**Supplementary Table S1**. Cytokines analysed by Mesoscale.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cytokines**  **(n=30)** | **Number of samples analyzed** | | **% Detected above LLOQa** | | **Excluded**  **(n=10)b** |
|  | **SLE** | **Control** | **SLE** | **Control** |  |
| INF-γ | 422 | 317 | 98 | 98 |  |
| IL-12p70 | 422 | 317 | 19 | 10 | x |
| IL-1β | 433 | 319 | 8 | 1 | x |
| IL-4 | 433 | 319 | 3 | 0 | x |
| IL-8 | 433 | 319 | 100 | 98 |  |
| GM-CSF | 423 | 316 | 16 | 5 | x |
| IL-15 | 434 | 318 | 99 | 96 |  |
| IL-17A | 434 | 318 | 23 | 8 | x |
| IL-5 | 423 | 316 | 8 | 3 | x |
| TNF-β | 434 | 318 | 22 | 17 | x |
| Eotaxin | 434 | 318 | 99 | 100 |  |
| IL-8 HL | 434 | 318 | 2 | 0 | x |
| MCP-1 | 434 | 318 | 99 | 99 |  |
| MDC | 434 | 318 | 100 | 100 |  |
| MIP-1β | 434 | 318 | 100 | 100 |  |
| IL-10 | 422 | 317 | 80 | 52 |  |
| IL-13 | 433 | 319 | 3 | 3 | x |
| IL-2 | 433 | 319 | 7 | 6 | x |
| IL-6 | 433 | 319 | 89 | 64 |  |
| TNF-α | 433 | 319 | 100 | 100 |  |
| IL-12/IL-23p40 | 434 | 318 | 100 | 100 |  |
| IL-16 | 434 | 318 | 98 | 99 |  |
| IL-1α | 412 | 298 | 96 | 94 |  |
| IL-7 | 432 | 318 | 94 | 88 |  |
| VEGF | 434 | 318 | 100 | 100 |  |
| *Eotaxin-3* | *434* | *318* | *49* | *37* |  |
| IP-10 | 334 | 318 | 99 | 100 |  |
| MCP-4 | 434 | 318 | 100 | 100 |  |
| *MIP-1α* | *434* | *318* | *62* | *24* |  |
| TARC | 434 | 318 | 95 | 99 |  |

The number of samples successfully analysed and the number (%) of quantifiable samples are reported.

a Number of samples in percent that were above lower limit of quantification (LLOQ) and included in the calculations. Eotaxin-3 and MIP-1α were detected above LLOQ in less than 50% of the controls (highlighted in italic) and IL-10 and IL-6 in less than 65% of the controls (n>160). All other included cytokines were detected in >85% of the samples.

b Only cytokines detected above LLOQ in more than 25% of the samples in SLE or control were included from further analysis. Ten cytokines were excluded.

