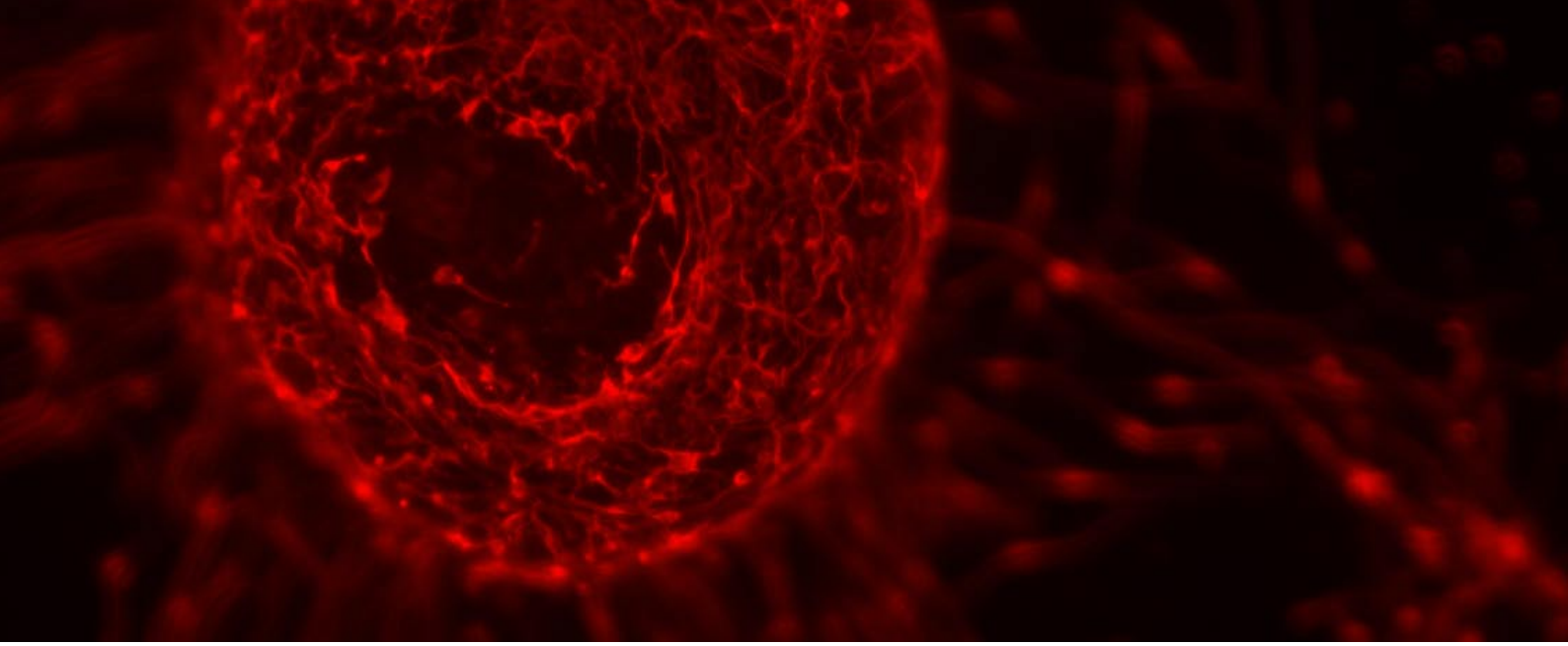

Annual Report 2008

CAST
CANCER • STEM CELL INNOVATION CENTER

Established by the Research Council of Norway
sfi Centre for Research-based Innovation
ULLEVÅL University Hospital
RIKSHOSPITALET
UNIVERSITY OF OSLO

Address of the chairman of the board

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

Indeed, 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 getting 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 center application, really does turn into solid scientific evidence and subsequently forms the basis for product development with high innovative potential and commercial value.

I am pleased to see that SFI-CAST has used the first 2 years of its existence to establish a portfolio of tools and cell lines that comprise a solid basis for the projected therapy development with our industry partners. We now look forward to 2009 where the center enters the crucial phase in which the basic academic research at SFI-CAST starts to turn into the initiation of commercial product development. We have no illusions: very substantial challenges lie ahead of the center in this critical face, both scientifically and financially. But we face these challenges with the confidence that the chosen strategy is correct.

I want to use this opportunity to thank the research council of Norway for its support to the SCI-CAST innovation center and to thank the academic researchers and our industry partners for their outstanding commitment.

Finally, I would like to express that the ongoing research is not only about innovation and scientific or commercial value, it is about saving lives. More than 50% of the population will get cancer; many will be uncurable and dye slowly and cruel. In this context we feel privileged to be able to contribute at the cutting edge of science and technology to the development of potential future cancer cures.

Steinar Funderud

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summary

About Stemcellness in cancer

Tumours contain heterogeneous cell populations with respect to growth kinetics, drug resistance, and metastatic potential. Many of these identities are directed by stem cell pathways. The advances in understanding pathways and mechanisms that determine stemcellness open new possibilities for improved strategies within detection and treatment of cancer.

About SFI-CAST

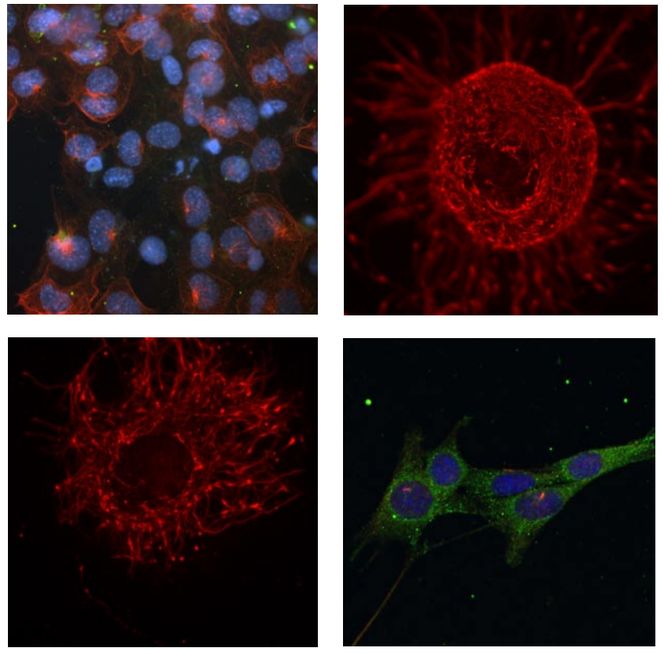
SFI-CAST is an integrated biomedical centre that works towards the identification and characterization of stem cell parameters in tumours. SFI-CAST develops innovative approaches for finding small drugs, cancer vaccines and antibodies that address specifically stem cell issues in cancer. Furthermore, SFI-CAST develops high resolution visualization of specific cell sub-populations in the body as a tool for tracking therapeutic success.

goals

The goals of SFI-CAST are (i) to characterize with innovative approaches heterogeneity in tumours and provide methods for identifying, validating, isolating and targeting cell subpopulations in the tumour. (ii) to develop diagnostic methods based on subpopulations with stem cell characteristics, and (iii) to develop experimental therapies based on subpopulations with stem cell characteristics.

highlights 2008

In 2008 the concept of subpopulations of cells with stem cell characters in cancer has seen further validation. It is now clear that such cells exist in various solid tumours, and that they raise important diagnostic and therapeutic issues. As such, SFI-CAST is well placed at the cutting edge of advancing future cancer diagnosis and therapy. SFI-CAST has identified, characterized and validated stem cell markers in pancreas adenocarcinoma, lung carcinoma, oesophagus carcinoma, sarcoma and breast carcinoma. Members of SFI-CAST have furthermore identified substantial stemcellness in glioblastoma and melanoma. Together with the industry partner PCI Biotech AS, a technology is developed to use stem cell surface markers for targeted internalization of photosensitizers. The industry partner Affitech AS has initiated an extensive search for antibodies directed towards cancer stem cells. Axellia Pharmaceuticals AS is currently in negotiations to set up targeted commercial activity to identify small drugs that specifically address cancer stem cells. In 2008, the first clinical trial based on SFI-CAST resources has been initiated. The clinical testing focuses on immuno-gene therapy targeting cancer stem cells in patients with glioblastoma.



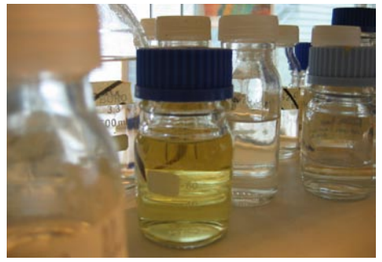
NORSK HYDRO'S
FUND FOR CANCER RESEARCH

Cancer Stem Cell Symposium 2009

Norsk Hydros Fund for Cancer Research has awarded SFI-CAST a grant to arrange in 2009 a cancer symposium, titled: "Frontiers in Cancer Stem Cell Research - **From basic science towards a cure**". The symposium will be arranged in Oslo December 2 -4, 2009, and will enlist top international speakers in the field. More information on www.cancersymposia.no

Clinical Testing of glioblastoma treatment

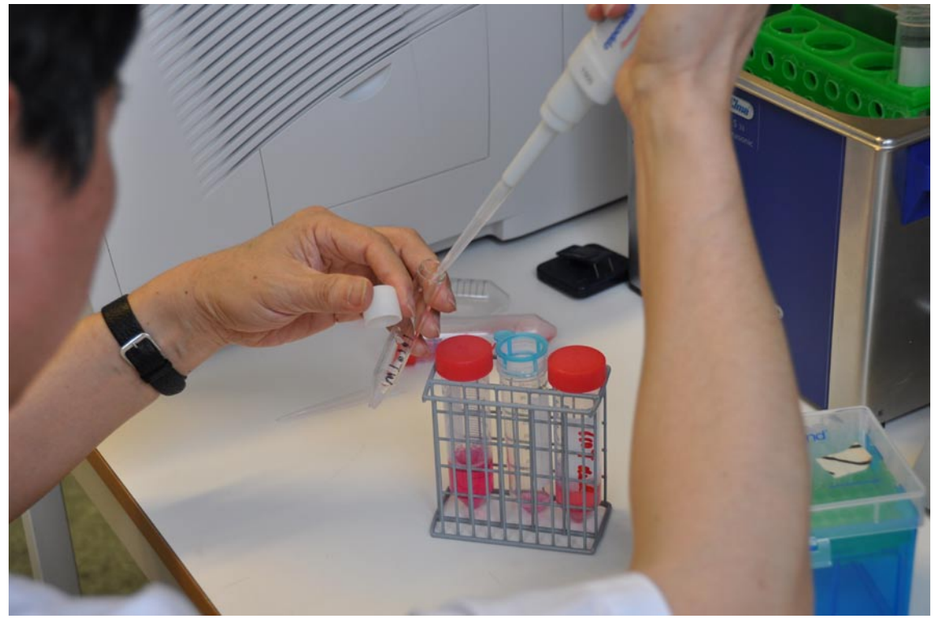
June 2008



We are proud to announce that SFI-CAST is ready to start the first clinical testing of new cancer treatment targeting cancer stem cells.

