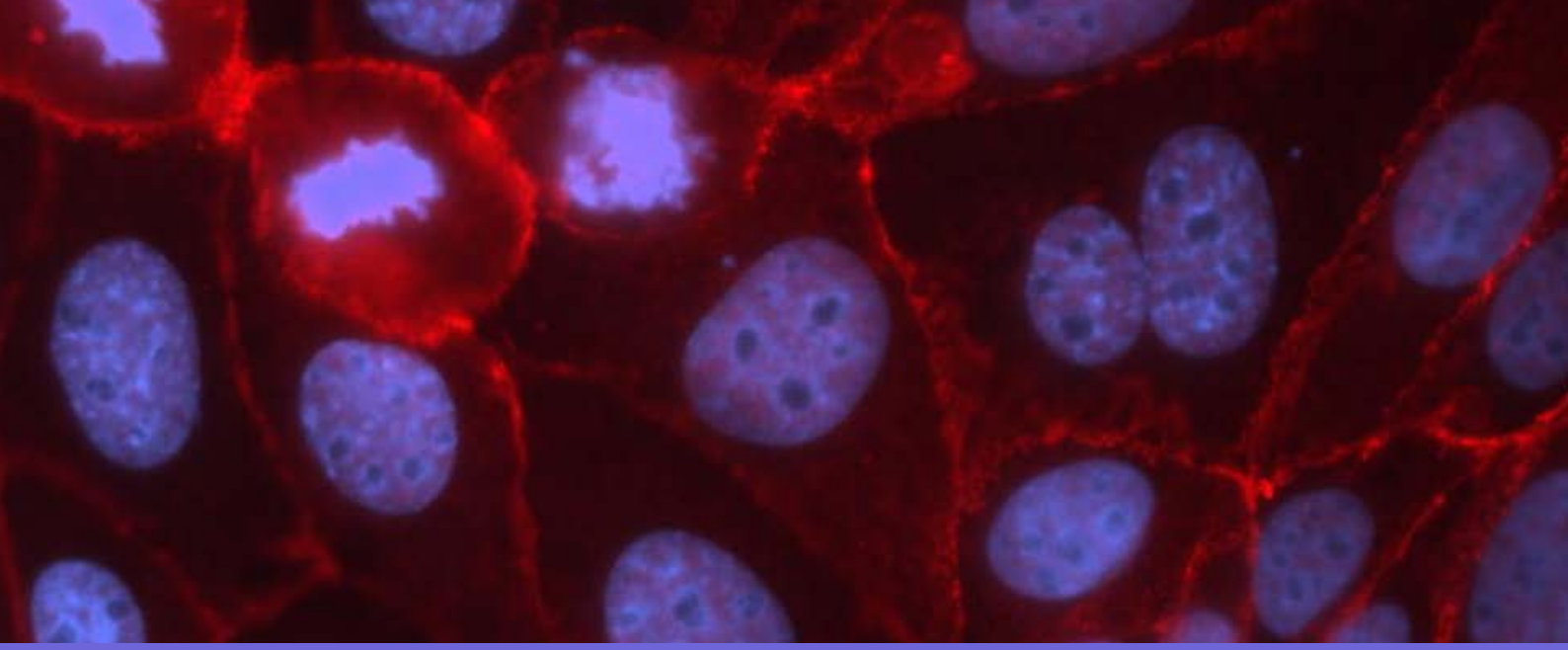

2010 Annual Report

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 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 cancer 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.

In the 4 years of its existence, SFI-CAST researchers have established analytical tools that provide a solid basis for industry development. A series of validated cancer cell lines has been established that provide a frame for *in vitro* and *in vivo* tests. A pioneering clinical trial based on an in-house developed immunotherapy protocol is in progress. Finally, a spin-off company based on SFI-CAST technology is developing.

The year 2010 has been a critical milestone for SFI-CAST, as the centre was going through a mid-term evaluation.

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 supportive to the implementation of our commercialisation 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

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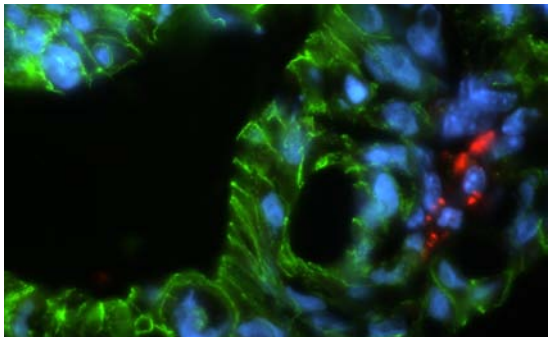


Panc03.27 tumours were established in mice using unsorted, DiI labeled cells (day 0) and harvested after 51 days to select for label-retaining DiI+/slow cycling cells in vivo. Photo shows E-cadherin staining (green, 488) of a tumour section, demonstrating the loss of E-cadherin in the DiI+/slow cycling cells (red) (J. Dembinski).

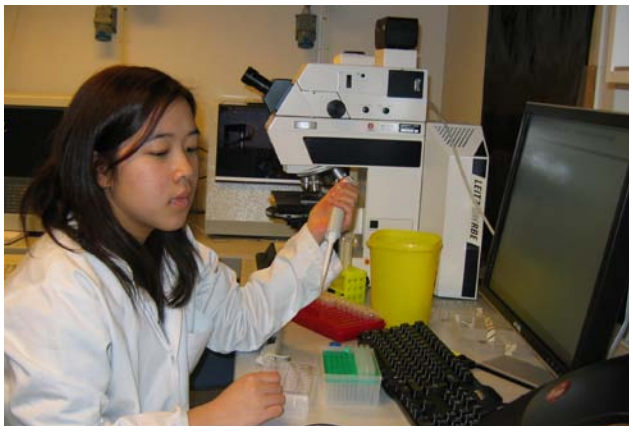
Summary

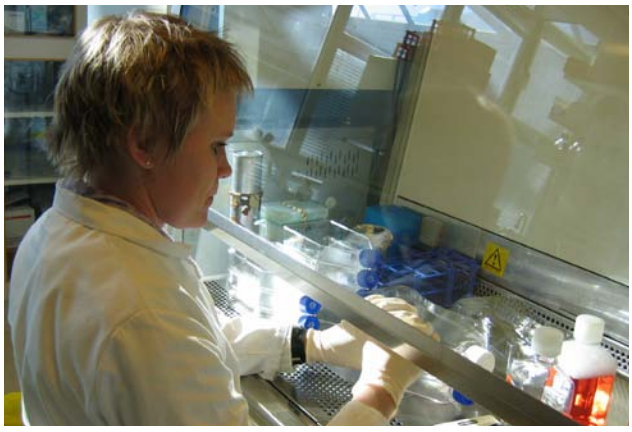
During the last decade, cancer research has gained substantial knowledge by applying a multidisciplinary developmental understanding of tumour formation and progression, as well as a precise analysis on individual differences in tumours with single cell resolution.

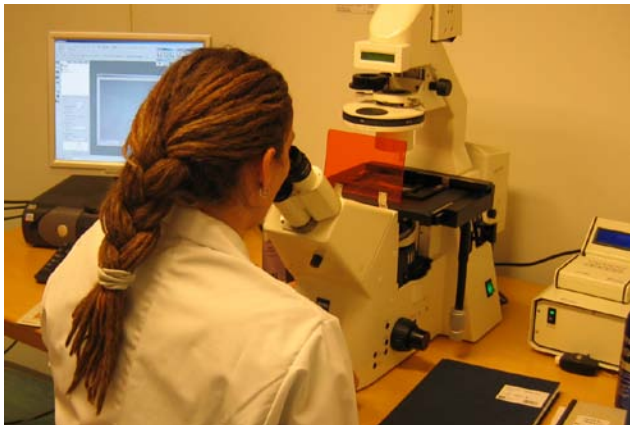
It is now becoming increasingly evident that cancer cells comprise a heterogeneous cell population with dynamic sub-populations of cells showing different biological profiles including cell proliferation, invasiveness and metastatic potential. The temporal and spatial dynamics of heterogeneity appear 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 providing single cell (or sub cellular) resolution and high sensitivity, 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 tumour 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 characterisation of stem cell parameters in tumours. SFI-CAST develops innovative approaches for finding small drugs, cancer vaccines and antibodies that address specifically stem cell issues in cancer. Furthermore, SFI-CAST works towards high resolution visualisation of specific cell sub-populations in the body as a tool for tracking therapeutic success.



