72° CONGRESSO NAZIONALE FIMMG - METIS
MEDICINA DI FAMIGLIA: CAMBIARE PER MANTENERE I PROPRI VALORI

PERCORSI SIMPeSV PER UN AMBULATORIO DEGLI STILI DI VITA:

Alimentazione e stili di vita
nei disturbi funzionali gastrointestinali

Impatto della dieta sulle modificazioni del microbiota

Lorenzo M Donini

SIMPeSV
Società Italiana
di Medicida di Prevenzione
e degli Stili di Vita

3/8 Ottobre 2016
Complesso Chia Laguna
Domus de Maria (CA)

- **Ruolo dell’alimentazione**
    - ***nel favorire la genesi di IBD***
    - ***nelle alterazioni del microbiota***

- **Comportamento alimentare nei soggetti con IBD**

ELSEVIER

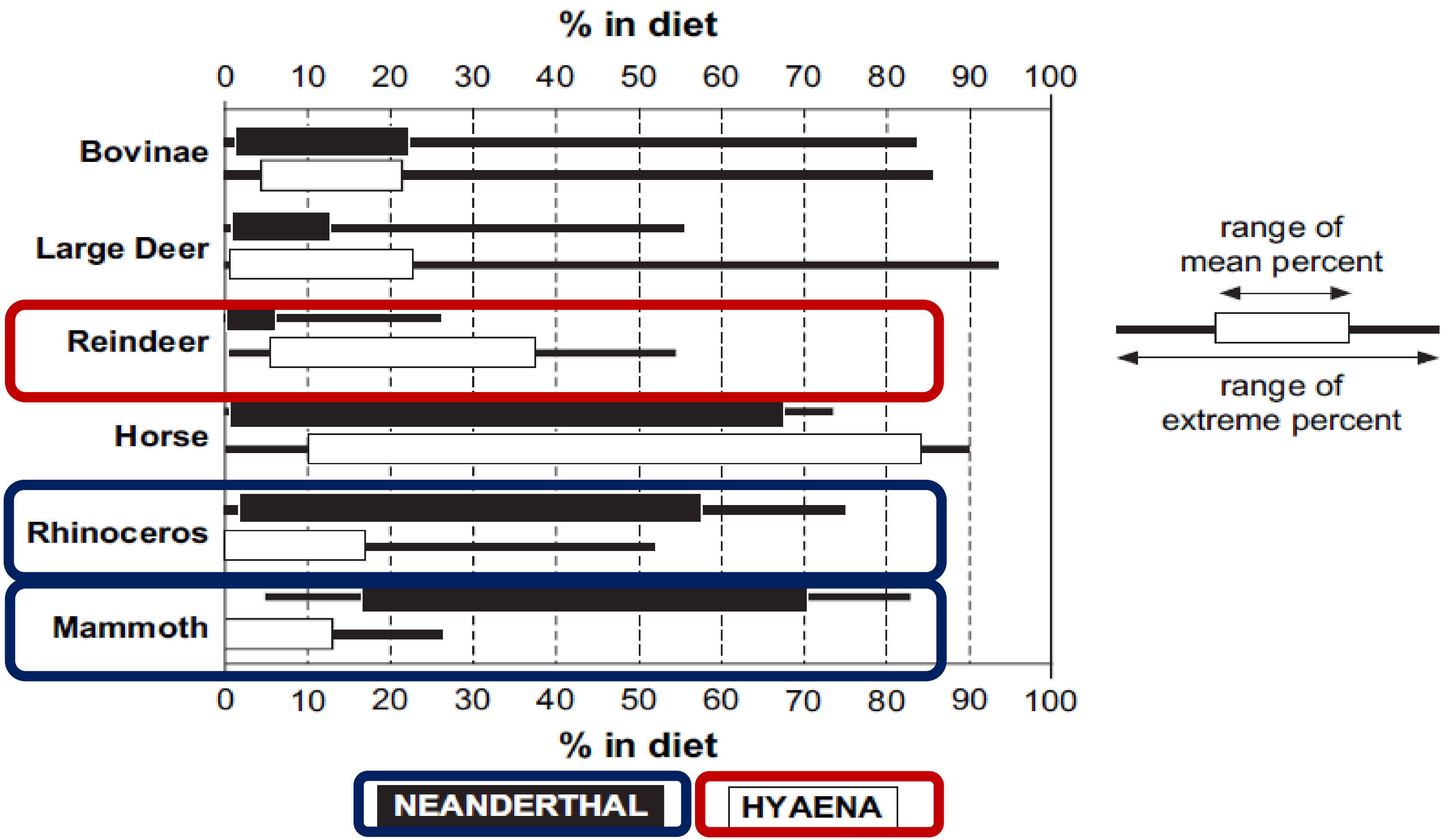
Available online at www.sciencedirect.com
SCIENCE DIRECT

Journal of Human Evolution 49 (2005) 71–87

JHE

Isotopic evidence for diet and subsistence pattern of the Saint-Césaire I Neanderthal: review and use of a multi-source mixing model

Hervé Bocherens [a,b,*], Dorothée G. Drucker [c], Daniel Billiou [d], Marylène Patou-Mathis [e], Bernard Vandermeersch [f]



Trois Néandertaliens reconstitués par Elizabeth Daynès. A gauche, Pierrette, réalisée à partir du moulage du crâne trouvé dans la grotte de Saint-Césaire en France

Hyenadon

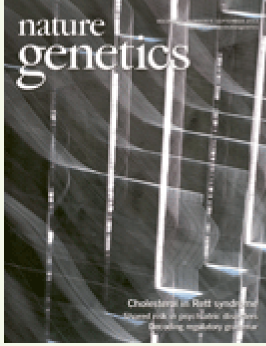
NATURE GENETICS | LETTER

日本語要約

Sequencing ancient calcified dental plaque shows changes in oral microbiota with dietary shifts of the Neolithic and Industrial revolutions

Christina J Adler, Keith Dobney, Laura S Weyrich, John Kaidonis, Alan W Walker, Wolfgang Haak, Corey J A Bradshaw, Grant Townsend, Arkadiusz Sołtysiak, Kurt W Alt, Julian Parkhill & Alan Cooper

Nature Genetics **45**, 450–455 (2013) doi:10.1038/ng.2536



- Calcified dental plaque (dental calculus) on ancient teeth preserves a detailed genetic record
- Aim of the study was to see how dietary changes affected the oral microbiome by analyzing the ancient microbial DNA in the calcified dental plaque from 34 early European skeletons.
- The skeletons included both sexes, ranging in age from <20- to >60-years old and dating from the Mesolithic to Medieval times.

The composition of oral microbiota remained unexpectedly constant between Neolithic and Medieval times, after which cariogenic bacteria became dominant, apparently during the Industrial Revolution.

1. **hunter-gatherers** (HGs) dental calculus had fewer bacterial related to caries or periodontal diseases
2. in **Neolithic farmers** (NFs) these bacteria are more frequent (⇐ increased use of soft CHO foods)
3. oral microbiome remains stable in the **medieval farmers’** (MFs)
4. **post-industrial modern humans** (MHs) carry dominantly cariogenic bacteria, (e.g. S. mutans) and show less diversity in the oral cavity.