The treatment takes place at the Norwegian Radium Hospital in co-operation with Ullevål University Hospital and involves several departments and laboratories. The clinical testing focuses on immunogene therapy targeting cancer stem cells in patients with glioblastoma. The protocol has been approved by the Norwegian Medical Authority, the Regional Ethical Committee and the Institutional Review Board. Kick-off is planned next week and the first patients will be included after the summer. By this the SFI-CAST innovation center is ahead of schedule, which refers to efficient interdisciplinary cooperation between the different sections of SFI-CAST and hospitals in Oslo.

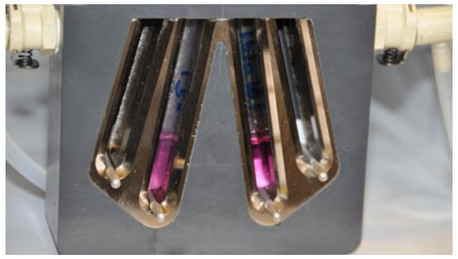
Charities at the Norwegian Radiumhospital (Radiumhospitalets legater) supported SFI-CAST by donating 4,435 Mkr for establishing a state of the art high speed flow cytometry unit. Essential upgrades for creating a core sorting facility was made possible by a donation of 1,4 Mkr from the Jeanette and Søren Bothners legat. Thanks to the donation, SFI-CAST has unique possibilities for advanced identification and sorting of tumour stem cells



The SFI-CAST innovation centre has a work program aimed at advancing basic research on tumour stem cells towards experimental clinical trials. Based on the outcome of this effort, several interactive biotechnology pipelines are fed. (i) Human therapeutic antibodies against tumour stem cells are identified (with industry partner Affitech AS). The antibodies will be used to identify novel epitopes and therapeutic targets. (ii) Novel whole cell reporters that are capable of distinguishing molecular signalling in stem cells and tumour stem cells are developed. (iii) Tumour stem cell pathways are used for differential high throughput screens for drugs (as a projected collaboration with industry partner Axellia Pharmaceuticals AS). (iv) High resolution cell imaging of tumour stem cells *in vivo* using cutting edge magnetic resonance imaging (MRI) techniques is developed in animal models. (v) Ways to find improved immunotherapy protocols and targets are being explored and tested. (vi) Antibodies are tested for improved therapeutic photo-internalization (with industry partner PCI Biotech AS).

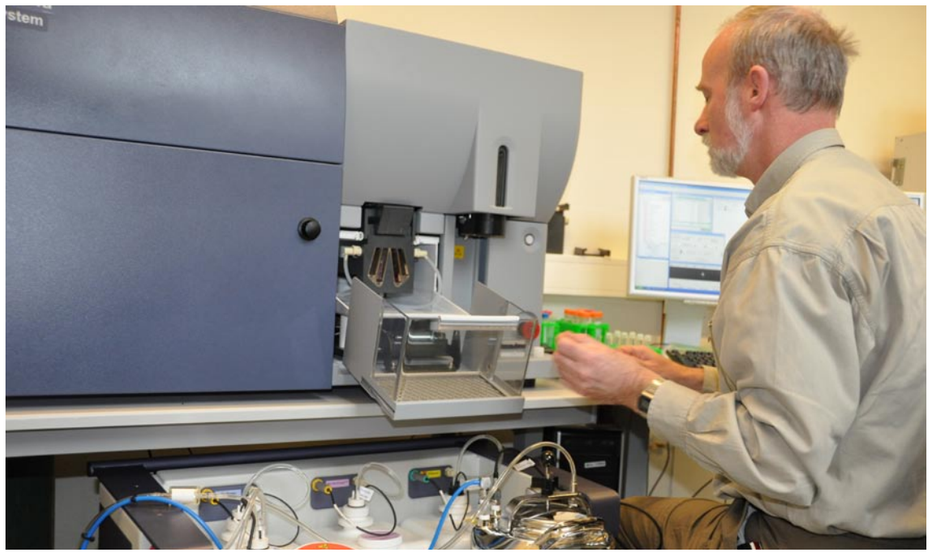
A major focus of the centre is translational research. Partners at the Norwegian Radiumhospital have been responsible for more than 25 phase I/II clinical trials of cancer vaccines and immunogene therapy, and will co-operate with clinicians involved in the project to initial the first clinical trials targeting TSC (Tumour Stem Cells) from the very beginning of the project. This ensures a swift start of the translational aspect as well as provides clinical material for the individual work programs.

The first stage of SFI-CAST was dedicated to establish the SFI-CAST core facility, including sophisticated flow cytometry. Next a panel of assays for stem cell phenotypes were established and put into use on a wide range of cancer types. Furthermore >20 novel primary cancer cell lines have been established from surgical samples. This required extensive collaborations within CAST, both among the academic groups, and with industry partners. This work led to a series of publications and work on patenting key results is pending.



Small subpopulations of cancer cells with stem-like phenotypes have been purified and shown to contain most of the colony-forming capacity of the original population. Phenotypes include ability to export or metabolize xenobiotics, various surface protein markers, and slow cell cycle progression. Studies are on-going to characterise the stem-like cells by various phenotype assays, including global expression profiling, and experimental therapeutic targeting based on surface markers are in process. Furthermore, *in vivo* results using mouse models, are accumulating.

Finally, a SFI-CAST-initiated clinical vaccine trial targeting stem-like brain cancer cells has been approved. In collaboration with Oslo Cancer Cluster (OCC), a business development plan has been elaborated for innovation based on the cellular models established within SFI-CAST.



Management and organization

SFI-CAST is headed by Stefan Krauss (Director) and Ola Myklebost (Assistant Director). The Centre has a project leadership group that meets on a regular basis. This group consists of the ten Primary Investigators (PI) of each research group and leaders of industry partners of the consortium. In 2008 the Centre's activities were mainly located in the Norwegian Radiumhospital, the Oslo Research Park, the University of Oslo, Domus Medica, the Chemistry Department and Ullevål University Hospital. In 2009 a majority of the academic SFI-CAST partners will co-localize in the novel research building at the Norwegian Radiumhospital.

The board

The Board is responsible for ensuring that SFI-CAST is developed in accordance with the current research plan. The members are:

Prof. Steinar Funderud, Rikshospitalet University Hospital HF (Chairman)

Director Karen Marie Ulshagen, University of Oslo

Division director, prof. Lars Engebretsen, Ullevål University Hospital

CEO Martin Welschof, Affitech AS

Chief Scientific Officer (CSO) Steinar Pedersen, Axellia Pharmaceuticals AS

Director of Research and Development Oguz Ersoy, Invitrogen-Dynal AS

CEO Anders Høgset, PCI Biotech AS

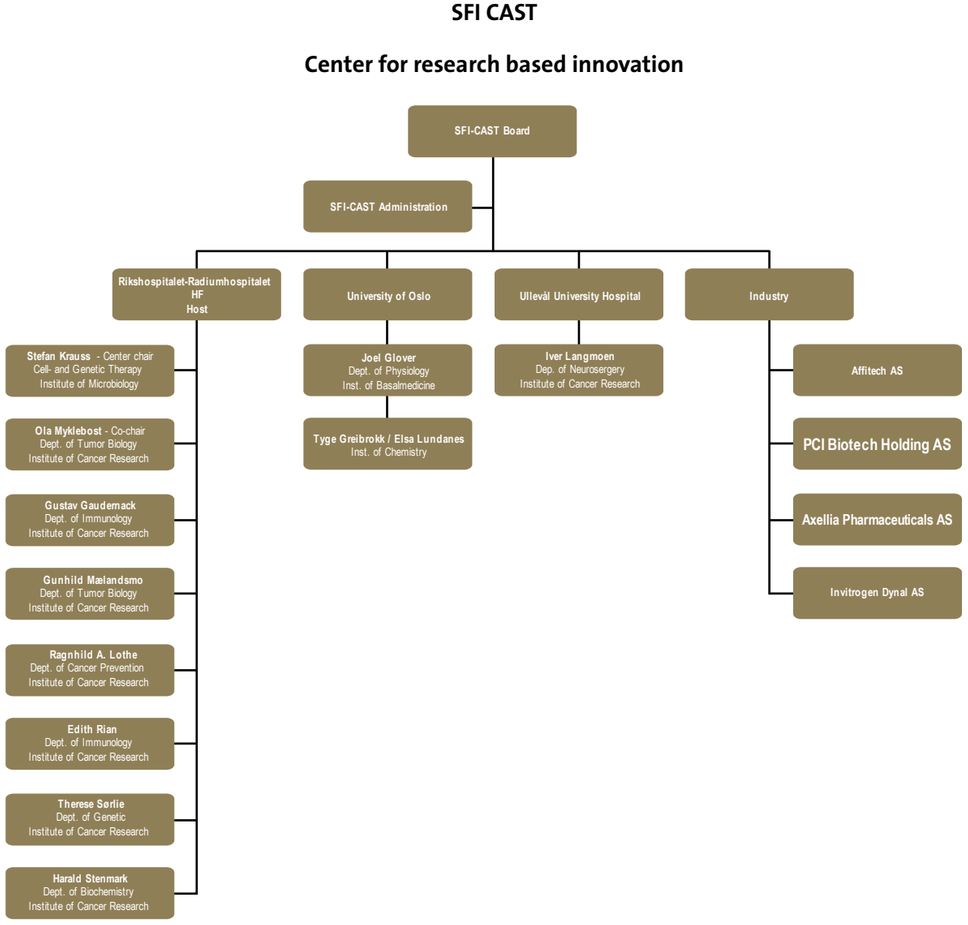
Prof. Lars Nordsletten, Ullevål University Hospital, Substitute member,

