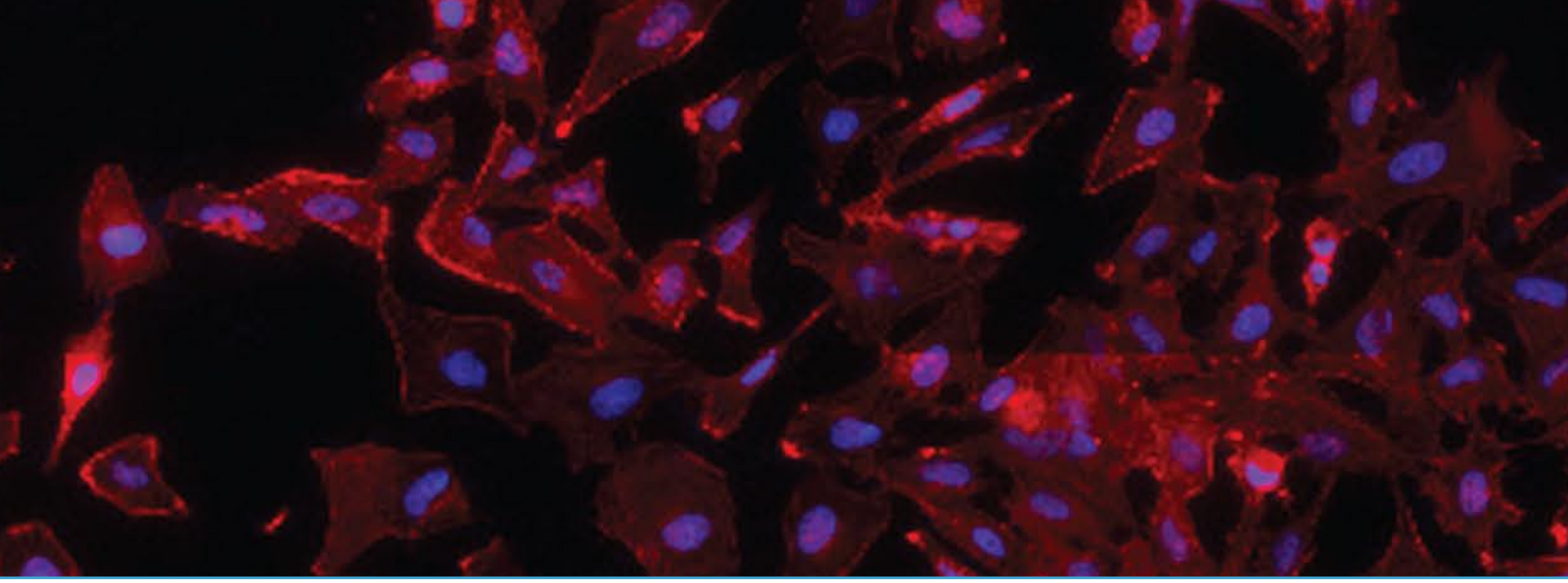


Centre for Cancer Biomedicine

ANNUAL REPORT 2008

2008

SUMMARY

CCB was inaugurated in September 2007, and 2008 therefore represented the Centre's first operational year. It has been a rather busy year with strong focus on the Centre's founding idea – to unite scientists across academic disciplines for breaking new grounds in cancer research. The Centre's annual gathering was held at Losby in September. We had inspiring scientific seminars, including a lecture about the challenges of prostate cancer by the Centre's first guest professor Manuel R.Teixeira, and fruitful group discussions. The first season of the CCB seminars has been dedicated to internal education about the cancer types studied by the Centre, in particular colorectal cancer, prostate cancer and lymphomas - and by the various signalling pathways that are deranged in cancers and that can serve as benchmarks for novel diagnostics. We have consciously stimulated collaborations across the Centre's research groups, and amongst others established the CCB's Postdoc and PhD student forums. Several joint projects have been initiated, and we expect to publish several multidisciplinary papers on cancer research in the coming years. Indeed, the identification of a strong predictor of survival for patients with a malignancy arising in the peripheral nerves has recently been published jointly by members from three CCB groups (Brekke et al., Neuro Oncology, 2009).

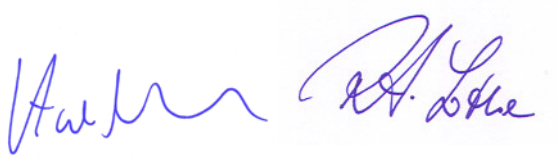
CCB had set ambitious scientific milestones for 2008, including the characterization of the "methylomes" for 26 cancer cell lines and the establishment of a model for invasive growth in Drosophila. These milestones have been obtained, and the Centre also has made additional accomplishments that actually had been planned for the following years. One of the principal aims of CCB is to identify novel biomarkers for cancer for future use within diagnostics and therapy. CCB,

represented by Erlend Smeland, participates in a multinational co-operation within subclassification of lymphomas. This co-operation has now resulted in the identification of the CARD11 protein as a novel biomarker for one of the most common types of lymphomas. This protein is an attractive target for future therapy (Lenz et al., Science, 2008). The results of a large study of B-cell lymhpoma patients showed that survival after combined chemotherapy is determined by several factors that are reflected in gene signatures (Lenz et al., New England Journal of Medicine, 2008). CCB scientists have recently identified a group of genes that become chemically modified already during early stages of colorectal cancer, thereby representing promising biomarkers for this disease (Lind et al., J Transl Med., 2008; Ahlquist et al., Molecular Cancer, 2008; Lind et al.,submitted). The centre also has a major focus on the identification of molecular mechanisms that regulate cell proliferation. An important progress in this context was the identification of the protein Eps15B, which contributes to attenuate the cell's response to growth signals from surrounding tissue (Roxrud et al., Journal of Cell Biology, 2008). The Centre's scientists have also identified novel connections between intracellular signalling and trafficking pathways (Wälchli et al., Molecular Biology of the Cell, 2008; Haugsten et al., Molecular Biology of the Cell, 2008) and spearheaded investigations concerning the intracellular fate of internalized nanoparticles (Tekle et al., Nano Letters, 2008).

CCB has experienced a rapid growth during its first year and currently consists of as many as 108 members. It is a special pleasure to welcome our first guest professors, Manuel R. Teixeira and Bo van Deurs. These internationally acclaimed scientists provide valuable contributions to CCB with their expertise in translational cancer medicine and basic cell biology, respectively. We are also very pleased that Edgar Rivedal's group joined CCB during 2008 as part of the Lothe lab. This group will strengthen CCB's research on intercellular communication, a topic of high significance to the cancer field.

CCB is concerned with equal opportunities in science, and has appointed a committee for equal opportunities, chaired by Kirsten Sandvig. Among several actions to improve the career development of female scientists, with a particular focus on women in leading positions, CCB recently announced its first researcher position earmarked for women, supported by the Research Council of Norway. Given the number of highly qualified women in the junior ranks of CCB, we expect to obtain a better gender balance in leading positions within the near future.

Finally, we would like to take this opportunity to acknowledge our host institutions, the University of Oslo and Rikshospitalet University Hospital, and the Research Council of Norway for supporting our activities in 2008. Special thanks also to our external funding bodies, especially the Norwegian Cancer Society, which provides invaluable support of our research.



Harald Stenmark *Ragnhild A. Lothe*

TABLE OF CONTENTS

VISION AND AIMS 5

HIGHLIGHTS AND MEDIA 6

RESEARCH GROUPS 8

INTERACTION ACTIVITIES 15

FORUMS 17

VISITORS 17

EDUCATION ACTIVITIES 18

PRIZES AND AWARDS 18

PUBLICATIONS & PRESENTATIONS 19

ABOUT CCB 22

FUNDING AND COSTS 24

PEOPLE 25




VISION AND AIMS

Cancer is a highly complex invasive cell disease, unique to small patient groups or even to single patients. Improvement of prognostics, diagnostics and therapy requires an integrated approach based on tumour parameters and patient specific properties. In Centre for Cancer Biomedicine more than 100 scientists from different disciplines share the common focus of disease understanding and development of affordable tools for early detection and tailored treatment of cancer.

Vision

The overall vision is to unite basic and translational research for the benefit of the cancer patient.

The efforts of the centre are aimed towards a better understanding of the complex dynamics of cancer evolution, a more accurate prediction of cancer prognosis and response to treatment and more powerful molecular based treatment. Scientific aims

- Identify genetic, epigenetic and morphological characteristics of cancer cells
- Develop and implement bioinformatic and biostatistical tools for handling of complex data sets from canceromics and image analyses
- Identify and characterize molecular and cellular mechanisms for regulation of cell growth, proliferation, survival, differentiation and motility – and link these to potential cancer biomarkers
- Identify potential biomarkers for cancer, and validate their clinical utility

CCB scientist published findings about entry of nanoparticles into cells

Senior CCB scientist Tore-Geir Iversen published a paper entitled "Cellular trafficking of Quantum dot-Ligand bioconjugates and their induction of changes in normal routing of unconjugated ligands", in the June 21st. issue of "Nano Letters" (impact factor: 10.0).

CCB group leader Kirsten Sandvig and visiting professor Bo van Deurs wrote 'News & Views' in Nature, about viruses exploiting the endocytic machinery in cells

CCB group leader, professor Kirsten Sandvig, was invited by the editors of Nature to comment on findings on the uptake mechanism of vaccinia virus. Sandvig is working with endocytosis and intracellular transport and is highly cited for her work (Hirsch factor 59). She has together with Prof. Bo van Deurs written an article entitled "Viruses in camouflage", which was published in the "News and views" section in the May 22nd issue of Nature (impact factor 27).