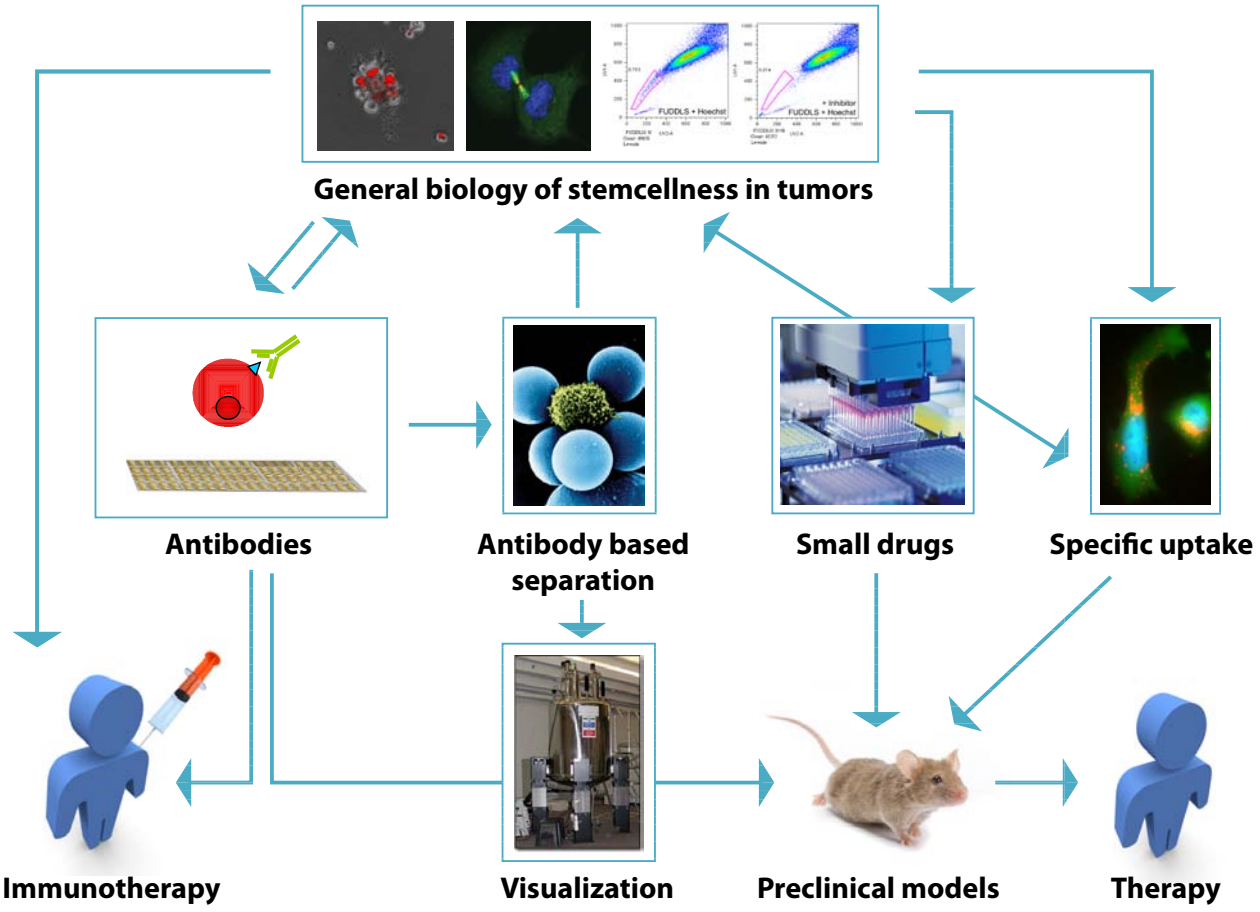




Goals and research strategy

The SFI-CAST biomedical innovation centre has a work program aimed at advancing basic research on 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 identified with industry partner Affitech AS. The antibodies will be used to identify novel epitopes and therapeutic targets. (ii) Tumour stem cell pathways are used for differential high throughput screens for drugs (a biotechnology startup company will be established for this goal in spring 2010). (iii) High resolution cell imaging of tumour stem cells *in vivo* using magnetic resonance imaging (MRI) techniques is developed in animal models. (iv) Ways to find improved immunotherapy protocols and targets are being explored and tested. (vi) Specific receptors 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 Radiumhospital 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 to initial the first clinical trials targeting TSC (Tumour Stem Cell) from the very beginning of the project. This ensures a swift start of the translational aspect as well as providing clinical material for the individual work programs.



Innovative highlights of the SFI-CAST biomedical innovation centre

Determining parameters that influence heterogeneity in solid tumours is the core activity of the SFI-CAST consortium. The SFI-CAST researchers work on breast cancer, melanoma, lung cancer, colon cancer, oesophagus carcinoma, mesenchymal tumours and pancreas adenocarcinoma.

A broad range of early stage discovery programs are in progress at SFI-CAST.

As part of the SFI-CAST core facility, a "Cancer Stem Cell Validation Platform" has been further expanded. With the aim of creating a large panel of proprietary cancer cell lines for use within CAST, the Gaudernack group has established > 20 primary lung cancer cell lines and 10 primary prostate cancer cell lines, starting from fresh surgical specimens. In addition, 2 primary pancreas cancer cell lines have been established. These cell lines constitute a master cell bank. A further objective is to offer these models for validation of candidate treatments.

The Lothe laboratory has focused on molecules which are specific to cancer cells with stemness properties and which can be used both as cancer biomarkers and as targets for therapy. The laboratory has continued to investigate exon-resolution genome-wide expression analysis comparing embryonal carcinoma and embryonic stem cells. Sorting for pluripotent populations in both cell types allowed the identification of malignancy-specific gene expression and alternative splicing events between the two cell types, several of which have been both technically validated and clinically validated in an extended series of cancer samples. The group has also developed a new strategy for detection of oncogenic fusion genes, and highlighted that fusion genes are in general specific to the cancer types from which they were originally discovered.

In the breast cancer arena, the Mælandsmo group has isolated and characterised tumour cell populations from two orthotopically growing breast cancer xenograft models. In both cancer subtypes (luminal and basal-like) all tumour cells expressed EpCAM, and *in vivo* experiments showed that the luminal like EpCAM subpopulation had the highest tumour initiating potential. Further analysis of the luminal-like EpCAM population revealed population heterogeneity with respect to cell surface markers and *in vivo* tumourigenicity. In collaboration with T. Sørlie whole genome expression analysis have been performed, and the results indicate that the population with the highest *in vivo* tumourigenic potential contain cells with a more basal-like transcriptional profile, while the most benign population has a transcriptome more similar to a luminal-like expression profile.

In the melanoma arena, research in the Mælandsmo group suggests that most of melanoma cells have the potential to exhibit "stemcellness". This is in agreement with the new theory, which proposes that acquisition of CSC (Cancer Stem Cell) characteristics in melanoma might be a dynamic process and most of melanoma cells can switch into a transient CSC-like phenotype given appropriate signals from the microenvironment. This signifies the importance of a better understanding of the microenvironment-driven signals that might regulate phenotype-switching, i.e. generation of invasive/metastatic, therapy-resistant, stem-like subpopulations. The group has developed *in vitro* and *in vivo* melanoma models allowing investigation of tumour-microenvironment interaction and its role on the phenotype and functional properties of melanoma cells.

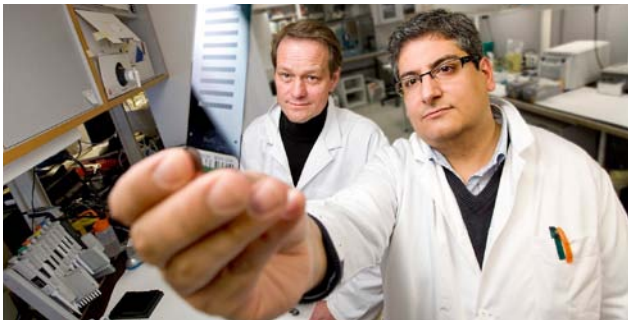
Also, selected cell lines derived from various other solid tumours, including lung cancer, oesophagus cancer, mesenchymal tumours and pancreas adenocarcinoma depict various degrees of heterogeneity. In pancreas adenocarcinoma, the Krauss laboratory has identified a slower cycling sub-population of cells at the invasive edge that show differential drug response and migration as well as tumour initiation potential. The Myklebost laboratory has continued the search for CSCs in mesenchymal, breast, and lung cancers, identifying various sub-populations, by metabolic labelling, surface staining, and label retention (slow cycling), and investigating their stem cell properties, in particular colony-forming ability *in vitro* and tumour-initiating ability in mice. A particular focus has been on the HMGA2 protein, which together

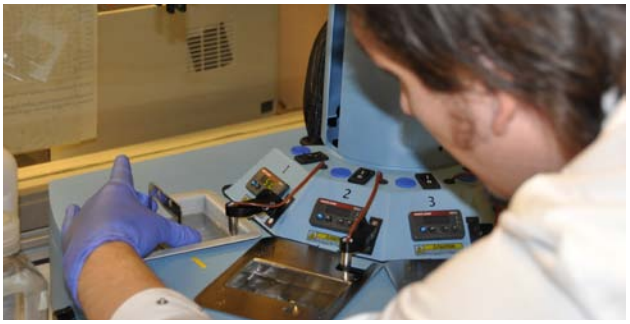
with its antagonist microRNA let-7 is an important regulator of stem cell phenotypes. The Glover group used Phospho-flow studies to study phosphoprotein dynamics in primary glioblastoma cells and CSCs from different tumours.

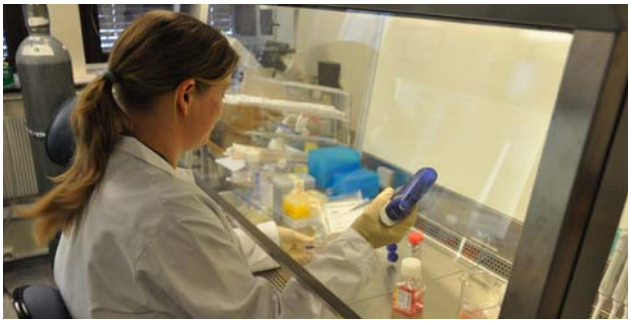
The SFI-CAST consortium has put a major focus on cellular signals that determine stemcellness. In particular, the role of canonical Wnt signalling in stemcellness and cancer was studied in a number of tumours and cancer stem cell models. Based on this research, two novel inhibitors of canonical Wnt signalling have been identified that specifically block nuclear presence of β-catenin. Using a new nanoflow liquid chromatography technology, signalling and signal inhibition dependent alterations in metabolites are currently studied.

A further highlight in 2010 was the identification of a Class III PI 3-kinase as a novel regulator of cell division via production of PtdIns3P by Harald Stenmark. Furthermore, the PtdIns3P-binding protein FYVE-CENT was identified as a key regulator of cytokinesis. Another regulator of cytokinesis was also identified, CIN85, and its function was studied *in vivo*. Integrin degradation via ubiquitination and lysosomal sorting was established as a novel mechanism involved in cell migration. A novel mechanism of cell death regulation was uncovered – triggering of apoptosis through autophagic degradation of an apoptosis inhibitor.

Finally, in 2010, a Phase I/II clinical trial of glioblastoma vaccine based on dendritic cells transfected with amplified glioblastoma stem cell (neurosphere) mRNA was continued. Fourteen patients have been included and preliminary results demonstrate that immune responses may be obtained in vaccinated patients and are associated with a favourable clinical response. Another clinical protocol along the same line as the glioblastoma protocol, but targeting ovarian cancer stem cells has been submitted to the regulatory authorities for approval. The protocol was approved in February 2010 and patient recruitment has started.







Organisation

Management and members

SFI-CAST consists of 10 research groups; 8 groups at the Oslo University Hospital and 2 groups at the University of Oslo. There are three industry partners in the consortium. In 2010 the centre's activities were located at the Norwegian Radium Hospital, Oslo Research Park, Rikshospitalet, Ullevål Oslo University Hospital, and at Domus Medica and the Department of Chemistry (University of Oslo) as well as in the different industries. In total SFI-CAST employs 90 scientific staff.