Director, Finance Hans Petter Tjeldflaat, Affitech AS, Substitute member,

Researcher Karoline W. Schjetne, Invitrogen-Dynal AS, Substitute member,

Special counsellor, Øystein Rønning, Norwegian Research Council, Observer

Organisation structure



SFI-CAST members

Stefan Krauss, Center director, Cell- and Genetic Therapy, Inst. of Microbiology, Rikshospitalet University Hospital HF

Ola Myklebost, Center assistant director, Dept. of Tumour Biology, Institute of Cancer Research, The Norwegian Radium Hospital

Gustav Gaudernack, Dept. Of Immunology, Institute of Cancer Research, The Norwegian Radium Hospital

Joel Glover, Dept. of Physiology, Institute of Basic Medical Sciences, University of Oslo

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

Ragnhild A. Lothe, Dept. of Cancer Prevention, Institute for Cancer Research, Norwegian Radium Hospital

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

Gunhild Mælandsmo, Dept. of Tumour Biology, Institute of Cancer Research , The Norwegian Radium Hospital

Edith Rian (resigned as member in July 2008), Dept. Of Immunology, Institute of Cancer Research, The Norwegian Radium Hospital

Harald Stenmark, Dept. of Biochemistry, Institute of Cancer Research, The Norwegian Radium Hospital

Therese Sørlie, Dept. of Genetics, Institute of Cancer Research, The Norwegian Radium Hospital

SFI-CAST administration

Karina Saksberg, Cell- and Genetic Therapy, Inst. of Microbiology, Rikshospitalet University Hospital HF

Peder Heyerdahl Utne, Forskningsstøtte, Rikshospitalet University Hospital HF

Kassahun Zelleke, Forskningsstøtte, Rikshospitalet University Hospital HF

Industry Partners

Affitech AS

Axellia Pharmaceuticals AS

PCI Biotech Holding ASA

Invitrogen Dynal Inc.

co-operation between partners in the center

The SFI-CAST innovation center is designed as a highly integrated structure where the academic partners are exchanging technology, materials and know how while the industry partners can connect at any point when they see potential for innovation. Examples of close collaborations between the academic partners, and the academic partners and industry are:

- Molecular profiling on various cancer cell populations.
- Novel biomarkers that affect the decision between symmetric and asymmetric division, a topic that is of central importance in creating heterogeneity and regulating stemcellness.
- Correlation between surface antibodies, dye exclusion, dye dilution and biomarkers in various tumour types, issues that are key to identifying and validating tumour stem cells.
- Development of validation assays.
- Co-operation on stem cells and proteomics.
- Joint development of a immuno-vaccine program for glioblastoma.
- Joint program for live imaging of tumour stem cells using sarcoma, glioblastoma and pancreas adenocarcinoma models.
- Joint collaborations to develop xenograft models.
- Collaborative program to analyze links between Epithelial Mesenchymal Transition (EMT) and induction of a stem cell-like phenotype in breast cancer.
- Collaborative program for targeted drug discovery.
- Joint development for targeting breast cancer, sarcoma, and pancreas cancer stem cells with industry partner PCI Biotech.
- Joint development for identifying novel antibodies that target cancer stem cells in pancreas adeno-carcinoma with industry partner Affitech. Following its CAST participation, Affitech has selected cancer stem cells as one of its 2 major future research areas.
- Joint program of a phase I/II clinical trial of immuno-gene therapy targeting glioblastoma cancer stem cells. Ongoing, 2/20 patients included.
- Joint project on developing and characterization of a large panel of proprietary primary cell lines for various solid tumours.

co-operation between sfi-cast and other national institutions

There is also extensive collaboration between academic partners of SFI-CAST and other national institutions, Examples of these are:

The FUGE Nuclear Programming Consortium at the University of Oslo, the Norwegian Microarray Consortium / FUGE Platform; The FUGE Imaging platform, St. Olavs Hospital, Trondheim; the CMBN Center for Molecular Biology and Neuroscience and the National Center for Stem Cell Research

Awards and Doctoral Degrees

Awards 2008

SFI-CAST scientist Rolf I. Skotheim received the Young Investigator Award at Oncology Forum, Bergen 2008, Annual Meeting for Oncologists, Norway.

SFI-CAST scientists Rolf I. Skotheim, Gard Thomassen, Guro E. Lind, Torbjørn Rognes and Ragnhild A. Lothe, received the 1st runner up Medinnova Idea prize 2008 for the project “Fusion gene microarray”.

Doctoral Degrees 2008

Mercy Varghese defended her PhD dissertation with the title ”Isolation and Characterization of Stem Cells from the Adult Human Central Nervous System and Brain Tumours”, at the Medical Faculty, University of Oslo, 2008. The candidate was supervised by group leader Iver Langmoen.

Stine H. Kresse defended her PhD dissertation with the title “Chromosomal aberrations in human sarcomas identified using genomic microarrays”, at University of Oslo 2008. The candidate was supervised by group leader Ola Myklebost.

Seminars / Student Group Activities

SFI-CAST Practical Discussion Forum

The SFI-CAST practical discussion forum is a forum where SFI-CAST members discuss practical problems, perform troubleshooting and share knowledge and observations relevant for cancer stem cell research. The topics discussed include detailed methodology, project presentations, and recent findings from the literature as well as discussions of the “bigger questions” such as how to define a cancer stem cell. SFI-CAST members with particular expertise on the chosen topics are asked to present. The forum is arranged approximately every 6 weeks and is attended by SFI-CAST post doc’s, research assistants, technicians and PhD students.

SFI-CAST Seminars

The plenum SFI-CAST seminars are arranged as one day retreats. At the retreats all SFI-CAST staff meets and discusses scientific and administrative issues. To some of the retreats external partners are invited to stimulate collaborations and internationalization. During 2008 two SFI-CAST seminars have been arranged:

• Holmenkollen Park Hotel, 24th April

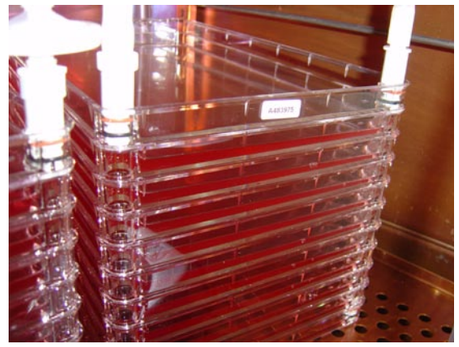
• Holmenkollen Park Hotel, 10th November

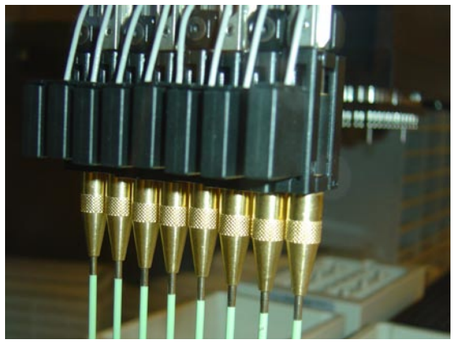
Tarjei Mikkelsen, div. Health Sciences and Technology, MIT, Broad Inst. Harvard and MIT, gave a guest lecture at SFI-CAST seminar, Oslo 10th November 2008 with the title “Epigenomes and cellular states”.

Neil J. Harrison, dep. Biomedical Science, Univ. of Sheffield, gave a guest lecture at SFI-CAST seminar, Oslo 10th November 2008 with the title “Culture adaptation of human embryonic stem cells: a paradigm for germ cell tumorigenesis.”

SFI-CAST is recruiting scientists, post docs and PhD-students nationally and internationally. Whereas in the first phase mostly post docs were recruited, we now have established sufficient technologies and have a level of progression where we can take on PhD students, and have recruited a number of these by external funds. Totally about 60 people work within the centre and by the end of 2008 about 20 scientists, post docs and PhD-students from abroad were funded by the centre or work in close relationship within the centre.

In 2008 there were three visiting scientists within the centre, they were working within the topics prostate cancer stem cell cooperation and isolation of cell populations from breast cancer cell lines.





international networks

ZNIP, LSHB-CT2006-037783, “Therapeutic in vivo DNA repair by site-specific double-strand breaks” 2007-2009.

EuroSTELLS, 04-ESTELLS-F01-029, “Translational stem cell research: from basic biology to regenerative medicine” 2006-2008.

”Network of Excellence on Bone Tumours” (euroboet.eu).

NANOMEDPART:”Targeting cancer stem cells by nanoparticles”.

SFI-CAST has an extensive network of international collaborators, and the different scientific groups have several international partners. Co-operations with both other academic partners and industry exist. Examples of these close collaborations are:

- Joint program between Gaudernack and Fujirebio: Screening for antibodies selectively removing the side population in cancer cell lines using their panel of stem cell reactive antibodies.

- The Lothe group's main collaborating partner is Professor Peter Andrews and members of his lab., University of Sheffield, including studies of embryonal stem cells and their malignant counterpart embryonal carcinomas. This co-operation includes exchange of personnel on a regular basis.

