

The Gut-Brain Axis...

The impact of the microbiome on brain and cognitive development

Diane Stadler, PhD, RD

**Oregon Health & Sciences University, Portland, Oregon
Lao-American Nutrition Institute**

With acknowledgements to:

Robert Martindale PhD, MD

**Chief, Division of General and Gastrointestinal Surgery
Medical Director Hospital Nutrition Support
Oregon Health & Sciences University, Portland, Oregon**

Our Gut Microbiome

- **Human GI tract**
 - **Surface area: 300 to 400 square-meters**
 - **100 trillion living bacteria**
 - **~ 10 trillion cells in human body**
 - **Several thousand species in colon**
 - **Primarily made up of 4 phyla:**
 - **Actinobacteria** **Firmicutes**
 - **Bacteroidetes** **Proteobacteria**
- **Function to:**
 - **Digest “undigestable” foods**
 - **Produce essential cofactors and vitamins**
 - **Stimulate of the immune system**



Development of Our GI Microbiome

Newborns are exposed to pro-and prebiotics before, during, and after birth:

- **Vaginal vs C-section delivery—**
 - In the US, 1/3 by C-section
- **Breastfeeding vs Formula feeding**
 - Majority are formula-fed
 - Breastfeeding encourages bifidobacteria growth
 - Formula feeding associated with bifidobacteria, bacteroides, clostridia, streptococci
 - Breast milk composition influenced by maternal weight
 - 13 - 15% of CHO in breast milk not absorbed by infant

By ~2 years the microbiome resembles the adult bacterial profile; “blend” of bacteria based on environmental exposure

Evolution of Our Gut Microbiome

- Major Changes in Diet and Activity
 - Fats, protein, fiber, food additives, sweeteners
 - Sedentary lifestyles, obesity
- Enhanced use of immunizations & antibiotics
- Reduced parasitic infection
- Urban life in cities and concrete
- Reduced exposure to animals, livestock
- Improved refrigeration, sanitation and hygiene
- Introduction of solid foods, types of foods, and nutrients like iron and fatty acids impact diversity and composition of gut bacteria



Criteria for Probiotic Designation

WHO, FAO Definition

Live microorganisms in which when administered in adequate amounts confer a health benefit on the host”

- Human origin
- Viable / hardy in human GI tract
- Acid and bile stable
- Adhesion to mucosa
- Clinically demonstrated benefit
- Safe