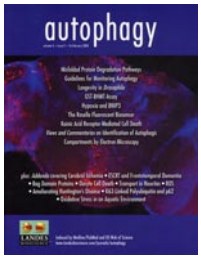
CCB team discovered new protein involved in growth factor downregulation

A new ubiquitin-binding protein that mediates sorting of endocytosed growth factor receptors from endosomes to lysosomes was discovered by Ingrid Roxrud *et al.* at Centre for Cancer Biomedicine, as reported in Journal of Cell Biology.

When cells are exposed to high levels of growth factors, the growth factor receptors become internalized by endocytosis and subsequently degraded in lysosomes as a mechanism to prevent overactivation of growth factor signalling pathways that mediate cell proliferation. Because growth factor signalling is often strongly upregulated in cancers, researchers are trying to elucidate the molecular mechanisms of growth factor-induced receptor downregulation. It has been known for some time that a protein called Eps15 facilitates endocytosis of epidermal growth factor receptors (EGFRs). Now, PhD student Ingrid Roxrud in Harald Stenmark's group has identified a "cousin" of Eps15, called Eps15b, which plays a different role in EGFR downregulation. While Eps15 works at the plasma membrane, Eps15b works at early endosomes, where it binds to the sorting protein Hrs and mediates sorting of EGFRs to lysosomes for degradation. EGFRs are known to become ubiquitinated when activated by growth factor, and both Eps15b and Hrs are ubiquitin binding proteins that presumably interact directly with the ubiquitinated receptor to mediate its sorting.

Illustration from CCB senior scientist Anne Simonsen's article on the cover of "Autophagy"

A figure from a paper by Anne Simonsen and co-workers was given the cover space of the February 16th issue of the journal Autophagy (impact factor 6,7). Results presented in the article indicate that induction of autophagy in the neurons of aging flies strongly increases their life span.



The e-published version of the article, "Promoting basal levels of autophagy in the nervous system enhances longevity and oxidant resistance in adult Drosophila" - was previously dedicated an editorial ("Editor's choice") in Science.

The image shows protein aggregates (red) that accumulate in the brain of a fruit fly defective in autophagy. Cell nuclei are shown in blue.

CCB group leader Erlend Smeland contributed to paper on oncogenic mutation in DLBC Lymphoma, published Science

Erlend B. Smeland and Jan Delabie co-authored an article entitled “Oncogenic CARD11 Mutations in Human Diffuse Large B Cell Lymphoma”, published in Science in Mar 2008 (impact factor 30). These important findings came as a result of an international collaborative effort involving prominent scientists from cancer centres in the USA, Canada, Gerrmany, Spain and Norway.

New England Journal of Medicine article by CCB group leader Smeland and collaborators links gene expression signatures to survival in lymphoma patients

The results of a large study of B-cell lymphoma patients showed that survival after combined chemotherapy was determined by differences in immune cells, fibrosis, and angiogenesis in the tumour microenvironment. This was reflected in the gene expression signatures (Lenz et al., New England Journal of Medicine, 2008).

The NEW ENGLAND JOURNAL of MEDICINE

Important findings on formation of protein aggregates in the brain, published by CCB scientists in JCB

CCB senior scientists Ioannis Nezis (left) and Andreas Brech (right) found that the Drosophila homologue of mammalian the protein p62 was required for formation of protein aggregates in the brain.

The results were published in Journal of Cell Biology (impact factor 10) in Mar 2008.

CCB Group leader Sjur Olsnes interviewed in The Cancer Society Journal.

We had no idea what were to come...

Prof. Sjur Olsnes was interviewed by The Cancer Society about cancer research since his early days. He states that ‘tremendous of progress has been made’.

RESEARCH GROUPS

Lothe's lab

Project

Understanding molecular mechanisms underlying human tumor development is essential to improve the diagnosis and treatment of the cancer patient. To gain knowledge of the complex dynamics of these abnormal processes the Lothe lab combines large-scale and detailed biology research using *in vitro* models and human samples arising from different embryonic germ layers.

Colorectal cancer and the many clinical challenges yet unresolved are the crux of the department research activity. They aim to identify and validate biomarkers for early detection and risk assessment, and predictive and prognostic molecular signatures.

Through creation and integration of in-lab datasets of the genome, transcriptome and epigenome of high quality clinical series they identify short gene lists of interest according to specific hypotheses. These genes and encoded products are then studied in detail to reveal molecular disease mechanisms, and potential biomarkers are validated in large independent clinical series.

Recent discoveries

During the last 2 years the Lothe lab have published all together 22 scientific papers, finished 4 MSc degrees and filed two patents.

The group recently used a combined strategy of epigenetic drug treatment of cell lines with expression studies of primary tumors to identify targeted genes (Lind et al., Cell Oncol 2006). Following up on these epigenetic gene lists by downstream studies they have recently identified novel methylated target genes in colorectal cancer (Lind et al., Gastroenterology 2007; J Transl Medicine 2008;) , ovarian cancer (Wu et al., Mol Cancer 2007; Epigenetics 2007) and nerve sheath tumors (unpublished). They further identified methylation markers for early colorectal tumor stages and a classifier of microsatellite unstable colorectal carcinomas (Ahlquist et al., 2008). Furthermore, they have validated a robust set of biomarkers with high sensitivity and specificity for both adenomas and carcinomas in independent clinical series (unpublished; patented).

By genetic studies of signaling pathways affected in colorectal cancer the group showed that the NF1 gene encoding neurofibromin, an inhibitor of RAS, are altered preferentially in tumors with the microsatellite instability phenotype and that the mutation profile of NF1 is different from that of the NF1 patients and their tumors (Ahlquist et al., Neoplasia 2008; J Pathol in press). They also identified novel mutations of the PTEN gene mutually exclusive with TP53 changes and present in at least 10% of all colorectal cancers (Danielsen et al., 2008 Human Mutation).

During the last two years the lab has developed a new microarray design to detect fusion genes by a simple universal assay. The proof-of-principle was recently published (Skotheim et al., Mol Cancer Jan 2009 "Highly accessed"), and has great potential for use in diagnostics and in research (patented).

Sandvig's lab

Project

Uptake of receptors and ligands and correct intracellular sorting of endocytosed molecules are crucial for maintenance of a normal differentiated phenotype. Protein toxins such as Shiga toxin are now well established as markers for studies of membrane traffic and as tools in molecular cell biology. In addition, the toxins are used in cancer diagnosis and therapy. The Shiga toxin receptor is overexpressed by a number of human tumors. Shiga toxin or its binding subunit can be used for *in vivo* tumor targeting and imaging. Importantly, a number of the protein toxins, such as ricin, diphtheria toxin and Shiga toxin are of interest also in connection with targeted drug delivery of toxin conjugates.

To construct active toxin conjugates, it is important to know which part of the toxin molecule to include, and whether the construct needs targeting to a specific intracellular compartment. For this purpose, knowledge about the relationship between toxin structure and function and the mechanisms involved in intracellular sorting is essential. By using a combination of morphological, biochemical and molecular biological approaches, Sandvig's group is investigating the various aspects of intracellular transport.

Specific aims

Errors in trafficking and signaling are associated with cancer, and the differences in expression of surface molecules and transport/signaling can be exploited to detect and kill tumor cells using drugs based on protein toxins. This project aims at increasing our knowledge about transport and signaling both in normal and tumor cells, and the results will provide a rational basis for treatment and prevention of disease.

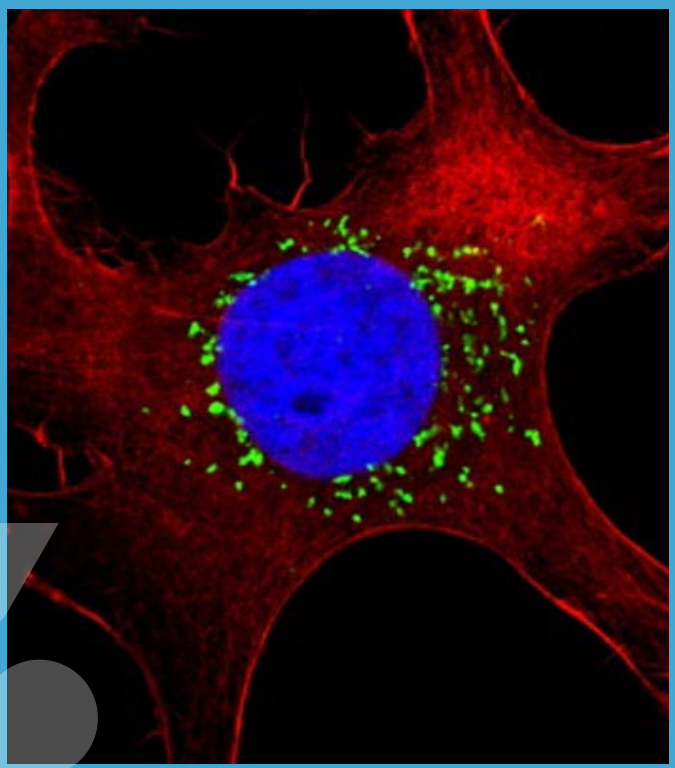
Recent discoveries

Sandvig's group was the first to publish that a molecule can be transported all the way from the cell surface, through endosomes, to the Golgi apparatus and then retrogradely to the endoplasmic reticulum (Sandvig et al., Nature 358(1992)510-512). Toxins as well as viruses have proven useful as tools to elucidate transport mechanisms (Sandvig and van Deurs, Nature 2008, Sandvig et al., Histochem.Cell Biol. 129(2008)267-276). Toxins are used to investigate the complexity of endocytic mechanisms, the pathways between endosomes and the Golgi apparatus, as well as transport to the ER (Recent findings from the group: Skånland et al., Cell. Microbiol. 2009, In press; Wälchli et al., Mol.Biol.Cell 19(2008)95-104; Torgersen et al., J.Biol.Chem. 282(2007)16317-16328; Utskarpen et al., Biochem.Biophys.Res.Commun. 358(2007)566-570; Skånland et al., Traffic 8(2007)297-309). Sandvig's group has recently found, by comparing different toxins, that retrograde transport seems to consist of several pathways that are controlled by both lipids and protein complexes. Importantly, the transport is regulated by kinases such as p38 and protein kinase C delta, and remarkably Shiga toxin activates the same kinases that regulate its transport. In addition to studies with toxins Sandvig's group has recently started to investigate the interaction between uptake of nanoparticles and the transport machinery in cells (Tekle et al., Nanoletters, 8(2008)1858-1865).

