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The type I interferon system in SLE and Sjögren´s syndrome

Systemic lupus erythematosus (SLE) and primary Sjögren's syndrome (SS) are two systemic autoimmune diseases. SLE is characterized by an inflammation in multiple organs and SS by inflammation in the lacrimal and salivary glands. In both SLE and SS, autoantibodies against nucleic acids and their associated proteins are produced, i.e. anti-SS-A, SS-B, RNP and Sm antibodies, which form immune complexes that can induce IFN-α production in the plasmacytoid dendritic cells (PDCs). PDCs have been detected in the skin of SLE patients and in the minor salivary glands of SS patients. IFN-α exerts a pleiotropic effect on the immune system and increased serum levels of IFN-α correlates with skin rash, fever and leucopenia in SLE.

Gene expression profiling of cells from SLE patients and salivary glands from SS patients has shown an up-regulation of IFN-stimulated genes, a so called IFN signature. In addition, polymorphisms in two genes in the type I IFN system, the interferon regulatory factor 5 (IRF5) and signal transducer and activator of transcription 4 (STAT4) genes, have shown an association with both SLE and SS, where the STAT4 risk variant correlates with anti-dsDNA antibodies and nephritis in SLE.

There are several potential therapeutic targets within the type I IFN system and monoclonal anti-IFN-α antibodies have been shown to reduce disease activity in SLE clinical trials.