

## **Supplementary Information**

**Genetic variations in Toll-like receptors (TLRs 3/7/8) are associated with systemic lupus erythematosus in a Taiwanese population**

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**Table 1** Association of TLR 7 and TLR8 SNPs with SLE clinical phenotypes and autoantibodies in the male SLE patients

| Clinical characteristics | TLR7                          |                               |                               |                               | TLR8                          |                               |                               |                               |
|--------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
|                          | rs3853839                     |                               | rs5935436                     |                               | rs179010                      |                               | rs3764880                     |                               |
|                          | Type of analysis <sup>a</sup> | P <sub>FDR</sub> <sup>b</sup> | Type of analysis <sup>a</sup> | P <sub>FDR</sub> <sup>b</sup> | Type of analysis <sup>a</sup> | P <sub>FDR</sub> <sup>b</sup> | Type of analysis <sup>a</sup> | P <sub>FDR</sub> <sup>b</sup> |
| Oral ulcer               | + vs. -                       |                               | C vs.G                        |                               | C vs.T                        |                               | T vs.C                        |                               |
|                          |                               | 0.9587                        | 1.05 (0.20-5.65)              | 0.9587                        | 0.98 (0.04-23.05)             | 0.2182                        | 3.29 (0.94-11.50)             | 0.9587                        |
| Arthritis                | + vs. Normal                  |                               | G vs.C                        |                               | C vs.T                        |                               | T vs.C                        |                               |
|                          |                               | 0.4797                        | 1.72 (0.38-7.87)              | 0.4797                        | 1.00 (0.06-17.49)             | 0.1056                        | 3.36 (1.08-10.43)             | 0.4797                        |
| Malar rash               | + vs. -                       |                               | G vs.C                        |                               | C vs.T                        |                               | C vs.T                        |                               |
|                          |                               | 0.3115                        | 3.45 (0.81-14.74)             | 0.8650                        | 1.28 (0.08-21.35)             | 0.8650                        | 1.14 (0.43-3.05)              | 0.3115                        |
| Discoid rash             | + vs. Normal                  |                               | G vs.C                        |                               | C vs.T                        |                               | T vs.C                        |                               |
|                          |                               | 0.0546                        | 3.55 (1.07-11.76)             | 0.7331                        | 1.42 (0.18-10.90)             | 0.7331                        | 1.23 (0.62-2.44)              | 0.0514                        |
| Photosensitivity         | + vs. -                       |                               | G vs.C                        |                               | C vs.T                        |                               | C vs.T                        |                               |
|                          |                               | 0.8988                        | 1.19 (0.31-4.57)              | 0.8988                        | 1.20 (0.07-20.01)             | 0.1509                        | 2.88 (1.05-7.92)              | 0.8988                        |
| Pleural effusion         | + vs. Normal                  |                               | G vs.C                        |                               | C vs.T                        |                               | C vs.T                        |                               |
|                          |                               | 0.3404                        | 1.94 (0.74-5.10)              | 0.7534                        | 1.38 (0.18-10.60)             | 0.6829                        | 1.28 (0.61-2.71)              | 0.1618                        |
|                          | + vs. -                       |                               | G vs.C                        |                               | C vs.T                        |                               | T vs.C                        |                               |
|                          |                               | 0.9002                        | 1.30 (0.25-6.86)              | 0.9002                        | 1.28 (0.05-29.86)             | 0.9002                        | 1.35 (0.43-4.21)              | 0.9002                        |
|                          | + vs. Normal                  |                               | G vs.C                        |                               | C vs.T                        |                               | T vs.C                        |                               |
|                          |                               | 0.4330                        | 2.20 (0.49-9.82)              | 0.4330                        | 1.23 (0.07-21.30)             | 0.4330                        | 1.64 (0.60-4.48)              | 0.4330                        |
|                          | + vs. -                       |                               | G vs.C                        |                               | T vs.C                        |                               | T vs.C                        |                               |
|                          |                               | 0.5136                        | 2.15 (0.25-18.80)             | 0.5136                        | 4.50 (0.26-77.14)             | 0.5136                        | 1.50 (0.44-5.09)              | 0.5136                        |
|                          | + vs. Normal                  |                               | G vs.C                        |                               | T vs.C                        |                               | T vs.C                        |                               |
|                          |                               | 0.3866                        | 3.45 (0.44-26.99)             | 0.4577                        | 2.17 (0.27-17.56)             | 0.3866                        | 1.80 (0.60-5.44)              | 0.1530                        |
|                          | + vs. -                       |                               | G vs.C                        |                               | C vs.T                        |                               | C vs.T                        |                               |
|                          |                               | 0.5064                        | 2.15 (0.25-18.80)             | 0.5064                        | 0.89 (0.04-21.01)             | 0.0753                        | 8.87 (1.07-73.45)             | 0.2641                        |
|                          | + vs. Normal                  |                               | G vs.C                        |                               | T vs.C                        |                               | G vs.A                        |                               |
|                          |                               | 0.5064                        | 2.15 (0.25-18.80)             | 0.5064                        | 0.89 (0.04-21.01)             | 0.0753                        | 8.87 (1.07-73.45)             | 0.2641                        |
|                          | + vs. -                       |                               | G vs.C                        |                               | T vs.C                        |                               | G vs.A                        |                               |
|                          |                               | 4.70 (0.25-86.95)             |                               | 4.70 (0.25-86.95)             |                               | 4.70 (0.25-86.95)             |                               | 4.70 (0.25-86.95)             |

|  | + vs. Normal | G vs.C            | C vs.T            | C vs.T            | G vs.A            |                   |                   |                    |                   |
|--|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|
|  | 0.2794       | 3.45 (0.44-26.99) | 0.4971            | 0.92 (0.05-16.16) | 0.1573            | 5.23 (0.67-40.85) | 0.1530            | 8.66 (0.51-147.60) |                   |
| Pericardial effusion                               | + vs. -      | G vs.C            | T vs.C            | T vs.C            | A vs.G            |                   |                   |                    |                   |
|  |              | 0.5533            | 2.40 (0.28-20.85) | 0.5192            | 4.50 (0.26-77.14) | 0.9851            | 1.01 (0.29-3.50)  | 0.5192             | 2.40 (0.51-11.24) |
|  | + vs. Normal | G vs.C            | T vs.C            | T vs.C            | G vs.A            |                   |                   |                    |                   |
|  | 0.6960       | 3.76 (0.48-29.21) | 0.7816            | 2.17 (0.27-17.56) | 0.7816            | 1.31 (0.42-4.07)  | 0.7816            | 1.20 (0.33-4.43)   |                   |
| Ascites  | + vs. -      | C vs.G            | C vs.T            | C vs.T            | A vs.G            |                   |                   |                    |                   |
|  |              | 0.7199            | 3.06 (0.25-37.35) | 0.8582            | 0.19 (0.01-5.19)  | 0.8582            | 1.25 (0.11-14.51) | 0.7199             | 3.50 (0.28-43.16) |
|  | + vs. Normal | C vs.G            | C vs.T            | T vs.C            | A vs.G            |                   |                   |                    |                   |
|  | 0.9674       | 1.59 (0.14-17.69) | 0.9674            | 0.23 (0.01-4.75)  | 0.9674            | 1.05 (0.09-11.66) | 0.9674            | 1.39 (0.13-15.45)  |                   |
| Nephritis  | + vs. -      | C vs.G            | C vs.T            | C vs.T            | A vs.G            |                   |                   |                    |                   |
|  |              | 0.4011            | 2.33 (0.45-12.02) | 0.6236            | 2.00 (0.12-33.51) | 0.2297            | 2.42 (0.86-6.80)  | 0.2297             | 4.89 (0.57-41.79) |
|  | + vs. Normal | G vs.C            | C vs.T            | C vs.T            | G vs.A            |                   |                   |                    |                   |
|  | 0.7845       | 1.41 (0.64-3.11)  | 0.8110            | 1.69 (0.22-12.92) | 0.8779            | 1.05 (0.54-2.03)  | 0.7845            | 1.62 (0.73-3.57)   |                   |
| Neuropsychiatric manifestations                    | + vs. -      | G vs.C            | C vs.T            | C vs.T            | G vs.A            |                   |                   |                    |                   |
|  |              | 0.7300            | 1.69 (0.19-15.03) | 0.7300            | 0.71 (0.03-16.92) | 0.1866            | 6.82 (0.81-57.41) | 0.7300             | 1.47 (0.16-13.23) |
|  | + vs. Normal | G vs.C            | C vs.T            | C vs.T            | G vs.A            |                   |                   |                    |                   |
|  | 0.4083       | 2.82 (0.35-22.48) | 0.5353            | 0.77 (0.04-13.68) | 0.4083            | 4.28 (0.54-34.07) | 0.4083            | 3.25 (0.41-25.89)  |                   |
| Leukopenia (WBC count < 3500/uL)                   | + vs. -      | G vs.C            | C vs.T            | T vs.C            | G vs.A            |                   |                   |                    |                   |
|  |              | 0.4720            | 2.57 (0.65-10.16) | 0.7852            | 1.54 (0.09-25.72) | 0.4720            | 1.86 (0.66-5.21)  | 0.7852             | 1.22 (0.30-5.03)  |
|  | + vs. Normal | G vs.C            | C vs.T            | T vs.C            | G vs.A            |                   |                   |                    |                   |
|  | 0.1004       | 2.82 (0.98-8.08)  | 0.6761            | 1.54 (0.20-11.80) | 0.1684            | 1.65 (0.87-3.14)  | 0.1004            | 2.53 (0.97-6.59)   |                   |
| Anemia (Hb < 9 g/dL)                               | + vs. -      | C vs.G            | C vs.T            | C vs.T            | G vs.A            |                   |                   |                    |                   |
|  |              | 0.7402            | 1.33 (0.24-7.32)  | 0.7402            | 0.80 (0.03-18.97) | 0.5398            | 3.27 (0.65-16.52) | 0.7402             | 1.67 (0.19-14.89) |
|  | + vs. Normal | G vs.C            | C vs.T            | C vs.T            | G vs.A            |                   |                   |                    |                   |
|  | 0.6607       | 1.41 (0.30-6.61)  | 0.6607            | 0.85 (0.05-15.01) | 0.6457            | 2.14 (0.46-10.02) | 0.6457            | 3.61 (0.46-28.47)  |                   |
| Thrombocytopenia (Plat count <10 <sup>5</sup> /uL) | + vs. -      | G vs.C            | T vs.C            | C vs.T            | G vs.A            |                   |                   |                    |                   |

