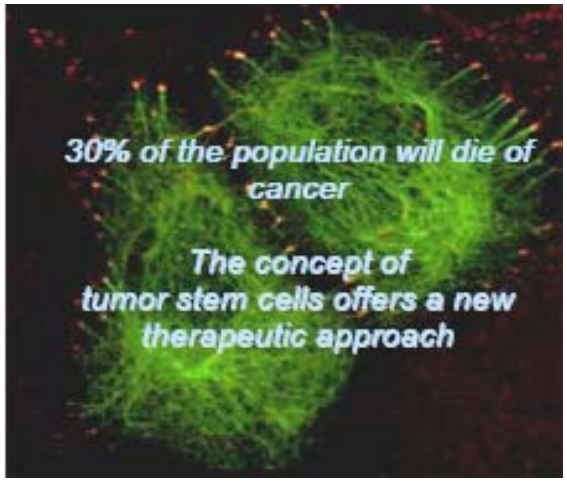
Annual report 2007
SFI - CAST

Cancer Stem Cell Innovation Center



Effective therapies for cancer patients require a thorough understanding of mechanisms leading to tumour development and drug resistance.

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Summary

It has long been known that tumours contain heterogeneous cell populations with respect to growth kinetics, drug resistance, and metastatic potential. Advances in understanding pathways and mechanisms that determine stem cell ness open new possibilities for improved strategies within detection and treatment of cancer.

The CAST centre for innovation based research works towards:

(i) The identification and characterization of cell populations (side-populations) enriched for cells with high tumourigenic potential.

(ii) The development of innovative approaches for finding small drugs, cancer vaccines and antibodies that destroy specifically stem-like cancer cells.

(iii) High resolution visualization of specific cell sub-populations in the body as a tool for tracking therapeutic success, and possible future diagnosis.





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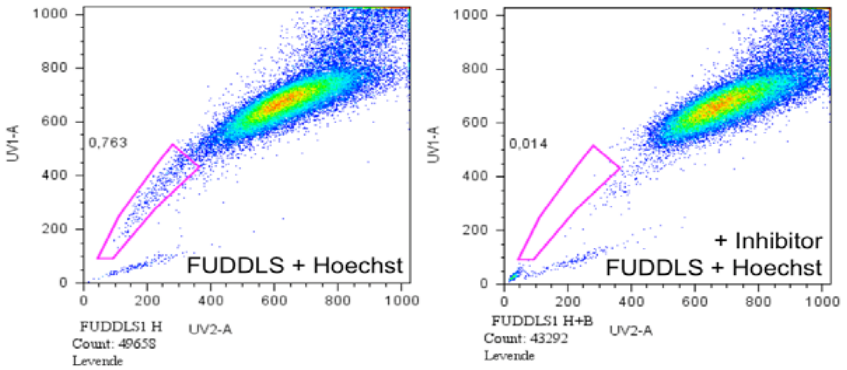
CAST – Vision and background

Effective therapies for cancer patients require a thorough understanding of mechanisms leading to tumour development and drug resistance. For many severe cancer types, including melanoma, glioblastoma, pancreas carcinoma and breast tumour, patients are given very aggressive treatments to improve their chances of survival. Unfortunately, these treatments often have serious side effects. Moreover, conventional treatments are often not even effective in fighting the most serious forms of these cancers.

Evidence suggests that at many tumours derived from cells with stem cell like character that function as the "root" of the tumour (TSC's). Therefore, substantial effort is done to understand stem cells, and to identify cells with TSC properties in cancer. By defining the biological properties of TSC's, highly targeted approaches to treating the roots of these cancers can be developed. There is now accumulating substantial evidence that this new approach could improve cancer therapy and reduce harmful side effects.



Side population in a mesenchymal tumour as determined by classical Hoechst stain exclusion (Myklebost laboratory).

If parallels are drawn with normal stem cells one would expect that cancer cells in many tumours still follow hierarchical structures and thus develop heterogeneous population of cancer cells.

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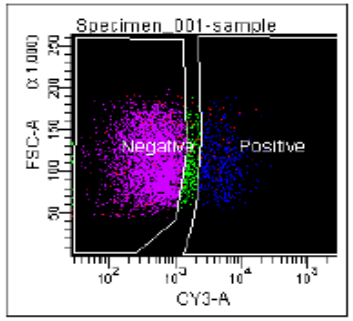
In particular, tumours, whether they are solid tumours (e.g., breast and lung) or hematological (e.g., leukemia), are predicted to be heterogeneous with respect to their cycling states. Cells that contain high proliferate potential but are in a reversible state of slow cycling – as frequently observed in stem cells – would easily escape traditional treatment.

Furthermore, depending on the status of various stem cell pathways that may be active in the tumour cells, tumour cells may be heterogeneous in the potential to metastasize. Thus, the molecular machinery used by normal stem cells for homing to or mobilizing from the niche may be "hijacked" by cancer stem cells for invasion and metastasis.

Recently it also got evident that the micro-environment of stem cells and cancer cells is important in understanding cancer and developing treatment. The stem cell niche in adult somatic tissues plays an essential role in maintaining stem cells or preventing tumour genesis by providing primarily inhibitory signals for both proliferation and differentiation. However, the niche also provides transient signals for stem cell division to support ongoing tissue regeneration. The balance between proliferation-inhibiting and proliferation-promoting signals is the key to homeostatic regulation of stem cell maintenance versus tissue regeneration.

