasiliauskaite**, *Tumour microenvironment interactions in malignant melanoma: impact on metastasis and sensitivity to therapy.* Vilnius University, Lithuania. Supervisor: Lina Prasmickaite

- **Maria Rist,** *Effect of tumour microenvironment-derived factors on melanoma growth and drug-response: an in vitro study in three-dimensional cultures.* Department of Pharmacy, University of Tromsø. Supervisor: Lina Prasmickaite

International cooperation

International Networks

- Eurobonet (www.eurobonet.eu) (OM)
- International Liposarcoma consortium (www.liposarcomaresearch.org) (OM)
- EuroStars (PCI Biotech)
- Nordforsk network on cilia and centrosomes, Nordic autophagy network (HS)

International collaborations

- Alan Mackay-Sim, Australian National Adult Stem Cell Centre, Brisbane, Australia (IL)
- Nobuo Tanaka, Kyoto Institute of Technology, Japan (academic). Collaboration in development of high resolution, high speed chromatography for proteomics applications (EL)
- Yasuhiro Watanabe, Tottori University, Japan (IL)
- Charles Liu, University of Southern California, Los Angeles, USA (IL)
- David Tirrell, California Institute of Technology, Los Angeles, USA (IL)
- Dolph Hatfield, NIH, Washington, USA (IL)
- Katherine Mc Glynn and Stephen Chanock, NCI, NIH, Bethesda, MA, USA. Genome-wide association study of testicular germ cell cancers (RAL)
- Luke Tolley, University of Southern Illinois, USA (academic). Collaboration in development of methodology for drug/protein interaction studies (EL)
- Meenhard Herlyn, Wistar Inst., Philadelphia, USA. Cooperation on studies of melanoma heterogeneity and the role of tumour microenvironment on melanoma properties by using 3D *in vitro* systems (GMM)
- Michael Rosenblum, MD Anderson Cancer Center, USA, academic collaboration (PCI)
- Mina Bissell and Mark LaBarge, Lawrence Berkeley National Laboratory, Berkeley, CA, USA. Collaboration on stem cells and tumour-microenvironment interactions in breast cancer (GMG)
- Mirna therapeutics and Dr. Bader, Austin, Texas, USA. Collaboration on testing the effects of let-7 mimics provided by Mirna therapeutics in our lipo- and osteosarcoma, as well as breast cancer cell lines (OM)
- Nai Wen Chi, Scripps, San Diego USA. Collaboration on tankyrase (SK)
- Sendurai Mani, MD Anderson Cancer Centre, Houston Texas, USA. Collaboration on investigating the role of HMGA2 and let-7 in his human EMT models. (OM)
- Soldano Ferrone, University of Pittsburgh Cancer Institute (CCC), USA, academic collaboration (PCI)
- Sonja Hess, Proteome Exploration Laboratory (PEL), California institute of Technology (Caltech), Pasadena, California, USA. Collaboration regarding selective enrichment and determination of N-linked glycoproteins (EL)
- Winston Hide, Harvard University, MA, USA (IL)
- Elisabetta Marangoni, Curie Institute, Paris, France (academic). Collaboration on Orthotopic xenograft models of breast cancer subtypes (TS)
- Elisabetta Marangoni and Paul Cotton, Curie Institute, Paris, France. Collaboration on exchange of orthotopic breast cancer models of luminal and basal-like breast cancer (GMM)
- Dietmar Gradl, Universität Kalrsruhe, Germany. Collaboration on animal models (SK)

- Ivan Dikic, University of Frankfurt, Germany. Collaboration on ubiquitin regulation of cell signalling (HS)
- Jens Peter von Kries, Leibniz-Institute Für Moleculare Pharmakologie, Berlin, Germany. Collaboration on HTS screens (SK)
- Pål Johansen, University Hospital Zürich, Switzerland, academic collaboration (PCI)
- Colin Hopper, University College London Hospitals, England, academic collaboration (PCI)
- Peter W. Andrews and Neil Harrison, University of Sheffield, Sheffield, UK. Comparative analyses of embryonal carcinomas and embryonic stem cells (RAL)
- Anders Björklund, Wallenberg Center/University of Lund, Sweden (IL)
- Ernest Arenas, Karolinska Institute, Stockholm, Sweden (IL)
- Ernest Arenas, Karolinska Institute, Stockholm, Sweden. Collaboration on stemcells (SK)
- Denator, Göteborg, Sweden (IL)
- Herwig Schuler, Karolinska Institute, Stockholm, Sweden. Collaboration on crystallography (SK)
- Lars Åhrlund-Richter, Department of Woman and Child Health, Karolinska Institute, Stockholm, Sweden. Collaboration on stem cells and invasive properties of melanoma cells. Use engraftment of human melanoma cells in human environment by prior injection of embryonic stem cells and formation of teratoma in nude mice (GMM)
- Ludesi, Malmö, Sweden (IL)
- Monica Nistér, Karolinska Institute, Stockholm, Sweden (IL)
- SpectraCure AB, Sweden, industry collaboration (PCI)
- Tobias Jonnson, Merck Sequent, Umeå, Sweden (academic/industry). Collaboration on understanding and application of novel (HILIC) LC columns. (EL)
- Ole W Petersen, Department of Cellular and Molecular Medicine, The Panum Building, University of Copenhagen, Denmark (academic). Collaboration on heterogeneity and tumourigenicity of subpopulations of cells from breast cancer cell lines and tumours (TS)
- Ole W. Pettersen, Department of Medical Anatomy, The Panum Institute, University of Copenhagen, Denmark. Collaboration on stem cells and tumour-microenvironment interactions in breast cancer. (GMM)

