IBD and the Functional Provider Pt II

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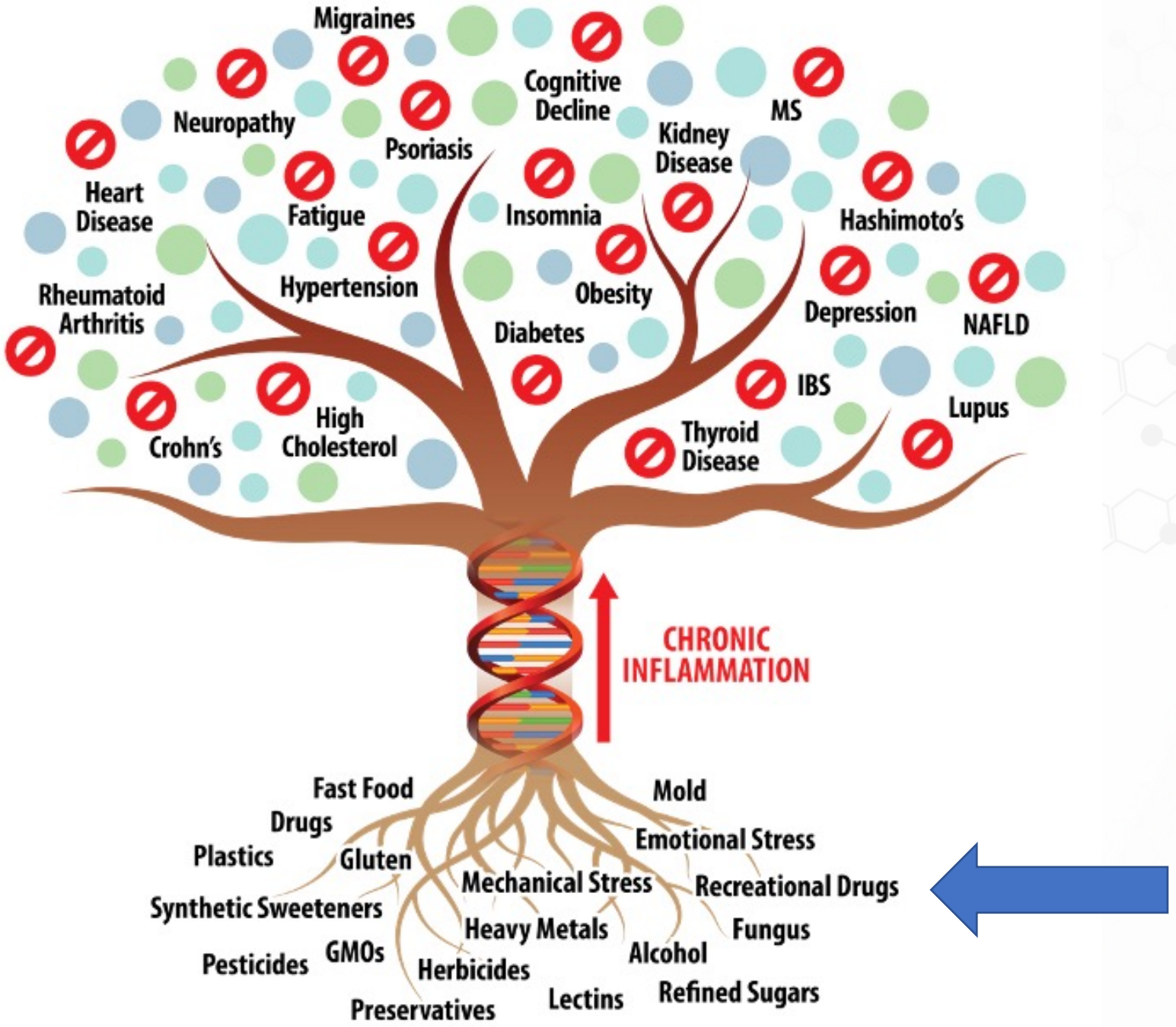
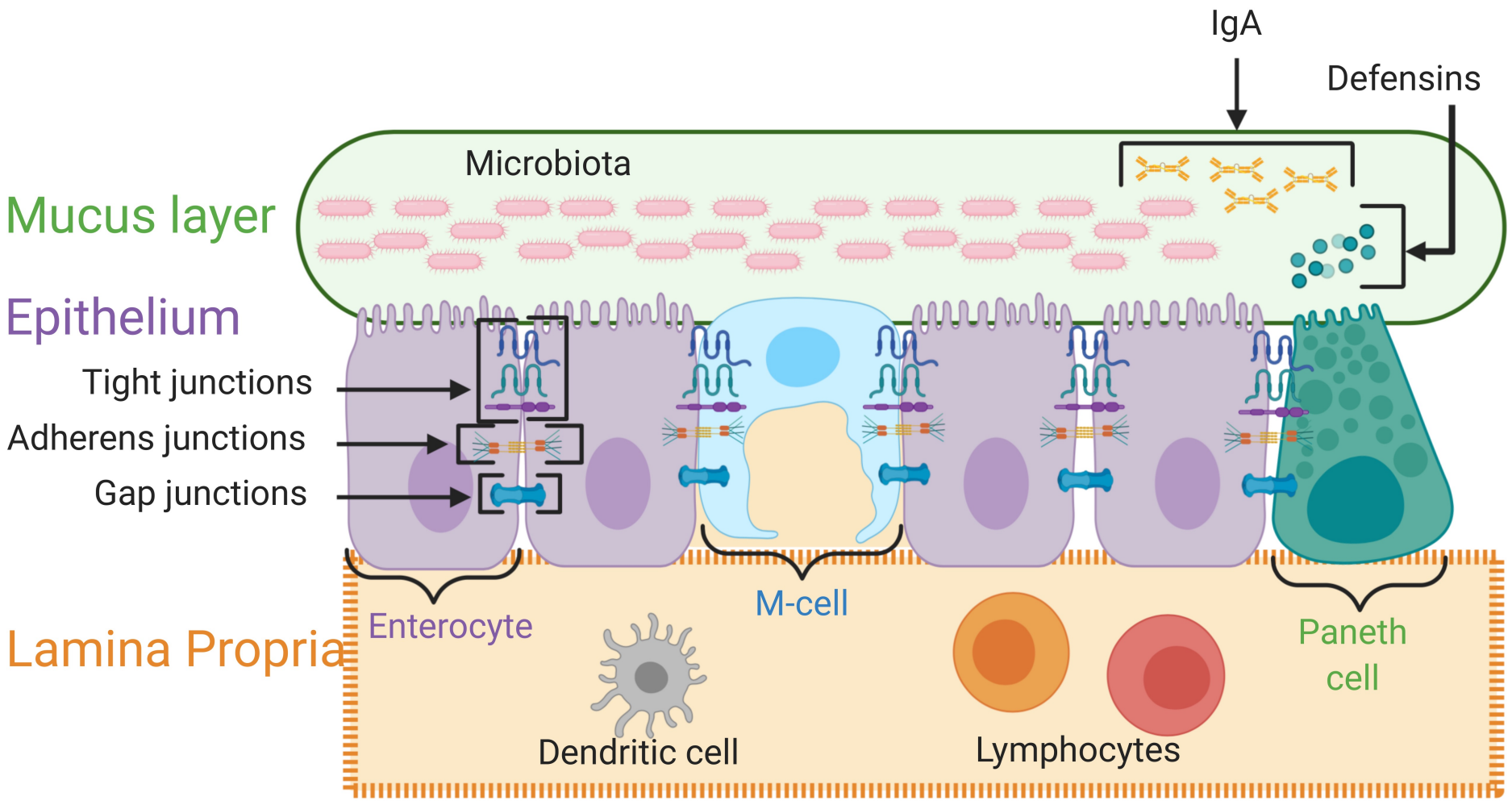