Most Common Commercial Probiotics

Lactobacillus acidophilus/johnsonii/gasseri

Lactobacillus casei

Lactobacillus paracasei

Lactobacillus rhamnosus

Lactobacillus plantarum

Lactobacillus reuteri

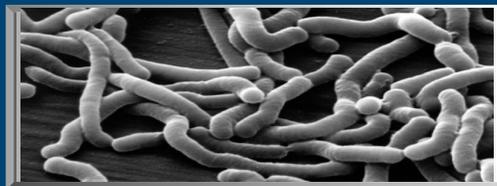
Bifidobacterium animalis/lactis

Bifidobacterium bifidum

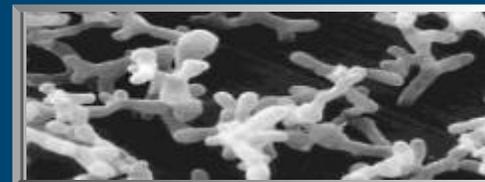
Bifidobacterium breve

Bifidobacterium longum

Bifidobacterium adolescentis

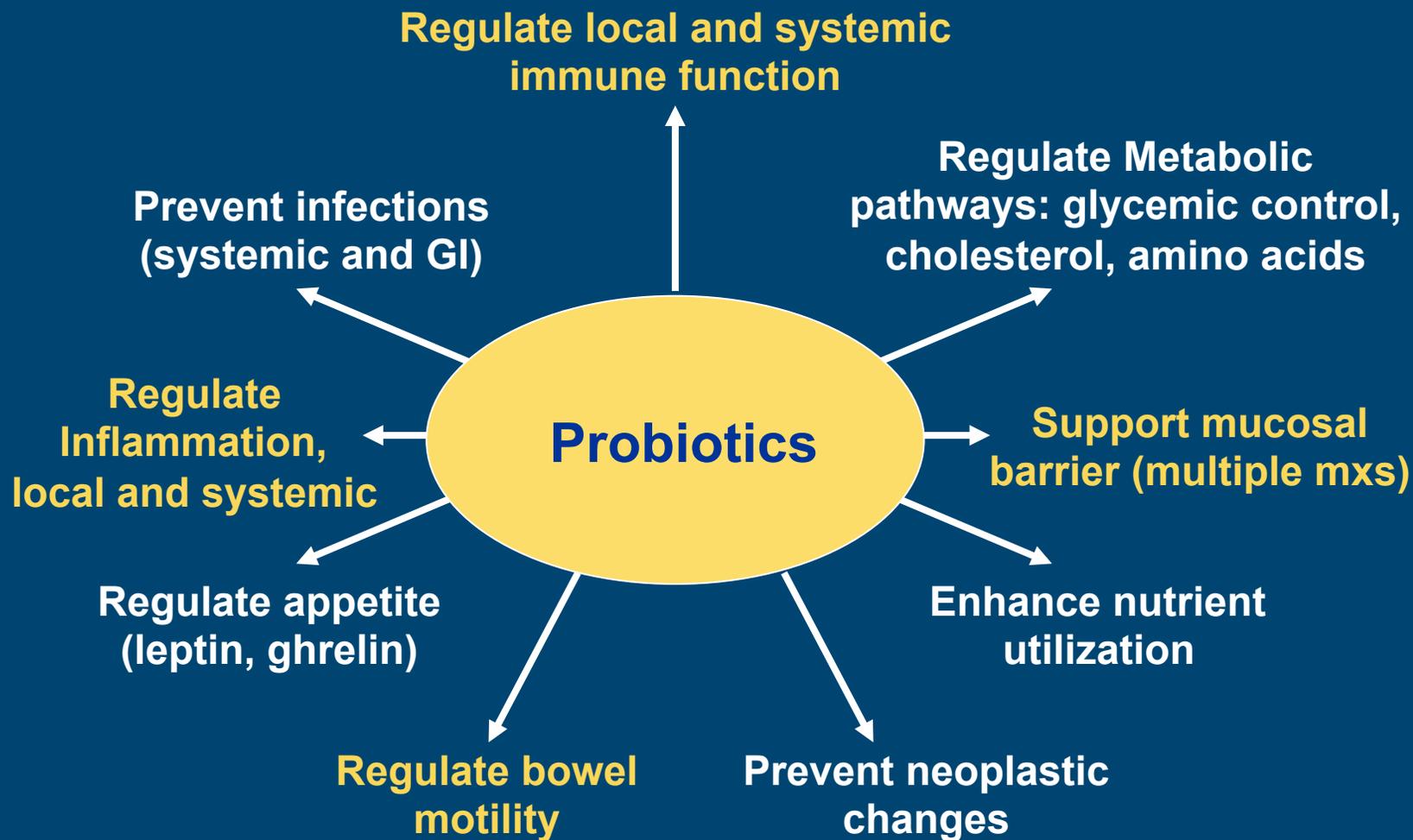


Lactobacillus

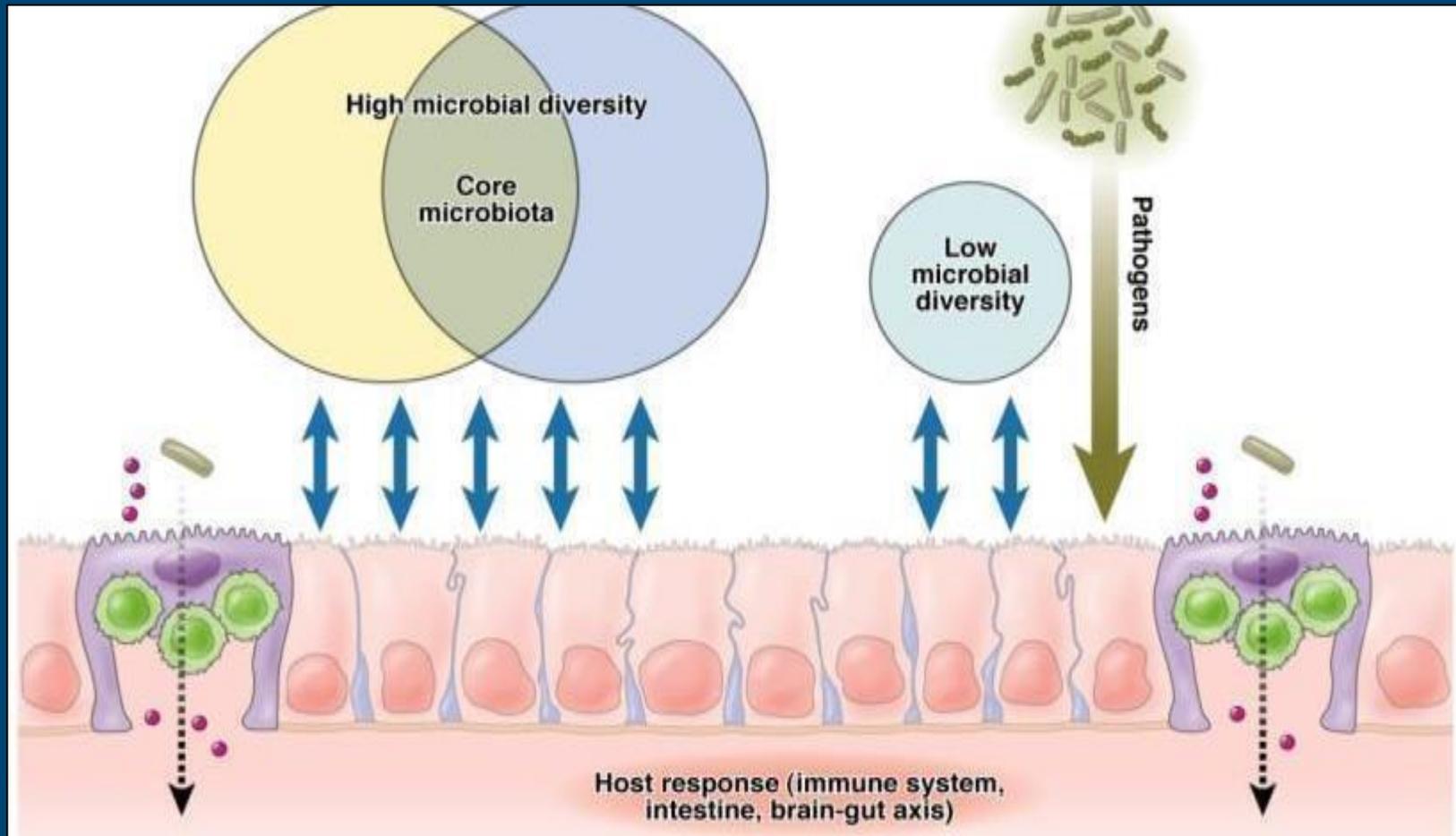


Bifidobacteria

Mutually Beneficial Effects of Bacteria and Their Substrates in Humans

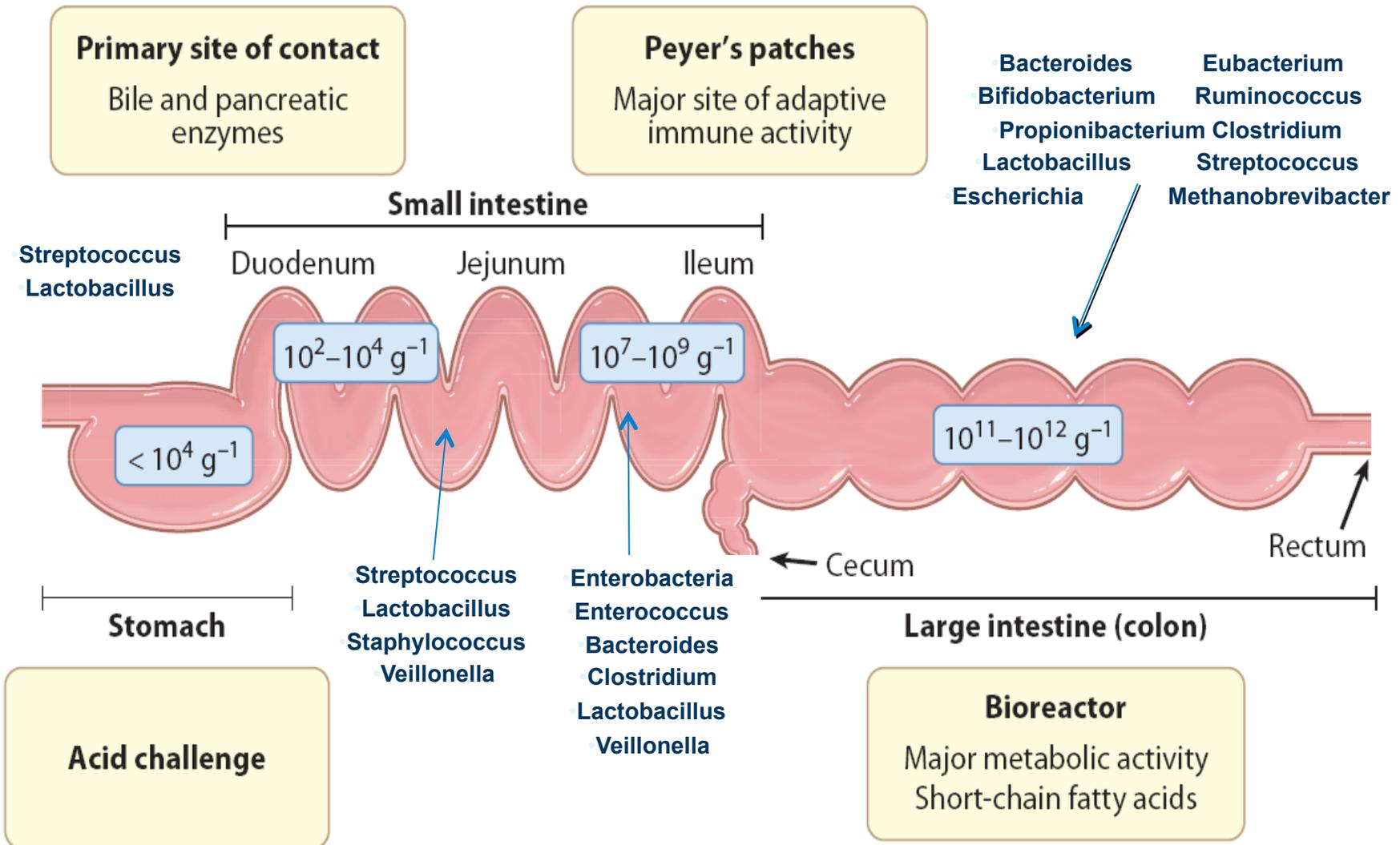


What is a healthy gut?

