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## **Involvement of genetic variation and related gene expression changes on acute rejection in renal transplant recipients**

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**Objectives:** Acute rejection is one of the major risk factors for renal allograft loss. The effect of genetic factors on the transplant outcomes has been clear. However, the correlation between genetic variation and acute rejection remains undetermined.

**Methods:** We collected blood samples from recipients with acute rejection (n = 82) and with stable graft function (n = 70). Gene expression data was pooled from RNA microarray and RNA sequencing. Integrative analysis combining genome-wide association studies (GWAS) and expression quantitative trait locus (eQTL) was used to identify single nucleotide polymorphisms (SNPs) for acute rejection.

**Results:** In eQTL analysis, we detected potential 47 SNPs, which correlated with 4700 genes whose expression differs between patients with stable graft and with acute rejection. We also analyzed rejection related SNPs in GWAS, and finally detected 10 overlapped SNPs in integrative analyses of eQTL and GWAS. Of these, the strongest association with clinical phenotype was observed in rs3934007 on chromosome 11q23.2. This genetic variant significantly increased the expression of *TMPRSS5* gene, and linear regression analysis revealed that A allele induced 2.5-fold risk of acute rejection compared to G allele.

**Conclusions:** Our integrated analysis of GWAS and eQTL, which helps to find relevant genes in a small number of patients population, identify novel acute rejection susceptibility loci in renal transplant recipients.