National Cooperation

National Cooperation

- Anne-Lise Børresen-Dale, Department of Genetics, Institute for Cancer Research, Oslo University Hospital. Partner in OSBREAC and Head, KGJ-Center - Collaborator on molecular characterization (GMM).
- Daniela-Elena Costea and Anne Chr. Johannessen, Department of Pathology, Gade Institute, University of Bergen: Stem cells and epithelial-mesenchymal transition (EMT) in oral cancer and breast cancer (GMM)
- Ingrid Gribbestad, Norwegian University of Science and Technology, Department of Circulation and Medical Imaging, Trondheim (academic) (TS)
- Ingrid Gribbestad, Department of Circulation and Medical Imaging Norwegian University of Science and Technology. Partner in OSBREAC and the KGJ-Center – Collaborator on function and molecular MR spectroscopy (GMM)
- Ian Mills, NCMM Oslo, chromatin IP (SK)
- Jens Preben Morth, NCMM Oslo, crystallography (SK)
- Kjetil Tasken, NCMM Oslo and the Chemical Biology Screening Platform, the Biotechnology Centre, UiO, collaboration on screening of inhibitors of S100A4-induced EMT (GMM)
- Lars Akslen, Department of Pathology, Gade Institute, University of Bergen. Collaborator on tumour-stroma interactions in breast cancer and melanomas with special focus on vascularisation and endothelial markers (GMM).
- Malcom Reid, NIVA (academic). Collaboration on application of AFFL-SPE-LC technology for analysis of pharmaceuticals and metabolites (EL)
- Olav Haraldseth, Fuge MIC Trondheim. Collaborated on MRI-based tracking of MPIOs in mouse brain and other tissues (JG)
- Terje Johansen, University of Tromsø. Collaboration on protein aggregation in cell signalling and pathologies (HS)
- Toni Hurtado , NCMM Oslo, will be collaborating with OSBREAC on molecular characterization of breast cancer and the involvement of stem cell subpopulations (GMM)
- Partner in OSBREAC and K.G.Jebsen Center for Breast Cancer Research (GMM):
  - OSBREAC – Oslo Breast Cancer Research Consortium is headed by Steering Group leader Prof. emeritus Rolf Kåresen, OUS Ullevål. The groups participating in OSBREAC perform molecular and functional characterization of breast cancer patients/ cells at different steps during cancer development with the aim of identifying biomarkers to be utilized for stratification into more personalized treatment regimes for the patient.
  - The K.G. Jebsen Center for Breast Cancer Research is headed by Prof. Anne-Lise Børresen-Dale and is based on the OSBREAC initiative.

Communication and dissemination activities

MEDIA COVERAGE

TV

- Steven Ray Wilson: Interview on Norwegian television (Østlandsendingen, NRK) about cancer, drug discovery and technology (November 2011).

Newspapers

- Dagens Næringsliv, *artikkel om innovasjon i forskning*, article about innovation and research, (page24-25), 16th Aug 2011 (R.A. Lothe)

- Dagens Næringsliv, article about PCI Biotech, 28th Aug 2011


LIVSSTIL

Ikke helt patent

Jumboplass: Norge har langt færre patentsøknader enn Sverige og Danmark.
Ikke kultur: Det er ikke kultur i Norge for å kommersialiere gode ideer, ifølge eksperter.

Jordnær salgstrening

Jørgen Juel Larsen

Vil høste resultater

Må profesjonaliseres


Gode kreft-nyheter i kø

Å gjenoppbygge omdømmet

pwc

Clavis Pharma

PCI Biotech

Mindre Audi for pengene

Nye Audi A1 fra kr 198.700,-

Internet

The Norwegian Cancer Society: www.kreftforeningen.no; Research project of the month: "Kreftspredning - kan det forhindres" 3rd Aug 2011 (G. Mælandsmo)

Forskning.no: "På sporet av spredningsgåten", 4th Jan 2011 (G. Mælandsmo)

Forskning.no: "Vi kan hindre kreftspredning", 26th Jan 2011, (G. Mælandsmo)

Helse Sør-Øst: www.helse-sorost.no; Dr. Mælandsmo: "Researcher of the month"; "Metastaseforskning - et stort puslespill", September 2011 (M. Mælandsmo)

Dr. Pål Selbo was interviewed in connection with the European Cancer Organization (ECCO) in Stockholm, September 24th. The interview was published on ecancer.tv and was rated as "editors pick" in the "Technologies" category; http://ecancer.org/tv/pubdate/1162

Articles about PCI Biotech winning the DNB Innovation Prize:

http://www.forskningsradet.no/no/Nyheter/Innovasjonspris_til_PCI_Biotech/1253968916092?lang=no

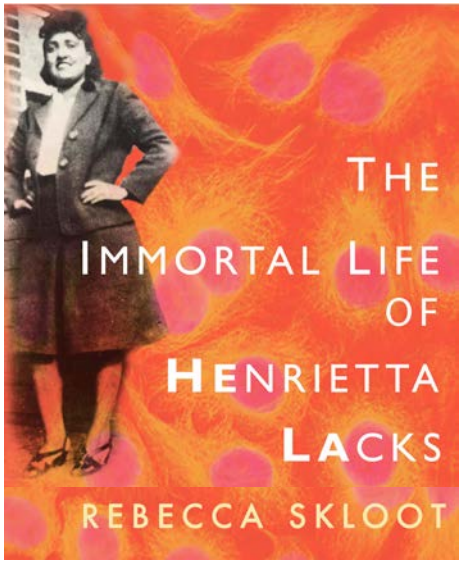
http://www.hegnar.no/bors/article650626.ece

Per Walday (CEO of PCI Biotech) held this lecture under the Norwegian Research Council's Business seminar (Forskningsrådets næringslivsdag) http://www.youtube.com/watch?v=AqreKujXSXU

Radio

Steven Ray Wilson: Interview on Norwegian radio (NRK) on "Analytical tools and doping in sports": http://nettradio.nrk.no/

- Ola Myklebost: Interviewed in Ekko on NRK P2: HeLa-cellene, - Henrietta Lacks udødelige liv, 27th Oct 2011. Viten: "HeLa-cellene - Ny kreftbehandling". The book about Henrietta Lacks immortal life, just been published in Norwegian, is the story of Henrietta and her cancer cells and the enormous importance they have had and still have in research.



