Supplemental Table 1. Summary of primary Sjögren's syndrome (pSS) and Sicca patient samples utilized in analysis of viral profiles present in Sjögren's syndrome patient cohorts at NIH and in UK.

NIH Patient ID	Sex	Schirmer's Test	Unstimulated Saliva Flow	Focus Score (≥1)	Autoantibody	Diagnosis
pSS-1	Male	Negative	Low Flow	Negative	Positive	pSS
pSS-2	Female	Positive	Low Flow	Positive	Positive	pSS
pSS-3	Male	Positive	Low Flow	Positive	Positive	pSS
pSS-4	Female	Negative	Low Flow	Positive	Positive	pSS
pSS-6	Female	Positive	Low Flow	Positive	Positive	pSS
pSS-7	Male	Negative	Low Flow	Positive	Positive	pSS
pSS-9	Female	Positive	Low Flow	Negative	Positive	pSS
pSS-10	Female	Positive	Low Flow	Positive	Positive	pSS
pSS-11	Male	Positive	Normal Flow	Positive	Positive	pSS
pSS-12	Female	Positive	Low Flow	Positive	Negative	pSS
pSS-13	Female	Positive	Low Flow	Positive	Negative	pSS
pSS-14	Female	Negative	Normal Flow	Positive	Positive	pSS
pSS-15	Male	Negative	Low Flow	Positive	Positive	pSS
pSS-19	Male	Positive	Normal Flow	Positive	Positive	pSS
pSS-20	Male	Positive	Normal Flow	Positive	Positive	pSS

UK Patient ID	Sex	Schirmer's Test	Unstimulated Saliva Flow	Focus Score (≥1)	Autoantibody	Diagnosis
UK-1	Female	Positive	Normal Flow	Positive	Positive	pSS
UK-2	Male	Positive	Normal Flow	Positive	Positive	pSS
UK-3	Female	Positive	Low Flow	Positive	Positive	pSS
UK-4	Female	Positive	Low Flow	Positive	Positive	pSS
UK-5	Female	Positive	Low Flow	Positive	Positive	pSS
UK-6	Female	Negative	Normal Flow	Positive	Positive	pSS
UK-7	Female	Positive	Low Flow	Positive	Positive	pSS
UK-8	Female	Positive	Low Flow	Positive	Positive	pSS
UK-9	Female	Positive	Low Flow	Positive	Positive	pSS
UK-10	Female	Positive	Normal Flow	Positive	Positive	pSS
UK-11	Female	Positive	Normal Flow	Positive	Positive	pSS
UK-12	Male	Positive	Normal Flow	Positive	Positive	pSS
UK-13	Female	Positive	Low Flow	Negative	Negative	Sicca
UK-14	Female	Negative	Normal Flow	Negative	Negative	Sicca
UK-15	Female	Negative	Normal Flow	Negative	Negative	Sicca
UK-16	Female	Negative	Normal Flow	Negative	Negative	Sicca
UK-17	Female	Positive	Low Flow	Negative	Negative	Sicca
UK-18	Male	Positive	Low Flow	Negative	Negative	Sicca
UK-19	Female	Positive	Low Flow	Negative	Negative	Sicca
UK-20	Female	Negative	Normal Flow	Negative	Negative	Sicca
UK-21	Female	Positive	Normal Flow	Negative	Negative	Sicca
UK-22	Female	Positive	Normal Flow	Negative	Negative	Sicca

All pSS patients met diagnosis criteria based on the American European consensus group (AECG).

Supplemental Table 2. Viral microarray analysis identified 9 viral probes with significantly different intensity between the collective pSS patient population compared to healthy controls.

