LC- and GC-MS based non-targeted metabolomics in the study of chronic kidney disease

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The progressive loss in renal function in chronic kidney disease (CKD) results in the accumulation of potentially toxic compounds. Early detection of an impaired kidney function is primordial towards disease management; hence, there is a clear need for novel biomarkers. The objective of this work was to perform a proof-of-concept metabolomics discovery study for CKD.

Serum samples from CKD patients at stage 3 (n=20), at stage 5 on hemodialysis (n=19) and from healthy controls (n=20) were monitored on a holistic metabolomics platform combining reversed-phase liquid chromatography coupled to high-resolution quadrupole time-of-flight mass spectrometry (LC-Q-TOF MS) in both negative and positive ionization mode and gas chromatography coupled to quadrupole mass spectrometry (GC-MS). The methodological validity was ensured by use of quality control (QC) samples in the analytical setup, and by a thorough data analysis strategy for both the GC-MS and the LC-MS part.

A substantial portion of the serum metabolome was covered. Ninety-one metabolites were identified. Forty-nine metabolites were already known in the context of CKD (7 downregulated and 42 upregulated) while 42 metabolites were yet unknown (11 downregulated and 31 upregulated). Of the latter, 5 metabolites were found to be significantly increased (fold change≥5) at CKD stage 3 compared to control. These metabolites were 2-hydroxyhippuric acid glucuronide, 2-/3-hydroxyhippuric acid sulfate, hydroxypyridine, methoxy-hydroxyphenylglycol glucuronide and a hexose based tetrasaccharide.

Further targeted analysis in an increased study population will be performed to validate these novel, potential biomarkers across all CKD stages.