Butyrate: Bridging Bench to Bedside -- Bringing Hope for Better Diagnostic and Therapeutic Options for Peanut Allergies

Heffernan, Isabella (School: Saint Mary Academy Bayview)

Background: Distinctive roles for T-lymphocyte:Bacteroides fragilis cross-talk occurs in dampening peanut allergic responses. Butyrate is key to B.fragilis regulation of immune homeostasis. Current peanut allergy diagnostics and therapeutics are unreliable and may induce allergic reactions. Safer ex-vivo, non-allergen based diagnostics and therapies are critically needed. Methods: T-cells, B-cells and mast cells plus Ara-h-2 peanut allergen(PA) comprised the allergic model. For clinical translation, T-cells from individuals with vs without a peanut allergy were used. Microbes included B.fragilis(WT vs D-PSA-B.frag). Angiopoetin-1(protective) and Angiopoetin-2(induces pulmonary capillary leakage) from pulmonary endothelial cells measured end-organ response. Multiple PA exposure (up to 14 days) created a long-term, persistent T-cell allergic model. Results: Repeated dosing of either WT B.fragilis or butyrate, but not D-PSA-B.frag, prevented long-term T-cell allergic responses(dampening IL-4). Repeat butyrate dosing induced a (protective)CD-3+:PD-1-high phenotype. Butyrate could not rescue T-cells after PA exposure. Within pulmonary endothelial cell: immune model, PA induced decreased Ang-1 and increased Ang-2, IL-4, IL-6 and histamine expression. Butyrate prevented this response. To assess potential diagnostic test, T-cells from allergic individuals exposed to PA demonstrated distinct profile (increased PD-1+(60% vs 91%) and IL-4). As a potential therapeutic agent, butyrate prevented an allergic T-cell response, and induced a distinctive CD-3:PD-1-high subpopulation phenotype(<5% vs ~20%). Conclusion: This lays the basis for safe ex-vivo peanut allergy diagnostic test. B. fragilis derived butyrate may prove an effective, long-term, therapeutic option for peanut allergies.

Awards Won:

First Award of $5,000