Other

- Therese Sørlie; "Congress update newsletter" after ECCO 16 in Stockholm: http://stockholm2011.ecco-org.eu/News-and-alerts/~/media/ECCO%20documents/Stockholm%202011/News%20and%20alerts/Congress%20update%20services/Edition%2010%20October%202011%20web.ashx

- Harald Stenmark interviewed in Journal of Cell Biology: http://jcb.rupress.org/content/192/4/544.long

Appendix

PERSONNEL

Principal Investigators
Stefan Krauss
Ola Myklebost
Joel Glover
Iver Arne Langmoen
Ragnhild A. Lothe
Elsa Lundanes
Tyge Greibrokk
Gunhild Mari Mælandsmo
Harald Stenmark
Therese Sørlie
Anders Høgset
Alexander Duncan

Administrative Manager
Bie Ekblad

Senior Scientists
Leonardo Meza-Zepedea
Lina Prasmickaite
Pål Selbo
Rolf I. Skotheim

Postdoctoral Researchers
Andrey Voronkov
Anne-Mari Håkelien
Biljana Stangeland
Else Munthe
Eva Wessel Stratford
Gabor Halasi
Helle Malerød
Jean-Luc Boulland
Jennifer L. Dembinski
Kristin Andresen
Lene Malerød
Marianne Stabell
Nina Marie Pedersen
Nina Therese Solberg
Ondrej Machon
Petter A. Olsen
Sharmini Alagaratnam
Silje Lauvrak
Steven R. Wilson

PhD students
Cecilie Sandberg
Einar Vik-Mo
Eldrid borgan
Elin Johnsen
Hanne K. Hustoft
Heidi Namløs
Ingrid Johanne Bettum
Jo Waaler
Kaja Lund
Magnus Røgeberg
Martin F. Strang
Mrinal Joel
Nirma Skrbo
Ping Wang
Viola Lobert

Master students
Anastassia Serguienko
Andreas Hoff
Anders Grimsmo
Hanne Røberg-Larsen
Hemaseh Bideli
Hong Diem Nguyen
Kirsten Strømme
Khanh Quang Huynh
Kotryna Vasiliauskaite
Maria Rist
Marius Strømbo Eng
Rebecca C. Frøen
Svein R. Angel
Tore Vehus

Technical personnel
Anna-Berit Wennerström
Anne Cathrine Bakken
Birthe Mikkelsen
Huyen Mong Thi Dinh
Jeanette Daffinrud
Kobra Sultani
Menaka Sathermugathevan
Monica Bostad
Monika Gelazauskaite
Nirma Skrbo
Nomdo A.C. Westerdaal
Olga Machonova
Petros Gebregziabher
Russel Castro
Victoria Edwards

ACCOUNTS

Funding and Cost

Funding

		Amount
The Research Council	The Norwegian Research Council	10 895
The Host Institution	Oslo University Hospital (Rikshospitalet) HF	7 287
Research Partners	University of Oslo	1 298
Enterprise partners	PCI Biotech AS	1 228
	Affitech AS, in kind	963
Total		21 671

All figures in 1000 NOK

Costs

		Amount
The Host Institution	Oslo University Hospital (Rikshospitalet) HF	16510
Research Partners	University of Oslo	2 668
Enterprise partners	PCI Biotech AS	1 530
	Affitech AS	963
Total		21 671
All figures in 1000 NOK		

PUBLICATIONS

Journal papers 2011

Abrahamsen H and Stenmark H, Growth signaling from inside. **Science**, 2011, 334: 611-612

Alagaratnam S, Lind GE, Kraggerud SM, Lothe RA, and Skotheim RI. The testicular germ cell tumour transcriptome. **Int J Androl.** 2011 Aug;34(4 Pt 2):e133-50; discussion e150-1. doi: 10.1111/j.1365-2605.2011.01169.x. Epub 2011 Jun 9. Invited review.

Andersen K, Mori H, Fata J, Bascom J, Oyjord T, Mælandsmo GM, Bissell M. The metastasis-promoting protein S100A4 regulates mammary branching morphogenesis. **Dev Biol**. 2011 Apr 15;352(2):181-90. Epub 2010 Dec 31.

Berg K, Nordstrand S, Selbo PK, Tran DT, Angell-Petersen E, Høgset A. Disulfonated tetraphenyl chlorin (TPCS2a), a novel photosensitizer developed for clinical utilization of photochemical internalization. **Photochem Photobiol Sci.** 2011 Oct;10(10):1637-51. Epub 2011 Jul 20.

Berge G, Pettersen S, Grotterød I, Bettum IJ, Boye K, Mælandsmo GM. Osteopontin--an important downstream effector of S100A4-mediated invasion and metastasis. **Int J Cancer**. 2011 Aug 15;129(4):780-90. doi: 10.1002/ijc.25735. Epub 2011 Mar 11.

Buddingh EP, Kuijjer ML, Duim RA, Bürger H, Agelopoulos K, Myklebost O, Serra M, Mertens F, Hogendoorn PC, Lankester AC, Cleton-Jansen AM, Tumor-infiltrating macrophages are associated with metastasis suppression in high-grade osteosarcoma: a rationale for treatment with macrophage activating agents. **Clin Cancer Res**. 2011 Apr 15;17(8):2110-9.