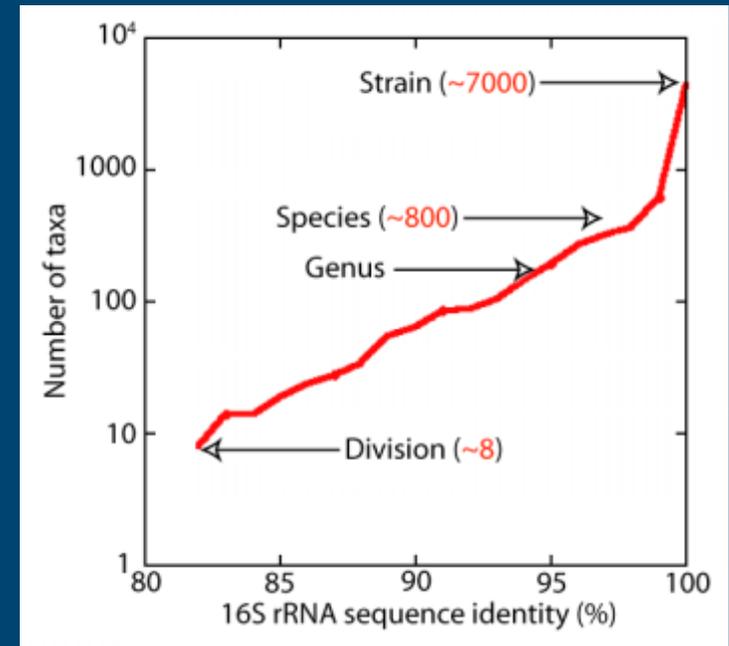
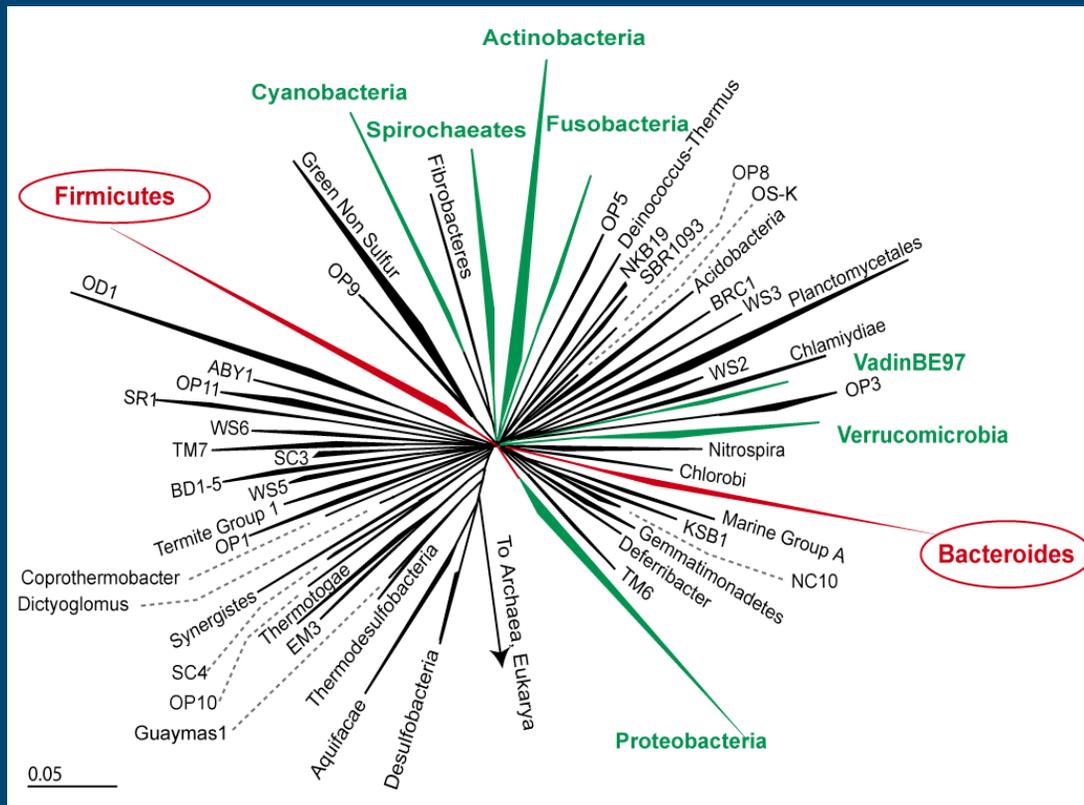


Host response
(immune system, intestine, brain-gut axis)

Regional distribution of the gut microbiota



Composition of the Human Gut Microbiota

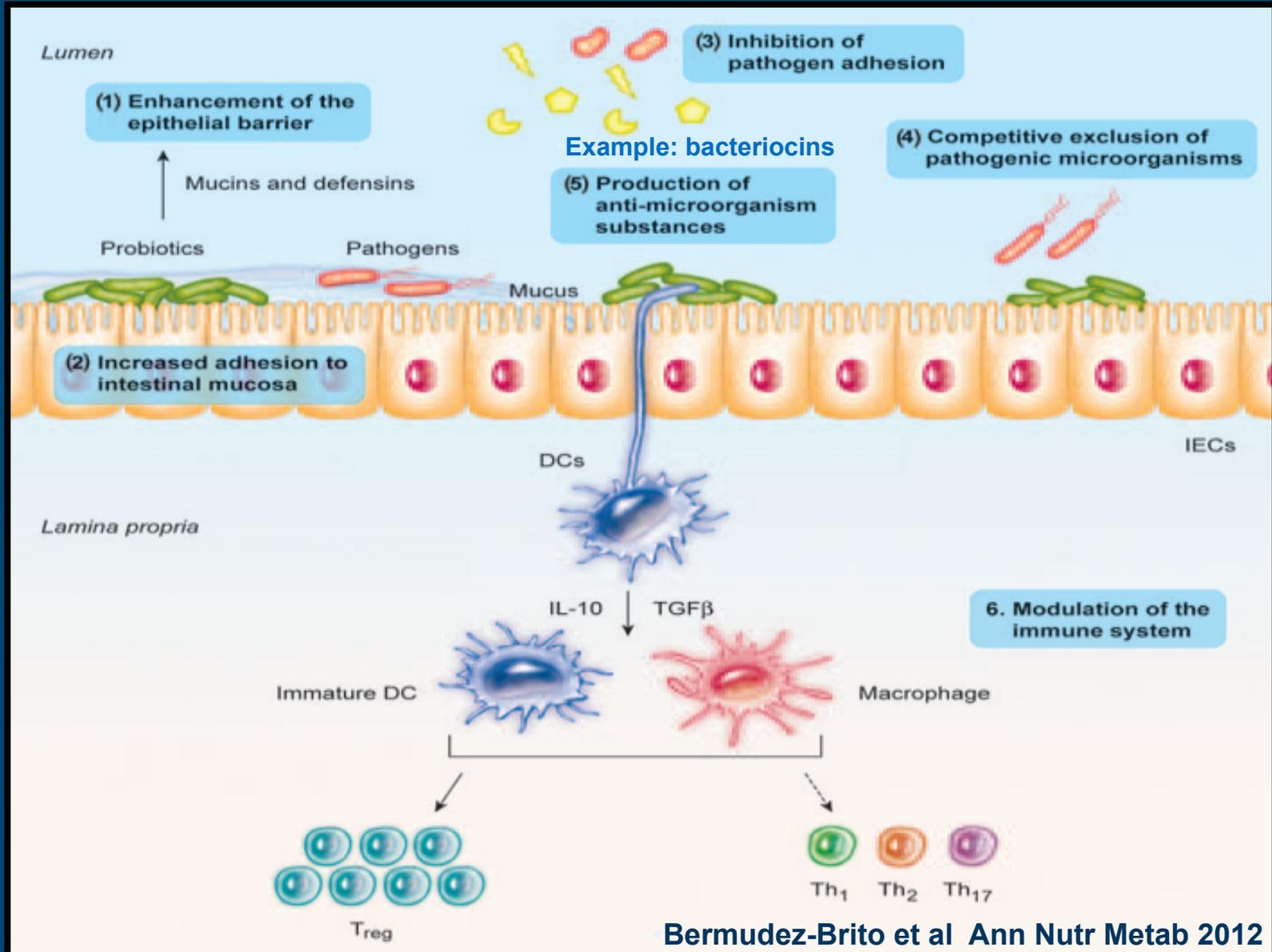


Only 9 bacterial divisions detected but extremely diverse

Gut has strong selection for bacteria and redundancy of functions

Variety is thought to yield resilience to insults

Mechanisms of Action



Use of Probiotics during Pregnancy and Maternal Outcomes



- Finland N=256
- GDM defined by GTT
- 3 groups
 - Control-SOC
 - Placebo
 - Probiotics
- Results: ↓ GDM
 - Control 36%
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Luoto R British J Nutrition 2010

