Ending the EpiPen Epidemic: Creating an Intestinal Organoid to Understand the Immune Mechanisms Involved in a Peanut Allergy

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Background: Peanut allergies are an epidemic with no cure. Microbiome alterations favoring Bacteroides fragilis can dampen a peanut allergy. To clinically translate prior findings, a complex immune cell and intestinal organoids(miniature intestine) model was developed. Methods: Intestinal organoids grew from Lgr5+ intestinal stem cells. A semi-solid extracellular matrix allowed 3-dimensional organ growth. Organoids were followed for confluence, budding and development of intestinal lumens. T-cells, B-cells and mast cells (Immune model(IM)) were combined with peanut extract to create an allergic reaction. B.fragilis or L.acidophilus represented microbiome components. ELISA measured IL-4, histamine, IgE, and α-defensin levels. Microscopy for cell/organoid interactions. Western blot analyzed Stat1, Stat4 and Stat6. Results: The IM peanut extract required T-cells to induce markers of allergy(elevated IL-4, IgE and histamine). Responses were dampened with B.fragilis but not L.acidophilus. IM/Organoid alone did not significantly affect cytokine or histamine levels. Addition of peanut induced allergy markers and cell influx towards and within the organoids. B.fragilis did not affect IL-4 but mildly elevated IgE and histamine and induced mild cellular influx. L.acidophilus markedly elevated IL-4, histamine and IgE. L.acidophilus within peanut/IM/Organoid induced considerable immune cellular influx. Both B.frgailis and L.acidophilus induced organoid production of α-defensin, not seen with IM alone. Discussion: Intestinal organoids avoid murine models while studying cross-talk between microbe, immune cell, and intestinal physiology. Harvesting the properties of T-cells and Bacteroides to foster a homeostatic response will aid targeted probiotic-based cures for peanut allergies.

Awards Won:

Third Award of $1,000