The role of FcgammaRIIA and IIIA polymorphisms in autoimmune diseases.

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Source
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Abstract
Our knowledge about the role of human Fc receptors for IgG (FcgammaR) has increased considerably within the last several years. These receptors vary in their affinity for IgG, their preferences for IgG subclasses, the cell type-specific expression patterns, and the intracellular signals that they elicit. Additional FcgammaR heterogeneity is introduced by the presence of well characterized genetic polymorphisms. Allelic variants of FcgammaR genes may influence phagocyte biologic activity, providing a basis for inherited predisposition to disease. Recent evidence suggests that certain FcgammaR alleles are genetic risk factors for systemic autoimmune diseases and the development of major manifestations of these diseases. The FcgammaRIIA-R/H131 polymorphism is an important determinant of predisposition to systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS). FcgammaRIIA-R131, the low-binding IgG2 allele, seems to confer risk for APS under a recessive model, whereas its effect on SLE susceptibility probably has a dose-response character. The population-attributable fraction of lupus cases due to the R131 allele is 13% and for APS cases is at least 10%, in subjects of European descent. The FcgammaRIIIA-V/F158 polymorphism has a significant impact on renal involvement in lupus patients. The proportion of nephritis cases that could be attributed to the low-binding IgG1 and IgG3 F158 allele is approximately 10-14%. These genetic associations have been well documented in meta-analyses including a large number of studies. Besides the epidemiologic and pathophysiologic interest, this knowledge may be of use in the future in designing novel therapeutic interventions.

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