



Newsletter

CREATE Health - a Strategic Centre for Clinical Cancer Research at Lund University February-2010

CREATE Health

CREATE Health is a Strategic Centre for Clinical Cancer research located at the Biomedical Centre in Lund. The vision of CREATE Health is to use an integrative approach to develop novel diagnostics and therapeutics, based on identified markers and molecular signatures and to create a substantial social impact for the patient, through direct application of research for selection of an optimal, individually-based, cancer treatment. "After four years of successful research we have come very close and in some cases even fulfilled this vision, says professor Carl Borrebaeck, Program Director of CREATE Health.

New Technology for Diagnosis of Hereditary Breast Cancer

Next generation sequencing technology, using the Illumina Genome Analyzer Iix system with Agilent SureSelect genome fragment capture protocols, will in 2010 be introduced into a clinical setting for mutations screening in hereditary breast cancer. Roughly 10 % of all breast cancers occur in women with a strong familial history of breast and/or ovarian cancer, a major part of which can be explained by germline mutations in the breast cancer susceptibility genes BRCA1 or BRCA2 that confer a high life-time risk of disease development. **Therese Törngren** and **Anders Kvist**, Dept of Oncology in Lund, working together with **Åke Borg** at CREATE Health, have developed sequencing protocols enabling faster screening and more precise detection of BRCA1 and BRCA2 mutations in blood or tissue samples. Lund is providing a nation-wide health care service for BRCA mutation screening, including more than 500 families annually. New technology is urged not only by increasing awareness and counseling at oncogenetic clinics, but also by demands of screening at primary breast cancer diagnosis due to the development of new therapy targeting the DNA deficiency characteristics of BRCA-associated tumors.

Diagnosis of pancreatic cancer patients using a blood sample

Serum, representing the most common clinical specimen, contains thousands of different proteins and consequently withholds a wealth of information. Furthermore, since the immune system is one of the earliest responders to disease, researches at CREATE Health have tried to decipher this information by monitoring changes in the expression patterns of immuno-regulatory proteins. This approach is based on so called antibody microarrays, where hundreds or thousand of antibodies are spotted on to a small plastic chip, no larger than a finger nail, which is then subjected to a serum sample. The different protein expression patterns, formed by molecules derived from the tumor secretome, as well as from the systemic response against the tumor, are interpreted by the bioinformatics experts at the center. In a recent collaborative study with Karolinska Institute, scientists at CREATE Health found a serum biomarker signature that was able to discriminate between proteomes derived from healthy individuals and pancreatic cancer patients. Recently, this study was extended, and it was further demonstrated that the pancreatic cancer proteome displayed different biomarker patterns as compared to those of acute, chronic and autoimmune pancreatitis, further validating the initial discovery. These are the first pancreatic cancer studies, in which a small biomarker signature has

been pre-validated in several independent test sets of patients, demonstrating the potential and clinical applicability of such an approach.

Seeing early stage tumors in patients

Common for all cancers the rule is – the earlier the detection, the better the chances of a complete cure. But how do we find a tumour today? The current approach measures changes of certain hormones or diagnostic markers in the blood. However this means the tumour cells must leak out these proteins and this usually occurs after the early stages. A promising way to detect tumours in the body is to label them with fluorescent dyes. We have recently developed a method to identify the proteins present on the surface of tumour and normal cells. This will allow to construct fluorescent or radioactive antibodies which can be injected into the patient and used to localise the tumour. It may also be used for treatment, by coupling toxins to the antibody which are then taken only to tumour cells where they are released and selectively kill the tumour cell.

Why CREATE Health?

Lars-Erik Arvidsson, Vice President AstraZeneca R&D Lund. CREATE Health is a truly translational centre embracing the scientific skills, technologies and collaborative culture needed to develop diagnostics and therapeutic approaches to deliver the right cancer treatment, for the right patient at the right dose. I am convinced that this will lead to hallmarks of future cancer diagnosis and treatment.



Per Eriksson, Vice Chancellor Lund University.

Lund University supports strong research and innovation milieu, i.e. excellent research groups that also address innovation as an important mission. CREATE Health is one of the best examples, and has an excellent name that communicates its purpose of research and innovation.



The SCAN-B project

The South Sweden Cancerome Analysis Network – Breast initiative (SCAN-B) will implement routine gene expression and genomic tumor profiling in the clinical setting of breast cancer, eventually including all new breast cancer cases in southern Sweden. SCAN-B will provide novel clinical tools for a more refined, individualized, and optimized medical decision-making process, including diagnostic tests for tumor classification, prognosis and treatment response. SCAN-B aims to build knowledge and confidence in the genomics technology and facilitate clinical trials and interactions with the pharma industry. This will be accomplished by a network of scientist at CREATE Health, SCIBLU Genomics and Dept of Oncology in Lund, together with a panel of physicians and the cancer registry in South Sweden. SCAN-B has support from the South Sweden Breast Cancer Group and funding was also recently secured by a grant from the Berta Kamprad Foundation to **Åke Borg**.

