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## **Clinical significance of CD8<sup>+</sup> T cell subset analysis for the prediction of acute allograft rejection in kidney transplant recipients**

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**Objectives:** In this study, we performed multi-color flowcytometry to analyze the CD8<sup>+</sup>T cell subsets in KTRs with acute rejection in comparison with KTRs with different clinical status.

**Methods:** At first, we included 121 KTRs from three transplant centers and we isolated PBMC at the time of allograft biopsy. They were divided into 3 groups according to the pathologic diagnosis; Normal biopsy control (NC) (n=32), Acute rejection (AR) (n=50), long term graft survival (LTGS) (n=39). **We** performed multi-color flowcytometry analysis using following platform. We also did microarray analysis to investigate the significant changes in gene expression associated with cell types using SAM analysis.

**Results:** The percentage of CCR7<sup>+</sup>CD8<sup>+</sup> T cells showed significant decrease in the AR group compared to NC group or LTGS group (P<0.05 for each). In contrast, the percentage of CD28<sup>null</sup>CD57<sup>+</sup> T cell and CCR7<sup>-</sup>CD45RA<sup>+</sup>/CD8<sup>+</sup> T cells and showed increase in AR group in comparison with other groups. Both effector CD8<sup>+</sup> T cells showed significant negative correlation to CCR7<sup>+</sup>CD8<sup>+</sup> T cells in an ex vivo and also in an vitro conditions. In microarray analysis from blood of KTRs, we identified significant genes associated with CCR7<sup>-</sup>CD45RA<sup>+</sup>/CD8<sup>+</sup> T and CD28<sup>null</sup>CD57<sup>+</sup>/CD8<sup>+</sup> T cells by SAM analysis. Moreover, some of significant genes associated with CCR7<sup>-</sup>CD45RA<sup>+</sup>/CD8<sup>+</sup> T cells and CD28<sup>null</sup>CD57<sup>+</sup>/CD8<sup>+</sup> T cells showed negative correlation to expressed genes in CCR7<sup>+</sup>CD8<sup>+</sup> T cells. ROC analysis showed that the ratio between CCR7<sup>+</sup>CD8<sup>+</sup> T cells and CD28<sup>null</sup>CD57<sup>+</sup> CD8<sup>+</sup> T cells showed best prediction for AR in the whole clinical cohort (AUC=0.800, P<0.01).

**Conclusions:** This study suggests that combined monitoring of the ratio between CCR7<sup>+</sup> and CD28<sup>null</sup>CD57<sup>+</sup> T in CD8<sup>+</sup> T gaing may be useful for the prediction of AR. Validation of this result in the prospective cohort may be required.