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Editorial Open Access

iNKT Cells in Lupus Development

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Editorial

Invariant natural killer T (iNKT) cells are a new subset of T cells that bridge innate and acquired immunity and play important roles in both protective and regulatory responses in a variety of diseases [1,2]. Our group has worked on the role and the underlying molecular mechanisms of iNKT cells in lupus development for more than a decade and published a dozen of research articles in peer reviewed journals. Here, we briefly summarize and comment our findings.

Several promising and important findings are made on the features and roles of iNKT cells in three murine models of lupus. Firstly, we revealed for the first time that iNKT cells were deficient in both number and function in lupus-prone MRL-*lpr* mice. Moreover, repeated administration of α-GalCer, a glycolipid and natural activator of iNKT cells, expanded iNKT cell number and function in these mice [3]. This finding revealed that α-GalCer was able to induce iNKT cell expansion *in vivo*. Before that, NKT cells were generally believed to undergo apoptosis upon α-GalCer treatment. Consistent to this finding, MRL-*lpr* mice with CD1d-deficiency, which blocks iNKT cell development, exacerbated the frequency and severity of skin lesions [4]. Treatment with α-GalCer ameliorated the dermatitis in MRL-*lpr* mice [3]. Secondly, in an induced lupus model in BALB/c mice by hydrocarbon oil pristane (2,6,10,14-tetramethylpentadecane, TMP), iNKT cells were found to be functionally insufficient. CD1-deletion in these mice further increased the level of serum autoAbs and induced more severe glomerulonephritis [5]. In addition, repeated α-GalCer treatment of pristane-inoculated BALB/c mice prior to the onset of florid disease suppressed proteinuria [6]. Thirdly, (NZB × NZW) F1 (BWF1) mice showed intrinsic deficiency of iNKT cell function [7]. Deficiency of CD1 in BWF1 mice further worsened the glomerulonephritis as compared to wild-type mice [8]. Similar findings are evident in β2-microglobulin knockout BWF1 mice, where iNKT cells are also deficient as CD1 knockout mice [9]. Interestingly, activation of iNKT cells with α-GalCer in BWF1 mice at an early age by short term ameliorated the glomerulonephritis [10]. Moreover, iNKT cells can directly regulate autoreactive B cells in a contact and CD1-dependent manner. This regulation was related to the impaired IL-10 production from B cells, reduced number and function of marginal zone B cells and involved Fas pathway [11,12].

The above studies indicate the regulatory role of iNKT cells in lupus development. These findings should be helpful to delineate the pathogenesis of lupus and may have the potential leading to new therapeutics for lupus, and perhaps other autoimmune diseases, based on manipulation of iNKT cells. Further in-depth studies are needed to explore the underlying molecular mechanisms how iNKT cells control lupus development.

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