Engesæter BO, Sathermugathevan M, Hellenes T, Engebråten O, Holm R, Flørenes VA, Mælandsmo GM. Targeting inhibitor of apoptosis proteins in combination with dacarbazine or TRAIL in melanoma cells, **Cancer Biol Ther**. 2011 Jul 1;12(1):47-58. doi: 10.4161/cbt.12.1.15714. Epub 2011 Jul 1.

Haglund K, Nezis IP and Stenmark H. Structure and functions of stable intercellular bridges formed by incomplete cytokinesis during development. **Commun Integr Biol**. 2011 Jan;4(1):1-9.

Hjortland GO, Meza-Zepeda LA, Beiske K, Ree AH, Tveito S, Hoifodt H, Bohler PJ, Hole KH, Myklebost O, Fodstad O, Smeland S, Hovig E. Genome wide single cell analysis of chemotherapy resistant metastatic cells in a case of gastroesophageal adenocarcinoma. **BMC Cancer** 2011 Oct 20;11:455.

Hurley JH and Stenmark H. Molecular mechanisms of ubiquitin-dependent membrane traffic. **Annu Rev Biophys**. 2011 Jun 9;40:119-42.

Hustoft HK, Reubsaet L, Greibrokk T, Lundanes E, Malerod H, Critical assessment of accelerating trypsination methods, **J. Pharm. Biomed. Anal**. 56, 5, 15, 1069–1078

Jing Y, Machon O, Hampl A, Dvorak P, Xing Y, Krauss S. *In vitro* differentiation of mouse embryonic stem cells into neurons of the dorsal forebrain. **Cell Mol Neurobiol.** 2011 Jul;31(5):715-27. doi: 10.1007/s10571-011-9669-2. Epub 2011 Mar 20.

Johnsen E, Wilson SR, Odsbu I, Krapp A, Malerod H, Skarstad K, Lundanes E. Hydrophilic interaction chromatography of nucleoside triphosphates with temperature as a separation parameter. **J Chromatogr A**. 2011 Sep 2;1218(35):5981-6. Epub 2011 Jan 27.

Kuijjer ML, Namløs HM, Hauben EI, Machado I, Kresse SH, Serra M, Llombart-Bosch A, Hogendoorn PC, Meza-Zepeda LA, Myklebost O, Cleton-Jansen AM, mRNA expression profiles of primary high-grade central osteosarcoma are preserved in cell lines and xenografts. **BMC Med Genomics** 2011 Sep 20;4:66.

Lassen B, Helseth E, Rønning P, Scheie D, Johannesen TB, Mæhlen J, Langmoen IA. Meling TR, Surgical mortality at 30 days and complications leading to recraniotomy in 2630 consecutive craniotomies for intracranial tumors. **Neurosurgery**. 2011 May;68(5):1259-68.

Lilletvedt M, Smistad G, Tonnesen HH, Hogset A, Kristensen S. Solubilization of the novel anionic amphiphilic photosensitizer TPCS 2a by nonionic Pluronic block copolymers. **Eur J Pharm Sci** 2011 Jun 14;43(3):180-7.

Lilletvedt M, Tonnesen HH, Hogset A, Sande SA. Kristensen S. Evaluation of physicochemical properties and aggregation of the photosensitizers TPCS2a and TPPS2a in aqueous media. **Pharmazie**. 2011 May;66(5):325-33.

Lind GE, Raiborg C, Danielsen SA, Rognum TO, Thiis-Evensen E, Nesbakken A, Stenmark H and Lothe RA. SPG20, a novel biomarker in colorectal carcinogenesis, encodes a regulator of cytokinesis. **Oncogene**. 2011 Sep 15;30(37):3967-78. doi: 10.1038/onc.2011.109. Epub 2011 Apr 18.

Liu H, Tekle C, Chen YW, Kristian A, Zhao Y, Zhou M, Liu Z, Ding Y, Wang B, Mælandsmo GM, Nesland JM, Fodstad O, Tan M. B7-H3 silencing increases paclitaxel sensitivity by abrogating Jak2/Stat3 phosphorylation, **Mol Cancer Ther**. 2011 Jun;10(6):960-71. Epub 2011 Apr 25.

Lobert VH and Stenmark H, Cell polarity and migration: Emerging role for the endosomal sorting machinery. **Physiology** 2011, 26: 171-180.

Løvf M, Thomassen GOS, Bakken AC, Celestino R, Fioretos T, Lind GE, Lothe RA and Skotheim RI. Fusion gene microarray reveals cancer type-specificity among fusion genes, **Genes Chromosomes Cancer**. 2011 May;50(5):348-57. doi: 10.1002/gcc.20860. Epub 2011 Feb 8.

Malerød L, Pedersen NM, Lobert VH, Leithe E, Wegner CES, Brech A, Edgar Rivedal E, Liestøl K and Stenmark H. Cargo-dependent degradation of ESCRT-I as a feedback mechanism to modulate endosomal sorting. **Traffic**. 2011 Sep;12(9):1211-26. doi: 10.1111/j.1600-0854.2011.01220.x. Epub 2011 Jun 13.

Ohnstad HO, Paulsen EB, Noordhuis P, Berg M, Lothe RA, Vassilev LT, Myklebost O. MDM2 antagonist Nutlin-3a potentiates antitumour activity of cytotoxic drugs in osteosarcoma cell lines. **BMC Cancer**. 2011 May 30;11:211:1-11. doi: 10.1186/1471-2407-11-211.

Olstorn H, Varghese M, Murrell W, Moe MC, Langmoen IA. Predifferentiated brain-derived adult human progenitor cells migrate toward ischemia after transplantation to the adult rat brain. **Neurosurgery**. 2011 Jan;68(1):213-22.