Sajantila *Investigative Genetics* 2013, **4**:10
http://www.investigativegenetics.com/content/4/1/10

Investigative Genetics

EDITORIAL Open Access

Major historical dietary changes are reflected in the dental microbiome of ancient skeletons

Antti Sajantila

At least two major shifts have occurred in the nutritional history of humans:

- use of CHO-rich diets adopted around 10,000 years BP due to Neolithic farming
- influence of industrially processed flour and white sugar after the industrial revolution in the 1850s

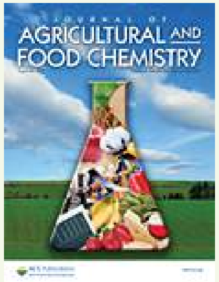
⇒ **evolution of commensal microbiota**

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Review

pubs.acs.org/JAFC

dx.doi.org/10.1021/jf4029046 | *J. Agric. Food Chem.* 2013, 61, 9559−9574



Emerging Aspects of Food and Nutrition on Gut Microbiota

Xuan He,[†,‡] Maria L. Marco,[‡] and Carolyn M. Slupsky*[,†,‡]

- Unlike the diets of other higher primates, which consist of mainly fiber-rich plants supplemented with insects and a small amount of animal flesh, humans consume **easily digested, energy-dense food**. This distinction has resulted in substantial **differences in the human GI tract** including a smaller gut volume, longer small intestine, smaller cecum and colon, and faster gut passage rate.
- The **discovery of fire and use of cooking techniques** are also contributed to the evolution of **human GI physiology** by softening food texture, elevating calorie density, and reducing toxins.
- Another major advancement in human evolution was **the shift from hunting and gathering to agriculture involving the domestication of animals and crops**. Domesticated plants provided more calories than non-domesticated plants, which consequently drove the dietary pattern to focus more on a **limited variety of foods, with a reduction in nutrient diversity**

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

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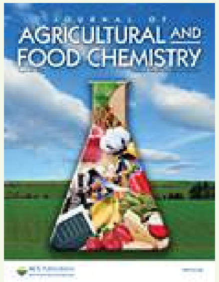
pubs.acs.org/JAFC

dx.doi.org/10.1021/jf4029046 | J. Agric. Food Chem. 2013, 61, 9559−9574



Emerging Aspects of Food and Nutrition on Gut Microbiota

Xuan He,[†,‡] Maria L. Marco,[‡] and Carolyn M. Slupsky*[,†,‡]

- The increasing use of **sanitization and antibiotics** in food processing may contribute to a profound impact on the gut microbiome.

- The activity and composition of the gut microbiome is also affected by an **individual's attitudes**, taste preference, and dietary habits that are likewise influenced by culture, the global food industry, and media.

- Furthermore, there is growing evidence that the human diet has undergone **profound simplification** since industrialization, which has occurred too recently on an evolutionary time scale for the human genome to adapt.

- This **maladaptation to the modern diet** has been hypothesized to be the underlying evolutionary origin of "civilization diseases," such as cardiovascular disease, in the 21st century.

Review

MOLECULAR METABOLISM

MOLECULAR METABOLISM 5 (2016) 737–742

The changing microbial landscape of Western society: Diet, dwellings and discordance

CrossMark

Josiane L. Broussard [1], Suzanne Devkota [2,*]

- **Gut microbiota of individuals in the United States** is far less diverse than the microbiota of native Amazonian and Malawian populations. Moreover the **composition of bacteria** is different as well
- Increased **bacterial diversity** in the gut is generally accepted as a marker of health.
- The microbial differences in richness and diversity emerge post-weaning upon adaptation to the native diet.
- One possible mechanistic underpinning for these potentially deleterious microbial changes may be **decreased consumption of microbially accessible carbohydrates** (MACs) in the form of fiber-rich foods.

Review

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The changing microbial landscape of Western society: Diet, dwellings and discordance

Josiane L. Broussard [1], Suzanne Devkota [2,*]

- In rodents, decreased consumption of MACs over successive generations could result in **complete loss of entire genera or species of microbiota**, highlighting that "unhealthy" microbiomes can be permanently inherited if diets continue to lose their fiber component.

- Moreover **re-introduction of MACs** into the diet may be unable to recover the lost species to a greater and greater degree with each subsequent generation, suggesting extinction from the gut microbiota.

Review

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Josiane L. Broussard[1], Suzanne Devkota[2,*]

- Among the long-term consequences of specific species extinction there are a **decrease in bacterially-produced short-chain fatty acids** (SCFA's) over time.
- To the microbiota, these are a necessary waste product to balance the redox equivalent product in the gut anaerobic environment, but to the **intestinal colonocytes**, SCFAs are the primary source of energy, comprising 60e70% of their energy supply.
- The gradual loss of SCFA's over generations could result in **serious defects in gut health.**
- The clinical importance of these SCFAs to intestinal health and homeostasis has been demonstrated in several studies in which **administration of SCFA's orally or via direct irrigation** to patients with ulcerative colitis, Crohn's disease, and antibiotic-resistant diarrhea has shown amelioration of symptoms

Review

MOLECULAR METABOLISM

MOLECULAR METABOLISM 5 (2016) 737–742

The changing microbial landscape of Western society: Diet, dwellings and discordance

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Josiane L. Broussard [1], Suzanne Devkota [2,*]

- While diet is accepted as one of the most potent driving forces shaping gut microbial communities other aspects of Westernization that contribute to disease need to be considered beyond changes in diet and **physical activity**.

- Our **physical environment** is another important determinant of microbial communities.
- As individuals, we each possess our own personal bacterial clouds that we carry with us throughout the day, and which can interact with, and be deposited in, the physical world.

Review

MOLECULAR METABOLISM

MOLECULAR METABOLISM 5 (2016) 737–742

The changing microbial landscape of Western society: Diet, dwellings and discordance

Josiane L. Broussard [1], Suzanne Devkota [2,*]

- During **circadian misalignment**, behaviors occur at inappropriate biological times. For example, during the circadian misalignment that typically accompanies jetlag and shift work, sleep is often attempted during the day, and wake/eating occurs at night.
- Circadian misalignment are associated with higher risks of diabetes, cardiovascular disease, and cancer; with alterations in energy balance that may predispose individuals to weight gain, with reduced insulin sensitivity and larger impairments in glucose tolerance.
- **Intestinal microbiota** exhibits diurnal oscillations, driven primarily by the food intake rhythms of the host organism, leading to rhythmic composition and functional profiles of intestinal bacteria: gut microbiota has differential circadian variations in the microbial structure, depending on dietary composition of the host
- Experimental circadian misalignment alters the gut microbiome in a way that promotes increased energy absorption and positive energy balance due to changes in gut microbial community and structure

Ruolo dell’alimentazione nel favorire la genesi di IBD anche attraverso cambiamenti del microbiota

Dietary management of IBD—insights and advice

Nat. Rev. Gastroenterol. Hepatol. **12**, 133–146 (2015);

nature REVIEWS GASTROENTEROLOGY & HEPATOLOGY

Emma P. Halmos and Peter R. Gibson

IDENTIFICATION OF CANDIDATE DIETARY FACTORS IN IBD PATHOGENESIS.

- alteration of **bacterial exposure** in childhood (the so-called cold-chain hypothesis)
- **impairment of the epithelial barrier** by multiple food components that have included emulsifiers, fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) in Crohn's disease, and foods that induce excessive nitric oxide and sulphide production in the lumen of the large bowel in ulcerative colitis
- **direct modulation of the control of mucosal inflammatory processes** by indigestible particles or exposure to various combination or individual lipids.

