The Minor Protective Allele at rs1876453 is Associated with Increased Age of Onset of Systemic Lupus Erythematosus


BACKGROUND

rs1876453 in CR2 is associated with decreased susceptibility to lupus (p = 0.0045) (Zhao et al, Ann Rheum Dis 75:242, 2016).

• This association was particularly striking when subjects with lupus were stratified based on sex, females with the protective allele had significantly delayed onset of lupus (p = 0.0045) (Zhao et al, Ann Rheum Dis 75:242, 2016).

• Anti-dsDNA antibodies are detected in patients with lupus a mean of 1.2 years before their initial symptom and a mean of 2.2 years before their diagnosis (Artuculie et al, N Engl J Med 348:1926, 2003).

HYPOTHESIS

• Lupus patients with the minor protective allele at rs1876453 will have delayed onset of lupus compared to patients with the major allele.

METHODS

• DNA from 5382 patients with SLE recruited from multiple sites was genotyped for rs1876453 on the Oklahoma Medical Research Foundation (OMRF) Illumina iSelect platform as part of the Large Lupus Association Study 2 (LLAS2).

• Global ancestry was estimated based on the genotype of ancestry informative markers.

• Age of onset was collected by chart review.

• Kruskal-Wallis and Mann Whitney tests were used to detect differences between groups. A p value of <0.05 was considered significant. Statistics and graphs were generated using GraphPad Prism software.

• Institutional review board approval was obtained for LLAS2 at OMRF and at each of the contributing sites.

CONCLUSIONS

• The minor protective allele at rs1876453 delays onset of lupus.

• Subjects with one copy of the protective allele develop lupus a median of 2 years later than subjects without the protective allele.

• These data confirm the relevance of this polymorphism in lupus pathogenesis.

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