Paus E, Haugen MH, Olsen KH, Flatmark K, Maelandsmo GM, Nilsson O, Röijer E, Lundin M, Fermér C, Samsonova M, Lebedin Y, Stigbrand T. TD-11 workshop report: characterization of monoclonal antibodies to S100 proteins. **Tumour Biol**. 2011 Feb;32(1):1-12. Epub 2010 Jul 24.

Platta HW, Stenmark H. Endocytosis and signaling. **Curr Opin Cell Biol**. 2011 Aug;23(4):393-403. Epub 2011 Apr 5. Review.

Raiborg C and Stenmark H. A helix for the final cut. **Science**. 2011 Mar 25;331(6024):1533-4.

Rogeberg M, Wilson SR, Malerod H, Lundanes E, Tanaka N, Greibrokk T. High efficiency, high temperature separations on silica based monolithic columns. **J Chromatogr A**. 2011 Oct 14;1218(41):7281-8. Epub 2011 Aug 23.

Sagona AP, Nezis IP, Bache KG, Haglund K, Bakken AC, Skotheim RI, Stenmark H. A tumor-associated mutation of FYVE-CENT prevents its interaction with Beclin 1 and interferes with cytokinesis. **PLoS One**. 2011 Mar 24;6(3):e17086.

Schink KO, Stenmark H. Cell differentiation: midbody remnants - junk or fate factors? **Curr Biol**. 2011 Dec 6;21(23):R958-60. Epub 2011 Dec 5.

Skårn M, Namløs HM, Noordhuis P, Wang MY, Meza-Zepeda LA, Myklebost O, Adipocytic differentiation of human bone marrow-derived stromal cells is modulated by microRNA-155, microRNA-221, and microRNA-222. **Stem Cells Dev**. 2011 Aug 24. Epub ahead of print.

Strand MF, Wilson SR, Dembinski JL, Holsworth DD, Khvat A, Okun I, Petersen D, Krauss S. A novel synthetic smoothened antagonist transiently inhibits pancreatic adenocarcinoma xenografts in a mouse model, **PLoS One.** 2011;6(6):e19904. Epub 2011 Jun 15.

Stratford EW, Castro R, Wennerstrøm A, Holm R, Munthe E, Lauvrak S, Bjerkehagen B and Myklebost O. Liposarcoma cells woth aldefluor and cd133 activity have a cancer stem cell potential. **Clinical sarcoma research** 2011. 1:8.

Svendsen KO, Larsen HR, Pedersen SA, Brenna I, Lundanes E, Wilson SR. Automatic filtration and filter flush for robust online solid-phase extraction liquid chromatography. **J Sep Sci**. 2011 Nov;34(21):3020-2. doi: 10.1002/jssc.201100553. Epub 2011 Sep 15.

Szokol K, Glover JC, Perreault MC. Organization of functional synaptic connections between medullary reticulospinal neurons and lumbar descending commissural interneurons in the neonatal mouse. **J Neurosci.** 2011 Mar 23;31(12):4731-42.

Tekle C, Nygren MK, Chen YW, Dybsjord I, Nesland JM, Maelandsmo GM, Fodstad O. B7-H3 contributes to the metastatic capacity of melanoma cells by modulation of known metastasis-associated genes, **Int J Cancer.** 2011 Jun 13. doi: 10.1002/ijc.26238. [Epub ahead of print].

Vik-Mo EO, Sandberg C, Joel M, Stangeland B, Watanabe Y, Mackay-Sim A, Moe MC, Murrell W, Langmoen IA. A comparative study of the structural organization of spheres derived from the adult human subventricular zone and glioblastoma biopsies. **Exp Cell Res**. 2011 Apr 15;317(7):1049-59.

Waaler J, Machon O, von Kries JP, Wilson SR, Lundenes E, Wedlich D, Gradl D, Paulsen JE, Machonova O, Dembinski JL, Dinh H, Krauss S. Novel synthetic antagonists of canonical Wnt signaling inhibit colorectal cancer cell growth, **Cancer Res**. 2011 Jan 1;71(1):197-205.

Wegner CS, Rodahl LM and Stenmark H. ESCRT proteins and cell signaling. **Traffic**. 2011 Oct;12(10):1291-7. doi: 10.1111/j.1600-0854.2011.01210.x. Epub 2011 May 13. Review.

Weyergang A, Selbo PK, Berstad ME, Bostad M, Berg K. Photochemical internalization of tumor-targeted protein toxins. **Lasers Surg Med**. 2011 Sep;43(7):721-33. doi:10.1002/lsm.21084.

Journal papers 2012

Abu-Yousif AO, Moor AC, Zheng X, Savellano MD, Yu W, Selbo PK, Hasan T. Epidermal growth factor receptor-targeted photosensitizer selectively inhibits EGFR signaling and induces targeted phototoxicity in ovarian cancer cells. **Cancer Lett**. 2012 Aug 28;321(2):120-7. Epub 2012 Jan 18. http://dx.doi.org/10.1016/j.canlet.2012.01.014

Boulland JL, Leung DS, Thuen M, Vik-Mo E, Joel M, Perreault MC, Langmoen IA, Haraldseth O, Glover JC. Evaluation of intracellular labeling with micron-sized particles of iron oxide (MPIOs) as a general tool for in vitro and in vivo tracking of human stem and progenitor cells. **Cell Transplant**. 2012 Mar 27. doi: 10.3727/096368911X627598. [Epub ahead of print]

Fossdal G, Vik-Mo EO, Sandberg C, Varghese M, Kaarbø M, Telmo E, Langmoen IA, Murrell W. Aqp 9 and brain tumour stem cells. **ScientificWorldJournal**. 2012;2012:915176. Epub 2012 Jan 4.