|                      |              |        |                   |        |                    |        |                   |        |                   |
|----------------------|--------------|--------|-------------------|--------|--------------------|--------|-------------------|--------|-------------------|
|                      |              | 0.3159 | 5.66 (0.67-47.81) | 0.6753 | 2.00 (0.12-33.51)  | 0.6753 | 1.25 (0.44-3.55)  | 0.6753 | 1.99 (0.38-10.47) |
|                      | + vs. Normal | G vs.C |                   | T vs.C |                    | T vs.C |                   | G vs.A |                   |
|                      |              | 0.1118 | 6.90 (0.92-51.72) | 0.8733 | 1.18 (0.15-9.22)   | 0.8733 | 1.12 (0.47-2.69)  | 0.1118 | 3.79 (0.88-16.38) |
| Complement depressed | + vs. -      | G vs.C |                   | T vs.C |                    | T vs.C |                   | A vs.G |                   |
|                      |              | 1.0000 | 1.00 (0.19-5.39)  | 0.9538 | 1.02 (0.04-24.00)  | 1.0000 | 1.05 (0.30-3.65)  | 0.9538 | 2.18 (0.25-19.18) |
|                      | + vs. Normal | G vs.C |                   | T vs.C |                    | T vs.C |                   | G vs.A |                   |
|                      |              | 0.3327 | 1.72 (0.79-3.75)  | 0.9796 | 1.02 (0.23-4.50)   | 0.3672 | 1.38 (0.77-2.47)  | 0.3175 | 1.98 (0.91-4.31)  |
| Anti-dsDNA           | + vs. -      | C vs.G |                   | T vs.C |                    | C vs.T |                   | A vs.G |                   |
|                      |              | 0.8232 | 1.21 (0.23-6.42)  | 0.6376 | 1.20 (0.05-28.07)  | 0.6376 | 1.52 (0.48-4.85)  | 0.6376 | 2.60 (0.30-22.65) |
|                      | + vs. Normal | G vs.C |                   | T vs.C |                    | T vs.C |                   | G vs.A |                   |
|                      |              | 0.3721 | 1.69 (0.77-3.69)  | 0.9587 | 1.04 (0.24-4.60)   | 0.7033 | 1.21 (0.67-2.19)  | 0.3635 | 1.94 (0.89-4.23)  |
| Anti-Sm              | + vs. -      | C vs.G |                   | T vs.C |                    | T vs.C |                   | G vs.A |                   |
|                      |              | 0.5704 | 2.27 (0.49-10.52) | 0.4472 | 5.28 (0.23-122.27) | 0.6469 | 1.40 (0.50-3.96)  | 0.6469 | 1.43 (0.31-6.62)  |
|                      | + vs. Normal | G vs.C |                   | T vs.C |                    | T vs.C |                   | G vs.A |                   |
|                      |              | 0.5230 | 1.38 (0.51-3.72)  | 0.4426 | 2.08 (0.46-9.43)   | 0.3753 | 1.68 (0.77-3.67)  | 0.2978 | 2.89 (0.86-9.75)  |
| Anti-RNP             | + vs. -      | G vs.C |                   | T vs.C |                    | T vs.C |                   | G vs.A |                   |
|                      |              | 0.6498 | 1.83 (0.32-10.32) | 0.7848 | 1.48 (0.09-24.88)  | 0.6498 | 1.62 (0.56-4.69)  | 0.5200 | 4.76 (0.53-42.39) |
|                      | + vs. Normal | G vs.C |                   | T vs.C |                    | T vs.C |                   | G vs.A |                   |
|                      |              | 0.1557 | 3.45 (0.80-14.88) | 0.9068 | 1.13 (0.14-8.81)   | 0.2205 | 1.78 (0.78-4.06)  | 0.0565 | 8.30 (1.11-62.05) |
| Anti-SSA             | + vs. -      | C vs.G |                   | C vs.T |                    | C vs.T |                   | G vs.A |                   |
|                      |              | 0.7585 | 1.27 (0.27-5.92)  | 0.7585 | 1.69 (0.10-28.93)  | 0.7585 | 1.43 (0.42-4.83)  | 0.4468 | 3.47 (0.71-16.99) |
|                      | + vs. Normal | G vs.C |                   | C vs.T |                    | T vs.C |                   | G vs.A |                   |
|                      |              | 0.9712 | 1.15 (0.46-2.90)  | 0.9712 | 1.04 (0.13-8.06)   | 0.1250 | 2.10 (0.98-4.51)  | 0.1250 | 3.01 (0.89-10.13) |
| Anti-SSB             | + vs. -      | C vs.G |                   | T vs.C |                    | T vs.C |                   | G vs.A |                   |
|                      |              | 0.6966 | 1.43 (0.24-8.65)  | 0.6966 | 5.14 (0.29-92.27)  | 0.6966 | 1.58 (0.33-7.59)  | 0.6966 | 1.63 (0.17-15.48) |
|                      | + vs. Normal | C vs.G |                   | T vs.C |                    | T vs.C |                   | G vs.A |                   |
|                      |              | 0.9410 | 1.06 (0.21-5.32)  | 0.3976 | 3.71 (0.43-31.69)  | 0.2804 | 3.51 (0.83-14.86) | 0.4957 | 2.53 (0.31-20.75) |

| Anti-cardiolipin IgG | + vs. -      | C vs.G |                  | C vs.T |                   | C vs.T |                   | A vs.G |                   |
|----------------------|--------------|--------|------------------|--------|-------------------|--------|-------------------|--------|-------------------|
|                      |              | 0.7601 | 1.32 (0.22-7.87) | 0.7601 | 0.65 (0.02-20.61) | 0.4156 | 2.70 (0.63-11.55) | 0.4156 | 2.83 (0.53-15.00) |
| Anti-cardiolipin IgM | + vs. Normal | G vs.C |                  | C vs.T |                   | C vs.T |                   | G vs.A |                   |
|                      |              | 0.7946 | 1.57 (0.34-7.26) | 0.7946 | 0.92 (0.05-16.16) | 0.7946 | 1.43 (0.38-5.35)  | 0.9067 | 1.08 (0.29-4.05)  |

  

| Anti-cardiolipin IgG | + vs. -      | C vs.G |                   | C vs.T |                  | C vs.T |                   | A vs.G |                   |
|----------------------|--------------|--------|-------------------|--------|------------------|--------|-------------------|--------|-------------------|
|                      |              | 0.7564 | 2.53 (0.22-29.25) | 0.7579 | 0.19 (0.01-6.59) | 0.7564 | 1.96 (0.19-20.44) | 0.7564 | 2.06 (0.18-23.21) |
| Anti-cardiolipin IgM | + vs. Normal | C vs.G |                   | C vs.T |                  | C vs.T |                   | G vs.A |                   |
|                      |              | 0.9581 | 1.06 (0.11-10.28) | 0.9581 | 0.31 (0.02-6.08) | 0.9581 | 1.43 (0.15-13.85) | 0.9581 | 1.08 (0.11-10.47) |

<sup>a</sup>The analysis was done by comparing allele frequencies in different clinical subgroups as described in the methods section. <sup>b</sup>P<sub>FDR</sub>: The p-value was adjusted after the FDR correction.

