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Autoreactive marginal B cells in drug-induced lupus

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Keywords

Autoreactive B cells, induced-SLE, tolerance

Context

Expansion of autoreactive B cells could explain the presence of autoantibodies in the autoimmune disease, systemic lupus erythematosus (SLE). To gain better insight into the production of autoreactive B cells, the authors have developed a drug-induced model of lupus in BALB/c mice transgenic for the heavy chain of an anti-DNA antibody. Normally, the transgenic mice display effective regulation of the transgene-expressing anti-DNA B cells. When treated with exogenous 17'-estradiol (E2), autoreactive B cells were activated and mice developed a lupus-like disease.

Significant findings

In this model, only a small population of B cells was activated, showing that the autoimmune disease does not result in polyclonal B-cell activation. However, the splenic B-cell development is altered by E2 treatment, with a decrease in transitional B cells and an increase in marginal zone B cells. Moreover, anti-DNA secreting B cells display a marginal zone B cell phenotype. These alterations do not result from $CD4^+$ T-cell activation.

Comments

These results demonstrate that an autoreactive marginal zone B-cell population proliferates during SLE development, and may be mechanistically involved in disease induction. The results are very interesting and should permit insights into both the mechanism of B-cell tolerance breakdown and the

role played by estrogens in this disease. However, these results were obtained in a nonautoimmune transgenic mouse strain, and the clinical manifestations are not spontaneous but are induced instead by a hormone.

Methods

Flow cytometry, immunochemistry, ELISPOT assay

Additional information

References

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