SFI-CAST is headed by Stefan Krauss (director) and Ola Myklebost (assistant director). The administrative manager of SFI-CAST is Line Mygland.

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

Academic SFI-CAST members

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

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

Gustav Gaudernack, Department of Immunology, Oslo University Hospital, the Norwegian Radium Hospital

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

Iver 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

Invitrogen Dynal AS

PCI Biotech Holding ASA

The Board

The board is responsible for ensuring that SFI-CAST is developed in accordance with the current research plan. In 2010 the board members were:

Steinar Funderud, Oslo University Hospital, Rikshospitalet (Chairman)

Karen Marie Ulshagen, University of Oslo

Lars Engebretsen, Oslo University Hospital, Ullevål University Hospital

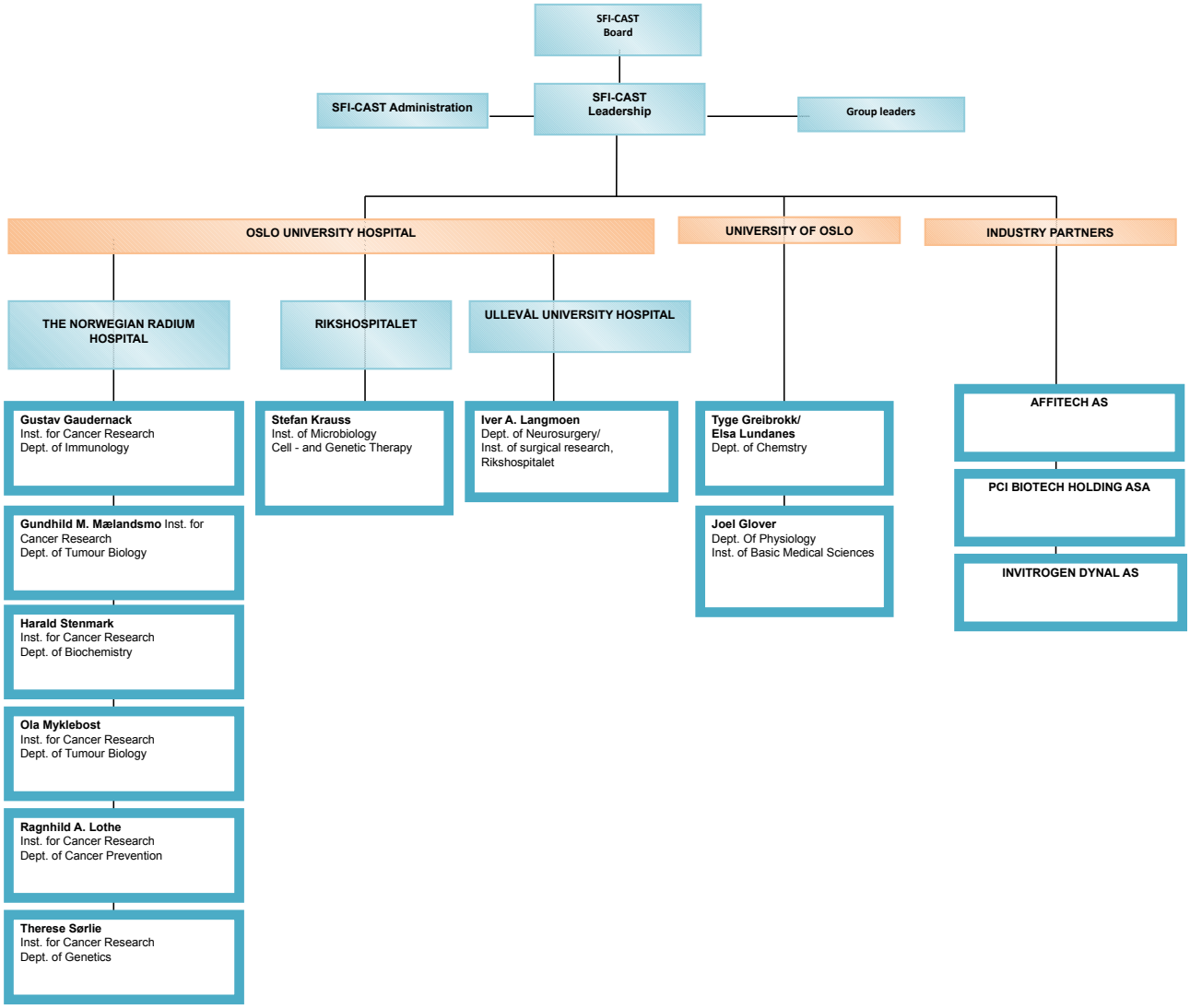
Martin Welschof, Affitech AS

Anders Høgset, PCI Biotech Holding ASA

Øystein Rønning, Norwegian Research Council, Observer

Research Building at the Norwegian Radium Hospital (O. Myklebost)

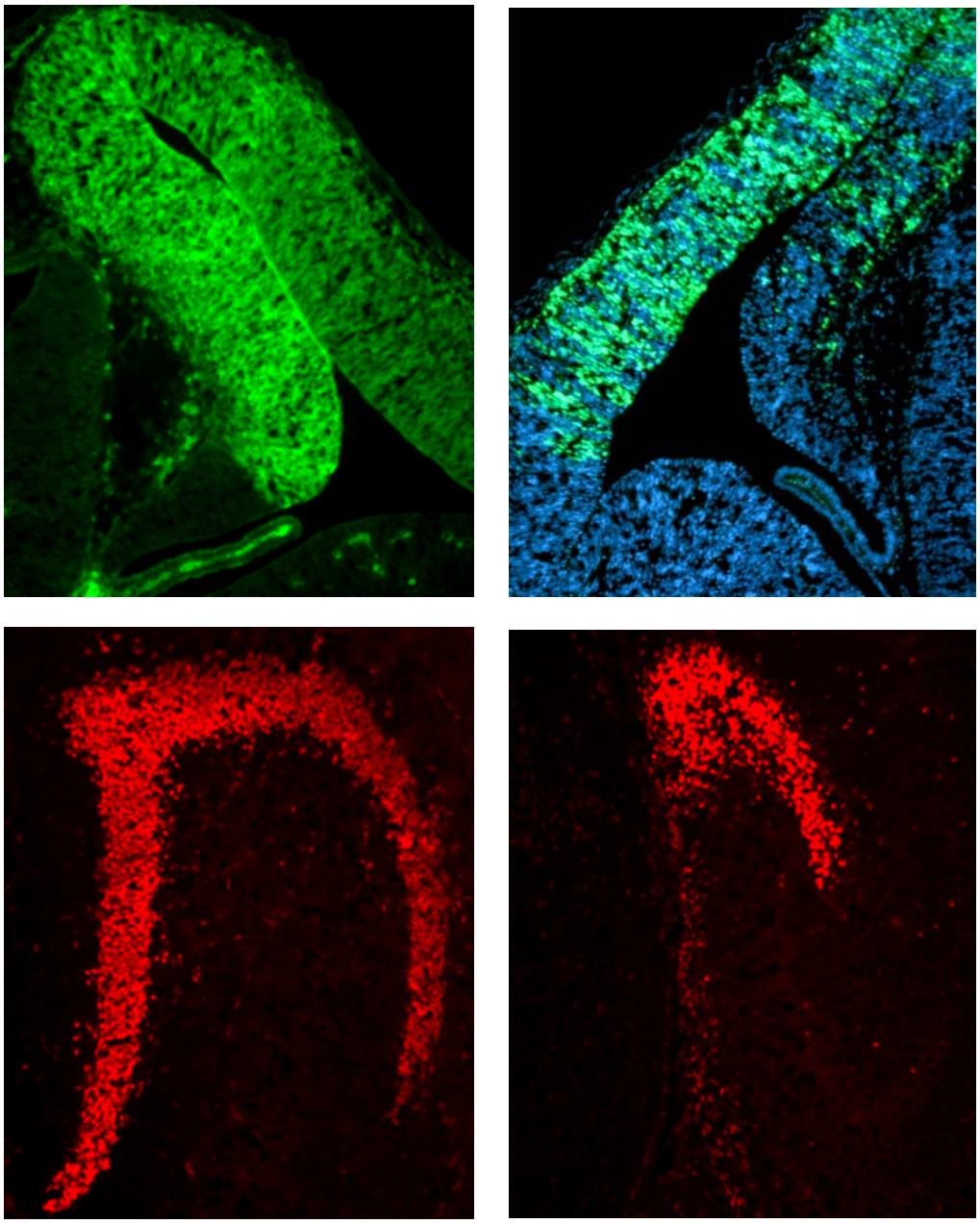
Organisation structure



Co-operation 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 a potential for innovation.

The collaborations between the academic partners and in selected areas with the industry include the SFI-CAST drug discovery platform, the SFI-CAST heterogeneity validated tumour cell bio bank, the antibody discovery platform, the immunotherapy platform and the photo internalization platform. Three retreats are annually organised to coordinate cooperation between the partners. In addition, project work groups are established.



Presentation of the research groups

Gustav Gaudernack-group Immunology

Aim

The major aim of the immunotherapy group within the framework of SFI-CAST is to develop novel forms of immunotherapy for cancer targeting cancer stem cell, and to test these in early phase clinical trials.

Status

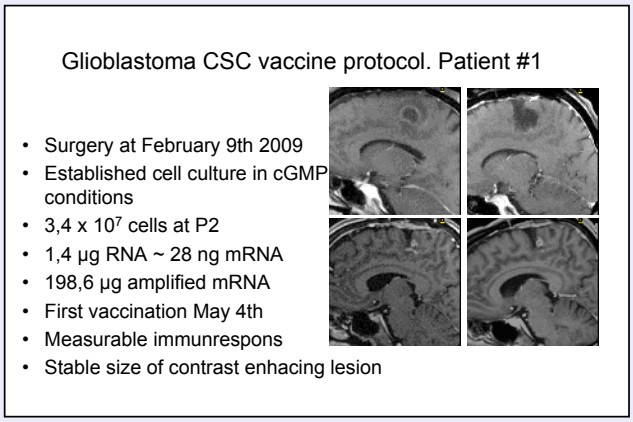
The glioblastoma clinical trials are continuing, and characterisation of immune responses in the vaccinated patients is ongoing. Detailed characterisation of the cancer stem cell component in the newly established lung cancer and prostate cancer cell lines is ongoing and will be completed in 2011.

