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RENAL DEVELOPMENT AND CYSTIC DISEASES

FP047 URINARY PROTEOMIC BIOMARKERS, A POWERFUL TOOL FOR PROGNOSIS OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE PROGRESSION

Martin Pejchinovski[1,2], Justyna Siwy[1,2], Jochen Metzger[1], Harald Mischak[1,3], Vera Jankowski[4], Arlene B Chapman[5] and Andreas D Kistler[6]

[1]Mosaiques Diagnostics GmbH, Clinical Proteomics, Hannover, Germany, [2]Charite-Universitätsmedizin, Department of Nephrology, Endocrinology and Transplantation Medicine, Berlin, Germany, [3]University of Glasgow, BHF Glasgow Cardiovascular Research Centre, Glasgow, United Kingdom, [4]Universitätsklinikum RWTH Aachen, Institute of Molecular Cardiovascular Research, Aachen, Germany, [5]Emory University School of Medicine, Atlanta Clinical & Translational Science Institute, Atlanta, GA, [6]University Hospital, Division of Nephrology, Zürich, Switzerland

Introduction and Aims: Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited renal disease. It accounts 5% of the patients with end stage renal disease (ESRD). Despite the fact that numerous treatment options are likely becoming available in the near future, predicting disease course would be of utmost importance to select high-risk patients for treatment. Up to now, we identified ADPKD-specific peptide markers that distinguish ADPKD patients from healthy state as well as patients with other renal diseases. In this study, we aimed to identify urinary peptide marker panel associated with future progression towards ESRD in ADPKD patients with an extended follow up time of 13 years. This work is supported by TranCYST and iMODE-CKD grant projects.

Methods: We used capillary electrophoresis online coupled with mass spectrometry to analyze the low molecular weight urinary proteome (0.8-20 kDa) of 14 ADPKD patients with progression to ESRD and 39 ADPKD patients with slow disease progression (as defined as a mGFR and eGFR slope of not more than -3 ml/min/1.73m2/year) over a follow up period of 13 years to establish a ESRD-predictive urinary peptide marker model.

Results: A multidimensional marker model established in training cohort consisting of 16 urinary peptides enabled the prediction of ESRD in an independent cohort of ADPKD patients (n=19; 5 reaching ESRD excluding those with age above 40 years at baseline and 14 without ESRD during follow up with age less than 24 at baseline) with an area under the curve value of 0.94 (less than 0.0001) and a 95% confidence interval ranging from 0.73 to 0.99 in receiver operating characteristic analysis. Sensitivity and specificity was 80% and 71% at the predetermined cut-off level of above -0.64. For further validation, we applied the proteomic model to young ADPKD patients (less than 24 years of age) to predict their progression to ESRD (i.e GFR change from baseline to year 8). In this group, the model showed a reasonable correlation with GFR slope (R2=0.29).

Conclusions: In our discovery and validation study, we identified urinary peptide markers that enabled prediction of ESRD in ADPKD patients with a prognostic accuracy similar to that of total kidney volume.