- The Lothe group collaborates with the group of Prof. Huirong Shi, The First Affiliated Hospital of Zhengzhou University for studies on female germ cell tumours.

- The Mælandsmo group collaborates with Ole W. Pettersen, The Panum Institute, University of Copenhagen, Denmark. Topic: Petersen and co workers have discovered a stem cell hierarch in normal human mammary gland and collaborates with SFI- CAST to investigate whether a similar hierarchy and sub-populations of cells also are present in breast cancer.

- Mina Bissel, Lawrence Berkeley National Laboratory, Berkeley, USA and the Mælandsmo group collaborate on studies on stem cells and the importance of particular proteins in differentiation measured as branching morphogenesis in 3D cultures

- The Mælandsmo group and the Krauss group furthermore collaborates with Lars Âhlund-Richter, Karolinska Institute, Stockholm, Sweden in studies of growth, differentiation and stem cell characteristics in human malignant melanoma and pancreas adenocarcinoma grown in a human microenvironment (teratoma)

- In collaboration with Charles Liu and David Tirrell at USC/ Caltech the Langmoen group have shown that modified artificial extracellular matrix affects differentiation and proliferation of normal and tumour stem cells.

- The Langmoen group collaborates with prof. Monica Nistér at Karolinska Institute on glioblastoma stem cells.

Further international collaborators are:

- Prof. Scott Fraser, California Institute of Technology (CalTech).
- Prof Robert Rees, John van Geest Cancer Research Center, School of Science and Technology, Nottingham Trent University, Nottingham UK
- Prof. Shin Hsin Lu, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing and Cancer Research Center, Zhengzhou University, Zhengzhou, Henan, China
- Prof. J.v. Kries Leibniz-Institut Für Molekulare Pharmakologie, FMP Berlin
- Prof. Bengt Norden, Chalmers, Sweden
- Dr Karperien et al, .University of Twente, The Netherlands
- Meenhard Herlyn, Wister Institute, Philadelphia, USA
- Prof. Michael Rosenblum, MD Anderson Cancer Center, Houston, Texas, USA
- Prof. Steve Bown, National Laser Center, University College London, England
- Prof. Gert Storm, University of Utrecht, The Netherlands
- Denator AB, Biotech Center, Gothenburg, Sweden
- Ludesi AB, Malmö, Sweden
- Prof Horst Bürger, University of Münster, Germany
- Prof Pancras Hogendoorn, University of Leiden, The Netherlands
- Prof Karl-Ludvig Schaefer, University of Düsseldorf, Germany
- Dr Massimo Serra, Rizzoli Institute, Bologna, Italy

SFI-CAST has a web presence www.cancerstemcell.no that provides information about the centre and its partners. The web presence includes an intranet with restricted access for SFI-CAST internal exchange of information.

P2 Akademiet

Ola Myklebost has given a lecture about "The dark side of stem cells" on the popular scientific programme "P2-akademiet" on one of the main Norwegian national radio channels (NRK P2), in February 2008.

"Verdt å vite", at NRK2

The Langmoen group presented in the radio programme "Verdt å vite", at NRK2 : information about immunization of patients operated for glioblastoma

Schrödingers katt

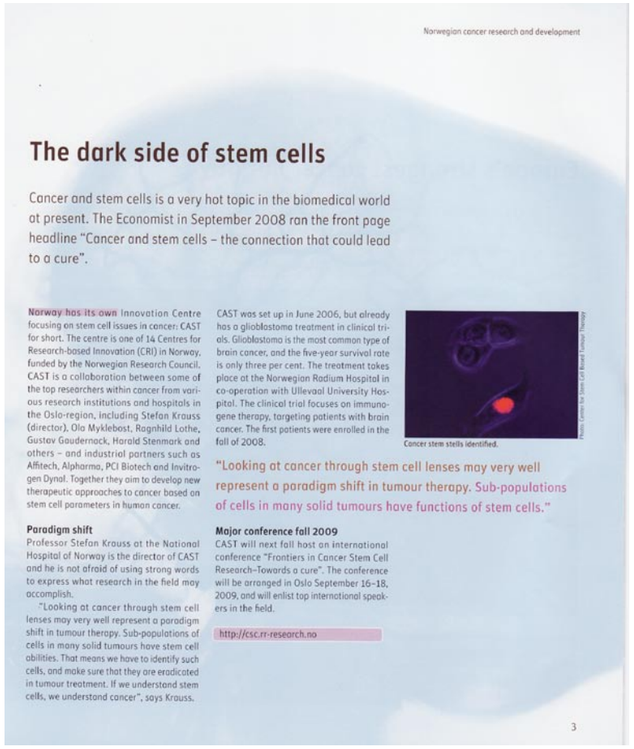
Steinar Funderud participated at the TV program "Schrödingers katt" at the national channel NRK1, in February 2008, on research results revolutionising the knowledge of cancer tumours.

Puls

Therese Sørlie was Interview in NRKs "Puls" 29th of September 2008

Genome Technology

June 2008, the Oslo area was featured as one of the top emerging places in the world for biotech research by the well-known magazine "Genome Technology". The Oslo Cancer Cluster (OCC), SFI-CAST and the Biotechnology Center were high lightened in the report.



Norwegian cancer research and development

The dark side of stem cells

Cancer and stem cells is a very hot topic in the biomedical world at present. The Economist in September 2008 ran the front page headline "Cancer and stem cells – the connection that could lead to a cure".

Norway has its own Innovation Centre focusing on stem cell issues in cancer: CAST for short. The centre is one of 14 Centres for Research-based Innovation (CRI) in Norway, funded by the Norwegian Research Council. CAST is a collaboration between some of the top researchers within cancer from various research institutions and hospitals in the Oslo-region, including Stefan Krauss (director), Ola Myklebost, Ragnhild Lothe, Gustav Gaudernack, Harald Stenmark and others – and industrial partners such as Affitech, Alpharma, PCI Biotech and Invitrogen Dynal. Together they aim to develop new therapeutic approaches to cancer based on stem cell parameters in human cancer.

CAST was set up in June 2006, but already has a glioblastoma treatment in clinical trials. Glioblastoma is the most common type of brain cancer, and the five-year survival rate is only three per cent. The treatment takes place at the Norwegian Radium Hospital in co-operation with Ullevaal University Hospital. The clinical trial focuses on immunogene therapy, targeting patients with brain cancer. The first patients were enrolled in the fall of 2008.

Cancer stem stells identified.

Photo: Centre for Stem Cell Based Cancer Therapy

"Looking at cancer through stem cell lenses may very well represent a paradigm shift in tumour therapy. Sub-populations of cells in many solid tumours have functions of stem cells."

Paradigm shift

Professor Stefan Krauss at the National Hospital of Norway is the director of CAST and he is not afraid of using strong words to express what research in the field may accomplish.

"Looking at cancer through stem cell lenses may very well represent a paradigm shift in tumour therapy. Sub-populations of cells in many solid tumours have stem cell abilities. That means we have to identify such cells, and make sure that they are eradicated in tumour treatment. If we understand stem cells, we understand cancer", says Krauss.

Major conference fall 2009

CAST will next fall host an international conference "Frontiers in Cancer Stem Cell Research–Towards a cure". The conference will be arranged in Oslo September 16–18, 2009, and will enlist top international speakers in the field.

http://csc.rr-research.no

3

Oslo Cancer Clusters magazine

December 2008 featured SFI-CAST "From cancer research to cure, Norwegian cancer research and development" .

Forskning.no

Forskning.no featured an article by the Langmoen group: http://www.forskning.no/artikler/2009/februar/209067

Kreft.no

The Lothe group was featured in Kreft.no in the context of the Young Investigator award

The Research Council of Norway's website

Joel Glover was featured in an article on the Research Council of Norway's website regarding the establishment of the Norwegian Centre for Stem Cell Research

Currently SFI-CAST consist of 10 academic research groups and four industry partners. In total about 60 people are involved full time or part time in the research at SFI-CAST. The SFI-CAST members are presented on the following pages.

Presentations of the Research Groups

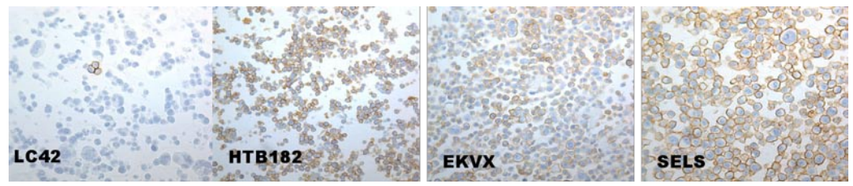
Gustav Gaudernack

Status

Within the framework of WP1, a large number of primary cancer cell lines have been established from fresh biopsy material using a serum free medium in combination with growth factors developed in co-operation with the Chinese Academy of Medical Sciences. Altogether 23 novel primary cancer cell lines have been established (6 lung adenocarcinoma cell lines, 7 squamous carcinoma lines, 1 large cell carcinoma, 1 small cell lung cancer, 1 carcinoid lung cancer, 6 prostate cancer and 1 ovarian cancer cell lines). The majority of cell lines are stable and have been passaged extensively *in vitro*. The panel of cell lines have been characterized phenotypically by flow cytometry and heterogeneity is seen in all of the cell lines. A distinctive subpopulation with phenotype (CD44++/CD90+) is associated with colony formation in vitro and with increase resistance to radiation. A method of selection for the CD44++/CD90+ by changing the culture conditions have been developed, and is presently being tested on cancers also of origin in other tissues.

Further research plans

Through the very good cooperation with the Center for lung cancer research, we are trying to further increasing the number of cell lines from this type of cancer, hopefully to obtain several cell lines also from the less frequent forms of lung cancer. A similar project is now established with the Department for Oncological Surgery (Karol Axcrona), who will provide prostate cancer material on a weekly basis. Recently a co-operation to obtain pancreas cancer material from Ullevål University Hospital, coordinated by Prof. T. Ikdahl, has been set up. The plan is to obtain a new panel of >5 primary cell lines from each of these cancer types within Q3 of 2009.
The already established cell lines are undergoing extensive studies *in vitro* and in animal models. The aim is to get information on side population, aldefluor positive cells and slow cycling cells in each of the cell lines and selected subpopulations (CD44++/CD90+), as well as soft agar colonies and *in vivo* growth.