Family Name	Probe Name	Sequence	p-value	p (Corr)	FC
Deltavirus	Deltavirus_13277517_18	GGTCAACCTCCTAAGTTCCTCTTCCTCCTCCTTGCTGAGGTTCTTTCCCCCCGCCGATAG	0.004	0.022	3.25
Herpesviridae	Herpesviridae_9629267_432	GCCCTGGGCCCCGAGGCCATCCAGGCGCGGCTGGAGGACGTGCGGATCCAGGCCCGCCGG	0.012	0.033	3.47
Astroviridae	Astroviridae_20514394_47	CAACCTCAACCTCAACCTCCTGCTCCTATTGAAGAAATACTTCTGCCTTTAGCAGAACTG	0.014	0.033	2.60
Adenoviridae	Adenoviridae_34303903_34	TTCACTAAGTTTGCCTCCAGCTCTACAAAAAATTTTAATTGAAATTTTTATTGGAAAATC	0.014	0.033	2.48
Retroviridae	Retroviridae_9629902_75	CATTGCAAGTTATTGCGATCATCTCTCTCCTCCTCGTTGGGGGGGCCAGTCAACCAGCTA	0.009	0.033	2.05
Circoviridae	Circoviridae_12280941_24	TGCCAACTTTGTAACCCCCTCCACCAACTTGGCCTATGACCCCTATATTAACTACTCCTC	0.023	0.044	2.86
Flaviviridae	Flaviviridae_157781216_244	TATACCAATGCTGTAACCTTGAACCGGAGGCCAGGAAAGTGATCTCCTCCCTCACGGAGC	0.003	0.022	-2.10
Poxviridae	Poxviridae_96980809_55	GCTTCCGCAAGGCGGTCGAGCGGCAGCTGGAGGAGGAGCAGGAGGTGAAGCTGAAGAGCC	0.003	0.022	-4.00
Poxviridae	Poxviridae_96980809_110	TCGAGCGGCAGCTGGAGGAGGAGCAGGAGGTGAAGCTGAAGAGCCTCGCGCGGCGCGAGT	0.016	0.033	-2.93

Six probes were increased in pSS compared to healthy controls and 3 probes were significantly decreased in pSS compared to healthy controls. (FC = Fold Change, p-value denotes t-test, p(Corr) denotes $p<0.05$, t-test, Benjamini-Hochberg correction n=14-15)

Supplemental Table 3. Analysis of viral microarray data for subgroups within the Sjögren's syndrome patient population identified 12 viral probes significantly increased in at least 25% of the patient co-hort.

Viral Family Name	Probe Name	Sequence
Astroviridae	Astroviridae_20514394_18	CCAACGACAGGAGCTCAACCTCAACCTCAACCTCCTGCTCCTATTGAAGAAATACTTCTG
Astroviridae	Astroviridae_20514394_47	CAACCTCAACCTCAACCTCCTGCTCCTATTGAAGAAATACTTCTGCCTTTAGCAGAACTG
Parvoviridae	Parvoviridae_51949963_15	ACACCATCTGGCTGTTTGGACCCGCCACCACCGGCAAGACCAACATTGCGGAAGCCATCG
Adenoviridae	Adenoviridae_46852402_27	ACCGCCTCCACCCTGGAGGCCATGCTGCGCAACGACACCAACAACCAAACCTTTATTGAC
Circoviridae	Circoviridae_12280941_24	TGCCAACTTTGTAACCCCCTCCACCAACTTGGCCTATGACCCCTATATTAACTACTCCTC
Herpesviridae	Herpesviridae_126882977_334	CAGCCCTCTCAGCCCAAAGCCATTACTAAAGTCCCGTTGTATGTACAAGCGCAAGAGGAA
Picornaviridae	Picornaviridae_9626123_24	ATAGCCTACACCCCGCCTGGTGCGGGAAAGCCCACCACCCGGGACCAAGCTATGCAGGCT
Picornaviridae	Picornaviridae_157939778_31	TCGAGAGCAACCCTGGCCCTCTGTATGTTTGTTCCCAACCAGGTAAGTGCGATCCATTTC
Herpesviridae	Herpesviridae_9629267_432	GCCCTGGGCCCCGAGGCCATCCAGGCGCGGCTGGAGGACGTGCGGATCCAGGCCCGCCGG
Deltavirus	Deltavirus_13277517_18	GGTCAACCTCCTAAGTTCCTCTTCCTCCTCCTTGCTGAGGTTCTTTCCCCCCGCCGATAG
Flaviviridae	Flaviviridae_157781208_384	TTTATCACAGCATGTCTCATGCCCGACCCCGCTATTTACTCCTGTGCCTACTCATACTTA
Parvoviridae	Parvoviridae_51593836_90	TCAACAAGAGGAACACCGTCTGGCTCTACGGACCCGCCACGACCGGCAAGACCAACATCG

Subgroup analysis was performed through identifying normalized probe intensity of each individual patient that was greater than the average +2 standard deviations. Probes selected for further analysis were found in >25% of the pSS samples tested.

