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# Supplemental Data

# Two Susceptibility Loci to Takayasu Arteritis Reveal a Synergistic Role of the *IL12B* and *HLA-B* Regions in a Japanese Population

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Figure S1. Manhattan plot based on imputed results

The horizontal line indicates the significant level based on Bonferroni's correction. The HLA locus on chromosome 6 and the *IL12B* region on chromosome 5 reached the significant level.

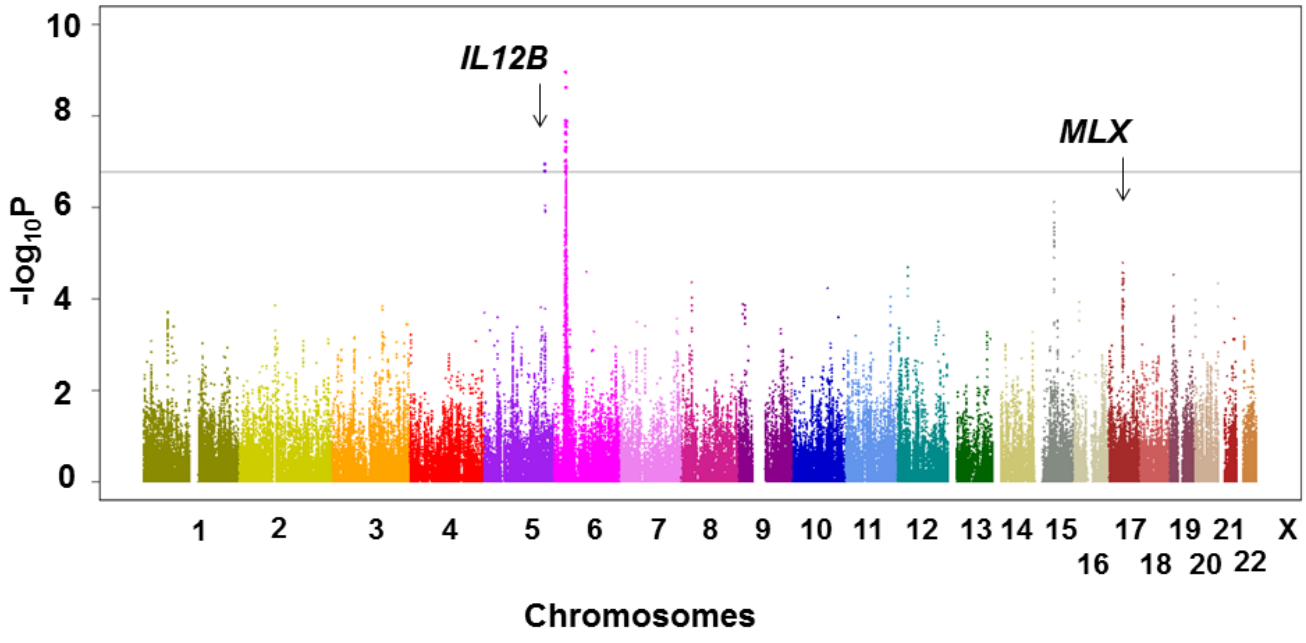

Figure S2. Associations between rs665268 genotypes and clinical manifestations of TAK.

An association between rs665268 genotypes and A) development of AR, B) severity of AR, and C) time-averaged CRP levels in TAK cases. The p-value was calculated by A) logistic regression analysis, B) linear regression analysis, and C) linear regression analysis with time-averaged dosage of prednisolone as covariate. The dominant model is applied to all calculations. Severity of 1 to 3 in AR corresponds to mild, moderate, and severe, respectively. Mean±SD are indicated for B) and C).

