A Molecular Diagnostic Approach to Management of Renal Transplant Recipients

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Precedures to diagnose renal allograft rejection depend upon detection of graft dysfunction and the presence of a mononuclear leukocytic infiltration; however, the presence of a modest cellular infiltrate is often not conclusive and can be detected in non-rejecting graft. We have pursued a molecular approach utilizing reversed transcripting (RT)-PCR to test the diagnostic accuracy of multiple immune activation gene analysis as means to diagnose renal allograft rejection. The magnitude of intragraft gene expression of 15 immune activation genes was qunatified by competitive RT-PCR in 60 renal allograft core biopsies obained for surveillance or to diagnose the etiology of graft dysfunction. Results were compared with a clinicopathological analysis based upon the histological diagnoses (Banff criteria) and the response to anti-rejection treatment. During acute renal allograft rejection intragraft expression of the interleukin (IL)-7 ($P<0.001$), IL-10 ($P<0.0001$), IL-15 ($P<0.0001$) and granzyme B($P<0.0015$), but not IL-2, interferon γ, or IL-4, genes is significantly heightened. Amplified RANTES and IL-8 gene transcripts are sensitive but non-specific markers of rejection. A simultaneous RT-PCR evaluation of perforin, granzyme B, Fas ligand identifies acute regection, including cases with and infiltration, with extraordinary sensitivity (100%) and specifictiy (100%). Effective anti-rejection therapy results in a rapid down-regulation of gene expression. The combined analysis of Fas ligand, perforin, and granzyme B gene expression by quantitative RT-PCR provides a reliable tool for diagnosis and follow-up of acute renal allograft rejection. Its accuaracy and a potential rapid application within few hours suggest its use in the clinical management of renal transplant patients.