**Supplementary Table S2.** Investigated potential biomarkers and their correlations to disease activity in patients without nephritis according to ACR criteria.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Concentrationa** | | | **p-valueb** | | | **SLE No Nephritis**  **Spearman’s Correlation to DAc** | | |
|  | **SLE No Nephritis**  (n=257) | **SLE**  **Nephritis**  (n=180) | **SLE No Nephritis**  **vs. SLE Nephritis** | | **SLE No Nephritis vs. Control** | **SLAMd**  (n=257) | | **SLEDAI-2Ke**  (n=257) | **PtGDAf**  (n=77) |
| Cytokines | | | | | | | | | |
| INF-γ | 10.9  (7.0-17.8) | 14.0  (7.1-27.7) | P=0.01 | | P<0.0001 | 0.04  (p=0.6) | | 0.05  (p=0.01) | -0.04  (p=0.7) |
| IL-8 | 5.1  (3.3-8.6) | 4.8  (2.9-8.9) | P=0.4 | | P<0.0001 | 0.09  (p=0.1) | | 0.15  (p=0.4) | 0.09  (p=0.4) |
| IL-15 | 2.8  (2.3-3.7) | 3.2  (2.4-5.0) | P=0.0003 | | P<0.0001 | **0.25**  **(p<0.0001)** | | 0.22  (p=0.0004) | 0.17  (p=0.14) |
| Eotaxin | 131.0  (94.4-184.5) | 142.5  (106.4-197) | P=0.2 | | p>0.0001 | 0.005  (p=0.9) | | 0.08  (p=0.2) | 0.22  (p=0.06) |
| MCP-1 | 108.0  (82.0-150.0) | 113.5  (85.0-162.3) | P=0.3 | | P<0.0001 | 0.16  P=0.01 | | 0.22  (p=0.0005) | **0.27**  **(p=0.02)** |
| MDC | 887.0  (659-1135) | 819.0  (611-1070) | P=0.07 | | P=0.02 | -0.10  (p=0.1) | | -0.10  (p=0.1) | -0.05  (p=0.6) |
| MIP-1β | 71.3  (51.4-106.8) | 75.0  (50.5-112.5) | P=0.7 | | P<0.0001 | 0.10  (p=0.1) | | 0.17  (p=0.007) | 0.23  (p=0.04) |
| IL-10 | 0.8  (0.5-1.4) | 0.9  (0.5-1.8) | P=0.09 | | P<0.0001 | 0.20  (p=0.005) | | **0.25**  **(p=0.0003)** | 0.14  (p=0.2) |
| IL-6 | 1.2  (0.8-2.1) | 1.4  (0.9-2.6) | P=0.05 | | P<0.0001 | 0.16  (p=0.02) | | 0.16  (p=0.02) | **0.38**  **(p=0.001)** |
| TNF-α | 4.1  (2.9-5.8) | 5.1  (3.6-6.8) | P<0.0001 | | P<0.0001 | 0.21  (p=0.0008) | | 0.18  (p=0.003) | 0.14  (p=0.2) |
| IL-12/IL-23p40 | 171.0  (115.3-278) | 192.0  (131-300.5) | P=0.8 | | P<0.0001 | 0.05  (p=0.4) | | -0.002  (p=0.97) | -0.01  (p=0.9) |
| IL-16 | 191.0  (145-260) | 244.0  (173-322) | P<0.0001 | | P=0.06 | 0.04  (p=0.6) | | 0.08  (p=0.2) | 0.03  (p=0.8 |
| IL-1α | 6.1  (3.2-11.5) | 6.8  (3.2-17.2) | P=0.1 | | P=0.7 | 0.10  (p=0.1) | | 0.20  (p=0.003) | -0.21  (p=0.07) |
| IL-7 | 5.1  (3.4-8.8) | 5.0  (2.9-8.4) | P=0.3 | | P<0.0001 | 0.09  (p=0.2) | | 0.11  (p=0.08) | 0.14  (p=0.2) |
| VEGF | 74.3  (46.5-121.3) | 80.0  (52.6-138.0) | P=0.3 | | P<0.0001 | 0.10  (p=0.1) | | **0.26**  **(p<0.0001)** | 0.07  (p=0.5) |
| Eotaxin-3 | 24.7  (19.3-35.5) | 23.6  (19.1-34.6) | P=0.6 | | P=0.001 | -0.04  (p=0.7) | | 0.05  (p=0.6) | -0.14  (p=0.4) |
| **IP-10** | 751.5  (460-1316) | 665.5  (425-1283) | P=0.2 | | P<0.0001 | 0.21  (p=0.001) | | **0.25**  **(p<0.0001)** | **0.26**  **(p=0.02)** |
| MCP-4 | 84.0  (54.0-126.0) | 73.0  (52.5-116.5) | P=0.07 | | P<0.0001 | -0.03  (p=0.6) | | -0.01  (p=0.8) | 0.09  (p=0.4) |
| MIP-1α | 20.9  (16.8-27.1) | 22.6  (17.7-32.0) | P=0.08 | | P<0.0001 | 0.17  (p=0.03) | | 0.16  (p=0.04) | 0.0003  (p=1.00) |
| TARC | 89.0  (53.6-154.0) | 79.3  (51.2-131.9) | P=0.3 | | P<0.0001 | 0.02  (p=0.7) | | 0.11  (p=0.08) | 0.12  (p=0.3) |
| Standard Clinical Laboratory Measurements | | | | | | | | | |
| ESR | 19  (10-33) | 19  (11-36) | P=0.5 | | P<0.0001 | ***0.40***  ***(p<0.0001)*** | | 0.17  (p=0.009) | 0.14  (p=0.2) |
| C4 | 0.15  (0.11-0.19) | 0.14  (0.08-0.2) | P=0.2 | | P<0.0001 | -0.11 (p=0.08) | | ***-0.29***  *(p<0.0001)* | -0.01  (p=0.9) |
| C3 | 0.9  (0.8-1.1) | 0.8  (0.6-1.0) | P=0.002 | | P<0.0001 | -0.06 (p=0.4) | | *-0.22*  *(p=0.0004)* | 0.09  (p=0.4) |
| p-albumin | 39  (37-42) | 38  (33-41) | P<0.0001 | | P<0.0001 | -0.17  (p=0.007) | | -0.12  (p=0.06) | **-0.36**  (p=0.001) |
| hsCRP | 1.7  (0.7-5.2) | 1.6  (0.7-5.3) | P=0.7 | | P<0.0001 | 0.10  (p=0.1) | | 0.12  (p=0.04) | **0.29**  (p=0.01) |
| anti-dsDNA | 4  (4-13) | 8  (4-30.75) | P<0.0001 | | P<0.0001 | 0.22  (p=0.0003) | | ***0.43***  *(p<0.0001)* | 0.12  (p=0.3) |
| U-albumin/  creatinine | 0.6  (0.4-1.3) | 8.4  (1.4-55.6) | P<0.0001 | | P<0.0001 | 0.17  (p=0.01) | | 0.09  (p=0.2) | 0.11  (p=0.4) |

