P040

P040 -Use of a gene panel for a diagnosis of cystic kidney disease and ciliopathy syndromes in an Omani population

Miss Intisar Al Alawi[1,2], Dr Adhra Al Mawali[2], Dr Issa Al Salmi[2], Professor John Sayer[1]
[1]Newcastle University, Newcastle, United Kingdom, [2]Royal Hospital, Ministry of Health, Muscat, Oman

Introduction

The genetic investigation of inherited ciliopathies and cystic kidney disease is important as it provides valuable diagnostic information and allows screening of at-risk individuals and genetic counseling to be undertaken. The continuous growing of the number of disease causative genes is making-routine clinical diagnosis through next-generation sequencing (NGS) technologies is consistent in routine clinical diagnosis. The Omani population has high rates of consanguinity making recessive diseases more frequent.

Methods
A comprehensive diagnosis panel targeting 49 genes associated with cystic kidney disease and ciliopathy syndromes were designed and validated using Agilent SureDesign tool. The captured and indexed libraries were prepared using HaloPlex HS Target Enrichment System and sequenced as a multiplex of 12 samples on an IlluminaMiSeq sequencer in 250 bp paired-end mode. The panel was used in 45 consecutive referred cases of inherited cystic kidney disease.

Results
The panel was efficient and specific at covering the candidate genes and providing rapid and accurate genetic diagnosis. Moreover, it was sensitive at detecting different types of mutations including missense, nonsense, small INDELS and whole gene deletion. A total of 11 unreported pathogenic mutations suspected as the causative genetic aetiology were detected by the NGS. These included variants in PKD1, PKHD1, SDCCAG8, WDR19, NPHP1, NPHP3 and NPHP4 genes. All suspected pathogenic mutations were validated by Sanger sequence. 12 patients had a genetic diagnosis for a dominant form of cystic kidney disease (PKD1 & HNF1B) and 23 had a genetic diagnosis for a recessive cystic kidney disease or ciliopathy. Overall, using this customized targeted NGS resulted in a comprehensive molecular genetics diagnosis in 35/45 patients (78%).

Conclusions
The high diagnostic yield and accuracy of this comprehensive targeted gene panel validate the use of broad NGS-based testing for patients with suspected inherited kidney disease in the Omani population.