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Autoantibodies to GPI in rheumatoid arthritis

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Keywords

Autoantibodies, mouse model, rheumatoid arthritis

Context

The study of the various animal models of rheumatoid arthritis (RA) has provided valuable information about the multiple pathways leading to the disease and enabled the evaluation of potential therapeutic treatments. A recently described K/BxN T-cell receptor transgenic mouse model spontaneously develops a disease with clinical, histological and immunological features of human RA; however, the presence of serum rheumatoid factors is not a feature of this model. Disease development in the transgenic mice is dependent on systemic T-cell self-reactivity, but disease progression is caused by the production of arthritogenic IgG antibodies to a ubiquitously expressed self-antigen, glucose-6-phosphate isomerase (GPI). As the effector phase of the disease is almost exclusively driven by GPI antibodies, this mouse model has been considered valuable for analyzing B cell effector pathways that contribute to arthritis. However, there has been no evidence that GPI autoantibodies are expressed in humans and the relevance to human RA has been questioned. To determine if there is a relationship between this animal model and human disease, the authors investigate if GPI is an autoantigen involved in human RA.

Significant findings

Increased levels of anti-GPI IgG were found in the sera (64%) and synovial fluid (33%) of RA patients, but in all other patient groups levels were less than 5%. Weak responses were detected in healthy controls at low frequency (3%). Some RA patients (73%) were also positive for rheumatoid factor, but no correlation with anti-GPI IgG levels was observed. Anti-GPI IgG titers were similar in RA sera and synovial fluid; however, GPI levels were twofold higher in synovial fluid. Further analysis of RA synovial fluid revealed that GPI and anti-GPI IgG were present as immune complexes. The anti-GPI IgG antibodies were characterized molecularly, using an IgG phage-display library generated from an RA patient with a high GPI serum titer. Sequence analysis revealed evidence of multiple somatic

mutations in several antibody clones, including two that exhibited strong binding affinity for GPI. Immunohistochemistry of RA synovium revealed intense staining for GPI on the endothelial cell surface of synovial arterioles, and along the surface lining of the hypertrophic synovium. Skin sections also revealed strong GPI staining of keratinocytes. The staining of synovial endothelium in particular may be an important mechanism by which GPI contributes to joint pathology, since these cells are known to be involved in a variety inflammatory processes.

Comments

The authors perform thorough analyses of sera and synovial tissue from RA patients and provide the first evidence that GPI may be an important autoantigen in human RA. Few details of patient demographics are provided, however, making it difficult to determine whether anti-GPI IgG responses are specific for a subset of patients with RA. The identification of common autoantigens are intriguing; however, the data presented are only correlative. Nevertheless, this study provides a basis for further investigation of the pathological mechanisms by which GPI autoantibodies may contribute to RA pathogenesis in the mouse model.

Methods

Phage display library, affinity gel chromatography, ELISA, DNA sequencing, immunoblotting, immunofluorescence, surface plasmon resonance

Additional information

References

1. Schaller M, Burton DR, Ditzel HJ: Autoantibodies to GPI in rheumatoid arthritis: linkage between an animal model and human disease. Nat Immunol. 2001, 2: 746-753.