Stenmark's lab

Project

Stenmark's group studies mechanisms that control the proliferation, growth and motility of cells, and how dysregulation of these processes may cause cancer. Cellular pathways of particular interest to the group include endocytosis and degradation of growth factor receptors, autophagy, and cytokinesis. All these processes are known to contribute to tumour suppression, and the group is trying to elucidate the underlying molecular mechanisms in the hope that these may reveal pathways that may be exploited diagnostically or therapeutically. The translation of this research into applications that benefit cancer patients occurs in close collaboration with biostatisticians and translational cancer researchers in CCB. The model systems employed by the group include fruit flies and cultured cancer cell lines, and a range of biochemical, molecular biological, genetic and cell biological methods are employed. In particular, confocal and electron microscopy is central to the group's work, and the CCB biostatisticians contribute with quantitative analyses of imaging data.



Specific aims

- To identify molecular mechanisms responsible for the regulation of growth factor receptor signalling, autophagy and cytokinesis.
- To clarify the contribution of such mechanisms to tumour suppression or promotion.

Recent discoveries

Identification of Rabaptin-5 as the first effector of the small GTPase Rab5 in endosome fusion (Stenmark et al., Cell, 1995). Identification of the conserved FYVE zinc finger, and demonstration that a FYVE finger mediates the endosomal localization of the early-endosomal autoantigen EEA1 (Stenmark et al., J.Biol.Chem.,1996). Demonstration that the FYVE finger binds specifically to the PI 3-kinase product, phosphatidylinositol 3-phosphate (PI3P) (Gaullier et al., Nature, 1998). Identification of EEA1 as an effector of Rab5 and PI3P in endosome fusion (Simonsen et al., Nature, 1998). Construction of a tandem FYVE domain (2xFYVE) as a probe for PI3P and demonstration that PI3P is specifically localized to endosomes (Gillooly et al., EMBO J., 2000). Demonstration that the PI3P-binding protein Hrs binds ubiquitin via a ubiquitin-interacting motif (UIM) and recruits ubiquitinated membrane proteins into clathrin-coated microdomains on endosomes for their targeting to lysosomes (Raiborg et al., Nat. Cell Biol., 2002). Discovery that Hrs recruits endosomal sorting complex required for transport (ESCRT)-I to endosome membranes (Bache et al., J. Cell Biol., 2003). Discovery that the steroid hormone ecdysone induces developmental autophagy in Drosophila through downregulating the class I PI 3-kinase pathway (Rusten et al., Dev. Cell, 2004). In collaboration with Marino Zerial's lab, identification of KIF-16B as a kinesin motor protein that binds PI3P and powers the motility of PI3P-containing endosomes in the plus direction along microtubules (Hoepfner et al., Cell, 2005). Identification of the cytokine-independent survival kinase, CISK, as a key factor in regulating stability of the chemokine receptor CXCR4 downstream of PI 3-kinase (Slagsvold et al., EMBO J., 2006). Identification of Eps15b as an Eps15-related protein on early endosomes that interacts with Hrs to mediate degradation of epidermal growth factor receptors (Roxrud et al., J. Cell Biol., 2008).

Danielsen's lab

Project

Cancer arises from a single or a few transformed cells, and by the time a cancer is diagnosed, it comprises billions of cells carrying multiple, and mostly different, DNA- and chromatin abnormalities. Today's powerful technologies are enabling these changes to the genome to be catalogued in detail. If these billions of cells in a given tumour were carrying a specific aberration that initiated malignant proliferation of the single or few transformed cells, one would expect that the initiator would be easily detected. If indeed a given cancer type is characterised by one or a few specific aberrations, one would expect that such "true oncogenes" would also be easily detected. Evidence is instead accumulating indicating a close link between genomic instability and cancer initiation and progression. Neoplastic cells typically possess numerous genomic lesions, which may include sequence alterations and/or gross structural abnormalities in one or more chromosomes. Furthermore karyotypic alterations, including whole chromosome loss or gain, ploidy changes (aneuploidy and polyploidy) and a variety of chromosome aberrations are common in tumour cells. The loss of genomic stability appears to be a key molecular and pathogenetic step that occurs early in the tumorigenesis process and serves to create a permissive environment for the occurrence of alterations in tumour suppressor genes and oncogenes.

Danielsen's group is developing high throughput methods for detection and characterisation of large-scale genomic instability (chromatin structure and ploidy), based on high-resolution digital microscopy and advanced image analysis. They are studying archival material at the time of diagnosis from patients with proper clinical follow-up and known prognosis, in large series of colorectal, breast, prostate and gynaecological cancers.

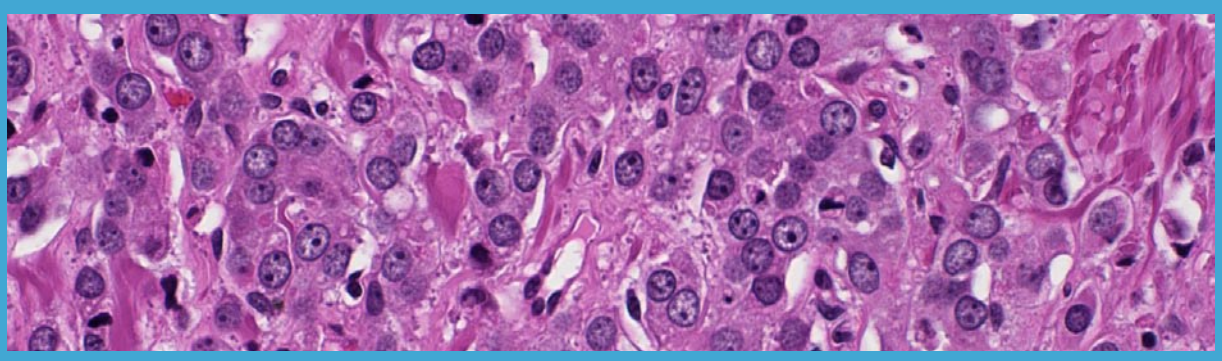
Specific aims

The first aim is to complete the methodology and develop a system that detects and classifies large scale genomic instability in tumours by analysing nuclei in routine histological biopsies, and to use this to analyse the large series of common cancers and define more precise prognostic markers for these cancer types. Results from different cancer types, as well as from different methods of instability indicators (DNA ploidy, Nucleotyping, CGH, Karyotyping), will be compared and analysed in an attempt to obtain new knowledge about the mechanistic and pathobiology of large scale genomic instability.

Detection and classification of genomic instability may be a key disease biomarker for cancer, and knowledge of the biochemical mechanisms behind it is likely to identify the next set of key therapeutic targets.

Recent discoveries and achievements

Methods and systems for high throughput analysis of chromatin structure and DNA ploidy in nuclei from routine biopsies are developed, and DNA ploidy have been shown to have independent prognostic power in Gleason 7 prostate cancers (Pretorius et al, Cellular Oncology, In press), and in uterine sarcomas (Kildal et al, Annals of Oncology, in press). A new high trougput method for analysing tissue micro arrays (TMA) based on virtual microscopy has also been completed (Brekke et al, Neuro Oncol. In press, and Arnoldussen et al, Cancer Res. 68(22)_9255-64, 2008). The use of texture analysis to study nuclear chromatin in cancers have been reviewed (Critical Reviews in Oncogenesis, 14(2), 89-164, 2008) and development of methods for automatic segmentation and classification of nuclei in histological sections have been completed .

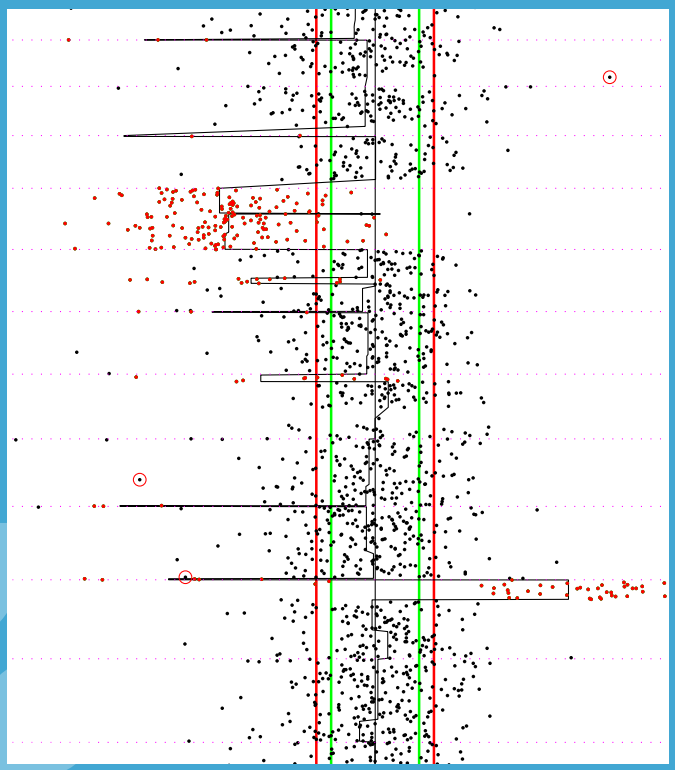


Liestøl's lab

Project

The Liestøl group is part of the Biomedical research group (BioMed) at the Department of Informatics, University of Oslo. The research activity in the BioMed group is directed towards methods development and applications of biostatistics, bioinformatics and computational science in the medical sciences, and in particular in medical genomics.

