Therapeutic dietary alterations: how a diverse gut microbiota can reduce the risk of chronic illness

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The Gut Microbiota

100 trillion bacteria cells make up the intestinal tract

- Gut microbiota of a person is determined by lifestyle habitats, exercise, diet, disease, and antibiotic use
- Contains species from each major life domain which are bacteria, archaebacteria, and eukaryotes
- An unhealthy diet alone can have a tremendous negative effect on the gut microbiota

Bacteria Amounts and Types

Beneficial Bacterial Species

- *Bacteroides thetaiotaomicron (B-theta)*
- *Firmicutes* (gram positive)

Pathogenic Bacterial Species

- *Salmonella typhi*
- *Bacillus anthracis*

Bacteria	Basic features	Associated physiologic changes	Associated disease states	References
Bifidobacterium spp.	Gram positive obligate anaerobe branched; nonmotile	SCFA production; improve gut mucosal barrier; lower intestinal LPS levels	Reduced abundance in obesity	[166, 167]
Lactobacillus spp.	Gram positive facultative anaerobe rod-shaped	SCFA production; anti-inflammatory and anti-cancer activities	Attenuate IBD	[168, 169]
Bacteroides spp.	Gram negative obligate anaerobe rod-shaped; variable motility	Activate CD4 + T cells	Increased abundance in IBD	[170–173]
Alistipes spp.	Gram negative obligate anaerobe rod-shaped; bile-resistant and pigment-producing*		Reported in tissue from acute appendicitis and perirectal and brain abscesses	[174]
Bilophila spp.	Gram negative obligate anaerobe urease-positive, bile resistant, catalase-positive	Promote pro-inflammatory T_H1 immunity	*B. wadsworthia* observed in colitis, perforated and gangrenous appendicitis, liver and soft tissue abscesses, cholecystitis, FG, empyema, osteomyelitis, and HS	[175, 176]
Clostridium spp.	Gram positive obligate anaerobe rod-shaped; spore-forming	Promote generation of T_H17 cells	Several spp. are pathogenic causing tetanus, botulism, gas gangrene, or pseudomembranous colitis	[177, 178]
Roseburia spp.	Gram variable obligate anaerobe curved rod-shaped; motile	SCFA production	Reduced abundance in IBD	[179]
Eubacterium spp.	Gram positive obligate anaerobe rod-shaped	SCFA production; form beneficial phenolic acids	Reduced abundance in IBD	[180, 181]
Enterococcus spp.	Gram positive facultative anaerobe cocci		Several spp. are pathogenic causing UTI, endocarditis, or bacteremia	[182]
Faecalibacterium prausnitzii	Gram positive obligate anaerobe rod-shaped; nonmotile	SCFA production; anti-inflammatory effects	Reduced abundance in IBD and obesity	[183, 184]
Akkermansia muciniphila	Gram negative obligate anaerobe oval-shaped; nonmotile	Anti-inflammatory effects	Reduced abundance in IBD, obesity, and psoriatic arthritis	[53, 133, 185]
Escherichia coli	Gram negative facultative anaerobe rod-shaped	TLR-activation	Increased abundance in IBD gastroenteritis, UTI, and meningitis	[186–188]
Helicobacter pylori	Gram negative microaerophilic helix-shaped; motile		Gastritis, ulcers, MALT cancers	[189, 190]
Streptococcus spp.	Gram positive facultative anaerobe cocci		Some spp. are pathogenic causing meningitis, pneumonia, and endocarditis	[191]

spp species, *SCFA* short chain fatty acid, *LPS* lipopolysaccharide, *IBD* inflammatory bowel disease, T_H T helper, *FG* Fournier's gangrene, *HS* hidradenitis suppurativa, *UTI* urinary tract infection(s), *TLR* toll-like receptor, *MALT* mucosa-associated lymphoid tissue

* *A. putredinis* does not produce pigment and is susceptible to bile

(Singh K., et al. 2017)

Bacteria Amounts and Types

Symbiotic Human-bacteria Relationship

- Allows the body to be able to adapt to sudden dietary changes
- Maximize the amount of energy obtained from a person's diet

- Symbiotic relationship between humans and bacteria due to an antibacterial lectin secreted by the epithelial surface which is known as *RegIIIy*
- Other animals that have positive symbiotic relationships with bacteria: termites, the Gypsy moth, the squid.

