

CHARACTERIZATION OF AN AUTOIMMUNE
GENE EXPRESSION SIGNATURE

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Autoimmune diseases affect approximately 5% of the human population and are believed to arise from immune mediated attack against self-antigen. Microarray studies demonstrate highly reproducible gene expression signatures in peripheral blood mononuclear cells (PBMC) of patients with a range of autoimmune disorders. Neither *in vivo* recapitulation of an immune response to foreign antigen or disease duration accounted for the autoimmune gene expression signature. However, unaffected first-degree relatives also contained this gene expression signature, suggesting that it arose from a heritable trait(s). The autoimmune signature includes, at least in part, under-expressed genes that encode proteins that inhibit cell cycle progression and stimulate apoptosis. We found that reduced TP53 gene expression and p53 protein levels are associated with selective loss of lymphocyte radiation-induced apoptosis in patients with rheumatoid arthritis. We hypothesize that these liabilities may contribute to autoimmunity.

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