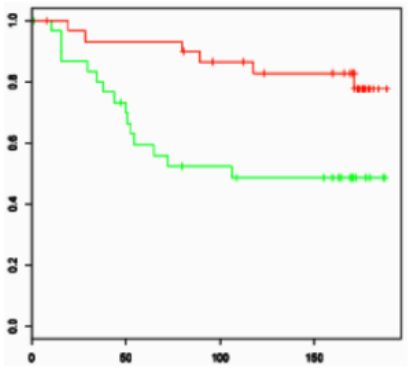
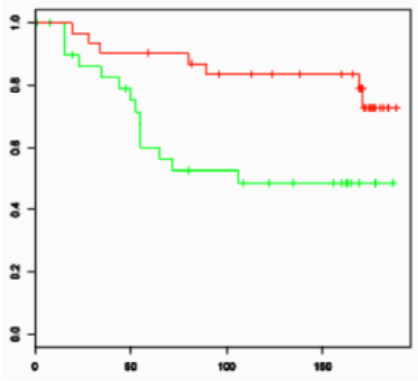
Sugars in circulating blood reflect breast cancer biology

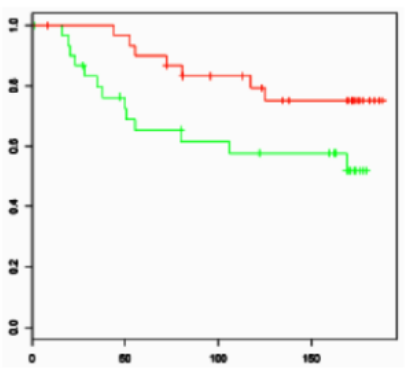
In our studies, consisting of measurements and analyses, we have shown that the sugar composition in the serum of breast cancer patients reflects the biology of their breast tumours. Patients with different kinds of breast tumours have different compositions of sugar structures in their blood. This is not linked to sugar consumption, but is likely to be a result of biological processes in the breast tumour combined with the body's response to the cancer. Our findings illustrate that cancer in one part of the body leads to complex alterations in different types of molecules in other parts of the body. Many of these molecular systems (including sugar structures) have been poorly characterised and improved knowledge may help us identify biological mechanisms that may be used for new diagnostics or treatment measures.



GP1, p=0.005, FDR=0.010



GP3, p=0.010, FDR=0.011



GP22, p=0.011, FDR=0.046

Three glycan structures (GP1, GP3 and GP22) have high abundance in the serum of patients with good prognosis and low abundance in the serum of patients with poor prognosis.

Cancer is a genetic disease as it is caused by alterations in the genomes of cells that transform the cell from a normal cell to a cancer cell. These alterations affect cell function by changing proteins and other functional molecules. Proteins are produced from DNA (genes) through RNA (gene transcripts) and are the molecules that drive activities in the cell. Cancer cells need increased proliferation, reduced cell death, capability to produce new blood vessels, avoid the immune system and spread to other organs.

Much cancer research work has been invested in identifying alteration at the gene (DNA) or transcript (RNA) level. Less has been done to characterize the protein profiles of cancer cells. This is much because the technology for these analyses have been lacking. Technology development has been a main goal of our project.

Protein analysis is even further complicated by the fact that one protein may have different

functions according to further molecular alterations of the protein that occur after it has been produced (synthesised). Such alterations are called post-translational modifications. One type of post-translational modification is glycosylation – the addition of sugars to proteins. Tumour cells shed some of their proteins and attached sugars (glycans) into the circulation. These proteins and sugars can be detected in the blood and reflect biological processes in the tumour and elsewhere in the body - such as infections or the body's systemic response to the cancer.

Despite the fact that molecules from the entire body find their way into the blood circulation, we found significant differences between the sugar (glycan) composition of the blood of healthy women compared with breast cancer patients and between breast cancer patients with different types of breast cancer. Specifically, we found associations between certain mRNA-transcripts in the tumour and glycan structures in the serum and we identified certain glycans associated with survival. These results can be used to explore which protein modifications are active in cancer and thereby point at therapies directed toward such alterations. The characterization of glycan profiles in accessible tissue such as blood also holds great potential to lead to cancer biomarkers that can help in early detection.

Publication

Serum N-glycan analysis in breast cancer patients - Relation to tumour biology and clinical outcome.
Haakensen VD, Steinfeld I, Saldova R, Shehni A, Kifer I, Naume B, Rudd PM, Børresen-Dale AL, Yakhini Z
Mol Oncol. 2015 Aug 19