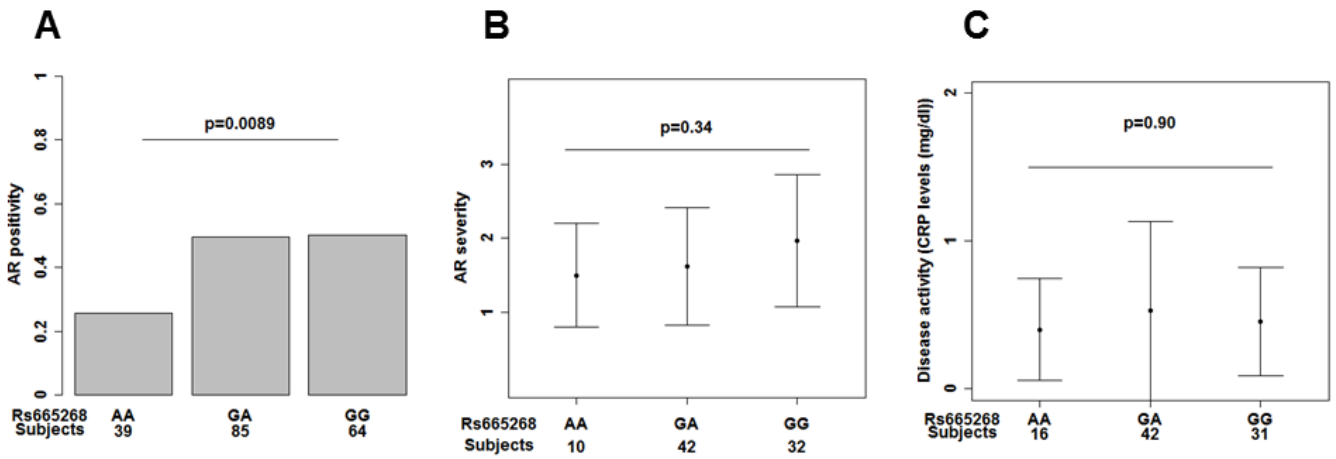

Figure S3. Associations between clinical manifestations and combinations of *IL12B* and HLA-B*52:01

The results of analyses for synergistic effects between rs6871626 and HLA-B*52:01 on A) existence of AR, B) severity of AR, and C) time-averaged CRP levels as disease activity. Mean±SD are indicated for B) and C).

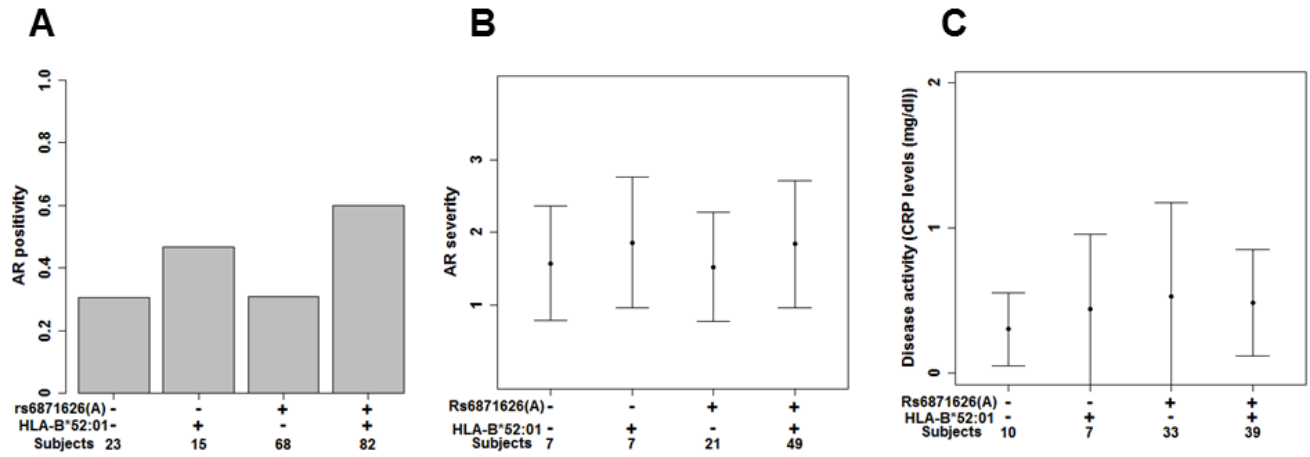

Figure S4. A synergistic effect between *MLX* and HLA-B*52:01 on TAK susceptibility

ORs are shown for the four strata of subjects according to combination of rs665268 and rs9263739 genotypes. Those who are negative for rs9263739 T allele, a proxy of HLA-B*52:01, and rs665268 G allele are used as reference. ORs and 95%CI are indicated.

