CREATE Health is a strategic centre for translational research focussing on the early diagnosis and prognosis of cancer. **Professor Carl Borrebaeck** explains how the project's research could have a substantial impact on diagnosis and treatment of the disease in the next five to 10 years

Cancer: how biotechnology is benefitting the patient

Despite recent progression in detection and therapy, cancer has remained a major health care problem. Every year over 3 mn people in Europe are diagnosed with cancer. More than 50 per cent of these will die as a result of the disease, thus making cancer the second main cause of death, after circulatory diseases. Treatment success is mainly limited due to difficulties in diagnosis in combination with the often late presentation of cancer.

Cancer is a disease caused by alterations of the genome as well as the proteome. These changes allow the cancer cell to evade normal cellular control mechanisms and to start growing uncontrolled. The major goal of cancer research is to identify these molecular defects and use this knowledge to develop effective diagnostic. treatment and prevention regimens. More specifically, researchers are looking for predictive molecular signatures or so called biomarkers. Biomarkers are molecules whose presence indicates various disease states. For example, a biomarker may be a protein whose expression levels correlate with the risk or progression of cancer. Once a proposed biomarker has been confirmed, it can be used to predict the disease risk, diagnose the disease, or even be used as an indicator of which treatment to use.

In 2005, the Center for Clinical Research using Emerging Advanced TEchnologies for Health (CREATE Health), funded by the Swedish Foundation for Strategic Research, was established to address these challenges. The centre is located at the Biomedical Centre at Lund University, Sweden. The centre has brought together, both physically and

"Our goal is to improve the early differential diagnosis of cancer to improve the selection of an optimal, individuallybased, cancer treatment. Our vision is that our research will have a substantial impact on how cancer is diagnosed and treated within the next 5-10 years."

Despite being only in its infancy, a few

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logistically, researchers from diverse fields, such as bioinformatics, nanotechnology, proteomics, transcriptomics, cancer genetics and tumour cell biology with clinical oncologists from Lund University Hospital, in order to create a unique integrative environment to solve complex clinical problems.

Carl Borrebaeck, CREATE Health's programme director, says: "By using the latest equipment within the 'omics area and in-house developed technology platforms we are focussing on defining gene and protein signatures that can differentiate between different cancer types and stages at an early phase.



Protein signitatures can be used to diagnose the presence of disease

projects within CREATE Health have already proven to be successful. For instance, genetic profiling of over 600 breast tumours has been completed with a matching proteomic analysis of over 400 of these. Breast cancer is the most common female malignancy in the Western world and the incidence has steadily increased over the past decades. It is a heterogeneous disease with respect to genetics, histology and clinical appearance. For example, 70 per cent of all breast cancer patients undergoing post-operative irradiation do not benefit from this treatment, and only 10 per cent of breast cancer patients receiving adjuvant chemotherapy benefit from these regimens, the remainder being either cured by surgery alone or relapse despite additional systemic treatment. Better predictive factors are thus needed for deciding optimal type of chemotherapy and response to drugs with specific cellular targets. CREATE Health has recently identified novel gene and protein profiles of breast cancer that are more effective than previous biomarkers in stratifying breast tumours into clinically relevant subtypes



Protein indication: Red for up-regulated, green for down-regulation. Black is no change

that have the potential to enable a more targeted treatment of the disease.

Another example is mantle cell lymphoma (MCL), a cancer form of the lymphatic system with poor survival, where correct diagnosis is crucial, e.g. to separate it from other types of lymphomas that require less harsh treatment strategies. In a combined genomic and proteomic approach researchers within CREATE Health have identified a range of novel MCL diagnostic and potentially therapeutic markers. In a first step, more than 12,000 genes of the human genome were analysed and approximately 100 gene-products differing between normal and MCL tissue were selected. In a second step, antibodies were used to analyse the expression patterns of the proteins corresponding to the selected genes in different types of malignant and normal tissue to evaluate the clinical significance of these gene products. Some proteins showed great promise in that they differentiated between both normal and malignant tissue as well as between different types of lymphomas.

One of these markers, Sox11, has further been evaluated and has been found to have an ability to completely discriminate MCL from all other lymphomas. Sox11 is not only complementing the current clinical markers that are used to diagnose MCL, but it also targets MCL-cases that were markers previously and have been lacking, this will provide a better indicator of which treatment to use. It will also likely replace the need for more time-consuming genetic analyses.

"The advent of biomarker pattern profiling is emerging as an extremely powerful tool in the fields of cancer diagnosis and drug discovery," says Carl Borrebaeck, "and we have already demonstrated the predictive power of multiplexed analysis in cancer research as the way forward".

Not only will these kinds of studies have a direct social impact for the patient, but they will also have major implications on healthcare costs. Early diagnosis of cancer has an enormous cost-saving potential, especially given the age profile of the population. The results generated are also of interest for the pharmaceutical industry. There is an upsurge of novel cancer drugs emerging for clinical trial. Efficient and successful utilisation of these will require more 'personalised medicine', i.e. customised treatment based on the genetic or proteomic profile from each individual patient. Utilisation of biomarkers as a diagnostic, prognostic and therapeutic tool is the future of medicine, one which CREATE Health is already contributing to. As Carl Borrebaeck concludes: "Today there is a serious and widening gap between basic and clinical research that must be addressed by targeting significant efforts and resources to translational research. The major challenge is to harness the enormous potential of biotechnology for the direct benefit of the patient."

The vision of CREATE Health is to develop new techniques and instruments for medical applications to be used to solve complex clinical cancer problems. More specifically, these tools will be used to achieve the following specific goals:

- For early diagnosis and disease evaluation
- For drug response prediction and patient stratification
- For identification and evaluation of drug targets

At a glance

The translation of basic discoveries to the clinic requires multidisciplinary collaborations involving basic researchers, clinicians, pathologists, patients, and regulatory bodies. All of which are represented within CREATE Health. More specifically, CREATE Health consists of the following partners:

Partners

Carl Borrebaeck, Proteomics and genomics Åke Borg, Genomics Peter James, Proteomics Carsten Peterson, Bioinformatics Thomas Laurell, Nanotechnology Sven Påhlman, Tumor Biology Carsten Rose, Clinical Oncology and Clinical Trial Unit

For further information please visit www.createhealth.lth.se

Professor Carl Borrebaeck



Director of CREATE HEALTH

Professor Borrebaeck graduated from Lund University in Sweden with a D. Sc. in 1979. Since 1989 he has been Professor and Chairman at the Department of Immunotechnology, Lund University. His research interests include antibody engineering and immunotherapy



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