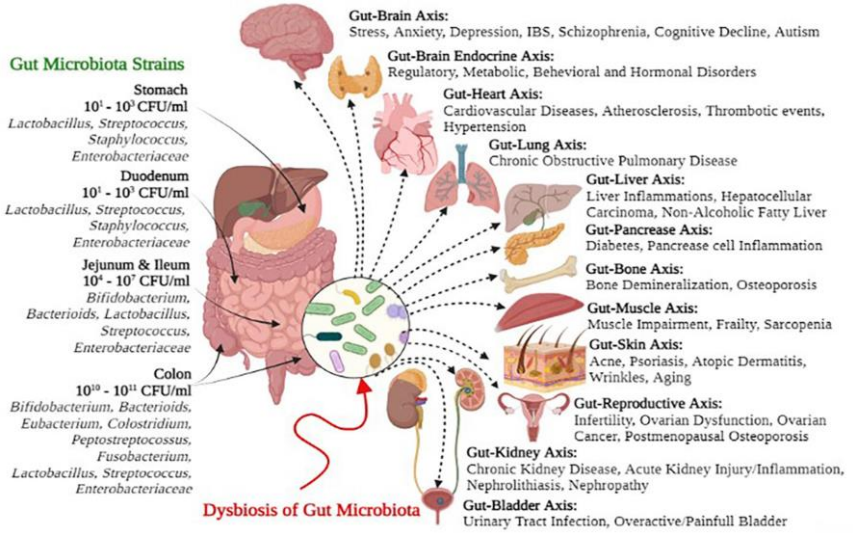
PROGRESSI E NUOVE FRONTIERE IN GASTROENTEROLOGIA ED ENDOSCOPIA DIGESTIVA

Belluno, 15-16 giugno 2023

MICROBIOTA E DISBIOSI

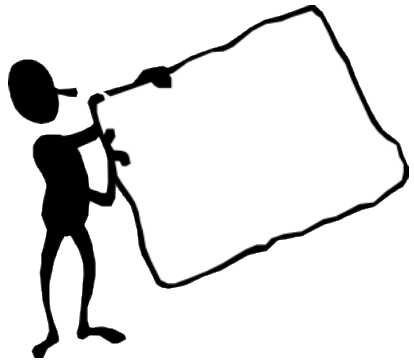


Cesare EFRATI

Responsabile UOS di malattie infiammatorie croniche intestinali

Ospedale Israelitico

- According to current estimates the human body harbors around **3.8×10^{13} microorganisms,** which is of the same order as the number of human cells
- Most of these microorganisms are bacteria, which outnumber eukaryotes (e.g. fungi) and archaea by 2–3 order of magnitude, and reside primarily in the gastrointestinal (GI) tract.
- They form a complex and diverse community, termed as bacterial gut microbiota (hereinafter simply referred to as gut microbiota), which is composed of more than 1000 different bacterial species, with more than 90% of the them belonging to two major phyla, the Firmicutes and Bacteroidetes.
- Less abundant, but still dominant gut phyla are Actinobacteria, Proteobacteria and Verrucomicrobia



Bacterial concentrations in the stomach and upper small intestine are considerably lower (~10^3 –10^4 organisms per ml of luminal contents) than in the ileum, and especially colon (~10^8 and 10^{11} bacteria/ml, respectively) (Sender et al., 2016).