CAST uses advanced stem cell understanding to develop new experimental therapeutic schemes for advanced cancer therapy.



Identification of cell cycle heterogeneity within a pancreas adenocarcinoma cell line creates a basis for advanced antibody and drug sreens (Krauss laboratory).

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CAST - strategy

The CAST innovation centre has a work program aimed at advancing from 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 tumour stem cells are identified (Affitech). The antibodies will be used to identify novel epitomes and therapeutic targets (Invitrogen).**
- **(i) Novel whole cell reporters that are capable of distinguishing molecular signalling in stem cells and tumour stem cells are developed.**
- **(i) Tumour stem cell pathways are used for differential high throughput screens that are coupled to combinatorial genetic platforms.**
- **(i) High cell resolution imaging of tumour stem cells *in vivo* using cutting edge magnetic resonance imaging (MRI) techniques is developed in animal models.**
- **(i) Ways to find improved immunotherapy protocols and targets are being explored and tested.**
- **(i) Antibodies are tested for improved therapeutic photo-internalization (Photo cure).**

SFI-CAST hosted by Rikshospitalet-Radiumhospitalet (RH HF)





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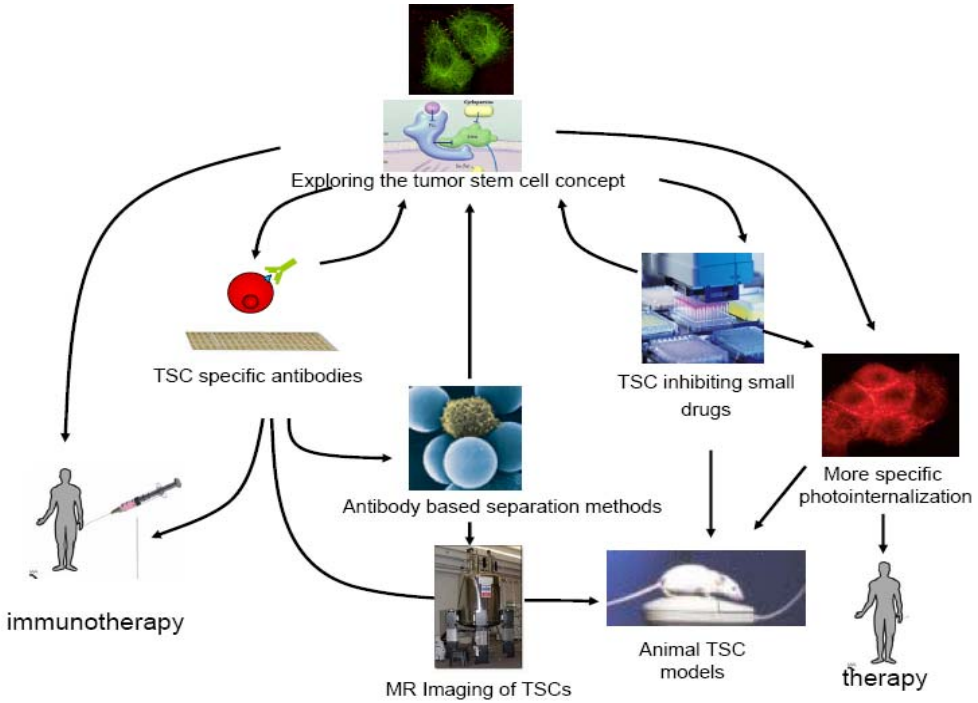
A major focus of the centre is translational research. Partners at the Radium hospital have been responsible for more than 20 phase I/II clinical trials of cancer vaccines and immune-gene therapy, and will cooperate with clinicians involved in the project to initial the first clinical trials targeting TSC from the very beginning of the project.

This ensures a swift start of the translational aspect as well as provide clinical material for the below work programs. For all central tasks the consortium has substantial international networks, including EU framework networks and European Science foundation networks.



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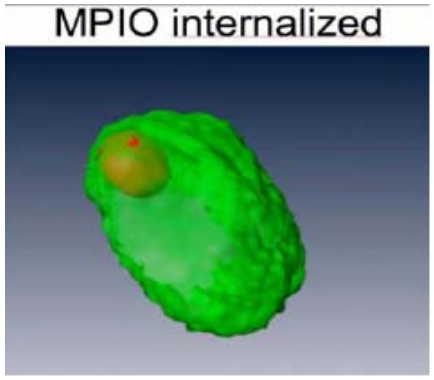
CAST- scientific activity2007

In 2007 CAST scientists have published 68 articles in international peer reviewed journals. A substantial number of these articles are in high impact journals.

CAST was established as a biomedical innovation center in June 2007. In the first project phase the main focus was in establishing the scientific and administrative infrastructure for the center.