- Systematic review: 189 articles
- Primary outcome
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Lindsay KL et al 2013 J Maternal-Fetal Neonatal Med

Microbial Enhancement: Use of probiotics to prevent necrotizing enterocolitis in neonates

- **N=566 infants**
 - Prospective RCT
 - 5 probiotic genera
 - 4 bifidobacteria, 1 lactobacillus
 - 2.0×10^9 CFU /day
- **Results**
 - ↓ NEC 9.8% vs 5.45 % (p<0.05)
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Microbiota and Brain Development

- In the absence of gut microbiota, mice have:
 - substantially ↑↑ corticosterone, a stress hormone in the hypothalamus
 - ↓↓ brain-derived neurotrophic factor (BDNF) a protein that stimulates:
 - neurogenesis
 - synaptic growth
 - modulates synaptic plasticity and transmission
- Partially reversed by re-colonization with a diverse microbiota
- Suggests that active signals from the microbiota play a critical role in brain development

Microbiome required for normal gut-brain signaling

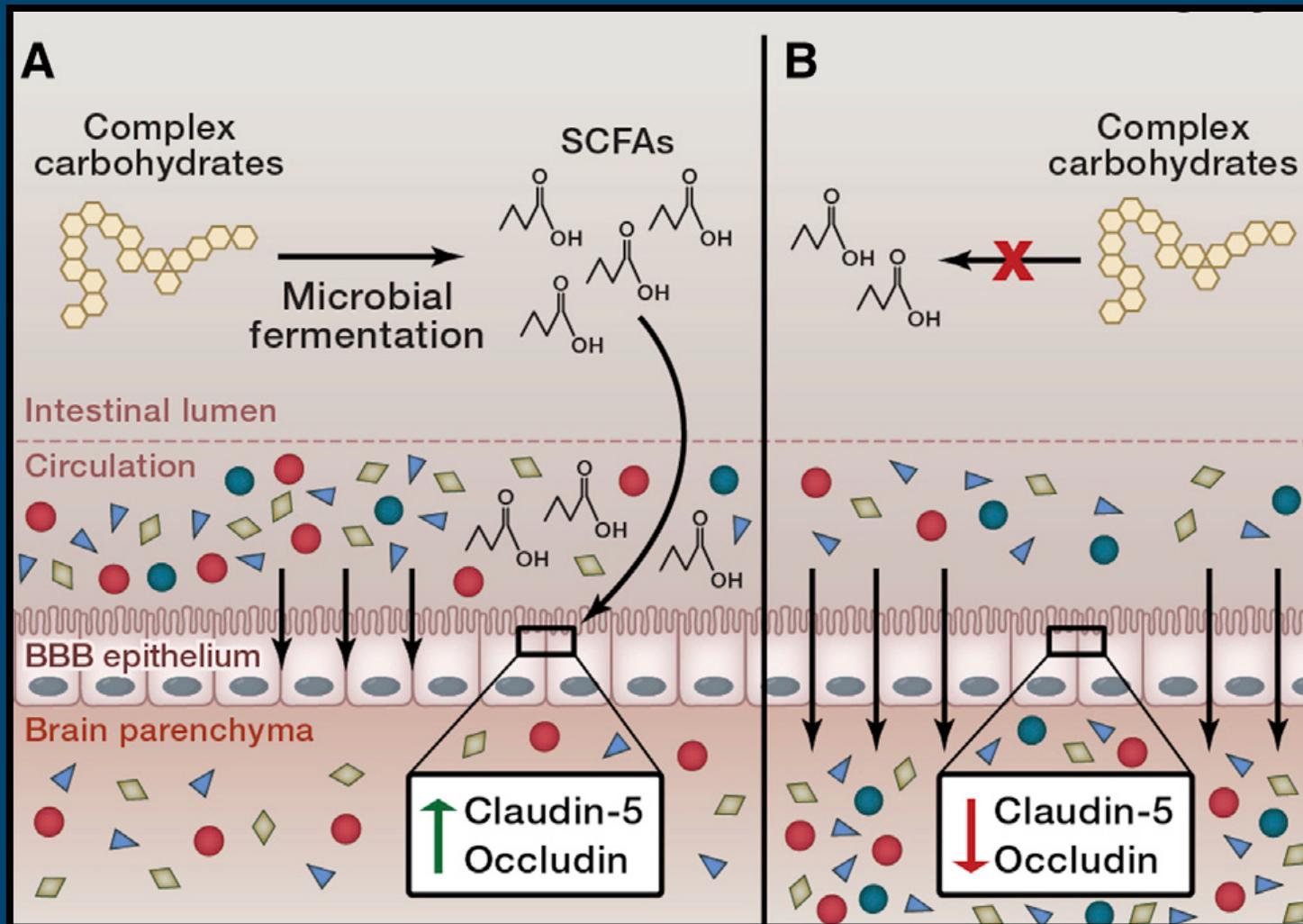
Bidirectional communication:

- ↑ Nerve Growth Factor (Lactobacillus sp)
- ↑ IL-10 (attenuates inflammation)
- Alters GABA in brain
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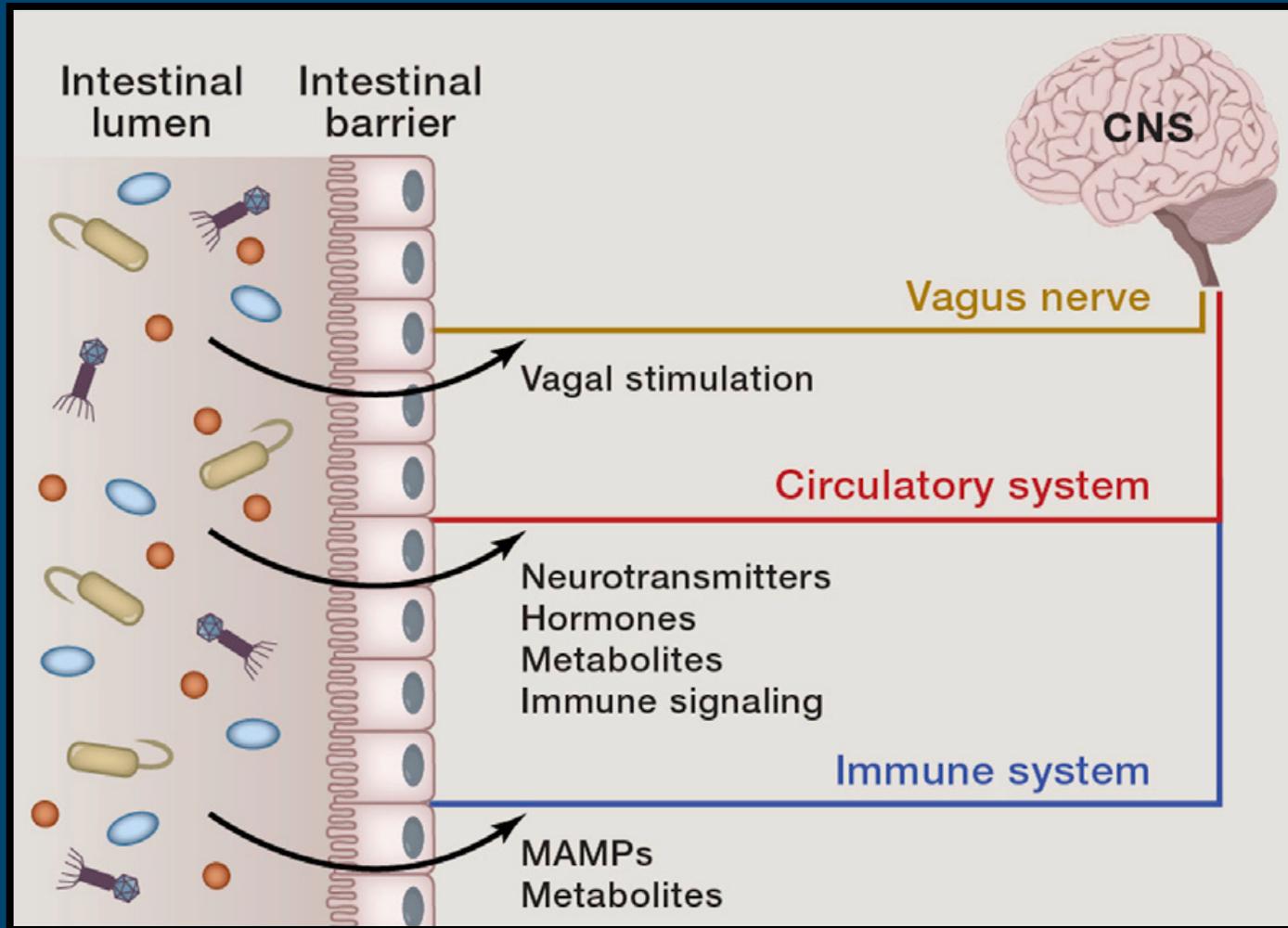
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Influence of the Microbiome on Blood Brain Barrier Integrity