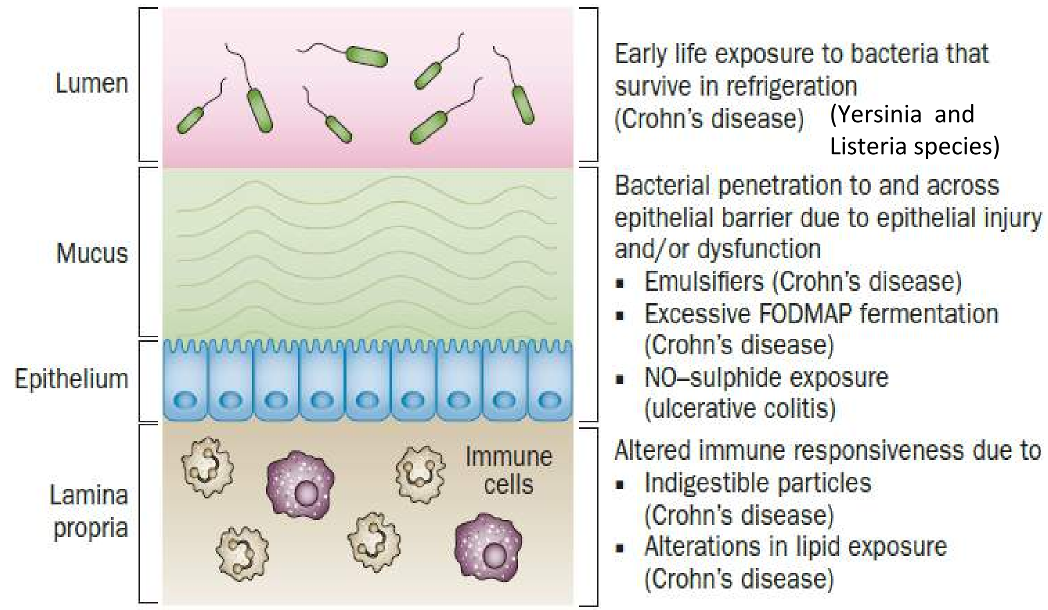

Figure 2 | Some of the dietary factors hypothesized to be involved in the pathogenesis of IBD. Ingestion of food might drive IBD via three broad mechanisms: by enabling exposure to specific microbiota in early life;[37] by enabling greater bacterial penetration of the epithelial barrier to induce inflammatory events;[38,39,127] and by directly altering immune responsiveness.[41,45] Abbreviations: FODMAP, fermentable oligosaccharide, disaccharide, monosaccharide and polypol; NO, nitric oxide.

Mol. Nutr. Food Res. 2016, 00, 1–13 DOI 10.1002/mnfr.201600129

REVIEW

Diet, gut microbes, and the pathogenesis of inflammatory bowel diseases

Kyle T. Dolan and Eugene B. Chang

Table 1. Prospective cohort studies of dietary influence on IBD risk

Diet factor	Sample features	Findings	Reference
A. European Prospective Investigation into Cancer and Nutrition (EPIC) (nested case-control studies)			
Dietary pattern	Cohort size = 366,351; UC: cases = 256, controls = 1022; CD: cases = 117, controls = 468	"Sugar and soft drinks" diet increased risk in UC cases diagnosed >2 years after diet survey (Highest versus lowest quintile: IRR 1.68, 95% CI 1.00-2.82, $p = 0.02$). Low vegetable intake enhanced risk associated with high sugar and soft drink intake. No pattern associated with CD. Mediterranean diet not associated with reduced risk for UC or CD.	Racine et al. 2016 [20]
Carbohydrates	Cohort size = 401,326; UC: cases = 244, controls = 976; CD: cases = 110, controls = 440	No associations between UC or CD risk and total carbohydrate, sugar, or starch intake	Chan et al. 2014 [21]
Fatty acids	Cohort size = 229,702; CD: cases = 73, controls = 292	DHA intake inversely associated with CD risk (trend across quintiles: OR 0.54, 95% CI 0.30-0.99, $p = 0.04$). No effect seen for intake of EPA, alpha-linolenic acid, linoleic acid, or oleic acid	Chan et al. 2014b [25]
Omega-3 PUFA	Cohort size = 25,639; UC: cases = 22, controls = 91	Association between DHA intake and reduced UC risk (trend across tertiles: OR 0.43, 95% CI 0.22-0.86, $p = 0.02$). Similar protective trends were observed for increasing intake of EPA ($p = 0.06$) and total omega-3 PUFA ($p = 0.10$)	John et al. 2010 [26]
Fatty acids	Cohort size = 203,193; UC: cases = 126, controls = 504	Increased linoleic intake associated with UC risk (trend across quartiles: OR 1.32, 95% CI 1.04-1.66, $p = 0.02$). DHA intake associated with decreased UC risk (trend: OR 0.59, 95% CI 0.37-0.94, $p = 0.03$). No association between EPA, alpha-linolenic acid, or oleic acid and UC risk.	Tjonneland et al. 2009 [27]
Various macronutrients and micronutrients	Cohort size = 260,686; UC: cases = 139, controls = 556	Trend suggestive of elevated risk from increased total PUFA intake (trend across quartiles: OR 1.19, 95% CI 0.99–1.43, $p = 0.07$). No other macronutrient or micronutrient showed association with altered risk of UC.	Hart et al. 2008 [24]

Mol. Nutr. Food Res. 2016, 00, 1–13 DOI 10.1002/mnfr.201600129

REVIEW

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B. Nurses' Health Study (cohort studies)			
Dietary fat	Cohort size = 170,805 women followed over 26 years; cases: UC = 338, CD = 269	Higher intake ratio of omega-3/omega-6 PUFA associated with reduced incidence of UC (trend across quintiles: HR 0.69, 95% CI 0.49–0.98, p = 0.03). Trend of inverse association between total omega-3 intake and UC risk (HR 0.72, 95% CI 0.51–1.02, p = 0.13). Trend of positive correlation between trans-unsaturated fat intake and UC risk (HR 1.34, 95% CI 0.94–1.46, p = 0.07). No associations between dietary fat intake and CD incidence observed.	Ananthakrishnan et al. 2014 [19]
Dietary fiber	Cohort size = 170,776 women followed over 26 years; cases: UC = 338, CD = 269	Higher intake of dietary fiber associated with lower incidence of CD (highest versus lowest quintile: HR 0.59, 95% CI 0.39–0.90). A strong negative correlation to CD risk was ascribed to fruit intake, and a weaker negative correlation to vegetable intake. No effects of dietary fiber on UC risk were observed.	Ananthakrishnan et al. 2013 [30]
C. Other			
Animal protein	E3N (France): cohort size = 67,581 women, mean follow-up time = 10.4 years; cases: UC = 44, CD = 30	Intake of total protein, but not total carbohydrate or fat, associated with higher risk of both UC (p = 0.06) and CD (p = 0.04). Higher intake of animal protein, particularly meat and fish, were positively associated with IBD risk.	Jantchou et al. 2010 [17]

Dig Dis Sci (2015) 60:290–298
DOI 10.1007/s10620-014-3350-9

REVIEW

Environmental Risk Factors for Inflammatory Bowel Diseases: A Review

Ashwin N. Ananthakrishnan

Vitamin D

- there is a geographic variation in IBD incidence even within a specific country and have suggested a greater incidence in areas associated with reduced exposure to UV light
- in the Nurses' Health Study cohort described above demonstrated a lower risk for both CD (HR 0.48, 95 % CI 0.30–0.77) and UC (HR 0.62, 95 % CI 0.42–0.90) in women residing in southern latitudes at age 30 compared to those residing in northern latitudes
- compared to women in the lowest quartile of predicted plasma vitD those in the highest quartile of predicted vitD had a **lower risk of CD** (HR 0.54, 95 % CI 0.30–0.99). Higher dietary vitD intake was inversely associated with **reduced risk of UC** ⇒ vitD may have a role in the pathogenesis of both diseases (greater strength of association for CD)
- lower plasma 25(OH)D was associated with an increased **risk of surgery** and IBD-related hospitalizations in both CD and UC (OR 0.56, 95 % CI 0.32–0.98)
- IBD patients with low plasma vitD may have increased **risk of cancers**, in particular colorectal cancer, and **clostridium difficile infection**
- in animal models **vitD administration** may reduce risk of relapses. Similar results seems to be present also in humans with a borderline statistically significant reduction in risk of relapse (13 vs. 29 %, p = 0.06) (1,200 IU vitD3 vs placebo for 12 months)