Selected scientific milestones that were reached in 2007 are:

- **Isolation and molecular characterization of various tumour stem cell populations**
- **Assay development for drug screening**
- **MPIO marking of tumour stem cell**
- **Stem cell/tumour stem cell pathway characterization**
- **Development of analytical tools**



Glioblastoma cell marked with magnetic fluorescent beads (MPIO) (Joel Glover laboratory)





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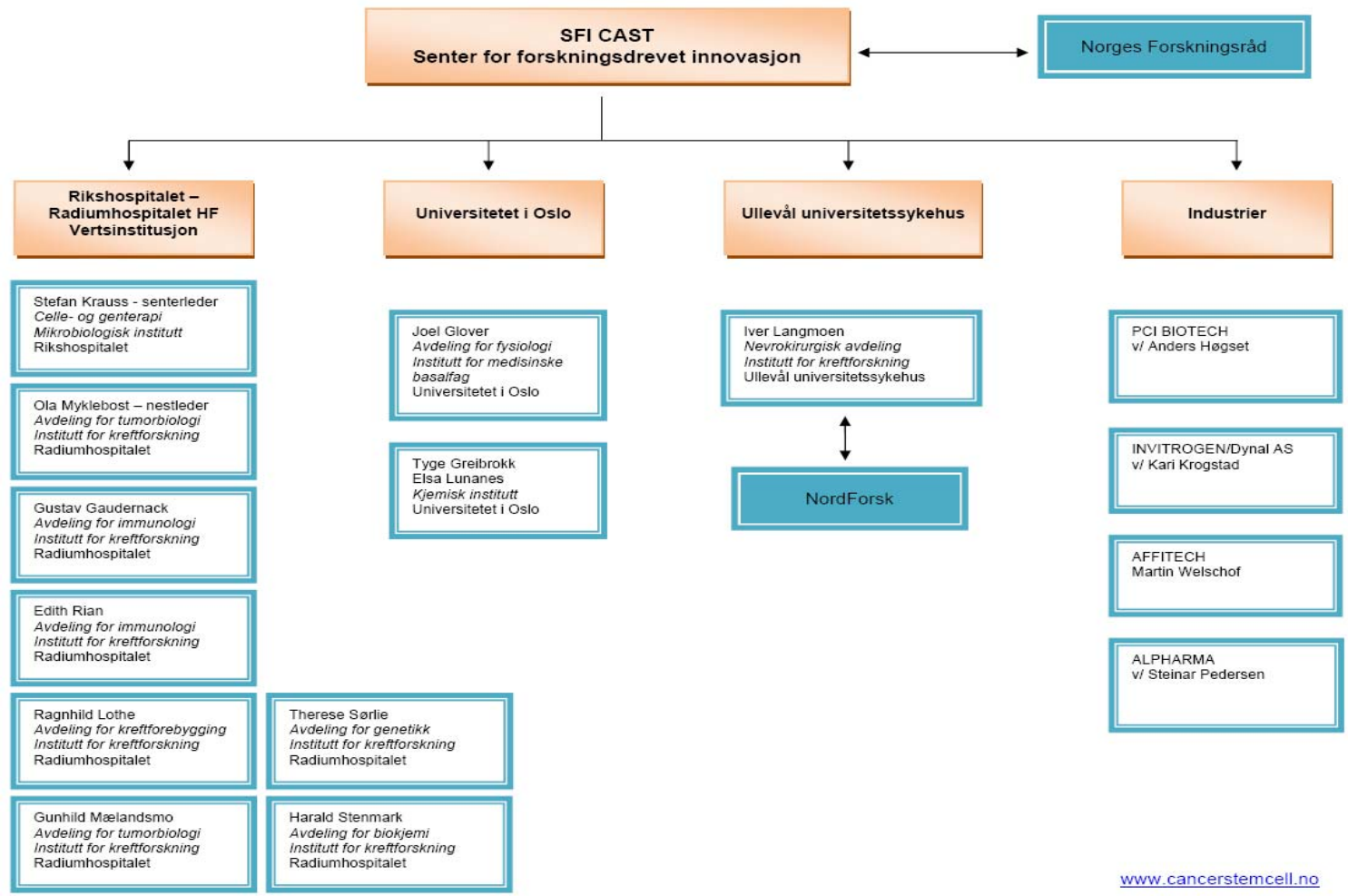
CAST- organization



www.cancerstemcell.no

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CAST- academic and administrative staff

Administration
Karina Saksberg
Line Mygland
Peder H. Utne
Kassahun Zelleke

Pi Edith Rian
Else Munthe – postdoctoral
Nomdo Westerdaal - cell sorter
Heidi Stubberud - cell sorter
Oleg Tsinkalovsky - cell sorter

Pi Stefan Krauss (centre chair)
Nina Solberg - PhD - student
Martin Strand – PhD - student
Ondrej Machon - postdoctoral
Olga Machonova – technician
Jennifer Dembinski – postdoctoral
Jo Waale – PhD - student

Pi Gustav Gaudernack
Ping Wang – PhD - student
Quanli Gao – postdoctoral

Pi Harald Stenmark

Pi Ola Myklebost (centre co-chair)
Hege Oma Ohnstad – PhD - student
Thea Sogn Smedsrud – engineer (over-)
Unn-Hilde Grasmo - postdoctoral
Russell Castro - engineer
Ingrid Østensen – engineer (over-)
Stine Kresse - postdoctoral
Eva Wessel Pedersen - postdoctoral
Leonardo Meza-Zepeda - postdoctoral

Pi Ragnhild Lothe
Rolf Skotheim - postdoctoral
Sharmini Alagaratnam - postdoctoral

Pi Iver Langmoen
Einar Vik-Mo - PhD - student
Cecilie Sandberg - PhD - student
Birthe Mikkelsen - engineer
Linda Paulsson – PhD - student
John Bianco – postdoctoral
Sandrine Pacchini – PhD - student