Migraines
Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Hashimoto's
Hypertension
Obesity
Depression
NAFLD
Rheumatoid Arthritis
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
CHRONIC INFLAMMATION
Fast Food
Mold
Drugs
Emotional Stress
Plastics
Gluten
Mechanical Stress
Recreational Drugs
Synthetic Sweeteners
Heavy Metals
Fungus
Pesticides
GMOs
Alcohol
Herbicides
Refined Sugars
Lectins
Preservatives



https://www.mdpi.com/microorganisms/microorganisms-08-01744/article_deploy/html/images/microorganisms-08-01744-g001.png

Revisiting Inflammatory Bowel Disease: Pathology, Treatments, Challenges and Emerging Therapeutics Including Drug Leads from Natural Products

by Karma Yeshi [1], Roland Ruscher [1], Luke Hunter [2], Norelle L. Daly [1], Alex Loukas [1] and Phurpa Wangchuk [1,*]

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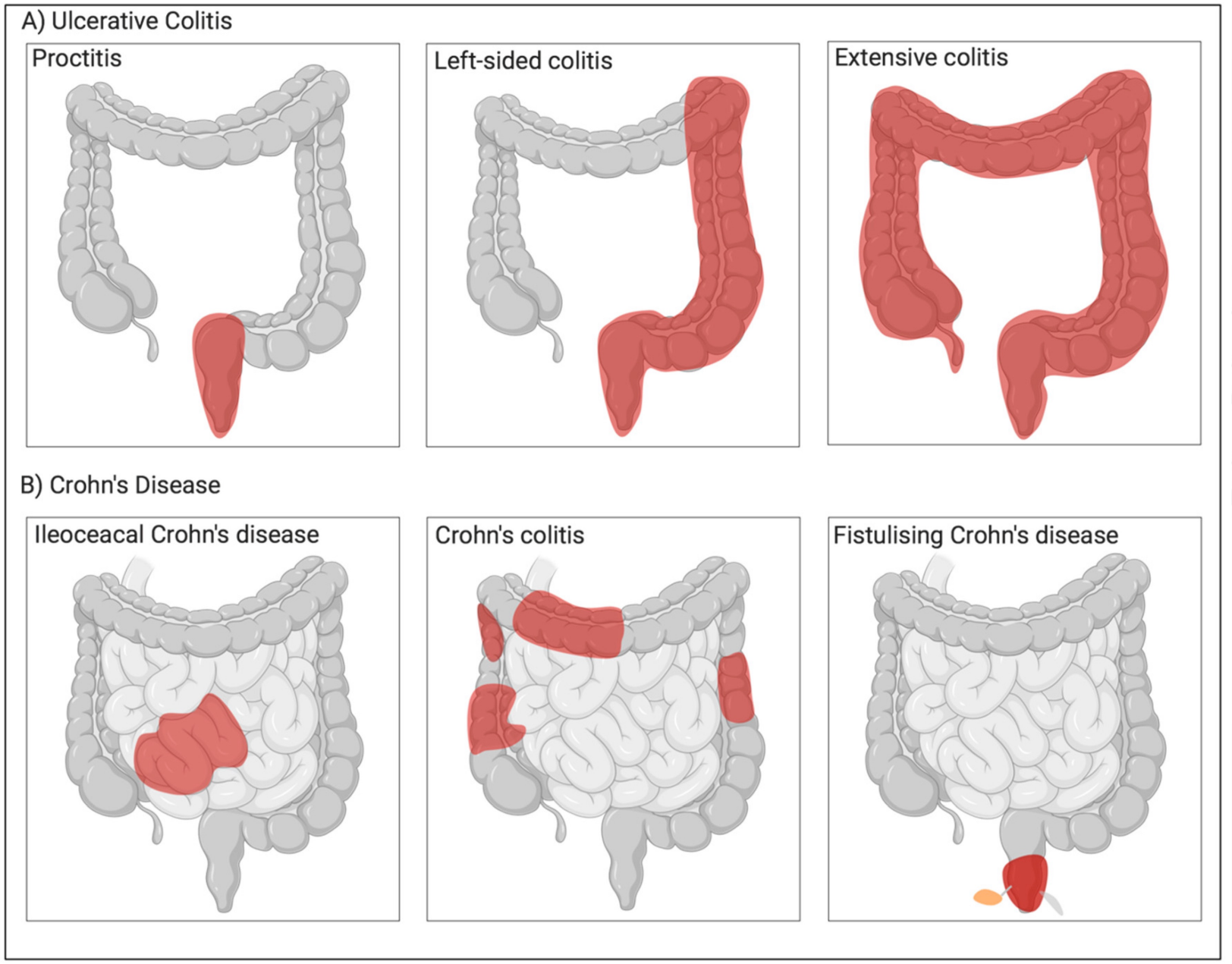
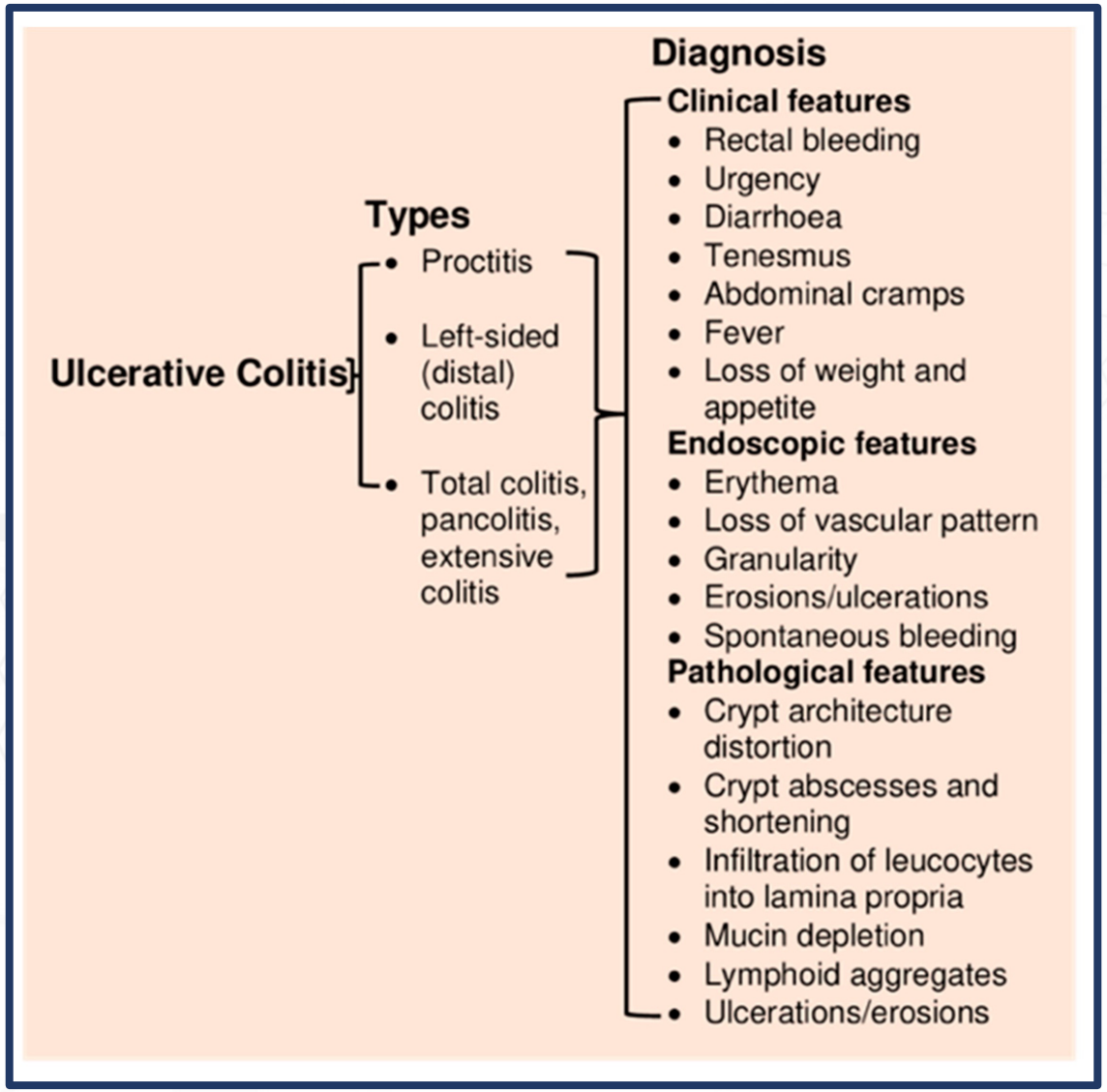
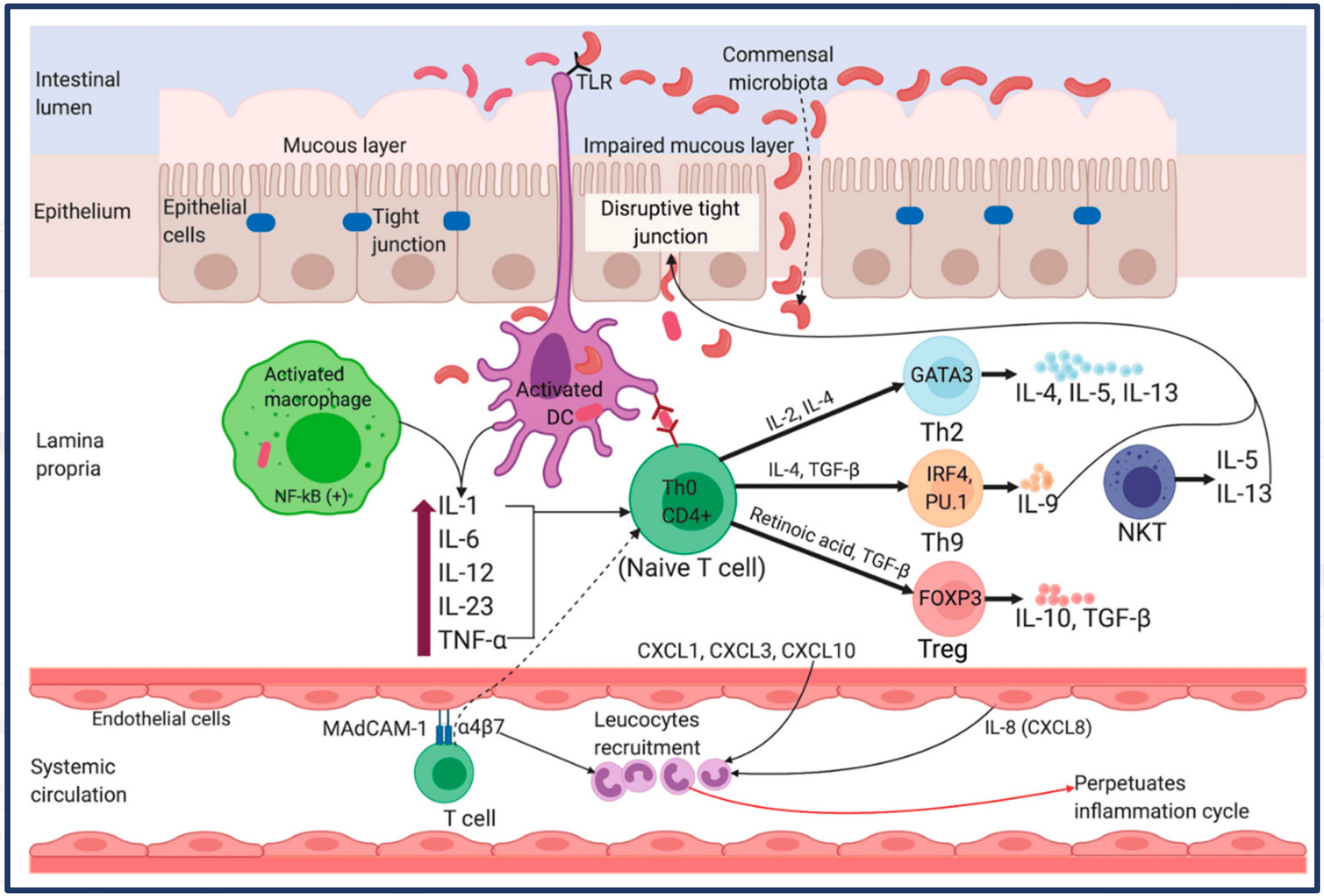
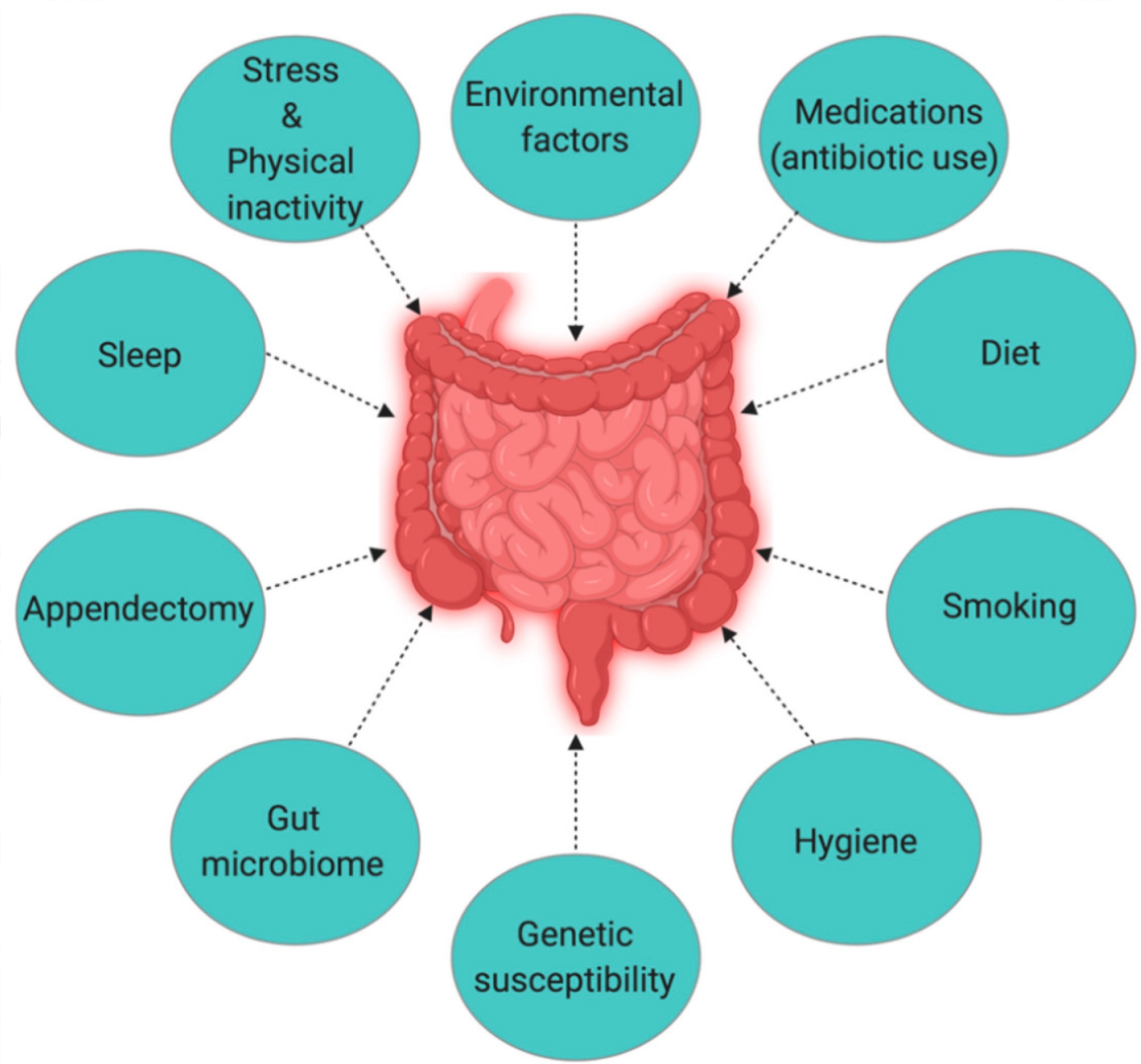
Both CD and UC show heterogeneity in many clinical and pathological features. They are distinguishable by their location and nature of inflammation (**Figure 1**). Unlike UC, which attacks colonic mucosa, CD can affect any part of the gastrointestinal (GI) tract [23]. Both conditions share clinical features like extra-intestinal manifestation, but hematochezia and passage of mucus or pus are common only in UC. Fistulas, perianal disease, colonic and small bowel obstruction is common in CD. Cryptitis and crypt abscesses are observed in both UC and CD, while crypt architecture is more distorted in the case of UC [24]. Both UC and CD show relapsing intestinal inflammation. Intermediate colitis (IC) sometimes does not present distinct clinical features of either UC or CD, particularly in colectomy specimens, rendering it hard to distinguish UC from CD. Although IC is not a unique disease or distinct clinical entity, it accounts for around 10% of the total IBD cases involving the colon [25], and this figure has not changed over the last 30 years [26]. Currently, IC is usually diagnosed when a distinction between UC and CD becomes difficult. A standard positive diagnostic test for IC is not yet available.