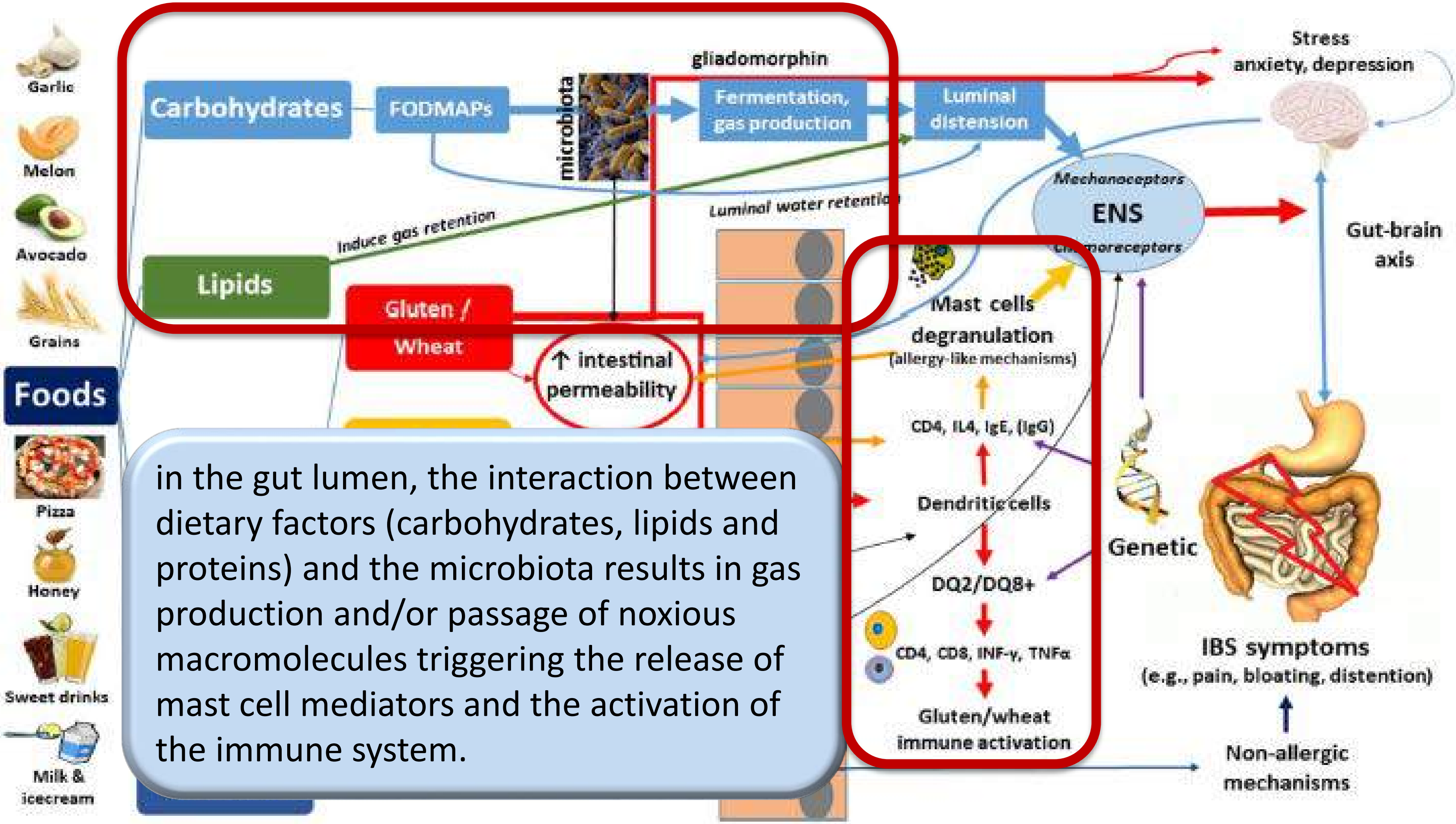
vitamin D deficiency may merely be a marker of severe disease and a confounder rather than a true biologic (immunological) mediator ??

SIMPeSV

Sensitivity to wheat, gluten and FODMAPs in IBS: facts or fiction?

Gut 2016;**65**:169–178. doi:10.1136/gutjnl-2015-309757

Roberto De Giorgio,[1] Umberto Volta,[1] Peter R Gibson[2]



in the gut lumen, the interaction between dietary factors (carbohydrates, lipids and proteins) and the microbiota results in gas production and/or passage of noxious macromolecules triggering the release of mast cell mediators and the activation of the immune system.

Sensitivity to wheat, gluten and FODMAPs in IBS: facts or fiction?

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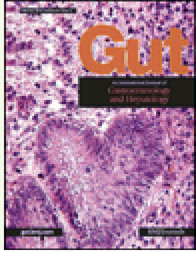

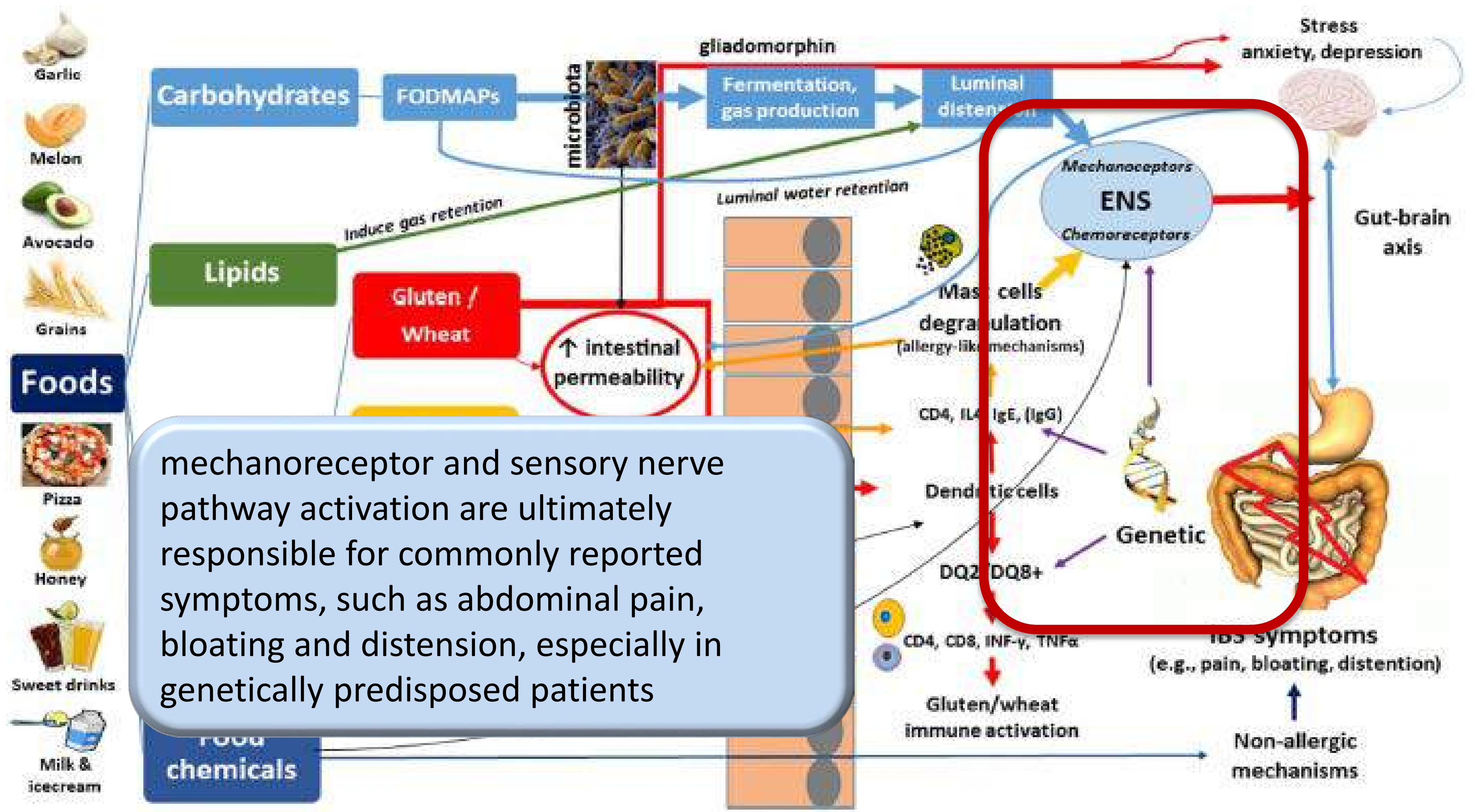

mechanoreceptor and sensory nerve pathway activation are ultimately responsible for commonly reported symptoms, such as abdominal pain, bloating and distension, especially in genetically predisposed patients

Sensitivity to wheat, gluten and FODMAPs in IBS: facts or fiction?

