Dissecting the genetic factors involved in systemic lupus erythematosus development

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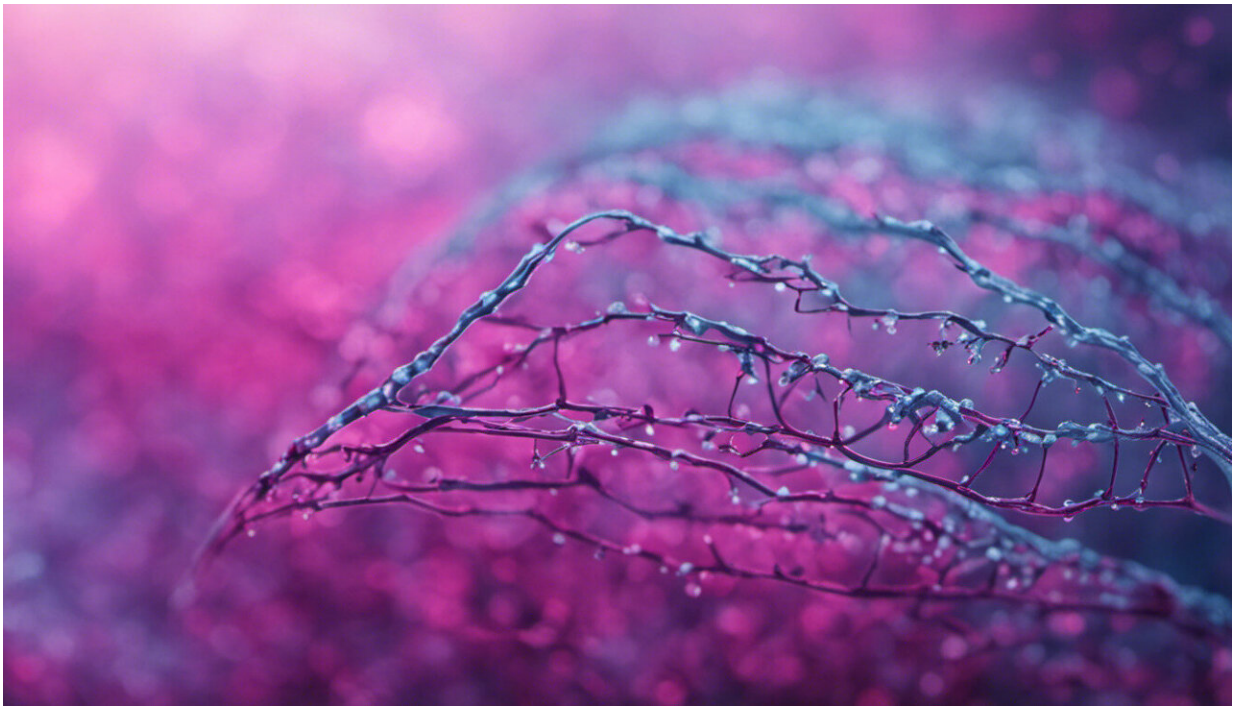

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Systemic lupus erythematosus (SLE) is a typical autoimmune rheumatic disease. This multifactorial condition results from a combination of multiple genetic and acquired factors. Human leukocyte antigen (HLA), which is responsible for individual differences in immune response, is one of the major genetic factors associated with SLE development.

However, its contribution to the pathogenesis of the disease has not been fully understood.

The gene sequence associated with SLE susceptibility occasionally varies among populations. In the Japanese population, the gene sequence type HLA-DRB1*15:01 is associated with SLE susceptibility.

In the European population, a very high proportion of individuals with HLA-DRB1*15:01 also have specific variants (individual differences in the DNA sequence) in the intergenic region, which is located in the adjacent XL9 region on the chromosome and regulates the expression of the HLA cluster. Consequently, it has been difficult to determine whether HLA-DRB1*15:01 itself or the variants in the XL9 region is important.

In this study, researchers observed that the combination of HLA-DRB1*15:01 and XL9 variants was not as prominent in the Japanese population compared to the European population. Using epidemiological analysis, they were able to distinguish the effects of HLA-DRB1*15:01 and XL9 variants.

Of the two, HLA-DRB1*15:01 was primarily associated with the SLE development in the Japanese population, and the association with the XL9 region was secondary, suggesting that differences in amino acid sequences based on the diversity of the HLA itself are likely to influence SLE development. The research is published in the journal *RMD Open*.

Furthermore, the study reaffirmed the usefulness of analyzing multiple populations with different genetic backgrounds for identifying genetic variants that contribute to the development of multifactorial diseases.

More information: Aya Kawasaki et al, Genetic dissection ofHLA-DRB1*15:01and XL9 region variants in Japanese patients with systemic

lupus erythematosus: primary role forHLA-DRB1*15:01, *RMD Open* (2023). DOI: 10.1136/rmdopen-2023-003214