https://www.mdpi.com/2077-0383/9/5/1273

Revisiting Inflammatory Bowel Disease: Pathology, Treatments, Challenges and Emerging Therapeutics Including Drug Leads from Natural Products

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Diet influences the composition of the microbiota and their metabolic activity in the human gut [86]. There is a growing concern that the western diet, rich in fats and sugars, is responsible for the change in the diversity and metabolic activity of human gut microbiota, thereby contributing to the increasing incidence of IBD [87,88]. The increase in the abundance of *Bilophila wadsworthia* due to an animal-based diet can facilitate the growth of microorganisms that can trigger IBD [87,88]. Moreover, *B. wadsworthia* also produces hydrogen sulfide that can cause damage to intestinal tissues [86]. Long-term dietary pattern influences the development of IBD [89]. For instance, the intake of fruits decreases the risks of developing CD [90], although the underlying mechanism is yet to be understood. Smoking is one of the contradictory factors linked to IBD. While smoking is harmful to CD patients, reports show beneficial in UC [63]. The positive effect of smoking in UC is evident from the "Boston Drugs Surveillance Program" [91], "UC patients in Birmingham, England" [92], and "Oxford Family Planning Association Contraceptive Study" [93]. Additionally, the transdermal treatment of active UC patients with nicotine patches also showed better remission compared to the placebo group [94]. However, it is still controversial, and more research is required to determine if nicotine is one of the active components of cigarette smoking that is responsible for the beneficial effects on the UC disease course.

