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MEETING ABSTRACT Open Access

Peripherally induced Foxp3$^+$ regulatory T cells mediates the immunomodulatory effect of intravenous immunoglobulin in an experimental model of allergic airway disease

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Background

IVIg is a polyclonal IgG preparation with potent immune-modulating properties. We demonstrated that IVIg protects against airway hyperreactivity (AHR) and airway inflammation in mouse models of allergic airway disease, accompanied by peripheral induction of Foxp3$^+$regulatory T-cells (iT$_{reg}$). The requirement of IVIg-induced iT$_{reg}$ and their antigen-specificity in attenuation of AHR and airway inflammation remains unknown.

Methods

We utilized DEREG mice, carrying a transgenic diphtheria toxin receptor under the control of the Foxp3 promoter, allowing for selective depletion of Foxp3$^+$T$_{reg}$ by the application of diphtheria toxin (DT). Mice were sensitized and challenged with ovalbumin (OVA) and treated with IVIg. AHR was measured using a FlexiVent small animal ventilator. Total and antigen-specific IgE, as well as pro-inflammatory cytokines levels were determined in serum and alveolar lavage, using ELISA.

Results

In the absence of Treg, due to multiple DT doses before and after the treatment, IVIg was not able to attenuate AHR, diminish IgE levels and Th-2 type cytokine production, nor alleviate airway inflammation. However, mice in which the pre-established T$_{reg}$ cells (nT$_{reg}$) were depleted before but not following IVIg treatment demonstrated an induction of Foxp3$^+$T$_{reg}$ to IVIg therapy and did not develop AHR and airway inflammation to allergen-challenge. Adoptive transfer of enriched IVIg-induced iT$_{reg}$ from OVA-IVIg treated mice failed to transfer protection to mice exposed to ragweed, but was protective in OVA-sensitized and challenged mice.

Conclusions

T$_{reg}$ can be induced from effector CD4$^+$T-cells in the absence of nT$_{reg}$. IVIg-induced antigen specific T$_{reg}$ are capable of suppressing all aspects of antigen-driven airway inflammation in an antigen-specific manner.

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