Lund University BioImaging Center

CREATE Health has established a collaboration with the recently inaugurated Lund University BioImaging Center (LBIC). The centre is equipped for front-end bioimaging research in the fields of MRI and PET for experimental and human use. “The possibility to use the advanced PET and MRI techniques, using our newly defined targets for diagnostics and therapy is a tremendous opportunity and adds a novel translational aspect to our research”, says **Carl Borrebaeck**, program director of CREATE Health”. **Freddy Ståhlberg**, director of LBIC, adds that “the interaction with a well established translational center as CREATE Health puts us in a unique position to deliver improved health care”



Prognostic prediction of HER2 positive breast cancer

HER2 gene amplification and over expression defines a clinically challenging subgroup of breast cancer with variable prognosis and response to therapy, including targeted drugs based on antibodies or kinase inhibitors. **Johan Staaf**, **Markus Ringnér** and **Åke Borg** at CREATE Health, used genomics to describe three biological subtypes of HER2+ breast cancer, and developed a gene predictor that classifies breast cancer patients with poor or better disease-free and overall survival. The study is published in the J. Clin. Oncol. and will be followed by studies including patients treated with adjuvant trastuzumab (Herceptin®) and chemotherapies. Herceptin is regarded as a success story in targeted cancer treatment, providing hope and cure for patients with the aggressive HER2+ disease, but many cases were found to have an intrinsic or acquired resistance against the drug. New means of disease stratification will enable more refined selection of patients for correct treatment.

Launching a new Proteomics Software Environment

CREATE Health is now launching the Proteios Software Environment (ProSE) that is built around a Web-based local data repository for proteomics experiments. The application features sample tracking, project sharing between multiple users, and automated data merging and analysis. ProSE has built-in support for several quantitative proteomics workflows, and integrates

searching in several search engines, automated combination of the search results with predetermined false discovery rates, annotation of proteins and submission of results to public repositories. ProSE also provides a programming interface to enable local extensions, as well as database access using Web services. ProSE provides an analysis platform for proteomics research and is targeted for multiuser projects with needs to share data, sample tracking, and analysis result. ProSE is open source software available at <http://www.proteios.org>. The proteomics field will greatly benefit from this user-friendly analysis and data management platform in which method developers can make their analysis tools available for the community. Read more in Jari Häkkinen, Gregory Vincic, Olle Månsson, Kristofer Wårell, and Fredrik Levander. Journal of Proteome Research 2009, 8, 3037–3043 3037 at <http://dx.doi.org/10.1021/pr900189c>

Pharmacogenetics

Constitutional variants of ADME (absorption, distribution, metabolism and elimination) related genes have been associated with pharmacokinetic properties of numerous drugs and may have clinical significance in predicting drug response and side effects. For instance, tamoxifen is a commonly used drug in therapy of breast cancer to prevent recurrence of estrogen receptor-positive disease, and the cytochrome P450 metabolic enzyme CYP2D6 has a major role in tamoxifen metabolism. The CYP2D6 gene is highly polymorphic with variants associated with enhanced, reduced or absent enzyme function, resulting in unexpected plasma levels of active tamoxifen metabolites, which has an impact on tamoxifen treatment efficacy. **Helena Jernström** in Lund, working with **Carsten Rose** and **Åke Borg** at CREATE Health, will initiate a study of CYP2D6 and of an additional ~2000 genetic variants in breast cancer. The project will utilize the SCIBLU Genomics Affymetrix unit expertise.

CREATE Health researcher expert in Cancéropôle

CREATE Health's **Carl Borrebaeck** has been appointed cancer expert in the French Cancéropôle Grand Sud-Ouest. It is one of the seven Cancéropôles of France, created in the context of the French government “Cancer Plan” to reinforce academic research in oncology and accelerate the rate of research transfer from bench to bedside. It gathers research teams through a network of research institutions and learning hospitals dedicated in order to federate oncology research in the South-West of France (Bordeaux, Nîmes-Montpellier, Toulouse and Limoges)

New employees



Helena Persson Ph.D. has joined the CREATE Health team after a year as post doc at University of Toronto, Canada. She is now building up a platform unit around high-throughput generation of recombinant antibodies, which is a corner stone of today's translational research. The expertise behind such a unit is a long sought after skill at CREATE Health. Access to high quality reagents is crucial in several of the cancer projects within the center, such as antibody microarray studies of breast cancer and antibody based therapy of cancer stem cells, as well as for technology development projects, such as acoustophoresis of phages and cells.