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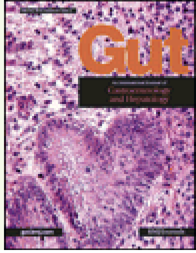

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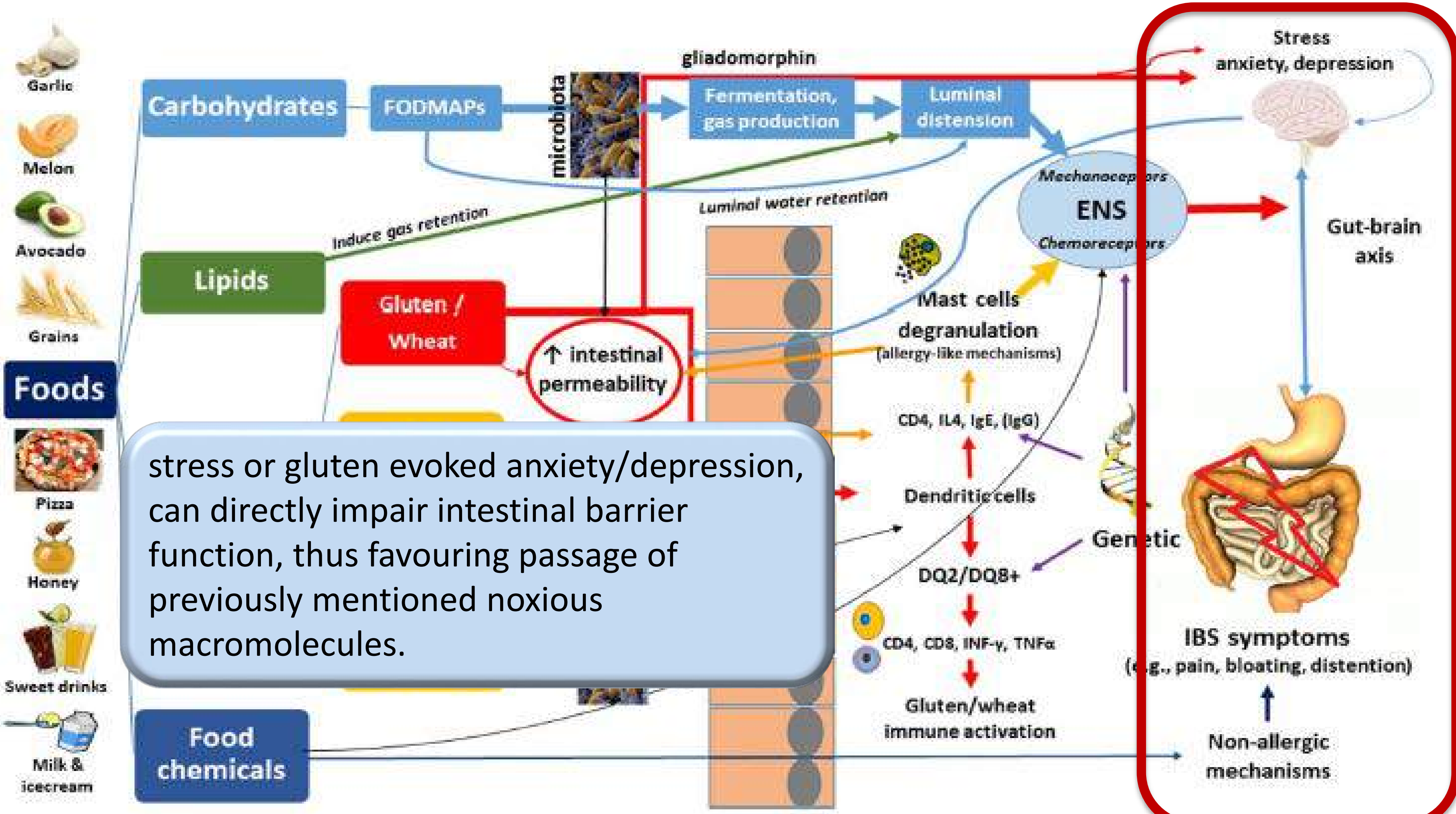

stress or gluten evoked anxiety/depression, can directly impair intestinal barrier function, thus favouring passage of previously mentioned noxious macromolecules.

Sensitivity to wheat, gluten and FODMAPs in IBS: facts or fiction?

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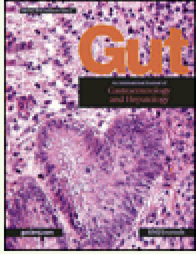


WHEAT SENSITIVITY

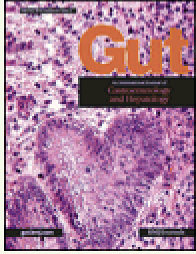
Wheat is considered one of the foods known to evoke IBS symptoms. However, which component(s) of wheat is/are actually responsible for these clinical effects still remain(s) an unsettled issue.

The two parts of wheat that are thought to have a mechanistic effect comprise **proteins** (primarily, but not exclusively, gluten) and **carbohydrates** (primarily indigestible short-chain components, FODMAPs).

Sensitivity to wheat, gluten and FODMAPs in IBS: facts or fiction?

Gut 2016;65:169–178. doi:10.1136/gutjnl-2015-309757

Roberto De Giorgio,[1] Umberto Volta,[1] Peter R Gibson[2]



The role of wheat proteins in IBS. Nomenclature evolution:

1. **non-coeliac gluten sensitivity (NCGS):** coeliac disease-like abnormalities, are triggered by gluten ingestion: IBS-like phenotype, along with an extra-intestinal phenotype (malaise, fatigue, headache, numbness, mental confusion, anxiety, sleep abnormalities, fibromyalgia-like symptoms and skin rash).
   Symptoms or other manifestations occur shortly after gluten consumption and disappear or recur in a few hours (or days) after gluten withdrawal or challenge.
   A fundamental prerequisite for suspecting NCGS is to rule out all coeliac disease, gluten ataxia, dermatitis herpetiformis and wheat allergy
2. **non-coeliac wheat sensitivity (NCWS) or non-coeliac wheat protein sensitivity (NCWPS)**: gluten is not the only one protein contained within wheat.
   amylase-trypsin inhibitors and wheat germ agglutinin are strong activators of innate immune responses (in monocytes, macrophages and dendritic cells) and epithelial-damaging effects

nutrients MDPI

Review

The Overlap between Irritable Bowel Syndrome and Non-Celiac Gluten Sensitivity: A Clinical Dilemma

Archita Makharia [1], Carlo Catassi [2] and Govind K. Makharia [1,*]

- Both IBS and NCGS are common in the general population and can **coexist** with each other independently without necessarily sharing a common pathophysiological basis.
- While the treatment of NCGS is exclusion of gluten from the diet, **some of the patients with IBS do improve with the gluten-free diet.**
- **Minimal inflammation in the gut** has been demonstrated in both IBS and NCGS. It is thus conceivable that ingestion of wheat containing ATIs (amylase-trypsin inhibitors), in the presence of intestinal inflammation enhances an innate immune response that plays a role in the generation of symptoms in patients with IBS, which then resolve when the patient takes up a gluten-free/wheat free diet.

Sensitivity to wheat, gluten and FODMAPs in IBS: facts or fiction?

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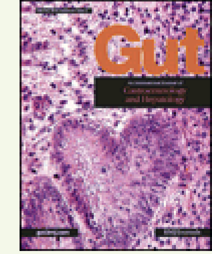


THE ROLE OF FODMAPS IN IBS

ingestion of certain short-chain carbohydrates (lactose, fructose, sorbitol, fructo-oligosaccharides and galacto-oligosaccharides) may induce IBS-like symptoms, and their restriction in the diet is associated with apparent improvement in symptoms in some patients with IBS.