Pi Joel Glover
Doreen Leung - postdoctoral
Nedim Kasumacic - postdoctoral

Pi Gunhild Mælandsmo
Olav Engebråten - postdoctoral
Geir Olav Hjortland - postdoctoral
Lina Prasmickaite - postdoctoral
Evy Storeng - engineer
Trine Lillehammer – PhD - student
Hanne K. Høifødt - engineer
Kari A. Aaslund - engineer
Alexander Kristian - engineer
Thomas Halvorsen – engineer

Pi Tyge Greibrokk
Elsa Lundanes - postdoctoral
Sandra Rinne Dahl – PhD - student
Steven Wilson - postdoctoral
Helle Malerød – PhD - student

Pi Anders Høgseth
Pål Kristian Selbo - postdoctoral
Victoria Tudor Edwards - engineer
Kristian Berg – postdoctoral

Pi Therese Sørlie
Anna Bergamaschi - postdoctoral
Anne-Lise B-Dahle - professor
Anita Langerød - postdoctoral





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CAST- international cooperation and networks (excerpts)

- **Prof. Peter W. Andrews, Department of Biomedical Science, University of Sheffield, UK**
  - ✓ Comparison Embryonic Stem Cells and Testicular Cancer
- **Prof. Scott Fraser, California Institute of Technology, USA**
  - ✓ Small animal imaging (MRI)
- **Prof. William Matsui, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA**
- **Dr. Christiane Bruns, Klinikum Grosshadern, University of Munich, Germany**
- **Prof. Bengt Norden, Chalmers, Sweden (former chairman of Nobel commission chemistry)**
  - ✓ Sterols in changing membrane embedding of signal receptors
- **Prof. Ahmen El Zewail, California Institute of Technology, Pasadena, USA (Nobel price chemistry 1998)**
- **European Network of Excellence on Bone Tumours**
  - ✓ Bone Tumour biology, incl. Cancer stem cells
- **European Science Foundation EUROSTELLS program (coordination)**
- **Several Cancer/Stem Cell groups**
  - ✓ D Prof Horst Bürger - University of Münster, NL Drs AM Cleton-Janssen - University of Leiden, S Prof F Mertens - University of Lund
- **Meenhard Herlyn, Program of Molecular and Cellular Oncogenesis, The Wistar Institute, Philadelphia, USA**
- **Prof. Lars Âhrlund-Richter, Karolinska Institutet, Stockholm, Sverige**
  - ✓ Studies of embryonal imprinting of melanoma
- **Prof. Ole W. Petersen, Panum Institute, Denmark**
  - ✓ Stem cell hierarchy in breast, cell sorting
- **Prof. Mina J. Bissell, Lawrence Berkeley Laboratory, California, USA**
  - ✓ Microenvironment in normal and malignant breast development
- **Several medical chemistry groups in Berlin, Germany (Jörg Rademann, Jens Von Kries)**
  - ✓ Designing drug screens





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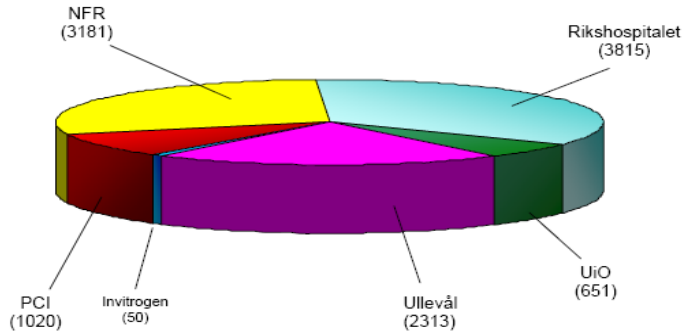
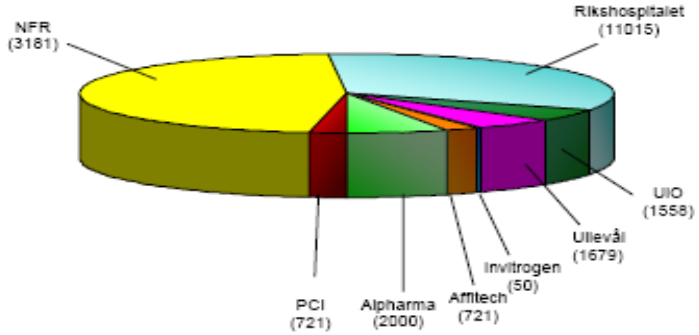
CAST-budget

Total budget 2007



Total budget 2008



CRI Annual Work Plan 2007 - FUNDING

Item	Type of research	Incentive effect	Bonus (2000)207	RCN Grant	Host	Other public	Other private	Skattefunn	University of Oslo	Ullevål univ. hospital	Affitech	Alpharma	Invitrogen	PCI	Total state aid	Total funding	State aid/ total funding
Type of Partner					P				R	P	SME	L	SME	SME			
Project WP1a	F	1111	1	2279	3 507				476	1677					2749	6130	0,34
Project WP1b	I	1111	0,65												0	0	
Project WP2a	F	1111	1												0	0	
Project WP2b	I	1111	0,65												0	0	
Project WP3a	F	1111	1	352	308				175	420					527	1271	0,41
Project WP3b	I	1111	0,65												0	0	
Project WP4a	F	1111	1												0	0	
Project WP4b	I	1111	0,65												0	0	
Project WP5a	F	1111	1												0	0	0,00
Project WP5b	I	1111	0,65	247										1020	247	1267	0,00
Equipment															0	0	0,00
Adm.				312											312	312	1,00
Total budget				3181	3815	0	0	0	651	2313	0	0	0	1020	3832	10980	0,35