Further research plans

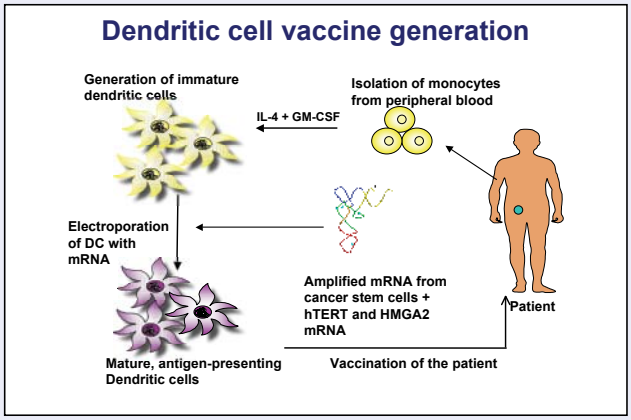
Characterisation of novel candidate cancer vaccine targets in cancer stem cells and determination of immunogenic epitopes. Patenting work and new phase I clinical trial based on peptide vaccine. Complete inclusion in ongoing and newly started clinical trial and publish trial results.

Cooperation with other academic partners in the centre

Our group cooperates with the Langmoen and Myklebost group and has been actively cooperating with the cell platform.



MRI image (top) of the brain of a vaccinated patient, indicating stable disease >12 months after surgery. In cooperation with I. Langmoens group. (I. Langmoen)



Overview of GMP production scheme for cancer stem cell mRNA transfected dendritic cells used as vaccines in glioblastoma and ovarian cancer.

Joel Glover-group
Imaging

Aim

Establish methods for non-invasive dynamic tracking of tumour cells and tumour stem cells in animal models.

Status

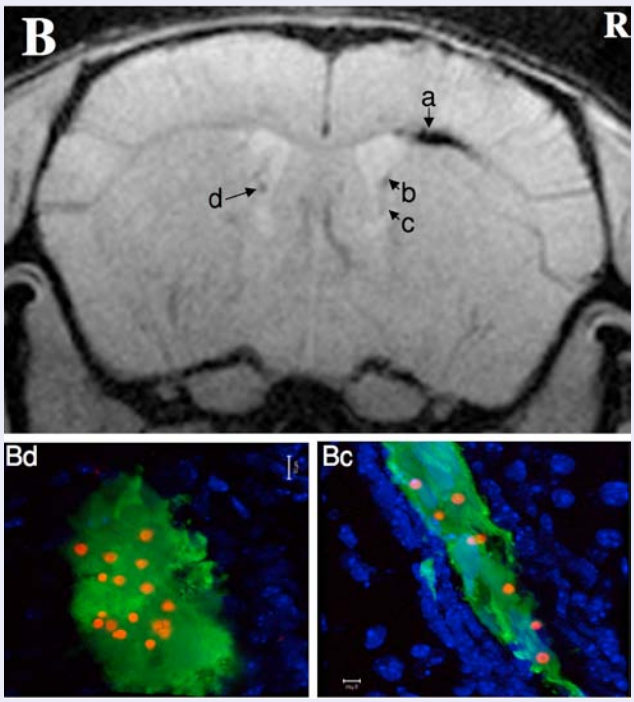
In 2010 the group completed a project investigating the utility of micron-sized particles of iron oxide for *in vivo* tracking of stem cells, which has been submitted for publication. It also established that glioblastoma cells exhibit arrested proliferation at the population level, altered patterns of differentiation and a lack of tumourigenicity when implanted into an embryonic tissue environment. The group has also begun a study of phosphoprotein dynamics in glioblastoma cells as a means of dissecting out signalling pathways in this tumour type.

Further research plans

In 2011 the group intends to 1) make a quantitative comparison of MRI and fluorescence-based *in vivo* tracking of stem cells in the mouse, and to develop MPIO-based methods for intracellular delivery of substances such as agonists and antagonists of signalling pathways, 2) continue to characterise signalling pathways in glioblastoma stem cells using phosphoflow technology, 3) continue to investigate the effects of embryonic microenvironments on the differentiation and tumourigenicity of glioblastoma cells.

Cooperation with other academic partners in the centre

The group has an active collaboration with the Langmoen group on glioblastoma projects.



MRI image (top) of the brain of a living mouse 2 weeks after injection of magnetic bead-labelled glioblastoma cells near site "a", and post-mortem fluorescence images of the cells (bottom). Glioblastoma cells (green, GFP) containing beads (red) have migrated to sites "c" and "d" where they can be detected as darker grey areas in the MRI image.

Stefan Krauss-group
Stem cell signalling

Aim

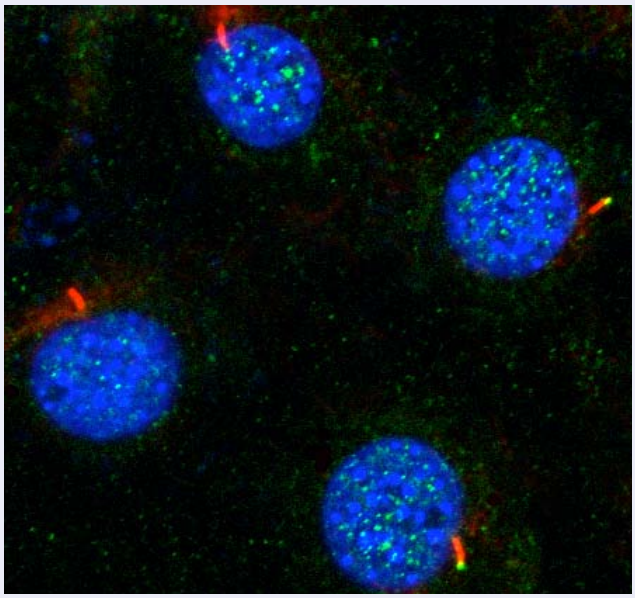
The main goal of the groups within SFI-CAST is to gain understanding on stemcellness in cancer, and to use this knowledge for developing antagonists to the stem cell pathways.

Status

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.

Our laboratory has put a particular focus on identifying a sub-population of stem cell-like, slow cycling cells in solid tumours. Using pancreas adenocarcinoma and colon cancer as models, we recognised that slow cycling cells (SSCs) have an increased potential to survive chemotherapeutic treatment, and are able to recreate the initial heterogeneous tumour cell population. In addition, SSCs show an increased invasive and tumourigenic potential including morphological changes resembling cells that have undergone an epithelial to mesenchymal transition (EMT).

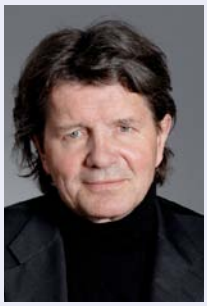
Based on this knowledge, we identified novel small molecules that specifically inhibit beta-catenin from entering the nucleus. The molecules are currently tested in various *in vitro*- and *in vivo* models with the aim of reaching clinical candidate status.



Shh-Light2 cells expression Gli2-Flag, stained with DAPI (nucleus-BLUE), anti acetylated tubulin (cilia-RED) and anti-flag (Gli2-GREEN) (M. F. Strand)

Further research plans

In the next period we will put a focus on increasing our understanding of the mechanisms that lead to cancer heterogeneity. In particular, we are interested in understanding the interplay between stem cell signalling (Wnt/Hh) and chromatin morphology. This knowledge should help us to develop further strategies to interfere with stemcellness in cancer. A central aim of this research is to identify and characterise druggable targets in stemcell pathways.



Iver Arne Langmoen-group
Malignant brain tumours

Aim

The group has previously worked on neural cell physiology and neuronal differentiation of adult human neural stem cells. The main focus of the group in the frame of SFI-CAST is on cultivation, identification and characterisation of brain tumour stem cells and identification of therapeutic targets through comparison of brain tumour stem cells vs neural stem cells and tumour stem cells from brain tumours.

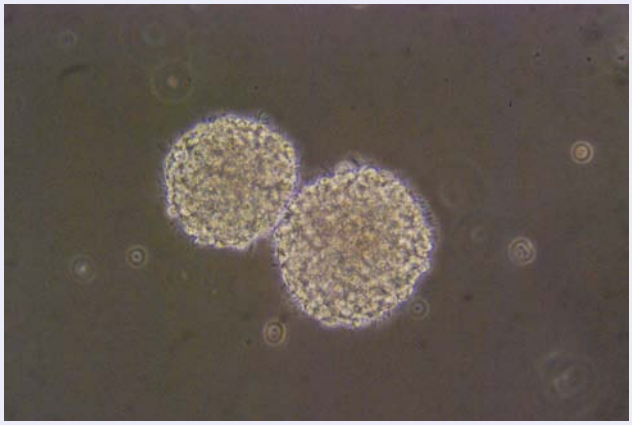
Status

Glioblastoma is the most common tumour of the brain parenchymas. Despite the combined effort of surgery, chemo- and radiotherapy the median survival of patients is only ≈ one year (15 months in selected groups).

Previously, we have characterised similarities and differences in cells with stem like characteristics from the adult human subventricular zone and glioblastoma on a cell biology level. We have developed a technique for analysing the gene expression of single cells in a tumour-sphere. We have now carried out microarray studies in order to compare gene expression in these cells. To be able to study the function of possible target genes, we have established nucleofection as an efficient technique for over-expression and siRNA knockdown in our cells. Using bioinformatics approach we identified 20 genes that were up-regulated and 50 gene loci that were down-regulated in all the included GBM (Glioblastoma Mulitforme) tumour cultures. Our preliminary data indicate that the genes that are up-regulated in tumours are involved in cell-cycle/division, epigenetic regulation, signalling or have unknown functions. Few candidates seem to be down-regulating known tumour-suppressors. Among the genes that are down-regulated in tumours we found several growth inhibitors and loci on chromosome 10. Several of these candidates do not correspond to known genes.

In order to identify potential therapeutic targets we also assess differences between brain tumour stem cells, normal neural stem cells and normal brain tissue with proteomics approaches.

Based on the results we have so far we have designed a clinical phase I/II trial targeting brain tumour stem cells in patients with glioblastoma. The study has been fully certified by relevant authorities, and is the first of its kind worldwide. The trial has commenced and so far recruited eleven patients. The study is done in collaboration with the program on immunotherapy/vaccination at the Norwegian Radiumhospital.