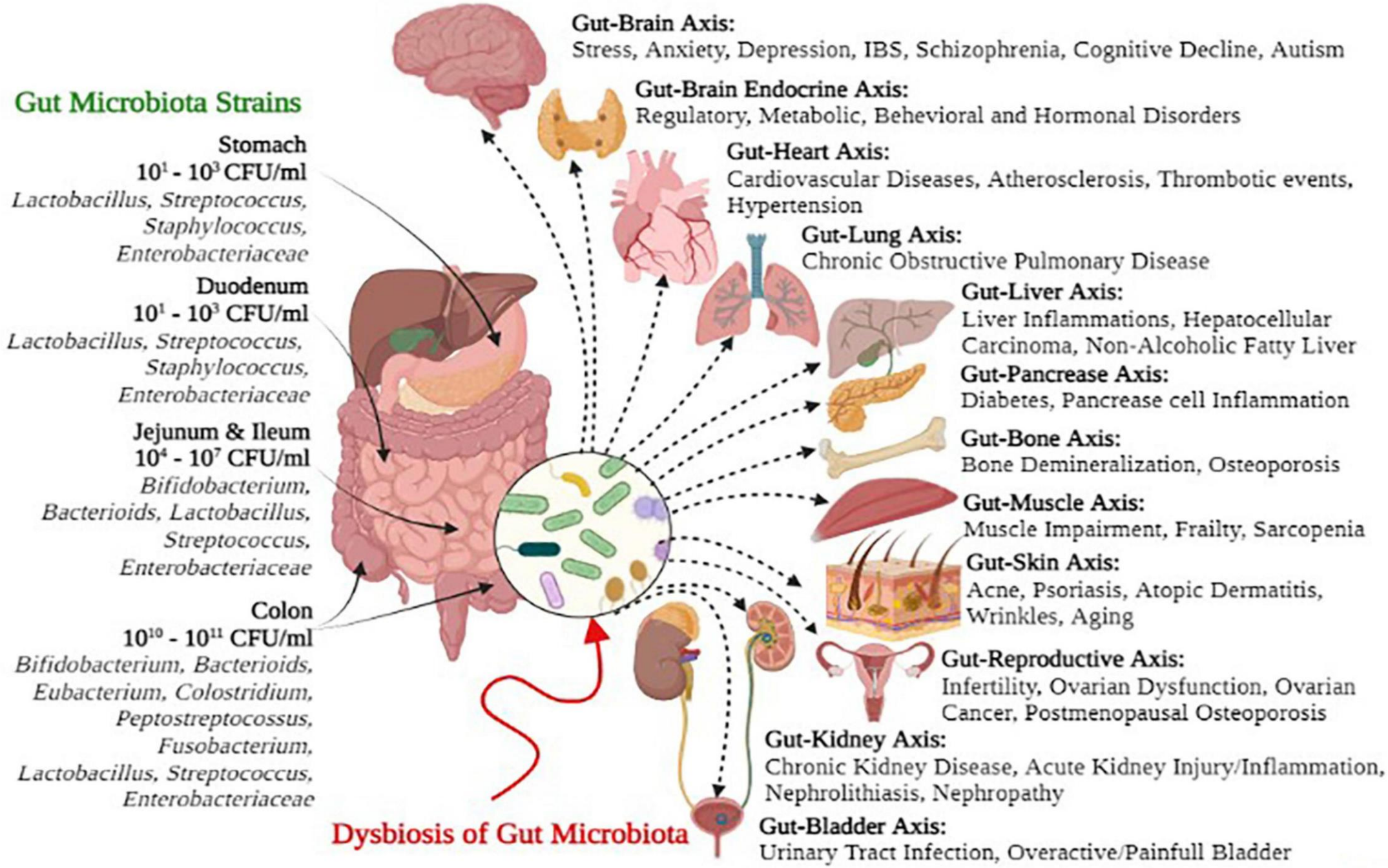
Not only the bacterial density, but also the relative abundance of distinct bacteria vary between the different segments of GI tract, due to differences in biochemical and physiological factors shaping its composition, such as **pH, oxygen, motility or bile acid**

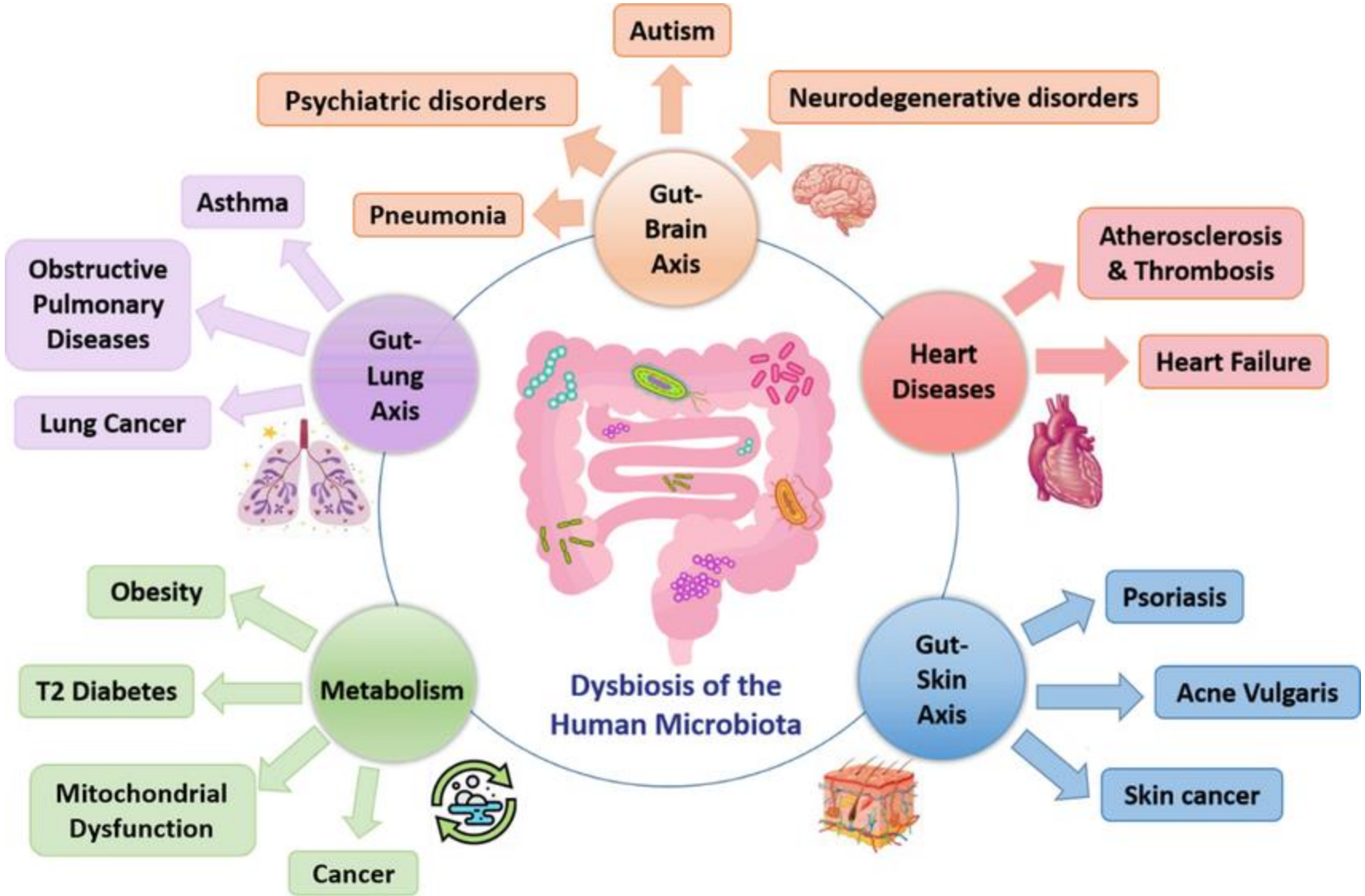
Over the past decades, it has been increasingly recognized that **gut microbiota has a crucial role in the regulation of host physiology.**