Concentrations of investigated potential biomarkers and u-albumin/creatinine in SLE patients without nephritis and in controls, their p-values comparing non-nephritis SLE patients and controls and their correlations to three different measurements of disease activity are reported. Biomarkers with correlations (ρ)≥|0.25| to all three disease activity measurements are highlighted in bold. Italic numbers indicates biomarkers which are included in the respective indices.

a Median (25% quantile - 75% quantile). Concentrations of cytokines are reported in pg/ml. Standard Clinical Laboratory Measurements reported as erythrocyte sedimentation rate (ESR) in mm/h, Complement factor C4 in g/L, Complement factor C3 in g/L, plasma albumin (p-albumin) in g/L, high-sensitivity (hs) CRP in mg/L, anti-dsDNA units, urinary (u-) albumin/creatinine mg/mmol.

b Mann Whitney U test. Not compensated for multiple testing (variables: n=26).

c Spearman’s correlation rho (p-value). Spearman’s ρ>0.25 are highlighted in bold. Spearmans’s ρ =|0.20-0.39| is considered as week correlation and ρ = 0.40-0.59 as moderate correlation. Italic values indicates variables included in SLAM, SLEDAI-2K or PtGDA.

d SLAM = SLE Activity Measure [4](#_ENREF_4).

e SLEDAI-2K = SLE Disease Activity Index [2](#_ENREF_2).

f PtGDA = Patients Global Disease Activity as determined by Systemic Lupus Activity Questionnaire (SLAQ) [7](#_ENREF_7).