These carbohydrates have several key features in common:

1. they are **small molecules**, containing only 1–10 sugars, and hence are possible osmotically active substances in the lumen of the intestine
2. they are **slowly absorbed** in the small intestine if monosaccharides are not absorbed at all if they contain more than one sugar due to lack of suitable hydrolases.

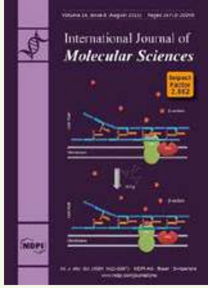
Hence, they are present in the small intestinal lumen for a prolonged time and do **increase the intestinal luminal water content**. Their malabsorption leads to their exposure to intestinal bacteria, which rapidly ferment them to release SCFA and gases (hydrogen, carbon dioxide and, in some people, methane).

Ruolo dell'alimentazione nelle alterazioni del microbiota

Impacts of Gut Bacteria on Human Health and Diseases

Yu-Jie Zhang [1], Sha Li [2], Ren-You Gan [3], Tong Zhou [1], Dong-Ping Xu [1] and Hua-Bin Li [1,]

Int. J. Mol. Sci. **2015**, *16*, 7493-7519; doi:10.3390/ijms16047493



Gut Bacteria and IBD

- disorders in bacterial recognition by macrophages are strongly related to pathogenesis of IBD
- IBD could results from an **abnormal immune response against the commensal microbiota in a genetically susceptible host**
- **bacterial products exacerbate acute inflammation** via TLR2- and TLR4-signaling and potentially trigger TLR-dependent accumulation of neutrophiles and T-cells.

Impacts of Gut Bacteria on Human Health and Diseases

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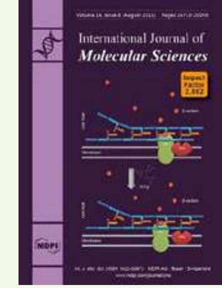

Gut Bacteria and IBD

- colonic bacterial communities from diseased mice are less complex, indicating **less diversity** of bacterial composition during acute inflammation
- **numbers of lactobacilli** are significantly lower during the active phase of UC, while lactobacilli communities differ in remission and acute phase
- percentages of **potentially protective bacterial species** (e.g., *Lachnospiraceae* and Ruminococcaceae) are lower in acute phase of UC
- families of bacteria of the **Clostridiales group** are more prominent in samples from the inflamed colon, indicating these bacteria might accumulate during colitis
- in Crohn’s disease (CD) the **fecal microflora** in patients with both inactive and active disease contained significantly more enterobacteria than in healthy subjects while 30% of the dominant bacteria did not belong to the usual dominant phylogenetic groups
- **four bacterial species** characterised dysbiosis in CD patients (decrease in *Dialister invisus*, *Faecalibacterium prausnitzii* and *Bifidobacterium adolescentis*, and an increase in *Ruminococcus gnavus*)

OPEN

Clinical & Translational Immunology (2016) 5, e82; doi:10.1038/cti.2016.29

www.nature.com/cti

REVIEW

Dietary metabolites and the gut microbiota: an alternative approach to control inflammatory and autoimmune diseases

James L Richards, Yu Anne Yap, Keiran H McLeod, Charles R Mackay and Eliana Mariño

- During fermentation of fibre, the **microbiota produces metabolites or short-chain fatty acids (SCFAs),** which can exert beneficial effects in health by maintaining the homeostasis of **metabolic function**, as well as having profound **anti-inflammatory effects** by modulating the development and priming of the immune system

- The **strong anti-inflammatory effects by SCFAs** may act via specific G protein-coupled receptors (GPCRs) and/or via inhibiting histone deacetylases (HDACs) ⇒ promoting **homeostasis of the gut epithelium**, a **tightly controlled border between gut microbes and host, better function of the immune cells** residing closely in the lymphoid compartments of the gut, or in peripheral tissues.

- **The amount of fibre and fat** in the diet shapes large-bowel microbial ecology that has been associated with many inflammatory diseases

- **Resistant starches** (obtained from vegetable, fruits, wheat, corn and nuts) mediate many of the effects ascribed to fibre, and their supply is critical for optimal gut In the mammalian gut, primarily the colon, resistant

- Starches are degraded and fermented by gut microbiota that subsequently produce metabolites, the most prominent being **SCFA**: acetate (two carbons), propionate (three carbons) and butyrate (four carbons)

OPEN

Clinical & Translational Immunology (2016) 5, e82; doi:10.1038/cti.2016.29

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REVIEW

Dietary metabolites and the gut microbiota: an alternative approach to control inflammatory and autoimmune diseases

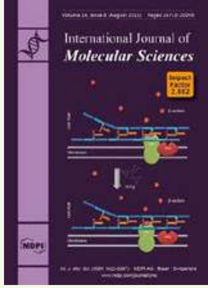
James L Richards, Yu Anne Yap, Keiran H McLeod, Charles R Mackay and Eliana Mariño

- A **'leaky gut'** in humans and mice, referring to increased gut permeability, disturbed microbial balance and impaired mucosal immunity, has been linked as the preceding step to the initiation of inflammatory diseases and autoimmunity.
- This is possibly because alteration in microbial ecology and decreased production of SCFAs altered mechanisms of **mucosal barrier function** ⇒ translocation of gut bacterial and contribution to autoimmune diseases (e.g. T1D, certain variants of inflammatory bowel disease)
- SCFAs produced from bacterial fermentation of fibre have **anti-inflammatory and immunomodulatory effects** through the impact of regulatory T (Treg) cells as an important factor in immune tolerance.
- The SCFA butyrate promotes inducible Treg (iTreg) number and function in the colon of mice.

Impacts of Gut Bacteria on Human Health and Diseases

Yu-Jie Zhang [1], Sha Li [2], Ren-You Gan [3], Tong Zhou [1], Dong-Ping Xu [1] and Hua-Bin Li [1,

Int. J. Mol. Sci. **2015**, *16*, 7493-7519; doi:10.3390/ijms16047493



Dietary Influence on Gut Bacteria

- **feeding ways of infants**
  - infants fed with breast milk have higher levels of *Bifidobacteria* spp., while infants fed with formula have higher levels of *Bacteroides* spp., *Clostridium coccoides* and *Lactobacillus* spp.
  - mice fed with Western-diet and low-fat-chow-diet display different structures of gut bacteria (increase of *Bacteroidetes and Proteobacteria*, decrease for *Firmicutes*
- **long-term diets**
  - enterotypes are strongly associated with protein and animal fat (*Bacteroides*) versus carbohydrates (*Prevotella*).
- **animal-based diet**
  - increases the abundance of bile-tolerant microorganisms (*Alistipes*, *Bilophila*, *Bacteroides*) and decreases the levels of *Firmicutes* that metabolize dietary plant polysaccharides
  - results in significantly lower levels of the products of CHO fermentation and a higher concentration of the products of AA fermentation compared with the plant-based diet

Impacts of Gut Bacteria on Human Health and Diseases

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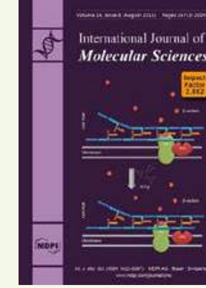


Dietary Influence on Gut Bacteria

- **bioactive molecules**
  - **phenolics** and their derivatives repress the growth of certain pathogenic bacteria such as *Clostridium perfringens*, *Clostridium difficile*, and *Bacteroides* spp., while they less severely affected commensal anaerobes, such as *Clostridium* spp., *Bifidobacterium* spp., and *Lactobacillus* sp. stimulates the production of SCFA by the gut bacteria
  - **fiber** fortified enteral formula have less negative symptoms related to bowel urgency, and decreases in total bacteria and *Bifidobacteria* were less severe compared with the fiber-free formula
  - **dietary iron** mostly from red meat and fortified cereals can also change the gut bacteria composition, increase the proliferation/virulence of gut bacteria and increase the permeability of the gut barrier.

