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A Proposal Concept of a Polygene Network in Systemic Vasculitis: Lessons from MRL Mouse Models

http://www.firstlight.cn 2007-06-18

In addition to the studies of cellular and molecular events in the pathogenesis of systemic vasculitis, a genome analysis of mouse models may shed some light on the complex clinicopathological manifestations of systemic vasculitis. In the study of susceptibility loci to vasculitis in MRL mouse models, we learned that systemic vasculitis developed in a cumulative effect of multiple gene loci, each of which by itself did not have a significant effect to induce the related phenotype, thus indicating a polygenic system. The mice developed vasculitis in an additive manner of multiple genes with a hierarchical effect. Some of the susceptibility loci seemed to be common to those in other collagen diseases as well. Moreover, the loci controlling tissue specificity of vasculitis were present. One of the positional candidate genes for vasculitis showed an allelic polymorphism in the coding region, thus possibly causing a qualitative difference in its function. As a result, a particular combination of polygenes with such an allelic polymorphism may thus play a critical role in leading the cascade reaction to develop vasculitis, and also a regular variation of systemic vasculitis. This is designated as the polygene network in systemic vasculitis.

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