Tumoursphere derived from glioblastom.

Further research plans/in progress

1. Confirmation of differentially regulated genes at the protein level
2. Investigation of differentially regulated genes by knock-down and functional testing *in vitro*
3. Investigation of differentially regulated genes by knock-down and functional testing *in vivo*
4. Further clinical projects against selected targets

Ragnhild Lothes-group
Stem cell biomarkers

Aim

We aim to identify and establish malignancy specific biomarkers in a stem cell context.

Status

Embryonal carcinoma cells found in testicular germ cell tumours are considered the malignant counterpart of embryonic stem cells. Both cell types are pluripotent, share cell surface markers and the overall gene expression programmes. In comparing the two, we access a non-malignant ("normal") counterpart of a cancer cell with stemness properties, and gain insights into the role of stem cells in the development and progression of stem cells related cancers.

We have performed exon microarray analyses from series of both types, at different conditions and passages. From the top-most differentially expressed genes and individual exons between ES and EC cells, we have now validated several genes and transcripts that we are in progress of defining their role in cancer.

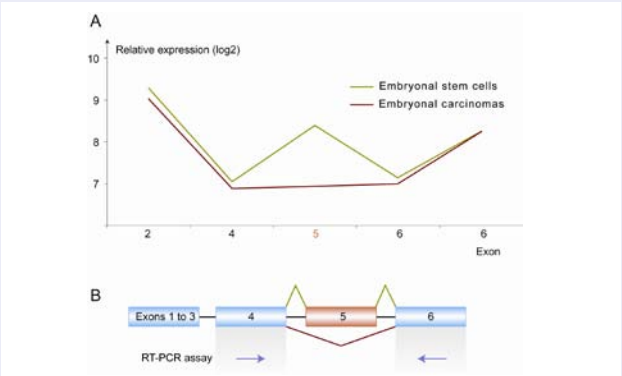
We have employed high-throughput RNA-sequencing to a pair of embryonal carcinoma and embryonic stem cells. This provides us with higher resolution data to their transcriptomes, and has in particular yielded a set of fusion transcripts from the embryonal carcinoma which have not yet been described in cancer (not published).

Further research plans

The malignancy specific transcripts of EC will be available to the consortium partners ahead of publication for comparison with tumour stem cells and stem cells isolated from adult tissues. We will ourselves seek collaborators for such studies on gastrointestinal cancers. We will perform DNA copy number profiling (array-CGH) on the embryonal carcinomas and embryonic stem cells for integrative studies with the transcriptome data already at hand.

Cooperation with other academic partners in the centre

We collaborate with the Myklebost group on setting up and running the deep sequencing platform.



A, *Candidate malignancy-specific splicing for a gene with differential exon-level expression pattern. The green and red lines represent the averages of four embryonic stem (ES) cell lines and three embryonal carcinoma (EC) cell lines, respectively.* B, *The anticipated splicing events assumed to be responsible for the interesting exon-wise plot are shown. The green and red lines represent the splicing events dominating in ES and EC cells, respectively.*

Cooperation with industry partners

Relevant patent applications are filed, and we work with the hospital's TTO, Inven2, for collaborations with aim of commercialisation.

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

Elsa Lundanes and Tyge Greibrokks-group
Analytical chemistry

Aim

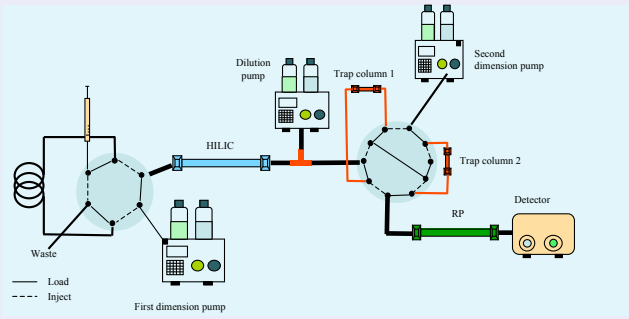
In the frame of the SFI-CAST, the analytical chemistry group is engaged in development of analytical methods for identifying proteome and metabolome markers for cancer stem cells and reagents that affect them.

Status

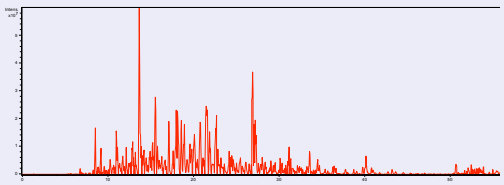
Some highly sensitive and selective automatable capillary LC-MS quantification methods for potential novel drugs in different types of organs as liver, kidney, plasma etc, as well as a highly sensitive and selective automatable capillary LC-MS quantification method for oxysterols have been developed in cooperation with Krauss and his group. Also in cooperation with Krauss, studies of possible new isomers of cyclopamine and investigations of new drugs from plants have been carried out and published in 2010. Miniaturised liquid chromatography mass spectrometric methods for identification of proteins and glycoproteins have been explored, in cooperation with Langmoen and his group. We have made porous layer open tubular (PLOT) columns with 10 µm inner diameter suitable for separation of low abundance proteins/peptides since protein markers for cancer stem cells are expected to be present at low concentrations. Work on open tubular columns with nanoparticle based stationary phases was initiated with the intention of including these columns in methods for determination of phosphatidylinositol phosphates in cooperation with Stenmark.

Further research plans

Development of methods for quantification of potential novel drugs and metabolites will be continued, as will protein and glycoprotein separation and identification methods based on miniaturised liquid chromatography and mass spectrometry. Trypsin and other enzyme PLOT columns will be explored in combination with PLOT protein separation column(s) in order to perform protein separation with subsequent on-line digestion and mass spectrometry (MS/MS) for protein identification. Work on development of nanoparticle based open tubular columns for use in methods for determination of the signalling molecules phosphatidylinositol phosphates (PIPs) in cells will be continued.



A 2D-LC system for separation of complex samples. HILIC is applied in the first dimension wheras RP is applied in the second dimension. The compounds are preconcentrated on two trap columns prior to the second dimension separation.



Trypsin digested cell lysate (from 1 million cells) separated on a monolithic column (1 m x 100 ffim i.d.) using a 60 minute long gradient. The LC gradient started at 5 % ACN + 0.1 % FA and increased up to 30 % ACN + 0.1 % FA in 45 minutes, and increased further up to 95 % ACN + 0.1 % FA in 15 minutes. The flow rate was sat to 2 ffiL/min and the injection volume was 18 ffiL (12% of sample). An IT-MS/MS was used for the peptide detection.

Cooperation with other academic partners in the centre

Cooperation with Stefan Krauss and his group on highly sensitive and selective automatable capillary LC-MS quantification methods for potential novel drugs and metabolites. Miniaturised liquid chromatography mass spectrometric methods for identification of proteins and glycoproteins are being explored, in cooperation with Iver Langmoen and his group. A project on development of methods for determination of the signalling molecules phosphatidylinositol phosphates (PIPs) in cells has been initiated in cooperation with Harald Stenmark.

Ola Myklebost-group
Mesenchymal Programming

Aim

The Myklebost group has a focus on mesenchymal cancer, sarcoma, and investigates the regulation and properties of stem cell-like sub-populations in such tumours, but extends the studies of the mechanisms identified also to breast cancer.

Status

The association of HMGA2, an architectural transcription factor that is amplified and rearranged in sarcomas, with stem cell properties both in sarcomas and breast cancer has been further investigated. As its levels are being regulated by the *Let*-7microRNA, models for investigation of this mechanism have also been developed. To be able to investigate primary cells, lentiviral vectors had to be developed, and we now have systems for a number of functional and tumour associated mutants of HMGA2, as well as reporters for *Let*-7. Expression profiles of mesenchymal stem-like cells have been obtained for all the different HMGA2 mutants, and those for knock-down of the amplified, tumour-associated variants are being generated.

Stem-like sarcoma cells have been strongly enriched by several means, cell sorting based on a $CD133^{Hi}$, ALH^{Hi} phenotype, label retaining (slowly dividing) phenotype, and a *Let*-7^{Lo} phenotype, all giving increased colony-forming ability *in vitro*. The former also showed enrichment for tumour-initiating ability *in vivo*, whereas the latter two phenotypes are being further investigated. The label-retaining cells showed $Sox2^{Hi}$, $HMGA2^{Hi}$, *Let*-7^{Lo} phenotypes, supporting our working hypothesis that these are stem-like cells, and the expected correlation with HMGA2 and *Let*-7.

The moving of our animal facility to the new research building has been severely delayed, but a new NOD/SCID colony is currently being established, which should give sufficient animals sometime in the summer 2011. The gradual closing down and bad state of the old facility is creating serious problems for the required animal studies. However, a number of xenograft lines have been established, e.g. for pancreatic cancer.

Further research plans

Following the recommendations of the NFR evaluation panel, we will focus more on stem cell programming by *Let*-7/HMGA2 and the possibilities for therapeutic applications both in sarcomas and epithelial cancers. The role of HMGA2 in TGF-beta-induced epithelial-mesenchymal transition (EMT) in breast cells and cancer, again with therapeutic possibilities, will be further investigated, in collaboration with Dr. Sendurai Mani at the MD Anderson Cancer centre. Therapeutic strategies based on *Let*-7 and miR34a will be evaluated in collaboration with Mirna Therapeutics (Austin). We have identified a collection of fusion genes by deep sequencing of osteosarcomas, of which we expect some recurrent variants to be deeply connected to disease etiology, and thus also required for stem-like tumour cells. The functions of these will be investigated, as will their use for disease monitoring and as therapeutic targets.

Cooperation with other academic partners in the centre

A project on immunotherapy based on tumour-associated HMGA2 in liposarcomas and novel fusion proteins in osteosarcomas will be pursued in collaboration with the Gaudernack group. Together with this group we are also establishing and characterising lung cancer cell and xenograft lines. Together with the Lothe group we have set up deep sequencing technology and are identifying fusion genes in tumours. We have assisted the Langmoen group by expression profiling of their brain cancer and stem cell models, and provided our mesenchymal stem cell model for imaging studies by the Glover group. Together with the Krauss group we are investigating the efficacy of their Wnt antagonists on our osteosarcoma models.

Cooperation with industry partners

Together with PCI Biotech we are testing out their targeted therapy on our stem-like cancer cells, both *in vitro* and *in vivo*. Preliminary data look very promising. We will also investigate the usefulness of their methodology in steering and facilitating microRNA-based therapies.

