association analyses. We analyzed the entire group and also the two largest strata by ethnicity (European and Asian, with outliers removed outside of PCA clusters).

Results: Out of 3284 unrelated subjects with post-QC genotypes and sufficient clinical data, patients were categorized for analysis as follows: high FS (n=636), normal FS (n=1968), high OSS (n=1333), normal OSS (n=857). A total of 1,550,200 SNPs with MAF ≥ 1% passed all QC filters and were fully analyzed. Not surprising in autoimmunity, the MHC was the most significantly associated with both traits in the full dataset (FS p=3e-22; OSS p=6e-12) and in Europeans (FS 375 SNPs p<5e-8, lowest 3e-17; OSS 60 SNPs p<5e-8, lowest p=4e-11). However, in Asians the MHC appears to have much less importance. There was only one suggestive MHC SNP (p=8e-6) for FS; the most associated FS gene in Asians was *PTPRD*, with 12 SNPs p<5e-6 (lowest p=1.8e-7). Outside of the MHC, some genes appear to influence both phenotypes while others are trait-specific. For example, *IRF5* is the highest-associated region for FS (p=2e-7) but not suggestive for OSS. The *XYLT1* region is the highest-associated region for OSS (p=1e-6) but is not implicated in FS. On the other hand, *STAT4* is among the most-associated regions for both FS (p=1e-6) and OSS (p=3e-6).

Conclusion: These results demonstrate that the ocular (OSS) and oral (FS) manifestations of SS are influenced by both shared and trait-specific genetic factors. Furthermore the genetic profile appears to be quite different for both depending on ancestry, in particular when comparing European and Asian SS patients. Additional work including imputed genetic data and more extensive ancestry analysis will provide more power for extending these findings and fully characterizing the genetic contribution to SS.

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A Descriptive and Comparative Study of the Transcriptome from Salivary Exosomes of Sjögren's Syndrome Patients Using RNA-Seq. Alessia Gallo[1], Mayank Tandon[2], Shyh-Ing Jang[2], Ana Paola Cotrim[1] and Ilias Alevizos[3]. [1]NIH, Bethesda, MD, [2]NIDCR, Bethesda, MD, [3]NIDCR/NIH #10 1N110, Bethesda, MD.

Background/Purpose: Saliva is a biofluid secreted by the salivary glands (SGs) that is critical for the health of the oral cavity. In Sjögren's Syndrome (SS), changes in salivary biomarkers are not only useful for diagnosis, but may also elucidate the mechanisms underlying SG dysfunction. The RNA content of saliva has been shown to be useful for monitoring the health of oral tissue and the oral microbiome. Next-Generation Sequencing (NGS) offers a high throughput method for comparing the salivary transcriptomes of SS patients and healthy volunteers (HV). We have previously shown that RNA is protected within exosomes and we focused this study in using salivary exosomes isolated from the parotid. Parotid saliva has the advantage of being pure without the contamination generated from all type of cells found in the whole saliva.

Methods: Total RNA was extracted from exosomes isolated from parotid saliva from 4 healthy volunteers and 4 primary SS patients. The amount and the quality of the RNA were assessed using Nanodrop, Qubit and Bioanalyzer. The Ion Torrent Proton sequencer was used sequencing according to manufacturer protocols. Reconstructed reads were aligned using the TMAP (Torrent Mapper) algorithm sequentially to miRBase 19, hg19, viral, and bacterial genomes, i.e. reads left unmapped were used as input for each subsequent step. The bacterial reference included 14,549 contigs representing 1,132 genomes retrieved from the Human Oral Microbiome Database, and the viral reference included 1,741 viruses retrieved using the NCBI assembled genomes FTP website. Read counts were generated using the HTSeq python module, and differential expression analysis was done in R using the DESeq2 package. Ingenuity Pathway Analysis (IPA) was used to analyze pathway enrichment and visualization. Microbial expression and taxonomy were analyzed used Pathosystems Resource Integration Center (PATRIC).

