ANALYSIS OF THE SPLEEN OF BFCRN TG MICE WITH AUGMENTED IMMUNE RESPONSE

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Introduction

The neonatal Fc receptor (FcRn) plays a key role in IgG and albumin homeostasis, and is involved in antigen presentation in case of antigen-IgG immune complexes. We have previously demonstrated that bovine FcRn (bFcRn) overexpression in transgenic (Tg) mice significantly augments the humoral immune response producing higher titer of antigen specific antibodies and increased number of antigen-specific B cells and hybridomas, offering a great advantage in polyclonal and monoclonal antibody production.

Methods

To gain further insight into the mechanisms of this enhanced humoral immune response we examined the spleen structure of untreated and immunized bFcRn Tg and wild type (wt) mice, and localized bFcRn positive cells with a newly developed bFcRn-specific monoclonal antibody.

Results

Thy-1, B220 and CR1/2 staining demonstrated normal localization of T and B-cell zones and follicular dendritic cells in the white pulp, both in untreated and immunized bFcRn Tg mice. Furthermore, MARCO and CD169 staining indicated a preserved distribution of marginal zone macrophages and marginal metallophilic macrophages in Tg mice. Germinal centers (GCs) formed in bFcRn Tg mice upon booster immunization with ovalbumin were twice as large as compared to wt animals, indicating improved recall response.
To determine the topographic relationship between bFcRn-expressing cells and GC formation, spleen sections were stained with our recently developed bFcRn-specific monoclonal antibody that does not cross-react with mouse FcRn. We detected strong bFcRn expression in the marginal zone macrophages and marginal metallophilic macrophages. In addition, other bFcRn-positive cells in the T-cell zone and red pulp were found, possibly corresponding to dendritic cells and red pulp macrophages.

Conclusions

The general lymphoid architecture of the spleen was unchanged in bFcRn Tg mice. The strong bFcRn expression of splenic macrophages that are essential for the formation of germinal centers and dendritic cells with highly effective immune complex presentation capacity probably contributes to the GC enlargement and augmented humoral immune response in bFcRn Tg mice.

Supported by grant K101364 from Hungarian Scientific Research Fund.