Interactions between the gut microbiota and the immune system

Relevance in human health and veterinary medicine

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THE MICROBIOTA

- Complex community of microorganisms found normally on the skin and mucous surfaces of all multicellular organisms in a symbiotic relationship.
- The role of the microbiota in homeostasis and in classic diseases has been re-discovered, enhancing the design of new therapeutic approaches.

FUNCTIONS OF THE INTESTINAL MICROBIOTA

- Microbial antagonism
- Optimization of nutrient absorption
- Immune System development

INTESTINAL MICROBIOME AND THE IMMUNE SYSTEM

CROSSTALK. The communication between microbiota and the host to adjust the antimicrobial program.

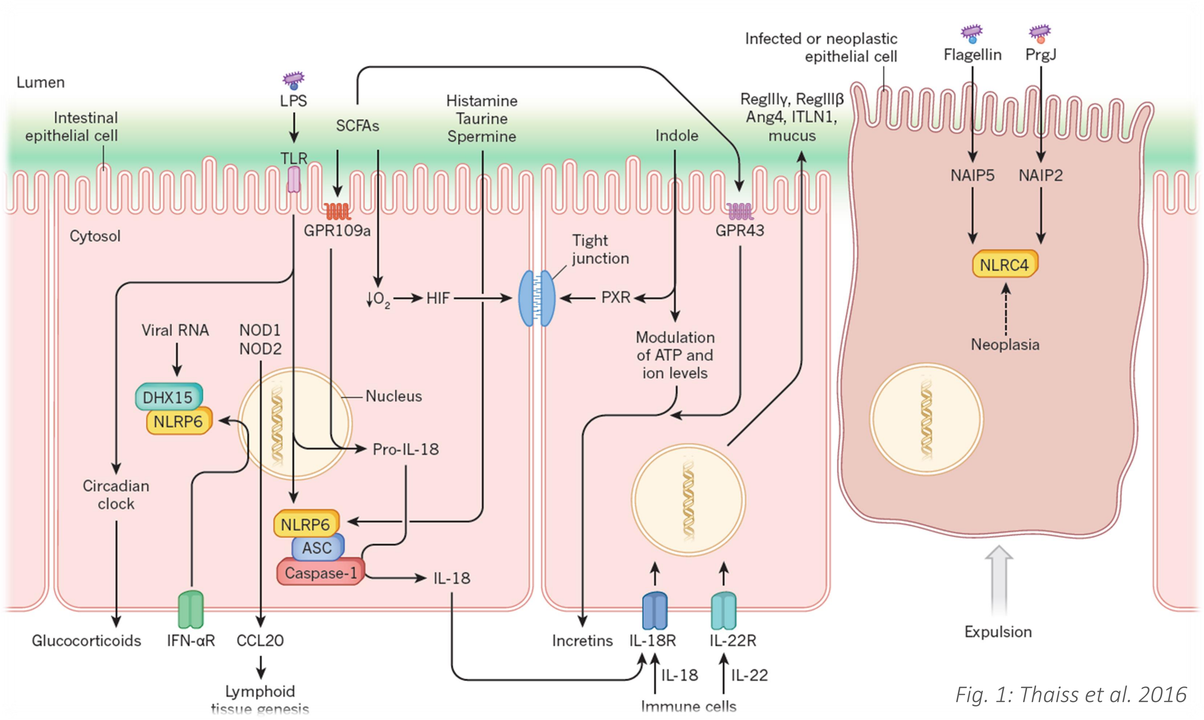

Fig. 1: Thaiss et al. 2016

- ***Objectives***: tolerance to the own microbiota and immune response against the foreign.
- ***Mechanisms:*** transcriptional reprogramming and epigenetic programming of host cells.
- ***Process and compounds:*** Recognition of bacterial patterns (PRRs) by specific epithelial receptors (PAMPs) to adjust the antimicrobial program (mucus, antimicrobial peptides, IgA, cytokines...). The own microbiota drives to a negative feedback. Bacterial metabolites, such SCFA, AA or Indole, also contribute to the crosstalk.

  Epithelial **NLRC4** expulse infected or carcinogenic enterocytes.

INNATE IMMUNE SYSTEM:

- **Myeloid cells:**
  Its production, maturation and biology depend on the complexity of bacterial antigens.
  Low microbial complexity is related to a major disease incidence.