Pathways linking the microbiome and CNS



Sampson, TR & SK Mazmanian, Cell Host & Microbe, 2015

What have we learned from germ-free mice...

- When the microbiota is absent:
 - Altered sociability, decreased memory, and increased stress responses
- Bacteria produce neurotransmitters
 - norepinephrine, serotonin, dopamine,
- Certain probiotic bacteria modulate the effects of neurotransmitters
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Summary

The microbiota:

- Is established early, it's diverse, and responds to environmental exposure
- Functions through a variety of mechanisms to enhance the integrity of the gut and the immune system
- Impacts brain and cognitive development early and throughout life
- The gut brain axis is bi-directional
- This field of study is relatively new and we have a lot to learn about the power of this system to promote health and prevent and treat disease



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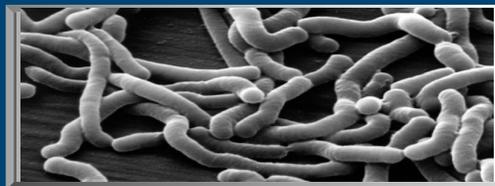
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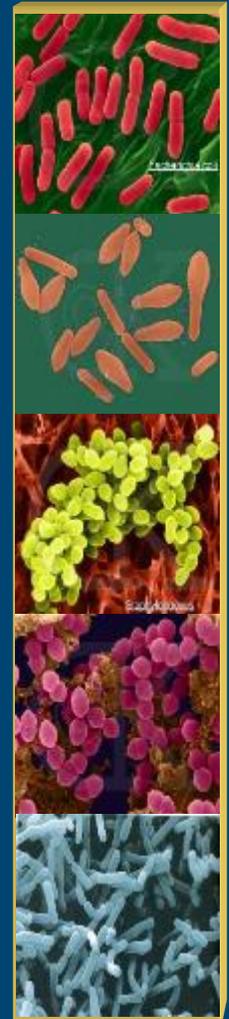
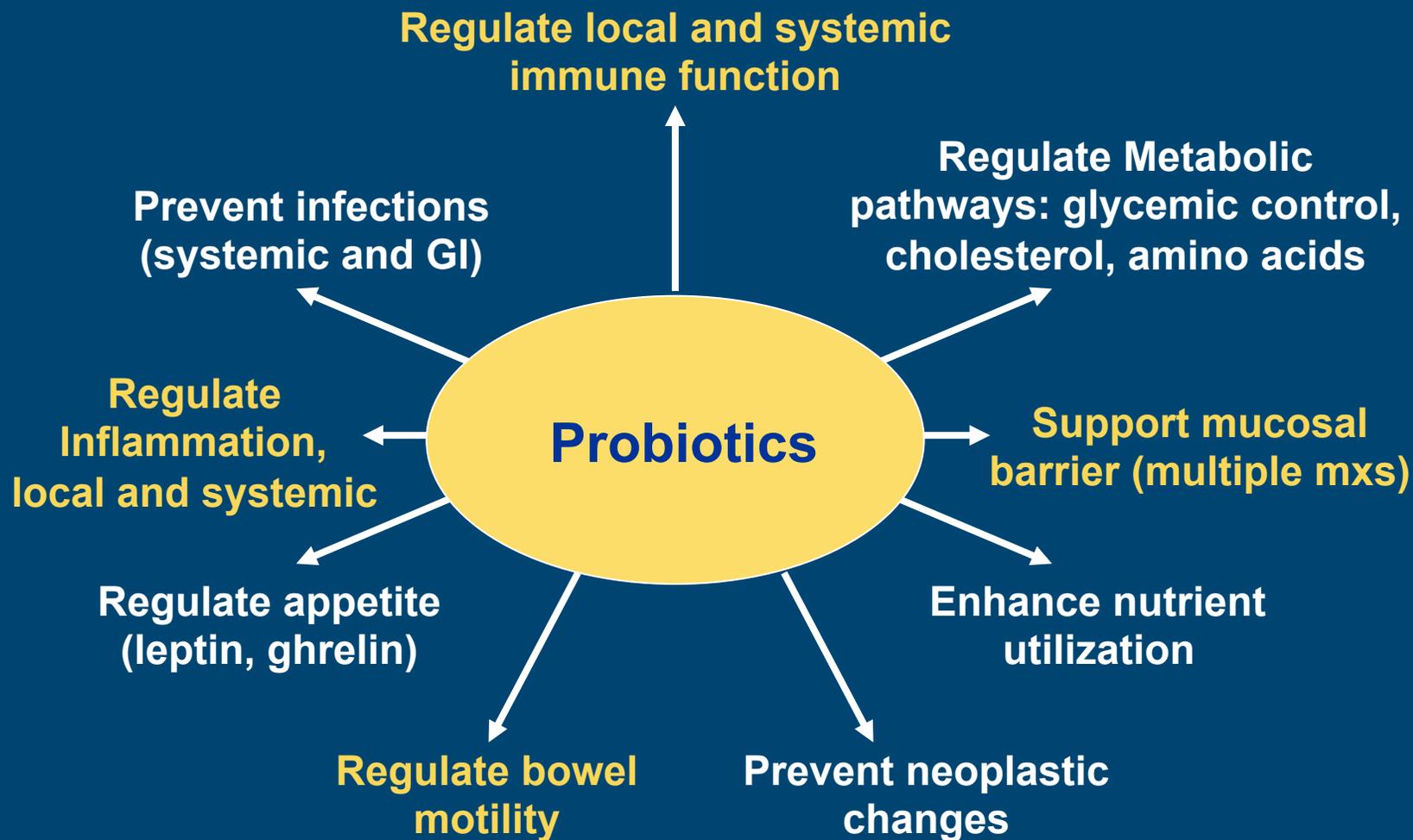


