

Johns Hopkins Engineering

Immunoengineering

Immunoengineering—Allergy and Autoimmunity

Discovering Therapeutic Targets



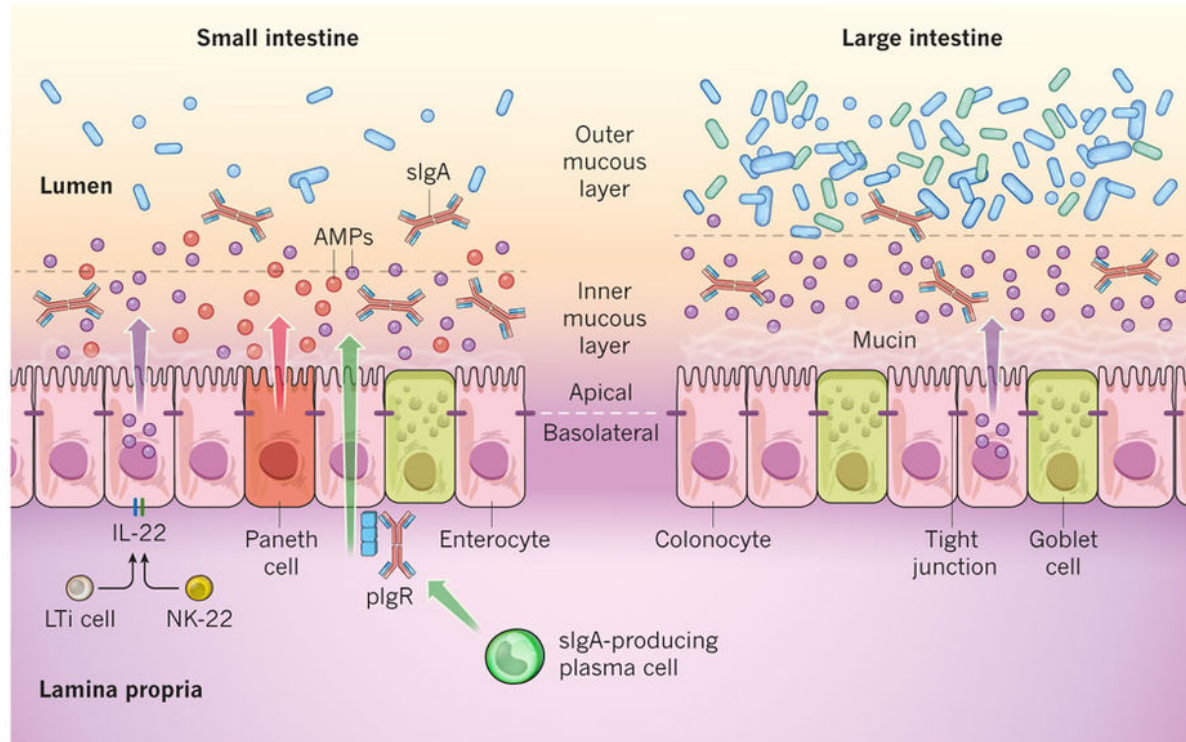
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Discovering Therapeutic Targets

1. Define disease phenotype
 - **Using patient samples**
 - **Where to get samples**
2. Replicate *in vitro* or *in vivo* models
3. Screen therapeutics
 - Large scale screens & mechanistically inspired
 - High throughput tools