CRI Annual Work Plan 2007 - Cost

Item	Host	University of Oslo	Ullevål univ. hospital	Affitech	Alpharma	Invitrogen	PCI	Total
Project WP1a	5103	546	2166					7849
Project WP1b								0
Project WP2a								0
Project WP2b								0
Project WP3a	826	352	575					1653
Project WP3b								0
Project WP4a								0
Project WP4b								0
Project WP5a								0
Project WP5b							1267	1267
Equipment								0
Adm.	312							312
Total budget	6070	900	2743	0	0	0	1267	10980





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Presentation of the partners

Stefan Krauss
The laboratory for cell signalling focuses on Shh and canonical Wnt signalling in development, stem cells, and tumors. Since its discovery in 1993 (Krauss et al., Cell 75, 1431-1444) Shh has shown to be a central signal in numerous developmental systems. Hh and Wnt signalling play important roles in various tumours and in stem cells. The laboratory currently works on pathways that feed into Hh and Wnt signalling, and on ways of influencing pharmaceutically Hh and Wnt signalling.

Mælandsmo
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 tumors grown as xenografts in nude mice. We are in the process of establishing optimized methods for preparing the tissue, isolating the tumor-initiating cell populations and cultivating the cells for maintenance of stemness characteristics and differentiation capability.

Tyge Greibrokk / Elsa Lundanes
We are developing highly sensitive and selective capillary LC-MS methods for potential novel drugs in different types of organs as liver, kidney, plasma etc, in cooperation with Stefan Krauss and his group, in order to determine if the drugs reach the target organs and for pharmacokinetic studies.
We are also developing miniaturized liquid chromatography methods for identification of proteins, especially membrane proteins, in cooperation with Iver Langmoen and his group. Novel separation technology in the nano-flow region will be explored for the ability to separate the hydrophobic membrane proteins.
On-line multidimensional capillary liquid chromatographic methods with mass spectrometric detection of peptides have already been developed for identification of the proteins.

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Therese Sørlie
Our research interests are in functional genomics and breast cancer. We are using DNA microarrays to study patterns of gene expression in clinical breast cancer samples. By using this technology in combination with statistical and bioinformatical tools, we have been able to identify specific patterns of gene expression that provided distinctive molecular portraits of breast tumors.

Ola Myklebost
The Mesenchymal Cancer Biology Group are studying sarcomas, malignant tumours with mesenchymal characteristics, and focus on osteo- and liposarcomas, as well as normal mesenchymal stem cells as model systems. Our CAST projects involve identification and characterization of stem-like cells in sarcomas, and the involvement of stem cell pathways in sarcoma development.

Harald Stenmark
Receptor signalling guides the maintenance and fate of stem cells and their progenitors, including renewal, proliferation and choice of differentiation pathways. Dysregulated receptor signalling is associated with oncogenesis and is probably a central cue in the development of cancer stem cells. Our group studies receptor signalling and how it is attenuated by endocytosis. In particular, we have been studying epidermal growth factor (EGF), a strong proliferative signal, and how EGF receptors become endocytosed and degraded after EGF binding. Ligand binding causes ubiquitination of EGF receptors, and we have identified and characterized a ubiquitin-binding endosomal machinery that recognizes ubiquitinated receptors in endosomes and mediates their sorting to lysosomes. Preliminary studies suggest that components of this machinery serve as tumour suppressors, and we are now performing further studies to characterize the functional mechanisms of endosomal sorting complexes in receptor downregulation and tumour suppression. As model systems we use cultured human cell lines as well as *Drosophila* models for cell signalling and oncogenesis. Confocal microscopy is central in our work, and in addition to characterizing stem cell relevant signalling pathways we will also contribute to the SFI project by characterizing the intracellular localization and trafficking of relevant cancer stem cell markers.





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Edith Rian

We recently got a new laboratory in Radiumhospitalet. Anna Wennerstrøm has been employed as an engineer. We have bought a Flow cytometer (special made FACSAria with 4 lasers) and this is now now running.
Our group has been identifying the factor of the transcription TIEG1, which is a possible mediator for TGFb/BMP6 and stroma mediated inhibitor of leukaemia cell dividing. This inhibitor is the rason why a larger part of leukaemia cells survive with cytostatika treatment. This task submits within June 1st, and will be presented (orally) at the European Hematology Association meeting in Copenhagen in June.
Furthermore we have showed that b-catenin is not passing on signals from Wnt16 in leukaemia cells with the translocation of E2A-PBX1. Instead, the b-catenin is connected to the N-cadherin mediated cell-cell adhesion. Until now this is the first time this type of interaction is shown for leukaemia cells.The connection between N-cadherin/b-catenin in adhesion of hematopoietic stem cells in the micro environment has been reported. This task is being submitted within June 15th.

Ragnhild Lothe

Germ cell tumors can develop in both males and females but are far more common among males. In fact, testicular cancer (usually of germ cell origin; TGCT) is the most common cancer type among young and adolescent males, and the incidence has almost quadrupled during the past 50 years. Pluripotent cells in TGCTs may differentiate along embryonic or extraembryonic lineages into various histological subtypes, and as such, the development of this cancer type is a caricature of the early embryogenesis. We and others have collected strong evidences for this also being the case for the transcriptional and epigenetic programs of these tumours. Genetic studies of embryonal stem cells and their adaptation to culturing have revealed striking similarities to genomic changes in the germ cell tumour genome, in particular embryonal carcinomas. By comparative studies of embryonic stem cells and *in vitro* cultures of their malignant counterparts, we aim to identify genes with malignancy-specific expression patterns in a stem cell context. The resulting markers will be functionally as well as clinically validated, the latter through the use of large patient series available in our department. Furthermore, the genes with malignancy–specific expression will be interrogated
from profiles of isolated side populations from other tumour types, as obtained by the other
consortium members.