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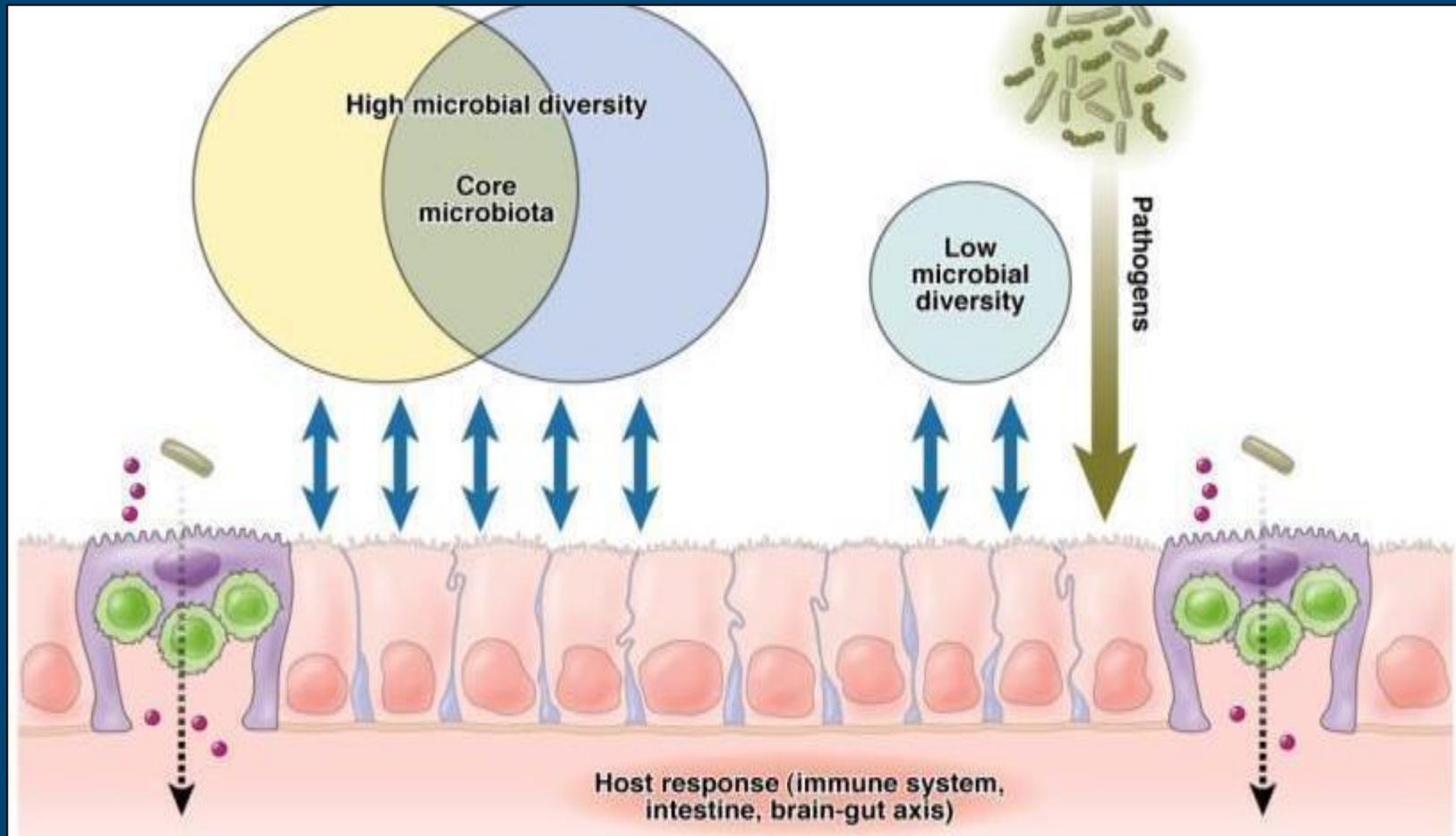


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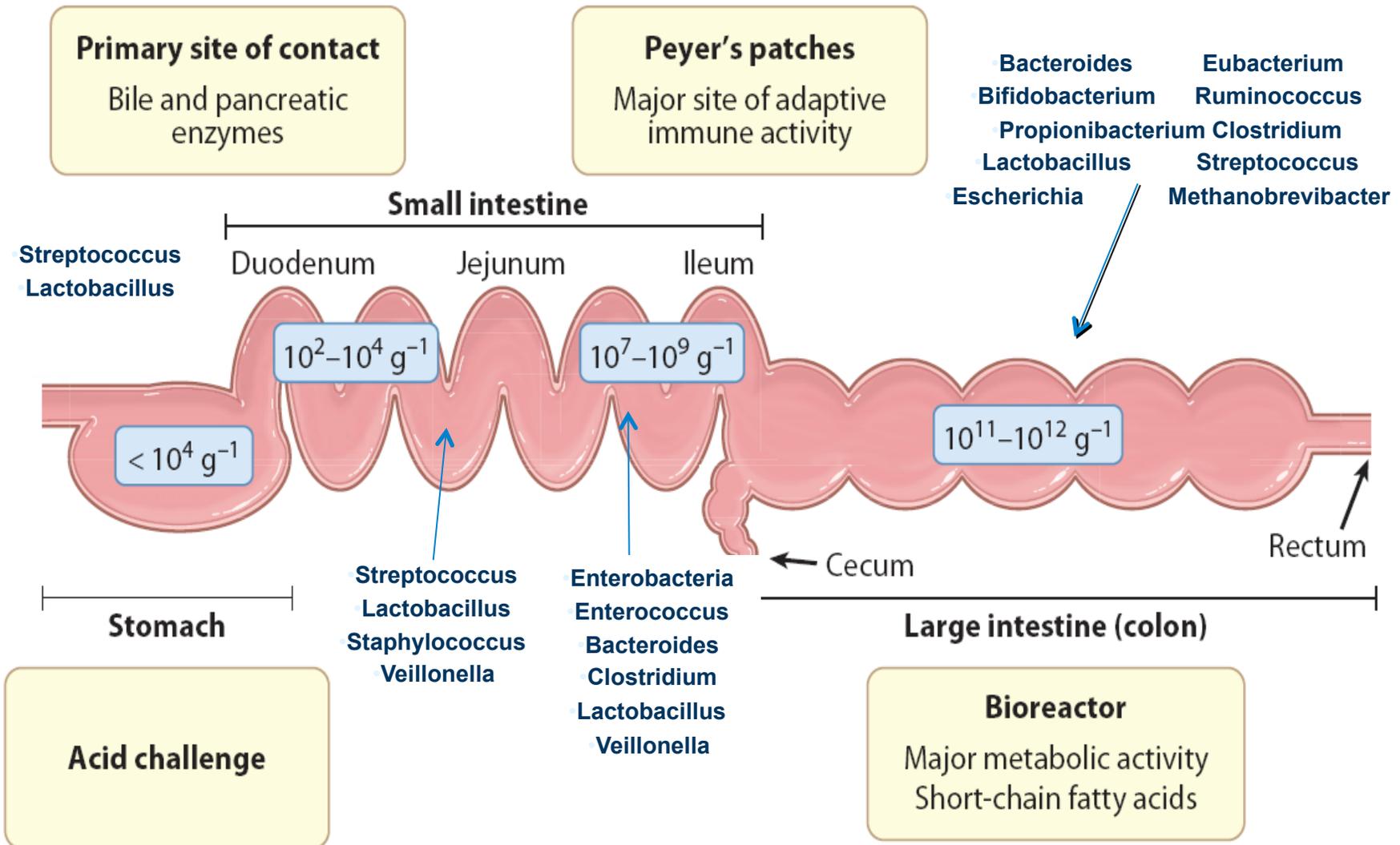