**Table 2 Association of TLR 7 and TLR8 SNPs with SLE clinical phenotypes and autoantibodies in the female SLE patients**

| Clinical characteristics | TLR7                          |                               |                         |                               | TLR8                    |                               |                               |                               |
|--------------------------|-------------------------------|-------------------------------|-------------------------|-------------------------------|-------------------------|-------------------------------|-------------------------------|-------------------------------|
|                          | rs3853839                     |                               | rs5935436               |                               | rs179010                |                               | rs3764880                     |                               |
|                          | Type of analysis <sup>a</sup> | P <sub>FDR</sub> <sup>b</sup> | Type of analysis        | P <sub>FDR</sub> <sup>b</sup> | Type of analysis        | P <sub>FDR</sub> <sup>b</sup> | Type of analysis <sup>a</sup> | P <sub>FDR</sub> <sup>b</sup> |
| Oral ulcer               | + vs. -                       | G vs.C                        | C vs.T                  | C vs.T                        | C vs.T                  | G vs.A                        |                               |                               |
|                          |                               | 0.6589 1.17 (0.85-1.60)       | 0.3192 1.72 (0.89-3.34) | 0.6589 1.09 (0.86-1.39)       | 0.0828 1.56 (1.10-2.21) |                               |                               |                               |
|                          |                               | GG vs.CC+CG                   | CC vs.CT+TT             | CC vs.CT+TT                   |                         | additive                      |                               |                               |
|                          |                               | 0.4059 1.22 (0.86-1.75)       | 0.2134 1.90 (0.95-3.82) | 0.4059 1.22 (0.88-1.70)       | 0.0816 1.55 (1.10-2.20) |                               |                               |                               |
|                          | + vs. Normal                  | G vs.C                        | C vs.T                  | T vs.C                        | G vs.A                  |                               |                               |                               |
|                          |                               | 0.0378 1.49 (1.10-2.02)       | 0.7986 1.26 (0.65-2.46) | 0.8567 1.05 (0.83-1.33)       | 0.0300 1.65 (1.17-2.32) |                               |                               |                               |
| Arthritis                | + vs. -                       | G vs.C                        | C vs.T                  | T vs.C                        | G vs.A                  |                               |                               |                               |
|                          |                               | 0.5250 1.22 (0.92-1.61)       | 0.7771 1.16 (0.69-1.95) | 0.7771 1.10 (0.88-1.37)       | 0.3168 1.34 (1.00-1.79) |                               |                               |                               |
|                          |                               | additive                      | additive                | additive                      | GG vs.AA+AG             |                               |                               |                               |
|                          |                               | 0.4936 1.22 (0.92-1.60)       | 0.7414 1.15 (0.69-1.92) | 0.7414 1.10 (0.88-1.36)       | 0.1369 1.47 (1.06-2.03) |                               |                               |                               |
|                          | + vs. Normal                  | G vs.C                        | T vs.C                  | T vs.C                        | G vs.A                  |                               |                               |                               |
|                          |                               | 0.0084 1.43 (1.15-1.78)       | 0.6067 1.15 (0.74-1.79) | 0.2100 1.16 (0.97-1.38)       | 0.0693 1.32 (1.04-1.67) |                               |                               |                               |
| Malar rash               | + vs. -                       | G vs.C                        | C vs.T                  | T vs.C                        | G vs.A                  |                               |                               |                               |
|                          |                               | 0.7255 1.05 (0.80-1.38)       | 0.6200 1.37 (0.82-2.28) | 0.6200 1.10 (0.89-1.36)       | 0.6200 1.16 (0.87-1.54) |                               |                               |                               |
|                          |                               | additive                      | CC vs.CT+TT             | TT vs.CC+CT                   | GG vs.AA+AG             |                               |                               |                               |
|                          |                               | 0.7042 1.05 (0.80-1.38)       | 0.5193 1.49 (0.88-2.53) | 0.5193 1.34 (0.88-2.04)       | 0.5312 1.17 (0.84-1.61) |                               |                               |                               |
|                          | + vs. Normal                  | G vs.C                        | T vs.C                  | T vs.C                        | G vs.A                  |                               |                               |                               |
|                          |                               | 0.0474 1.36 (1.09-1.70)       | 0.9001 1.04 (0.65-1.66) | 0.1952 1.17 (0.98-1.40)       | 0.1830 1.26 (0.99-1.60) |                               |                               |                               |

|                      |              | GG vs.CC+CG                            | additive                               | additive                               | GG vs.AA+AG                            |
|----------------------|--------------|--|--|--|--|
|                      |              | 0.0364 1.45 (1.11-1.88)                | 0.8572 1.04 (0.66-1.66)                | 0.1985 1.16 (0.97-1.39)                | 0.1684 1.31 (0.99-1.71)                |
| Discoid rash         | + vs. -      | C vs.G<br>0.9404 1.05 (0.74-1.49)      | C vs.T<br>0.9404 1.81 (0.81-4.02)      | T vs.C<br>0.9404 1.14 (0.87-1.50)      | G vs.A<br>0.9404 1.10 (0.76-1.60)      |
|                      |              | CC+CG vs.GG<br>0.8368 1.12 (0.76-1.67) | CC vs.CT+TT<br>0.4904 1.78 (0.79-3.99) | TT vs.CC+CT<br>0.1189 1.77 (1.10-2.85) | AG+GG vs.AA<br>0.7528 1.95 (0.45-8.47) |
|                      | + vs. Normal | G vs.C<br>0.4314 1.27 (0.90-1.78)      | C vs.T<br>0.5731 1.37 (0.61-3.07)      | T vs.C<br>0.4314 1.25 (0.95-1.64)      | G vs.A<br>0.4314 1.27 (0.88-1.84)      |
|                      |              | additive<br>0.3941 1.28 (0.91-1.80)    | CC vs.CT+TT<br>0.5090 1.38 (0.61-3.12) | TT vs.CC+CT<br>0.0680 1.85 (1.15-2.98) | additive<br>0.3941 1.28 (0.88-1.85)    |
| Photosensitivity     | + vs. -      | G vs.C<br>0.5462 1.29 (0.92-1.81)      | T vs.C<br>0.5462 1.39 (0.79-2.44)      | C vs.T<br>0.8964 1.03 (0.80-1.33)      | G vs.A<br>0.8964 1.06 (0.75-1.49)      |
|                      |              | additive<br>0.5074 1.28 (0.92-1.80)    | additive<br>0.5074 1.38 (0.79-2.41)    | CC+CT vs.TT<br>0.8404 0.95 (0.58-1.54) | AG+GG vs.AA<br>0.8404 1.12 (0.37-3.41) |
|                      | + vs. Normal | G vs.C<br>0.0264 1.61 (1.16-2.24)      | T vs.C<br>0.4404 1.55 (0.89-2.71)      | T vs.C<br>0.5881 1.10 (0.86-1.41)      | G vs.A<br>0.4404 1.23 (0.88-1.72)      |
|                      |              | additive<br>0.0251 1.63 (1.17-2.28)    | additive<br>0.3872 1.53 (0.89-2.66)    | additive<br>0.5795 1.09 (0.85-1.39)    | additive<br>0.4417 1.23 (0.88-1.72)    |
| Pleural effusion     | + vs. -      | G vs.C<br>0.7301 1.07 (0.76-1.51)      | T vs.C<br>0.7301 1.21 (0.66-2.23)      | T vs.C<br>0.1794 1.29 (0.99-1.68)      | G vs.A<br>0.7301 1.08 (0.75-1.55)      |
|                      |              | CG+GG vs.CC<br>0.6585 1.64 (0.48-5.56) | CT+TT vs.CC<br>0.6585 1.28 (0.69-2.40) | additive<br>0.1943 1.28 (0.99-1.66)    | additive<br>0.7024 1.07 (0.75-1.54)    |
|                      | + vs. Normal | G vs.C<br>0.1106 1.40 (1.00-1.97)      | T vs.C<br>0.3628 1.41 (0.76-2.60)      | T vs.C<br>0.0852 1.37 (1.05-1.78)      | G vs.A<br>0.3309 1.25 (0.87-1.79)      |
|                      |              | additive<br>0.0997 1.41 (1.00-1.99)    | additive<br>0.3123 1.43 (0.77-2.68)    | additive<br>0.0713 1.36 (1.05-1.76)    | additive<br>0.3123 1.25 (0.87-1.79)    |
| Pericardial effusion | + vs. -      | G vs.C                                 | T vs.C                                 | T vs.C                                 | G vs.A                                 |

