Effects of Steroids in Cultured human Type-2 Cytokine Producing Cells

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Background

Type-2 T helpers (Th2), type-2 cytotoxic T cells (Tc2), and group 2 innate lymphoid cells (ILC2) have been found to be important sources of type-2 cytokines and numbers are increased in blood and sputum in patients with severe asthma. Corticosteroids are potent anti-inflammatory treatment but patients with severe asthma have a diminished response. In our cohort study, ILC2 numbers in peripheral blood remained unchanged after treatment of oral corticosteroids. Here we have tested the hypothesis that ILC2 are resistant to the apoptotic effects of corticosteroids *in vitro* and have explored potential mechanisms.

Aims

We aimed to evaluate the apoptotic responses of the cultured human Th2, Tc2 and ILC2 to corticosteroids and confirm the steroid resistance of ILC2 *in vivo* (see another abstract by Shrimanker R. et al).

Methods

Human Th2 and Tc2 cells were isolated from CD Leucocyte Cones, and ILC2 cells were sorted from mononuclear cells of blood of healthy volunteers and cultured. The effect of serial concentrations (0.1nM to 1000nM) of dexamethasone with and without the multi-drug resistance protein 1 (MDR1) inhibitors, Tariquidar and Zosuquidar, were used to treat these three types of cells, and cell apoptosis was measured with Annexin V by using flow cytometry.

Results

Dexamethasone caused a concetration dependent increase in the percentage of apoptotic Th2, Tc2 and ILC2 increased. However the half maximal effective concentration (EC_{50}) of dexamethasone in ILC2 (5.467 nM) was much higher than that in Th2 (1.823 nM) and Tc2 (1.882 nM). Addition of Tariquidar (60 nM) and Zosuquidar (60 nM) did not enhance ILC2's response to dexamethasone.

Conclusions

ILC2 cells are less sensitive to dexamethasone induced apoptosis, compared to Th2 and Tc2. The responses of ILC2 to dexamethasone were not increased by MDR1 inhibitors, suggesting that MDR1 might not contribute to the apoptotic resistance of ILC2 to steroids.