From EpiPens to EpiGenetics: Understanding the Mechanisms Behind the Microbiome’s Impact on Peanut Allergies

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BACKGROUND: Peanut allergy therapies, such as EpiPens, treat anaphylactic reactions, but do not cure allergies. Previously, altering a monomicrobial microbiome with Bacteroides fragilis dampened the destructive T-cell peanut allergic response (IL-22). However, mechanisms driving the microbiome's alteration of T-cell responses remain unclear. T-cells are regulated by checkpoint proteins PD-1 and BTLA. T-cells can also produce the reparative cytokine IL-33. Recent data has shown epigenetic changes (DNA methylation) may explain individualized responses in varying diseases. I hypothesize Bacteroides impacts a combination of phenotypic and epigenetic changes. METHODS: T-cells were cultured in mono- or polymicrobial environments, dominated in Clostridium(C50), Bacteroides(B50), or Lactobacillus(L50). ELISA measured IL-22 over varying time points and IL-33. Global epigenetic changes(5-methylcytosine) were measured by ELISA. PD-1 and BTLA expression was measured by flow cytometry. RESULTS: Allergic reactions produce biphasic IL-22 responses, suggesting it is both preformed and de novo synthesized. Bacteroides dampened IL-22 and elevated IL-33 in a monomicrobial environment. In polymicrobial environments, C50 decreased IL-22, and C50 and B50 elevated IL-33. Only Bacteroides decreases PD-1 and BTLA expression, and induced a PD-1 high response.Peanut allergy induced T-cell epigenetic changes, which were decreased by both Bacteroides and B50. CONCLUSION: In mono- and polymicrobial environments, Bacteroides impacts allergic reactions producing a combination of protective T-cell phenotypes, cytokines, and epigenetic changes, while reducing the destructive IL-22 levels. This data paves the way for a potential cure for peanut allergies by changing the immune/microbiome interactions.

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