**Supplementary information**

**Supplementary table S1.** Norm values used for laboratory diagnosis.

| Immune Parameter | Reference Value |
|---|---|
| CD4+ T cells | 500-1500 cells/μl |
| CD8+ T cells | 250-1000 cells/μl |
| CD8-CD57+ NK cells | 30-180 cells/μl |
| CD3+16+56+ NKT cells | 20-220 cells/μl |
| CD3-CD16+CD56+ NK cells | 90-600 cells/μl |
| IgG | 7-16 g/l |
| IgA | 0.7-2.3 g/l |
| IgM | 0.4-2.3 g/l |
| IgG1 | 2.8-8.0g/l |
| IgG2 | 1.15-5.70g/l |
| IgG3 | 0.24-1.25g/l |
| IgG4 | 0.052-1.25g/l |
| MBL | <300ng/ml |
| C3c | 0.9-1.8 g/l |
| C4 | 0.1-0.4 g/l |

**Supplementary table S2.** Number of ME/CFS patients with reduced humoral immune parameters

| Parameter | No. of patients (95%CI) (n= 262) |
|---|---|
| **reduced IgG titers** | **17 (10-27)** |
| **reduced IgA titers** | **17 (10-27)** |
| **reduced IgM titers** | **13 (7-22)** |
| reduced IgG1 titers | 8 (3-16) |
| reduced IgG2 titers | 4 (1-10) |
| **reduced IgG3 titers** | **21 (13-31)** |
| **reduced IgG4 titers** | **13 (7-22)** |
| **reduced MBL levels** | **84 (69-100)** |
| **reduced C3c levels** | **41 (30-54)** |
| reduced C4 levels | 6 (2-13) |

**Supplementary table S3.** Differences of reduced immune parameters in male versus female ME/CFS patients

| parameter | male (n= 83) | female (n=179) | p-value |
|---|---|---|---|
| reduced IgG titers | 5 (6.0 %) | 12 (6.7%) | 1 |
| reduced IgA titers | 3 (3.6%) | 14 (7.8%) | 0.28 |
| **reduced IgM titers** | **8 (9.6%)** | **5 (2.8%)** | **0.02** |
| reduced IgG1 titers | 1 (1.2%) | 7 (3.9%) | 0.44 |
| **reduced IgG2 titers** | **4 (4.8%)** | **0** | **0.01** |
| reduced IgG3 titers | 10 (12.0%) | 11 (6.1%) | 0.14 |
| reduced IgG4 titers | 2 (2.4%) | 11 (6.1%) | 0.24 |
| reduced MBL levels | 30 (36.1%) | 54 (30.2%) | 0.39 |
| reduced C3c levels | 10 (12.0%) | 31 (17.3%) | 0.36 |

| | | | |
|---|---|---|---|
| reduced C4 levels | 1 (1.2%) | 5 (2.8%) | 0.67 |
| no immune changes | 35 (42.2%) | 76 (42.5%) | 1 |

For each parameter, frequencies were statistically compared by a Fisher exact test.

**Supplementary table S4.** Differences of reduced immune parameters in two age groups of ME/CFS patients

| parameter | 18-40 years (n= 131) | 41-80 years (n= 131) | p-value |
|---|---|---|---|
| reduced IgG titers | 6 (4.6%) | 11 (8.4%) | 0.32 |
| reduced IgA titers | 5 (3.8%) | 12 (9.2%) | 0.13 |
| reduced IgM titers | 6 (4.6%) | 7 (5.3%) | 1 |
| reduced IgG1 titers | 2 (1.5%) | 6 (4.6%) | 0.28 |
| reduced IgG2 titers | 4 (3.1%) | 0 | 0.12 |
| reduced IgG3 titers | 8 (6.1%) | 13 (9.9%) | 0.36 |
| reduced IgG4 titers | 9 (6.9%) | 4 (3.1%) | 0.25 |
| reduced MBL levels | 38 (29%) | 46 (35.1%) | 0.35 |
| reduced C3c levels | 26 (19.8%) | 15 (11.5%) | 0.09 |
| reduced C4 levels | 3 (2.3%) | 3 (2.3%) | 1 |
| no immune changes | 61 (46.6%) | 50 (38.2%) | 0.21 |

For each parameter, frequencies were statistically compared by a Fisher exact test.

**Supplementary table S5.** Immunodeficiencies in male versus female ME/CFS patients

| Parameter | Male (n= 53) | Female (n=114) | p-value |
|---|---|---|---|
| unclassfied antibody deficiency | 14 (26.4%) | 32 (28.1%) | 0.85 |
| selective IgA deficiency | 0 | 7 (6.1%) | 0.1 |
| IgA with IgG subclass deficiency | 1 (1.9%) | 4 (3.5%) | 1 |
| isolated IgG1 subclass deficiency | 0 | 2 (1.8%) | 1 |
| isolated IgG2 subclass deficiency | 1 (1.9%) | 0 | 0.32 |
| isolated IgG3 subclass deficiency | 6 (11.3%) | 9 (7.9%) | 0.56 |
| isolated IgG4 subclass deficiency | 0 | 7 (6.1%) | 0.1 |
| selective IgM deficiency | 3 (5.7%) | 2 (1.8%) | 0.33 |
| MBL deficiency | 7 (13.2%) | 11 (9.6%) | 0.59 |
| complement component C3 deficiency | 0 | 5 (4.4%) | 0.18 |
| complement component C4 deficiency | 0 | 1 (0.9%) | 1 |
| no immune changes | 22 (41.5%) | 39 | 0.39 |

For each parameter, frequencies were statistically compared by a Fisher exact test.

**Supplementary table S6.** Immunodeficiencies in different age groups of ME/CFS patients

| Parameter | 18-40 years (n= 86) | 41-80 years (n= 81) | p-value |
|---|---|---|---|
| unclassfied antibody deficiency | 23 (26.7%) | 23 (28.4%) | 0.86 |
| selective IgA deficiency | 2 (2.3%) | 5 (6.2%) | 0.27 |
| IgA with IgG subclass deficiency | 2 (2.3%) | 3 (3.7%) | 0.67 |
| isolated IgG1 subclass deficiency | 2 (2.3%) | 0 | 0.5 |
| isolated IgG2 subclass deficiency | 1 (1.2%) | 0 | 1 |
| isolated IgG3 subclass deficiency | 6 (6.9%) | 9 (11.1%) | 0.42 |
| **isolated IgG4 subclass deficiency** | **7 (8.1%)** | **0** | **0.01** |
| selective IgM deficiency | 3 (3.5%) | 2 (2.5%) | 1 |
| MBL deficiency | 9 (10.5%) | 9 (11.1%) | 1 |
| complement component C3 deficiency | 2 (2.3%) | 3 (3.7%) | 0.67 |
| complement component C4 deficiency | 1 (1.2%) | 0 | 1 |
| No immune changes | 30 (34.9%) | 31 (38.3%) | 0.75 |

For each parameter, frequencies were statistically compared by a Fisher exact test.