(Rajpal and Brown 2013)

Gut Microbiota Functions

- Major implication of digesting food, but it also plays a significant role in the development of the immune system and communicating with the brain
- Stimulation of naive T cells into T reg cells which suppresses inflammation

Metabolites	Related bacteria	Biological functions
SCFA	*Clostridial clusters* IV and XIVa, *Eubacterium*, *Roseburia*, *Faecalibacterium*, *Coprococcus*	Cholesterol synthesis, implicated in T2D, obesity, insulin resistance, colorectal cancer
Bile acids	*Lactobacillus*, *Bifidobacteria*, *Enterobacter*, *Bacteroides*, *Clostridium*	Absorb dietary fats, intestinal barrier function, signal systemic endocrine functions, energy homeostasis
Choline metabolites	*Faecalibacterium prausnitzii*, *Bifidobacterium*	Lipid metabolism and glucose homeostasis, involved in NAFLD, obesity, diabetes & CV disease
Phenolic, benzoyl and phenyl derivatives	*Clostridium difficile*, *F. prausnitzii*, *Bifidobacterium*, *Subdoligranulum*	Detox of xenobiotics, urinary metabolites
Indole derivatives	*Clostridium sporogenes*, *Escherichia coli*	Modulate pro-inflammatory genes, strengthen epithelial cell barrier, implicated in brain-GI axis
Vitamins	*Bifidobacterium*	Endogenous sources of vitamins, potential epigenetics
Polyamines	*Campylobacter jejuni*, *Clostridium saccharolyticum*	Exert genotoxic effects, potential anti-inflammatory & anti-tumor effects
Lipids	*Bifidobacterium*, *Roseburia*, *Lactobacillus*, *Clostridium*, *Proteobacteria*	LPS induction, intestinal permeability, brain-GI-liver axis & glucose homeostasis
Others: lactate, endocannabinoids, *etc.*	*Bacteroides*, *Pseudobutyrivibrio*, *Ruminococcus*, *Faecalibacterium*, *Lactobacillus*, *etc.*	Various pathways including endocannabinoid system

Germ-free Mice Research

- Raised in these germ-free conditions
- Do not develop a gut microbiota

- Germ-free mice that were compared to regular mice had to eat 20% more calories in order to maintain the same weight as normal mice
- Studies with germ-free animals has also demonstrated that bacteria is essential for immune cell recruitment

How the Gut Microbiota Guides Immune Cell Development

- Gut microbiota has the ability to develop immunity to pathogens
- Study indicates that the gut microbiota helps to inhibit pathogen colonization
- Germ-free mice have a greatly reduced ability to form an immune response to *Toxoplasma gondii*

- Microbiota diversity and density is greatly reduced when a person is being treated with antibiotics
- Patients need assistance to help reestablish gut microbiota balance after antibiotic consumption

Fecal Microbiota Transplantation

- Consumptions of antibiotics such as Vancomycin can potentially cause an overgrowth of *Clostridium difficile*
- Fecal sample administered into the ill patient endoscopically
- In a scientific trial of 516 patients, fecal microbial transplantation produced an 85% success rate compared to the 20% success rate of antibiotic treatment

