DOCTORAL CANDIDATE:

DEGREE:	Philosophiae Doctor
FACULTY:	Faculty of Mathematics and Natural Sciences
DEPARTMENT:	Department of Biosciences
AREA OF EXPERTISE:	Molecular biology
SUPERVISORS:	Doctor Ian G. Mills, Professor, MD, Olli Kallioniemi Professor Odd S. Gabrielsen
DATE OF DISPUTATION:	9th of May 2014
DISSERTATION TITLE:	Glycosylation in Prostate Cancer

Harri Itkonen har i sitt doktorgradsarbeid brukt prostatakreft-genuttrykkssprofiler som et utgangspunkt og har identifisert glykosylering som en viktig faktor for å øke kreftcellenes vekst og stresstoleranse.

Harri Itkonen's PhD work used prostate cancer gene expression profiles as a starting point and identified glycosylation as an important factor to enhance cancer cell proliferation and stress resistance.

Prostate cancer is the most frequently diagnosed cancer in men in the USA and Europe. Cancer cells acquire an ability to proliferate continuously and this is accompanied by alterations in the gene expression program. Cancer cells consume glucose in an energy-inefficient way that enables the build-up of carbon for fast dividing cells. In this work, Itkonen and co-workers used clinical gene expression data and identified the hexosamine biosynthetic pathway (HBP) as a process that is frequently up-regulated in clinical prostate cancer. This pathway supports a single enzyme (O-GlcNAc transferase, OGT) which modifies target proteins via single sugar modification. OGT was shown to be over-expressed in prostate cancer patients with poor prognosis. Inhibition of the OGT activity in cancer cell lines decreased the ability to proliferate, and Itkonen identified a well-described oncogene, MYC, to be lost in cancer cells if OGT activity was inhibited. In addition, Itkonen and co-workers showed that increased expression of the HBP enzymes is accompanied with increased end-product of the pathway, required for the production of secretory proteins. If

HBP activity is inhibited, cancer cells are sensitized to the drugs interfering with processing of secretory proteins, which was demonstrated by multiple markers including clinically used prostate cancer biomarker, prostate specific antigen.

In conclusion, Itkonen's Thesis identified a metabolic process that is hyperactivated in the cancer cells. This work identified new potential drug targets and serves as a starting point for a more detailed analysis of HBP activity and glycosylation in cancer cells.