**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 | 0.16P=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) | SLESLEDAI=0(n=115) | SLESLEDAI>0(n=322) | SLE all (n=437) | SLEDAI=0vs. 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.