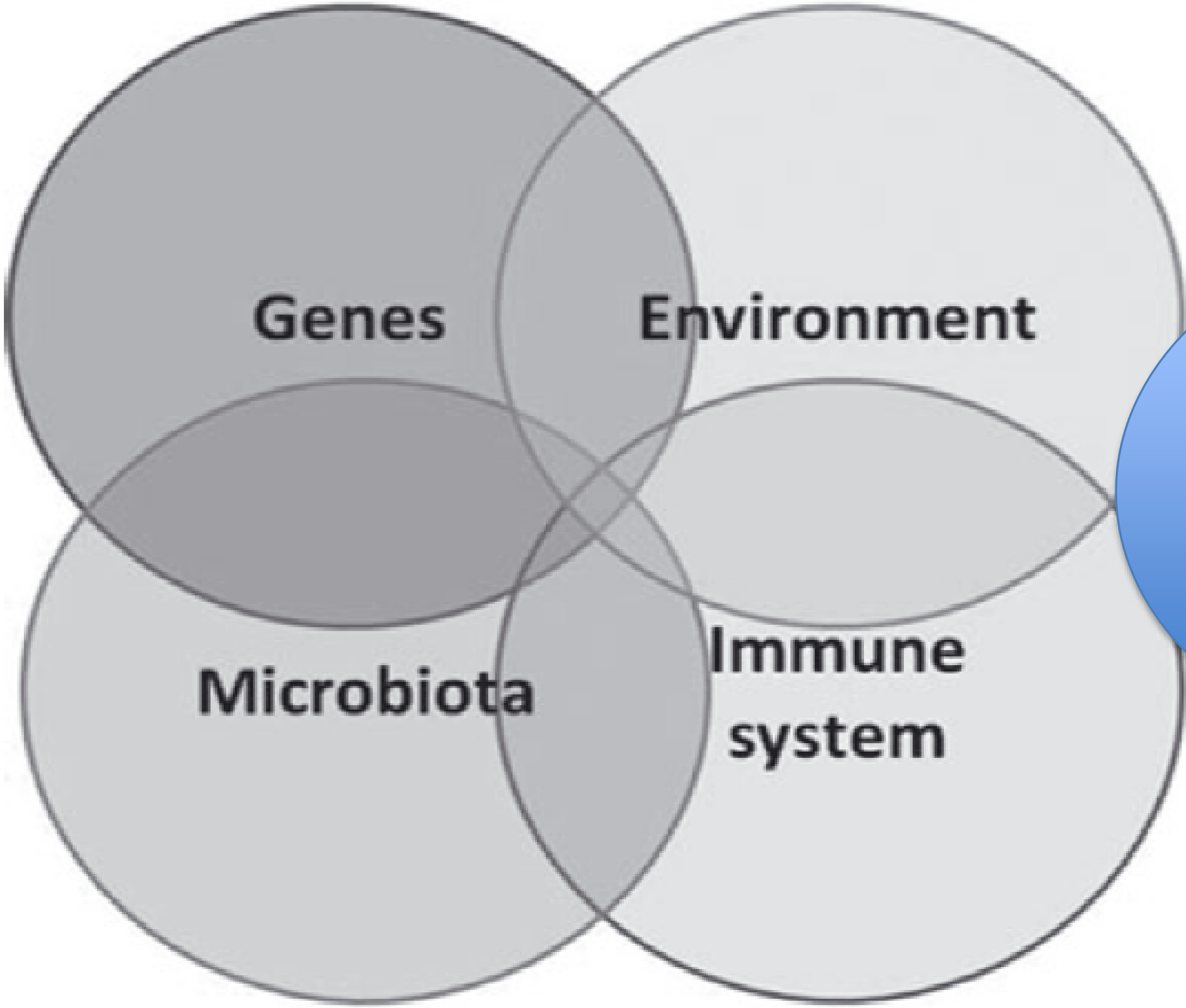
- **prebiotics** (CHO-like compounds, such as lactulose and resistant starch) can influence the composition of gut bacteria to benefit the host targeting bifidobacteria and lactobacilli, which are two kinds of probiotics

REVIEW

Role of nutrition and microbiota in susceptibility to inflammatory bowel diseases

Liljana Gentschew[1,2] *and Lynnette R. Ferguson*[1,2]

Mol. Nutr. Food Res. 2012, *56*, 524–535



Diet & physical activity

Comportamento alimentare nei soggetti con IBD

Dietary management of IBD—insights and advice

Nat. Rev. Gastroenterol. Hepatol. 12, 133–146 (2015);

Emma P. Halmos and Peter R. Gibson

- Diet is the primary behavioural factor manipulated by patients with IBD.
- Crucially, patients with IBD want to know what they should eat to improve their underlying condition.
- They generally find it a **frustrating trial-and-error process** of identifying foods that trigger symptoms.
- An examination of the top 30 hits on two popular search engines published in 2014 revealed a surfeit of advice for food choice in patients with IBD, but the **recommendations were often conflicting** (Hou JK et al: *Clin. Gastroenterol. Hepatol.* 2014).
- These findings are supported in a UK survey of patients with ulcerative colitis, in which **adherence to national dietary guidelines was poor and food avoidance strategies led to nutritional inadequacy** (Walton M, *Brit. J. Nutr.* 2014).

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What Are Adults With Inflammatory Bowel Disease (IBD) Eating? A Closer Look at the Dietary Habits of a Population-Based Canadian IBD Cohort

Kathy Vagianos, RD, MSc[1]; Ian Clara, PhD[2]; Rachel Carr, MSc[3];
Leslie A. Graff, CPsych, PhD[4]; John R. Walker, CPsych, PhD[5];
Laura E. Targownik, MD[6]; Lisa M. Lix, PhD, PStat[7]; Linda Rogala, BN[8];
Norine Miller, RN[8]; and Charles N. Bernstein, MD[9]

Table 2. Proportion of Participants With IBD Who Always Avoid Particular Food Items or Avoid When Disease Is Active.[a]

Food Item	Always Avoid, No. (%)	Normally Eat but Avoid When Disease Is Active, No. (%)
Alcohol	104 (31)	142 (42)
Popcorn	100 (30)	129 (38)
Legumes (beans, chickpeas, lentils)	103 (30)	96 (28)
Nuts and seeds (peanuts, almonds, walnuts, sunflower seeds, pumpkinseeds)	92 (27)	119 (35)
Deep-fried higher fat (food purchased at fast-food restaurants, fried potatoes, or burgers)	85 (25)	143 (42)
Processed deli meat (bologna, corned beef, or salami)	85 (25)	65 (19)
Tea or coffee	43 (13)	86 (25)
Milk/milk products (milk, cheese, yogurt, ice cream)	42 (12)	97 (29)
Salad or raw vegetables, any type	35 (10)	156 (46)
Tomato products (tomato sauce, tomato juice, or ketchup)	30 (9)	69 (20)
Red meat (ground beef, steak, or pork)	26 (8)	91 (27)
Raw fruit	22 (6.5)	100 (29)

[a]n = 319 participants with inflammatory bowel disease (IBD) participants; responses collected between 2006 and 2007.