Liestøl's group has its main activity within analysis of data from high throughput technologies in genetics and molecular biology. While rich in information, the complexity of these large data sets makes extraction of information a true challenge. As opposed to the typical situation in classical statistics, high throughput technologies require methods adapted to (relatively) few samples and high numbers of observations on each sample.



Specific aims

Liestøl's group philosophy is to work in close interaction with other biomedical research groups and also to obtain own competence in the application areas. Typically, projects in their group initially focus on a concrete biomedical problem; they then try to solve the problem in a broader context and finally develop adapted software tools. In the pre-CCB period, much of their applied work was directed towards coronary disease (risk factors, decision support for myocardial infarction), as well as ecological population dynamical processes and their interactions with genetical processes. On the methodological side, focus has been on survival analysis, nonparametric/nonlinear statistical modeling, and how to handle many covariates in regression.

Recent discoveries

After the establishment of CCB, the group has focused on analysis of copy numbers (including further development of the CGHExplorer system, *Bioinformatics* 2005, 21, 821-822.) and worked on survival analysis with complex covariate structures *(Biostatistics* 2003, 4,633-49, Lifetime data analysis, 2008, 14, 179-195). Additionally, they address other statistical problems arising in CCB, including problems related to cellular processes, biomarkers or in translational research

Olsnes' lab

Project

Growth factors and cytokins act in most cases by binding to specific receptors at the cell surface and transmit signals into the cell interior. A common way of signal transmitting is that the receptors which often contain a kinase domain form dimers with the help of the ligand. The dimerisation brings together the cytoplasmic part of the receptors. This leads to cross-phosphorylation of the two receptor molecules which triggers a phosphorylation cascade and physiological altering of the cell.

Several years ago the group discovered that there must be an alternative way of receptor-mediated signalling. The process that has been studied is the ability of FGF-1 to be translocated into cells, to the cytosol and to the nucleus. This translocation is receptor mediated, but the kinase domain of the receptor is not required. On the other hand, approximately 60 amino acids at the C-terminal tail of the receptor are required. The translocation appears to be regulated by p38MAP kinase. The group tries to elucidate the mechanism of translocation and the function of the internalized growth factor. In addition, the group studies the endocytic uptake and the intracellular sorting leading to down-regulation the 4 FGF receptors (FGFR1-4).

Specific aims

Elucidation of the structure and function of the apparatus that translocates the growth factor into the cells is the main aim. Identification of the molecular target of the growth factor in the nucleus likewise. The group looks for additional phenotypes linked to the translocation of the growth factor. FGFs play important roles in many cancers and the Olsnes'group studies if the malignant process is linked to the uptake of growth factor. They study endocytosis and down-regulation of FGF receptors.

Recent discoveries

Olsnes' group that FGF1 does not only act by transphosphorylation of the FGF receptor, but that the growth factor is transported into the cytosol and nucleus and stimulates DNA synthesis (Wiedlocha et al. **Cell** 78, 1994, 1039). This observation has been followed up by studies of various aspects of the translocation. The group has found that the membrane potential is required (Malecki et al. **EMBO J,** 21, 2002, 4480), that the growth factor is first translocated to the cytoplasm, then to the nucleus due to two nuclear localisation sequences (**Biochemistry,** 44(16), 2005, 6071) where it is phosphorylated by PKCdelta (Wiedlocha, **Mol. Biol. Cell** 16, 2005, 794) at an incomplete nuclear export site (Nilsen et al.**J.Biol. Chem.** 282, 2007, 26245) which is then activated. This leads to export of the growth factor from the nucleus. The group demonstrated that the C-terminal tail of the receptor is required for translocation and that a site on this tail regulated by p38 MAP kinase is essential for translocation (Sørensen et al. **Mol. Cell. Biol.** 28, 2008, 4129). Furthermore, they have demonstrated that of the four different FGF receptors only 2 are able to translocate FGF1 to cytosol and nucleus (Sørensen et al. **J. Cell Sci.** 119, 2006, 4332). The translocation apparatus can only accommodate proteins of a defined size and active heat shock protein 90 is a prerequisite for translocation (Wesche, **J.Biol.Chem**, 281, 2006, 11405).The group has previously shown that while FGFR1 is predominantly transported to lysosomes for degradation, FGFR4 is recycled back to the cell-surface after internalization (Haugsten et al. **J. Cell. Sci.,** 118:3869-81, 2005). The different fate of the receptors seems to be dictated by the level of ubiquitination. Even if ubiquitination was shown to be important for sorting of the receptors, it was shown to be unimportant for endocytosis (Haugsten et al. **Mol. Biol. Cell.**, 19:3390-403, 2008).

RESEARCH GROUPS

Smeland's lab

Projects

Malignant lymphomas represent a heterogeneous group of diseases with variable clinical course. Due to the complex biology, heterogeneous prognosis and the wide range of genetic alterations involved, there is a clear need for improved diagnostics and the development of novel therapeutic approaches. Smelands group has access to patient biopsies from retrospective and ongoing clinical studies through collaboration with the lymphoma milieu at our institution, as well as cell lines from various subtypes of lymphoma and normal lymphocytes isolated from blood or tonsils. The combination of a large tumour bank and a clinical database up to 25 years of follow-up, offers a unique opportunity for retrospective studies with correlation to clinical parameters, including long-time survival. Smeland's group studies genetic and epigenetic changes, as well as gene expression patterns at the mRNA and protein levels. They are also actively participating as one of four European groups in a large international collaborative project regarding molecular profiling of B-cell lymphomas (headed by Dr. Louis Staudt at NCI, Smeland is site-PI).

The functional studies currently concentrate on the role of the BMP/TGF- β pathways in normal and neoplastic B cells. The TGF-β family of cytokines are involved in many aspects of cell function including proliferation, apoptosis, differentiation, and morphogenesis, and alterations in the BMP/TGF-β signalling pathways have been detected in a variety of human cancers. We have previously studied the role of PI3-kinase signalling in hematopoietic progenitors, and have now initiated studies in normal and neoplastic B cells to examine the role of this pathway. Smeland's group has recently initiated collaboration with Stanford University regarding detection of phosphorylated signalling molecules in lymphoma cell suspensions by flow cytometry.

Specific aims

The transformation of normal cells to cancer cells is closely related to control mechanisms for cell growth and cell death. Smeland's group uses high-throughput analysis of genetic changes and gene expression in neoplastic cells combined with functional studies of normal and neoplastic cells to increase our knowledge about B lymphocyte biology and to identify novel diagnostic and therapeutic strategies in B cell lymphomas. Altered DNA methylation patterns may serve as biomarkers for cancer detection, assessment of prognosis, and prediction of response to therapy.

Recent discoveries

The leukemia and lymphoma molecular profiling project has characterized several major subgroups of B-NHL by expression profiling. The studies have revealed and characterized 3 previously unrecognized, distinct subgroups of DLBCL; ABC, GCB and PMBL with distinct gene expression profiles, distinct genetic abnormalities and different prognosis (Rosenwald et al., N Eng J Med 2002, 346:1937-47, Rosenwald et al., J Exp Med 2003, 198:851-62, Lenz et al, N Engl J Med 2008, 359:2313-23, Lenz et al., Proc Natl Acad Sci U S A 2008, 105:13520-5). Importantly, Smeland's group has also shown for DLBCL, MCL and FL that gene expression profiles correlate to prognosis. In addition, several follow-up studies have revealed insight into activation of signal pathways in lymphoma subsets. Importantly, it was recently shown that the CARD11 gene is an oncogene in lymphoma and harbours activating mutations in a subset of DLBCL (Science 2008; 319: 1676-9). Finally, the group has shown that the presence of TP53 mutation at diagnosis of follicular lymphoma identifies a high-risk group of patients with shortened time to disease progression and a poorer overall survival (O'Shea et al., Blood. 2008; 112: 3126-9).

Smeland's group has performed gene expression profiling of normal highly purified B cell progenitors after RNA amplification and characterized changes in gene expression during early stages of human B cell development (Hystad et al., J Immunol 2007;179: 3662-71).

Smeland's group was the first to demonstrate cytokine production in normal human B cells (Smeland et al., J Exp Med. 1989; 70:1463-8), and has for several years studied the effects of the TGF-β/ BMP family of cytokines on hematopoietic and lymphoid cells. They have in the recent years explored the role of BMP induced growth suppression in normal primary B and T lineage cells from blood and bone marrow (Kersten et al., BMC Immunol 2005, 6:9; Kersten et al., Exp Hematol 34:72-81, Sivertsen et al., Eur J Immunol 2007; 37: 2937-48).

INTERACTION ACTIVITIES

CCB seminars

Lymphomas
Time: Jan. 23rd
Speakers form 4 CCB groups.

Prostate cancer
Time: Feb. 28th
Speakers from 4 CCB groups

Growth Factors and Cancer
Time: April 3rd
Speakers from 4 CCB groups

Endocytosis and Cancer
Time: May 14th
Speakers from 4 CCB groups

PI3 Kinases and Cancer
Time: June 18th
Speakers from 4 CCB groups

The Losby seminar 2008

One of the winners of Best CCB article prize, Ellen Haugsten

The Annual CCB seminar was held at Losby Gods on sep. 15/16 .