With Texas-based Mirna Therapeutics we are investigating details of targeting cancer stem cells or stem cell function in cancer using *Let*-7 and miR34a microRNA-based strategies.

Gunhild Mælandsmo-group
Tumour heterogeneity

Aim

In the frame of SFI-CAST, the group is studying the impact of stem or progenitor cells for initiation and progression of breast cancer and malignant melanoma.

Status

We are utilising either clinical material obtained directly from the patients, or human tumours grown as xenografts in nude mice in our studies. A focus for the group has been to optimise methods for single cell preparation from tumour tissue, isolation of various cell populations from the heterogenous tumour mass and cultivation of the cells for maintenance and further evaluation of stemness characteristics and differentiation capability.

In the breast cancer project we utilise models representative for basal-like and luminal breast cancer grown orthotopically in nude mice. We have isolated and characterised tumour cell populations from two ortothopically growing breast cancer xenograft models. The luminal like tumour cell subpopulation had the highest tumour initiating potential of the two models. More detailed analysis of this population revealed population heterogeneity with respect to several cell surface markers. Re-injected pure subpopulations defined by chosen markers, indicated differential *in vivo* tumourigenicity as well as regenerative capacity. In collaboration with T. Sørlie whole genome expression analysis have been performed, and preliminar results suggest that the gene signature derived from the benign population of tumour cells can predict patients with a more favourable disease outcome.

Melanoma subproject. Our recent publications (Prasmickaite et al, Pigment Cell Melanoma Res. 2010 and PLoS One. 2010) suggests that melanoma does not follow the "classical" CSC model i.e. 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 the melanoma cells phenotype and functional properties linked to metastasis and drug-response. Thus, we have developed two melanoma models *in vitro* and *in vivo* based on the cells of a proliferative and an invasive phenotype, respectively. According to the literature, the invasive phenotype might me more stem-like. By using these models we are imaging metastasis formation *in vivo* and are characterising the cells, isolated from different microenvironments, by molecular and functional approaches.

Further research plans

Breast cancer:

We are searching for new candidate molecules that may be examined for the possible use as novel markers for stemness in breast cancer. For this purpose, we are currently expanding our panel of xenografts. The collaboration with K.G.Jebsen Centre for Breast Cancer Research, ensures access to fresh patient derived tumour material, and to already established xenografts models from international collaborators. Our goal is to reveal molecular differences between the most malignant populations and the benign tumour cell populations within breast tumours. Such differences will provide new interesting information on breast cancer development, and might represent new targets for personalised therapy.

Malignant melanoma. Based on *in vivo* studies in two different models, we expect to identify metastasis-implicated microenvironment factors, whose role on melanoma phenotype and functional properties will be studied further *in vitro* by using 3D cultures/co-cultures. We also plan to use these models in a drug discovery program; eventually we will focus on the cells that survived the treatment. Therapy-surviving cells should represent the most aggressive subpopulations and therefore, when characterised, could lead to discovery of resistance-associated factors - potential targets for therapy. We also plan to investigate how drug-sensitivity is modulated by the microenvironment factors.

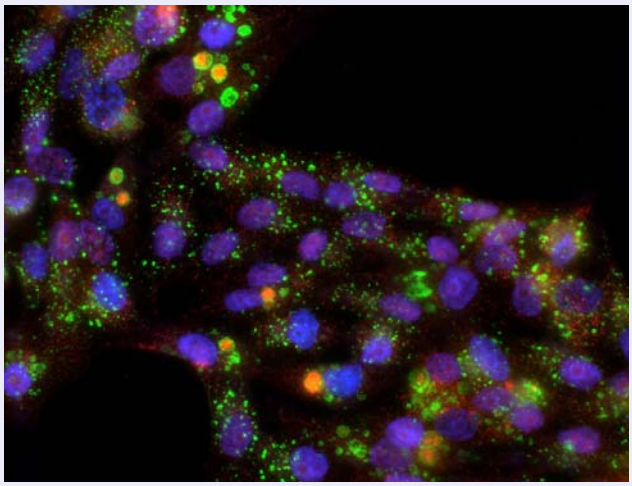
Harald Stenmark-group
Intracellular trafficking and signalling

Aim

In the frame of SFI-CAST, the group focuses on intracellular trafficking and signallling of receptors that control the maintenance and proliferation of stem cells.

Status

The group has made major progress in understanding how the endosomal sorting complex required for transport (ESCRT) machinery controls membrane dynamics. A recent development was the finding that an ESCRT-interacting protein, TTC19, regulates cytokinesis, and the group now has a strong focus on this cellular process. At the same time, the group is still pursuing research on how ESCRTs and other protein complexes regulate endosomes sorting.



The picture shows cancer cells with nuclei stained blue, early endosomes stained green and multivesicular endosomes stained red (N. M. Pedersen).

Further research plans

While major efforts have been made to understand how trafficking of growth factor receptors is regulated, also other receptors, including those involved in stem cell maintenance are now being studied.

Cooperation with other academic partners in the centre

Two collaborative papers on cytokinesis with Rolf Skotheim (Lothe Group), published in Nat.Cell Biol. (2010) and PLoS One (in press). One collaborative paper with Ragnhild Lothe on autophagy and cancer, published in Autophagy (2010).

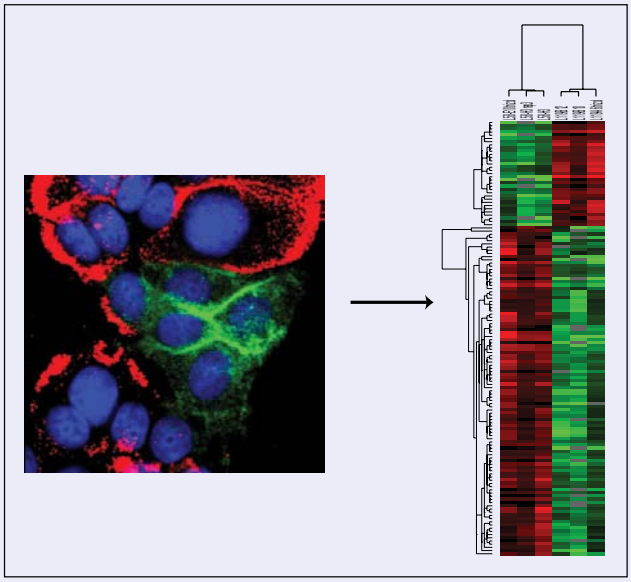
Therese Sørlies-group
Breast cancer heterogeneity

Aim

In the frame of SFI-CAST, our group works to identify and characterise tumour-initiating cells in breast tumours with the aim of identifying novel therapeutic targets.

Status

Breast cancer is heterogeneous and can be viewed as a collection of different diseases with different molecular characteristics. We are interested in the origin of this heterogeneity and how the different subtypes develop in light of a stem cell hierarchy. Using both breast cancer cell lines and xenograft models of different subtypes of breast cancer, we have identified subpopulations of cells characterised by specific cell surface markers that show differential tumourigenicity and invasiveness both *in vitro* and *in vivo*. These various subpopulations have been characterised by genome-wide microarray analyses (copy number, gene expression, miRNA) and we have identified markers that will be further studied.



Multicolour imaging of luminal-like cells (red = MUC1; green = NTR; blue = nuclei) and heat map showing gene expression differences of the representative FACS-sorted cells.

Further research plans

We will continue to study the tumourigenicity of the various subpopulations of cells from both cell lines and xenografts. Based on the microarray analyses, we will search for novel cell surface markers for further sorting of the tumour-initiating populations. We will also identify gene profiles specific for these populations and investigate their prognostic impact in gene expression data from large series of breast cancer cohorts, representing all different subtypes of breast cancer. The biological effects of the expression of the identified markers will be explored in functional studies by overexpressing the proteins in negative cell populations and knocking these factors out by siRNA in positive populations. On a more long term basis, we plan to use different types of mouse models to study the mechanisms regulating stem cells, focusing on the Hedgehog and the Wnt pathways.

Cooperation with other academic partners in the centre

We collaborate closely with the Mælandsmo group on the described projects.

CAST core facilities

The SFI-CAST animal and cell sorting core facility was established thanks to a grant from Radium Hospital Donations, and is now serviced by four technical employees that take care of these functions. This facility provides advanced cell and animal technology, in particular high-speed cell sorting, but also cell isolation, propagation, and analysis, as well as a NOD/SCID colony for *in vivo* experiments. The level of activity is high, and more or less every day is now booked for sorting experiments, isolating small number of cells with stem cell properties from cancer cell cultures. In addition to advanced flow sorting equipment, the core also has an automatic colony counter and time-lapse equipment.

In 2010 core activity has been increased further, as SFI-CAST has started to establish a heterogeneity validated cell culture biobank or cell culture platform. The main goal of the cell culture platform is to establish a collection of CSC model systems for several cancer types that are frequent and for which there is a lack of good therapies. The cell culture platform will be an important standard for internal CAST projects, but also for possible industry collaborations.

For the cell platform we will validate the CSC phenotype assays already established within CAST, including label retention (slow proliferation), aldehyde dehydrogenase, and cell surface markers relevant for the tissue type, combined with ability to form colonies without attachment. This work is headed by one of the CAST postdocs.

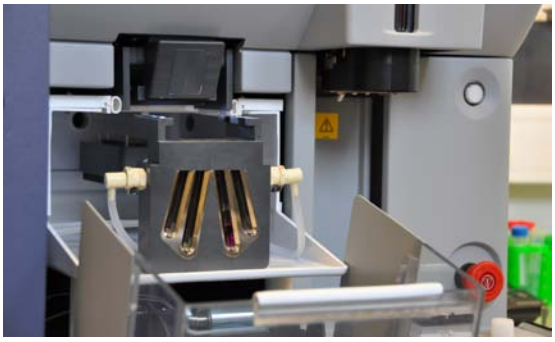
The objective is to establish at least 5 validated model systems for each selected cancer type. Initially we prioritise lung, pancreas and prostate cancer. The selection is governed by clinical urgency, and thus reflects in commercialisation potential.

The efficacy of candidate therapies, from within CAST or from commercial collaborators, will be investigated on CSC sub-populations, with regard to specific toxicity, reduced colony formation, and ability to alter cellular phenotypes. Promising candidates can then be assayed further for tumour initiating ability in our NOD/SCID *in vivo* models.

