Integrating Proteomics and Genomics for the Prediction of Cardiometabolic Disease

Background:
Diabetes increases the risk of heart failure (HF) and cardiovascular disease (CVD) independent of other traditional risk factors and ischemia. Although it is clear that patients with diabetes are at increased risk of CVD and HF, the causal mechanisms remain elusive and their identification poses a great challenge in order to provide new targets for treatment.

Methods:
Study populations
The Malmö Diet and Cancer study is a population based study that enrolled 28,449 individuals in 1991-1996. We used Mendelian randomization to examine if cystatin-C was causally associated with incident diabetes and the metabolic syndrome.

MPP Re-examination Study (MPP-RES) was conducted during 2002-2006. In a sample of 1,792 participants randomly selected based on glucometabolic status; echocardiography was performed. We used a novel multiplex proteomic proximity extension assay to examine associations with incident diabetes, CVD, mortality and echocardiographic parameters.

The HARVEST trial (HeART and brain failure InVESTigation) started in Malmoe 2014 and one of its main purposes is to explore existing and novel correlations between HF and biomarkers, echocardiographic parameters, cardiovascular magnetic resonance imaging, cognitive tests, head-up tilttest with cerebral oximetry. Analysis of biomarkers’ association with mortality and re-hospitalisation for HF.

Preliminary results


Article 4) Cardiovascular Biomarkers Predict Post-discharge Rehospitalization Risk and Mortality Among Swedish Heart Failure Patients. Data collection complete and statistical analysis ongoing.

Significance:
The core of this research is to bridge the surprisingly under-explored gap between the “omics” of epidemiology and biological and clinical function. Thus, a major component of this study
plan is to enhance the understanding of the causes of progressive diabetes and CVD and we invest large efforts in proteomics. The pandemic of cardiometabolic disease is perhaps the greatest challenge our healthcare system faces and constantly improving our prediction, prevention and basic understanding are key for us to be successful in facing this challenge.

**Publications:** Article 1) *Cystatin C and Risk of Diabetes and the Metabolic Syndrome - Biomarker and Genotype Association Analyses.* Published in PLOS One May 2016.