Expression of CD44 on four different cell lines (Ping Wang)

Joel Glover

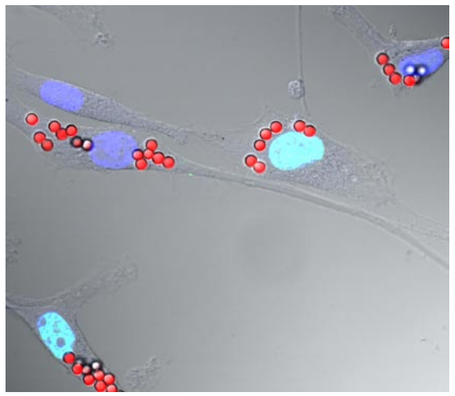
Status

The research interest of the group in the frame of CAST-SFI is to test and develop imaging systems that allow tracking tumour stem cells *in vivo*. In the longer term this will provide technologies for assessing treatment response and success We have labelled human mesechymal, adipose-derived, and fetal neural stem cells as well as human glioblastoma cells with MRI-detectable magnetic beads, after having transfected these cells with GFP using lentivirus. We have assessed several cell biological parameters (proliferation rate, duration of cytokinesis, migration rate, differentiation of specific characters) in vitro after labelling with beads. The main result is that cells labelled with beads behave nearly normally. Bead-labelled glioblastoma cells and mesenchymal stem cells have been injected into NOD-SCID mice of preliminary examinations have shown that they can be detected in vivo and thereafter found post-mortem by virtue of their GFP expression. The same cells have subsequently been injected into chicken embryos for analysis of differentiation potential and MRI detection.

We have also made co-cultures of human glioblastoma cells and cells from the neural tube of chicken embryos to assess interactions between the two cell types with respect to invasiveness and differentiation. Analysis of these co-cultures is underway.

Further research plans

The experiments described above will continue with the aim of establishing routine procedures for effective MRI-labelling and detection of tumour stem cells *in vivo* in animal models. Glioblastoma cells, mesenchymal tumour cells and pancreas adenocarcinoma cells will be the principal focus for the near future.



U87 cells labeled with micrometer-sized particles of iron oxide (MPIOs) can undergo mitotic process.

EdU (green), a nucleotide analog that incorporates in the DNA upon replication, is present in the nucleus of U87 cells that are labeled with MPIOs (red) while cells that are not replicating are only stained for DAPI (blue).

Stefan Krauss

Status

The main focus of the research group in the frame of SFI-CAST is to study stem cell signalling pathways and their role in development and cancer.

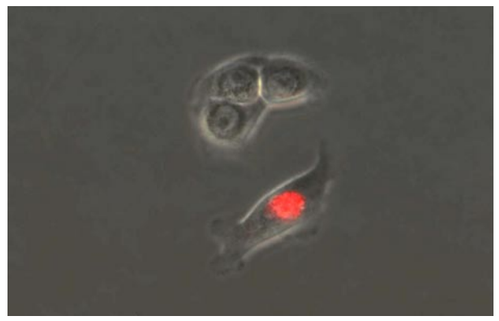
Evidence suggests that multiple tumours, display heterogeneity in parameters that are critical for tumour formation, progression and metastasis. We have identified a subpopulation of slow cycling cells (SCC) in pancreas adenocarcinoma and oesophagus carcinoma cells. SCC, which cycled on average 10-20 times slower than the fast cycling cell (FCC) population, showed only a partial overlap with known cancer stem cell markers, but they survived chemotherapeutic treatment, and were able to recreate the initial heterogeneous tumour cell population. The identified cells exhibited an increased invasive potential and morphological change resembling cells that have undergone an epithelial to mesenchymal transition (EMT). Furthermore, SCCs revealed a selective up-regulation of tell tale components of the Hedgehog (Hh)/TGFβ and Wnt pathways. These presented findings offer an expanded mechanistic understanding that tumour initiating potential with cycling speed and EMT, and provide a basis for novel diagnostic and therapeutic approaches, including targeted drug discovery to slow cycling tumour initiating cells.

With the aim of developing novel stem cell pathway specific antagonists we have established a drug discovery program for the Hh and Wnt pathways. Canonical Wnt signalling is over-activated in several tumours where it plays a central role in cell growth and tumour progression. Blocking canonical Wnt signalling has become a challenge in drug development. We identified three new small molecules that specifically inhibited canonical Wnt pathway at the level of activation of β-catenin. This specificity was verified in various cellular reporter systems, a *Xenopus* double axis formation assay and in gene expression profile analysis. Blockade of the Wnt controlled expression profile led to cell cycle arrest in the G1 phase, decreased proliferation rate of colorectal cells and inhibition of tumour growth in CB17/SCID mice. One lead substance has been selected for further preclinical development.

Further research plans

In the project period 2009-2010 we will extend our studies on understanding the mechanisms that control the transition between slow and fast cycling tumour cells. We will enlarge our drug discovery program on Hh and Wnt antagonists, and initiate a program for drug discovery using assay systems modelled for slow cycling tumour stem cells.

In collaboration with the biotechnology partners Affitech we will search for SSC specific therapeutic antibodies.



Slow dividing tumour stem cell side by side with fast cycling tumor cells derived from pancreas adenocarcinoma (J. Dembinski)

Iver Langmoen

Status

The main focus of the group in the frame of SFI-CAST is on neural stem cells and glioblastoma.

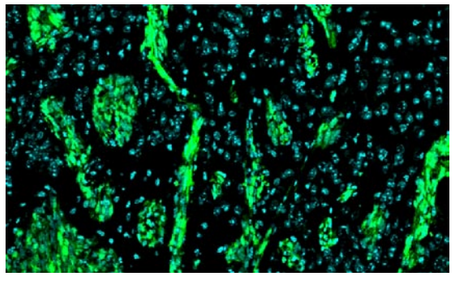
We have designed a clinical phase I/II study that has been fully certified by relevant authorities and opened for inclusion of patients. The study is based on 1) our previous work on cancer stem cells from glioblastomas and 2) the program on immunotherapy/vaccination by Guaudernack et al at the Norwegian Radiumhospital. We harvest tissue from patients undergoing surgery for glioblastoma and isolate/culture the stem cells. RNA from the stem cells is then isolated and introduced into dendritic cells harvested from the same patient. These dendritic cells, which now express the surface antigens of glioblastoma stem cells, are then used for immunization. The protocol is backed by the collaborations in SFI-CAST and includes both of the two neurosurgical and oncological departments in Oslo as well as the Departments of Clinical Cancer Research, Cell Therapy and Immunology at the Norwegian Radiumhospital and the Ex Vivo lab at Rikshospitalet University Hospital.

We have done microarray studies in order to compare gene expression in glioblastoma stem cells to normal stem cells from the adult human brain. 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. Furthermore, we have developed a technique for analysing the gene expression of single cells in a tumorsphere. We have performed a number of experiments studying the effect in vitro culturing of tumour stem cells has on the cells ability to form tumours, differentiate and on genotypic and expressional changes. These studies show that we can produce high numbers of tumour stem cells through limited expansions with insignificant changes in geno- and phenotype.

Finally, we have cultured stem cells from various regions of the adult human nervous system and eye, compared the geno- and phenotype of these cells and identified different patterns of differentiation both in these normal cells and in tumour stem cells.

Further research plans

To more accurately assess cell phenotype we will use a proteomic approach to compare two cell types at the membrane protein level to find specific surface markers from normal human neural stem cells and from tumour stem cells. The methodology will also be used in a study looking for proteins in the eye. We are exploring the cellular organization of neuro- and tumorspheres and looking at the cellular hetereogenity of such spheres. By sorting tumour cells based on surface antigens, we hope to establish methods for better identification of the progenitor population.



EGFP-expressing glioblastoma-derived stem cells showed aggressive invasion of the surrounding brain parenchyma (EGFP, green; nuclear marker TO-PRO3, blue).

Ragnhild A. Lothe

Status

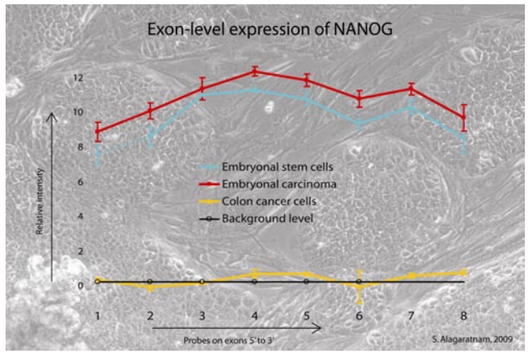
The main aim of the group in the frame of SFI-CAST is to identify novel genes that determine stemcellness, and to subsequently study these genes in the context of tumour/tumour stem cells

Embryonic stem cells and embryonal carcinoma cell lines have been cultured under identical conditions and an extensive transcriptomics analysis has been carried out. Bioinformatic analyses and laboratory validation of potentially interesting transcripts are ongoing and have provided preliminary results. From gene level analyses, known stem cell markers show expected expression levels (see figure below). From exon-level analyses, we have so far validated two genes as having differentially processed transcripts between embryonic stem cells and embryonal carcinomas. Ongoing are analyses of genome-wide DNA variation to be integrated with the transcript data set.

Further research plans

As an extension of the above studies, we are planning –omics analyses of primary germ cell tumours from males and females. For male germ cell tumours such datasets exist but they are few and only one integrative data set (genome and transcriptome of the same tumours) is available. Furthermore, none of the existing datasets are performed with the resolution level of the platforms currently used in the ongoing *in vitro* studies of the embryonic stem cells and their malignancy counterpart.
The direct comparison with the *in vitro* models will aid in identification of genes/transcripts that are associated with early stem cell adaptation, with transformation into malignancy. This “embryonic stem cell malignancy signature” will be analysed in comparison with stem cell signatures from adult tissues in order to potentially identify common tumour stem cell markers.

