AUTOIMMUNITY

Human SLE B cells lack self-control

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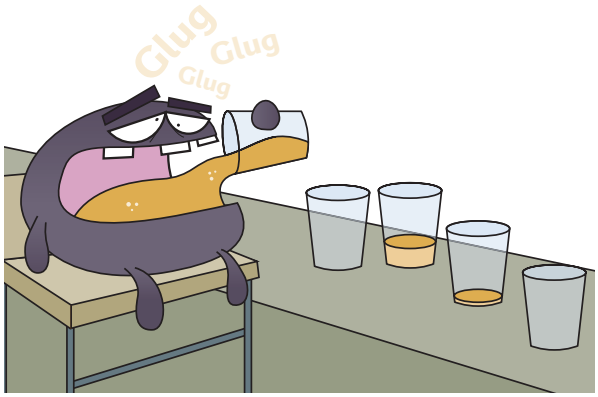
FcγRIIb
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=full_report&list_uids=2213

The autoimmune disease systemic lupus erythematosus (SLE) is characterized by the inappropriate activation and proliferation of autoreactive memory B cells in the periphery. Mouse models of SLE have shown a clear association between disease susceptibility and the amount of expression of the inhibitory IgG receptor FcγRIIb. Crosslinking of FcγRIIb and the B-cell receptor (BCR) — with IgG, for example — would normally inhibit BCR signalling, so it has been proposed that SLE can occur when B cells lack this self-control mechanism. However, human studies have been less conclusive, owing to a lack of specific serological reagents. Also, the role of FcγRIIb polymorphisms in the susceptibility of humans to SLE varies depending on the ethnicity of the population being studied.

This study used the recently developed monoclonal antibody 2B6, which can distinguish between FcγRIIa and FcγRIIb, to quantify the amount of FcγRIIb expressed at the surface of B cells from patients with SLE compared with those from non-autoimmune control individuals. Naive B cells from both control and disease populations expressed similar amounts of FcγRIIb. But, whereas memory B cells from control individuals upregulated expression of FcγRIIb, memory B cells from patients with SLE failed to do so. This failure of memory B cells to upregulate expression of FcγRIIb resulted in an inability to suppress the BCR-induced Ca^{2+} response, which activates B cells, when cells were stimulated with IgG. Therefore, decreased FcγRIIb expression by the memory B cells of patients with SLE could result in increased BCR-mediated B-cell activation.

In terms of clinical correlates, the authors could not show an association between the amount of FcγRIIb expressed by memory B cells and the disease course or severity. However, there was a statistically significant association between race and the amount of FcγRIIb expressed by memory B cells of patients with SLE; 55% of African-American patients showed downregulated FcγRIIb expression by memory B cells, in contrast to 27% of other patients. This finding indicates that failure to upregulate FcγRIIb might be the result of a genetic difference. Further work is required, however, to determine whether the decreased expression of FcγRIIb by memory B cells in this study is a result of one of the previously described polymorphisms of the transmembrane-encoding or promoter regions of the gene that encodes FcγRIIb in humans.

Kirsty Minton



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