

# 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.
- In patients with severe asthma, Th2, Tc2 and ILC2 are reported to be increased in both blood and sputum.
- 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 tested the hypothesis that ILC2 are resistant to the apoptotic effects of corticosteroids *in vitro* and have explored potential mechanisms.

## Aims

- To evaluate the apoptotic responses of the cultured human Th2, Tc2 and ILC2 to corticosteroids.
- To confirm the steroid resistance of ILC2 *in vitro* (see another abstract by Hynes G, et al).

## Bibliography

1. Smith SG, Chen R, Kjarsgaard M, et al. J Allergy Clin Immunol. 2016;137(1):75-86.e8.
2. Liu S, Verma M, Michalec L, et al. J Allergy Clin Immunol. 2018;141(1):257-268.e6

## Methods

- Human Th2 and Tc2 cells were isolated from CD Leucocyte Cones by MACS beads and cultured.
- Human ILC2 cells were sorted by BD FACS sorter from mononuclear cells of blood of healthy volunteers and cultured.
- Cells were treated with serial concentrations (0.1nM to 1000nM) of dexamethasone with or without the multi-drug resistance protein 1 (MDR1) inhibitors, Tariquidar and Zosuquidar.
- Cell apoptosis was measured with Annexin V by using flow cytometry.

## Results

- Dexamethasone caused a concentration dependent increase in the percentage of apoptotic Th2, Tc2 and ILC2.
- The half maximal effective concentration (EC<sub>50</sub>) of dexamethasone on ILC2 (5.467nM) was much higher than that in Th2 (1.823nM) and Tc2 (1.882nM).
- Addition of Tariquidar (60nM) and Zosuquidar (60nM) did not enhance ILC2's response to dexamethasone induced apoptosis.

## Conclusion

- 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.

### Dex Dose Curve in Th2 Tc2 ILC2

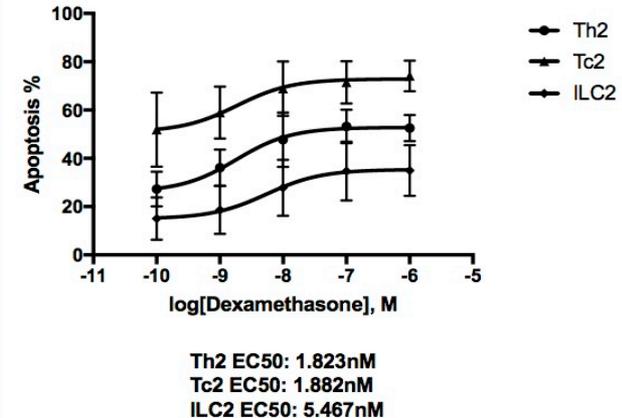


Figure 1 Dexamethasone induced cells apoptosis in Th2, Tc2 and ILC2.

### Dex Dose Curve in ILC2 with 60nM MDR1 Inhibitors

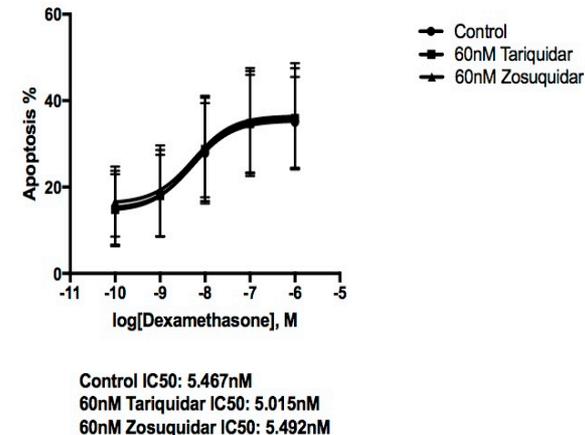


Figure 2 MDR1 inhibitor could not increase the sensitivity to dexamethasone induced cell apoptosis in ILC2