Halasi G, Søviknes AM, Sigurjonsson O, Glover JC. Proliferation and recapitulation of developmental patterning associated with regulative regeneration of the spinal cord neural tube. **Dev Biol.** 2012 May 1;365(1):118-32. Epub 2012 Feb 18.

Huuse EM, Moestue SA, Lindholm EM, Bathen TF, Nalwoga H, Krüger K, Bofin A, Maelandsmo GM, Akslen LA, Engebraaten O, Gribbestad IS. *In vivo* MRI and histopathological assessment of tumor microenvironment in luminal-like and basal-like breast cancer xenografts. **J Magn Reson Imaging**. 2012 May;35(5):1098-107. doi: 10.1002/jmri.23507. Epub 2011 Dec 14.

Kim J, Villadsen R, Sørlie T, Fogh L, Grønlund SZ, Fridriksdottir AJ, Kuhn I, Rank F, Wielenga VT, Solvang H, Edwards PA, Børresen-Dale AL, Rønnov-Jessen L, Bissell MJ, Petersen OW. Tumor initiating but differentiated luminal-like breast cancer cells are highly invasive in the absence of basal-like activity. **Proc Natl Acad Sci U S A.** 2012 Apr 17;109(16):6124-9. Epub 2012 Mar 27.

Kresse SH, Meza-Zepeda LA, Machado I, Llombart-Bosch A, Myklebost O. Preclinical xenograft models of human sarcoma show nonrandom loss of aberrations. **Cancer**. 2012 Jan 15;118(2):558-70. doi: 10.1002/cncr.26276. Epub 2011 Jun 28.

Kuijjer ML, Rydbeck H, Kresse SH, Buddingh EP, Lid AB, Roelofs H, Bürger H, Myklebost O, Hogendoorn PC, Meza-Zepeda LA, Cleton-Jansen AM. Identification of osteosarcoma driver genes by integrative analysis of copy number and gene expression data. **Genes Chromosomes Cancer.** 2012 Jul;51(7):696-706. doi: 10.1002/gcc.21956. Epub 2012 Mar 27.

Lindholm EM, Kristian A, Nalwoga H, Krüger K, Nygård S, Akslen LA, Mælandsmo GM, Engebraaten O. Effect of antiangiogenic therapy on tumor growth, vasculature and kinase activity in basal- and luminal-like breast cancer xenografts. **Mol Oncol**. 2012 Mar 31. [Epub ahead of print]

Lobert VH and Stenmark H, The ESCRT machinery mediates polarization of fibroblasts through regulation of myosin light chain. **J.Cell Sci**. 2012, 125: 29-36

Namløs HM, Kresse SH, Müller CR, Henriksen J, Holdhus R, Sæter G, Bruland OS, Bjerkehagen B, Steen VM, Myklebost O. Global gene expression profiling of human osteosarcomas reveals metastasis-associated chemokine pattern. **Sarcoma**. 2012;2012:639038. Epub 2012 Feb 28.

Nezis IP, Stenmark H. p62 at the Interface of Autophagy, Oxidative Stress Signaling, and Cancer. **Antioxid Redox Signal**. 2012 Jan 11. [Epub ahead of print]

Nunes AR, Chavez-Valdez R, Ezell T, Donnelly DF, Glover JC, Gauda EB. Effect of development on [Ca2+] i transients to ATP in petrosal ganglion neurons: a pharmacological approach using optical recording. **J Appl Physiol**. 2012 Apr;112(8):1393-402. Epub 2012 Jan 12.

Platta HW, Abrahamsen H, Thoresen SB and Stenmark H, Nedd4-dependent lysine-11-linked polyubiuqitination of the tumour suppressor Beclin 1. **Biochem. J**. 2012, 441: 399-406

Roberg-Larsen H, Strand MF, Grimsmo A, Olsen PA, Dembinski JL, Rise F, Lundanes E, Greibrokk T, Krauss S, Wilson SR. High sensitivity measurements of active oxysterols with automated filtration/filter backflush-solid phase extraction-liquid chromatography-mass spectrometry. **J Chromatogr A**. 2012 Feb 28. [Epub ahead of print]

Selbo PK, Weyergang A, Eng MS, Bostad M, Mælandsmo GM, Høgset A, Berg K. Strongly amphiphilic photosensitizers are not substrates of the cancer stem cell marker ABCG2 and provides specific and efficient light-triggered drug delivery of an EGFR-targeted cytotoxic drug. **J Control Release.** 2012 Apr 30;159(2):197-203. Epub 2012 Feb 10. http://dx.doi.org/10.1016/j.jconrel.2012.02.003

Slipicevic, A., Holm, R., Emilsen, E., Rosnes, A. K. R., Welch, D., Mælandsmo, G. M. And Flørenes, V. A.: Cytoplasmic BRMS1 expression in malignant melanomais associated with increased disease-free survival, **BMC Cancer.** 2012 Feb 22;12(1):73. [Epub ahead of print]

Solberg N, Machon O, Krauss S. Characterization and functional analysis of the 5'-flanking promoter region of the mouse Tcf3 gene. **Mol Cell Biochem**. 2012 Jan;360(1-2):289-99. Epub 2011 Sep 21.

Solberg N, Machon O, Machonova O, Krauss S. Mouse Tcf3 represses canonical Wnt signaling by either competing for β-catenin binding or through occupation of DNA-binding sites. **Mol Cell Biochem**. 2012 Jun;365(1-2):53-63. Epub 2012 Jan 22.

Stratford EW, Castro R, Daffinrud J, Skarn M, Lauvrak SU, Munthe E and Myklebost O. Characterization of a liposarcoma cell line panel with focus on tumor formation, stem-ness and differentiation. **Sarcoma**. 2012 [In press].