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Table 3. Proportion of Participants With IBD Reporting Particular Reasons for Avoiding Food Item.[a]

Food Avoided (No. of Responses)	GI Upset (24 h), %	GI Upset (Days to Weeks), %	Heard "Should Avoid," %	Professional Advice, %	Do Not Like, %	Other, %
Alcohol (n = 96)	14	8	1	3	70	4
Popcorn (n = 93)	24	14	3	10	45	4
Legumes (n = 97)	16	7	4	0	69	3
Nuts and seeds (n = 88)	38	10	2	3	32	15
Deep-fried/higher fat food (n = 78)	40	8	1	9	32	10
Processed deli meat (n = 73)	15	5	1	3	67	8
Tea or coffee (n = 36)	8	3	3	3	81	3
Milk/milk products (n = 41)	51	15	0	15	12	7
Salad and raw vegetables (n = 35)	71	17	0	6	6	0
Tomato products (n = 29)	55	10	3	3	24	3
Red meat (n = 25)	44	4	4	4	36	8
Raw fruit (n = 20)	40	15	5	5	25	10

[a] n = 319 participants with inflammatory bowel disease (IBD) participants; responses collected between 2006 and 2007. Response options for food avoidance: (1) eating this food causes me to have gastrointestinal (GI) upset with symptoms that last up to 24 hours, (2) eating this food causes me to have GI upset with symptoms that last days to weeks, (3) I have read/heard that people with IBD should avoid this food, (4) a health professional has advised me to avoid this food, (5) I do not like this food, and (6) other.

Original Communication

What Are Adults With Inflammatory Bowel Disease (IBD) Eating? A Closer Look at the Dietary Habits of a Population-Based Canadian IBD Cohort

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Table 4. Mean Number of Weekly Portions of Sugar-Laden Food and Drink Among Participants With IBD Comparing Those With Inactive and Active Disease and Comparing IBD Subtypes.[a]

Food (Portion Size)	Active IBD	Inactive IBD	CD	UC
Sugar (tsp)	10.1	11.2	11.7	9.7
Candy (1 candy)	4.5	5.9	5.7	4.7
Chocolate (bar = 70 g)	1.5	1.3	1.2	1.6
Pastries (1 piece)	3.3	3.1	3.3	3.1
Jam or jelly (1 tsp)	2.8	2.7	2.5	3
Regular soft drinks (can = 355 mL)	3.4	3.1	3.8	2.8
Diet soft drinks (can = 355 mL)	4.4	4.0	4.4	4.2
Sports drinks (bottle = 591 mL)	2.3[b]	1.0	2.03	1.4
Fruit juice (250 mL)	6.3	6.6	7.1	5.9
Sweetened drinks (1 cup)	5.1[b]	2.6	4.0	3.5

[a] n = 319 participants with inflammatory bowel disease (IBD) participants; responses collected between 2006 and 2007.
[b] $P = .05$ was for mean comparisons between active and inactive disease and between ulcerative colitis (UC) and Crohn's disease (CD).

- A survey of Canadian adults with IBD showed that **food avoidance was far more common than in the general population**, …
- … but **sugar consumption from sweetened beverages was far greater** in those with active IBD, potentially giving rise to undernutrition or overnutrition.

Neurogastroenterology & Motility
NGM
Neurogastroenterol Motil (2016) doi: 10.1111/nmo.12894

Adolescents with irritable bowel syndrome report increased eating-associated symptoms, changes in dietary composition, and altered eating behaviors: a pilot comparison study to healthy adolescents

B. REED-KNIGHT,* M. SQUIRES,† D. K. CHITKARA‡ & M. A. L. VAN TILBURG†

- A total of 99 adolescents between 15 and 21 years-of-age participated (n = 48 IBS; n = 51 Healthy Controls-HC). All subjects completed three 24-h dietary recalls and questionnaires on Eating Associated Symptoms (EAS) and disordered eating.

Key Results

- IBS patients were more likely to report **EASs** than HC (91.7% vs 28%, $p < 0.001$).
- Eating-associated symptoms were controlled by **avoiding the offending food (97.7%), not eating any food even when hungry (43.2%), or vomiting after eating (13.6%).**
- Compared to HC, IBS patients reported **reduced daily intake** of overall calories (1828 vs 2139; $p < 0.05$), fat (65.4 g vs 81.4 g, $p < 0.05$), and lactose (8.2 g vs 12.8 g, $p < 0.01$).
- No differences were found between IBS and HC in screening for **disordered eating patterns** or BMI, though IBS patients endorsed using potentially unhealthy eating behaviors in an attempt to control symptoms

SIMPeSV

Dietary management of IBD—insights and advice

Nat. Rev. Gastroenterol. Hepatol. **12**, 133–146 (2015);

Emma P. Halmos and Peter R. Gibson

nature REVIEWS GASTROENTEROLOGY & HEPATOLOGY

- **Dietary history** (retrospective questioning of usual dietary intake; by 24 h recall; or by a 3–7 day documented food record)

  ⇒ detection of **normal dietary variation**, for example, on weekends compared with weekdays, meal pattern and portions, food variety, snacking between meals

  ⇒ an **estimated energy, macronutrient and micronutrient intake** should be ascertained

  - 67% of patients **under-report** their intake compared with both weighed food record and energy intake calculated to basal metabolic rate. Moreover, patients with a BMI >30 kg/m^2 seem to under-report to a greater degree than those of normal weight

NUTRITION ISSUES IN GASTROENTEROLOGY, SERIES #5

Series Editor: Carol Rees Parrish, M.S., R.D., CNSD

PRACTICAL GASTROENTEROLOGY • MAY 2003

Nutritional Considerations in Inflammatory Bowel Disease

Factors Altering Nutritional Status in Patients with IBD

- Decreased nutrient intake
  - Anorexia
  - Fear of eating
- Nausea, vomiting, abdominal pain, diarrhea
- Restrictive diets
- Side effects of medications
- Appetite suppression, taste changes
- Oral aphthous ulcerations
- Protein losses from inflamed, ulcerated mucosal
- Increased needs for healing
- Surgical resections
- Increased vitamin and mineral needs
- Bacterial overgrowth
- Malabsorption
- Blood loss

Implications of IBD on Nutrition

- Reduced absorption may lead to nutritional deficiencies

Iron
- Decreased absorption
- Bleeding

Vitamin B_{12}
- Ileal resection

Vitamin D
- Intestinal surgery
- Common deficiency in CD

Zinc
- Chronic diarrhea
- Fistula

Dietary management of IBD—insights and advice

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Indications for referral to dietitian	Grounds for increased risk of overnutrition	Grounds for increased risk of undernutrition
Skipping breakfast, lunch or dinner	Overeating at other meals of the day	Not able to meet energy, macronutrient and/or micronutrient intake
Continual grazing	Low volumes of food are not stimulating satiety and enables overeating	Small volumes are inadequate over the day
Inappropriate eating times (e.g. overnight)	Overeating from additional meals	Avoiding or eating less at traditional meal times
Extreme dietary restriction due to philosophy, religion or cultural beliefs	Food restriction resulting in compensation of other foods of higher energy	Food restriction resulting in undereating
Similar diet everyday	Diet providing more nutrients than required	Diet providing less nutrients than required and limited variety
Poor knowledge of intake	Overnutrition from food choice	Undernutrition from food choice
Fussy eater	Including only foods of high energy	Including insufficient energy intake and limited variety
Excessive attention to food and/or disordered eating	Episodes of binging leading to overnutrition	Intentional and inappropriate food restriction leading to undernutrition

*Indications might arise from taking a dietary history, and possible attributing factors to overnutrition and undernutrition are listed.

Dietary management of IBD—insights and advice

Nat. Rev. Gastroenterol. Hepatol. **12**, 133–146 (2015);

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- Dietary history

- **Nutritional status evaluation**:
  - anthropometry (minimum: BMI)
  - protein status (minimum: visual assessment of skeletal muscle mass)
  - energy status (minimum: assessment of subcutaneous fat stores), laboratory assessment (negative acute-phase proteins albumin, prealbumin and transferrin)

  - Undernutrition is common in active IBD due to any combination of anorexia or poor dietary intake associated with being unwell, increased nutritional requirements resulting from inflammation and impairment of nutrient absorption related to small bowel inflammatory disease

CANT-Z. 515 idrovolante quadrimotore a galleggianti (motori Piaggio P. XII R.C. 35, 1.500 CV. al decollo e 1.350 in quota); primo volo 15.10.1940