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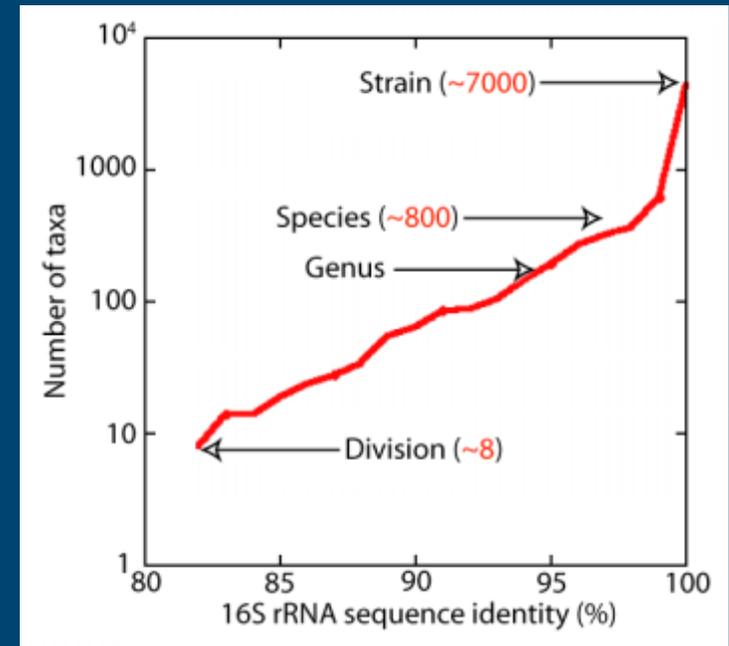
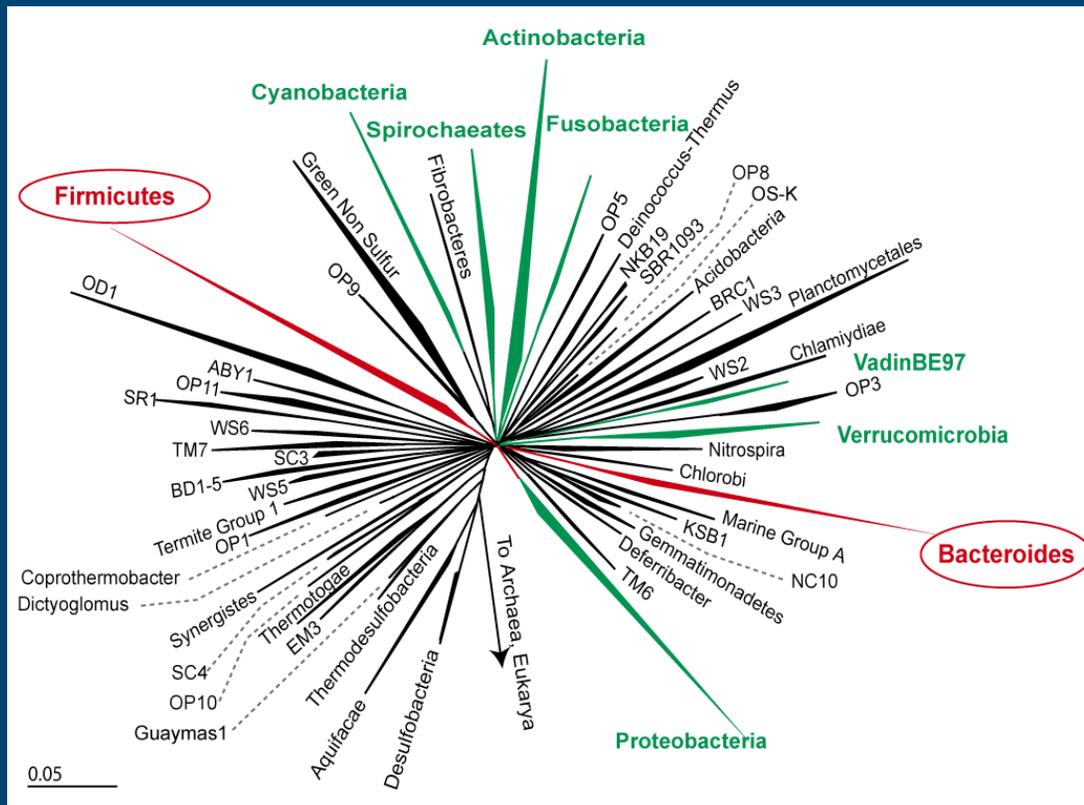


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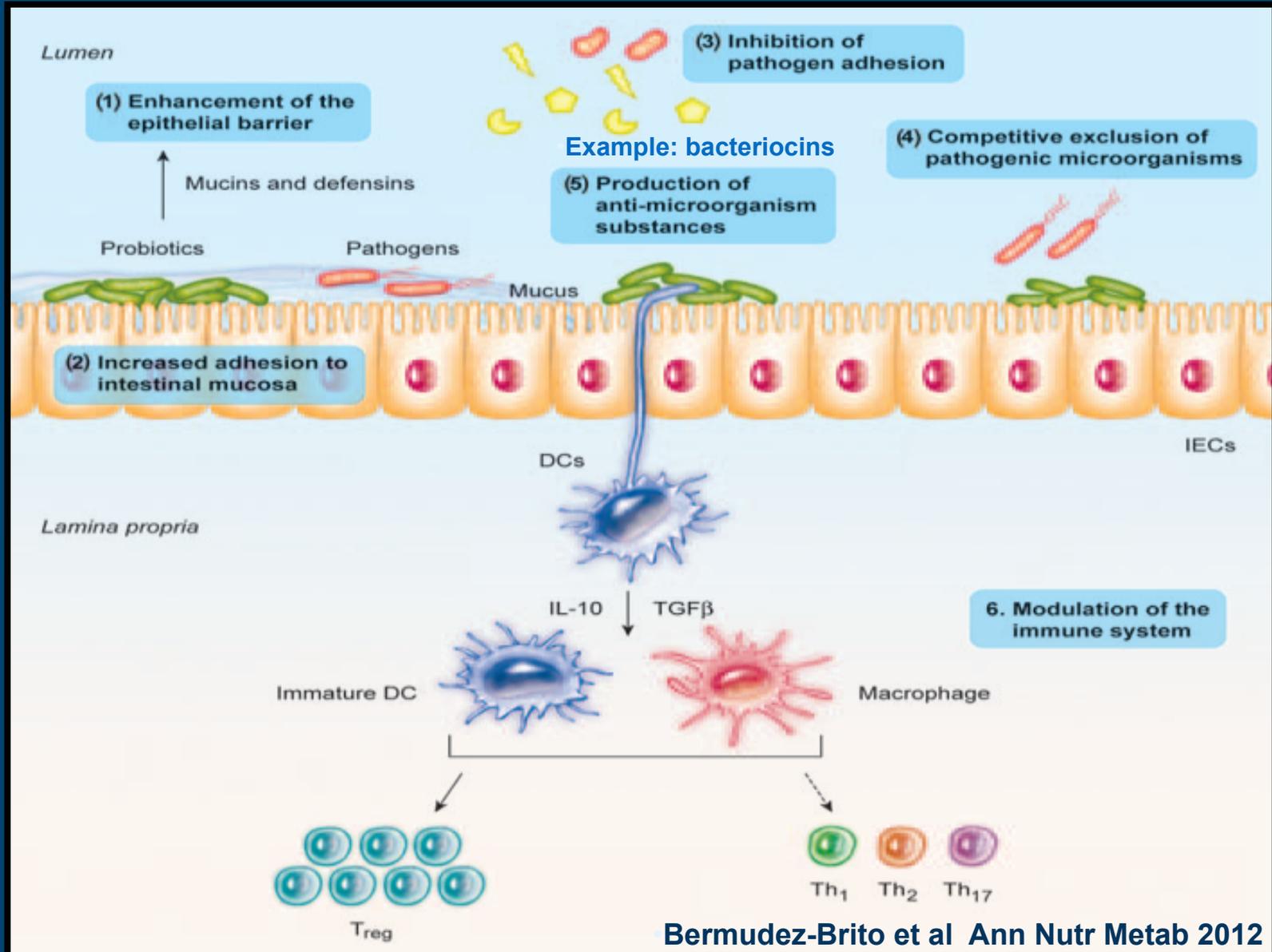


