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Investigation of killer immunoglobulin-like receptor (KIR) and HLA genotypes to predict the occurrence of acute allograft rejection after kidney transplantation

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Background: After kidney transplantation, natural killer (NK) cells as a component of innate immune system play a pivotal role in triggering the immune response to the allogeneic grafts primarily by their killer-cell immunoglobulin-like receptors (KIR). This process may be one mechanism that contributes to graft rejection. In this study, we have evaluated whether acute rejection after kidney transplantation was associated with predicted NK cell alloreactivity based on KIR gene and ligand along with KIR/HLA compound genotype analysis.

Material & Methods: DNA from 65 patients with biopsy-proven acute kidney allograft rejection (AKAR), 61 clinically well graft function (WGF) recipients and 176 healthy subjects was identified for the presence or absence of 10 variable KIR genes (both activating and inhibitory receptors) and their HLA ligands using polymerase chain reaction-sequence specific primers (PCR-SSP) assay.

Results: Although no significant difference in the frequency of individual KIR genes, the gene content and the haplotypic distribution between the three categories was detected, the frequency of the KIR3DL1+HLA-Bw4* A allele combination was significantly lower in AKAR patients compared to SGF recipients (p=0.004, OR=0.34, CI =0.16-0.72) and healthy subjects (p=0.019, OR=0.47, CI=0.25-0.89). Kaplan-Meier survival test showed that the KIR3DL1+HLA-Bw4* A allele combination could be considered protective for AKAR (p=0.04 by log-rank).

Conclusion: The results of this study suggest that KIR/HLA polymorphism may be a genetic susceptibility factor to alloreactivity dysfunction in the NK cells of patients with AKAR. It is likely that a KIR/HLA combinatorial study can be beneficial in predicting AKAR occurrence for the purpose of selecting donors appropriately.

Effect of age and CMV latent infection on NKT-like cells frequency and functionality

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Changes in the T-cell pool caused by CMV infection have been proposed to contribute to immunosenescence. However, this detrimental role of CMV has been questioned and although it is clear that CMV contributes to immune cell senescence, it also has beneficial effects in young individuals improving the immune response to other pathogens. T-cells expressing NK cell receptors (NKT-like cells) such as CD56, expand with age and CMV infection and play an important role in the immune response against cancer, yet little information about their contribution to the response to infections is known. Here we propose an analysis of NKT-like cells responses to Staphylococcal Enterotoxin-B (SEB), in the context of CMV latent infection and aging. Our results show that NKT-like cell percentage increases with a combination of CMV latent infection and age. The response to SEB and the poly functional index of NKT-like cells also increase with age in CMV-seropositive individuals. Besides, in young individuals, CMV infection induces a shift on the poly functional profile of CD8+CD56− T-cells, but not on NKT-like's. We have as well confirmed that in both subsets, i.e., independently of CD56 expression, CD57+ cells are more poly functional than their CD57− counterparts and are expanded in CMV-seropositive individuals.