Clinical Correlations and Expression Pattern of the Autoimmunity Susceptibility Factor Diora-1 in Primary Sjögren's Syndrome

Abstract # 1582

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Background/Purpose:
Genome-wide association studies of multiple autoimmune diseases, including primary Sjögren's syndrome (pSS), systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) have revealed an association with the chromosome 8 locus *FAM167A-BLK*. The disease-associated genotypes of SNPs in the locus have been linked to a significantly increased expression of FAM167A in B cells. While BLK (B lymphocyte kinase) has a well-established role in B cells, little is known about FAM167A (family with sequence similarity 167 member A). We recently cloned and investigated the gene product of FAM167A, identifying an encoded protein with high content of intrinsic disorder which we denoted Disordered Autoimmunity 1 (DIORA-1). In the present study we investigated the expression of DIORA-1 in human immune cells and in salivary glands of patients with pSS, as well as assessed DIORA-1 expression in relation to pSS clinical manifestations to begin understanding the role of DIORA-1 in rheumatic disease pathogenesis.

Methods:
Primary cells were purified from peripheral blood or buffy coats by MACS beads, and cell lines representing discrete differentiation stages of B cells were cultured under standard conditions. DIORA-1 mRNA expression was assessed by qPCR. Immunohistochemistry was performed to identify DIORA-1 expressing cells in salivary gland biopsies, and characterization of the cells and DIORA-1 localization performed by immunofluorescence using double staining. Characterization of DIORA-1 expressing cells was performed by immunofluorescence. In all, 55 patients with pSS, 20 sicca patient controls and 29 healthy donors were included in the study.

Results:
We observed expression of DIORA-1 in CD19+ B cells from peripheral blood, while CD3+ T cells and CD14+ monocytes expressed little or no DIORA-1. To further define the expression pattern of DIORA-1 in B cells, we analyzed cell lines representing discrete differentiation stages of B cells. Interestingly, we observed a graded expression of DIORA-1 in these various cell lines, with the highest expression found in the two plasma cell myeloma lines and intermediate expression in other B cell lines, whereas little or no expression was observed in T cells and other investigated cell lines. CD138+ plasma cells expressing DIORA-1 intracellularly were observed

within the salivary glands of pSS patients. Spatially, DIORA-1+ cells were detected within the focal infiltrates and interstitially in salivary gland biopsies. Notably, expression of DIORA-1 correlated to salivary gland focus score, as well as serum IgG levels and the presence of Ro/SSA autoantibodies.

Conclusion:
These findings indicate a role for DIORA-1 in select B cell subsets, and moreover suggest that DIORA-1 potentially contribute to the inflammatory process and disease pathogenesis in pSS through B cell involvement.

Disclosure:
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