|                                 |              |        |                   |        |                  |        |                  |        |                   |  |
|---------------------------------|--------------|--------|-------------------|--------|------------------|--------|------------------|--------|-------------------|--|
|                                 |              | 0.2388 | 1.71 (1.04-2.81)  | 0.4668 | 1.52 (0.76-3.05) | 0.3510 | 1.31 (0.94-1.82) | 0.4668 | 1.31 (0.81-2.12)  |  |
|                                 |              |        | additive          |        | additive         |        | additive         |        | GG vs.AA+AG       |  |
|                                 |              | 0.2179 | 1.70 (1.04-2.79)  | 0.4196 | 1.51 (0.76-2.99) | 0.3372 | 1.30 (0.94-1.79) | 0.2890 | 1.50 (0.87-2.59)  |  |
|                                 | + vs. Normal |        | G vs.C            |        | T vs.C           |        | T vs.C           |        | G vs.A            |  |
|                                 |              | 0.0132 | 2.15 (1.31-3.53)  | 0.1977 | 1.74 (0.86-3.52) | 0.1110 | 1.42 (1.02-1.97) | 0.1977 | 1.49 (0.92-2.41)  |  |
|                                 |              |        | additive          |        | additive         |        | additive         |        | additive          |  |
|                                 |              | 0.0134 | 2.19 (1.33-3.61)  | 0.1708 | 1.80 (0.87-3.70) | 0.1119 | 1.41 (1.02-1.96) | 0.1708 | 1.49 (0.93-2.41)  |  |
| Ascites                         | + vs. -      |        | C vs.G            |        | C vs.T           |        | C vs.T           |        | A vs.G            |  |
|                                 |              | 1.0000 | 1.05 (0.58-1.90)  | 1.0000 | 1.12 (0.34-3.66) | 1.0000 | 1.12 (0.69-1.81) | 1.0000 | 1.31 (0.73-2.34)  |  |
|                                 |              |        | CC+CG vs.GG       |        | additive         |        | CC+CT vs.TT      |        | AA+AG vs.GG       |  |
|                                 |              | 0.8158 | 1.23 (0.63-2.41)  | 0.8830 | 1.12 (0.35-3.58) | 0.8158 | 1.51 (0.53-4.30) | 0.8158 | 1.44 (0.73-2.81)  |  |
|                                 | + vs. Normal |        | G vs.C            |        | T vs.C           |        | T vs.C           |        | A vs.G            |  |
|                                 |              | 1.0000 | 1.27 (0.70-2.30)  | 1.0000 | 1.09 (0.33-3.59) | 1.0000 | 1.01 (0.62-1.63) | 1.0000 | 1.10 (0.62-1.97)  |  |
|                                 |              |        | additive          |        | additive         |        | TT vs.CC+CT      |        | additive          |  |
|                                 |              | 0.9746 | 1.28 (0.70-2.33)  | 0.9746 | 1.09 (0.33-3.66) | 0.7310 | 0.80 (0.28-2.30) | 0.9746 | 1.10 (0.61-1.98)  |  |
| Nephritis                       | + vs. -      |        | C vs.G            |        | T vs.C           |        | T vs.C           |        | G vs.A            |  |
|                                 |              | 0.8813 | 1.09 (0.83-1.43)  | 0.8813 | 1.18 (0.70-1.98) | 0.8813 | 1.11 (0.90-1.38) | 1.0000 | 1.00 (0.75-1.33)  |  |
|                                 |              |        | additive          |        | additive         |        | additive         |        | AG+GG vs.AA       |  |
|                                 |              | 0.8307 | 1.09 (0.83-1.42)  | 0.8307 | 1.17 (0.70-1.96) | 0.8307 | 1.11 (0.90-1.37) | 0.8562 | 0.92 (0.37-2.30)  |  |
|                                 | + vs. Normal |        | G vs.C            |        | T vs.C           |        | T vs.C           |        | G vs.A            |  |
|                                 |              | 0.2028 | 1.28 (1.02-1.60)  | 0.3066 | 1.30 (0.84-2.02) | 0.2517 | 1.18 (0.98-1.42) | 0.3066 | 1.18 (0.93-1.50)  |  |
|                                 |              |        | GG vs.CC+CG       |        | additive         |        | additive         |        | GG vs.AA+AG       |  |
|                                 |              | 0.1174 | 1.37 (1.05-1.77)  | 0.2901 | 1.31 (0.84-2.03) | 0.2569 | 1.17 (0.98-1.40) | 0.2766 | 1.23 (0.94-1.61)  |  |
| Neuropsychiatric manifestations | + vs. -      |        | G vs.C            |        | T vs.C           |        | T vs.C           |        | G vs.A            |  |
|                                 |              | 0.9439 | 1.02 (0.71-1.47)  | 0.3162 | 1.81 (1.01-3.25) | 0.9439 | 1.04 (0.78-1.38) | 0.9439 | 1.19 (0.80-1.77)  |  |
|                                 |              |        | CG+GG vs.CC       |        | CT+TT vs.CC      |        | CT+TT vs.CC      |        | AG+GG vs.AA       |  |
|                                 |              | 0.2894 | 4.48 (0.60-33.18) | 0.2715 | 1.78 (0.96-3.31) | 0.8449 | 1.06 (0.71-1.58) | 0.3166 | 3.64 (0.49-27.22) |  |

|  | + vs. Normal | G vs.C                   | T vs.C                  | T vs.C                  | G vs.A                  |
|--|--------------|--------------------------|-------------------------|-------------------------|-------------------------|
|  |              | 0.2692 1.35 (0.94-1.94)  | 0.1866 1.94 (1.08-3.49) | 0.4455 1.16 (0.87-1.54) | 0.2692 1.36 (0.92-2.02) |
|  |              | CG+GG vs.CC              | additive                | CT+TT vs.CC             | additive                |
|  |              | 0.2124 5.36 (0.73-39.40) | 0.1559 1.96 (1.09-3.54) | 0.4406 1.20 (0.81-1.78) | 0.2474 1.37 (0.92-2.03) |
| Leukopenia (WBC count < 3500/uL)                   | + vs. -      | C vs.G                   | T vs.C                  | T vs.C                  | A vs.G                  |
|  |              | 1.0000 1.02 (0.78-1.34)  | 1.0000 1.00 (0.60-1.67) | 1.0000 1.08 (0.87-1.34) | 1.0000 1.08 (0.81-1.44) |
|  |              | CC+CG vs.GG              | CT+TT vs.CC             | CT+TT vs.CC             | AA+AG vs.GG             |
|  |              | 0.9531 1.02 (0.75-1.40)  | 0.9531 1.09 (0.64-1.86) | 0.9531 1.05 (0.78-1.42) | 0.9531 1.04 (0.75-1.43) |
| Anemia (Hb < 9 g/dL)                               | + vs. Normal | G vs.C                   | T vs.C                  | T vs.C                  | G vs.A                  |
|  |              | 0.0978 1.31 (1.05-1.64)  | 0.4199 1.21 (0.77-1.89) | 0.3678 1.16 (0.97-1.39) | 0.3678 1.14 (0.90-1.44) |
|  |              | GG vs.CC+CG              | additive                | TT vs.CC+CT             | additive                |
|  |              | 0.0723 1.38 (1.07-1.80)  | 0.3882 1.22 (0.78-1.93) | 0.2298 1.27 (0.89-1.81) | 0.3462 1.14 (0.90-1.44) |
| Thrombocytopenia (Plat count <10 <sup>5</sup> /uL) | + vs. -      | C vs.G                   | C vs.T                  | T vs.C                  | A vs.G                  |
|  |              | 1.0000 1.00 (0.75-1.34)  | 1.0000 1.09 (0.63-1.89) | 0.9782 1.11 (0.89-1.39) | 0.9782 1.12 (0.83-1.51) |
|  |              | additive                 | additive                | additive                | AA vs.AG+GG             |
|  |              | 0.9771 1.00 (0.75-1.34)  | 0.9771 1.09 (0.63-1.88) | 0.9543 1.11 (0.89-1.39) | 0.1934 2.37 (0.95-5.88) |
|  | + vs. Normal | G vs.C                   | T vs.C                  | T vs.C                  | G vs.A                  |
|  |              | 0.2414 1.32 (1.01-1.73)  | 0.6732 1.14 (0.66-1.97) | 0.2414 1.21 (0.97-1.50) | 0.6732 1.09 (0.82-1.44) |
|  |              | GG vs.CC+CG              | CT+TT vs.CC             | additive                | AG+GG vs.AA             |
|  |              | 0.1141 1.38 (1.01-1.89)  | 0.6274 1.15 (0.66-2.00) | 0.2289 1.20 (0.97-1.49) | 0.6274 0.68 (0.31-1.48) |
|  | + vs. -      | G vs.C                   | T vs.C                  | C vs.T                  | A vs.G                  |
|  |              | 1.0000 1.00 (0.73-1.37)  | 1.0000 1.21 (0.69-2.12) | 1.0000 1.03 (0.81-1.32) | 1.0000 1.01 (0.73-1.40) |
|  |              | CG+GG vs.CC              | CT+TT vs.CC             | CC+CT vs.TT             | AA+AG vs.GG             |
|  |              | 0.8146 1.24 (0.45-3.36)  | 0.8146 1.28 (0.72-2.28) | 0.8146 1.43 (0.86-2.38) | 0.8989 0.98 (0.68-1.41) |
|  | + vs. Normal | G vs.C                   | T vs.C                  | T vs.C                  | G vs.A                  |
|  |              | 0.4224 1.33 (0.99-1.80)  | 0.5319 1.39 (0.80-2.43) | 0.5920 1.09 (0.86-1.39) | 0.5319 1.16 (0.85-1.59) |
|  |              | GG vs.CC+CG              | additive                | CT+TT vs.CC             | additive                |
|  |              |                          |                         |                         |                         |