Recently we have shown proof-of-principle of a novel fusion genes microarray This will be used (in-lab platform) in search for known fusion genes among the *in vitro* models as well as primary tumours, but also potential novel targets identified through the –omics studies will be included in this custom made array.



Elsa Lundanes / Tyge Greibrokk

Status

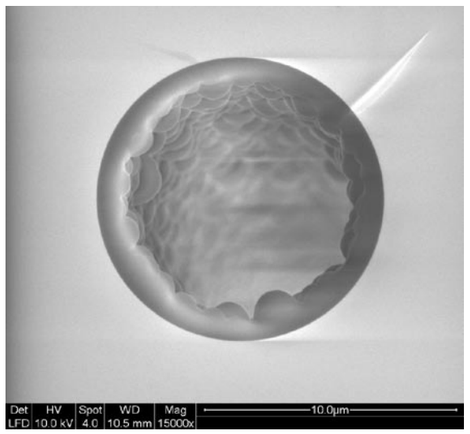
In the frame of the SFI-CAST, the group is engaged in analytical chemistry of cancer stem cells and reagents that affect cancer stem cells.
We have developed some highly sensitive and selective capillary LC-MS quantification methods for potential novel drugs in different types of organs as liver, kidney, plasma etc, in cooperation with Stefan Krauss and his group. Studies of possible new isomers of cyclopamine have also been performed using capillary LC-MS. Investigations of new drugs from plants are also ongoing.

We are also exploring miniaturized liquid chromatography methods for identification of proteins, especially membrane proteins, in cooperation with Iver Langmoen and his group

Further research plans

We will develop new miniaturized liquid chromatography columns for separation of low abundance proteins/peptides, since protein markers for cancer stem cells are expected to be present at low concentrations.

The liquid chromatography methods for determination of drugs developed in 2008 will be automated for high throughput analyses in 2009.



Scanning electron micrograph of the end section of a 10 µm inner diameter polystyrene-divinylbenzene porous layer open tubular (PLOT) column made at the Department of Chemistry and intended used for peptide and protein separations for identification of cancer stem cell markers.

Ola Myklebost

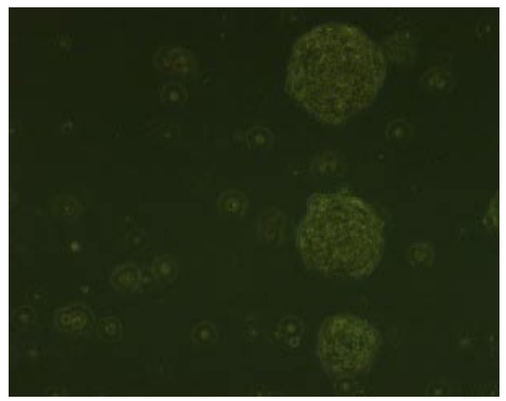
Status

The Myklebost group has for many years focused on mesenchymal cancer, sarcoma, and uses various functional genomics approaches to identify gene aberrations involved in their etiology. As part of this approach, normal mesenchymal stem cell systems have been established to investigate the function of the candidate proteins. One such candidate protein is HMGA2, an architectural transcription factor that is amplified and rearranged in sarcomas and that has shown to be central in the regulation of self-renewal and differentiation and also in the regulation of the stem cell phenotype especially in epithelial cancers. We have therefore in 2008 intensified our research on HMGA2, and have set up number of assays to investigate its intracellular level in individual cells by flow cytometry, its subcellular localization by confocal microscopy, its regulation by microRNAs, and experimental systems to study its posttranslational modifications. Investigations have been initiated to characterize how this protein affects the stem-like phenotype in our cancer stem cell models, and in particular the connection between TGF-beta and HMGA2 for the epithelial-mesenchymal transition in breast and pancreatic cancezr is investigated

Furthermore, using various assays, subpopulations have been identified in sarcoma cultures that are highly enriched for colony-forming ability. Work is in progress with reporter assays for Let-7 microRNA activity (which regulates levels of HMGA2 and ras). A colony of NOD/SCID immunodeficient mice has been established and assays of tumour-initiating potential of the various stem-like cell populations are on-going.

Further research plans

The studies on HMGA2 are being expanded, and the involvement of this protein its regulator, the Let-7 microRNA, and TGF-beta in the epithelial-mesenchymal transition (EMT) in carcinomas will be further investigated. Work is initiated to establish a number of cancer stem cell models from lung, prostate and pancreatic cancer, for use as drug validation systems.



Cancer cells grow as spheroids in stem cell culture.

Gunhild Mælandsmo

Status

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. In our studies we are utilizing either clinical material obtained directly from the patients, or human tumours grown as xenografts in nude mice. A focus for the group has been to optimize 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 utilize models representative for the basal-like and luminal subtypes of human breast cancer grown orthotopically in nude mice. The primary purpose of the project is to investigate whether any of the two subtypes of breast cancer originate from cells with stem cell-like properties, and furthermore to study whether the ER negative basal-like subtype descend from a more primitive/less differentiated, potential pluripotent, stem cell compared to the ER positive luminal subtype.

In the melanoma project primary cells have been cultivated as monolayer cultures and as 3D structures (melanomspheres), of which the latter growth condition seems to enrich for the cells ability to self-renew in nude mice. When single unsorted melanoma cells are seeded in vitro a surprisingly high percentage of the cells have the ability to form spheres, suggesting that a higher fraction than earlier anticipated might harbour stem cell-like properties. These cells are currently further analyzed.

Further research plans

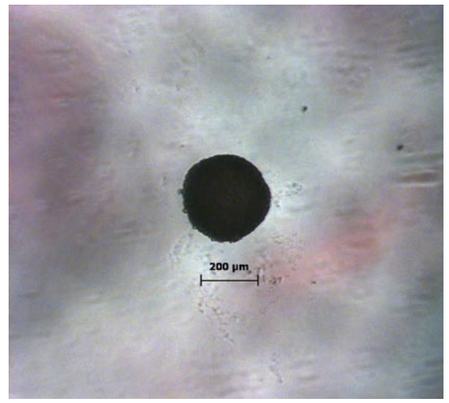
Breast cancer:

Test isolated subpopulations and implant form three-dimensional cultures in NOD-SCID mice studying tumour take from sorted cells and/or organotypic cultures. In addition we are searching for candidate molecules that may be examined for the possible use as novel markers for breast cancer cell stemness. Such markers will be examined in the available assays for the possible enrichment of tumour cells with stem cell characteristics.

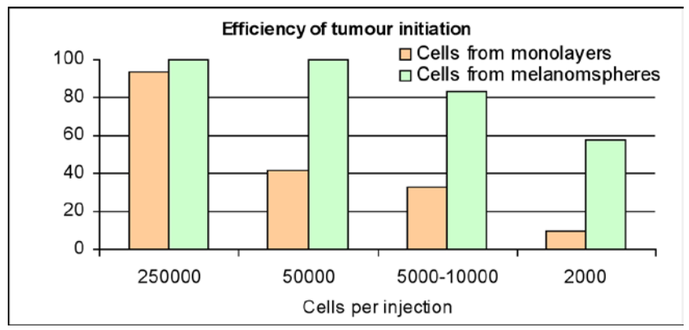
Malignant melanoma:

To investigate further the notion that aggressive melanoma, compared to other cancer forms, might contain quite frequent cells that have the potential for self-renewal and tumour initiation. Our in vitro data suggest that this is the case, and, therefore, we plan to carry out comprehensive in vivo studies to support this conclusion and to investigate whether those frequent cells have enhanced stem cell features.

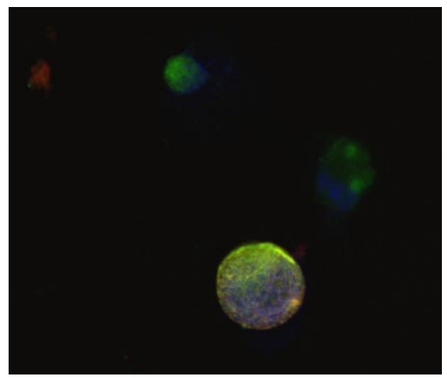
Furthermore, we are collecting and are planning to characterize paraffin-embedded archived material from the biopsies (primary melanoma - lymph node metastases – distant metastases) of several metastatic melanoma patients with respect to expression of differentiation (melanocytic) and de-differentiation (primitive, stem-like) markers and compare to clinicopathological parameters.



A) Microtumour-like melanomsphere, derived from a single melanoma cell, reflects a high self-renewal potential of the cell. 30-50% of cells from melanoma models *in vitro* and *in vivo* show the capacity for self-renewal.



B) Cells isolated from melanomspheres (like in A) have higher abilities to initiate tumours in nude mice than melanoma cells from adherent monolayer cultures suggesting that spheres might be enriched for stem cell properties.



Confocal image of CD49f expressing tumour cells isolated from a basal like mammary cancer xenograft. The Cd49f positive tumour cell subpopulation was smeared onto glass slides, fixed and immunolabelled with anti-cytokeratin 14 (green) and anti-cytokeratin 19 (red). The nuclei were counterstained with DAPI (blue). The yellowish colour occurs on double positive cells, indicating that this cell expresses both markers, suggesting that this might be a tumour cell of mammary progenitor lineage.

Harald Stenmark

Status

In the frame of SFI-CAST the group focuses on intracellular trafficking and cell signalling.

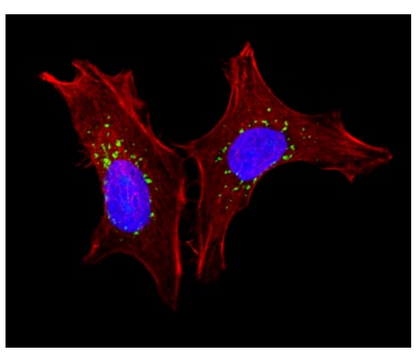
We have recently identified several endosomal proteins that attenuate downregulation of EGF receptors, and we are currently studying how these serve to modulate EGF signalling. In addition, we have performed a microarray analysis of EGF-stimulated fibroblasts and investigated how gene transcription is affected by EGF and how such signalling is modulated by regulators of membrane traffic.

