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Genetics of ADPKD, ADTKD, and Adult Proteinuria

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Next generation sequencing, such as exome sequencing, are widely used in the genetic analysis of various diseases. Today, my topics will included these three categories. In Taiwan, the incidence or prevalence of ADPKD is unknown. According to the Taiwan health registration record, ADPKD contributes only 2.25% of the KF population (8-10% in Western countries) where this number may be under-estimated due to incomplete disease coding. The Taiwan PKD mutation landscape is similar to other cohorts, that PKD1 is the most common, followed by PKD2. Disease-causing mutations were identified in 634 families, and detection PKD1, PKD2, PKHD1, GANAB, ALG8 pathogenic variants. In the Taiwan ADPKD, the PKD2 Arg803* mutation represented 17% of diagnosed individuals. We proved this is a founder mutation, and the founder most likely first migrated to Punghu island, then to Taiwan island more than 300 years (or 13 generation) ago. ADTKD is not as common as the ADPKD in our daily practice. Although positive family history of chronic kidney disease is commonly seen, their presentation can be quite different. For examples, gout attack is absence in some individuals. Recent studies have shown that ADTKD represents up to 0.3~2% of all CKD patients. Disease causing genes included: UMOD, MUC1, HNF1B, REN, and SEC61A1. In our cohort, we collect about 1,800 individuals in 15 years. Our panel contains 21 genes related to adult nephrotic syndrome. We Identified 113 variants are pathogenic or likely pathogenic, with an estimated ~6.3% may have genetic causes in our cohort. We found that COL4A is the most common genetic causes, which represented more than >50% of our cases. In term of clinical presentation, we found there is significant variability the genotype-phenotype-pathology.

Keywords: ADPKD, ADTKD, proteinuria