This year the abilities of the facility have been extended with an Incucyte time-lapse station, by which CAST researchers can monitor a number of properties of their cell cultures in multiple formats, and access their data on-line.

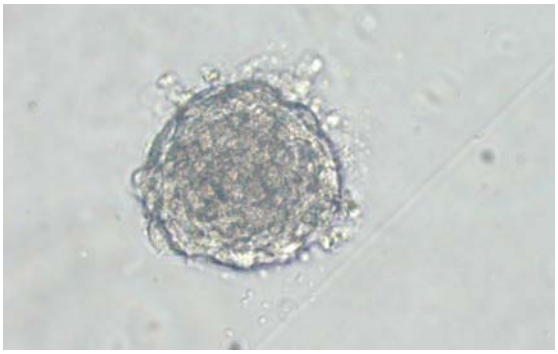
Personnel

Anna Berit Wennerström, Cell technician, Petros Gebregziabher, Animal technician, Nomdo Westerdaal, Flow sorting technician, Else Munthe, Project leader, Postdoc (50%) and Menaka Sathermugathevan, Technician.



Flow cytometry (O. Myklebost)

Flow sorting technician Nomdo Westerdaal (O. Myklebost)



Cancer cells grow as spheroids in 3D-assays (E. Munthe, A. Wennerström)

Presentation of industry partners

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 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. http://www.affitech.com/

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, which started in October 2010, is funded by the Research Council of Norway through the Industrial PhD scheme.

INVITROGEN DYNAL AS

About the company

Invitrogen Dynal`s AS interest is to commercialise identified cancer stem cell markers to generate laboratory research reagents and diagnostic assays. Dynabeads® revolutionised separation methodologies in the 1980s. Today these magnetic beads are used in countless scientific applications and cited in thousands of published articles. Dynal® is committed to delivering absolute consistency and to reducing variability in your studies, diagnostic assays and therapeutic protocols.

SFI-CAST interaction

Invitrogen Dynal aims to develop cell isolation products based on antibodies specific for surface markers specifically expressed on cancer stem cell populations. Invitrogen Dynal has a long term commitment to SFI-CAST and will provide competence and scientific personnel in the context of surface antigen based cell separation. Invitrogen Dynal has many years of experience with immunomagnetic beads and cell isolation and will be responsible for implementation of cell isolation of cancer stem cells that SFI-CAST has identified and characterised.

PCI BIOTECH HOLDING ASA

About the company

PCI Biotech® has developed a unique and patented photochemical drug delivery technology for use in cancer therapy and other diseases (Fig 1). The company's lead candidate drug is the proprietary photosensitiser Amphinex®.

Our vision is to make cancer medicines better by improving drug delivery by photochemical internalization.

Completed the inclusion of patients in its phase I/II study of its lead candidate PC-A11 in cancer patients. The last patient has been treated with the company's proprietary photosensitizer Amphinex® used in combination with the cytotoxic agent bleomycin at University College Hospital (UCH) in London. Principal Investigator, Colin Hopper said: "We at UCH are proud of being the first in the world to use the PCI technology in the treatment of cancer patients. The results have been very positive, with strong tumour response in all the treated patients, and we look forward to take part in the further development of PC-A11 in the treatment of Head and Neck cancer patients."

SFI-CAST interaction

PCI biotech has together with several SFI-CAST partners (Myklebost, Mælandsmo, Krauss) initiated targeting of different cancer cells (sarcoma, carcinoma of breast and pancreas) expressing relevant stem cell markers. Data obtained from *in vitro/in vivo* assays are very promising which warrant further preclinical evaluation of the technology. We have also initiated a collaboration with Stenmark group regarding cellular trafficking of cancer stem cell markers and antibody-drug conjugates (Fig 2).

Goals for 2011: We aim to further document the concept of combining PCI with cancer stem cell targeting toxins *in vivo*.

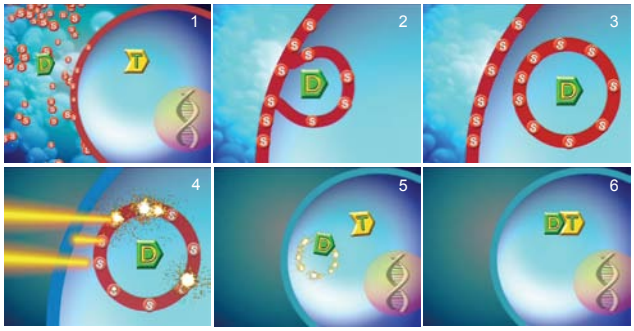


Fig. 1
Principle of the PCI technology. 1, Administration of photosensitizer (S) and drug (D). 2, D an S is taken up by endocyosis and 3, sequester in endo-lysosomal vesicles. 4, Light activation of (S) leads to formation of reactive oxygen species, which burst the mebrane of the vesicles leading to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

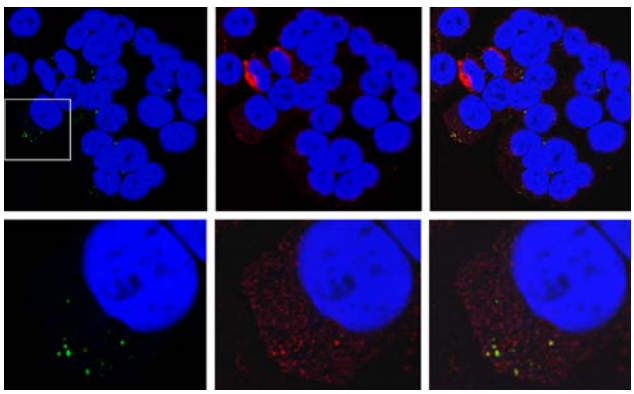


Fig. 2
Co-localisation of a cancer stem cell-targeting antibody (green) with lysosomal marker LAMP2 (red). Nucleus stained with DAPI.

Oslo Cancer Cluster

Oslo Cancer Cluster – From Cancer Research to Cure

Oslo Cancer Cluster is a non-profit member organisation committed to improve the lives of cancer patients by accelerating the development of new cancer diagnostics and medicines. In June 2007 the cluster became a Norwegian Centre of Expertise (NCE).

Oslo Cancer Cluster is built on strong foundations dating from the early 1930s; Oslo's Radium Hospital is now Northern Europe's largest comprehensive cancer centre. Already, together with the Centre for Cancer Research and the Norwegian Cancer Registry, the Norwegian Radium Hospital has built a dynamic biomedical cluster for research into cancer and commercial spinout of cancer diagnostics and therapies.

Oslo Cancer Cluster has more than 60 members, including industrial companies, academic research institutions, health initiatives and support groups in the field of biotechnology with the main focus on cancer.

The cancer research and its application are in world-class in terms of innovation and quality.

The region has also a unique infrastructure – from biobanks to extensive patient registries - that in Norway help accelerate the translational research crucial to converting ideas from the lab into diagnostics and treatment.

2010 has been an exciting year for the Oslo Cancer Cluster. 14 new and active members, promising clinical trials, important partnership deals and extensive media-exposure - our members continue their committed work to improve the lives of cancer patients by accelerating the development of new cancer diagnostics and treatments.

International partnerships are vital in order to support our members in commercialisation and in the search for investors/partners. Along with Cancer-Bio-Santé in Toulouse, we organised the second European Cancer Cluster Partnering (ECCP) meeting in September 2010 in Oslo. The conference was a great success, bringing more than 400 people from 21 nations and 203 different companies together to exchange knowledge and set up collaborations. In 2011 ECCP will again be arranged in Toulouse, and we hope that our members will actively support ECCP by participating at the conference, partnering meetings and investor streams. Save the date for ECCP2011: September 14th – 16th, Toulouse, France: http://www.ecc-partnering.com

The development of the Innovation Park next door to the Institute of Cancer Research where the majority of the SFI-CAST laboratories are located, was voted upon in Oslo City Council in October 2010 and the politicians gave their support to build the Innovation Park. The Oslo Cancer Cluster Innovation Park will physically integrate cancer research, clinical trials facility, biotech and biopharma companies with the purpose of accelerating innovation – and last, but not least, Ullern High School. Oslo Cancer Cluster and Ullern High School have a close educational collaboration on educating tomorrow's researchers and entrepreneurs.

Find more information about Oslo Cancer Cluster on our website www.oslocancercluster.no

Bjarte Reve
CEO of Oslo Cancer Cluster

Other achievements

INTERNATIONAL CONFERENCES/ SYMPOSIA ORGANISED BY SFI-CAST

Annual Retreat of the Norwegian Stem Cell Network, Losby, Norway October 18.-19. Chief organiser Stefan Krauss, 99 participants.

DOCTORAL AND MASTER DEGREES

In 2010 SFI-CAST supervised 23 PhD-students and 10 master students. 4 PhD-students and 7 master students were examined.

Doctoral degrees

Ali Areffard
Ovarian cancer; results of an immunoproteomic analysis and correlation to clinical data and immunohistochemistry.
3rd of June 2010
Supervised by Gustav Gaudernack.

Helle Malerød
Multidimensional miniaturized LC based methods – developments and applications.
11th of June 2010
Supervised by Elsa Lundanes and Tyge Greibrokk.

Nina Therese Solberg
Aspects of canonical Wnt signalling in the developing mouse forebrain.
1st of September 2010
Supervised by Stefan Krauss.

Jean-Sébastien Renaud
Developmental patterning of hindbrain sensory and sensorimotor systems.
28th of September 2010
Supervised by Joel Glover.

Master degrees

Stine Maria Bråtesveen
Screening and examination of small molecules to find inhibitors and synergists of the canonical Wnt signalling pathway.
Supervised by Stefan Krauss and Elsa Lundanes.

Elin Johnsen
Hydrophilic interaction chromatographic separation of 8 deoxynucleotide phosphates (dNTPs) and nucleotide triphosphates (NTPs).
Supervised by Elsa Lundanes and Tyge Greibrokk.

Kristin Opsal
Determination of a novel cancer stem cell drug candidate in blood plasma by LC-UV-MS.
Supervised by Elsa Lundanes and Tyge Greibrokk.

Eline Suzanne Buchman
Investigation of potential Hedgehog signalling pathway inhibitors
Supervised by Stefan Krauss and Elsa Lundanes.

