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L14 Down-Modulation of Cockroach (CR) Allergen-specific Th2 Cell Responses Following Subcutaneous German Cockroach Allergen Immunotherapy (SCIT)

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RATIONALE: The responses of T cells to subcutaneous allergen immunotherapy (SCIT) are not fully elucidated. We conducted a functional immunological evaluation of cockroach (CR) allergen-specific CD4+ T cell reactivity in the double-blinded, placebo-controlled, multi-center CRITICAL study.

METHODS: Participants (8-17 years of age) with mild to moderate, well-controlled asthma received 12 months of maintenance dosing of CR SCIT (n=20) or placebo (n=26). Peripheral blood mononuclear cells (PBMC) were isolated prior to, and after 12 months of therapy. CD4+ T cell responses at baseline and after treatment were assessed using overlapping peptide pools derived from 11 well-defined CR allergens and intracellular cytokine staining for IL-4, IFNg, and IL-10 production. T cell responses were further evaluated in terms of magnitude, cytokine polarization, and allergen immunodominance.

RESULTS: Significant down-modulation of the total magnitude of CD4+ T cell responses was observed with SCIT but not placebo, with a significant change between groups (-4.46±0.82 vs. −1.81±0.72, respectively, $p = 0.020$). Responses were driven by a decrease in IL-4 (-4.87±0.86 vs. −1.09±0.75, $p = 0.002$) with unaltered IFNg and IL-10 production, reflecting a shift towards a Th1 polarization profile (1.35±0.58 vs. −0.37±0.50, in SCIT and placebo respectively, $p = 0.031$). The largest effects were observed against the allergens Bla g 5 and Bla g 9, which are dominantly recognized, suggesting that dominant responses are susceptible to modulation.

CONCLUSIONS: Our results demonstrate a significant down-regulation of CR-specific Th2 cell responses in urban children with asthma who received SCIT, compared with those who received placebo.

L15 Investigating the Interplay Between Gut Microbiome and Immune Landscape in Sarcoidosis

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RATIONALE: Sarcoidosis is a chronic systemic inflammatory disease characterized by granulomatous infiltration of affected organs, predominantly the lungs, with unclear etiology. Prior studies implicate microbial antigens as a trigger for inflammation driving granuloma formation. Considering potential cross-interactions along the lung-gut axis, we examine the relationship between gut microbiome and host immunity in sarcoidosis.

METHODS: Subjects with sarcoidosis (n=50) were recruited from the University of Illinois Hospital and Health Sciences System and matched with controls (n=50). Stool samples were collected for metagenomic sequencing of the gut microbiome and blood samples for RNA-seq of the immune transcriptome. Taxonomic classification was performed using *Kraken2* with *Bracken* and gene annotation using *AnnotationHub* with human *ensembldb*. Differentially abundant species and expressed genes (DEGs) were identified using *edgeR* and correlated by Spearman's correlation and hierarchical clustering. DEGs were functionally organized using the blood transcription module (BTM) framework.

RESULTS: In the sarcoidosis microbiome, 27 species significantly increased while 239 decreased compared to controls (FDR<0.05). The sarcoidosis transcriptome featured upregulated BTMs for monocytes and heme biosynthesis and downregulated BTMs for dendritic cells and leukocytes (FDR<0.05). Association analysis revealed 8 clusters of correlated species displaying unique correlation patterns with 3 clusters of correlated BTMs, represented as general immune activation, monocyte activity, and heme-related inflammation. Notably, the heme cluster positively correlated with *Cereibacter sphaeroides*, which participates in heme synthesis, and negatively correlated with *Roseburia hominis*, which produces a heme chaperone.

CONCLUSIONS: Our findings highlight the interplay between microbial and host immune regulation of heme-related inflammation that may drive granuloma formation in sarcoidosis.