Supplemental Table 4. Significant pairwise correlations identified between probes significantly increased in >25% of the pSS patient population compared to healthy controls.

Variable	by Variable	Correlation	Count	Lower 95%	Upper 95%	Signif Prob
Deltavirus_13277517_18	Astroviridae_20514394_47	0.9268	15	0.7892	0.9758	<.0001
Flaviviridae_157781208_384	Parvoviridae_51949963_15	0.9121	15	0.7506	0.9708	<.0001
Parvoviridae_51593836_90	Picornaviridae_9626123_24	0.9097	15	0.7443	0.97	<.0001
Parvoviridae_51593836_90	Flaviviridae_157781208_384	0.9056	15	0.7336	0.9685	<.0001
Flaviviridae_157781208_384	Picornaviridae_9626123_24	0.8666	15	0.6373	0.9549	<.0001
Circoviridae_12280941_24	Astroviridae_20514394_18	0.8614	15	0.6248	0.9531	<.0001
Parvoviridae_51593836_90	Parvoviridae_51949963_15	0.8607	15	0.6231	0.9528	<.0001
Circoviridae_12280941_24	Astroviridae_20514394_47	0.8038	15	0.4956	0.9322	0.0003
Deltavirus_13277517_18	Circoviridae_12280941_24	0.8094	15	0.5076	0.9343	0.0003
Astroviridae_20514394_47	Astroviridae_20514394_18	0.7947	15	0.4764	0.9288	0.0004
Parvoviridae_51593836_90	Herpesviridae_9629267_432	0.7615	15	0.4087	0.9163	0.001
Herpesviridae_9629267_432	Parvoviridae_51949963_15	0.7122	15	0.3148	0.8972	0.0029
Herpesviridae_9629267_432	Picornaviridae_157939778_31	-0.7074	15	-0.8952	-0.306	0.0032
Picornaviridae_9626123_24	Parvoviridae_51949963_15	0.7059	15	0.3034	0.8947	0.0033
Deltavirus_13277517_18	Parvoviridae_51949963_15	-0.6949	15	-0.8903	-0.2837	0.004
Deltavirus_13277517_18	Astroviridae_20514394_18	0.6884	15	0.2721	0.8877	0.0045
Flaviviridae_157781208_384	Deltavirus_13277517_18	-0.6727	15	-0.8813	-0.2447	0.006
Flaviviridae_157781208_384	Herpesviridae_9629267_432	0.6656	15	0.2326	0.8784	0.0068
Parvoviridae_51949963_15	Astroviridae_20514394_47	-0.6512	15	-0.8724	-0.2084	0.0086
Parvoviridae_51593836_90	Deltavirus_13277517_18	-0.6162	15	-0.8577	-0.1519	0.0144
Herpesviridae_9629267_432	Picornaviridae_9626123_24	0.5904	15	0.112	0.8466	0.0205
Flaviviridae_157781208_384	Astroviridae_20514394_47	-0.5871	15	-0.8452	-0.107	0.0214
Herpesviridae_9629267_432	Herpesviridae_126882977_334	0.5414	15	0.0403	0.8249	0.0371
Picornaviridae_157939778_31	Parvoviridae_51949963_15	-0.5293	15	-0.8194	-0.0233	0.0425
Flaviviridae_157781208_384	Picornaviridae_157939778_31	-0.5287	15	-0.8191	-0.0225	0.0428
Deltavirus_13277517_18	Picornaviridae_9626123_24	-0.5253	15	-0.8176	-0.0179	0.0443

Significant pairwise correlations between viral probes revealed two distinct viral profiles present within the pSS patient population. (PCC, n=15, p<0.05. Table is ranked on statistical significance of correlation.

A.

