IMMUNOREGULATORY EFFECTS OF $\alpha$-GALCER IN A MURINE MODEL OF AUTOIMMUNE MYOCARDITIS

Li Shuqing  Department of Cardiology, The First Affiliated Hospital, Harbin Medical University

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Objective This study was designed to investigate the immunoregulatory role of $\alpha$-galactosylceramide ($\alpha$-GalCer), a ligand for invariant natural killer T (iNKT) cells, on experimental autoimmune myocarditis (EAM) induced in Balb/c mice, and to explore the underlying mechanisms of its action.

Methods Balb/c mice were immunised on day 0 with porcine cardiac myosin to establish the EAM model. All the immunised mice were divided into two groups, the $\alpha$-GalCer treated group and the EAM group. A dose of $\alpha$-GalCer (2 μg/mouse/injection) or vehicle (1% phosphate-buffered saline, PBS) was given intraperitoneally at the time of immunisation, and then $\alpha$-GalCer or PBS was injected on alternate days for 6 weeks. Untreated Balb/c mice (n=10) served as normal controls.

Results All animals were euthanised 1 day after the last injection. Myocardial inflammation was evaluated by H & E staining and the expression levels of C/EBPβ and $\alpha$-SMA were determined by immunohistochemistry. CD4 $^+$ CD25 Foxp3$^+$ Tregs and iNKT cells were analysed and sorted by flow cytometry. Western blot analysis was performed to detect MMP-2 and MMP-9 protein expression. Following $\alpha$-GalCer treatment for 6 weeks, myocardial inflammation improved significantly in the $\alpha$-GalCer treated group compared to the EAM group. The proportions of CD4 $^+$ CD25 Foxp3$^+$ regulatory T cells and NK1.1$^+$ iNKT cells were statistically increased in the $\alpha$-GalCer treated group compared to the EAM and normal control groups. In contrast to the EAM group, $\alpha$-GalCer treatment significantly increased myocardial MMP-2 and MMP-9 expression. Expression of C/EBPβ increased significantly in the EAM group compared to the $\alpha$-GalCer treated group and the normal control group. In contrast, the expression of $\alpha$-SMA in the myocardium did not differ significantly among the three groups.

Conclusion This study demonstrated that $\alpha$-GalCer alleviates experimental autoimmune myocarditis in Balb/c mice. Thus, $\alpha$-GalCer represents a potential therapeutic target for autoimmune-inflammation mediated cardiac damage. This study revealed that $\alpha$-GalCer protects experimental autoimmune myocarditis through upregulation of the proportion of iNKT and Tregs and increased expression of myocardial MMP-2 and MMP-9.
Immunoregulatory effects of α-GalCer in a murine model of autoimmune myocarditis

Li Shuqing

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