The seminar is the main gathering for the centre, and was in 2008 very successful, judging from feedback by the participants. The focus was mainly *centre aims and how to fulfill them.* There were project presentations by the group leaders and a lecture by visiting professor Manuel Teixeira. The three best CCB papers in 2008 were awarded and presented during the seminar. Group work with several tasks was arranged. This resulted in a number of actions to improve interaction in the centre, among them the establishment of Postdoc- and PhD forums.

Lecturer, proff. Manuel Teixeira

Serious work in the groups

Anne Simonsen presenting group work

…and not so serious dancing at night…

FORUMS

PhD forum

The PhD Forum was established after the Losby meeting, and is meant to be an arena where the PhD students of the centre can get to know each other, learn about and discuss topics relevant for their work. By December 2008 there were more than 30 PhD students associated with the centre and these will be gathered six times per year for a two hour meeting. The PhD board is responsible for the organization of the meetings and consists of one PhD student from each group. The PhD students from each group will take turns in hosting the meetings and give a short presentation of their group's work.

The topics will be of science matters as well as pedagogic (e.g. learn to write and present science). Once or twice a year there will also be a social event following the meeting.

Postdoc forum

It was decided in the Losby seminar, to establish a Postdoc forum for the approx. 30 CCB postdocs. The intention is to improve interaction, contribute to more collaboration and increase the sense of belonging to CCB. The activity plan for 2009 has been made, and focus will initially be directed towards methods and instruments within the centre. Speakers will also be invited to the forum.

VISITORS

Several scientists came to visit CCB labs the past year:

John Poulton, guest senior scientist

Prof. Manuel Teixeira, visiting professor

Vera Costa, guest scientist

Franclim Ricardo da Silva Ribeiro, guest scientist

Jedrzej Malecki, guest senior scientist




EDUCATION ACTIVITIES

Courses:

Pregraduate course

MBV3020, “Molecular genetics and development”, Institute for Molecular Biosciences, Faculty of Mathematics and Natural Sciences.

Graduate course

MBV4240, “Biochemical mechanisms in intracellular transport”, Institute for Molecular Biosciences, Faculty of Mathematics and Natural Sciences.

MOL8006, “Receptor signalling and trafficking”, Faculty of Medicine of the Norwegian University of Science and Technology.

M.Sc, degrees 2008:

June 2008

Hilde Honne, M.Sc. “Identification of novel epigenetic biomarkers in colorectal cancer”

Okt 2008

Jarle Bruun, M.Sc. “ Effect of Connexin 43 transcfection on growth characteristics of the human colon adenocarcinoma cell line HT29”

Des 2008

Marthe Eken, M.Sc. in Molecular Biosciences. “Identification of cancer-specific transcripts: With emphasis on the hunt for fusion genes in colorectal cancer.”

PRIZES AND AWARDS

Dr. Ragnar Mørk legacy prize 2008 to Tor Erik Rusten

This year’s prize from “Dr. Ragnar Mørk legacy” went to Tor Erik Rusten, senior scientist in CCB. This award is given annually to a scientist who has achieved excellent results throughout years of outstanding research.

The ceremony took place in the seminar room at the Institute for Cancer Research on Friday 7th of November. Rusten gave a lecture summarizing his work.

Young Investigator Award to Rolf Skotheim

Rolf Skotheim received the price for Young Researcher at Oncological Forum in Bergen. The price of 25 000 NOK will finance projects in his project group of Genome Biology (Lothe’s group), in CCB.

The Onkologisk Forum young researcher is an annual price awarded to an investigator younger than 40 years who has contributed significantly within the field of cancer research.

Fusion Gene Project - first runner up

An idea from Department of cancer prevention “Fusion gene microarray” received recognition and a diploma for having been in the final round of the price, Idea Prize 2008 (Medinnova). The idea fusion gene microarray is patent applied by Rolf Skotheim, Ragnhild A Lothe, Guro E Lind, Gard Thomassen, and Torbjørn Rognes, researchers from Department of Cancer Prevention at the Norwegian Radium Hospital and the Institute for Informatics at University of Oslo. They present a novel general test for identification of fusion genes in cancer. Proof-of-principle data have been successfully obtained from prostate cancers clinical samples and leukaemia cell lines, indicating the usefulness of this universal tool for fusion gene detection. For further development of this invention the Project Group of Genome Biology recently received funding from the FORNY-program of the Norwegian Research Council.

Chinese government scholarship for Outstanding Students to CCB PhD student

The Chinese government awarded CCB PhD student Yan Zen Outstanding student abroad. This award was only given to 130 Chinese abroad students throughout the world, and is based solely on scientific activity.

PUBLICATIONS & PRESENTATIONS

Publications

Ahlquist T, Lind GE, Costa VL, Meling GI, Vatn M, Hoff GS, Rognum TO, Skotheim RI, Thiis-Evensen E, Lothe RA. Gene methylation profiles of normal mucosa, and benign and malignant colorectal tumors identify early onset markers. Mol Cancer. 2008 Dec 31;7(1):94.

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Selected Presentations

Gordon Research Conferences (GRCs), Growth factors and Signalling. Regulation of Growth factor signalling by ESCRT proteins. Invited speaker.

PEN conference, Rome, Italy. “Entry of Shiga toxin into cells”, invited speaker.

FEBS Workshop, Lipids as regulators of cell function, Spetses, Greece. Involvement of sorting nexins in endosome to Golgi transport of Shiga toxin.

Norwegian State visit to Portugal. Biotechnology seminar, University of Porto. Early detection of colorectal cancer. Invited delegate.

European Testis Workshop, Naantali, Finland.

Genome biology of human testicular tumourigenesis. Invited speaker.

Nordic conference, Urotheraputic association, Oslo, Norway.

Cancer and diet. Invited speaker.

National conference. Screening av tykk- og endetarmskreft? Helse og Sosialdirektoratet, Oslo, Norway. Tidligdiagnostikk ved kolorektal cancer. Invited speaker.

The 14th International Charles Heidelberger Symposium on Cancer Research, Urumqi, China. Mechanisms for Down-Regulation of Gap Junction Intercellular Communication in Cancer. Invited speaker.

Workshop: Translational research-based decision-making in CRC, Taormina, Italy.

Novel epigenetic biomarkers for early detection of colorectal tumors. Invited EACR delegate

Biomarker Discovery Europe 2008, GTCbio, Dublin, Irland.

Identification of novel biomarkers for early detection of colorectal tumors. Invited speaker

Connective Tissue Oncology Society 14th Annual Meeting, London UK. Nuclear tp53 expression in malignant peripheral nerve sheath tumours is an independent marker of poor survival.

Oncological Forum, Bergen, Norway. Young Investigator award lecture 2008

Cancer specific RNA in search for biomarkers and targets for treatment.

Genesis, London, UK. Novel epigenetic biomarkers for early detection of colorectal tumors. Invited speaker, delegate of Oslo Cancer Cluster.

ISCO Congress 2008, Amsterdam, NL. Genomic Instability as Measured by DNA Ploidy in a Total Population of Uterine Sarcomas.

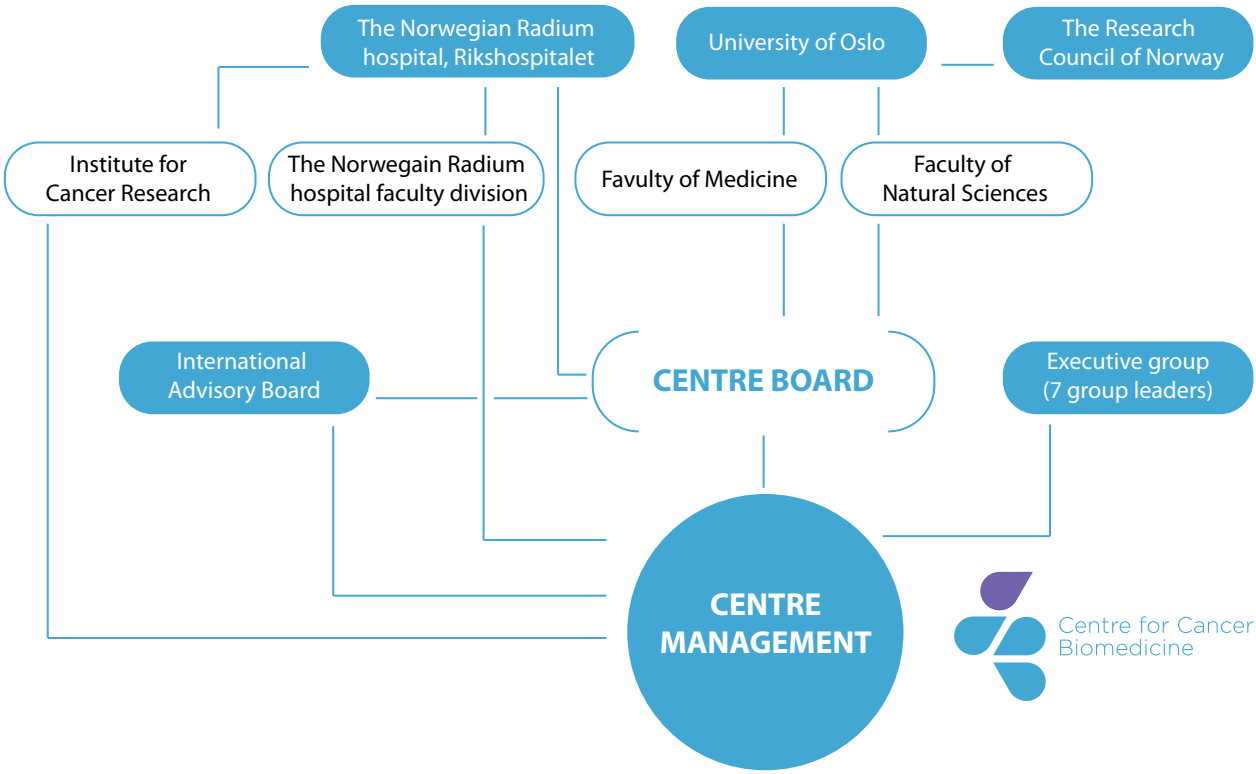
ISCO Congress 2008, Amsterdam, NL. Correlation Between Textural Analyses of Cell Nuclei and Gene-Copy Number Variations.