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HDV_M21012_nt883-nt1287      GAGATGCCATGCCGACCCGAAGAGGAAAGAAGGACGCGAGACGCAAACCT 50
pSS-20                       GAGATGCCATGCCGACCCGAAGAGGAAAGAAGGACGCGAGACGCAAACCT 50
pSS-3                        GAGATGCCATGCCGACCCGAAGAGGAAAGAAGGACGCGAGACGCAAACCT 50
pSS-9                        GAGATGCCACGCCGACCCGAAGAGGAAAGAAGGACGCGAGACGCAAACCT 50
pSS-7                        TAGATGCCATGCCGACCCGAAGAGGAAAGAAGGACGCGAGACGCAAACCT 50
                              ******** ****************************************

HDV_M21012_nt883-nt1287      GTGAGTGGAAACCCGCTTTATTCACTGGGGTCGACAACTCTGGGGAGAAA 100
pSS-20                       GTGAGTGGAA-CCCGCTTTATTCACTGGGGTCGACAACTCTGGGGAGAAA 99
pSS-3                        GTGAGTGGNAACCCGCTTTATTCACTGGGGTCGACAAYTCTGGGGAGAAA 100
pSS-9                        GTGAGTGGNAACCCGCTTTATTCACTGGGGTCGACAACTCTGGGGAGAAA 100
pSS-7                        GTGAGTGGNAACCCGCTTTATTCACTGGGGTYGACAACTYTGGGGAGAAA 100
                             ******** * ******************** ***** * **********

HDV_M21012_nt883-nt1287      AGGGCGGATCGGCTGGGAAGAGTATATCCTATGGAAATCCCTGGTTTCCC 150
pSS-20                       AGGGCGGATCGGCTGGGAAGAGTATATCCCATGGAAATCCCTGGTTTCCC 149
pSS-3                        AGGGCGGATCGGCTGGGAAGAGTATATCCTATGGAAATCCCTGGTTTCCC 150
pSS-9                        AGGGCGGATCGGCTGGGAAGAGTATATCCTATGGAAATCCCTGGTTTCCC 150
pSS-7                        AGGGCGGATYGGCTGGGAAGAGTATATCCTATGGAAATCCCTGGTTTCCC 150
                             ********* ****************** *********************

HDV_M21012_nt883-nt1287      CTGATGTCCAGCCCCTCCCCGGTCCGAGAGAAGGGGGACTCCGGGACTCC 200
pSS-20                       CTGATGTCCAGCCCCTCCCCGGTCCGAGAGAAGGGGGACTCCGGGACTCC 199
pSS-3                        CTGATGTCCAGCCCCTCCCCGGKCCGAGAGAAGGGGGACTCCGGGACTCC 200
pSS-9                        CTGATGTCCAGCCCCTCCCCGGTCCGAGAGAAGGGGGACTCCGGGACTCC 200
pSS-7                        CTGATGTCCAGCCCCTCCCCGGTCCGAGAGAAGGGGGACTCCGGGACTCC 200
                             ********************** ***************************

HDV_M21012_nt883-nt1287      CTGCAGATTGGGGACGAAGCCGCCCCCGGGCGCTCCCCTCGATCCACCTT 250
pSS-20                       CTGCAGATTGGGGACGAAGCCGCCCCCGGGCGCTCCCCTCGATCCACCTT 249
pSS-3                        CTGSAGATTGGGGACGAAGCCGCCCCCGGGCGCTCCCCTCGATCCACCTT 250
pSS-9                        CTGCAGATTGGGGACGAAGCCGCCCCCGGGCGCTCCCCTCGATCCACCTT 250
pSS-7                        CTGCMGATTGGGGACGAARCCSCCCCCGGGCGCTCCCCTCGATCCACCTT 250
                             ***  ************* ** ****************************

HDV_M21012_nt883-nt1287      CGAGGGGGTTCACACCCCCAACCGGCGGGCCGGCTACTCTTCTTTCCCTT 300
pSS-20                       CGAGGGGGTTCACACCCCCAACCGGCGGGCCGGCTACTCTTCTTTCCCTT 299
pSS-3                        CGAGGGGGTTCACACCCCCMACCGGCGGGCCGGCTACTCTTCYTTCCCTT 300
pSS-9                        CGAGGGGGTTCACACCCCCAACCGGCGGGCCGGCTACTCTTCTTTCCCTT 300
pSS-7                        CGAGGGGGTTCACACCCCCAACCGGCGGGCCGGCTACTCTTCTTTCCCTT 300
                             ******************* ********************** *******