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Invitrogen Dynal

Dynabeads® which are magnetic polystyrene beads have revolutionized separation technology ever since their inception and can be used to separate both biomolecules and cells in countless scientific applications. They are especially known for their consistency based on their narrow size distribution.

As an industrial partner of the SFI consortium, Invitrogen Dynal is committed to provide its cell-isolation and analysis tools and know-how for all applicable needs of the other partners of the consortium. This includes generation of specific cell-isolation beads for cancer stem cells of different cancer origin by targeting unique markers that are being discovered within the consortium. We will also contribute to the *in vitro* culture of these cells with our custom-made cell-culture media, provide specific labeling tools for cancer stem cells based on our FACS dies just to name a few of our input.

Alpharma

Alpharma AS is one of the leading Norwegian biotech companies, with more than 50 years of experience in development and manufacturing of antibiotics. Alpharma is recognized for its expertise in fermentation and specialized recovery and purification technologies. During the later years, Alpharma has also established a solid platform in chemical synthesis and semi-synthesis. Alpharma's predominant role within CAST is to assist in industrializing new products developed by the SFI-members, both biologicals/fermentation based in addition to synthetic and semi-synthetic products. Furthermore, Alpharma will have particular focus on small, chemically synthesized molecules with a potential of interfering with signal pathways of cancer stem cells and will attempt to increase input of candidate molecules through collaboration with other companies.

Affitech

Affitech is still waiting for a suitable target cell population before we can start the work for the SFI CAST project.

Once the work is started one whole project will take 2-3 full-time scientists (depending on the complexity of the target population) and 1 full-time senior scientist (Ph.D.) for 1 year and 4 months (timeline also depending on complexity of the project).

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Selected publications of CAST- associated scientists

Almstrup K, Leffers H, Lothe RA, Skakkebæk NE, Sonne SB, Nielsen JE, Rajpert-De Meyts E, and Skotheim RI (2007). Improved gene expression signature of testicular carcinoma in situ. Int J Androl. 30(4):292-303.

Berg K, Folini M, Prasmickaite L, Selbo PK, Bonsted A, Engesaeter BØ, Zaffaroni N, Weyergang A, Dietze A, Maelandsmo GM, Wagner E, Norum OJ, Høgset A. Photochemical internalization: a new tool for drug delivery. Curr Pharm Biotechnol. 2007 Dec;8(6):362-72.

Cabezón T, Celis JE, Skibshøj I, Klingelhöfer J, Grigorian M, Gromov P, Rank F, Myklebust JH, Maelandsmo GM, Lukanidin E, Ambartsumian N. Expression of S100A4 by a variety of cell types present in the tumor microenvironment of human breast cancer. Int J Cancer. 2007 Oct 1;121(7):1433-44.

Faedo A, Tomassy GS, Ruan Y, Teichmann H, Krauss S, Pleasure SJ, Tsai SY, Tsai MJ, Studer M, Rubenstein JL. COUP-TFI Coordinates Cortical Patterning, Neurogenesis, and Laminar Fate and Modulates MAPK/ERK, AKT, and {beta}-Catenin Signaling. Cereb Cortex. 2007 Dec 28; [Epub ahead of print] (Impact 6.368)

Feugaing DD, Tammi R, Echtermeyer FG, Stenmark H, Kresse H, Smollich M, Schönherr E, Kiesel L, Götte M. Endocytosis of the dermatan sulfate proteoglycan decorin utilizes multiple pathways and is modulated by epidermal growth factor receptor signaling. Biochimie. 2007 May;89(5):637-57. Epub 2007 Jan 21.

Filimonenko M, Stuffers S, Raiborg C, Yamamoto A, Malerød L, Fisher EM, Isaacs A, Brech A, Stenmark H, Simonsen A.Functional multivesicular bodies are required for autophagic clearance of protein aggregates associated with neurodegenerative disease. J Cell Biol. 2007 Nov 5;179(3):485-500.

Francis P, Namløs HM, Müller CR, Edén P, Fernebro J, Ritz C, Berner JM, Bjerkehagen B, Åkerman M, PO Bendahl, Isinger A, Rydholm A, Myklebost O, Nilbert M (2007) Diagnostic and prognostic gene expression signatures in 177 soft tissue sarcomas: hypoxia-induced transcription profile signifies metastatic potential. BMC Genomics 2007, 8:73

Greibrokk T. Looking into the world of biomarkers by chromatography and electrophoresis. J Sep Sci. 2007 Feb;30(2):147.

Greibrokk T.With emphasis on nano LC-MS. J Sep Sci. 2007 Sep;30(14):2177.

Gunn Hildestrand, Dzung Diep, David Kunke, Mattias Backman, Nils Bolstad, Magnar Bjørås, Stefan Krauss and Luisa Luna. The capacity to remove 8-oxoG is enhanced in neural stem/progenitor cells and decreases with age and upon cell differentiation (2007) DNA repair Jun 1;6(6):723-32

Haglund K, Rusten TE, Stenmark H. Aberrant receptor signaling and trafficking as mechanisms in oncogenesis. Crit Rev Oncog. 2007;13(1):39-74.