Rafika Rahho
Organic polymer monolithic columns for separation of small molecules and proteins
Supervised by Elsa Lundanes and Tyge Greibrokk.

Ingrid Johanne Bettum
Studier av proteiner involvert I metastaseprosessen – Betydning av S100A4 og osteopontin.
Supervised by Gisle Berge and Gunhild M. Mælandsmo.

Anoek Zomer
Isolation and characterisation of cancer stem cells (CSCs) using a cellular reporter system utilising the Let-7 miRNA.
Supervised by Ola Myklebost.

SPECIAL AWARDS

- At the 2010 FEBS Congress in Gothenburg, Harald Stenmark was awarded the Sir Hans Krebs Medal.
- An advanced grant from the European Research Council was given to Harald Stenmark. 2.272 mill. Euro over 5 years starting 01.01.2010.

INTERNATIONAL AND NATIONAL COLLABORATIONS BETWEEN SFI-CAST MEMBERS AND OTHER ACADEMIC RESEARCH INSTITUTIONS

The academic partners of SFI-CAST have established an extensive network of international and national collaborations.

International collaborations

Gaudernack-group
- The ACT project network partners

Glover-group
- Outi Hovatta, Karolinska Institute
- Sascha du Lac, The Salk Institute for Biological Studies

Krauss-group
- Bengt Norden, Chalmers University, Gothenburg, Sweden
- Jens v Kries, Leibniz-Institut Für Molekulare Pharmakologie, Berlin, Germany
- Ernest Arenas, Karolinska Institute, Stockholm, Sweden
- Dietmar Gradl, Universität Karlsruhe, Germany
- Ian Mills, University of Cambridge, UK

Langmoen-group
- Peter Andrews, University of Sheffield, UK
- Katherine McGlynn/Stephen Chanock, National Cancer Institute, National Institutes of Health (NIH)

Lundanes/Greibrokk-group
- Steven Wilson has with Stefan Krauss a collaboration with Professor Luke
- Tolley and his group, University of Southern Illinois, USA

Myklebost-group
- David Thomas, Peter MacCallum Cancer Centre, Melbourne, Australia
- Jordi Barretina Broad Inst, Boston, USA
- Tarjei Mikkelsen, Broad Inst, Boston, USA
- Sendurai Mani, MD Anderson Cancer Centre, Houston Texas, USA
- Marcel Karperien, University of Twente/Faculty of Science & Technology, Enschede, the Netherlands

Mælandsmo-group
- Lars Åhrlund-Richter, Department of Woman and Child Health, Karolinska Institutet, Stockholm, Sweden
- Prof. Meenhard Herlyn, Wistar Inst., Philadelphia, USA
- Ole W. Pettersen, Department of Medical Anatomy, The Panum Institute, University of Copenhagen, Denmark
- Mina Bissell and Mark LaBarge, Lawrence Berkeley National Laboratory, Berkeley, CA, USA
- Elisabetta Marangoni and Paul Cotton, Curie Institute, Paris, France

Stenmark-group
- Ivan Dikic, Frankfurt, Germany

Sørlie-group
- Ole W. Petersen, Department of Cellular and Molecular Medicine, The Panum Building, University of Copenhagen, Denmark

International research networks

Gaudernack-group
- ACT consortium (Activated T cell Therapy network)

Krauss-group
- EU Network "targeted sequence alteration"

Myklebost-group
- International Liposarcoma Consortium (liposarcomaresearch.org), funded by the US Shriver Foundation
- EURAMOS International clinical trial organisation, Translational studies group
- EU network of excellence on bone tumours, Eurobonet.EU
- Network of Excellence, the EurocanPlatform

Stenmark-group
- European Science Foundation network "Tracking of phosphoinositide pools"
- Nordforsk network on "Cilia and centrosomes"

National collaborations

Glover-group
- Iver Langmoen, OUS-RH
- Olav Haraldseth, St. Olavs Hospital
- Torunn Berge, Oslo Biotechnology Centre

Krauss-group
- Centre for Molecular Biology and Neuroscience (CMBN)
- Norwegian Stem Cell Centre
- Norwegian Centre for Molecular Medicine (NCMM)

Lothe-group
- Sophie D. Fosså/Gustav Lehne, Division for Surgery and Cancer Medicine, Oslo University Hospital (Urology programme)

Lundanes/Greibrokk-group
- Cooperation on analytical proteomics with the Department of Pharmacy, UiO; within the platform Bioanalytics@UiO, an "emerging top-tier group" at the Faculty of Mathematics and Science.

Myklebost-group
- Vidar Steen, UiB, and Arne Sandvik, NTNU, Technological collaboration on running the national platform for microarrays and deep sequencing under the NFR Functional Genomics Programme (FUGE)

Mælandsmo-group
- OSBREAC and K.G.Jebsen, Centre for Breast Cancer Research, partner
- Toni Hurtado, group leader NCM, collaboration with OSBREAC
- Kjetil Taskén and the Chemical Biology Screening Platform, the Biotechnology Centre, UiO
- Lars Akslen, Department of Pathology, Gade Institute, University of Bergen
- Daniela-Elena Costea and Anne Chr Johannessen, Department of Pathology, Gade Institute, University of Bergen

Stenmark-group
- Terje Johansen, University of Tromsø
- Terje Espevik, Institute for Cancer Research and Molecular Medicine, NTNU, Trondheim

Sørlie-group
- Ingrid Gribbestad, Norwegian University of Science and Technology, Department of Circulation and Medical Imaging

RECRUITMENT

Visiting scientists in 2010 include Prof. Nobuo Tanaka (full time at GL Sciences, and part time at Kyoto Institute of Technology, Japan), Paula Paulo (Portuguese Oncology Institute), Ricardo Celestino (Manuel Sobrinho Simões), Paula Soares group (Institute of Molecular Pathology and Immunology of the University of Porto (IPATIMUP)) and MSc student Kotryna Vasiliauskaite (Vilnius University, Lithuania).

CAST CORE FACILITY

Anna-Berit Wennerström, Cell technician
Else Munthe, Project leader
Menaka Sathermugathevan, technician
Nomdo Westerdaal, Flow sorting technician
Petros Gebregzibher, Animal technician

PERSONNEL

Principal investigators
Gustav Gaudernack
Tyge Greibrokk
Joel Glover
Stefan Krauss
Iver Arne Langmoen
Ragnhild A. Lothe
Elsa Lundanes
Ola Myklebost
Gunhild Mari Mælandsmo
Harald Stenmark
Therese Sørlie

Administrative manager
Line Mygland

Senior Scientists
Anders Høgset
Leonardo Meza-Zepeda
Lina Prasmickaite
Marie-Claude Perreault
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FUNDING AND COST

Statement of Accounts

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
	Invitrogen Dynal AS, in kind (lab supplies)	0
	Affitech AS, in kind	963
	Total	21 671

All figures in 1000 NOK

Costs

		Amount
The Host Institution	Oslo University Hospital (Rikshospitalet) HF	18 806
Research Partners	University of Oslo	2 456
Enterprise partners	PCI Biotech AS	1 033
	Affitech AS	963
Equipment		
	Total	21 671

All figures in 1000 NOK

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- Screen using selected cancer cells; United Kingdom Patent Application No. 0907514.4 (priority date; April 30, 2009)
- Compounds; CFS/107741 priority date 7.12.2010

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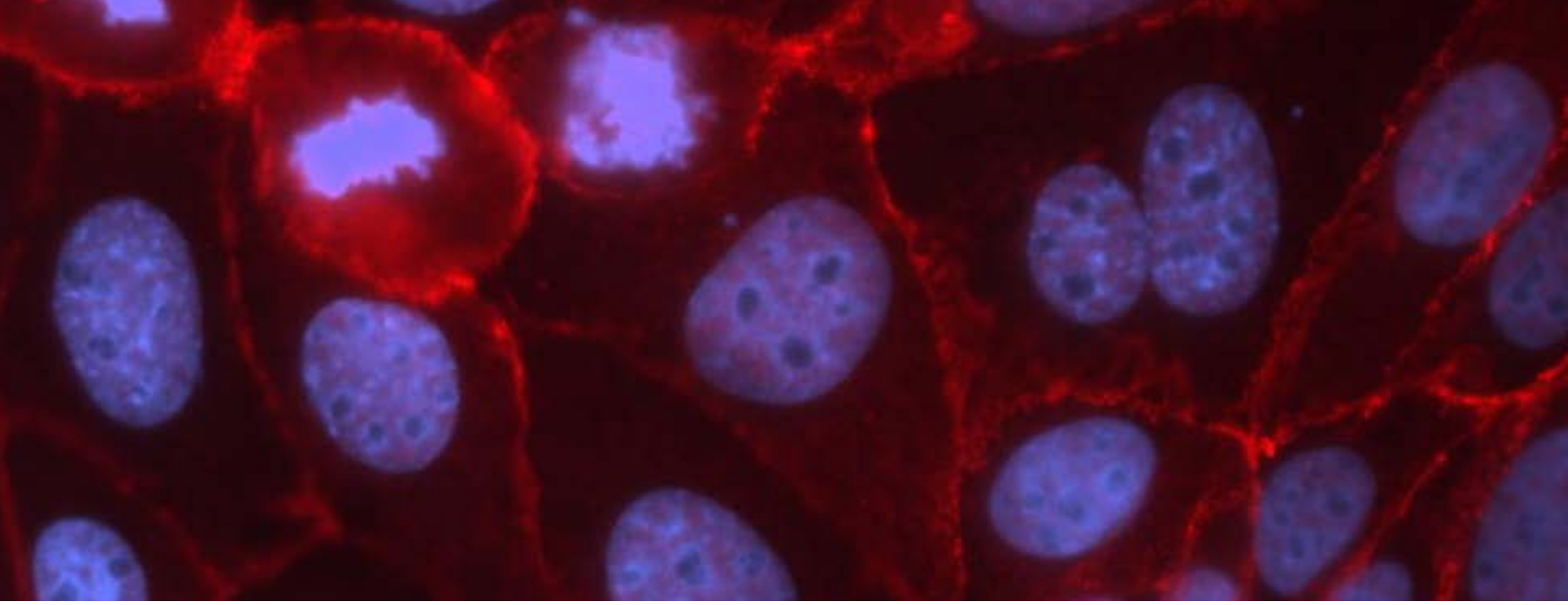

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