HDV_M21012_nt883-nt1287      CTCTCGTCTTCCTCGGTCAACCTCCTGAGTTCCTCTTCTTCCTCCTTGCT 350
pSS-20                       CTCTCGTCTTCCTCGGTCAACCTCCTGAGTTCCTCTTCTTCCTCCTTGCT 349
pSS-3                        CTCTCGTCTTCCTCGGTCAACCTCCTGARTTCCTCTTCTTCCTCCTTGCT 350
pSS-9                        CTCTCGTCTTCCTCGGTCAACCTCCTGAGTTCCTCTTCTTCCTCCTTGCT 350
pSS-7                        CTCTCGTCTTCCTCGGTCAACCTCCTGAGTTCCTCTTCTTCCTCCTTGCT 350
                             **************************** *********************

HDV_M21012_nt883-nt1287      GAGGTTCTTGCCTCCCGCCGATAGCTGCTTCTTCTTGTTCTCGAGGGCCT 400
pSS-20                       GAGG-TCTTGCCTCCCGCCGATAGCTGCTTCTTCTTGTTCTCGAGGGCCT 398
pSS-3                        GNAGTTCTTGCCTCCCGCCGATAGCTGCTTCTTCTTGTTCTCGAGGGCCT 400
pSS-9                        GTGKTTCTTGCCTCCCGCCGATAGCTGCTTCTTCTTGTTCTCGAGGGCCT 400
pSS-7                        GAGGTTCTTGCCTCCCGCCAATAGCTGCTTCTTCTTGTTCTCAAGGGCCT 400
                             *    ************** ********************** *******

HDV_M21012_nt883-nt1287      TCCTT 405
pSS-20                       TCCTT 403
pSS-3                        TCCTT 405
pSS-9                        TCCTT 405
pSS-7                        TCCTT 405
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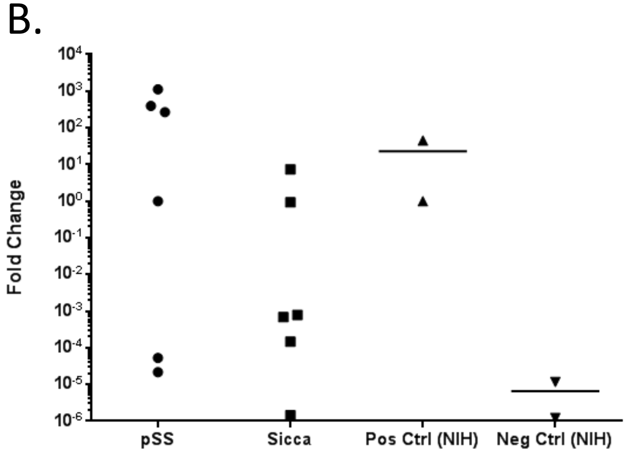


Supplemental Figure 1. HDV sequence was detected in salivary glands obtained from pSS and sicca patients. A) Nested PCR was used to detect HDV genomic sequence in minor salivary gland tissue. Sequence homology (98.5% (97.3%-99.3%)) was observed within nested PCR. B) Nested qPCR retargeted to the region encompassing HDAg transcript and genome was used to confirm the viral sequence present in a second pSS cohort and in a selection of patients experiencing sicca symptoms but did not meet full criteria for diagnosis. Two samples identified as positive and two samples identified as negative by qPCR performed on UK co-hort were independently processed and utilized as positive and negative controls in independent confirmation of HDV by nested qPCR in additional UK co-hort.

Supplemental Table 5. Evidence of past or current hepatitis B virus (HBV) infection or antibodies to HDV not detected in HDV positive pSS patients.

Detection by Elisa	Healthy Controls (%)	primary Sjögren's syndrome (%)
HBsAg	0/11 (0%)	0/13 (0%)
Anti-HBc Elisa	1/8(12.5%)	1/13 (7.7%)#
Anti-HBc LIPS	2/7(28.6%)	1/12(8.3%)#
Anti-HDAg Elisa	0/8 (0%)	0/21(0%)
Anti-HDAg LIPS	0/7(0%)	0/10(0%)

Antibodies to HDAg and Hepatitis B virus core (HBc) and HBV surface antigen (HBsAg) were quantified in serum by ELISA and the LIPS assay. [#]The pSS patient positive for anti-HBc was negative for HDV within the salivary gland.

Supplemental Table 6. Analysis of Hepadnaviridae probes on viral microarray did not find evidence of HBV differentially expressed in pSS or in pSS that possessed HDV in salivary gland tissue relative to healthy controls.

