

Logistic regression and stratified analyses for rs3789327

Logistic regression of the SNP

| Rs3789327 | OR (95% CI) | P |
|---------------------|------------------|------|
| CC vs. Carrier of T | 1.13 (0.89-1.44) | 0.30 |

SNP adjusted by sex, HLA and clinical form

| Rs3789327 | OR (95% CI) | P |
|---------------------|-------------------|--------|
| CC vs. Carrier of T | 1.06 (0.77-1.47) | 0.71 |
| Sex male | 1.52 (1.13-2.03) | 0.005 |
| Sex female | 4.13 (1.06-16.11) | 0.041 |
| HLA-DRB1*1501 | 3.10 (2.23-4.31) | <0.001 |
| Clinical form | -- | -- |

Analysis stratified by sex

| ARNTL rs3789327 | FemaleMS | | FemaleControls | | p |
|--------------------|----------|--------------|----------------|------|-----------------------------|
| | N | % | N | % | |
| TT | 165 | 26.4 | 87 | 24.0 | |
| TC | 324 | 51.9 | 175 | 48.3 | |
| CC | 135 | 21.6 | 100 | 27.6 | 0.07* |
| CC vs Carrier of T | 489 | 78.4 | 262 | 72.4 | 0.04 (OR=1.38 [1.02-1.86])* |
| Male MS | | MaleControls | | | |
| TT | 78 | 25.2 | 51 | 22.1 | |
| TC | 157 | 50.6 | 130 | 56.3 | |
| CC | 75 | 24.2 | 50 | 21.6 | 0.92 |
| CC vs Carrier of T | 235 | 75.8 | 181 | 78.4 | 0.53 |

*Statistical comparisons do not stand Bonferroni correction (p^*2)

Analysis stratified by clinical form

| ARNTLrs3789327 | RR | SP | | PP | | |
|----------------|-----|------|----|------|---|------|
| | | N | % | N | % | |
| TT | 111 | 25.4 | 23 | 27.1 | 3 | 16.7 |
| CT | 226 | 51.7 | 43 | 50.6 | 7 | 38.9 |
| CC | 100 | 22.9 | 19 | 22.4 | 8 | 44.4 |

RR vs SP p=0.79 RR vs PP p=0.07* SP vs PP p=0.08*

RR: Relapsing remitting
SP: secondary progressive
PP: primary progressive

*Statistical comparisons do not pass Bonferroni correction (p^*2). The size of the PP group is too small to draw solid conclusions

Analysis stratified by HLA DRB*15:01 status

| <i>ARNTL</i> rs3789327 | MS | | Controls | | |
|----------------------------------|-----|------|----------|------|------|
| Not HLA-DRB1*15:01 | N | % | N | % | P |
| TT | 152 | 24.8 | 100 | 24.6 | 0.42 |
| CT | 329 | 53.6 | 204 | 50.3 | |
| CC | 133 | 21.6 | 102 | 25.1 | |
| HLA-DRB1*15:01 / X | | | | | |
| TT | 82 | 28.3 | 14 | 25.4 | 0.79 |
| CT | 139 | 47.9 | 31 | 56.4 | |
| CC | 69 | 23.8 | 10 | 18.2 | |
| HLA-DRB1*15:01 homozygote | | | | | |
| TT | 7 | 24.1 | 0 | 0 | 0.61 |
| CT | 12 | 41.4 | 2 | 66.7 | |
| CC | 10 | 34.5 | 1 | 33.3 | |

*Statistical comparison does not pass Bonferroni correction (p^*2). The control group is small and does not allow drawing solid conclusions.

Logistic regression and stratified analysis for rs6811520

Logistic regression of the SNP

| Rs6811520 | OR (95% CI) | P |
|---------------------|-----------------|------|
| Cc vs. Carrier of T | 0.97 (0.72-1.3) | 0.82 |

SNP adjusted by sex, HLA and clinical form

| Rs6811520 | OR (95% CI) | P |
|----------------------|-------------------|--------|
| CC vis. Carrier of T | 1.09 (0.74-1.63) | 0.645 |
| Sex male | 1.56 (1.17-2.08) | 0.002 |
| Sex female | 4.03 (1.03-15.75) | 0.045 |
| HLA-DRB1*1501 | 3.31 (2.40-4.58) | <0.001 |
| Clinical form | -- | -- |

Analysis stratified by sex

| CLOCK rs6811520 | Female MS | | Female Controls | | p |
|-----------------|-----------|---------------|-----------------|------|------|
| | N | % | N | % | |
| TT | 265 | 41.5 | 154 | 42.1 | |
| CT | 292 | 45.8 | 167 | 45.6 | |
| CC | 81 | 12.7 | 45 | 12.3 | 0.83 |
| Male MS | | Male Controls | | | |
| TT | 127 | 41.1 | 90 | 37.3 | |
| CT | 137 | 44.3 | 112 | 46.5 | 0.37 |
| CC | 45 | 14.6 | 39 | 16.2 | |

Analysis stratified by clinical form

| CLOCK rs6811520 | RR | SP | | PP | | |
|-----------------|-----|------|----|------|----|------|
| | | N | % | N | % | |
| TT | 179 | 41.7 | 28 | 34.6 | 10 | 55.5 |
| CT | 199 | 46.4 | 42 | 51.9 | 2 | 11.2 |
| CC | 51 | 11.9 | 11 | 13.6 | 6 | 33.3 |

RR vs SP p=0.27; RR vs PP p=0.64; SP vs PP p=0.95

| |
|---------------------------|
| RR: Relapsing remitting |
| SP: secondary progressive |
| PP: primary progressive |

Analysis stratified by HLA DRB*15:01 status

| <i>CLOCK</i> rs6811520 | MS | | Controls | | |
|----------------------------------|-----|------|----------|------|-------|
| Not HLA-DRB1*15:01 | N | % | N | % | p |
| TT | 244 | 39.7 | 159 | 37.9 | 0.26 |
| CT | 292 | 47.5 | 193 | 46.1 | |
| CC | 79 | 12.8 | 67 | 16.0 | |
| HLA-DRB1*15:01 / X | | | | | |
| TT | 132 | 44.9 | 31 | 55.4 | 0.04* |
| CT | 124 | 42.2 | 23 | 41.1 | |
| CC | 38 | 12.9 | 2 | 3.5 | |
| HLA-DRB1*15:01 homozygote | | | | | |
| TT | 12 | 38.7 | 2 | 66.7 | 0.23 |
| CT | 9 | 29.0 | 1 | 33.3 | |
| CC | 10 | 32.3 | 0 | 0 | |

*Statistical comparison does not pass Bonferroni correction (p^*2). The control group is small and does not allow drawing solid conclusions.