KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Abstract Submission No. : 9993

Genetic Aspects of IgA Nephropathy

Krzysztof Kiryluk
College of Physicians & Surgeons, Columbia University, USA

IgA nephropathy (IgAN) represents the most common form of primary glomerulonephritis worldwide. The genetic architecture of IgAN is complex, likely involving multifactorial contributions from common and rare variants. The contribution of genetic factors is supported by numerous reports of familial aggregation of the disease, as well as ancestral differences in disease susceptibility. The disease is most common in individuals of East Asian ancestry, intermediately common in Europeans, and relatively infrequent in individuals of African descent. To date, several GWAS studies for IgAN have been performed and defined multiple risk loci. These loci implicate several pathways in the pathogenesis of IgAN, including antigen processing and presentation (e.g. *MHC* region), the complement system (e.g. *CFH* locus), regulation of mucosal IgA production (e.g. *TNFSF13* locus), and innate immunity against pathogens (e.g. *DEFA, CARD9, ITGAX* loci). GWAS-based pathway enrichment analyses point to the "*Intestinal Immune Network for IgA Production*" as the most significant pathway, providing potential targets for therapeutic interventions. However, for many of the genetic loci, the specific causal genes are still not known.

Ongoing studies and newer approaches to understand the genetic mechanisms underlying IgAN will be discussed, including GWAS fine-mapping and sequencing efforts, and genetic studies of related phenotypes including IgA vasculitis, serum IgA levels, or IgA glycosylation defects. Focusing future genetic studies on pediatric patients may be especially fruitful, since early onset of IgAN has already been correlated with higher burden of GWAS risk alleles and Mendelian forms of disease may also be more common in children. Integrative genetic analyses that combine human genome sequence data with comprehensive blood and kidney tissue transcriptomic, proteomic, and epigenetic profiles in large cohorts may enhance our ability to interpret GWAS loci. These efforts are likely to be further enhanced by new developments in single cell sequencing technologies applied to kidney tissue. These exciting new methods may be able to identify specific kidney cell types along with precise immune cell subtypes that are most critical to the pathogenesis of IgAN.