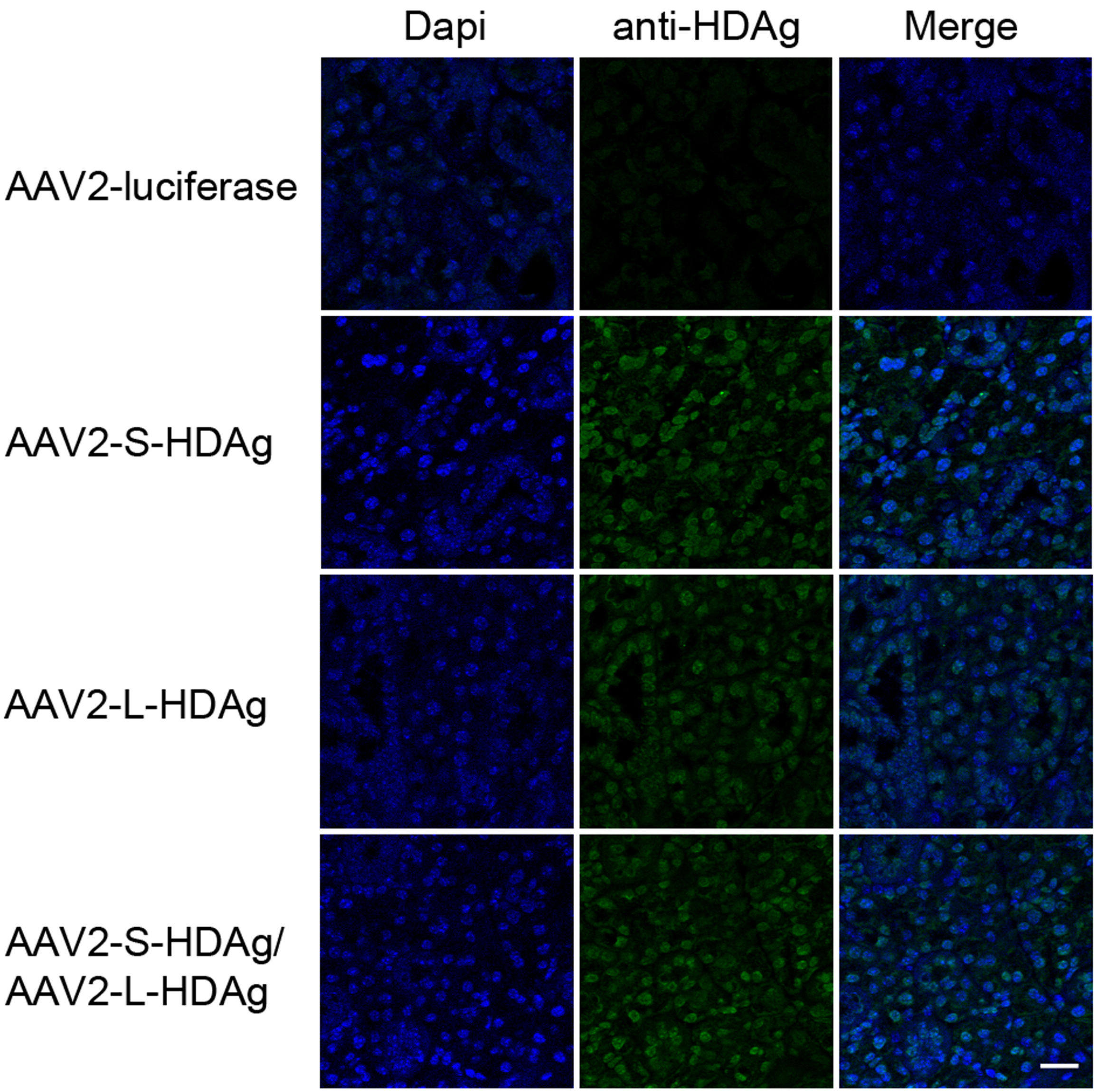
		pSS versus Healthy Controls		HDV+pSS versus Healthy Controls		HDV- pSS versus Healthy Controls	
Family Name	**Probe Name**	**p (Corr)**	**FC**	**p (Corr)**	**FC**	**p (Corr)**	**FC**
Hepadnaviridae	Hepadnaviridae_9626719_104	0.92	1.05	0.80	1.33	0.84	-1.34
Hepadnaviridae	Hepadnaviridae_48696569_109	0.88	-1.25	0.80	-1.69	0.85	1.26
Hepadnaviridae	Hepadnaviridae_48696604_116	0.84	-1.44	0.80	-1.52	0.85	-1.34
Hepadnaviridae	Hepadnaviridae_22256030_12	0.72	-1.23	0.80	-1.21	0.84	-1.26
Hepadnaviridae	Hepadnaviridae_9630370_13	0.51	-1.91	0.62	-2.02	0.84	-1.75
Hepadnaviridae	Hepadnaviridae_21326584_14	0.88	-1.15	0.91	1.08	0.84	-1.59
Hepadnaviridae	Hepadnaviridae_9630370_14	0.77	1.59	0.88	1.27	0.78	2.21
Hepadnaviridae	Hepadnaviridae_9630370_15	0.88	1.20	0.80	1.42	0.91	-1.08
Hepadnaviridae	Hepadnaviridae_21326584_16	0.72	-2.05	0.80	-2.60	0.85	-1.43
Hepadnaviridae	Hepadnaviridae_21326584_16	0.72	1.38	0.80	1.37	0.84	1.38
Hepadnaviridae	Hepadnaviridae_9628827_17	0.77	1.13	0.92	-1.02	0.54	1.38
Hepadnaviridae	Hepadnaviridae_48696604_18	0.91	-1.23	0.80	-1.53	0.91	1.13