Increased cell migration is a hallmark of many invasive cancers, but the mechanisms are incompletely understood. We have recently obtained evidence that degradation of integrins plays a crucial role in cell migration, and we are currently pursuing these results in order to elucidate the precise mechanisms involved. This study involves a combination of siRNA knock-downs and live-cell microscopy.

Finally, we study a class III PI-3-kinase that is a known tumour suppressor, but the molecular mechanisms are controversial. We have been investigating three cellular pathways controlled by this enzyme complex, namely endocytic membrane traffic, autophagy and receptor signalling. In addition, we have recently uncovered a function for class III PI 3-kinase in cytokinesis. We are currently continuing these studies in cell culture and Drosophila models to elucidate the tumour suppressor function of class III PI 3-kinase both *in vitro* and *in vivo*.

Further research plans

We will fucus on deepening the functional characterisation of protein complexes that mediate lysosomal degradation of endocytosed EGF receptors. We will carry out cluster analysis of EGF-activated genes that are sensitive to manipulation of the EGF receptor degradation machinery. Uncover the molecular mechanisms of integrin degradation, and establish their importance in cell migration. Furthermore, we will establish the function of class III PI 3-kinase and its downstream effectors in cytokinesis, cell signalling and tumour suppression.



The image shows cells in which ESCRT-III is inactivated. This causes redistribution of the Golgi complex (green). Actin is shown in red and nuclei are in blue. This image was selected for the cover of the 2009 edition of *Experimental Cell Research*.

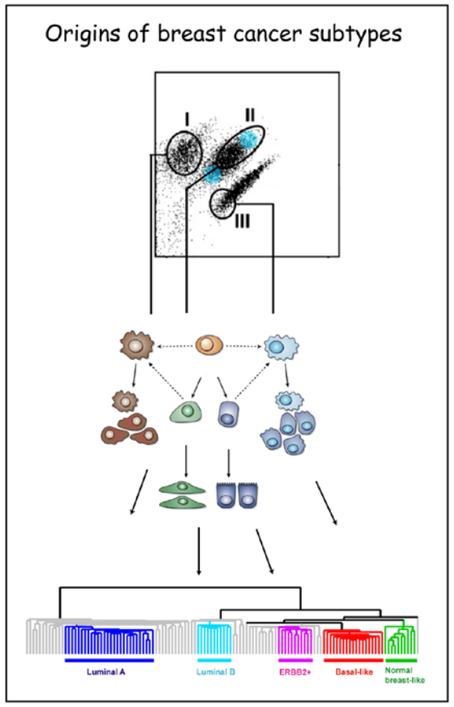
Therese Sørlie

Status

In the frame of SFI-CAST the group is focusing on stemcell parameters in breast cancer. We have characterized several subpopulations from the breast cancer cell line MCF7 by using microarray technology. More specifically, cells were sorted based on several potential markers for tumour initiating cells by our collaborators in Copenhagen. Copy number variations, expression of mRNA and miRNA were analyzed in these cells. Based on the gene expression patterns, selected genes were further analyzed by RT-PCR. Gene expression patterns of the various cells are clearly different and can be related to differentiation as well as the subtype specificity seen in primary tumours. These results will complement several functional assays as well as animal studies in a publication administered by the O. Petersen group. The challenge is to analyze enough biological replicates for robust conclusions of the data.

Further research plans

The work on the MCF7 cell line as well as other breast cancer cell lines will continue. We will include more biological replicates to confirm the results from MCF7 and in other cell lines. Furthermore, we are characterizing in a similar manner using whole-genome microarray technologies, several different cell populations from two xenograft models of breast cancer. This work is in close collaboration with Mælandsmo group. The goal here is to identify other markers that can help identify tumour initiating cells from these models. The initial markers were selected based on their possible definition of a stem cell niche in normal breast. The cells will be tested for stem cell-like characteristics by different functional assays and they will also be implanted into mice to analyze their tumour-forming capabilities.



AFFITECH AS

In the frame of SFI-CAST Affitech searches for antibodies or fragments thereof which bind to cancer stem cells.

Affitech is in the forefront of discovering and developing the new generation of drugs based on fully human antibodies for cancer and other key disease areas. Affitech does this by utilizing a fully integrated antibody library and its proprietary screening platform, in partnership with pharma and biotechnology companies as well as through the development of a proprietary portfolio of product candidates.

In November 2008, Affitech started an antibody discovery project in collaboration with SFI-CAST with the goal to find antibodies that preferentially bind to the slow cycling (SC) pancreatic cancer cells with cancer stem cell like characteristics (as determined by the collaborators). Affitech has managed to select a few scFv clones potentially specific for the slow cycling cells with cancer stem cell properties. Further characterization of the selected clones is ongoing.

Further research plans

An increased supply of sorted slow and fast cycling cell populations together with a routine quality control is planned for the future discovery activities, which involve using alternative selection strategies to enrich for more binders specific for the slow cycling cells of pancreatic adenocarcinoma

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AXELLIA PHARMACEUTICALS AS

(former Alpharma AS)

Axellia Pharmaceuticals AS (Axellia) is one of the leading Norwegian biotech companies, with more than 50 years of experience in the development and manufacture of antibiotics. Axellia is recognized for its expertise in fermentation and specialized recovery and purification technologies. During recent years, the company has also established a solid platform in chemical synthesis and semi-synthesis. Axellia`s interest in the frame of SFI-CAST is to help develop small, organically synthesized molecules that can be demonstrated to have a potential for blocking pathways/preventing tumour cell proliferation/killing cancer cells.

Further research plans

Axellia in collaboration with CAST-SFI plans to develop antagonists of the stem cell pathways Hh and Wnt to the stage of clinical candidates.

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INVITROGEN DYNAL AS

Invitrogen Dynal`s AS interest is to commercialise identified cancer stem cell markers to generate laboratory research reagents and diagnostic assays.

Dynabeads® revolutionized 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.

Invitrogen Dynal has the intentions to have long-term commitment to SFI-CAST and will provide competence and scientific personal in the context of surface antigen based cell separation. Invitrogen-Dynal AS 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 characterized.

Further research plans

Future plans for Invitrogen Dynal will be to develop cell isolation products based on antibodies specific for surface markers specifically expressed on cancer stem cell populations.

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PCI BIOTECH AS

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. The PCI technology has potential to improve the effect both of existing drugs and of emerging treatments such as gene therapy and other therapies based on nanotechnology or on biotechnological principles. In the frame of SFI-CAST PCI Biotech's interest is treatment of cancer stem cells involving photochemical reactions induced by a photosensitizing compound and illumination. A method for targeted therapy of stem cells is being developed, which *in vitro* is efficient with very low drug concentrations.

Further research plans

PCI Biotech aims to further document the concept of combining PCI with cancer stem cells (CSC) -targeting drugs, exploiting characteristic features of stem cells to achieve highly specific therapy. PCI Biotech has initiated collaboration with the Myklebost group for the targeting of sarcoma CSCs. In addition PCI Biotech has initiated collaboration with the Krauss group for the targeting of CD24+ slow-growing pancreas carcinoma cells.

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Bjarte Reve, CEO

www.oslocancercluster.no

Oslo Cancer Cluster – From cancer research to cure

Oslo Cancer Cluster is a research- and industry cluster within the field of cancer, in the Oslo-region of Norway, established as a result of more than 80 years of excellence in cancer research. The Norwegian government has appointed Oslo Cancer Cluster as a Norwegian Centre of Expertise (NCE). Oslo Cancer Cluster NCE is a non-profit organization with broad public funding and support.

Oslo Cancer Cluster is solely focused on developing new cancer treatments and diagnostics for the benefit of cancer patients. The cluster works to accelerate development of new cancer diagnostics and treatment.

One of nine emerging clusters

2008 was overall an exciting and fulfilling year for Oslo Cancer Cluster. The choice of Oslo as one of nine emerging clusters in biotechnology by the renowned magazine Genome Technology, sums up the many achievements made by the Oslo Cancer Cluster through the year. In 2008 Oslo Cancer Cluster managed to fully establish itself as an emerging cluster, both nationally and internationally. A whole range of new members came onboard, strengthening the research and development of cancer diagnostics and treatment in the cluster further. The cluster now has one of the strongest clinical pipelines in cancer outside of the pharmaceutical industry in the world.

Ten percent of the world's cancer products

Oslo Cancer Cluster fuses together Norway's world-class cancer research, unique healthcare infrastructure such as the Cancer Registry and the biobanks, with innovative biotechnology companies. Oslo Cancer Cluster´s member companies are strong in product development with over 50 products in clinical trials, ten percent of the overall cancer products in clinical trials worldwide. "We have more than 50 members from the government, research institutions, patient organisations, life sciences industry and hospitals. Our members come from the whole of Norway and abroad", says CEO Bjarte Reve.

Innovation Park in 2012

In August 2008 Oslo Cancer Cluster signed an agreement with the Oslo Council to build the Oslo Cancer Cluster Innovation Park next to the Radium Hospital. The Park is due for completion July 2012. It will include an incubator, AstraZeneca, GSK and biotechs, the Norwegian Cancer Registry, biobanks, the phase 1 unit at the Radium hospital and a fully integrated High School.

CAST is a valued member of the cluster

Oslo Cancer Cluster is proud to have the Norwegian Innovation Centre focusing on stem cell issues in cancer as a member. This is collaboration between some of the top researchers within cancer from various research institutions and hospitals in the Oslo-region. Cancer and stem cells is a very hot topic in the biomedical world at the present, and might represent the connection that could lead to a cure.

