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382 Salmonella-Induced Changes in Immunoregulatory Bacteria and the Impact on Transcriptional Activity of the Foxp3 and Roryt genes in Rat GALT

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RATIONALE: Intestinal microbiome supports immune homeostasis. Segmental filamentous bacteria (SFB) induce differentiation of Th17-cells in enteric-associated lymphoid tissue (GALT). Clostridium (cluster IV and XIVa) and Bacteroidesfragilis (polysaccharide A) stimulate the formation of T-regulatory cells (Treg) and production of suppressor cytokine IL-10.
METHODS: Metabolites of B. fragilis, short-chain fatty acids (SCFA), activate GALT cells through the FFAR2 receptor. Decrease in the concentration of SCFA decreases the number of Treg and disrupts the balance of Th17/Treg, which leads decreased level of FFAR2, Foxp3 mRNA and an increase in RORγt in GALT. Vancomycin and salmonella were given to rats and the levels of SFB assessed.
RESULTS: SFB increased and A.muciniphila, F.prausnitzii decreased post Vancomycin and salmmonella. In rats infected with salmonella after pretreatment with vancomycin, the number of SFBs increased with a marked decrease in the Bacteroides-Prevotela group, A.muciniphila, Clostridium spp. clusters XIV, IV, and F.prausnitzii, leading to a decrease in the expression level of Foxp3 + gene mRNA and an increase in Rorγt +. The introduction of B. fragilis to animals receiving Salmonella on the background of pre-treatment with vancomycin caused a decrease in the level of SFB and mRNA of Rorγt +, and, conversely, increased the number of Bacteroides-Prevotela group, A.muciniphila, Clostridium spp. clusters XIV, IV, F.prausnitzii and expression of Foxp3 + genes, indicative of restoration of intestinal microbiome homeostasis.
CONCLUSIONS: Salmonella-induced changes in immunoregulatory bacteria impacts transcriptional activity of the Foxp3 and Roryt genes in rat GALT.

383 miR-511-3p protects against cockroach allergen-induced airway inflammation

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RATIONALE: Plasma miR-511-3p levels are lower in asthmatics compared to healthy controls. MiR-511-3p, encoded within the mannose receptor (*Mrc1*) gene, is transcriptionally co-regulated with Mrc1. MiR-511-3p delivery reversed the increased airway inflammation in cockroach allergen (CRE)-induced mouse model of asthma due to Mrc1-deficiency. We provided additional evidence to support the protective role of miR-511-3p in allergen-induced airway inflammation.
METHODS: miR-511-3p-deficient (miR-511-3p$^{-/-}$) mice were generate using the CRISPR-Cas9 system and back-crossed with WT mice for a minimum of five generations. miR-511-3p$^{-/-}$ genotype was confirmed by sequencing. MiR-511-3p$^{-/-}$ and WT mice were subjected to our well-established CRE-induced asthma model.
RESULTS: Backcrossed miR-511-3p$^{-/-}$ mice were confirmed by genotyping and Sanger sequencing. MiR-511-3p levels are increased in WT, but were undetectable in miR-511-3p$^{-/-}$ mice after CRE-challenge. Similar expression of Mrc1 was observed in both animals. Interestingly, MiR-511-3p$^{-/-}$ mice have higher airway inflammation after CRE-challenged compared to WT controls. Histological examination showed increased dense peribronchial infiltrates, goblet hyperplasia, higher recruitment of inflammatory cells to the lungs, especially with eosinophils, elevated levels of serum titers of cockroach-specific IgE/IgG1, levels of IL-4 and IL-13, but lower levels of IFN-gamma, in the BALFs of miR-511-3p$^{-/-}$ compared to WT controls.
CONCLUSIONS: Our initial findings firmly support a protective role of miR-511-3p in allergen-induced allergic inflammation making it an attractive therapeutic agent for the treatment of asthma and allergic diseases.

384 Lymphocyte Transformation Test Effectivity based on the Antigen presenting Cells Employed in Immediate Allergic Reactions to Betalactams

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RATIONALE: Lymphocyte transformation test (LTT) is a reliable test that allows to determine cells proliferation in response to drugs/allergens. Its value in drug-immediate allergic reactions is not well-established. Its sensitivity varied depending on the antigen presentation cells (APCs) used. Therefore, we aimed to study LTT effectivity using pre-primed monocyte-derived dendritic cells (moDCs) or myeloid dendritic cells (mDCs) as APCs, comparing them with conventional LTT, carried out with peripheral blood mononuclear cells (PBMCs).
METHODS: Monocytes and mDCs were isolated from 10 controls, and from 10 clavulanic acid (CLV) and 10 amoxicillin (AX) allergic patients. Monocytes were cultured with GM-CSF and IL-4 to differentiate to moDCs. Both APCs were cultured with drugs and with lymphocytes later. Proliferative response was assessed in CD3^{+}, CD4^{+}, CD8^{+}, CD4^{+}Th2 and Treg cells using Carboxyfluorescein succinimidyl ester (CFSE) by flow cytometry. Results were expressed as Proliferation Index (PI).
RESULTS: Higher PI was obtained in both, AX and CLV patients compared with controls, independently of the type of APCs tested. Interestingly, increased percentage of positive cases was observed when mDCs were used in AX-allergic-patients (50% with PI>2), compared with moDCs or PBMCs (<20% for both). Surprisingly, sensitivity in CLV allergic patients was lower (25%), independently of the APCs used. No positive proliferation was observed in controls.
CONCLUSIONS: The employment of mDCs as APCs improves the sensitivity of LTT to diagnose immediate allergic reactions to AX. Nevertheless, no differences were observed in CLV immediate allergic reactions. This could be due to the non-inclusion of the specific determinants that induced the reaction.

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