Discovery of Novel Biomarkers for Progression of Chronic Kidney Disease

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Introduction
Type 2 diabetes is the leading cause of renal failure in most industrialized countries and because of the epidemiological increase, this is likely to become the case in most industrialized countries. As a consequence, many people are at risk of chronic kidney disease and do not get the right treatment in time. Since early detection can help to postpone the progression of chronic kidney disease, discovering new and sensitive biomarkers is of crucial importance.

Study Overview
To study the progression of CKD, samples from six cohorts, diabetics and non-diabetics at different disease stages were measured using liquid chromatography coupled with mass spectrometry (LC-MS). The approach was validated on 460 compounds by using an AB Sciex API 4000 QTRAP with electrospray ionization. Additionally, 160 fatty acids were quantitated in plasma and 270 in urine including the classes amino acids, biogenic amines, polypeptides, and others.

Results and Discussion
The study confirmed already established makers such as cystatin C and other well-studied markers for the kidney injury or kidney function (Table 1). Tyrosine / phenylalanine ratios were upregulated (Fig. 4). The steep change in the kynurine / Trp ratio suggests that there is a substantial increase of activity of the enzyme indoleamine 2,3-dioxygenase (IDO). This phenomenon could partially be explained by albumin depletion since the protein arginine N-methyltransferases (PRMT) seem to be an additional test substance (Fig. 1). SDMA was confirmed to be present in higher concentrations in non-diabetics. This ratio has the potential to serve as a stable end-point for the progression of CKD.

Conclusions
Both known and novel metabolic biomarkers for progression of CKD could be identified in this study. Further research is needed to confirm these results in larger cohorts and to develop potential strategies to delay the progression of CKD. Future work should also include a comprehensive analysis of the biological samples to identify potential pathways and mechanisms underlying the observed changes in metabolites. This approach will help to better understand the disease and to develop targeted therapeutic strategies.