Tekle C, Nygren MK, Chen YW, Dybsjord I, Nesland JM, Maelandsmo GM, Fodstad O. B7-H3 contributes to the metastatic capacity of melanoma cells by modulation of known metastasis-associated genes. **Int J Cancer.** 2012 May 15;130(10):2282-90. doi: 10.1002/ijc.26238.

Waaler J, Machon O, Tumova L, Dinh H, Korinek V, Wilson SR, Paulsen JE, Pedersen NM, Eide TJ, Machonova O, Gradl D, Voronkov A, von Kries JP, Krauss S. A Novel Tankyrase Inhibitor Decreases Canonical Wnt Signaling in Colon Carcinoma Cells and Reduces Tumor Growth in Conditional APC Mutant Mice. **Cancer Res**. 2012 Jun 1;72(11):2822-2832. Epub 2012 Mar 22.

Published Conference Papers

Invited lecture

2011 European Multidisciplinary Cancer Congress, Stockholm:

Selbo PK and Berg K. Fluorescence Guided Cancer Therapy. European Journal of Cancer Volume 47, Supplement 1, September 2011, Pages S27

Abstracts

Greibrokk T., Lundanes E., Wilson S.R., Malerod H., Hustoft H. K., Rogeberg M. Recent advances in two-dimensional capillary LC (Oral). ISCC 2011, 35th Int. Symp. Cap. Chrom. San Diego, US, 1-5. May

Johnsen E, Wilson SR, Krapp A, Odsbu I, Malerod H, Skarstad K, Lundanes E. HILIC separation of Nucleoside Triphosphates with Temperature as a Separation Parameter (Poster). HPLC 2011, 36th international symposium on high-performance liquid phase separations and related techniques. Budapest, Hungary: 19-23 June

Malerod H, Hustoft HK, Wilson SR, Reubsaet L, Lundanes E, Greibrokk T, Evaluating accelerating methods for trypsin digestion in LC-MS based proteomics (Poster). HPLC 2011, 36th international symposium on high-performance liquid phase separations and related techniques. Budapest, Hungary: 19-23 June_

Mughal Ahmad A. "Knock-down of a chromatid segregation mediator gene impairs tumor growth in Glioblastoma Multiforme.", Molecular Targets and Cancer Therapeutics, 2011, Nov. 12-16, San Francisco, CA

Rogeberg M, Wilson SR, Malerod H, Lundanes E, Tanaka N, Greibrokk T. Monolithic Silica Based Columns for Fast, High Temperature Peptide Separations in Proteomics (poster). HPLC 2011, 36th international symposium on high-performance liquid phase separations and related techniques. Budapest, Hungary: 19-23 June

Stangeland B.. "Identification of new molecular targets in glioblastoma.", Molecular Targets and Cancer Therapeutics, 2011, nov. 12-16, San Francisco, CA

Wilson S. R. Automation and On-line Hyphenations for Trace Analysis (Oral). European Lab Automation, Hamburg, Germany: 21-22 June

Books

Glover JC (2011). Therapeutic strategies for repairing motor functions of the spinal cord. In: **Motor Functions of the Spinal Cord**, Transworld Research Network, Kerala, India: ISBN: 978-81-7895-512-4 Editor: András Birinyi.

Hustoft HK, Malerød H, Wilson, SR, Reubsaet L, Lundanes E, Greibrokk T (2012). A critical review of trypsin digestion for LC-MS based proteomics, In Eastwood Lueng (ed.), ***Proteomics / book2***. Intech. ISBN 979-953-307-693-4.

Reports

PCI Biotech 2011:

http://www.oslocancercluster.no/News/tabid/69/articleType/ArticleView/articleId/103/PCI-Biotech-study-shows-great-results.aspx

http://www.oslo.teknopol.no/MainMenu/news2/News/PCI-Biotech--Winner-of-both-DnB-NORs-Innovation-prize-2011-and-the-Peoples-award/

http://ecancer.org/tv/pubdate/1162

Patents

Krauss-group
Patent 1
Title: Azole derivates as Wnt pathway inhibitors (title on published WO patent application)
Priority application: EP09251497.5, Priority date 05.06.23009
PCT application: PCT/GB2010/001118, International filing date 07.06.2010
Publication: WO2010139966, International publication date 09.12.2010
The application is filed in US, EPO, Canada, Australia, Japan, China and India.

Patent 2
Title: Compounds
Priority application: US 61/420,942, 08.12.2010
PCT application: PCT/GB2011/052441, 08.12.2011

Patent 3
Title: Wnt pathway inhibitors
Priority application: US61/579094, 22.12.2011

Lundanes-group
Wilson SR, Svendsen K, Larsen HR. "On-line filtration and filter wash for chromatography systems", patent application filed 21 June 2011, DOFI 11019.

