[gw22-e0219]

IMMUNOREGULATORY EFFECTS OF α -GALCER IN A MURINE MODEL OF AUTOIMMUNE MYOCARDITIS

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10.1136/heartjnl-2011-300867.604

Objective This study was designed to investigate the immunoregulatory role of α -galactosylceramide (α -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 α -GalCer treated group and the EAM group. A dose of α -GalCer (2 μ g/mouse/injection) or vehicle (1% phosphate-buffered saline, PBS) was given intraperitoneally at the time of immunisation, and then α -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/EBP β and α -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 α -GalCer treatment for 6 weeks, myocardial inflammation improved significantly in the α -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 α -GalCer treated group compared to the EAM and normal control groups. In contrast to the EAM group, α -GalCer treatment significantly increased myocardial MMP-2 and MMP-9 expression. Expression of C/EBP β increased significantly in the EAM group compared to the α -GalCer treated group and the normal control group. In contrast, the expression of α -SMA in the myocardium did not differ significantly among the three groups.

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