EMBO Protein Translocation meeting in Ste Maxime, France. Invited speaker.

Gordon Research Conferences (GRCs), Fibroblast Growth Factor in Development and Disease, Lucca 2008. Role of p38 MAPK in translocation of FGF-1 into cells. Invited speaker.

Centre of Excellence

Centre for Cancer Biomedicine (CCB) at the University of Oslo (UiO) and Rikshospitalet HF has since September 1st 2007 been a Centre of Excellence, appointed by the Research Council of Norway. The centre is located at the Radium hospital, Rikshospitalet HF.



Management

CCB is managed by Harald Stenmark (director), Ragnhild A. Lothe (vice director) and Jannikke Ludt (administrative coordinator). The director collaborates closely with the Executive Group, consisting of the additional six Principal Investigators, in scientific matters.

Board

The centre management reports to the centre board. The board was constituted in 2008, and the members are:

Prof. Sigbjørn Fossum (UiO), chair

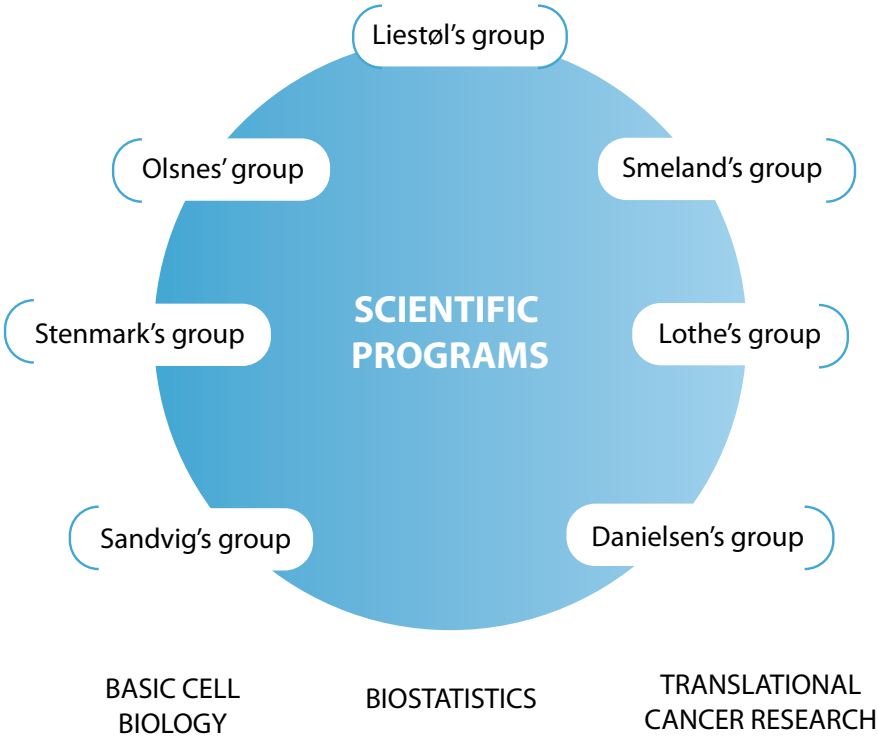
Prof. Anders Elverhøi (UiO)

Prof. Karl-Erik Giercksky (Rikshospitalet HF)

Prof. Erlend Smeland (Rikshospitalet HF)

7 Research groups

CCB is a constellation of 7 research groups cooperating to reach the aims of the centre, headed by the P.I.s: Harald Stenmark, Ragnhild A. Lothe, Sjur Olsnes, Kirsten Sandvig, Erlend Smeland, Håvard E. Danielsen and Knut Liestøl/Ole Crisitian Lingjærde.



Advisory board

The International Advisory Board gives scientific advice to Centre for Cancer Biomedicine.

Leader: Professor Manuel Sobrinho-Simões

Professor Lena Claesson-Welsh

Professor David J. Kerr

Professor Marja Jäättelä

Professor Olli Kallioniemi

Visiting professors

CCB has, in 2008, associated to professors to the centre:

Professor Bo van Deurs,
Planum Institute, University of Copenhagen

And

Professor Manuel Teixeira,
Portugese Oncology institute, Porto

FUNDING AND COSTS

Funding

The total funding of CCB was 106.3 mill NOK in 2008. This includes estimated infrastructure costs* (indirect costs, 28,7 mill NOK).

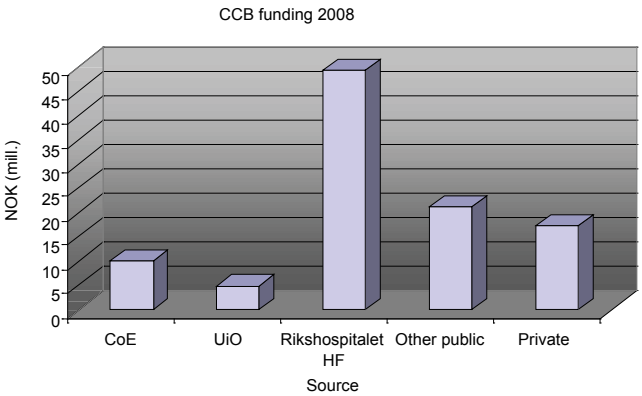
CoE funding is the SFF grant from RCN.

UiO funding includes: SFF funding (2 mill. NOK) and funding + infrastructure* for Liestøl's/Lingjærde's research activity.

Funding by Rikshospitalet HF includes salary, running costs and estimated costs of infrastructure* for all people physically working at the hospital (28.3 mill NOK).

Other public funding includes grants of 14 mill NOK from RCN and 3 mill NOK from Helse Sør-Øst.

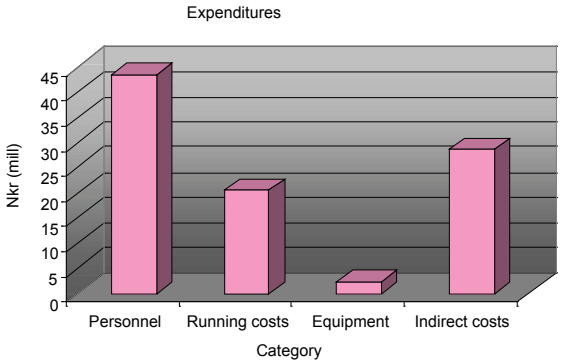
Private funding is mainly accounted for by The Norwegian Cancer Society (17.3 mill NOK).



Expenditures

The total costs for CCB were 94.1 mill NOK.

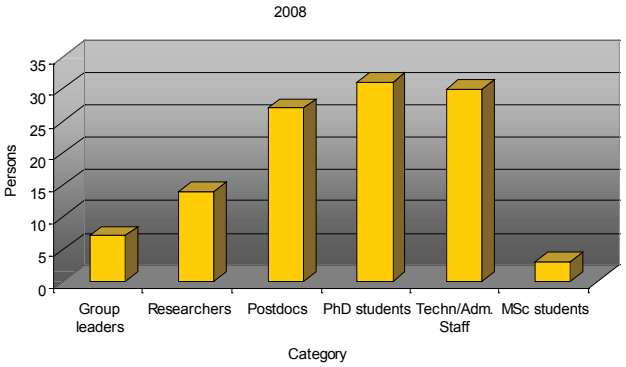
Personnel accounts for 43.5 mill NOK, running costs for 20.4 mill NOK and investment in equipment for 2.2 mill NOK. Indirect costs is the cost of infrastructure which is mainly accounted for by Rikshospitalet HF (28.3 mill NOK).



**Costs of infrastructure is estimated by formulas given by UiO (scientific personnel; 360 000 NOK/ year, technicians; 270 000 NOK/year and adm. staff; 80 000 NOK/year)*

PEOPLE

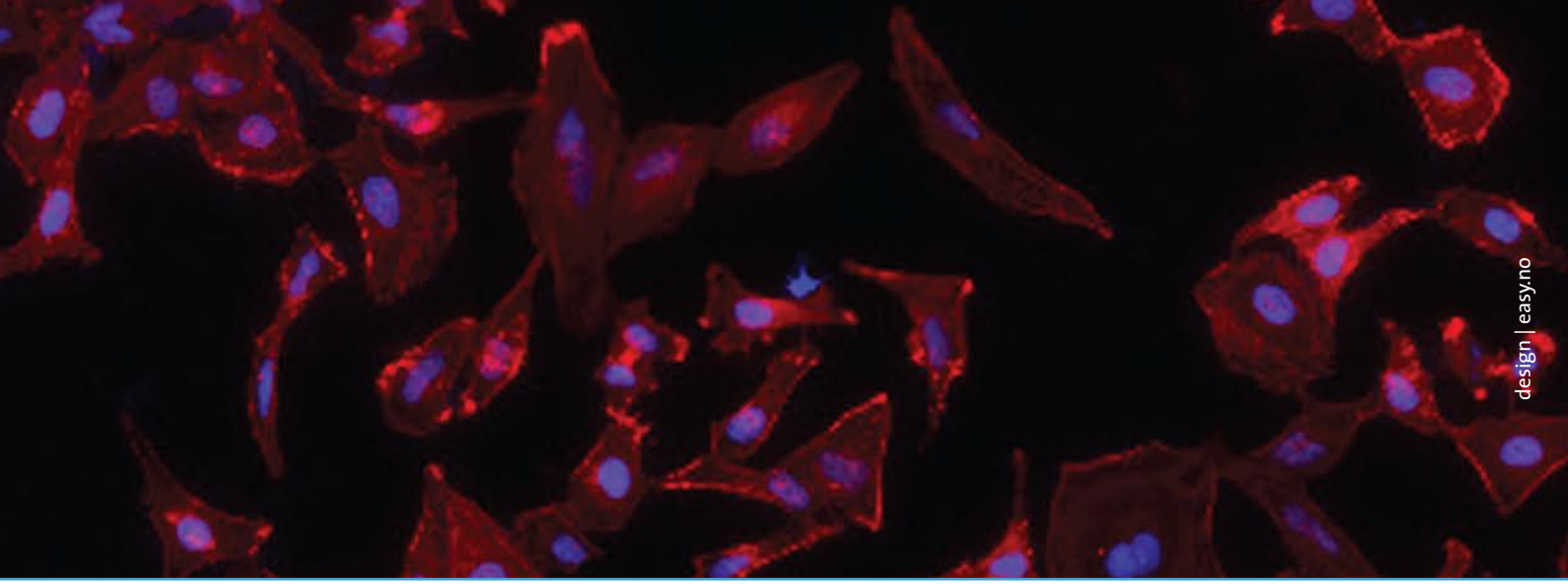
The centre is staffed by 109 persons. When categorized by position, the profile is 7 group leaders, 14 researchers (senior scientists), 27 post docs and 31 PhD students. Technical and Administrative staff are 30 persons, and 3 MSc students are affiliated to CCB.