Hoei-Hansen CE, Kraggerud SM, Abeler VM, Kærn J, Rajpert-De ME, and Lothe RA (2007). Ovarian dysgerminomas are characterised by frequent KIT mutations and abundant expression of pluripotency markers. Mol.Cancer 6(1): 12.

Hystad ME, Myklebust JH, Bø TH, Sivertsen EA, Rian E, Forfang L, Munthe E, Rosenwald A, Chiorazzi M, Jonassen I, Staudt LM, Smeland EB. Characterization of early stages of human B cell development by gene expression profiling. J Immunol. 2007 Sep 15;179(6):3662-71.

Jarnjak-Jankovic, S., Hege Hammerstad, Stein Saeboe-Larssen, Gunnar Kvalheim and Gustav Gaudernack.A full scale comparative study of methods for generation of functional DCs for use as cancer vaccines BMC Cancer 2007 Jul 3;7:119

Jarnjak-Jankovic, S., Gunnar Kvalheim and Gustav Gaudernack. mRNA transfection of DCs in immature and mature state: Comparable in vitro priming of Th and CTL against DCs electroporated with tumor cell line derived mRNA. Cytotherapy 2007;9(6):587-9

Kleivi K, Lind GE, Diep CB, Meling GI, Brandal LT, Nesland JM, Myklebost O, Rognum TO, Giercksky K-E, Skotheim RI, and Lothe RA (2007). Gene expression profiles of primary colorectal carcinomas, liver metastases, and carcinomatoses. Mol Cancer. 6:2.





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Kristoffersen L, Øiestad EL, Opdal MS, Krogh M, Lundanes E, Christophersen AS. Simultaneous determination of 6 beta-blockers, 3 calcium-channel antagonists, 4 angiotensin-II antagonists and 1 antiarrhythmic drug in post-mortem whole blood by automated solid phase extraction and liquid chromatography mass spectrometry. Method development and robustness testing by experimental design. J Chromatogr B Analyt Technol Biomed Life Sci. 2007 May 1;850(1-2):147-60. Epub 2006 Dec 18.

Kyte JA, Kvalheim,G, Lislerud K, thorStraten P, Dueland S, Aamdal S, Gaudernack G. T cell responses in tumour patients after vaccination with mRNA-transfected dendritic cells. Cancer Immunol. Immunother. 56:659-675 (2007)

Lillehammer T, Engesaeter BO, Prasmickaite L, Maelandsmo GM, Fodstad O, Engebraaten O. Combined treatment with Ad-hTRAIL and DTIC or SAHA is associated with increased mitochondrial-mediated apoptosis in human melanoma cell lines. J Gene Med. 2007 Jun;9(6):440-51.

Lind GE, Ahlquist T, and Lothe RA (2007). DNA hypermethylation of MAL – a promising diagnostic biomarker for colorectal tumors. Gastroenterology. 132(4):1631-2.

Lind GE, Skotheim RI, and Lothe RA (2007). The epigenome of testicular germ cell tumors. APMIS. 115(10):1147-60.

Machon, Ondrej, Mattias Backman, Olga Machova, Zbynek Kozmik, Tomas Vacik, Lill Andresen, Stefan Krauss. Dynamic gradients o Wnt signaling controls neurogenis in the mammalian cortex. (2007) Dev Biol Nov 1;311(1):223-37. Epub 2007 Aug 28. (Impact 4.89)

Malerød L, Stenmark H. ESCRTs. Curr Biol. 2007 Jan 23;17(2):R42-3..

Malerød L, Stuffers S, Brech A, Stenmark H. Vps22/EAP30 in ESCRT-II mediates endosomal sorting of growth factor and chemokine receptors destined for lysosomal degradation. Traffic. 2007 Nov;8(11):1617-29. Epub 2007 Aug 20.

Meza-Zepeda LA, Noer A, Dahl JA, Micci F, Myklebost O, Collas P (2007) High-resolution analysis of genetic stability of human adipose tissue stem cells cultured to senescence. J Cell Mol Med in press

Mmatli EE, Malerød H, Wilson SR, Abegaz B, Greibrokk T, Lundanes E, Malterud KE, Petersen D, Rise F.Identification of major metal complexing compounds in Blepharis aspera.Anal Chim Acta. 2007 Jul 30;597(1):24-31. Epub 2007 Jun 27.

Müller CR, Paulsen EB, Noordhuis P, Peudeutour F, Sæter G, Myklebost O (2007) Potential For Treatment Of Liposarcomas With The MDM2 Antagonist Nutlin-3a Int J Cancer 121:199-205

M. Müller Kloster, T. Tolesa Hafte, L. Román Moltzau, E. Hallan Naderi, M. Krudtaa Dahle, B. S. Skålhegg, G. Gaudernack, F.O. Levy, S. Naderi, H. K. Blomhof , EBV infection renders B cells resistant to growth inhibition via adenylyl cyclase. Cell Signalling (in press)

Naoko Fujimura, Tomas Vacik, Ondrej Machon, Cestmir Vladec, Simon Scalabrin, Martin Speth, Stefan Krauss, Zbynek Kozmik. The transcription factor Sp5 is a direct downstream target of Wnt/b-catenin signaling that attenuates Sp1 regulated transcription (2007). J Biol Chem 282(2):1225-37)

Oldenburg J, Kraggerud SM, Cvancarova M, Lothe RA, and Fosså SD (2007). Cisplatin-Induced Long-Term Hearing Impairment Is Associated With Specific Glutathione S-Transferase Genotypes in Testicular Cancer Survivors. J.Clin.Oncol.