|                      |              |             |                  |             |                  |             |                  |             |                  |
|----------------------|--------------|-------------|------------------|-------------|------------------|-------------|------------------|-------------|------------------|
|                      |              | 0.3664      | 1.37 (0.97-1.94) | 0.4708      | 1.41 (0.80-2.49) | 0.4885      | 1.24 (0.89-1.73) | 0.5131      | 1.16 (0.85-1.59) |
| Complement depressed | + vs. -      | G vs.C      |                  | C vs.T      |                  | C vs.T      |                  | G vs.A      |                  |
|                      |              | 0.6123      | 1.29 (0.94-1.77) | 0.7147      | 1.26 (0.69-2.30) | 0.6123      | 1.18 (0.91-1.53) | 0.7147      | 1.10 (0.78-1.55) |
|                      |              | GG vs.CC+CG |                  | CC vs.CT+TT |                  | CC vs.CT+TT |                  | GG vs.AA+AG |                  |
|                      |              | 0.5183      | 1.36 (0.93-1.96) | 0.5183      | 1.34 (0.72-2.47) | 0.5183      | 1.25 (0.87-1.80) | 0.5183      | 1.17 (0.79-1.72) |
|                      | + vs. Normal | G vs.C      |                  | T vs.C      |                  | T vs.C      |                  | G vs.A      |                  |
|                      |              | 0.0102      | 1.39 (1.13-1.71) | 0.6622      | 1.11 (0.73-1.69) | 0.5365      | 1.07 (0.91-1.26) | 0.2850      | 1.20 (0.97-1.49) |
|                      |              | GG vs.CC+CG |                  | additive    |                  | additive    |                  | GG vs.AA+AG |                  |
|                      |              | 0.0075      | 1.48 (1.17-1.88) | 0.6311      | 1.11 (0.73-1.68) | 0.5340      | 1.07 (0.90-1.26) | 0.1745      | 1.25 (0.98-1.60) |
| Anti-dsDNA           | + vs. -      | G vs.C      |                  | C vs.T      |                  | C vs.T      |                  | G vs.A      |                  |
|                      |              | 0.8156      | 1.15 (0.84-1.57) | 0.6522      | 1.44 (0.83-2.51) | 0.8565      | 1.03 (0.80-1.32) | 0.8565      | 1.07 (0.77-1.49) |
|                      |              | GG vs.CC+CG |                  | additive    |                  | CC+CT vs.TT |                  | GG vs.AA+AG |                  |
|                      |              | 0.6957      | 1.19 (0.83-1.71) | 0.6145      | 1.43 (0.83-2.47) | 0.8323      | 1.08 (0.67-1.75) | 0.8211      | 1.11 (0.76-1.61) |
|                      | + vs. Normal | G vs.C      |                  | T vs.C      |                  | T vs.C      |                  | G vs.A      |                  |
|                      |              | 0.0204      | 1.37 (1.11-1.69) | 0.6637      | 1.11 (0.72-1.70) | 0.3306      | 1.11 (0.94-1.31) | 0.2604      | 1.19 (0.96-1.48) |
|                      |              | GG vs.CC+CG |                  | additive    |                  | additive    |                  | GG vs.AA+AG |                  |
|                      |              | 0.0116      | 1.47 (1.15-1.87) | 0.6410      | 1.11 (0.72-1.70) | 0.3284      | 1.11 (0.94-1.31) | 0.1743      | 1.24 (0.97-1.59) |
| Anti-Sm              | + vs. -      | G vs.C      |                  | C vs.T      |                  | T vs.C      |                  | G vs.A      |                  |
|                      |              | 0.9318      | 1.15 (0.84-1.58) | 1.0000      | 1.05 (0.57-1.93) | 0.9318      | 1.07 (0.84-1.37) | 0.9318      | 1.25 (0.89-1.75) |
|                      |              | GG vs.CC+CG |                  | additive    |                  | TT vs.CC+CT |                  | GG vs.AA+AG |                  |
|                      |              | 0.5008      | 1.29 (0.90-1.86) | 0.8821      | 1.05 (0.57-1.91) | 0.5008      | 1.26 (0.79-2.00) | 0.5008      | 1.28 (0.88-1.86) |
|                      | + vs. Normal | G vs.C      |                  | T vs.C      |                  | T vs.C      |                  | G vs.A      |                  |
|                      |              | 0.0726      | 1.45 (1.09-1.93) | 0.7745      | 1.10 (0.62-1.94) | 0.4826      | 1.14 (0.91-1.43) | 0.1578      | 1.36 (1.00-1.85) |
|                      |              | GG vs.CC+CG |                  | additive    |                  | TT vs.CC+CT |                  | additive    |                  |
|                      |              | 0.0161      | 1.65 (1.19-2.31) | 0.7268      | 1.11 (0.62-1.97) | 0.0952      | 1.39 (0.91-2.12) | 0.1519      | 1.36 (1.00-1.85) |
| Anti-RNP             | + vs. -      | C vs.G      |                  | C vs.T      |                  | C vs.T      |                  | G vs.A      |                  |
|                      |              | 1.0000      | 1.03 (0.76-1.40) | 0.4488      | 1.86 (0.98-3.51) | 1.0000      | 1.01 (0.79-1.28) | 1.0000      | 1.01 (0.73-1.39) |

|                      |              | CC vs.CG+GG             | CC vs.CT+TT             | CC vs.CT+TT             | GG vs.AA+AG             |
|----------------------|--------------|-------------------------|-------------------------|-------------------------|-------------------------|
|                      |              | 0.1972 2.91 (1.10-7.73) | 0.1972 1.84 (0.96-3.52) | 0.7694 1.11 (0.80-1.54) | 0.7694 1.09 (0.76-1.56) |
|                      | + vs. Normal | G vs.C                  | C vs.T                  | T vs.C                  | G vs.A                  |
|                      |              | 0.2826 1.31 (1.01-1.71) | 0.6204 1.30 (0.71-2.39) | 0.6204 1.07 (0.86-1.33) | 0.6204 1.18 (0.89-1.56) |
|                      |              | GG vs.CC+CG             | CC vs.CT+TT             | TT vs.CC+CT             | GG vs.AA+AG             |
|                      |              | 0.0537 1.51 (1.11-2.06) | 0.4639 1.31 (0.71-2.43) | 0.3054 1.30 (0.87-1.96) | 0.3054 1.26 (0.92-1.73) |
| Anti-SSA             | + vs. -      | G vs.C                  | T vs.C                  | T vs.C                  | G vs.A                  |
|                      |              | 0.6965 1.12 (0.80-1.58) | 1.0000 1.04 (0.53-2.06) | 0.0366 1.47 (1.11-1.94) | 0.6965 1.11 (0.77-1.60) |
|                      |              | CG+GG vs.CC             | CT+TT vs.CC             | CT+TT vs.CC             | additive                |
|                      |              | 0.6316 0.56 (0.18-1.73) | 0.8683 1.14 (0.56-2.32) | 0.0037 1.93 (1.33-2.81) | 0.6745 1.12 (0.77-1.61) |
| Anti-SSB             | + vs. Normal | G vs.C                  | T vs.C                  | T vs.C                  | G vs.A                  |
|                      |              | 0.0804 1.36 (1.06-1.74) | 0.7028 1.11 (0.68-1.82) | 0.0804 1.25 (1.03-1.52) | 0.1572 1.26 (0.97-1.64) |
|                      |              | GG vs.CC+CG             | additive                | additive                | additive                |
|                      |              | 0.0248 1.51 (1.13-2.01) | 0.6648 1.12 (0.68-1.85) | 0.0840 1.24 (1.02-1.51) | 0.1548 1.27 (0.98-1.65) |
| Anti-cardiolipin IgG | + vs. -      | G vs.C                  | T vs.C                  | T vs.C                  | G vs.A                  |
|                      |              | 0.8785 1.06 (0.73-1.54) | 0.8573 1.28 (0.64-2.58) | 0.8785 1.03 (0.77-1.38) | 0.2052 1.48 (0.97-2.26) |
|                      |              | CG+GG vs.CC             | CT+TT vs.CC             | TT vs.CC+CT             | additive                |
|                      |              | 0.3558 0.51 (0.19-1.35) | 0.4487 1.35 (0.66-2.76) | 0.2673 0.58 (0.32-1.08) | 0.2005 1.50 (0.98-2.31) |
|                      | + vs. Normal | G vs.C                  | T vs.C                  | T vs.C                  | G vs.A                  |
|                      |              | 0.2248 1.34 (0.95-1.90) | 0.4629 1.31 (0.68-2.51) | 0.4629 1.12 (0.85-1.48) | 0.1200 1.61 (1.08-2.40) |
|                      |              | GG vs.CC+CG             | additive                | TT vs.CC+CT             | additive                |
|                      |              | 0.0746 1.57 (1.05-2.36) | 0.4236 1.32 (0.68-2.56) | 0.0776 0.84 (0.46-1.53) | 0.1105 1.63 (1.09-2.44) |
|                      | + vs. -      | C vs.G                  | T vs.C                  | C vs.T                  | A vs.G                  |
|                      |              | 1.0000 1.13 (0.81-1.58) | 1.0000 1.08 (0.59-1.97) | 1.0000 1.07 (0.82-1.39) | 1.0000 1.01 (0.71-1.44) |
|                      |              | CC+CG vs.GG             | CT+TT vs.CC             | CC vs.CT+TT             | AA vs.AG+GG             |
|                      |              | 0.8819 1.17 (0.80-1.73) | 0.8819 1.15 (0.62-2.13) | 0.8427 1.21 (0.84-1.75) | 0.8427 1.77 (0.67-4.71) |
|                      | + vs. Normal | G vs.C                  | T vs.C                  | T vs.C                  | G vs.A                  |
|                      |              |                         |                         |                         |                         |