Hepadnaviridae	Hepadnaviridae_9626719_20	0.72	1.50	0.80	1.63	0.85	1.31
Hepadnaviridae	Hepadnaviridae_9630370_20	0.72	-1.15	0.88	-1.06	0.78	-1.31
Hepadnaviridae	Hepadnaviridae_21326584_21	0.77	-1.77	0.80	-2.07	0.85	-1.39
Hepadnaviridae	Hepadnaviridae_22256030_22	0.76	1.29	0.80	1.45	0.86	1.08
Hepadnaviridae	Hepadnaviridae_9628827_22	0.45	1.52	0.27	1.74	0.78	1.24
Hepadnaviridae	Hepadnaviridae_9630370_23	0.91	-1.16	0.92	1.06	0.85	-1.60
Hepadnaviridae	Hepadnaviridae_22256030_29	0.51	1.36	0.55	1.51	0.84	1.15
Hepadnaviridae	Hepadnaviridae_9628827_29	0.45	1.52	0.27	1.79	0.84	1.18
Hepadnaviridae	Hepadnaviridae_9628827_3	0.72	1.34	0.80	1.23	0.53	1.53
Hepadnaviridae	Hepadnaviridae_9630370_3	0.98	1.01	0.91	1.11	0.85	-1.15
Hepadnaviridae	Hepadnaviridae_9628827_8	0.91	1.07	0.80	-1.36	0.54	1.87
Hepadnaviridae	Hepadnaviridae_9630370_8	0.92	1.06	0.91	1.11	0.99	-1.01
Hepadnaviridae	Hepadnaviridae_21326584_9	0.72	1.51	0.80	1.84	0.85	1.12
Hepadnaviridae	Hepadnaviridae_22256030_9	0.77	1.25	0.88	-1.12	0.48	2.06
Hepadnaviridae	Hepadnaviridae_9630370_9	0.88	1.22	0.80	1.54	0.85	-1.17