Dx: Ulcerative Colitis

1. What is your current lifestyle/environment?
2. What does the microbiome landscape look like?
3. Any identifiable food triggers (labs, experience, or otherwise)?

SAD →

Modern Med:
- Low Meat
- Heavy vegetable
- Moderate fruit
- Complex carbohydrates

→ AIP → Carnivore

Inflamm Bowel Dis. 2017 Nov; 23(11): 2054–2060.
Published online 2017 Aug 29. doi: 10.1097/MIB.0000000000001221

PMCID: PMC5647120
NIHMSID: NIHMS889275
PMID: 28858071

Efficacy of the Autoimmune Protocol Diet for Inflammatory Bowel Disease

Gauree G. Konijeti, MD, MPH,[✉*†] NaMee Kim, MD,[‡] James D. Lewis, MD, MSCE,[§] Shauna Groven, BS,[‖] Anita Chandrasekaran, MD, MPH,[*] Sirisha Grandhe, MD,[*] Caroline Diamant, MD,[*] Emily Singh, MD,[*] Glenn Oliveira, BS,[†¶] Xiaoyun Wang, MS,[†] Bhuvan Molparia, MS,[¶†] and Ali Torkamani, PhD[¶†]

Despite diet being implicated in the pathogenesis of IBD,[4] we have limited data to guide the use of nutritional therapy as either primary or adjunctive treatment for these conditions. Conventional medical therapy for IBD focuses on suppression of the immune system by targeting a variety of pathways, yet response rates continue to remain suboptimal. Therefore, there is an important need to study dietary factors that may not only help improve response to conventional treatment but also potentially be used as primary therapy or maintenance therapy for patients with IBD. A Western diet, high in refined carbohydrates, omega-6 fatty acids, saturated fat, low in fiber, vitamins, and generally nutrient dense foods, are associated with an increased risk of IBD.[4] Recent albeit limited data suggest that a semivegetarian diet[5] (allowing milk and eggs, fish once per week, and other meat once every 2 weeks), specific carbohydrate diet[6–8] (removal of all grains, most dairy products, and sweeteners except for honey), or anti-inflammatory diet[9] (modified carbohydrate and fatty acid intake, and increased prebiotic/probiotic ingestion) can be associated with improved rates of achieving or maintaining clinical response.

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The autoimmune protocol (AIP) diet is an extension of the Paleolithic diet[10] and incorporates some of the dietary changes previously studied in IBD, including avoidance of gluten and refined sugar. The AIP diet focuses on an initial elimination phase of food groups including grains, legumes, nightshades, dairy, eggs, coffee, alcohol, nuts and seeds, refined/processed sugars, oils, and food additives.[10,11] The rationale is to avoid foods, additives, or medications (e.g., nonsteroidal anti-inflammatory drugs) that can trigger intestinal inflammation, dysbiosis, and/or symptomatic food intolerance.[10,12–14] It also emphasizes consumption and preparation of fresh, nutrient dense foods, bone broth, and fermented foods, while addressing factors that are known to associate with disability due to IBD, such as sleep and sleep hygiene, stress management, forming a support system, and physical activity.[15] The elimination phase is followed by a maintenance phase, the duration of which can vary by individual, until they achieve a measurable improvement in their symptoms and overall well-being. Staged reintroduction of food groups is then initiated gradually, as patients identify unique foods or food groups that may contribute to symptoms while liberalizing their diet.[10,11]

Based on increasing evidence suggesting an impact of diet on clinical disease activity and IBD, and our clinical experience with patients pursuing the AIP diet for their symptomatic IBD, we performed a prospective study to evaluate the potential efficacy of the autoimmune protocol (AIP) diet in patients with active CD and UC.

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Increasing evidence suggests that dietary modification can modulate inflammation and improve clinical responses in IBD. Our prospective observational study indicate that an AIP diet, involving an elimination phase followed by a maintenance phase, demonstrates preliminary efficacy in patients with active IBD. We also identified improvements in FC along with endoscopic improvements in the mucosal appearance in most patients undergoing follow-up endoscopy.

Our results support the use of dietary modification as an adjunct to IBD therapy. Clinical remission was achieved by week 6 by 11/15 (73%) of study participants, and all 11 maintained clinical remission during the maintenance phase of the study. We did not hypothesize, a priori, that clinical remission would be achieved so early (week 6). Indeed, this proportion of participants with active IBD (HBI ≥ 5 or partial Mayo clinic score ≥3, and objective evidence of active inflammation) achieving clinical remission by week 6 rivals that of most drug therapies for IBD; importantly, our dietary study was performed as an adjunct to medical therapy, and almost 50% of patients in our study were on biological therapy. Therefore, our results suggest that dietary modification can be used as an adjunct to conventional IBD therapy, even among those with moderate-to-severe disease.

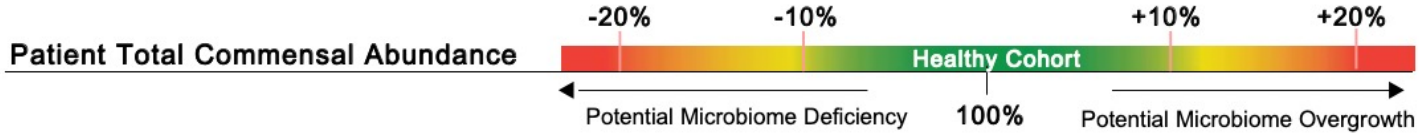
Functional Imbalance Scores

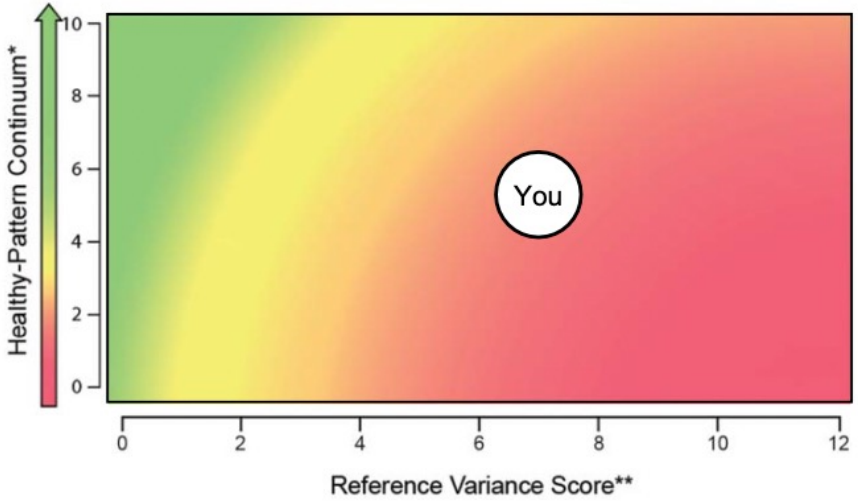
Key (< 2) : Low Need for Support (2-3) : Optional Need for Support (4-6) : Moderate Need for Support (7-10) : High Need for Support