|                      |              |             |                  |          |                  |             |                  |             |                  |
|----------------------|--------------|-------------|------------------|----------|------------------|-------------|------------------|-------------|------------------|
|                      |              | 0.6774      | 1.28 (0.94-1.75) | 0.6774   | 1.38 (0.77-2.47) | 0.6796      | 1.08 (0.84-1.39) | 0.6774      | 1.22 (0.87-1.70) |
|                      |              | GG vs.CC+CG |                  | additive |                  | TT vs.CC+CT |                  | additive    |                  |
|                      |              | 0.2948      | 1.33 (0.93-1.91) | 0.5405   | 1.40 (0.77-2.53) | 0.5444      | 1.24 (0.77-2.01) | 0.5405      | 1.22 (0.88-1.69) |
| Anti-cardiolipin IgM | + vs. -      | G vs.C      |                  | C vs.T   |                  | C vs.T      |                  | A vs.G      |                  |
|                      |              | 0.8009      | 1.18 (0.65-2.13) | 0.8135   | 1.15 (0.40-3.27) | 0.4518      | 1.55 (0.97-2.46) | 0.8009      | 1.39 (0.81-2.39) |
|                      |              | GG vs.CC+CG |                  | additive |                  | additive    |                  | AA vs.AG+GG |                  |
|                      |              | 0.7211      | 1.32 (0.67-2.59) | 0.7934   | 1.15 (0.41-3.19) | 0.3968      | 1.54 (0.97-2.44) | 0.4447      | 2.61 (0.72-9.54) |
|                      | + vs. Normal | G vs.C      |                  | T vs.C   |                  | C vs.T      |                  | A vs.G      |                  |
|                      |              | 0.6660      | 1.63 (0.91-2.92) | 0.8921   | 1.18 (0.42-3.35) | 0.6660      | 1.34 (0.85-2.12) | 0.8921      | 1.07 (0.63-1.82) |
|                      |              | GG vs.CC+CG |                  | additive |                  | CC vs.CT+TT |                  | additive    |                  |
|                      |              | 0.2767      | 1.93 (0.99-3.76) | 0.8138   | 1.19 (0.41-3.44) | 0.5532      | 1.29 (0.72-2.32) | 0.8138      | 1.07 (0.63-1.81) |

<sup>a</sup>The analysis was done by comparing allele frequencies in different clinical subgroups as described in the methods section. After testing for the additive, dominant and recessive models, only the model which provided the smallest p-value was presented in this table. <sup>b</sup>P<sub>FDR</sub>: The p-value was adjusted after the FDR correction.

**Table 3 Association of TLR 3 SNPs with SLE clinical phenotypes and autoantibodies in the male and female SLE patients**

| Clinical manifestation | Male                          |                  |                               |                  | Female                        |                  |                               |                  |
|------------------------|-------------------------------|------------------|-------------------------------|------------------|-------------------------------|------------------|-------------------------------|------------------|
|                        | TLR3                          |                  |                               |                  | TLR3                          |                  |                               |                  |
|                        | rs3775291                     |                  | rs3775296                     |                  | rs3775291                     |                  | rs3775296                     |                  |
|                        | Type of analysis <sup>a</sup> |                  | Type of analysis <sup>a</sup> |                  | Type of analysis <sup>a</sup> |                  | Type of analysis <sup>a</sup> |                  |
|                        | P <sub>FDR</sub> <sup>b</sup> | OR (95%CI)       |
| Oral ulcer             | + vs. -                       | G vs.A           |                               | G vs.T           |                               | G vs.A           |                               | G vs.T           |
|                        | 0.2082                        | 2.70 (0.95-7.70) | 0.9021                        | 1.53 (0.48-4.87) | 1.0000                        | 1.00 (0.78-1.28) | 0.6589                        | 1.09 (0.83-1.43) |
|                        |                               |                  |                               |                  | GG vs.AA+AG                   |                  | GG vs.GT+TT                   |                  |
|                        |                               |                  |                               |                  | 0.5975                        | 0.91 (0.66-1.27) | 0.5674                        | 1.13 (0.81-1.57) |
|                        | + vs. Normal                  | G vs.A           |                               | G vs.T           |                               | G vs.A           |                               | T vs.G           |
|                        | 0.3908                        | 2.19 (0.82-5.86) | 0.3908                        | 1.96 (0.67-5.74) | 0.7986                        | 1.09 (0.86-1.38) | 0.9479                        | 1.01 (0.78-1.32) |
|                        |                               |                  |                               |                  | GG vs.AA+AG                   |                  | TT vs.GG+GT                   |                  |
|                        |                               |                  |                               |                  | 0.5501                        | 1.12 (0.81-1.55) | 0.5501                        | 1.23 (0.63-2.42) |
| Arthritis              | + vs. -                       | G vs.A           |                               | T vs.G           |                               | G vs.A           |                               | G vs.T           |
|                        | 0.2006                        | 1.88 (0.92-3.83) | 1.0000                        | 1.07 (0.46-2.48) | 0.7771                        | 1.04 (0.83-1.30) | 0.7771                        | 1.06 (0.83-1.35) |
|                        |                               |                  |                               |                  | additive                      |                  | additive                      |                  |
|                        |                               |                  |                               |                  | 0.7585                        | 1.03 (0.83-1.28) | 0.7414                        | 1.06 (0.83-1.36) |
|                        | + vs. Normal                  | G vs.A           |                               | G vs.T           |                               | G vs.A           |                               | T vs.G           |
|                        | 0.5248                        | 1.28 (0.77-2.14) | 0.5248                        | 1.34 (0.76-2.37) | 0.4628                        | 1.10 (0.92-1.31) | 0.6067                        | 1.05 (0.86-1.28) |
|                        |                               |                  |                               |                  | GG vs.AA+AG                   |                  | TT vs.GG+GT                   |                  |
|                        |                               |                  |                               |                  | 0.2425                        | 1.21 (0.95-1.54) | 0.4500                        | 1.26 (0.76-2.10) |
| Malar rash             | + vs. -                       | G vs.A           |                               | T vs.G           |                               | A vs.G           |                               | T vs.G           |
|                        | 0.7010                        | 1.32 (0.65-2.67) | 0.1656                        | 2.50 (1.01-6.16) | 0.6200                        | 1.11 (0.89-1.38) | 0.7255                        | 1.06 (0.84-1.34) |
|                        |                               |                  |                               |                  | additive                      |                  | TT vs.GG+GT                   |                  |
|                        |                               |                  |                               |                  | 0.5842                        | 1.10 (0.89-1.36) | 0.5193                        | 0.71 (0.39-1.29) |
|                        | + vs. Normal                  | G vs.A           |                               | T vs.G           |                               | G vs.A           |                               | T vs.G           |

|                  |              |        |                  |        |                  |             |                  |             |                  |          |  |
|------------------|--------------|--------|------------------|--------|------------------|-------------|------------------|-------------|------------------|----------|--|
|                  |              | 0.9696 | 1.09 (0.66-1.80) | 1.0000 | 1.04 (0.61-1.77) | 0.8533      | 1.04 (0.87-1.25) | 0.5433      | 1.10 (0.90-1.35) |          |  |
|                  |              |        |                  |        |                  |             | GG vs.AA+AG      |             |                  | additive |  |
|                  |              |        |                  |        |                  | 0.5843      | 1.12 (0.87-1.44) | 0.4930      | 1.11 (0.90-1.36) |          |  |
| Discoid rash     | + vs. -      | A vs.G |                  | G vs.T |                  | G vs.A      |                  | G vs.T      |                  |          |  |
|                  |              | 0.8472 | 1.90 (0.85-4.26) | 0.9767 | 1.16 (0.42-3.17) | 0.9404      | 1.09 (0.82-1.44) | 0.9404      | 1.02 (0.75-1.38) |          |  |
|                  |              |        |                  |        |                  | AG+GG vs.AA |                  | GG+GT vs.TT |                  |          |  |
|                  |              |        |                  |        |                  | 0.7528      | 1.41 (0.78-2.57) | 0.7528      | 1.92 (0.75-4.92) |          |  |
|                  | + vs. Normal | A vs.G |                  | G vs.T |                  | G vs.A      |                  | T vs.G      |                  |          |  |
|                  |              | 0.2801 | 1.69 (0.83-3.42) | 0.4169 | 1.55 (0.63-3.81) | 0.4365      | 1.16 (0.88-1.53) | 0.7536      | 1.06 (0.78-1.44) |          |  |
|                  |              |        |                  |        |                  | additive    |                  | TT vs.GG+GT |                  |          |  |
|                  |              |        |                  |        |                  | 0.4145      | 1.17 (0.88-1.55) | 0.5090      | 0.72 (0.28-1.88) |          |  |
| Photosensitivity | + vs. -      | G vs.A |                  | G vs.T |                  | G vs.A      |                  | G vs.T      |                  |          |  |
|                  |              | 0.7817 | 1.29 (0.51-3.23) | 1.0000 | 1.11 (0.38-3.26) | 0.8964      | 1.02 (0.79-1.32) | 0.5462      | 1.20 (0.90-1.60) |          |  |
|                  |              |        |                  |        |                  | AG+GG vs.AA |                  | GG+GT vs.TT |                  |          |  |
|                  |              |        |                  |        |                  | 0.7757      | 1.19 (0.71-2.00) | 0.1465      | 3.30 (1.17-9.30) |          |  |
|                  | + vs. Normal | G vs.A |                  | G vs.T |                  | G vs.A      |                  | G vs.T      |                  |          |  |
|                  |              | 0.8389 | 1.18 (0.51-2.74) | 0.6044 | 1.50 (0.56-4.02) | 0.5881      | 1.10 (0.85-1.42) | 0.6640      | 1.07 (0.81-1.42) |          |  |
|                  |              |        |                  |        |                  | additive    |                  | GG+GT vs.TT |                  |          |  |
|                  |              |        |                  |        |                  | 0.5795      | 1.11 (0.86-1.42) | 0.4374      | 2.18 (0.77-6.22) |          |  |
| Pleural effusion | + vs. -      | A vs.G |                  | G vs.T |                  | G vs.A      |                  | T vs.G      |                  |          |  |
|                  |              | 0.7223 | 1.39 (0.56-3.42) | 0.7874 | 1.36 (0.42-4.36) | 0.7301      | 1.06 (0.81-1.39) | 0.1794      | 1.37 (1.03-1.82) |          |  |
|                  |              |        |                  |        |                  | additive    |                  | additive    |                  |          |  |
|                  |              |        |                  |        |                  | 0.7024      | 1.05 (0.81-1.37) | 0.1902      | 1.37 (1.03-1.83) |          |  |
|                  | + vs. Normal | A vs.G |                  | G vs.T |                  | G vs.A      |                  | T vs.G      |                  |          |  |
|                  |              | 0.6222 | 1.37 (0.60-3.12) | 0.5313 | 1.79 (0.61-5.28) | 0.3689      | 1.13 (0.86-1.48) | 0.0852      | 1.38 (1.04-1.83) |          |  |
|                  |              |        |                  |        |                  | GG vs.AA+AG |                  | additive    |                  |          |  |
|                  |              |        |                  |        |                  | 0.1173      | 1.26 (0.88-1.81) | 0.0713      | 1.40 (1.05-1.86) |          |  |

