relevance of variants in these genes for kidney diseases. As such, there is a clear need for methods that predict the phenotypic consequences of gene expression in a way that is as unbiased as possible.

We have recently done this using public RNA sequencing (RNA-seq) data and shown that our method substantially improves the diagnostic yield of clinical exome sequencing in rare disease (Deelen et al., 2019). We have now extended upon this work by developing a kidney-specific gene network -KidneyNetwork- similar to www.genenetwork.nl using a combined approach of non-specific human RNA-seq data and human kidney-derived RNA-seq data.

Methods: We calculated gene co-expression in 878 publicly available kidney RNA-seq samples and combined this with the calculated co-expression in the general human RNA-seq dataset. These expression patterns were used to predict genes involved in kidney related phenotypes as established in the HPO database. We used ‘leave-one-out’ cross validations to determine the prediction accuracy (AUC) of our predictions. The KidneyNetwork was applied to prioritize variants in 13 undiagnosed kidney patients for whom WES data were available.

Results: In KidneyNetwork, we observe a significantly improved prediction accuracy of kidney-related pathways as compared to GeneNetwork. Moreover, the total number of significantly predicted pathways has increased (Figure 1).

For each HPO term, all genes are assigned a z-score representing their potential involvement in the respective pathway. Genes with a known association to that pathway are expected to have high scores and genes unknown for their involvement with high scores are potential new candidate disease genes.

Based on the HPO terms “Polycystic kidney dysplasia” and “Hepatic cysts”, combined with information on potentially harmful variants in one of the undiagnosed patients with mild ADPKD/PCLD, we propose “gene X” (proper name will be revealed at the conference) as a new candidate gene. Gene X bears resemblance to other genes implicated in this phenotype. Two patients included in the Genomics England dataset with a similar phenotype have suspected deleterious variants in gene X.

Conclusions: The improvement of KidneyNetwork relative to www.genenetwork.nl, has enabled us to more accurately predict candidate genes involved in renal disease. By analysing 13 undiagnosed patients, for which we found gene X (name will be revealed at the conference) to be a highly promising candidate gene, we have shown the added benefit of KidneyNetwork for the research community and the clinic.

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POS-422

ADPKD: A GLOBAL ONLINE PLATFORM TO EXPLORE THE CHILDHOOD PHENOTYPE OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

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Introduction: Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the 4th common cause of renal replacement therapy worldwide. As the disorder has been historically considered an adult-onset disease, there is a lack of longitudinal data from large pediatric cohorts. However, evidence is growing that first manifestations of ADPKD may be detected in childhood and children represent a specific target population for future treatment, allowing a better chance of preserving long term kidney function. To better define the pediatric spectrum of the disease, a global multicenter observational study on childhood-diagnosed ADPKD was launched in 2017.

Methods: The ADPedKD registry is a worldwide web-based database, including both retrospective and prospective longitudinal data from young ADPKD patients (< or equal to 19 years). Australia, North America and the United Kingdom joined the initiative with their source databases, namely the KidGen Collaborative (KidGen), NIH-funded Hepato-Renal Fibrocystic Disease (HRFD) and National Registry of Rare Kidney Diseases (RaDaR). Under informed consent, de-identified patient data, including genetics, radiological and laboratory findings, treatments and follow-up were enrolled in the database accessible via https://www.ADPedKD.org/.

Results: 952 ADPKD children (from 89 centers and 33 countries) are enrolled in the registry of which 167 patients from RaDaR, 17 from KidGen, 11 from HRFD and 757 from ADPedKD (370 male/387 female) with a mean (+/-SD) age at diagnosis of 6.0 +/- 5.2 years. 72 children (9.5%) were diagnosed prenatally at a mean gestational age of 38.2 weeks (+/-2.2 SD). Reasons for initial visit were: family screening in 293 (38.7%), postnatal antenatal finding in 205 (27.1%), presenting features (such as hema-turia, hypertension, urinary tract infections and flank or back pain) in 130 (17.2%) or unknown/not available in 129 (17.0%). Genetic testing was performed in 41.9% of the population, with the following results: PKD1 mutation (84.4%), PKD2 mutation (8.7%) and others (6.9%).

Conclusions: The ADPedKD registry is a unique source of clinical observational data that will provide deep phenotyping of children with ADPKD and will allow to define unified diagnostic, treatment and follow-up recommendations. No conflict of interest

POS-423

MAINSTREAMING GENETIC TESTING FOR ADULT NEPHROLOGY: A MODEL FOR A PUBLICLY FUNDED HEALTHCARE SYSTEM FOR AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE AND FOCAL SEGMENTAL GLOMERULOSCLEROSIS

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