	Need for Digestive Support	Need for Inflammation Modulation	Need for Microbiome Support	Need for Prebiotic Support	Need for Antimicrobial Support
	MALDIGESTION	INFLAMMATION	DYSBIOSIS	METABOLIC IMBALANCE	INFECTION
	6	10	5	4	0
Biomarkers	Pancreatic Elastase ▽ Products of Protein Breakdown ● Fecal Fats ●	Calprotectin ▲ Eosinophil Protein X ● Secretory IgA ● Occult Blood ●	PP Bacteria/Yeast △ Reference Variance △ IAD/Methane Score ● Total Abundance N/A	Total SCFA's ▽ n-Butyrate Conc. ▽ SCFA (%) ▽ Beta-glucuronidase ●	PP Bacteria/Yeast △ Parasitic Infection ● Pathogenic Bacteria ● Total Abundance N/A
Therapeutic Support Options	• Digestive Enzymes • Betaine HCl • Bile Salts • Apple Cider Vinegar • Mindful Eating Habits • Digestive Bitters	• Elimination Diet/ Food Sensitivity Testing • Mucosa Support: Slippery Elm, Althea, Aloe, DGL, etc. • Zinc Carnosine • L-Glutamine • Quercetin • Turmeric • Omega-3's • GI Referral (If Calpro is Elevated)	• Pre-/Probiotics • Increase Dietary Fiber Intake • Consider SIBO Testing • Increase Resistant Starches • Increase Fermented Foods • Meal Timing	• Pre-/Probiotics • Increased Dietary Fiber Intake • Increase Resistant Starches • Increase Fermented Foods • Calcium D-Glucarate (for high beta-glucuronidase)	• Antibiotics (if warranted) • Antimicrobial Herbal Therapy • Antiparasitic Herbal Therapy (if warranted) • *Saccharomyces boulardii*

74yo female, 2 dm2, 1 statin, 3 bp, 1 kidney remains, BMI 44.

Commensal Abundance



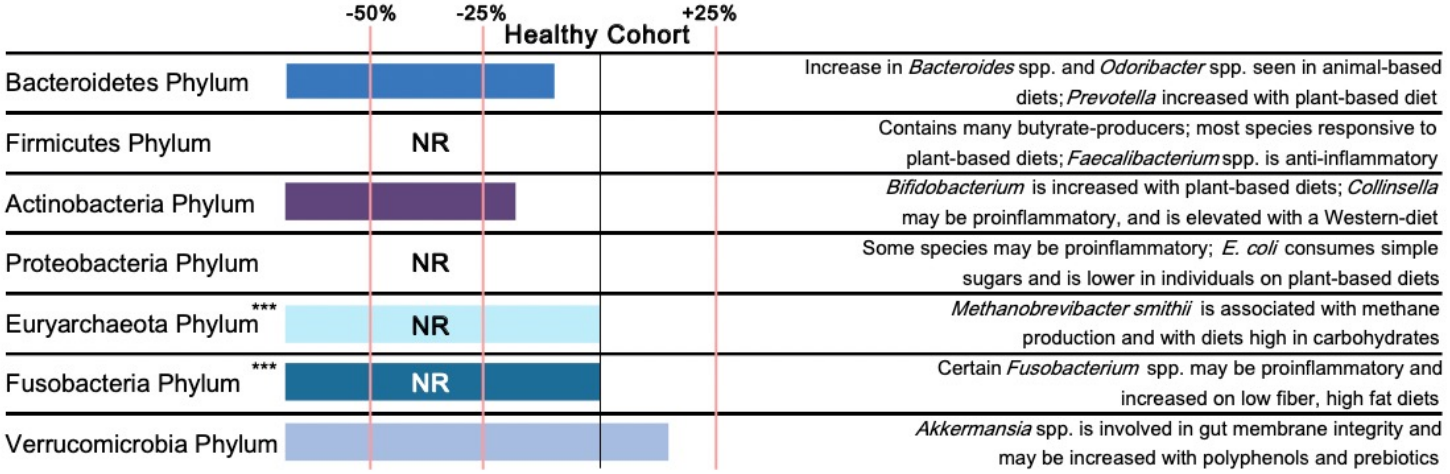


Balanced	Represents 95% of healthy individuals
Borderline	Represents 5% of healthy individuals
Imbalanced	Represents 60% of unhealthy individuals

*A progressive ranking scale based on a Genova proprietary algorithm that differentiates healthy and unhealthy commensal patterns.

**The total number of commensal bacteria (qPCR) that are out of balance for this individual on a scale of 0 to >12.

Relative Commensal Abundance



74yo female, 2 dm2, 1 statin, 3 bp, 1 kidney remains, BMI 44.

Inflammation and Immunology

Calprotectin † ◆	695 H	50 / 100	<50 mcg/g
Eosinophil Protein X (EPX) †	0.3	0.5 / 2.7	<=2.7 mcg/g
Fecal secretory IgA	<150	680 / 2040	<=2,040 mcg/mL

Additional Bacteria

Salmonella spp.		NG
Shigella spp.		NG
alpha haemolytic Streptococcus	1+	NP
Staphylococcus aureus	1+	NP
Klebsiella oxytoca	4+	PP

> Chemosphere. 2022 Jan;287(Pt 2):132160. doi: 10.1016/j.chemosphere.2021.132160. Epub 2021 Sep 5.

