Genetic variant tied to MS and systemic lupus identified

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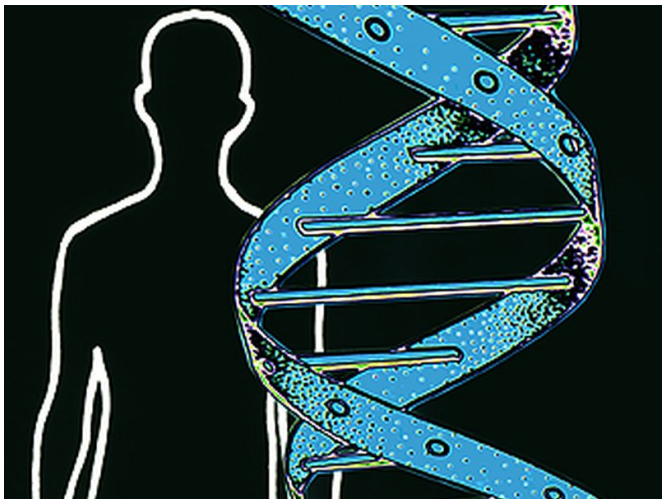

(HealthDay)—A genetic variant that is associated with both multiple sclerosis and systemic lupus erythematosus (SLE) has been identified, according to a study published online April 26 in the *New England Journal of Medicine*.

Maristella Steri, Ph.D., from Istituto di Ricerca Genetica e Biomedica in Italy, and colleagues conducted a genome-wide association study in multiple sclerosis as well as *TNFSF13B* locus-specific association testing in SLE. To identify the causal variant and determine its mechanism of action, they performed extensive phenotyping of quantitative immune variables, sequence-based fine mapping, cross-population and cross-phenotype analyses, and gene expression studies.

The researchers found that a variant in *TNFSF13B*, encoding the cytokine and drug target B-cell activating factor (BAFF), was associated with both multiple sclerosis and SLE. There was also an association between the disease-risk allele and up-regulated humoral immunity through increased levels of soluble BAFF, B lymphocytes, and immunoglobulins. An insertion-deletion variant, GCTGT?A (in which A is the risk allele) was identified as the causal variant and yielded a shorter transcript that escaped microRNA inhibition and increased production of soluble BAFF. This in turn up-regulated humoral immunity. This autoimmunity variant has been evolutionarily advantageous, based on population genetic signatures, most likely by augmenting resistance to malaria.

"Overall, the evolutionary scenario we propose is that BAFF-var was selected as an adaptive response to malaria infection, resulting in an increased present-day risk of autoimmunity," conclude the authors.

More information: Abstract/Full Text (subscription or payment may be required)