| Pericardial effusion               | + vs. - | G vs.A |                    | T vs.G |                   | A vs.G      |                  | T vs.G      |                  |
|------------------------------------|---------|--------|--------------------|--------|-------------------|-------------|------------------|-------------|------------------|
|                                    |         | 1.0000 | 1.04 (0.42-2.55)   | 0.6456 | 1.56 (0.58-4.19)  | 0.7299      | 1.07 (0.76-1.50) | 0.5485      | 1.17 (0.82-1.68) |
| + vs. Normal                       |         |        |                    |        |                   | AA vs.AG+GG |                  | TT vs.GG+GT |                  |
|                                    |         | 1.0000 | 1.01 (0.45-2.29)   | 1.0000 | 1.03 (0.43-2.48)  | 0.9303      | 1.02 (0.73-1.43) | 0.3415      | 1.23 (0.86-1.76) |
| Ascites                            | + vs. - |        |                    |        |                   | GG vs.AA+AG |                  | TT vs.GG+GT |                  |
|                                    |         | 0.4320 | 7.02 (0.38-128.47) | 1.0000 | 1.31 (0.15-11.69) | 1.0000      | 1.14 (0.70-1.86) | 1.0000      | 1.16 (0.68-1.99) |
| + vs. Normal                       |         |        |                    |        |                   | AG+GG vs.AA |                  | GG+GT vs.TT |                  |
|                                    |         | 0.6222 | 6.27 (0.35-112.58) | 1.0000 | 1.79 (0.21-15.39) | 1.0000      | 1.23 (0.75-2.01) | 1.0000      | 1.07 (0.62-1.84) |
| Nephritis                          | + vs. - |        |                    |        |                   | additive    |                  | additive    |                  |
|                                    |         | 0.2422 | 1.70 (0.82-3.54)   | 0.2422 | 2.16 (0.81-5.78)  | 0.8813      | 1.04 (0.84-1.29) | 0.8813      | 1.12 (0.88-1.42) |
| + vs. Normal                       |         |        |                    |        |                   | additive    |                  | TT vs.GG+GT |                  |
|                                    |         | 0.8491 | 1.16 (0.73-1.85)   | 0.8491 | 1.10 (0.67-1.81)  | 0.5163      | 1.07 (0.89-1.28) | 0.3066      | 1.13 (0.92-1.38) |
| Neuropsychiatric<br>manifestations | + vs. - |        |                    |        |                   | GG vs.AA+AG |                  | TT vs.GG+GT |                  |
|                                    |         | 1.0000 | 1.02 (0.38-2.76)   | 0.7713 | 2.60 (0.57-11.94) | 0.9439      | 1.01 (0.75-1.35) | 0.9439      | 1.07 (0.78-1.46) |
|                                    |         |        |                    |        |                   | AG+GG vs.AA |                  | TT vs.GG+GT |                  |

|                                       |              |                  |                  |                   |                  |                  |                  |                  |
|---------------------------------------|--------------|------------------|------------------|-------------------|------------------|------------------|------------------|------------------|
|                                       |              |                  |                  |                   | 0.2715           | 0.64 (0.38-1.07) | 0.5018           | 1.65 (0.82-3.34) |
| + vs. Normal                          | A vs.G       | G vs.T           | G vs.A           | T vs.G            |                  |                  |                  |                  |
|                                       | 1.0000       | 1.03 (0.41-2.60) | 0.2550           | 3.21 (0.74-13.93) | 0.5654           | 1.10 (0.82-1.47) | 0.5654           | 1.13 (0.83-1.55) |
|                                       |              |                  | AG+GG vs.AA      | TT vs.GG+GT       |                  |                  |                  |                  |
|                                       |              |                  | 0.2124           | 0.65 (0.39-1.09)  | 0.2440           | 1.88 (0.93-3.83) |                  |                  |
| Leukopenia (WBC count < 3500/uL)      | + vs. -      | G vs.A           | T vs.G           | G vs.A            | T vs.G           |                  |                  |                  |
|                                       |              | 0.3842           | 1.69 (0.83-3.46) | 1.0000            | 1.02 (0.44-2.39) | 1.0000           | 1.04 (0.84-1.29) | 1.0000           |
|                                       |              |                  |                  | AG+GG vs.AA       | GT+TT vs.GG      |                  |                  |                  |
|                                       |              |                  | 0.9531           | 1.01 (0.66-1.55)  | 0.9531           | 1.08 (0.81-1.45) |                  |                  |
| Anemia (Hb < 9 g/dL)                  | + vs. Normal | G vs.A           | G vs.T           | G vs.A            | T vs.G           |                  |                  |                  |
|                                       |              | 0.6544           | 1.19 (0.73-1.94) | 0.4488            | 1.37 (0.79-2.38) | 0.3678           | 1.10 (0.92-1.32) | 0.3678           |
|                                       |              |                  |                  | GG vs.AA+AG       | TT vs.GG+GT      |                  |                  |                  |
|                                       |              |                  | 0.2369           | 1.24 (0.96-1.59)  | 0.2298           | 1.37 (0.82-2.29) |                  |                  |
| Thrombocytopenia (Plat count <105/uL) | + vs. -      | G vs.A           | T vs.G           | A vs.G            | T vs.G           |                  |                  |                  |
|                                       |              | 0.2754           | 2.83 (0.90-8.91) | 0.5026            | 2.07 (0.75-5.71) | 1.0000           | 1.01 (0.80-1.27) | 0.9782           |
|                                       |              |                  |                  | AA vs.AG+GG       | TT vs.GG+GT      |                  |                  |                  |
|                                       |              |                  | 0.9203           | 1.18 (0.76-1.84)  | 0.0244           | 2.41 (1.33-4.39) |                  |                  |
|                                       | + vs. Normal | G vs.A           | T vs.G           | G vs.A            | T vs.G           |                  |                  |                  |
|                                       |              | 0.3462           | 2.35 (0.79-7.00) | 0.6271            | 1.31 (0.53-3.25) | 0.6732           | 1.08 (0.87-1.35) | 0.2414           |
|                                       |              |                  |                  | additive          |                  |                  |                  |                  |
|                                       |              |                  |                  | 0.2289            | 1.21 (0.96-1.53) |                  |                  |                  |