Analyzing the synergistic adverse effects of BPA and its substitute, BHPF, on ulcerative colitis through comparative metabolomics

Feiying Yin [1], Xue Huang [2], Xiao Lin [3], Ting Fung Chan [3], Keng Po Lai [4], Rong Li [5]

Affiliations expand

PMID: 34

Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) that causes long-term inflammation and ulcers in the colon and rectum. Approximately 3 million adults were diagnosed with IBD in the US in 2015, and its incidence rate is estimated to increase by 4-6 times in 2030. Industrial pollutants are largely responsible for this significant increase in UC cases. Several epidemiological and animal studies have demonstrated the correlation between pollutants and gastrointestinal diseases, but detailed molecular mechanisms responsible for adverse effects of environmental pollutants on UC are still unknown. In the present study, we used a dextran sulfate sodium (DSS)-induced colitis mouse model, comparative metabolomics analysis, and systematic bioinformatics analysis to delineate the synergistic adverse effects of bisphenol A (BPA) and its substitute fluorene-9-bisphenol (BHPF) on UC. Subsequently, a significant alteration in gut metabolites was observed by the BPA and BHPF treatments. Furthermore, the bioinformatics analysis indicated deregulation of sugar and fatty acid metabolisms in the DSS-induced colitis model by the BPA and BHPF treatments, respectively. Additionally, both the treatments induced an inflammatory response in the model. Particularly, some DSS-deregulated metabolites, which play important roles in gut inflammation, were synergistically induced or reduced by the BPA and BHPF treatments. To the best knowledge of the authors, the synergistic adverse effects of the BPA and BHPF treatments on UC were demonstrated for the first time through gut metabolism alterations. Therefore, the present study provides novel insights in the role of environmental pollutants, such as BPA and BHPF, in UC development.

> Ecotoxicol Environ Saf. 2022 Sep 1:242:113897. doi: 10.1016/j.ecoenv.2022.113897. Epub 2022 Aug 6.

Uncovering the functions of plasma proteins in ulcerative colitis and identifying biomarkers for BPA-induced severe ulcerative colitis: A plasma proteome analysis

Chen

Affili

PMI

Ulcerative colitis (UC), a long-term inflammation of the colon, is a worldwide disease. Accumulating reports have suggested the contribution of environmental pollutants to UC development. As such, the identification of biomarkers to evaluate pollutant-induced UC could provide a better assessment on the world's pollution problem. In the present study, we applied the plasma proteome to profile the plasma protein changes in three models: dextran sulfate sodium (DSS)-induced colitis, bisphenol A (BPA), and BPA-severe colitis. We aimed to investigate the functional roles of plasma proteins related to colitis development and further understand the synergistic effect of BPA on colitis. In addition, we aimed to identify novel biomarkers for UC non-invasive diagnosis and assessment of BPA-induced colitis. Our results showed a significant dysregulation of plasma proteins in these three models. Bioinformatics analysis, including gene ontology, Kyoto Encyclopedia of Genes and Genomes pathway enrichment analysis, and Ingenuity Pathway Analysis, highlighted the important effects of these dysregulated plasma proteins in immune and inflammatory responses through the regulation of CCR3 signaling in eosinophils, PI3K signaling in B lymphocytes, CD28 signaling in T helper cells, and leukocyte extravasation signaling in DSS-induced colitis model. Furthermore, our data suggested that BPA exposure altered the plasma proteins involved in lipid-related metabolic processes, leukocyte cell-cell adhesion and cytokine response. More importantly, we identified plasma proteins, ALB, APOA4, C3, CFB, DPEP1, HP, LTF, and Retnlg as biomarkers for assessing BPA-induced colitis.

Med Sci Monit Basic Res. 2014; 20: 47–54.
Published online 2014 Apr 10. doi: 10.12659/MSMBR.890644
PMCID: PMC3997203
PMID: 24717721

A novel pathway by which the environmental toxin 4-Nonylphenol may promote an inflammatory response in inflammatory bowel disease

Albert Kim,[A,B,C,D,E,F] Byeong Ho Jung,[B,C,D,F] and Patrick Cadet[A,E,G]

Abstract

Go to: ▸

Background

4-Nonylphenol is a ubiquitous environmental toxin that is formed as a byproduct in the manufacturing and/or sewage treatment of regular household items. Previous work in our lab has implicated 4-NP in the progression of autoimmune diseases such as inflammatory bowel disease in which macrophages mistakenly attack the intestinal linings, causing chronic inflammation. Several key pro-and anti-inflammatory molecules have been shown to be involved in the manifestation of this disease, including IL-23A, COX-2, IL-8, TLR-4, and IL-10.

Material/Methods

4-NP's effects on these known mediators of IBD were effectively analyzed using a novel model for IBD, by which 4-NP may promote an inflammatory response. Data were collected using DNA Microarray, RT-PCR, and ELISA, after 48 hour treatment of U937 histiocytic lymphocyte cells and COLO320DM human intestinal epithelial cells with 1 nM and 5 nM concentrations of 4-NP.

Int J Mol Sci. 2021 Feb; 22(3): 985.
Published online 2021 Jan 20. doi: 10.3390/ijms22030985
PMCID: PMC7863964
PMID: 33498177

Inflammatory Bowel Disease: New Insights into the Interplay between Environmental Factors and PPARγ

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Iwona Bogacka, Academic Editor

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Abstract

Go to:

The pathophysiological processes of inflammatory bowel diseases (IBDs), i.e., Crohn's disease (CD) and ulcerative colitis (UC), are still not completely understood. The exact etiology remains unknown, but it is well established that the pathogenesis of the inflammatory lesions is due to a dysregulation of the gut immune system resulting in over-production of pro-inflammatory cytokines. Increasing evidence underlines the involvement of both environmental and genetic factors. Regarding the environment, the microbiota seems to play a crucial role. Peroxisome proliferator-activated receptors (PPARs) are nuclear receptors that exert pleiotropic effects on glucose homeostasis, lipid metabolism, inflammatory/immune processes, cell proliferation, and fibrosis. Furthermore, PPARs modulate interactions with several environmental factors, including microbiota. A significantly impaired PPARγ expression was observed in UC patients' colonic epithelial cells, suggesting that the disruption of PPARγ signaling may represent a critical step of the IBD pathogenesis. This paper will focus on the role of PPARγ in the interaction between environmental factors and IBD, and it will analyze the most suitable in vitro and in vivo models available to better study these relationships.

Review > Sci Total Environ. 2022 Oct 10:842:156776. doi: 10.1016/j.scitotenv.2022.156776.
Epub 2022 Jun 17.

