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Increased T Cell Percentage and Enhanced Bioenergetics in T Cell-Mediated Renal Transplant Rejection

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Objectives : In this study, we investigated the role of T cells in renal transplant rejection, focusing on their abundance and metabolic activity.
Methods : T cell mediated transplant rejection patients (N=40) were enrolled in the study; all were biopsy proven, Control were transplant patients with stable graft function (N=40). The T cell markers in the PBMCs were evaluated by flowcytometry, the metabolic status of T cells was studied using the SCNIETH assay. Gene expression analysis was studied using qPCR.
Results : Our findings reveal a marked increase in the percentage of T cells infiltrating the grafts during episodes of rejection compared to non-rejecting controls (Th1, Th2, Th17, Tregs, in all subtypes $p<0.0001$). These T cells exhibited enhanced bioenergetics (glycolysis 84%, OXPHOS 27%), characterized by elevated oxidative phosphorylation and glycolysis ($p<0.001$), suggesting a metabolic reprogramming that supports their heightened proliferative and effector functions. This metabolic shift correlates with increased expression of key transcription factors (T bet, GATA3, FOXP3, ROR Gamma T, $p<0.001$) and cytokines involved in T cell activation and differentiation (IFN-gamma, IL-17, IL4 $p<0.0001$). AMPK1 was observed to be the master regulator, and the gene expression was reduced in transplant biopsies ($p<0.001$).
Conclusions : Our results highlight the importance of T cell metabolism in the pathogenesis of TCMR and suggest that targeting metabolic pathways may offer a novel approach to modulate T cell activity and improve graft survival. These findings provide new insights into the cellular and metabolic dynamics of T cell-mediated renal transplant rejection and open avenues for the development of metabolic interventions in transplant immunology.