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Abstract #517

Overexpression of BMP6 Is Associated with Loss of Salivary Gland Activity in Sjögren's Syndrome Patients and Mice

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Background/Purpose:

A hallmark of Sjögren's syndrome (SS) is the loss of activity in secretory epithelia, specifically the lacrimal and salivary glands. The mechanism(s) driving this disorder are poorly understood and may involve a combination of environmental and genetic factors. To date extensive efforts have been focused on understanding the changes in the immune system in these patients, however little is understood regarding the changes in the epithelia associated with the loss of gland activity.

Methods:

To identify genes associated with changes in the epithelia, RNA was isolated from patients with both low flow and low lymphocytic infiltrates (focus score) and used to probe customized high density microarrays. After normalization, the signal from the patient RNA samples was then compared to the signal from RNA isolated from healthy volunteers. The list of differentially expressed genes was then filtered for genes associated with salivary gland specific cell types.

Results:

A significant increase in expression of the bone morphogenic protein 6 (BMP6) was observed in RNA isolated from patients compared with healthy volunteers. Overexpression of BMP6 locally in the salivary gland or lacrimal glands of mice resulted in the loss of fluid secretion as well as changes in the connective tissue of the salivary gland. Assessment of the fluid movement in either isolated acinar cells of mice overexpressing BMP6 or HSG cells cultured in the presence of BMP6 identified a loss in volume regulation in these cells. Loss of fluid movement also correlated with a decrease in sodium concentration in the saliva. Lymphocytic infiltration in SMG of BMP6 overexpressing mice was increased. No significant changes were found in proinflammatory cytokines production, neither the auto-antibodies associated with SS, such as anti-Ro/SSA, anti-La SSB and anti-nuclear antibody (ANA) after BMP6 overexpression.

Conclusion:

Our study identified BMP6 as a novel gene associated with xerostomia associated with Sjögren's syndrome, which may become a new target for therapeutic intervention. In mice, a loss of salivary and lacrimal gland function can be induced by overexpression of BMP6, which further support our finding in patients. This study suggests the loss of salivary gland function can be separated from the autoantibodies and proinflammatory cytokines associated with this disease.