Triclosan and triclocarban as potential risk factors of colitis and colon cancer: Roles of gut microbiota involved

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Affiliations + expand

PMID: 35724794 DOI: 10.1016/j.scitotenv.2022.156776

Abstract

In recent decades there has been a dramatic increase in the incidence and prevalence of inflammatory bowel disease (IBD), a chronic inflammatory disease of the intestinal tissues and a major risk factor of developing colon cancer. While accumulating evidence supports that the rapid increase of IBD is mainly caused by exposure to environmental risk factors, the identities of the risk factors, as well as the mechanisms connecting environmental exposure with IBD, remain largely unknown. Triclosan (TCS) and triclocarban (TCC) are high-volume chemicals that are used as antimicrobial ingredients in consumer and industrial products. They are ubiquitous contaminants in the environment and are frequently detected in human populations. Recent studies showed that exposure to TCS/TCC, at human exposure-relevant doses, increases the severity of colitis and exacerbates colon tumorigenesis in mice, suggesting that they could be risk factors of IBD and associated diseases. The gut toxicities of these compounds require the presence of gut microbiota, since they fail to induce colonic inflammation in mice lacking the microbiota. Regarding the functional roles of the microbiota involved, gut commensal microbes and specific microbial β-glucuronidase (GUS) enzymes mediate colonic metabolism of TCS, leading to metabolic reactivation of TCS in the colon and contributing to its subsequent gut toxicity. Overall, these results support that these commonly used compounds could be environmental risk factors of IBD and associated diseases through gut microbiota-dependent mechanisms.

Keywords: Colon cancer; Gut microbial metabolism; Gut microbiota; Inflammatory bowel disease (IBD); Triclocarban (TCC); Triclosan (TCS).

High (>95th percentile)

Environmental Toxins

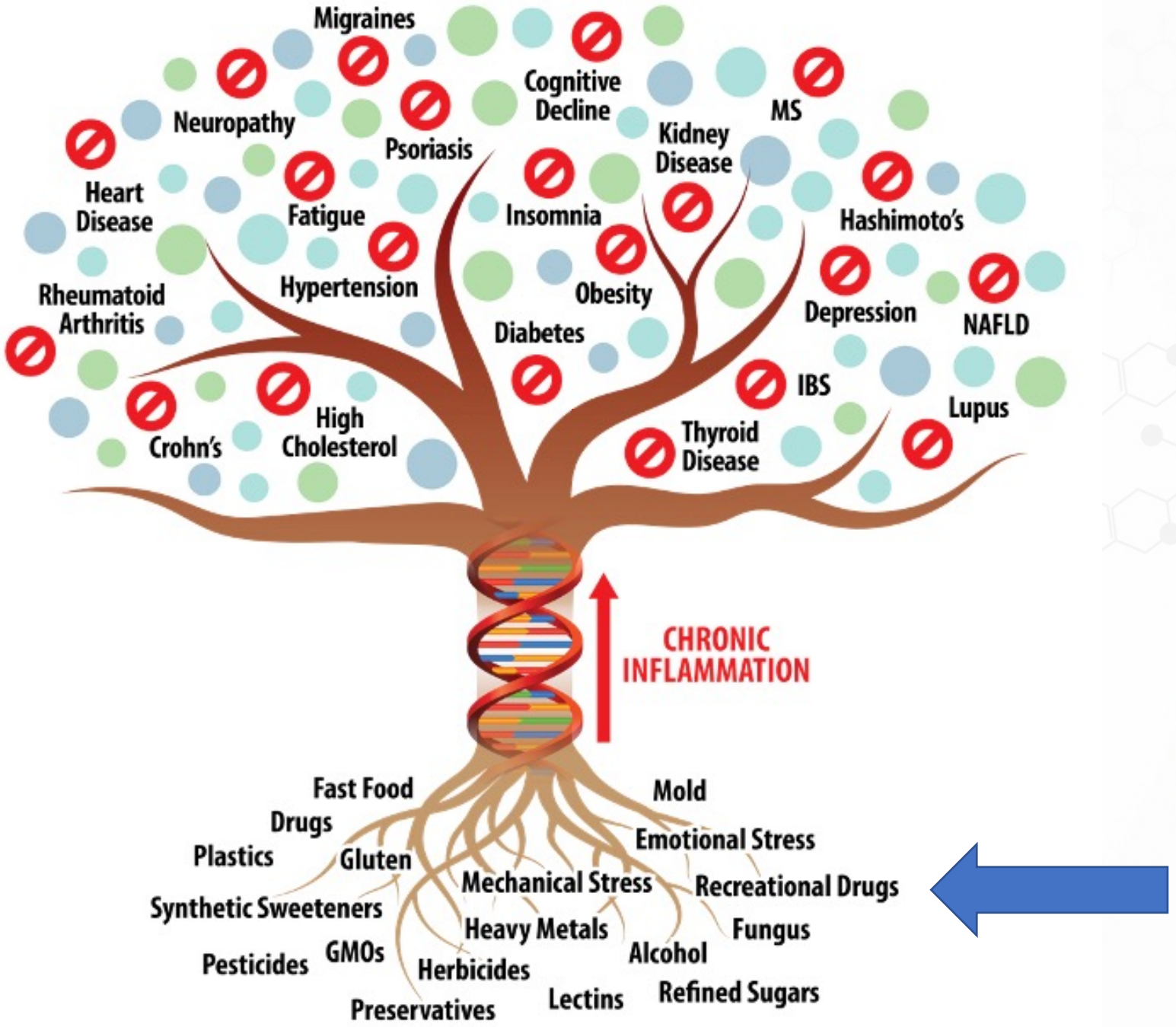
TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT / PREVIOUS RESULT	REFERENCE
4-Nonylphenol	6.08		0 0.42 2.06	≤2.06 ug/g

Moderate (75th-95th percentile)

Heavy Metals, Environmental Toxins

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT / PREVIOUS RESULT	REFERENCE
Cadmium*	0.32		0 0.29 0.8	≤0.8 ug/g
Platinum*	0.22		0 0.1 0.9	≤0.9 ug/g
Bisphenol A (BPA)*	4.89		0 2.12 5.09	≤5.09 ug/g
Butylparaben*	1.75		0 0.25 4.39	≤4.39 ug/g

* Indicates NHANES population data reference ranges.


Migraines
Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Hashimoto's
Hypertension
Obesity
Depression
NAFLD
Rheumatoid Arthritis
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
CHRONIC INFLAMMATION
Fast Food
Mold
Drugs
Emotional Stress
Plastics
Gluten
Mechanical Stress
Recreational Drugs
Synthetic Sweeteners
Heavy Metals
Fungus
Pesticides
GMOs
Alcohol
Herbicides
Refined Sugars
Lectins
Preservatives