Results: Overall the percentage of all reads mapping to each reference were similar between SS and HV: miRBase (5.96% in HV, 5.427% in pSS), hg19 (81.82% HV, 81.96% pSS), viral (6.94% HV, 3.26% pSS), and bacterial (1.121% HV, 1.737% pSS). On average, 4.14% of the input was left unmapped in HVs and 7.62% in pSS patients after all mapping. The differences between percent input reads in patients and HVs was only significant for the bacterial reference, and for unmapped reads. Expression pairing between miRNAs and their target genes using IPA showed significant enrichment for canonical pathways for pancreatic adenocarcinoma signaling, and estrogen-mediated S-phase Entry. Top differentially regulated bacterial genera (fold-change greater than or less two and FDR-corrected p-value less than 0.01) include Streptococcus, Selenomonas, and Actinomyces. Notable upregulated viruses include Tomato yellow leaf curl virus and streptococcus phage Cp-1. Human papillovirus, type 41 was found to be significantly downregulated in pSS patient saliva.

Conclusion: This is the first known effort to compare the transcriptome of SS patients' salivary exosomes versus healthy controls. Using RNA-Seq, we were able to identify important human genes as well as alterations in the salivary microbiome that could shed light on the mechanisms of salivary dysfunction in pSS.

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Salivary Expression of S100A7/Psoriasin and Oral Damage in Primary Sjögren's Syndrome and Overlapping Disorders. Francesca Sernissi[1], Chiara Baldini[1], Daniela Martini[1], Leonardo Lorenzini[1], Laura Bazzichi[1], Antonietta Raffaella Maria Sabbatini[1], Giada Marchi[1], Camillo Giacomelli[1], Marta Mosca[2] and Stefano Bombardieri[2]. [1]Rheumatology Unit, Pisa, Italy, [2]Rheumatology Unit, University of Pisa, Pisa, Italy.

Background/Purpose: S100A7/psoriasin, a 11.4kDa protein belonging to the S100A family of Ca2+-binding proteins, is known to exhibit an antimicrobial activity at skin level, but has also been implicated in the regulation of cell proliferation, differentiation, invasion and metastasis. By using a proteomic approach, S100A7/psoriasin has been recently identified in the whole saliva of patients with Systemic Sclerosis as a potential disease biomarker. The aims of the present study were (1) to compare the expression of salivary S100A7/psoriasin in patients with Sjögren's Syndrome associated to anti-centromere antibodies (ACA) positive Systemic Sclerosis (SS-SSc), versus patients with primary Sjögren's Syndrome (pSS), and (2) to explore any correlation between salivary S100A7/psoriasin and oral damage.

Methods: Unselected pSS and SS-SSc patients (AECG 2002) were consecutively recruited in the study. Unstimulated salivary flow (USF) rate were measured according to the sialometry protocol, and saliva samples were collected on ice, centrifuged and stored at -80°C. S100A7/psoriasin levels were determined by CircuLex S100A7/psoriasin ELISA kit (MBL International Corporation), according to manufacturer's instructions. All subjects had a standardized evaluation for pSS which included oral and ophthalmologic examinations, laboratory testing and a rheumatologic evaluation.

Results: Eighteen SS-SSc and 33 pSS female patients were included in the study. SS-SSc patients had a mean age ± standard deviation (SD) of 65.6 ± 11.3, which did not differ from that of pSS (59.8 ± 11.3). S100A7/psoriasin levels were significantly higher in SS-SSc subjects (p=0.02). S100A7/psoriasin salivary levels negatively correlated with the USF rate (r=−0.27, p<0.05), particularly in pSS subjects (r=−0.508, p=0.003), and were significantly higher in patients with a USF <1.5 ml/15 minutes (p=0.006). Regarding the relationship between S100A7/psoriasin and patients' oral damage, we found that the salivary expression of the protein was significantly associated with the Sjögren's Syndrome disease damage index (SSDDI) (p<0,05) and specifically with the complete loss of teeth (p=0.02).

Conclusion: Salivary S100A7/psoriasin might be useful in differentiating pSS from SS-SSc and seems to be able to reflect oral damage in both pSS and SS overlapping disorders. The potentially predictive value of this biomarker for oral damage accrual in SS calls for further studies.

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Calcium-Calcineurin-NFAT Signaling Pathway Regulates AQP5 Expression in Primary Salivary Gland Acinar Cells. Shyh-Ing Jang[1], Hwei Ling Ong[1], Indu Ambudkar[2] and Illias Alevizos[1]. [1]NIDCR, Bethesda, MD, [2]NIH, Bethesda, MD.

Background/Purpose: Aquaporin (AQP) 5 belongs to a family of small integral membrane proteins which function as a water channels in cells. AQP5