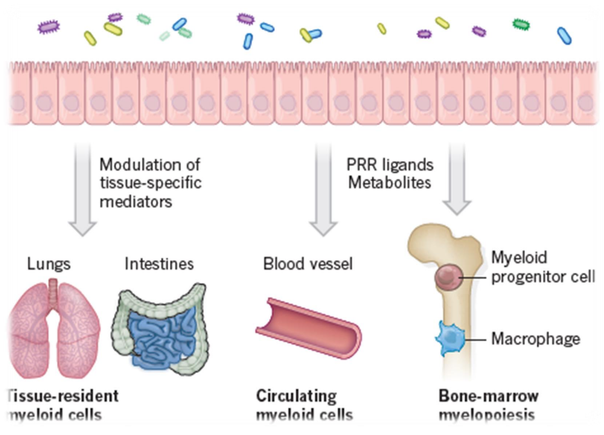

Fig. 2: Thaiss et al. 2016

ADDAPTATIVE IMMUNE SYSTEM

- **Mucosal IgA:** Produced by B cells, in the lamina propria (*Peyer Patch*). They prevent the microbial direct interaction with the host and regulate the composition of the microbiota, to keep it diversified.
- **T_H17 cells:** Prevent from extracellular infection (bacterial and fungi) and favor IgA synthesis. Some external factors favor its change to pathogenic cells, which can promote auto-antibodies production and autoimmune diseases in predisposed individuals.
- **T_{reg} cells:** Cut down T_{eff}, T_H17 and myeloid cell population, to promote intestinal tolerance. ***Bifidobacterium, Lactobacilli, Clostridium*** and ***Bacteroides fragilis*** enhance the T_{reg} cells population.

DYSBIOSIS AND CLASSIC DISEASES

- **Infection and chronic intestinal inflammation.**
- **Autoimmune diseases:** *Inflammatory bowel disease, allergen-induced airway hyperreactivity, DM-I.*
- **Metabolic syndrome** (*obesity and* DM-II) **and cardiovascular diseases** (*arteriosclerosis*)
- **Cancer:** bacterial substances that cause DNA damage directly or sustaining an inflammatory environment, and bacteria into neoplasia increase its growth.
- **Neurodegenerative disease:** ***Parkinson:*** α-syn pathology might be triggered in the gut by bacterial endotoxins and reach the brain via ENS (vagus nerve).

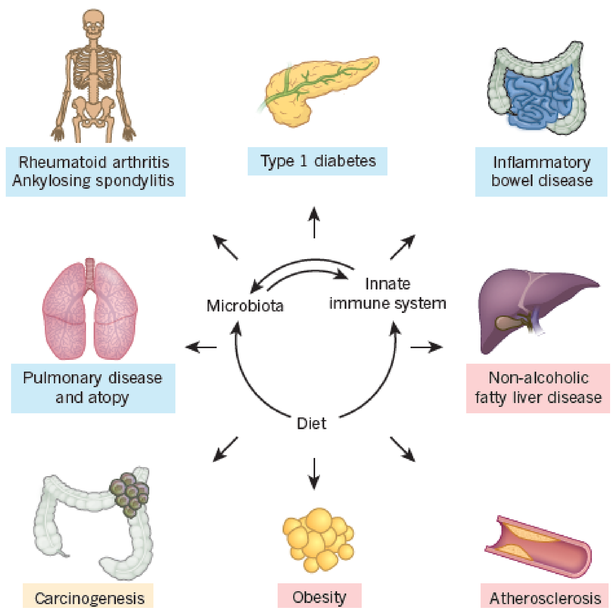

Fig. 3: Thaiss et al. 2016

NEW TREATMENT APPROACHES

Direct modification of microbiota

- **Antibiotics:** to treat disorders associated with a known pathobiont.
- **Faecal transplant:** Very effective for *Clostridium difficile* infections.
  It may be efficiency variations between individuals, risk of developing new diseases and the need of long-term repetitions.

Indirect modification of microbiota

- **Probiotics:** *Bifidocabteria, Lactobacilli, Streptococci*
- **Prebiotics:** *Fructo-oligosaccharides* and *inulin.*

They may help to reduce or prevent gastrointestinal signs.

CONCLUSIONS

- A new organ has just been discovered.
- Microorganisms modulate our immune system to promote self-tolerance and gut homeostasis.
- Correlations have been found between dysbiotic patterns and classic diseases.
- New therapeutic and diagnostic forms focused on the gut microbiota may be developed in the future.