"Quantitative serum metabolomics in large-scale epidemiology – A cost-effective base towards systems medicine"

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Date: October 27, 2015 (Tuesday)

Time: 2:30 p.m. – 3:30 p.m.

Venue: Alumni Chamber, 7/F, William M.W. Mong Block

Faculty of Medicine Building 21 Sassoon Road, Hong Kong

Abstract:

Metabolomics is becoming common in epidemiology due to recent developments in quantitative profiling technologies and appealing results from their applications for understanding health and disease. Our team has developed an automated high-throughput serum nuclear magnetic resonance (NMR) metabolomics platform that provides quantitative molecular data on 14 lipoprotein subclasses, their lipid concentrations and composition, apolipoprotein A-I and B, multiple cholesterol and triglyceride measures, albumin, various fatty acids as well as on numerous low-molecular-weight metabolites, including amino acids, glycolysis related measures and ketone bodies¹. The molar concentrations of these measures are obtained from a single sample with costs comparable to standard lipid measurements. The sample volume can be as low as 100 µl. We have already utilised this platform to analyse around 350,000 samples from >100 clinical and epidemiological studies and biobanks. The molecular data have been used to study type 1 diabetes, type 2 diabetes and cardiovascular disease aetiology as well as to characterize the molecular reflections of the metabolic syndrome, long-term physical activity, diet and lipoprotein metabolism. The results have revealed new biomarkers for early atherosclerosis, type 2 diabetes, diabetic nephropathy, cardiovascular disease and all-cause mortality. We have also combined genomics and metabolomics in diverse studies. We envision that quantitative high-throughput NMR metabolomics will be incorporated as a routine in

¹ Soininen P, Kangas AJ, Würtz P, Suna T, Ala-Korpela M. Quantitative serum nuclear magnetic resonance metabolomics in cardiovascular epidemiology and genetics. Circ Cardiovasc Genet. 2015;8:192-206.

large epidemiological and genetic studies as well as in biobanks; this would make perfect sense both from the biological research and cost point of view – the standard output of around 250 molecular measures would vastly extend the relevance of the sample collections and make many separate clinical chemistry assays redundant. Various systems epidemiology applications incorporating extensive data from the abovementioned platform will be presented, including a systems medicine concept to link microbial inflammatory response with glycoprotein-associated mortality risk² and also results from our recent studies on the systemic metabolic effects of hormonal contraception³ and statins⁴.

Bio-sketch:

Professor Mika Ala-Korpela is a Professor of Computational Medicine at the Medical Faculty, University of Oulu, Finland and at the School of Social and Community Medicine, University of Bristol, UK. He is one of the senior staff at the UK Medical Research Council Integrative Epidemiology Unit at the University of Bristol.

His research focuses on lipoprotein and lipid metabolism, development and applications of multivariate data analysis methods for metabolic phenotyping and risk assessment, and the utilisation of various 'omics technologies in clinical and systems epidemiology to study the aetiology of metabolic diseases. He has published around 150 articles in international peer-reviewed journals. Professor Ala-Korpela has more than two decades of experience in biomedical nuclear magnetic resonance (NMR) spectroscopy and has pioneered high-throughput applications of NMR-based metabolomics in molecular epidemiology and functional genetics. He is one of the founders of Brainshake Ltd., a company offering NMR-based metabolic profiling.

During the last ten years Professor Ala-Korpela's Computational Medicine Research Team has focused on developing an NMR-based quantitative high-throughput metabolomics platform for human serum and plasma. This novel methodology has now been used to analyse over 300,000 serum samples (in about 6.5 years). The methodology provides information on around 250 metabolic measures with clear biochemical interpretation and significance. This platform has recently been applied in various large-scale epidemiological and genetic studies, the results of which have been published in the leading scientific journals. Several new NMR laboratories are

² Ritchie SC, Würtz P, ..., Ala-Korpela M, Kettunen J, Inouye M. Systems medicine links microbial inflammatory response with glycoprotein-associated mortality risk. Cell Systems 2015; in press.

³ Wang Q, Würtz P, ..., Lawlor DA, Kettunen J, Ala-Korpela M. Effects of hormonal contraception on systemic metabolism: Evidence from cross-sectional and longitudinal studies. 2015; submitted.

⁴ Würtz P, Wang Q, ..., Chaturvedi N, Kettunen J, Ala-Korpela M. Metabolomics profiling of statin use and genetic inhibition of HMG-CoA reductase. 2015; submitted.



currently being set up to apply the aforesaid metabolomics platform in large-scale epidemiology and systems medicine; more and up-to-date information at http://computationalmedicine.fi.