**Supplementary information for the manuscript:**

**"Sjögren's and non-Sjögren's sicca share a similar symptom burden but with a distinct symptom-associated proteomic signature"**

Valentina Pucino[1,2*], Jason D. Turner[1*], Saba Nayar[1], Florian Kollert[3], Saaeha Rauz[1,4], Andrea Richards[5], Jon Higham[5], Ana Poveda-Gallego[1,5], Simon J. Bowman[1,2], Francesca Barone[1,2,6] and Benjamin A. Fisher[1,2]

**Supplementary Table 1 – Associations between proteins and symptoms (ESSPRI).** Values shown are the unstandardized coefficients and 95% confidence intervals.

| Proteins vs ESSPRI | SjS (n = 53) | | Sicca (n = 60) | |
|---|---|---|---|---|
| | B (95% CI) | P value | B (95% CI) | P value |
| ADM | 0.15 (-1.22 to 1.53) | 0.83 | 2.2 (1.44 to 3) | **<0.0001** |
| TNFRSF13B | -0.3 (-1.5 to 0.9) | 0.60 | 1.9 (0.64 to 3.17) | **0.004** |
| FGF_23 | 0.7 (-0.42 to 1.82) | 0.21 | 1.9 (0.70 to 3.1) | **0.005** |
| CD40 | -0.1 (-2.1 to 1.9) | 0.92 | 2.9 (1.5 to 4.4) | **0.0001** |
| IL_10RB | 0.35 (-1.77 to 2.48) | 0.74 | 3.5 (1.6 to 5.4) | **0.001** |
| CD5 | -0.5 (-2.65 to 1.64) | 0.63 | 1.9 (0.53 to 3.34) | **0.008** |
| CD4 | -1.3 (-3.44 to 0.82) | 0.22 | 2.6 (1.2 to 4.04) | **0.001** |
| ACE2 | 0.75 (-0.48 to 1.99) | 0.23 | 1.7 (0.88 to 2.47) | **<0.0001** |
| LEP | 0.2 (-0.64 to 1.04) | 0.80 | 0.8 (0.21 to 1.35) | **0.009** |
| TRAIL_R2 | -0.04 (-1.60 to 1.52) | 0.75 | 2.1 (0.90 to 3.33) | **0.001** |

| | | | | |
|---|---|---|---|---|
| **SPON2** | -4.3 (-8.28 to -0.33) | **0.03** | 4.3 (1.1 to 7.8) | **0.01** |
| **PD_L1** | -0.24 (-0.42 to 0.19) | 0.42 | 1.35 (0.26 to 2.45) | **0.02** |
| **SLAMF1** | 0.4 (-1.15 to 2.01) | 0.73 | 1.4 (0.32 to 2.5) | **0.01** |
| **CSF_1** | -0.03 (-3 to 2.94) | 0.98 | 4.4 (1.82 to 7.05) | **0.001** |
| **IL_1ra** | 0.35 (-0.73 to 1.43) | 0.52 | 0.96 (0.1 to 1.8) | **0.03** |
| **Gal_9** | -0.7 (-2.67 to 1.13) | 0.42 | 2.3 (0.82 to 3.86) | **0.003** |
| **TNFRSF10A** | -0.3 (-1.97 to 1.35) | 0.71 | 1.7 (0.37 to 3) | **0.01** |
| **IL_12B** | -0.02 (-0.98 to 0.93) | 0.06 | 0.4 (-0.04 to 0.90) | **0.07** |
| **TNFRSF9** | 0.01 (-1.28 to 1.3) | 0.98 | 1.4 (0.39 to 2.43) | **0.008** |
| **TNFRSF11A** | 0.01 (-1.51 to 1.69) | 0.91 | 1.4 (0.28 to 2.91) | **0.02** |

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance
placed on this supplemental material which has been supplied by the author(s)

*RMD Open*

**Supplementary Table 2 – Results of multiple regression analysis model (forward) for proteins and symptoms in sicca patients.** Values shown are the unstandardized coefficients and 95% confidence intervals.

| Variables vs ESSPRI | Model (Forward) | |
|---|---|---|
| | B (95% CI) | P value |
| ADM | 2.5 (1.6-3.6) | < 0.0001 |
| CD40 | 2.5 (1.1-3.8) | < 0.0001 |
| SPON2 | -4.6 (-8.6-1.2) | 0.009 |