**Supplementary Table S3.** Comparison of patients with SLEDAI-2K =0 to controls and to patients with SLEDAI-2K >0

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Controls  (n=322) | SLE  SLEDAI=0  (n=115) | SLE  SLEDAI>0  (n=322) | SLE all (n=437) | SLEDAI=0  vs. Controls a | SLEDAI=0  vs  SLEDAI>0 a |
| Cytokines b | | | | | | |
| INF-γ | 6.1  (4.6-9.9) | 10.8  (6.6-17.2) | 12.3  (7.4-20.9) | 11.7  (7.0-20.2) | **P<0.0001** | P=0.065 |
| IL-8 | 3.0  (2.2-4.0) | 4.5  (3.0-6.7) | 5.2  (3.1-9.6) | 4.9  (3.1-8.7) | **P<0.0001** | P=0.047 |
| **IL-15** | 2.1  (1.8-2.4) | 2.6  (2.3-3.2) | 3.1  (2.4-4.3) | 2.9  (2.3-4.1) | **P<0.0001** | **P=0.0003** |
| Eotaxin | 88.4  (70-114) | 131.2  (99.9-186) | 134.2  (97.6-186) | 133.5  (97.6-186) | **P<0.0001** | P=0.9 |
| MCP-1 | 69.0  (55-85) | 100.3  (77-139) | 113.5  (85-162) | 109.5  (83-152) | **P<0.0001** | P=0.01 |
| *MDC* | 939.0  (764-1109) | 886.4  (740-1164) | 836.3  (625-1094) | 844.0  (640-1120) | P=0.38 | P=0.03 |
| MIP-1β | 43.8  (33-56) | 67.8  (50-92) | 74.5  (51-114) | 72.7  (51-108) | **P<0.0001** | P=0.03 |
| IL-10 | 0.3  (0.2-0.4) | 0.69  (0.4-1.0) | 0.89  (0.5-1.7) | 0.8  (0.5-1.5) | **P<0.0001** | P=0.0048 |
| IL-6 | 0.6  (0.5-0.9) | 1.2  (0.8-2.0) | 1.3  (0.8-2.5) | 1.2  (0.7-2.2) | **p<0.0001** | P=0.087 |
| **TNF-α** | 2.3  (2.0-2.8) | 3.6  (2.9-5.4) | 4.7  (3.3-6.4) | 4.5  (3.1-6.2) | **P<0.0001** | **P=0.0003** |
| IL-12/IL-23p40 | 131.0  (99.5-179) | 168.9  (121-263) | 185.8  (124-295) | 181.0  (123-286) | **P<0.0001** | P=0.17 |
| *IL-16* | 182.0  (147-225) | 202.2  (147-254) | 215.5  (154-300) | 214.0  (152-287) | P=0.02 | 0.11 |
| *IL-1α* | 6.4  (3.4-11.7) | 5.0  (2.8-10.1) | 6.9  (3.4-15.0) | 6.3  (3.2-12.8) | P=0.067 | P=0.007 |
| IL-7 | 3.7  (2.5-5.5) | 4.2  (2.8-6.4) | 5.7  (3.6-9.3) | 5.0  (3.2-8.7) | p=0.07 | **P=0.0003** |
| VEGF | 56.7  (41-81) | 60.2  (41-101) | 82.7  (53-134) | 77.1  (48-124) | P=0.25 | **P=0.0004** |
| *Eotaxin-3* | 20.8  (15-26) | 24.4  (21-34) | 24.3  (19-35) | 24.4  (19-35) | P=0.004 | P=0.7 |
| **IP-10** | 352.0  (259-479) | 587.0  (377-950) | 775.5  (477-1471) | 725.0  (446-1309) | **P<0.0001** | **P=0.0010** |
| MCP-4 | 56.0  (41-81) | 74.9  (51-122) | 79.0  (54-124) | 78.0  (54-124) | **P<0.0001** | P=0.8 |
| MIP-1α | 12.0  (8.8-18) | 19.7  (16-25) | 21.6  (18-30) | 21.5  (17-29) | **P<0.0001** | P=0.09 |
| TARC | 54.4  (37-85) | 74.2  (51-123) | 87.4  (54-153) | 85.3  (52-150) | **P<0.0001** | P=0.15 |
| Standard Clinical Laboratory Measurements b | | | | | | |
| **ESR** | 8.5  (5-13) | 15.5  (9-28) | 21  (11-37) | 19  (11-34) | **P<0.0001** | **P=0.0003** |
| **C4** | 0.21  (0.17-0.25) | 0.18  (0.14-0.22) | 0.13  (0.09-0.18) | 0.15  (0.1-0.2) | **P=0.0001** | **P<0.0001** |
| **C3** | 1.04  (0.9-1.2) | 0.96  (0.8-1.1) | 0.84  (0.7-1.0) | 0.88  (0.7-1.0) | **P=0.0004** | **P<0.0001** |
| p-albumin | 42  (41-44) | 40  (37-42) | 39  (35-41) | 39  (36-41) | **P<0.0001** | P=0.008 |
| hsCRP | 0.93  (0.4-2.1) | 1.4  (0.6-4.2) | 1.7  (0.7-5.6) | 1.7  (0.7-5.3) | **P=0.0008** | P=0.14 |
| **Anti-dsDNA** | 4  (4-4) | 4  (4-4,5) | 8  (4-27) | 5  (4-19.5) | **P<0.0001** | **P<0.0001** |

a Mann Whitney U test. Not compensated for multiple testing. P-values <0.002 are highlighted in bold, i.e significant p-values after Bonferroni correction (26 variables).

b Variables highlighted in bold show differences both when comparing patients with SLEDAI-2K=0 to controls and to patients with SLEDAI-2K>0. Variables highlighted in italic did not show any differences when comparing patients with SLEDAI-2K=0 and controls nor with patients with SLEDAI-2K>0.