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신장 이식환자 혈액에서 전사체를 이용한 비침습적 거부반응 진단 후보물질 발굴

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서정우, 문해나, 이아라, 김세연, 김양균, 정경환, 문주영, 이상호

Discovery of Peripheral Blood Biomarkers for Non-invasive Diagnosis of Acute Rejection in Kidney Transplantation

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Background: Immunosuppressive drugs have improved to reduce renal allograft rejection, but renal allograft failure has not markedly diminished. The discovery of sensitive non-invasive diagnosis and the development of immune management in the renal allograft recipients are required for long-term graft survival. Although the several studies have identified numerous genetic biomarkers, they were not sufficient to detect renal graft injury. In this study, we performed DNA microarray and real-time PCR to investigate and confirm candidate genes of acute rejection (AR) in peripheral blood.

Methods: 48 Blood samples were collected from 47 transplant recipients (17 and 10 biopsy-proven acute cellular rejection (ACR) and acute antibody-mediated rejection (AMR), 21 stable (STA) patients). Gene expression was profiled using DNA microarray, and the diagnostic candidates for AR were classified by significance analysis of microarray (SAM) analysis. Real-time PCR was performed to validate the candidates.

Results: In microarray results, 1868 transcripts were up-regulated and 3312 were down-regulated in ACR recipients than in stable patients. There were 1604 up-regulation and 4732 down-regulation in AMR patients compared with stable patients. 24-positive and 13-negative significant genes (FDR <0.05) in ACR and 5-positive and 3-negative significant genes (FDR <0.05) in AMR were classified using SAM analysis. 9 candidates among the significant genes were selected in ACR. Real-time PCR was performed to confirm potential biomarkers of ACR in microarray-dependent samples (12 ACR, 8 AMR, and 18 STA). 2 genes among the 9 candidate genes these candidates were significant in ACR patients.

Conclusion: We investigated genetic biomarkers of AR from peripheral blood of kidney transplanted patients by transcriptome analysis. The genes validated from our study may be used as a non-invasive assay for AR detection in kidney transplantation. These potential biomarkers will need to be further validated in independent samples.

Key Words: 신장이식, 거부반응, 말초혈액
Kidney transplantation, Acute rejection, Peripheral blood