CONTACT INFORMATION

Academic Partners

Stefan Krauss - Center Director
Unit for Cell Signalling
Dept. of Microbiology
Oslo University Hospital HF, Rikshospitalet
stefan.krauss@rr-research.no
+47 22 95 81 52

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

Iver A. Langmoen
Department of Neurosurgery
Oslo University Hospital HF, Ullevål Univ. Hospital/ Rikshospitalet
iver.a.langmoen@rr-research.no
+47 23 01 54 62

Ragnhild A. Lothe
Department of Cancer Prevention
Institute for Cancer Research, Oslo University Hospital, Radium Hospital
rlothe@rr-research.no
+47 22 78 17 28

Elsa Lundanes
Department of Chemistry
University of Oslo, P.O. Box 1033 Blindern, NO-0315 Oslo
elsa.lundanes@kjemi.uio.no
+47 22 85 55 53

Tyge Greibrokk
Department of Chemistry
University of Oslo, P.O. Box 1033 Blindern, NO-0315 Oslo
tyge.greibrokk@kjemi.uio.no
+47 22 85 50 27

Gunhild Mari Mælandsmo
Department of Tumor Biology
Institute for Cancer Research, Oslo University Hospital, The Norwegian Radium Hospital
gunhild.mari.mælandsmo@rr-research.no
+47 22 78 18 79

Harald Stenmark
Department of Biochemistry
Institute for Cancer Research, Oslo University Hospital, Radium Hospital
h.a.stenmark@medisin.uio.no
+47 22 78 18 18

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

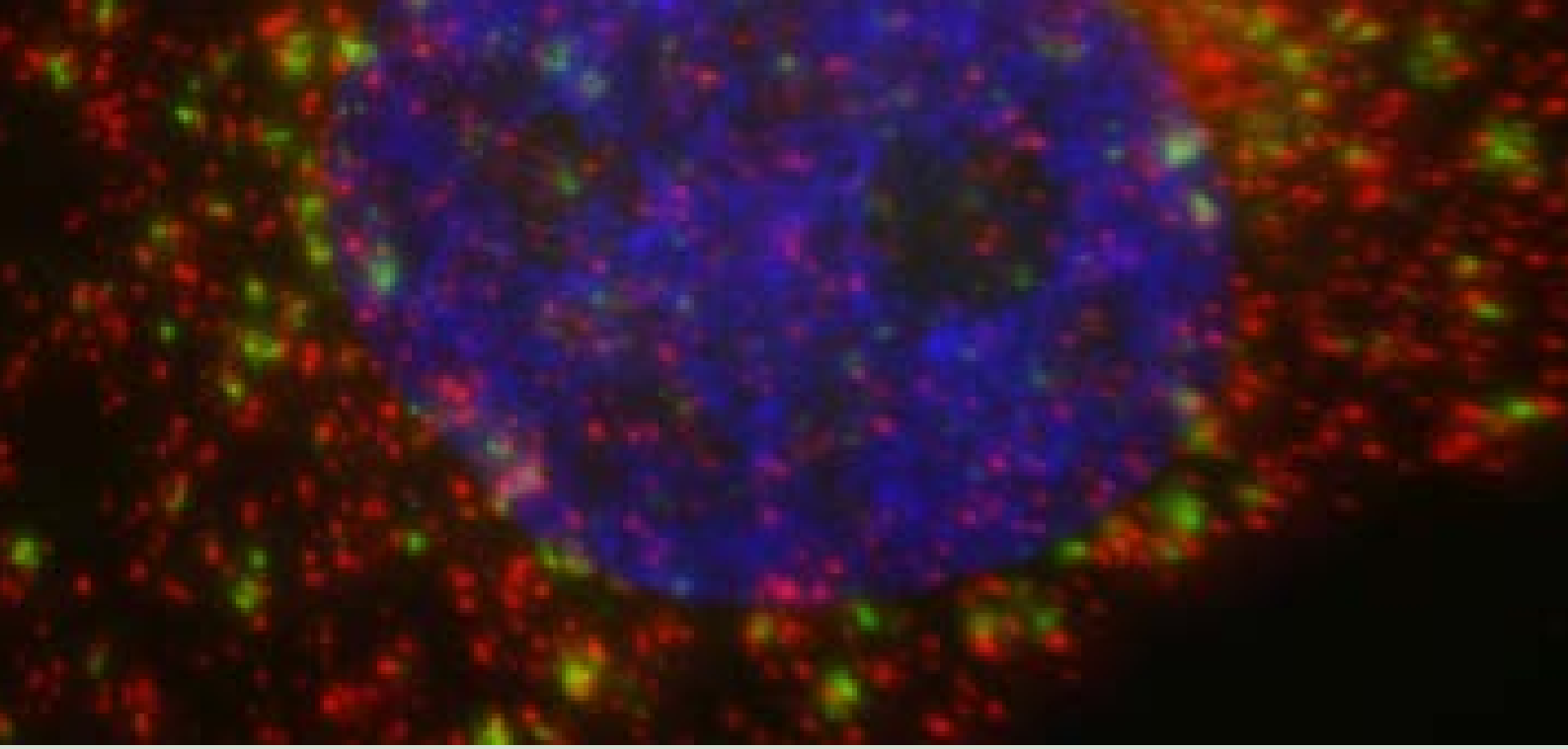
Joel Glover
Department of Physiology
Institute of Basic Medical Sciences
University of Oslo
joel.glover@medisin.uio.no
+47 22 85 12 30

Industry Partners

Affitech Research AS
Jenny Karlsson
Oslo Research Park
Gaustadalleen 21
0349 Oslo, Norway
j.karlsson@affitech.com
Tel +47 22 95 86 03
http://www.affitech.com

PCI Biotech Holding ASA
Anders Høgset
Strandveien 55
1366 Lysaker, Norway
anders.hogset@pcibiotech.no
Tel +47 67 11 54 04
http://www.pcibiotech.no

Photo: Affitech Research AS



CAST
CANCER • STEM CELL
INNOVATION CENTER

www.cancerstemcell.no

SFI CAST

Oslo University Hospital HF,
Rikshospitalet
Forskningsparken
Gaustadalleen 21
0349 Oslo, Norway

Managing Director
Prof. Stefan Krauss
stefan.krauss@rr-research.no
+47 22 95 81 52

Assistant Managing Director
Prof. Ola Myklebost
ola.myklebost@imbv.uio.no
+47 22 78 17 79

Administrative Manager
Line Mygland
line.mygland@rr-research.no
+47 22 95 81 55

design | essenz.no