**BACKGROUND**

- Allergy is characterized by a Th2-biased immune response.
- Allergen-specific immunotherapy (SIT) is the curative treatment for allergy and involves subcutaneous injection of increasing doses of allergen extract (SCIT) or sublingual administration of allergen extract (SLIT).
- The focus of SIT is to shift Th2 bias to Th1.

**METHODS**

**Sample collection:** Whole blood was collected from subjects with allergy to Timothy grass pollen under an IRB approved protocol. The allergy to Timothy grass pollen was confirmed by skin prick test or RAST blood test. Peripheral blood mononuclear cells (PBMC) were isolated from whole blood by using Ficoll gradient centrifugation and cells were cryopreserved for batch analysis.

**PBMC culture and cytokine measurement:** PBMC were cultured with grass pollen Phleum pretense extract (10 µg/mL, Greer, Cat # XP01602), with or without GLA (1 µg/mL) for 6 days. Cytokine production was measured by ELISA and Lumineex assays kits by BD Biosciences and Bio-Rad.

**IL-12 blockade:** Anti-iL12p70 neutralizing antibody (clone 20C2, Bioxcell, Cat#: BE0234) were added to PBMC culture before the addition of PH extract and GLA. The neutralizing antibody was included during the 6 days incubation period.

**RESULTS**

**Proposed MOA of GLA in Allergy**

- GLA modulates the Th1/2 cytokine profiles in allergy patient PBMC by decreasing Th2 cytokines and increasing Th1 cytokines.
- The Th1-polarizing effects of GLA in allergy PBMC is dependent on IL-12.
- Results from current study suggest GLA may be a promising adjuvant in SIT for pollen allergy that warrants further development.

**Fig. 1 TLR4 agonists induce Th1 cytokines and type 1 IFN**

**Fig. 2 A potent inducer of innate immune genes**

**Fig. 3 GLA Decreases the Production of Th2 Cytokines**

**Fig. 4 GLA Increases the Production of Th1 Cytokines**

**Fig. 5 IL-12-polarizing IL-12 and Tolerogenic IL-10**

**SUMMARY**

- GLA shifts the Th1/2 balance via induction of IL-12 and by reversing the effect of GLA-induced type 1 IFN.
- The Th1-polarizing effects of GLA in allergy PBMC is dependent on IL-12.
- Results from current study suggest GLA may be a promising adjuvant in SIT for pollen allergy that warrants further development.

**REFERENCES**