|            |              |                         |                         |                         |                         |
|------------|--------------|-------------------------|-------------------------|-------------------------|-------------------------|
|            |              |                         |                         | GG vs.AA+AG             | TT vs.GG+GT             |
|            |              |                         |                         | 0.4005 1.12 (0.80-1.56) | 0.4005 1.53 (0.80-2.91) |
| Complement | + vs. -      | G vs.A                  | T vs.G                  | G vs.A                  | G vs.T                  |
| depressed  |              | 0.2790 2.47 (1.03-5.91) | 0.7458 2.24 (0.62-8.11) | 0.7147 1.09 (0.84-1.42) | 1.0000 1.00 (0.75-1.33) |
|            |              |                         |                         | GG vs.AA+AG             | GG vs.GT+TT             |
|            |              |                         |                         | 0.5183 1.21 (0.84-1.74) | 0.8919 1.03 (0.72-1.46) |
|            | + vs. Normal | G vs.A                  | G vs.T                  | G vs.A                  | T vs.G                  |
|            |              | 0.7872 1.11 (0.72-1.70) | 0.6362 1.22 (0.76-1.96) | 0.5365 1.09 (0.92-1.29) | 0.5365 1.08 (0.90-1.30) |
|            |              |                         |                         | GG vs.AA+AG             | TT vs.GG+GT             |
|            |              |                         |                         | 0.1745 1.22 (0.97-1.53) | 0.4855 1.28 (0.79-2.07) |
| Anti-dsDNA | + vs. -      | G vs.A                  | T vs.G                  | G vs.A                  | T vs.G                  |
|            |              | 0.5018 1.80 (0.79-4.11) | 0.5018 2.70 (0.75-9.68) | 0.4284 1.26 (0.98-1.62) | 0.8565 1.06 (0.80-1.40) |
|            |              |                         |                         | AG+GG vs.AA             | TT vs.GG+GT             |
|            |              |                         |                         | 0.3423 1.57 (0.99-2.50) | 0.8211 1.16 (0.57-2.38) |
|            | + vs. Normal | G vs.A                  | G vs.T                  | G vs.A                  | T vs.G                  |
|            |              | 0.8986 1.08 (0.70-1.66) | 0.7206 1.19 (0.74-1.92) | 0.2604 1.15 (0.97-1.36) | 0.4189 1.10 (0.91-1.33) |
|            |              |                         |                         | GG vs.AA+AG             | TT vs.GG+GT             |
|            |              |                         |                         | 0.1408 1.26 (1.00-1.59) | 0.3605 1.34 (0.82-2.17) |
| Anti-Sm    | + vs. -      | A vs.G                  | T vs.G                  | G vs.A                  | T vs.G                  |
|            |              | 1.0000 1.03 (0.49-2.17) | 0.3614 2.11 (0.88-5.05) | 0.9318 1.07 (0.83-1.37) | 0.9331 1.04 (0.79-1.36) |
|            |              |                         |                         | GG vs.AA+AG             | additive                |
|            |              |                         |                         | 0.5008 1.21 (0.86-1.69) | 0.8821 1.04 (0.79-1.37) |
|            | + vs. Normal | A vs.G                  | T vs.G                  | G vs.A                  | T vs.G                  |
|            |              | 0.7711 1.13 (0.64-1.99) | 0.7661 1.18 (0.65-2.15) | 0.4826 1.13 (0.90-1.42) | 0.6296 1.09 (0.85-1.40) |
|            |              |                         |                         | additive                | TT vs.GG+GT             |
|            |              |                         |                         | 0.4624 1.13 (0.90-1.41) | 0.0952 1.18 (0.61-2.28) |
| Anti-RNP   | + vs. -      | A vs.G                  | T vs.G                  | A vs.G                  | G vs.T                  |

|                      |         |        |                  |        |                   |             |                  |             |                  |  |  |
|----------------------|---------|--------|------------------|--------|-------------------|-------------|------------------|-------------|------------------|--|--|
|                      |         | 0.6869 | 1.26 (0.59-2.70) | 0.5002 | 1.81 (0.76-4.30)  | 1.0000      | 1.00 (0.78-1.27) | 1.0000      | 1.11 (0.85-1.45) |  |  |
|                      |         |        |                  |        |                   | AA vs.AG+GG |                  | GG vs.GT+TT |                  |  |  |
|                      |         |        |                  |        |                   | 0.7725      | 1.07 (0.67-1.72) | 0.7694      | 1.12 (0.80-1.55) |  |  |
| + vs. Normal         |         | A vs.G |                  | T vs.G |                   | G vs.A      |                  | T vs.G      |                  |  |  |
|                      |         | 0.7977 | 1.25 (0.69-2.26) | 0.8890 | 1.15 (0.61-2.18)  | 0.6204      | 1.08 (0.87-1.34) | 1.0000      | 1.00 (0.79-1.27) |  |  |
|                      |         |        |                  |        |                   | GG vs.AA+AG |                  | additive    |                  |  |  |
|                      |         |        |                  |        |                   | 0.3054      | 1.22 (0.91-1.64) | 0.9834      | 1.00 (0.79-1.28) |  |  |
| Anti-SSA             | + vs. - | A vs.G |                  | G vs.T |                   | G vs.A      |                  | T vs.G      |                  |  |  |
|                      |         | 1.0000 | 1.10 (0.45-2.67) | 1.0000 | 1.42 (0.50-4.04)  | 0.6965      | 1.18 (0.90-1.55) | 0.6965      | 1.11 (0.82-1.50) |  |  |
|                      |         |        |                  |        |                   | AG+GG vs.AA |                  | GT+TT vs.GG |                  |  |  |
|                      |         |        |                  |        |                   | 0.5455      | 1.43 (0.85-2.42) | 0.6580      | 1.16 (0.80-1.68) |  |  |
| + vs. Normal         |         | A vs.G |                  | G vs.T |                   | G vs.A      |                  | T vs.G      |                  |  |  |
|                      |         | 0.9034 | 1.15 (0.66-2.01) | 0.4208 | 1.64 (0.82-3.30)  | 0.2501      | 1.14 (0.93-1.39) | 0.2501      | 1.16 (0.93-1.44) |  |  |
|                      |         |        |                  |        |                   | additive    |                  | TT vs.GG+GT |                  |  |  |
|                      |         |        |                  |        |                   | 0.2285      | 1.14 (0.94-1.40) | 0.1638      | 1.12 (0.62-2.02) |  |  |
| Anti-SSB             | + vs. - | A vs.G |                  | G vs.T |                   | G vs.A      |                  | T vs.G      |                  |  |  |
|                      |         | 1.0000 | 1.04 (0.34-3.18) | 0.8772 | 1.93 (0.40-9.39)  | 0.2052      | 1.34 (0.99-1.82) | 0.8573      | 1.13 (0.82-1.55) |  |  |
|                      |         |        |                  |        |                   | additive    |                  | GT+TT vs.GG |                  |  |  |
|                      |         |        |                  |        |                   | 0.2005      | 1.32 (0.98-1.78) | 0.4487      | 1.17 (0.78-1.74) |  |  |
| + vs. Normal         |         | A vs.G |                  | G vs.T |                   | G vs.A      |                  | T vs.G      |                  |  |  |
|                      |         | 0.9558 | 1.15 (0.41-3.19) | 0.3917 | 2.50 (0.56-11.07) | 0.1431      | 1.34 (1.01-1.79) | 0.2742      | 1.23 (0.91-1.66) |  |  |
|                      |         |        |                  |        |                   | additive    |                  | TT vs.GG+GT |                  |  |  |
|                      |         |        |                  |        |                   | 0.1288      | 1.35 (1.01-1.80) | 0.0746      | 1.21 (0.55-2.68) |  |  |
| Anti-cardiolipin IgG | + vs. - | A vs.G |                  | G vs.T |                   | A vs.G      |                  | G vs.T      |                  |  |  |
|                      |         | 0.4538 | 1.83 (0.72-4.67) | 0.9482 | 1.18 (0.39-3.61)  | 1.0000      | 1.06 (0.81-1.38) | 1.0000      | 1.00 (0.75-1.34) |  |  |
|                      |         |        |                  |        |                   | AA vs.AG+GG |                  | GG+GT vs.TT |                  |  |  |
|                      |         |        |                  |        |                   | 0.8427      | 1.23 (0.74-2.04) | 0.8819      | 1.14 (0.54-2.39) |  |  |

|                      | + vs. Normal | A vs.G                  | G vs.T                   | G vs.A                  | T vs.G                  |  |
|----------------------|--------------|-------------------------|--------------------------|-------------------------|-------------------------|--|
|                      |              | 0.7656 1.62 (0.72-3.65) | 0.7656 1.36 (0.50-3.68)  | 0.9493 1.01 (0.79-1.30) | 0.6796 1.09 (0.83-1.44) |  |
|                      |              |                         |                          | GG vs.AA+AG             | TT vs.GG+GT             |  |
|                      |              |                         |                          | 0.6294 1.15 (0.81-1.62) | 0.2948 1.20 (0.58-2.47) |  |
| Anti-cardiolipin IgM | + vs. -      | A vs.G                  | G vs.T                   | A vs.G                  | T vs.G                  |  |
|                      |              | 0.8197 1.87 (0.44-8.01) | 0.8197 2.26 (0.26-19.45) | 0.8009 1.12 (0.73-1.72) | 0.8009 1.17 (0.73-1.87) |  |
|                      |              |                         |                          | additive                | TT vs.GG+GT             |  |
|                      |              |                         |                          | 0.7442 1.11 (0.73-1.68) | 0.7211 0.59 (0.14-2.53) |  |
|                      | + vs. Normal | A vs.G                  | G vs.T                   | A vs.G                  | T vs.G                  |  |
|                      |              | 1.0000 1.91 (0.47-7.68) | 1.0000 2.50 (0.31-20.41) | 0.8921 1.08 (0.71-1.65) | 0.8921 1.22 (0.77-1.94) |  |
|                      |              |                         |                          | AA vs.AG+GG             | TT vs.GG+GT             |  |
|                      |              |                         |                          | 0.7792 1.36 (0.62-3.00) | 0.5377 0.81 (0.19-3.46) |  |

<sup>a</sup>For the male participants, the analysis was done by comparing allele frequencies in different clinical subgroups as described in the methods section. The additive, dominant and recessive models were further tested in the females, with only the model which provided the smallest p-value shown in this table. <sup>b</sup>P<sub>FDR</sub>: The p-value was adjusted after the FDR correction.