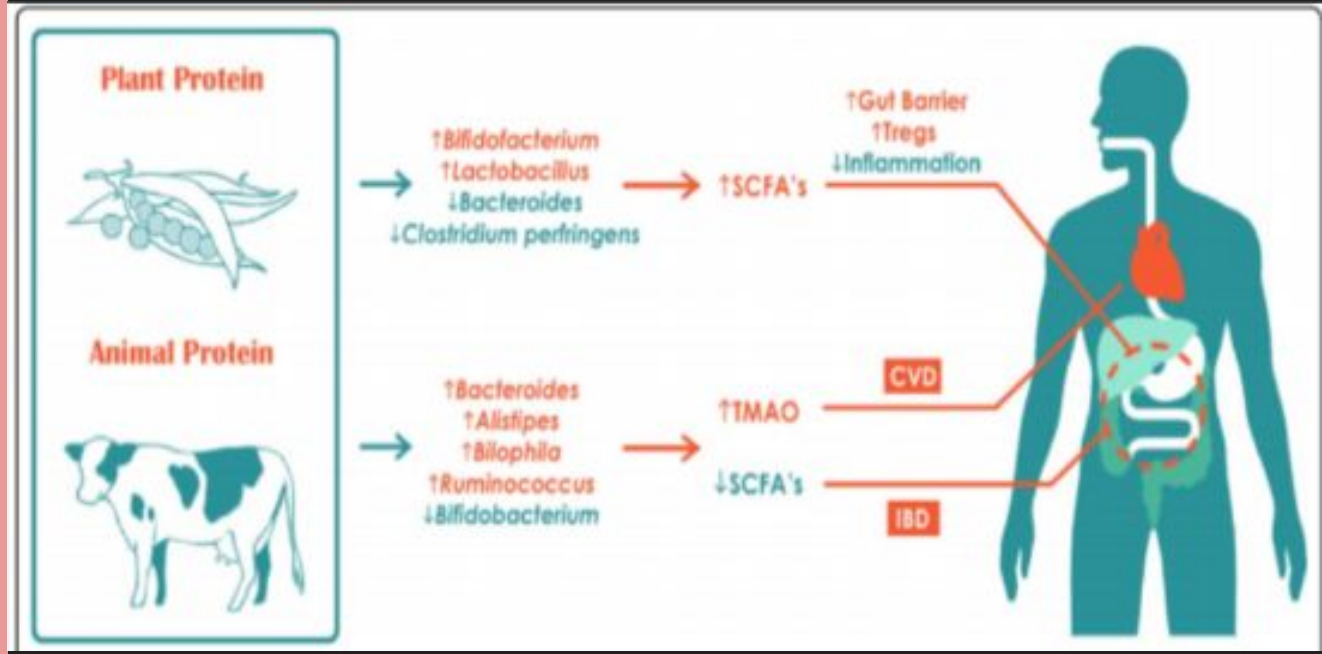
Food Types in Relation to Bacteria Composition in the Gut Microbiota

- Non-digestible carbohydrates such as fiber are considered to be “microbiota accessible carbohydrates (MACs), which allow microbes to supply their host with energy
- Soybeans, barley, and raw oats are prebiotic foods, and have shown to increase bacterial variety and density

- Fermented foods, which contain lactic acid bacteria, such as tempeh (fermented soybeans), have also shown to benefit intestinal health and are also known as probiotics
- A research study that was executed on 60 overweight adults were provided probiotic supplementation, and it resulted in an increased number in beneficial bacteria such as Bifidobacteria

Effects of Specific Diets on the Gut Microbiota

- Consuming red meat promotes a certain composition within the gut microbiota that is associated with increased levels of trimethylamine-N-oxide (TMAO)
- More studies need to be executed in order to gain more information concerning the effects of a vegan or vegetarian diet on the gut microbiota



Chronic Illnesses in Relation to Gut microbiota

- Correlation between the composition of the gut microbiota and different diseases such as type 2 diabetes, obesity, atherosclerosis, inflammatory bowel disease, atopic dermatitis, and autoimmune arthritis
- The gut microbiota of patients who are obese tend to have a higher concentration of *Firmicutes* bacteria within their intestines

- Mood disorders have also been demonstrated as a result of poor gut microbiota health.
- A distressed spatial relationship between the intestinal epithelial surface and gut microbiota correlates with IBD

Therapeutic Dietary Alterations to Increase Beneficial Bacteria Composition

- US National Institutes of Health (NIH) Human Microbiome Project was established in 2007
- EU MetaHIT Consortium; initiated in 2008
- Both developed to collect data concerning the microbiota of thousands of people from different backgrounds and different ages
- There needs to be more focus on restoration of the gut microbiota after consummation of antibiotics.
- Developments for antibiotics with specific bacterial targets will cause less distress on the gut microbiota balance.

Conclusions

- Healthy dietary changes are crucial in preventing chronic diseases
- The strong correlation between a dysbiosis of the gut microbiota and chronic illness is another reason why the gut microbiota needs to be considered more in every aspect when attempting to prevent or treat any chronic disease

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