**Supplementary Table 3 - Correlations between ADM and clinical/immunological variables.** Values shown are the unstandardized coefficients and 95% confidence intervals.

| ADM versus clinical parameters | SjS (n = 53) | | Sicca (n = 60) | |
| --- | --- | --- | --- | --- |
| | B (95% CI) | P value | B (95% CI) | P value |
| Age | 0.01 (0.003 to 0.02) | **0.01** | 0.02 (0.01 to 0.03) | **0.001** |
| BMI | 0.03 (0.01 to 0.05) | **0.01** | 004 (0.02 to 0.07) | **0.001** |
| Weight | 0.01 (0.0001 to 0.01) | **0.04** | 0.01 (0.003 to 0.20) | **0.01** |
| Fat mass | -0.005 (-0.003 to 0.01) | 0.22 | 0.004 (-0.003 to 0.01) | 0.25 |
| Free fat mass | 0.003 (-0.01 to 0.02) | 0.62 | 0.02 (-0.003 to 0.36) | 0.09 |
| Leptin | 0.2 (0.1 to 0.36) | **0.004** | 0.3 (0.15 to 0.41) | **<0.0001** |
| VAS global (patient) | -0.003 (-0.01 to 0.005) | 0.43 | -0.01 (-0.02 to -0.002) | **0.008** |
| EQ5D | 0.10 (-0.35 to 0.55) | 0.65 | -0.7 (-1.16 to -0.28) | **0.002** |
| IgG | -0.004 (-0.21 to 0.13) | 0.66 | 0.06 (-0.01 to 0.13) | 0.07 |
| C3 | 0.7 (0.19 to 1.23) | **0.008** | 0.6 (0.06 to 1.13) | **0.03** |

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

*RMD Open*

| | | | | |
|---|---|---|---|---|
| **C4** | 0.7 (-0.64 to 1.41) | 0.45 | 0.6 (-0.25 to 2.96) | 0.1 |
| **K/L free light chain quotient** | 0.01 (-0.12 to 0.14) | 0.86 | 0.33 (0.10 to 0.71) | **0.01** |
| **Focus score** | 0.01 (-0.14 to 0.17) | 0.86 | 0.01 (-0.47 to 0.48) | 0.98 |
| **Schirmer's test** | -0.01 (-0.02 to 0.005) | 0.09 | -0.01 (-0.02 to 0.003) | 0.13 |
| **Unstimulated salivary flow** | -0.1 (-0.35 to 0.09) | 0.24 | -0.15 (-0.27 to -0.02) | **0.02** |

**Supplementary Table 4 – Multiple regression analysis models for proteins and symptoms in sicca patients.** Values shown are the unstandardized coefficients and 95% confidence intervals.

| Variables vs ESSPRI | Individual predictors | | Model 1 (Multiple regression) | | Model 2 (Forward) | |
|---|---|---|---|---|---|---|
| | β (95% CI) | P value | β (95% CI) | P value | β (95% CI) | P value |
| Age | 0.06 (0.01-0.1) | **0.02** | -0.01 (-0.1-0.1) | 0.44 | - | - |
| BMI | 0.16 (0.06-0.26) | **0.002** | 0.06 (-0.1-0.2) | 0.16 | - | - |
| HADS D | 0.16 (0.03-0.3) | **0.01** | 0.1 (-0.1-0.3) | 0.07 | 0.2 (0.04-0.3) | **0.008** |
| C3 | 1.6 (-0.9-4.2) | 0.20 | -0.7 (-2.9-5.6) | 0.42 | - | - |
| Unstimulated salivary flow | -0.6 (-1.1—0.1) | **0.02** | -0.12 (-1.7-1.8) | 0.50 | - | - |
| ADM | 2.2 (1.4-3) | **< 0.0001** | 2.3 (1.3-3.5) | **<0.0001** | 2.5 (1.5-3.4) | **< 0.0001** |
| CD40 | 2.9 (1.5-4.4) | **< 0.0001** | 2.5 (1.2-3.8) | **0.001** | 2.5 (1.2-3.8) | **< 0.0001** |
| SPON2 | 4.3 (1.1-7.7) | 0.01 | -4.5 (-8--1.3) | **0.01** | -4.6 (-8.6-1.2) | **0.009** |