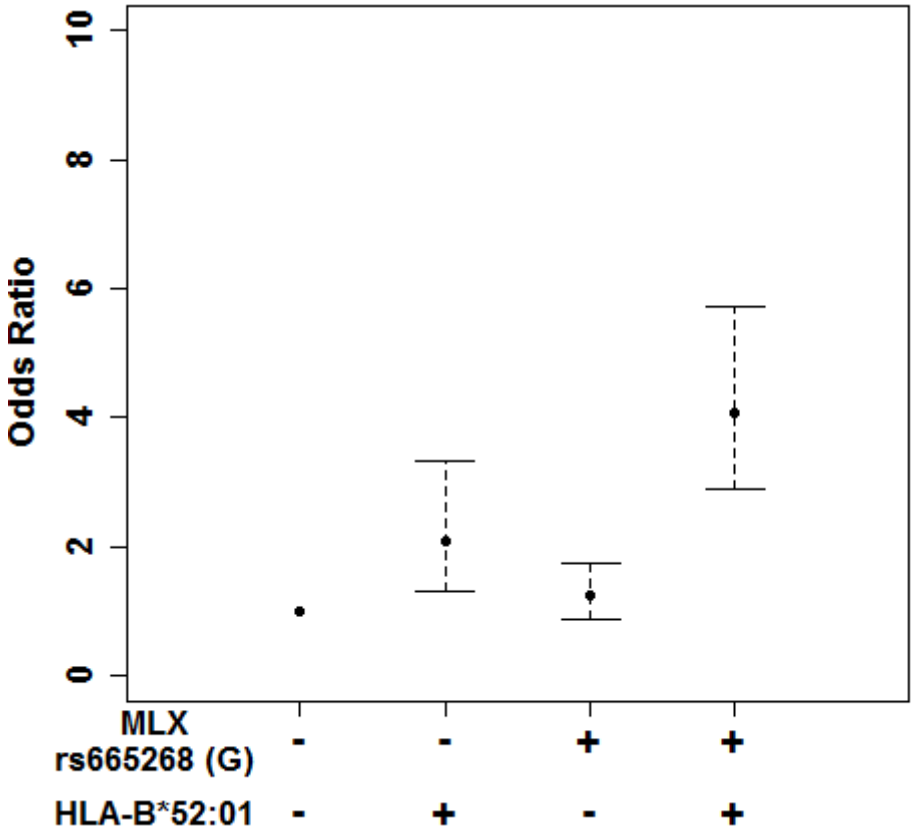

Figure S5. Associations between clinical manifestations and combinations of *MLX* and HLA-B*52:01

The results of analyses for synergistic effects between rs665268 and HLA-B*52:01 on A) existence of AR, B) severity of AR, and C) time-averaged CRP levels as disease activity. Mean±SD are indicated for B) and C).