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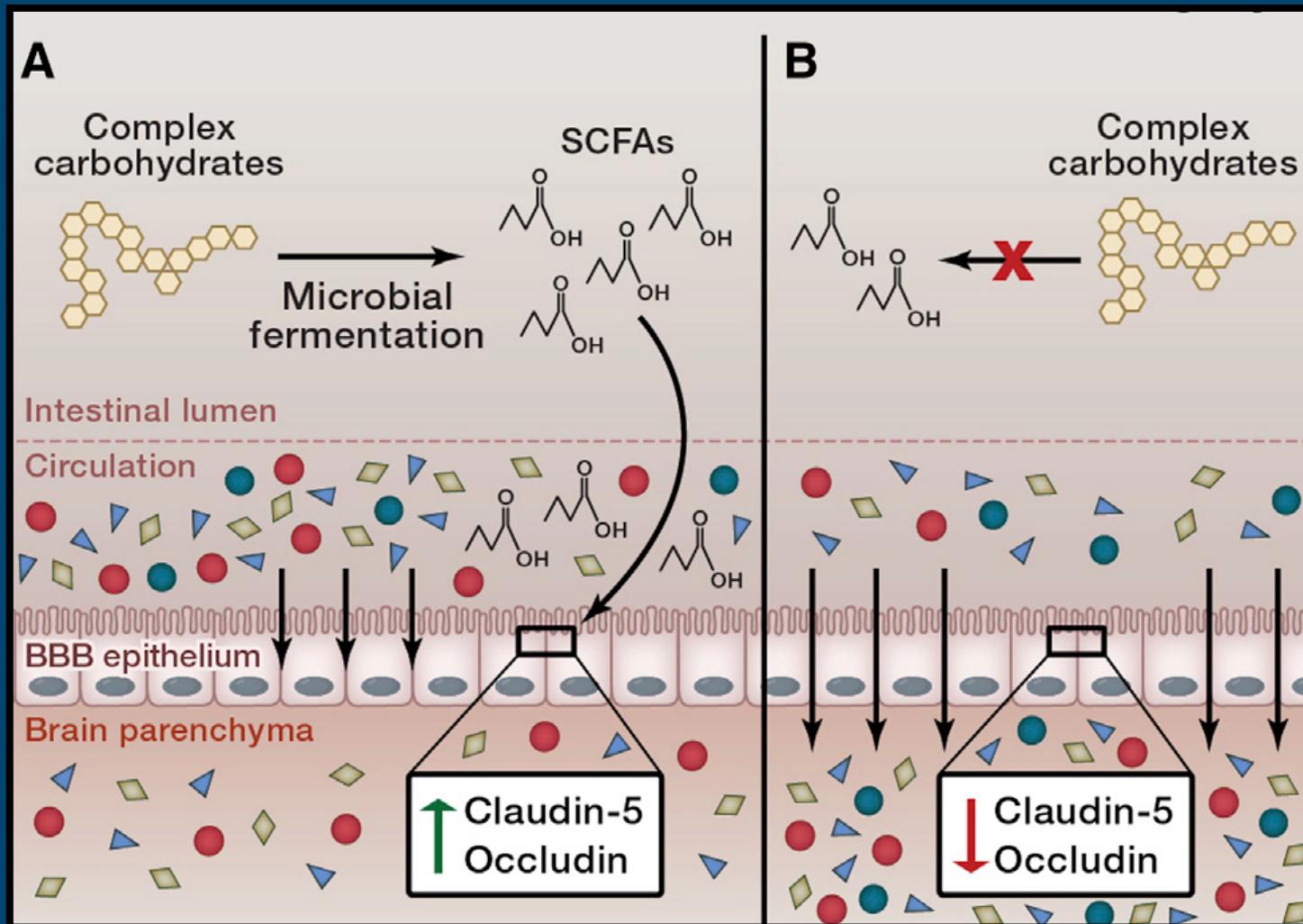
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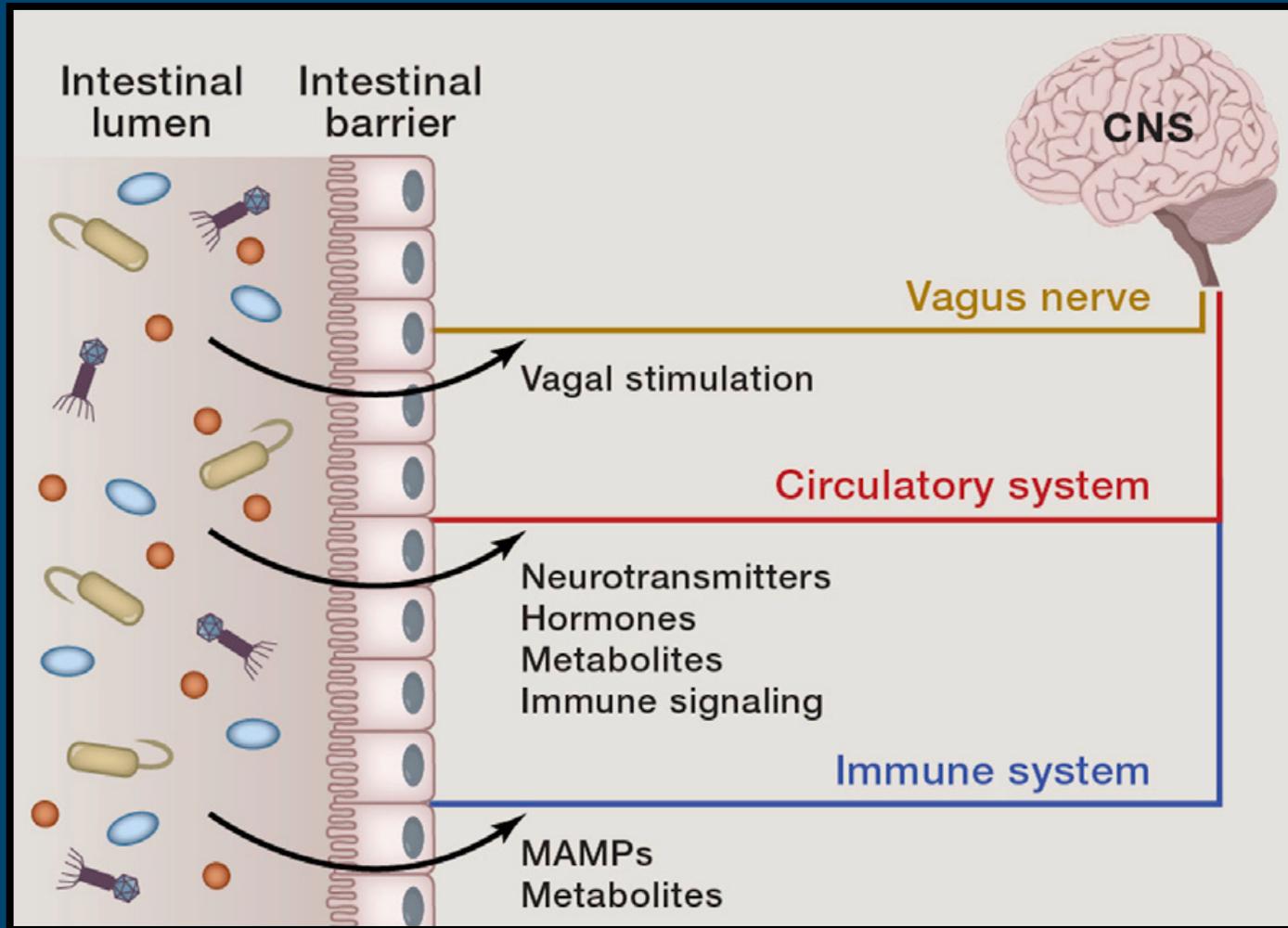
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