SEX AND ANDROGEN EFFECTS ON GENE EXPRESSION IN AUTOIMMUNE LACRIMAL GLANDS. R. Rahimi Darabad, S.M. Richards, D.A. Sullivan. Schepens Eye Research Institute and Harvard Medical School, Boston, MA

Purpose. Sjögren's syndrome (SS) is an incurable autoimmune disorder that occurs primarily in women, and is associated with extensive lacrimal gland (LG) inflammation, epithelial cell dysfunction and severe dry eye. We hypothesize that sex- and androgen-induced variations in LG gene expression and microenvironment contribute to the onset, progression and/or severity of the disease process. Our objective in this study was to begin to test this hypothesis.

Methods. LGs were collected from age-matched, adult, male and/or female mice, including MRL/Mp-lpr/lpr (MRL/lpr), a female SS model; non-obese diabetic (NOD), an anomalous SS model in which the male, but not female, LG is greatly inflamed; and C57Bl/6 and BALB/c controls. Animals were either untreated or treated with placebo or testosterone for 3 weeks. Glands were pooled according to sex, treatment and experiment and processed for the analysis of differentially expressed mRNAs by using CodeLink Bioarrays (n ~ 20,000 genes/array). Data were evaluated with bioinformatics and statistical software.

Results. Our results show that both sex and androgen treatment significantly influence the expression of thousands of genes in LGs of normal and autoimmune mice. The nature of the LG response, though, is very dependent upon the SS mouse model. For example, LGs of female, as compared to male, MRL/lpr mice contain a significant increase in the mRNA levels of numerous genes related to inflammatory responses, immune cell chemotaxis and antigen presentation. The expression of these immune-linked genes, in turn, is dramatically suppressed by androgen treatment. In contrast, NOD mice feature a very different pattern of LG gene expression, with immune-related genes upregulated in males and induced by testosterone in females. The C57Bl/6 and BALB/c control strains did not show analogous sex- and hormone-associated alterations in LG immune response genes.

Conclusions. These data support our hypothesis that sex- and androgen-related differences in gene expression contribute to LG disease in SS. We now seek to identify the factors in the LG microenvironment that mediate these sex and hormonal effects.