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Interleukin-4와 interleukin-4 수용체 유전자 polymorphism과 신이식 후 급성 거부반응의 관계

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Association between Interleukin-4 and Interleukin-4 Receptor Ggene Polymorphism and Acute Rejection after Kidney Transplantation

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Background: Acute rejection (AR) after kidney transplantation resulting from alloimmune responses has a negative effect on graft survival. AR is mainly caused by T-cell immune responses activated by cytokines, including interleukin (IL)-4. IL-4 is a cytokine produced by activated T cells, mast cells and basophils that plays a central role in the regulation of B cell-and T-cell-mediated immune responses. IL-4 exerts its biological effects through binding to the IL-4 receptor(IL-4R) complex on target cells. Consequently, IL-4 and IL-4R may be a good candidate gene to evaluate in kidney transplantation rejection. Previous report has shown that single nucleotide polymorphisms (SNPs) of IL-4R can affect the occurrence of AR. In this study, we investigated whether polymorphisms of the IL-4 and IL-4R gene were associated with susceptibility to kidney transplantation rejection.

Methods: We extracted genomic DNA from blood samples and amplified the genomic DNA using the primers for each SNP, which was sequenced.

We analyzed 2 SNPs of IL-4 (rs2243250, rs2070874) and 3 SNPs of IL-4R (rs1801275, rs2107356 and rs1805010) among 344 renal recipients, 62 of whom had developed an AR. 2 SNPs of the IL-4 genes included 1 promotor SNP (rs2243250) and 1 UTR SNP (rs2070874). 3 SNPs of IL-4R genes included 1 promotor SNP (rs2107356) and 2 missense SNP(rs1801275 and rs 1805010).

Results: The AR group included 62 patients, 45 male (38.3±11.9 year) and 17 female (38.9±11.32 year). There were no significant differences in follow up duration, age, sex, number of HLA mismatches, cause of renal failure, immunosuppressant regimen, and number of patients with previous transplants between the AR and non-AR groups.

We genotyped two selected SNPs in the IL-4 gene and three SNPs in the IL-4R gene using direct sequencing in 344 renal transplant recipients. Of the SNPs examined, one (rs1801275) showed a statistical association with acute rejection (p=.025, codominant model; p=.016, dominant model). Otherwise, no significant difference in genotype of the two SNPs of IL-4 (rs2243250 and rs2070874) and two SNPs of IL-4R (rs1801275 and rs2107356) was observed between non-AR and AR subjects.

Conclusion: One IL-4R gene polymorphisms was associated with acute rejection in kidney transplantation.

Key Words: 단일 염기 다형성, 신이식 거부반응, IL-4 수용체
Polymorphism, Kidney transplant rejection, IL4 receptor