Evaluation of HBV transcripts as detected by the viral microarray showed no significant difference in HBV transcripts levels between pSS patient samples and healthy controls showed. Evaluation of just the 9 samples that presented with HDV probe intensity above the 99%CI of HDV probe intensity of the healthy controls did not reveal a differential expression in pSS with HDV in salivary gland tissue compared to healthy controls. No significant difference in HBV probe intensity was noted between the HDV-negative pSS patients and healthy controls. (n=14-15, ttest, Benjamini-Hochberg correction (p Corr), was utilized to calculate statistical significance. FC = fold change)

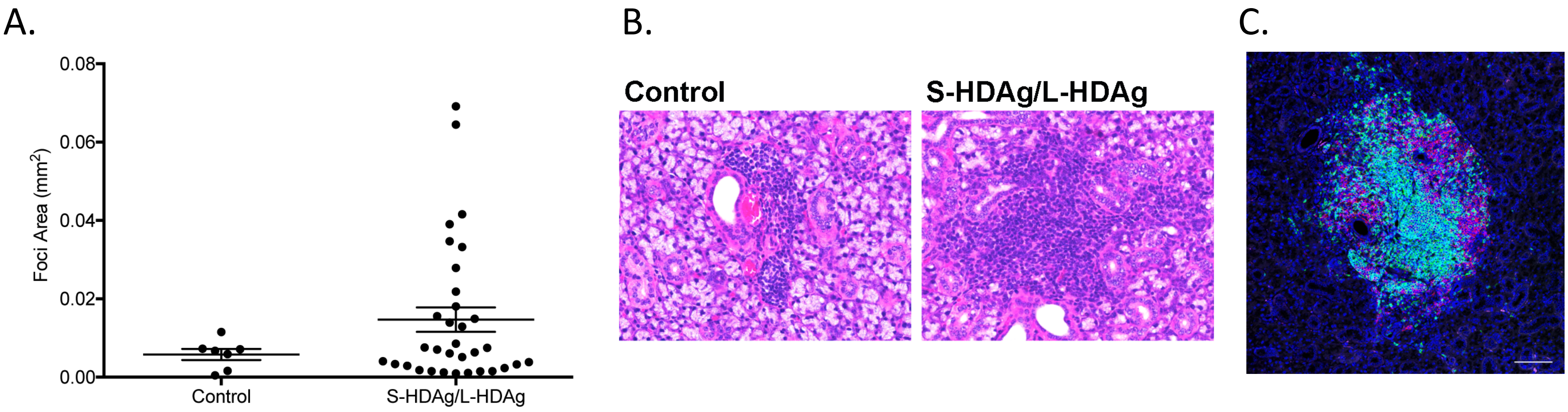
Supplemental Table 7. Correlations between clinical parameters and HDV levels in minor salivary gland biopsy.

Variable	By Variable	Correlation	Signif Prob
Anti-ANA Antibody	HDV	0.4475	0.0420*
Anti-SSA/Ro Antibody	HDV	0.5082	0.0187*
Anti-SSB/La Antibody	HDV	-0.0398	0.8639
Albumin	HDV	-0.0624	0.7937
Aspartate Aminotransferase (AST)	HDV	-0.1075	0.6519
Alanine Aminotransferase (ALT)	HDV	-0.2411	0.3058
Alkaline Phosphatase (ALP)	HDV	-0.277	0.2372

Select autoantibodies in serum significantly correlated with levels of HDV detected in minor salivary glands of healthy volunteers compared to patients diagnosed with primary Sjögren’s syndrome. Levels of ANA and Anti-SSA/Ro antibody significantly correlated with levels of HDV as determined by microarray detection. Liver function tests, including measurement of serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were all within normal range (data not shown) and did not significantly correlate with levels of HDV detected in salivary gland tissue. (PCC,*p<0.05, n=21-23).



Supplemental Figure 2. Detection of HDAg in mouse salivary gland tissue in mice cannulated with AAV-HDAg. Retrograde cannulation was used to delivery recombinant adeno-associated virus serotype 2 (rAAV-2) containing HDV genes to salivary gland tissue in female C57BL/6 mice. Salivary gland tissue was evaluated 4 months post cannulation for expression of HDAg (green), and dapi (blue) for nuclear localization. Scale bar 20μm



Supplemental Figure 3. Focal size of lymphocytic infiltrates were larger in mice expressing the combined S-HDAg and L-HDAg compared to foci size observed in mice expressing S-HDAg/L-HDAg in salivary gland tissue. A) Area of foci in mice expression a combination of both the small and large HDV antigen revealed an increase in size a subset of the observed foci (n.s., n=7-33). There was a significant increase in variance of size in the treated mice compared to the control mice (F-test, p=0.0008). B) Lymphocytic foci representative of the average size of foci present in control mice that expressed luciferase in salivary gland tissue (2.5E-3 mm^2). Average size of foci in the mice expressing S-HDAg/L-HDAg is 13.1E-3mm^2 in control mice. Images of lymphocytic foci representative of the average size of foci present. C) Ectopic lymphoid structures were evident in mice expressing combined S-HDAg/L-HDAg. Distribution of T-cell CD3 (green) and B-cell B220 (red) depict transition to organized lymphoid-like structures (bar 100um).