Name	Position	Group	Nationality	Employer	Academic title
Abrahamsen, Hilde	Senior scientist	Stenmark	Norway	Rikshospitalet HF	PhD
Ahlquist, Terje	PhD student	Lothe	Norway	Rikshospitalet HF	MSc
Ahmed Mohammed Ali, Deeqa	Master student	Lothe	Norway		
Alagaratnam, Sharmini	Postdoc	Lothe	Malaysia	Rikshospitalet HF	PhD
Andersson, Sofia	Postdoc	Sandvig	Sweden	Rikshospitalet HF	PhD
Andresen, Kim	PhD student	Lothe	Norway	Rikshospitalet HF	MSc
Bakkebø, Maren	PhD student	Smeland	Norway	Rikshospitalet HF	MSc
Bakken, Anne Cathrine	Master student	Lothe	Norway		
Bassols, Chema	Computer specialist	Olsnes	Spain	Rikshospitalet HF	
Berg, Marianne	PhD student	Lothe	Norway	Rikshospitalet HF	MSc
Bergan, Jonas	PhD student	Sandvig	Norway	Rikshospitalet HF	MSc
Bergersen, Anne Gro	Technician	Olsnes	Norway	Rikshospitalet HF	
Brech, Andreas	Project Leader, Senior Scientist (FUGE)	Stenmark	Norway	Rikshospitalet HF	PhD
Brekke, Helge	PhD student	Lothe	Norway	Rikshospitalet HF	MSc
Bruun, Jarle	Research fellow	Lothe	Norway	Rikshospitalet HF	MSc
Christensen, Inger	Technician	Lothe	Norway	Rikshospitalet HF	
Christensen, Svein Kjetil Fiane	Laboratory Assistant	Olsnes	Norway	Rikshospitalet HF	
Danielsen, Håvard	Group leader, professor	Danielsen	Norway	Rikshospitalet HF	Dr. Philos
Danielsen, Stine Aske	Ph.D. student	Lothe	Norway	Rikshospitalet HF	MSc
Dyve, Anne Berit	Ph.D. student	Sandvig	Norway	Rikshospitalet HF	MSc
Edvardsen, Anne Lise	Technician	Lothe	Norway	Rikshospitalet HF	
Eide, Marianne Brodtkorb	PhD student	Smeland	Norway	UiO	MD
Eiken, Hans Geir	Senior Scientist	Lothe	Norway	Rikshospitalet HF	PhD
Eken, Marthe	Master student	Lothe	Norway	Masterstudent	
Eknæs, Mette	Technician	Lothe	Norway	Rikshospitalet HF	
Engedal, Kim Nikolai	Postdoc	Sandvig	Norway	Rikshospitalet HF	PhD
Engen, Anne	Technician	Olsnes	Norway	Rikshospitalet HF	
Farstad, Benedikte	Technician (CCB)	Stenmark	Norway	Rikshospitalet HF	
Filimonenko, Maria	Ph.D. student (University of Oslo)	Stenmark	Norway	UiO	MSc
Forfang, Lise	Technician	Smeland	Norway	Rikshospitalet HF	
Frerker, Nadine	Post doc	Sandvig	Germany	Rikshospitalet HF	PhD
Guha, Nirmalendu	Laboratory assistant	Olsnes	Norway	Rikshospitalet HF	
Guldsten, Hanne	Technician	Olsnes	Norway	Rikshospitalet HF	
Haglund, Kaisa	Postdoc (Human Frontier Science Programme)	Stenmark	Sweden	Human Frontier Science program	PhD

Name	Position	Group	Nationality	Employer	Academic title
Haugsten, Ellen M.	Ph.D. student	Olsnes	Norway	Rikshospitalet HF	MSc
Hektoen, Merete	Technician	Lothe	Norway	Rikshospitalet HF	MSc
Hilden, Vera Irene	Technician	Smeland	Norway	Rikshospitalet HF	MSc
Homeide Aagesen, Trude	PhD student	Lothe	Norway	Rikshospitalet HF	MSc
Honne, Hilde	Research fellow	Lothe	Norway	Rikshospitalet HF	
Huse, Kanutte	PhD student	Smeland	Norway	Rikshospitalet HF	MSc
Hveem, Tarjei Sveinsgjerd	Developer	Danielsen	Norway	Rikshospitalet HF	MSc
Isakson, Pauline	Ph.D. student (FUGE)	Stenmark	Sweden	Rikshospitalet HF	MSc
Iversen, Tore-Geir	Senior Scientist	Sandvig	Norway	Rikshospitalet HF	PhD
Jenstad, Monica	Avdelingsingeniør	Danielsen	Norway	Rikshospitalet HF	MSc
Jin, Yi-xin	Post doc	Olsnes	China	Rikshospitalet HF	PhD
Johannessen, May Elisabeth	Secretary	Olsnes	Norway	Rikshospitalet HF	
Karerwa, Jeanne D'Arc	Technician	Danielsen	Norway	Rikshospitalet HF	
Kildahl, Wanja	PhD student	Danielsen	Norway	Rikshospitalet HF	MSc
Kjenseth, Ane Hansen	PhD student	Lothe	Norway	Rikshospitalet HF	MSc
Kjæreng, Marna Lill	Technician	Danielsen	Norway	Rikshospitalet HF	
Klokk, Tove Irene	Post doc	Sandvig	Norway	Rikshospitalet HF	PhD
Knævelsrud, Helene	PhD student	Stenmark	Norway	UiO	MSc
Kolberg, Matthias	Researcher	Lothe	Norway	Rikshospitalet HF	PhD
Kraggerud, Sigrid M.	Post doc	Lothe	Norway	Rikshospitalet HF	Dr. Philos
Lauvrak, Silje Anett Ugland	Postdoc	Sandvig	Norway	Rikshospitalet HF	PhD
Leithe, Edward	Post doc	Lothe	Norway	Rikshospitalet HF	PhD
Liestøl, Knut	Group leader, professor	Liestøl	Norway	UiO	Dr. philos
Lind, Guro Elisabeth	Post doc	Lothe	Norway	Rikshospitalet HF	Dr. philos
Lindmo, Karine	Postdoc	Stenmark	Norway	Rikshospitalet HF	PhD
Lindvall, Jessica	Post doc	Liestøl	Sweden	UiO	PhD
Lingjærde, Ole Christian	Associate Professor	Liestøl	Norway	UiO	PhD
Lobert, Viola	Ph.D. student	Stenmark	France	Rikshospitalet HF	
Lothe, Ragnhild A.	Group leader, professor	Lothe	Norway	Rikshospitalet HF	Dr. philos
Ludt, Jannikke	Administrative coordinator, Research Fellow	Olsnes	Norway	Rikshospitalet HF/UiO	PhD
Løvig, Tone	Technician	Lothe	Norway	Rikshospitalet HF	PhD
Malecki, Jedrzej	Guest Senior Scientist	Olsnes	Poland	Rikshospitalet HF	PhD
Malerød, Lene	Postdoc (FUGE)	Stenmark	Norway	Rikshospitalet HF	PhD
Merok, Marianne Aarstad	PhD student	Lothe	Norway	Aker / RH	MD
Mikalsen, Svein-Ole	Scientist	Lothe	Norway	Rikshospitalet HF	Dr. philos
Mjøen, Linda Uv	Economics Consultant	Lothe	Norway	Rikshospitalet HF	
Myklebust, June Helen	Post doc	Smeland	Norway	Rikshospitalet HF	PhD
Myrann, Anne Grethe	Technician	Sandvig	Norway	Rikshospitalet HF	
Nesheim, John Arne	Head of developement	Danielsen	Norway	Rikshospitalet HF	
Nezis, Ioannis	Postdoc (FUGE)	Stenmark	Greece	Rikshospitalet HF	PhD
Nielsen, Birgitte	Post doc	Danielsen	Norway	Rikshospitalet HF	PhD
Nilsgård, Siri	Laboratory assistant	Olsnes	Norway	Rikshospitalet HF	
Nybøen, Åsmund	Head of lab	Danielsen	Norway	Rikshospitalet HF	
Oksvold, Morten	Post doc	Smeland	Norway	Rikshospitalet HF	PhD
Olsnes, Sjur	Group leader, professor	Olsnes	Norway	Rikshospitalet HF	MD, PhD
Oppelt, Angela	PhD student	Olsnes	Germany	Rikshospitalet HF	MSc
Pedersen, Anne-Mari Gjestvang	Technician	Sandvig	Norway	Rikshospitalet HF	
Pedersen, Nina Marie	Postdoc (Helse Sør)	Stenmark	Norway	Rikshospitalet HF	PhD
Poulton, John	Postdoc	Stenmark	USA	Rikshospitalet HF	PhD
Pretorius, Maria	Administrative head	Danielsen	Norway	Rikshospitalet HF	MSc

