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Whole exome sequencing to find candidate variants for the prediction of kidney transplantation efficacy

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Introduction: Kidney transplantation is the optimal treatment strategy for some end-stage renal disease (ESRD); however, the graft survival and the success of the transplantation depend on several elements. The Human Leukocyte Antigens (HLAs) matching should be checked to ensure the minimal risk of graft rejection. There are some genes involved in graft survival, and in this study, we evaluate exon loci variants based on a high-resolution NGS method in that regard.

Methods: We evaluate Whole-Exome Sequencing (WES) of transplanted kidney recipients in a prospective study. We recruited the two target groups of low graft and high graft survival (more than five years) with five patients in each group. About five milliliters of blood were collected for DNA extraction, followed by whole-exome sequencing based on Molecular Inversion Probes (MIPs).

Results: The sequencing and variant filtering led to the identification of nine pathogenic variants in rejecting patients (low survival). The pathogenic or likely pathogenic single nucleotide and insertion/deletion variants were in three putative genes, including Zinc Finger Protein 806 (ZNF806), Hydrocephalus-inducing protein homolog (HYDIN), and Ataxin 3 (ATXN3). This was only one variant of Potassium Calcium-Activated Channel Subfamily N Member 3 (KCNN3), including insertion of fifteen nucleotides (GCTGCTGCTGCTGCT). Interestingly, in five patients with successful kidney transplantation, we found 86 SNPs in 63 genes that 61 were Variants of Uncertain Significance (VUS), 5 were likely pathogenic, and five were Likely Benign/benign. The only overlap between rejecting and non-rejecting patients was SNPs rs529922492 in rejecting and rs773542127 in non-rejecting patients' MUC4 gene.

Conclusion: We identified some genetic variants that may help predict transplantation's success using WES technology. Moreover, we suggest that some protective variants are still worth being studied.

Keywords: Whole-exome sequencing, single nucleotide polymorphisms, Kidney transplant, Exonic, Intronic.