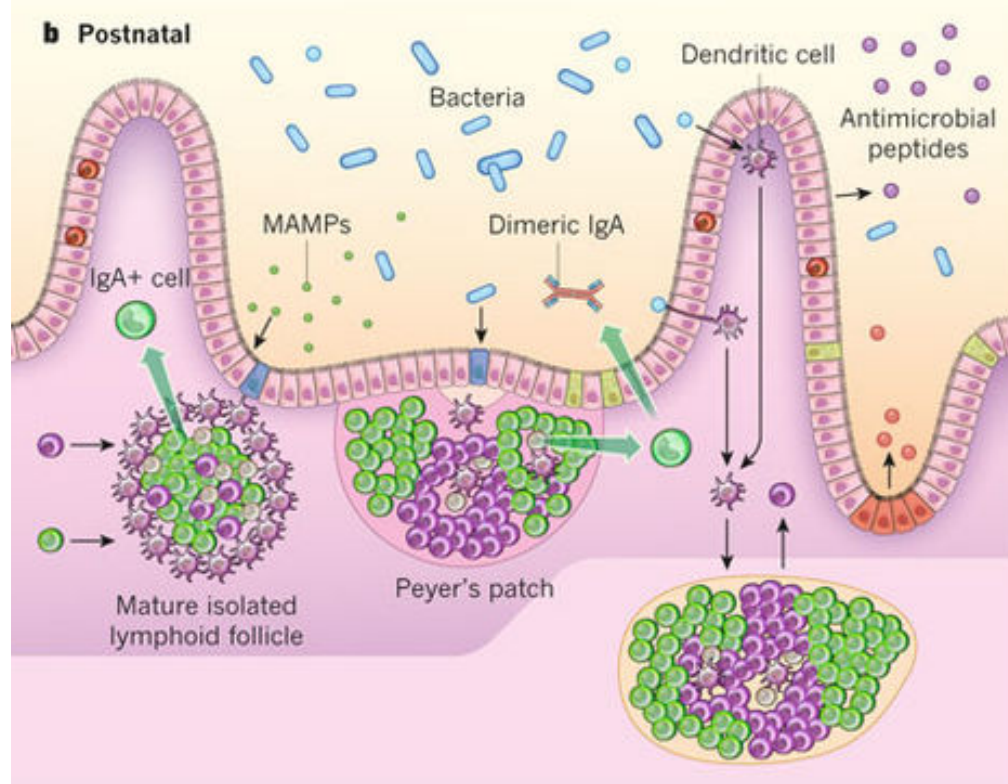
Microbiota – A part of the immune system?

- ~30 trillion bacteria inside us
- Layers of separation between gut and tissue
 - Mucus
 - Anti-microbial peptides
 - IgA
 - Epithelial barrier



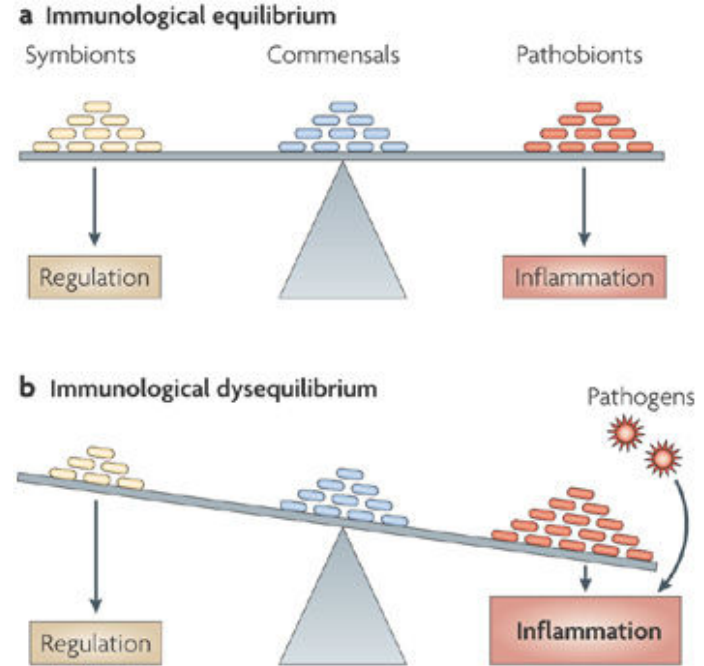
Microbiota – A part of the immune system?

- Interacts with immune system through:
 - Metabolites
 - DC antigen-sampling
 - MAMPs
 - Immune cell recruitment



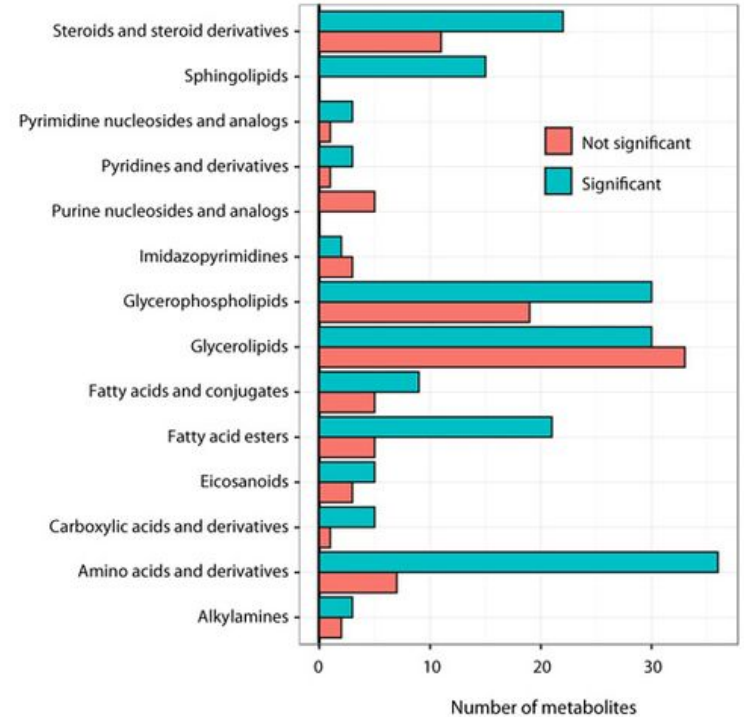
Microbiota – A part of the immune system?