Oldenburg J, Kraggerud SM, Brydøy M, Cvancarova M, Lothe RA, Fossa SD (2007). Association between long-term neuro-toxicities in testicular cancer survivors and polymorphisms in glutathione-s-transferase-P1 and -M1, a retrospective cross sectional study. J Transl Med. 5:70.

Olsen R, Backman J, Molander P, Øvrebø S, Thorud S, Lundanes E, Greibrokk T, Kronberg L. Characterization of adducts formed in the reaction of glutaraldehyde with 2'-deoxyadenosine. Chem Res Toxicol. 2007 Jun;20(6):965-74. Epub 2007 May 23.





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Olsen R, Thorud S, Hersson M, Ovrebø S, Lundanes E, Greibrokk T, Ellingsen DG, Thomassen Y, Molander P. Determination of the dialdehyde glyoxal in workroom air-development of personal sampling methodology. J Environ Monit. 2007 Jul;9(7):687-94. Epub 2007 Apr 4.

Olstorn H, Moe MC, Røste GK, Bueters T, Langmoen IA. Transplantation of stem cells from the adult human brain to the adult rat brain. Neurosurgery. 2007 Jun;60(6):1089-98; discussion 1098-9.

Progida C, Malerød L, Stuffers S, Brech A, Bucci C, Stenmark H. RILP is required for the proper morphology and function of late endosomes. J Cell Sci. 2007 Nov 1;120(Pt 21):3729-37.

Rinne S, Ramstad Kleiveland C, Kassem M, Lea T, Lundanes E, Greibrokk T. Fast and simple online sample preparation coupled with capillary LC-MS/MS for determination of prostaglandins in cell culture supernatants. J Sep Sci. 2007 Aug;30(12):1860-9.

Rusten TE, Stenmark H. Developmental biology: moonlighting at the pole.
Nature. 2007 Feb 1;445(7127):497-9.

Rusten TE, Vaccari T, Lindmo K, Rodahl LM, Nezis IP, Sem-Jacobsen C, Wendler F, Vincent JP, Brech A, Bilder D, Stenmark H. ESCRTs and Fab1 regulate distinct steps of autophagy. Curr Biol. 2007 Oct 23;17(20):1817-25. Epub 2007 Oct 11.

Rusten TE, Filimonenko M, Rodahl LM, Stenmark H, Simonsen A. SCRTing autophagic clearance of aggregating proteins. utophagy. 2007 Dec 10;4(2) [Epub ahead of print]

Røyrvik EC, Ahlquist T, Rognes T, Lothe RA (2007). Slip Slidin' Away: A Duodecennial Review of Targeted Genes in Mismatch Repair Deficient Colorectal Cancer. Crit Rev Oncog. 13(3):229-57.

Simonsen A, Stenmark H. Stimulating the cell's appetite for itself. Nat Chem Biol. 2007 Jun;3(6):304-6.

Skotheim RI and Nees M (2007). Alternative splicing in cancer: noise, functional, or systematic? Int.J.Biochem.Cell Biol. 39(7-8):1432-49.

Sørlie, T. Molecular classification of breast tumors: Toward improved diagnostics and treatments. Methods Mol Biol. 360. In"Target Discovery and Validation Reviews and Protocols: Emerging Strategies for Targets and Biomarker Discovery", Volume 1. 2007. Edited by M. Sioud. Humana Press. ISBN: 1-58829-656-3.

Tveito S, Maelandsmo GM, Hoifodt HK, Rasmussen H, Fodstad O. Specific isolation of disseminated cancer cells: a new method permitting sensitive detection of target molecules of diagnostic and therapeutic value. Clin Exp Metastasis. 2007;24(5):317-27. Epub 2007 May 26.

Wu Q, Lind GE, Aasheim HC, Micci F, Silins I, Tropé CG, Nesland JM, Lothe RA, Suo Z (2007). The EPH receptor Bs (EPHBs) promoters are unmethylated in colon and ovarian cancers. Epigenetics. 2(4):237-43.

Wu Q, Lothe RA, Ahlquist T, Silins I, Trope CG, Micci F, Nesland JM, Suo Z, Lind GE (2007). DNA methylation profiling of ovarian carcinomas and their in vitro models identifies HOXA9, HOXB5, SCGB3A1, and CRABP1 as novel targets. Mol Cancer. 6(1):45.

Wilson SR, Malerød H, Holm A, Molander P, Lundanes E, Greibrokk T. On-line SPE-Nano-LC-Nanospray-MS for rapid and sensitive determination of perfluorooctanoic acid and perfluorooctane sulfonate in river water. J Chromatogr Sci. 2007 Mar;45(3):146-52.

Wilson SR, Malerød H, Petersen D, Rise F, Lundanes E, Greibrokk T. An alternative multiple-trapping LC-SPE-NMR system. J Sep Sci. 2007 Feb;30(3):322-8.

Zangani MM, Frøyland M, Qiu1 GY, Meza-Zepeda LA, Kutok JL, Thompson KM, Munthe LA, Bogen B. Lymphomas can develop from B cells chronically helped by idiotype-specific T cells. Journal of Experimental Medicine 204(5):1181-91 (2007).





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