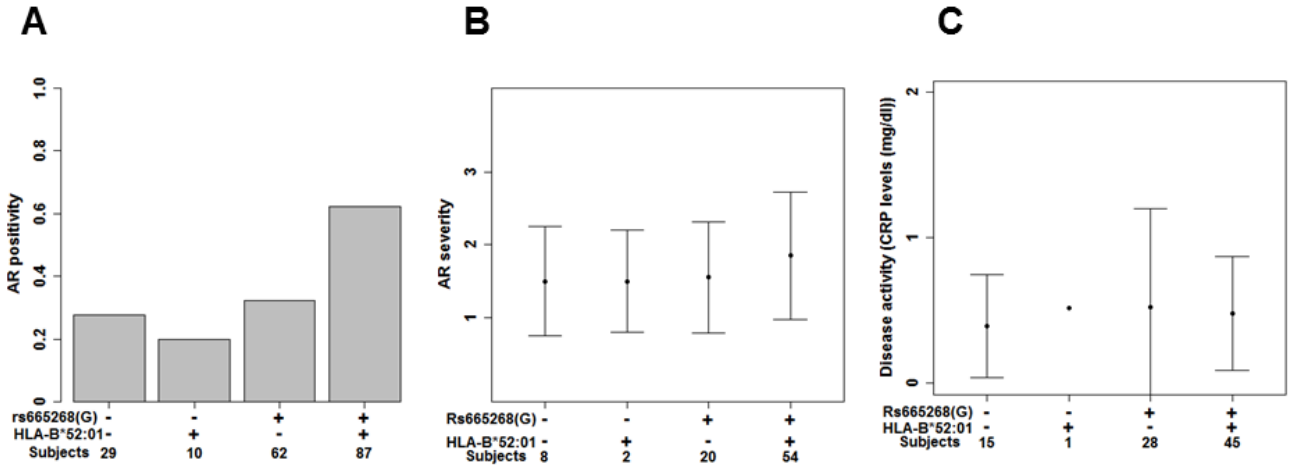

Figure S6. Associations between *IL23R/IL12RB2* and TAK susceptibility

Associations of SNPs in the *IL23R/IL12RB2* region are plotted according to the position of the markers. Red circles indicate results of the current genome-scanning. Blue circles indicate results of the imputation analysis based on the current results. The middle panel indicates recombination rates. The lower panel indicates LD of markers.

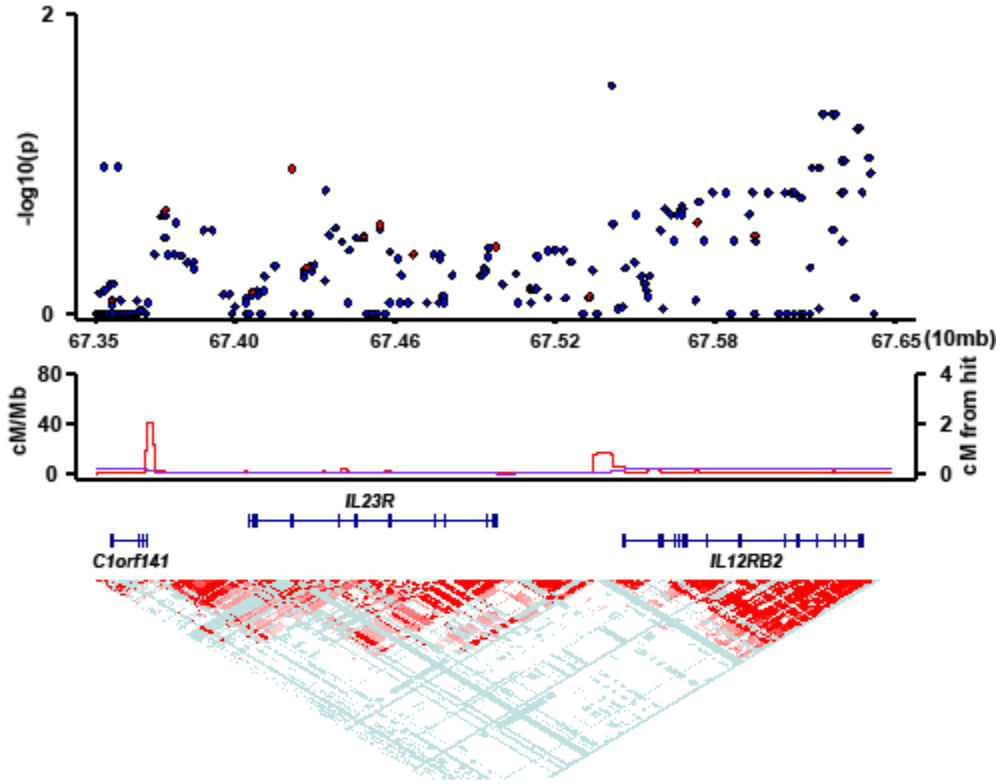

Table S1. Synergistic effects between *MLX* and HLA-B*52:01 in each study

| Study | RERI | | AP | | SI | |
|---|---|---|---|---|---|---|
| | (95%CI) | p | (95%CI) | p | (95%CI) | p |
| Genome-scanning | 2.55 (0.98-4.12) | 0.0015 | 0.67 (0.39-0.95) | $3.0x10^{-6}$ | 10.72 (0.10-1203.4) | 0.32 |
| Replication study | 0.95 (-0.68-2.58) | 0.25 | 0.23 (-0.14-0.61) | 0.23 | 1.45 (0.70-2.98) | 0.32 |
| Combined study | 1.73 (0.59-2.87) | 0.0029 | 0.43 (0.19-0.66) | 0.00046 | 2.29 (1.10-4.79) | 0.027 |

RERI: relative excess risk, AP: attributable proportion, and SI: synergy index, CI:confidence interval.