Canary in the Coalmine: Neonatal Gut Microbiome and Childhood Asthma Development

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Humans are Superorganisms

Microbial Biochemical

ECOSYSTEMS TO MOLECULES

Diversity

Watrous et al. PNAS 2012

The Gut Microbiome is Home to Several Trillion Microbes

Diet

Drug Metabolism

IBD

Obesity

The Gut Microbiome Influences Remote Organ and Immune Responses

Neurological

Respiratory

Cardiovascular

Immunity

Asthma is Prevalent in Westernized Nations

Risk Factors for Childhood Allergic Asthma Also Impact the Early-life Gut Microbiome

INCREASED RISK

Early-life gut microbial perturbation is associated with allergic sensitization in childhood.

Global initiative for Asthma

Asthma is Prevalent in Westernized Nations

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Global initiative for Asthma
Gut Microbial-derived Metabolites Influence Host Immunity

Poorly fermentable fiber (Control diet)
Highly fermentable pectin (High fiber)

House Dust Mite Airway sensitization
Airway Allergic Response


Daily gavage L. johnsonii 1x10^7 CFU


Gut Microbiome Manipulation Alters Airway Mucosal Response to Allergen Challenge or Viral Infection

L. johnsonii

Docosahexanoic Acid (DHA) inhibits RSV activation of
BMDC

Circulating Products of the L. johnsonii-supplemented Gut Microbiome
Down-regulate Pro-inflammatory Responses
Could Early-life Gut Microbiome Perturbation and Metabolic Dysfunction Relate to Childhood Atopy and Asthma?

Primary Succession as a Model for Human Gut Microbiome Development

Hypothesis:
High-risk for asthma neonates exhibit a distinct founder gut microbial population and an alternate trajectory of gut microbiota development

Wayne County Health, Environment, Allergy & Asthma Longitudinal Study (WHEALS)

Neonatal Gut Microbiota State is Associated with Risk of Childhood Atopy and Asthma

Inter-Kingdom Perturbation and Loss of Conserved Metabolic Pathways Associated with Increased Risk of Atopy and Asthma
Early-life Metabolic Dysfunction is Associated with Increased Risk of Childhood Atopy and Asthma

**TOLERGENIC GUT MICROBIOME**

**PRO-ALLERGIC GUT MICROBIOME**

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**Ex vivo DC/T-cells Assay to Assess Immunostimulatory Capacity Fecal Water**

**Products Associated with a High-risk Neonatal Gut Microbiota Induce Pro-allergic Inflammation and Suppress T-regulatory Cells**

**T2,13 DIHOME Suppresses T-regulatory cell Populations**

**Model for Childhood Atopic Asthma Development**
Summary

- Gut microbiome regulates local and remote immunity via metabolites
- Products of the 1 month old high-risk 1 for atopy/asthma gut microbiome induce allergic inflammation
- 12,13 diHOME is a gut bacterial produced oxylipin that reduces the frequency of regulatory T cell populations
- Neonates who develop disease in childhood may be identified using early life fecal microbiome risk genes and their products

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