- Microbiota is modular
 - Diet
 - Infection
 - Dysregulation of immune system
 - Trauma
 - Stress
 - Medication/antibiotics



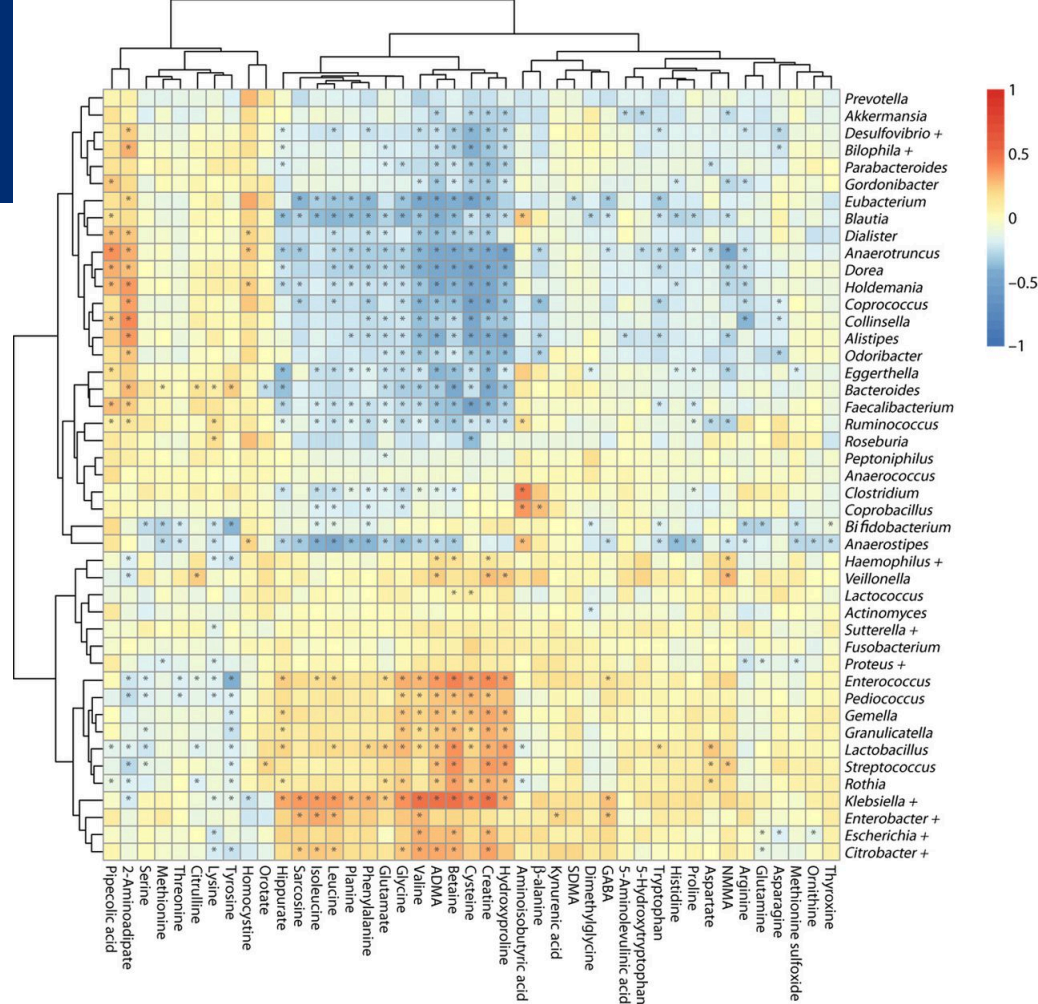
Example – Microbiota and Chron's disease

