Immune stimulation mediated by autoantigen binding sites within small nuclear RNAs involves Toll-like receptors 7 and 8.

Abstract:
Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the production of autoantibodies to certain cellular macromolecules, such as the small nuclear ribonucleoprotein particles (snRNPs), which had been considered to be passive targets of the autoimmune response. SLE is also characterized by the increased expression of type I interferon (IFN), which appears to be associated with the development and severity of disease. Here, we show that specific, highly conserved RNA sequences within snRNPs can stimulate Toll-like receptors (TLRs) 7 and 8 as well as activate innate immune cells, such as plasmacytoid dendritic cells (pDCs), which respond by secreting high levels of type I IFN. SLE patient sera containing autoantibodies to snRNPs form immune complexes that are taken up through the Fc receptor gammaRII and efficiently stimulate pDCs to secrete type I IFNs. These results demonstrate that a prototype autoantigen, the snRNP, can directly stimulate innate immunity and suggest that autoantibodies against snRNP may initiate SLE by stimulating TLR7/8.