A1 Personnel

Key Researchers

Name	Institution	Main research area
Stefan Krauss	Cell and Genetic Therapy Institute of Microbiology Rikshospitalet University Hospital HF	Shh and canonical Wnt signalling in development, stem cells, and tumors.
Ola Myklebost	Dept. of Tumor Biology Institute of Cancer Research The Norwegian Radium Hospital	Identification and characterization of stem-like cells in sarcomas, and the involvement of stem cell pathways in sarcoma development.
Gustav Gaudernack	Dept. Of Immunology Institute of Cancer Research The Norwegian Radium Hospital	Lung cancer and immunotherapy
Joel Glover	Dept. of Physiology Institute of Basic Medical Sciences University of Oslo	In vivo imaging for following the fate of tumor cells and potential tumor stem cells in animal models. Develop labeling and imaging protocols that facilitate non-invasive in vivo cell tracking at the highest possible spatial resolution.
Iver Langmoen	Dept. of Neurosurgery Ullevål University Hospital/ National Hospital, Norway	Stem cells from the adult human brain, including normal stem cells and tumor stem cells.
Ragnhild A. Lothe	Dept. of Cancer Prevention Institute for Cancer Research Norwegian Radium Hospital	Germ cells and testicular cancer
Elsa Lundanes Tyge Greibrokk	Department of Chemistry University of Oslo	Developing highly sensitive and selective capillary LC-MS methods for potential novel drugs in different types of organs in order to determine if the drugs reach the target organs and for pharmacokinetic studies.
Gunhild Mælandsmo	Dept. of Tumor Biology Institute of Cancer Research The Norwegian Radium Hospital	The group is studying the impact of stem or progenitor cells for initiation and progression of breast cancer and malignant melanoma.
Harald Stenmark	Dept. of Biochemistry Institute of Cancer Research The Norwegian Radium Hospital	Receptor signalling guides the maintenance and fate of stem cells and their progenitors, including renewal, proliferation and choice of differentiation pathways.
Therese Sørlie	Dept. of Genetics Institute of Cancer Research The Norwegian Radium Hospital	Functional genomics and breast cancer.
Pål Selbo	PCI Biotech AS	Cancer stem cells involving photochemical reactions induced by a photosensitizing compound and illumination.

Senior scientist

Name	Nationality	Topic
Rolf Skotheim	Norwegian	Testicular cancer
Lina Prasmickaite	Lithuanian	Melanoms
Tor Erik Rusten (10%)	Norwegian	Stem cell signalling using Drosophila melanogaster as model organism
Wayne Murrell	Australian	Stem cells, Parkinson

Visiting Researchers

Name	Affiliation	Nationality	Duration	Topic
Jiyoung Kim	University of Copenhagen	South Corean	26.05.08 - 08.06.08	isolated cell populations from breast cancer cell lines
Prof. Robert Rees	John van Geest Cancer Research Center, Nottingham Trent University	English	20.06.08 - 27.06.08	prostate cancer stem cell cooperation
Chungui Lu (postdoc)	John van Geest Cancer Research Center, Nottingham Trent University	Chinese	20.06.08 - 27.06.08	prostate cancer stem cell cooperation

Postdoctoral researchers with financial support from the Centre budget

Name	Nationality	Topic
Ondrej Machon	Check	Stem Cell Biology
Quanli Gao	Chinese	Lung cancer
Gabor Halasi	Hungary	Embryonic niches as model systems to test stem cell potential
Linda Paulson	Swedish	Proteomics
Sharmini Alagaratnam	Malaysian	How embryonal carcinomas are different from embryonal stem cells and what are the implications for cancer?
Steven R. Wilson	Norwegian	Developing capillary LC-MS methods for potential novel drugs
Eva Wessel Pedersen	Norwegian	Isolation and characterisation of mesenchymal cancer stem cells
Unn-Hilde Grasmo	Norwegian	Characterisation of the interaction of leukemia and mesenchymal stem cell niche
Else Munthe	Norwegian	Epithelial-mesenchymal transition in cancer stem cell biology
Silje Lauvrak	Norwegian	The cell biology of slowly cycling stem-like cells
Kristin Andersen	Norwegian	Breast cancer
Lene Malerød	Norwegian	Stem cell signalling
Anita Langerød (50%)	Norwegian	Molecular characterization of subpopulations from cell lines and xenografts

Postdoctoral researchers working on projects in the centre with financial support from other sources

Name	Funding	Nationality	Topic
Jennifer Dembinski	NFR	American	Stem cell biology
Petter A. Olsen	EU/Medinnova	Norwegian	Genetic therapy
Marianne Stabell	FUGE	Norwegian	Stem cell programming
Anne-Mari Håkelien	NFR Stem Cells.	Norwegian	Stem cell programming
Anne Jacob	FUGE	Norwegian	Mouse
Stine Kresse	DNK	Norwegian	Stem cell biology
Leonardo Meza-Zepeda	HSØ	Chilean	Stem cell biology
Doreen Leung	NFR	Chinese	Imaging
Jean-Luc Boulland	NEVRONOR	French	Imaging
John Bianco	NFR	Australian	Cellbiology
Geir Olav Hjortland (50%)	RH-HF	Norwegian	Stem cells in breast cancer

PhD students with financial support from the Centre budget

Name	Nationality	Topic
Nina Solberg	Norwegian	Stem cell biology
Ping Wang	Chinese	Identification and characterizaton of human lung cancer stem cells
Sandrine Pacchini	French	Effects on Ephrin receptor A4 expression on cancer stem cells compare to normal neural stem cells after stimulation and blocking'

Master degrees

Name	Topic
Eline Buchman	Stem cell biology
Rebecca C.Frøen	Medical student
Undis Ellevog	Solubility studies and development of liquid chromatographic method for determination of membrane proteins
Kristin Opsal	Quantification of cancer drugs in biological samples using liquid chromatographic methods

PhD students working on projects in the centre with financial support from other sources

Name	Funding	Nationality	Topic
Benoit Follin-Arbelet	NFR	French	stem cell biology
Jo Waaler	NFR	Norwegian	stem cell biology
Martin F. Strand	NFR	Norwegian	stem cell biology
Ying Jing	UiO	Chinese	stem cell biology
Hege Ohnstad	DNK	Norwegian	Side population cells in sarcomas
Magne Skårn	DNK	Norwegian	MicroRNA regulation of mesenchymal stem-like cells
Åshilde Breivik	Helse SørØst	Norwegian	HMGA2, regualtor of stem cell biology
Yishan Liu	Forskningsstiftelsen	Chinese	WP1 Prostata cancer stamcells
Ali Arrefard	Legatmidler	Norwegian	Ovariecancer
Cecilie Sandberg	Ullevål	Norwegian	Moecularbiology
Einar O. Vik-Mo	Ullevål	Norwegian	Cellbiology
Mrinal Joel	RH HF	Indian	Cellbiology
Mercy Varghese	Helse og rehab.	Indian	Cellbiology
Kirsten Strømme	RH HF	Norwegian	Frizzled-7 pathway
Helle Malerød	UiO	Norwegian	Developing methods for identification of membrane proteins by capillary LC-MS
Hanne Hustoft	UiO	Norwegian	Developing new columns in the nano-flow region for separation of proteins
Viola Lobert	DNK	French	stem cell biology
Eldrid Borgan	Norwegian Research Council	Norwegian	Integration of gene profiles in breast cancer

A2 Statement of Accounts

Funding

The Research Council	The Norwegian Research Council	13 579
The Host Institution	Rikshospitalet University Hospital HF	11 174
	Radiumhospitalets legater	3 200
Research Partners	University of Oslo	1 276
Enterprise partners	PCI Biotech AS	1 639
	Axellia Pharmaceuticals AS (former Alpharma)	1 000
	Invitrogen Dynal AS, in kind (lab supplies)	100
	Affitech AS, in kind	812
Public partners	Ullevål University Hospital	2 607
	Total	30 275

All figures in 1000 NOK

Costs

The Host Institution	Rikshospitalet University Hospital HF	22 355
Research Partners	University of Oslo	3 075
Enterprise partners	PCI Biotech AS	1 886
Public partners	Ullevål University Hospital	2 959
Equipment		0
	Total	30 275

All figures in 1000 NOK

A3 Publications

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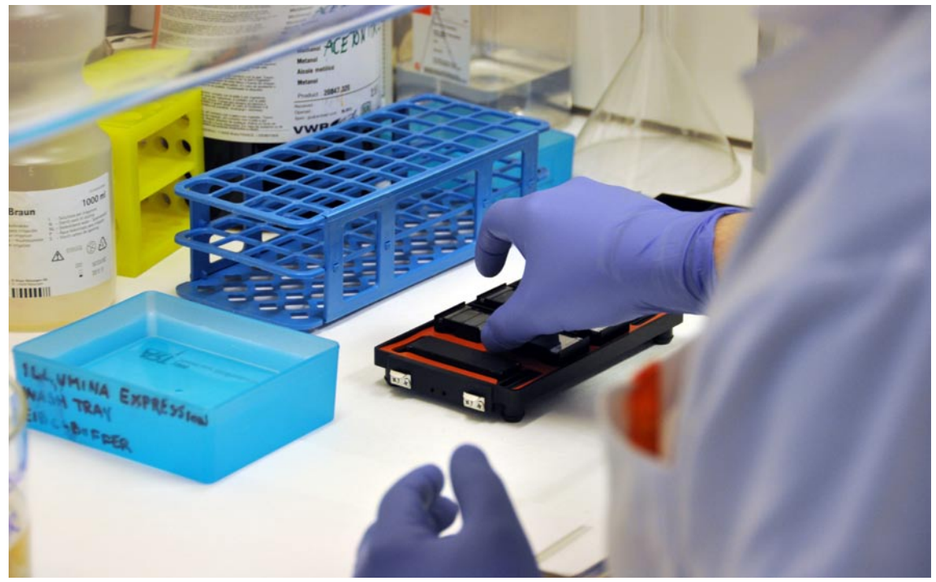

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