- Decrease in richness or diversity
- Increased in taxa belonging to the Proteobacteria phylum
- Differential metabolism of amino acids and derivatives



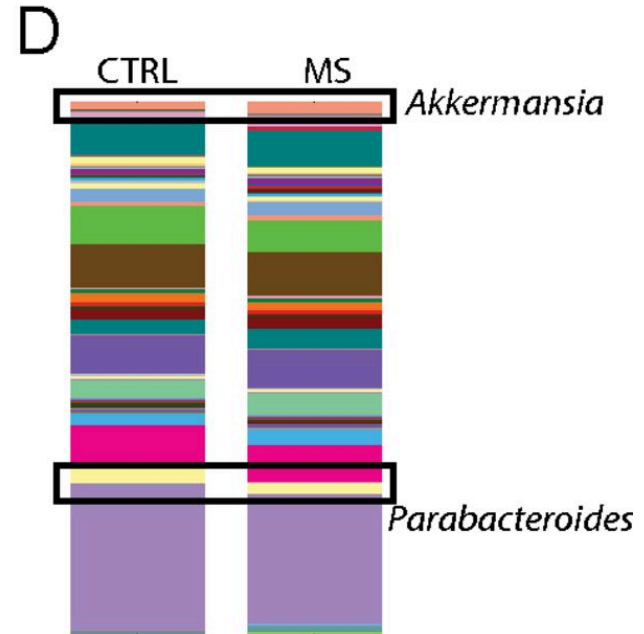
Example – Microbiota and Chron's disease

- Specific strains of bacteria associated with metabolic dysfunction
- Associated with increased urease expression by bacteria
- Further experiments revealed this can be changed by addition of beneficial bacteria



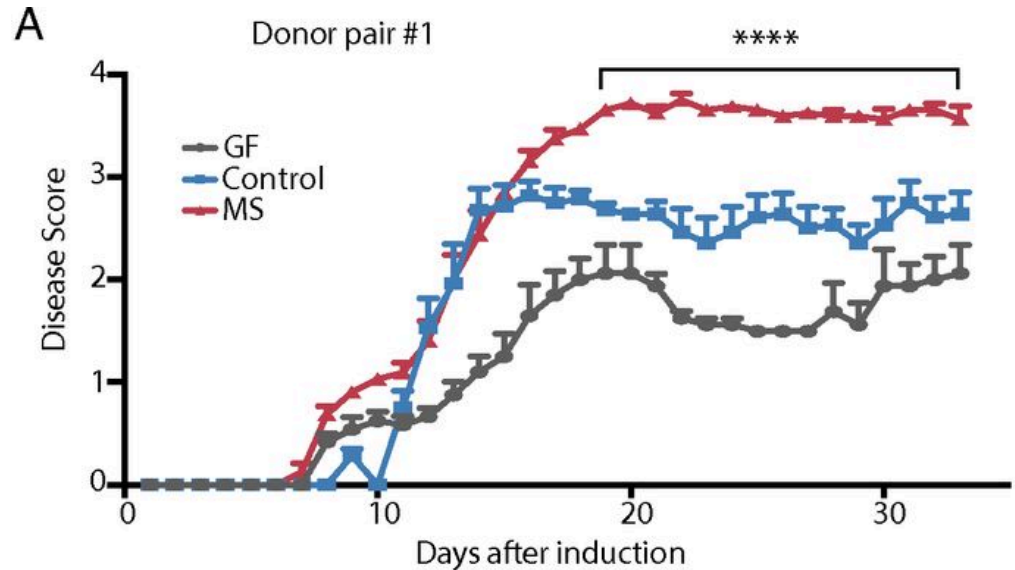
Example – Microbiota and Multiple Sclerosis

- *Akkermansia muciniphila* and *Acinetobacter calcoaceticus* both increased in MS patients
- *Parabacteroides distasonis* was reduced in MS patients
 - Found to stimulate antiinflammatory human CD4+CD25+ T cells and IL-10+FoxP3+ Tregs



Example – Microbiota and Multiple Sclerosis

- Microbiota transplants from MS patients or healthy controls into germ-free mice
- Experimental model of autoimmune encephalomyelitis
- More severe symptoms from MS patients & reduced proportions of IL-10⁺ Tregs



Questions to think about during your reading

- How might you develop an *in vitro* or *in vivo* models for drug discovery involving the role of the microbiota?
- How might you probe the efficacy of whether the microbiota contributes or provides therapy to disease *in vitro*?



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