Name	Position	Group	Nationality	Employer	Academic title
Pust, Sascha	Postdoc	Sandvig	Germany	Rikshospitalet HF	PhD
Raiborg, Camilla	Postdoc (the Norwegian Cancer Society)	Stenmark	Norway	Rikshospitalet HF	PhD
Rasmussen, Ida Løver	Laboratory Assistant	Olsnes	Norway	Rikshospitalet HF	
Rivedal, Edgar	Senior scientist	Lothe	Norway	Rikshospitalet HF	Dr. philos
Rodahl, Lina W.	Ph.D. student (EMBIO)	Stenmark	Norway	Rikshospitalet HF	PhD
Roxrud, Ingrid	Ph.D. student (the Research Council of Norway)	Stenmark	Norway	Rikshospitalet HF	MSc
Rusten, Tor Erik	Postdoc (FUGE)	Stenmark	Norway	Rikshospitalet HF	PhD
Rødland, Einar	Post doc	Liestøl	Norway	NR	PhD
Rønning, Eva	Head technician	Stenmark	Norway	Rikshospitalet HF	
Raa, Hilde	Ph.D. student	Sandvig	Norway	Rikshospitalet HF	MSc
Sagona, Antonia	Ph.D. student (EU)	Stenmark	Norway	Rikshospitalet HF	MSc
Sandvig, Kirsten	Group leader, professor	Sandvig	Norway	Rikshospitalet HF	Dr. Philos
Sem-Jacobsen, Catherine	PhD student (the Norwegian Cancer Society)	Stenmark	Norway	Rikshospitalet HF	MSc
Simonsen, Anne	Project Leader, Senior Scientist (the Norwegian Cancer Society)	Stenmark	Norway	Rikshospitalet HF	PhD
Sirnes, Solveig	PhD student	Lothe	Norway	Rikshospitalet HF	MSc
Skiple Skjerpen, Camilla	Post doc	Olsnes	Norway	Rikshospitalet HF	Dr. Philos
Skotheim, Rolf I.	Project leader, senior scientist	Lothe	Norway	Rikshospitalet HF	Dr. philos
Skånland, Sigrid	Ph.D. student	Sandvig	Norway	Rikshospitalet HF	MSc
Slåtta, Carina	Laboratory Assistant	Olsnes	Norway	Rikshospitalet HF	
Smeland, Erlend Bremertun	Group leader, professor	Smeland	Norway	Rikshospitalet HF	MD, PhD
Smestad, Marianne	Technician	Stenmark	Norway	Rikshospitalet HF	
Stenmark, Harald	Group leader, professor	Stenmark	Norway	Rikshospitalet HF/UiO	Dr. Philos
Stordal Bjørklund, Sunniva Maria	Ph.D. student	Olsnes	Norway	Rikshospitalet HF	MSc
Stuffers, Susanne	PhD student (FUGE)	Stenmark	Norway	Rikshospitalet HF	MSc
Sundet, Kristine Ingrid	Master student	Sandvig	Norway		
Sveen, Anita	PhD student	Lothe	Norway	Rikshospitalet HF	MSc
Sørensen, Vigdis	Post doc	Olsnes	Norway	Rikshospitalet HF	PhD
Tcatchoff, Lionel	Post doc	Sandvig	Norway	Rikshospitalet HF	PhD
Tengs, Torstein	Post doc	Danielsen	Norway	Rikshospitalet HF	PhD
Thomassen, Gard O. Sundby	PhD student	Lothe	Norway	Rikshospitalet HF	MSc
Thoresen, Sigrid Bratlie	PhD student	Stenmark	Norway	Rikshospitalet HF	MSc
Tolonen Egeberg, Nina Johanna	Technician (FUGE)	Stenmark	Finland	Rikshospitalet HF	
Torgersen, Maria Lyngaas	Postdoc	Sandvig	Norway	Rikshospitalet HF	PhD
Torres, Dafne Lemus	Ph.D. student	Stenmark	Mexico	Rikshospitalet HF	MSc
Utskarpen, Audrun	Ph.D. student	Sandvig	Norway	Rikshospitalet HF	MSc
Wesche, Jørgen	Project Leader, Senior Scientist (the Norwegian Cancer Society)	Olsnes	Norway	Rikshospitalet HF	Dr. Philos
Wiedlocha, Antoni	Project Leader, Senior Scientist	Olsnes	Norway	Rikshospitalet HF	Dr. Philos
Wæhre, Håkon	Senior scientist	Danielsen	Norway	Rikshospitalet HF	MD, PhD
Yadollahi, Mandana	Laboratory Assistant	Olsnes	Iran	Rikshospitalet HF	
Yohannes, Zeremariam	Technician	Lothe	Norway	Rikshospitalet HF	
Zakrzewska, Malgorzata	Post doc	Olsnes	Norway	Rikshospitalet HF	PhD
Zhen, Yan	Ph.D. student	Olsnes	Norway	Rikshospitalet HF	MSc



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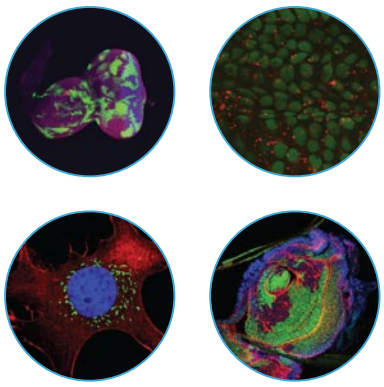

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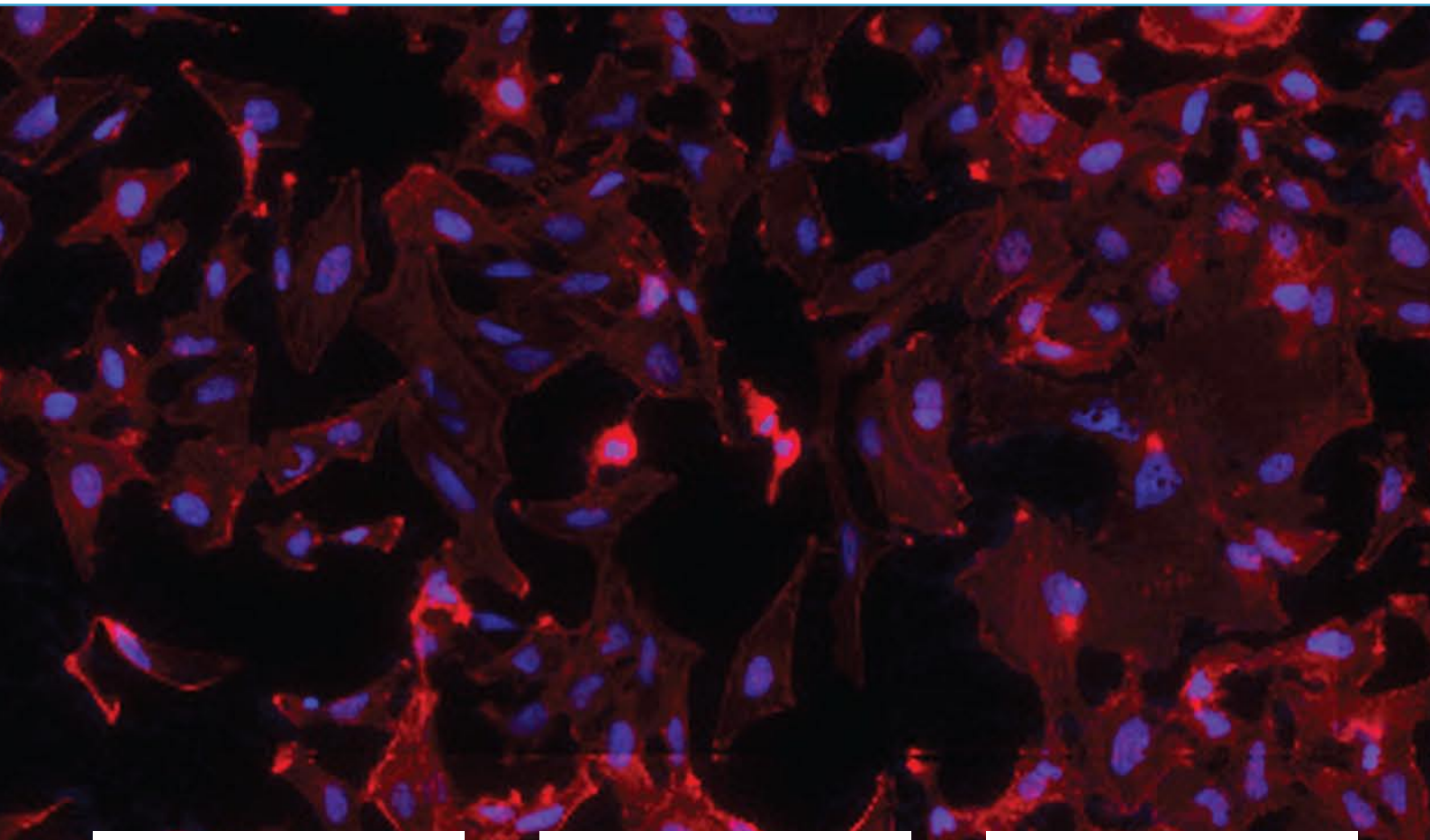

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