Interactions between the Microbiota and the Immune System

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Introduction

- Since birth, humans are colonized by a large number of microorganisms (10^{14} in the adulthood) which surpass the 10^{14} human eukaryotic cells; mostly found in the colon.
- The development of the gut associated lymphoid tissue (GALT) begins in mammals before birth and requires a microbiota for a proper development.
  1. Umbilical cord and amniotic fluid
  2. Mode of delivery
  3. Lactation
  4. Environment and diet exposure
- Intestinal microbiome
  - 75% Bacteria of the phylum Firmicutes, Bacteroidetes, Actinobacteria
  - Archaea such as Methanobrevibacter smithii and Methanosphaera stadtmanae
  - Fungi of the genus Candida and Saccharomyces

Stratification: minimizing direct contact between intestinal bacteria and the intestinal cell surface

- Mucus layer by Goblet cells
- Antibacterial proteins by Paneth cells
- β-defensins by Paneth cells
- Stomach pH
- Lactoferrin
- Catecholins by IECs
- Phospholipase A2
- Regilly by Paneth cells and enterocytes
- Proteins of the complement system
- Immunoregulatory cytokines and chemokines
- sIgA

Compartmentalization: confining the bacteria that are able to penetrate and limiting their exposure to systemic immune compartment

- Specific sIgA in the mesenteric lymph node by B cells activated when antigen presenting cells (APCs) sample microbial antigens
- Differential distribution of TLRs
- NOD and TLR9: located intracellularly
- T cell differentiation
- TLR5: basolateral distribution
- TLR4: internalized into endosomes

Microbiota Modulates the Immunity

Impact on the epithelial function and the lymphoid structure development

- Impact on the epithelial function and the lymphoid structure development
- Germ free animals have a scarce and inactive mucosal immune system
- Affects systemic immunity
- Control of IκB and IL-17 and IL-22-producing CD4+ T cells
- Can protect from autoimmune diseases

Clostridium clusters IV and XIVa

- Th17 and Th1 cells \(\rightarrow\) inflammatory state
- IL-10 and IFN-γ: producing CD4+ T cells
- SEGMENTED FILAMENTOUS BACTERIA

Bacillus fragilis polysaccharide A

- Systemic serum IgE
- iTREG induction \(\rightarrow\) anti-inflammatory state
- T CD4+ and Th1 cells
- IL-10 anti-inflammatory response
- iTREG induction

Prebiotics

Indigestible dietary fibers which selectively stimulate growth and bacterial activity, mostly from the genus Bifidobacterium and Lactobacillus.

V. g. Breast milk

Indigestible oligosaccharides (HMOs)

Saccharolytic fermentation

Short-chain fatty acids (SCFAs)

Antimicrobial effect by blocking bacterial adhesion to the intestinal barrier

Prevent an excessive permeability

IL-10 lymphocyte production

Probiotics

Live microorganisms, which if administered in appropriate quantities, can benefit the host’s health.

Lactobacillus

Bifidobacterium

Lactic acid bacteria (LAB)

Streptococcus

Enterococcus

Propionibacterium

Escherichia coli

Saccharomyces boulardii

Conclusions

- Deviations from proper microbiota establishment alter the immune system development and may lead to inflammatory disease emergence; such as inflammatory bowel disease (IBD) including Crohn’s disease and the ulcerous colitis. NEC as well as atopic and autoimmune diseases.
- Children microbiota is easily modulated as it is not consolidated.
- Probiotic, prebiotic and symbiotic use have led to heterogeneous effects and therefore cannot be a useful tool in this field.
- Further research Use genetically-modified commensal bacteria as liberation platforms for antimicrobial agents and vaccines

Goals

- Comprehension of the microbiota establishment and its affecting factors.
- Mechanisms description by which the immune system interacts with the microbiota and its relationship.
- Discussion about probiotic, prebiotic and symbiotic effects on the health of the host.

Metodology

- Reviews and Scientific Research Publications (NCBI and Google Scholar) with word limit: “immune system, intestinal microbiota, immunodiversity, maturation, mucosal immune response, gut, microbiota, probiotic, development”, in the last 15 years.
- MOOC Course “ Gut Check: Exploring Your Microbiome” by University of Colorado.
- VR Consortium “Societal Consequences of ImmunoLOGY” (SCI).

Results

Segemented filamentous bacteria

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- IL-10 and IFN-γ: producing CD4+ T cells

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