It is involved, among others, in glucose and **energy homeostasis**, in the education of the **immune system** and modulation of **GI sensory and motor functions**.

Not surprisingly, alterations in gut microbiota (termed as dysbiosis) may contribute to the development of numerous diseases, including **irritable bowel syndrome, endocrine, cardiovascular, autoimmune and even neuropsychiatric disorders**

Manipulation of gut microbiota with dietary interventions or fecal microbiota transplantation (FMT), therefore, may provide an attractive new way to improve health and prevent disease


Gut Microbiota Strains
Stomach
10^1 - 10^3 CFU/ml
Lactobacillus, Streptococcus, Staphylococcus, Enterobacteriaceae
Duodenum
10^1 - 10^3 CFU/ml
Lactobacillus, Streptococcus, Staphylococcus, Enterobacteriaceae
Jejunum & Ileum
10^4 - 10^7 CFU/ml
Bifidobacterium, Bacterioids, Lactobacillus, Streptococcus, Enterobacteriaceae
Colon
10^{10} - 10^{11} CFU/ml
Bifidobacterium, Bacterioids, Eubacterium, Colostridium, Peptostreptococcus, Fusobacterium, Lactobacillus, Streptococcus, Enterobacteriaceae
Dysbiosis of Gut Microbiota
Gut-Brain Axis:
Stress, Anxiety, Depression, IBS, Schizophrenia, Cognitive Decline, Autism
Gut-Brain Endocrine Axis:
Regulatory, Metabolic, Behevioral and Hormonal Disorders
Gut-Heart Axis:
Cardiovascular Diseases, Atherosclerosis, Thrombotic events, Hypertension
Gut-Lung Axis:
Chronic Obstructive Pulmonary Disease
Gut-Liver Axis:
Liver Inflammations, Hepatocellular Carcinoma, Non-Alcoholic Fatty Liver
Gut-Pancrease Axis:
Diabetes, Pancrease cell Inflammation
Gut-Bone Axis:
Bone Demineralization, Osteoporosis
Gut-Muscle Axis:
Muscle Impairment, Frailty, Sarcopenia
Gut-Skin Axis:
Acne, Psoriasis, Atopic Dermatitis, Wrinkles, Aging
Gut-Reproductive Axis:
Infertility, Ovarian Dysfunction, Ovarian Cancer, Postmenopausal Osteoporosis
Gut-Kidney Axis:
Chronic Kidney Disease, Acute Kidney Injury/Inflammation, Nephrolithiasis, Nephropathy
Gut-Bladder Axis:
Urinary Tract Infection, Overactive/Painfull Bladder


Autism
Psychiatric disorders
Neurodegenerative disorders
Gut-Brain Axis
Pneumonia
Asthma
Obstructive Pulmonary Diseases
Lung Cancer
Gut-Lung Axis
Atherosclerosis & Thrombosis
Heart Failure
Heart Diseases
Dysbiosis of the Human Microbiota
Obesity
T2 Diabetes
Metabolism
Mitochondrial Dysfunction
Cancer
Psoriasis
Acne Vulgaris
Skin cancer
Gut-Skin Axis

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microbiota and disbiosis

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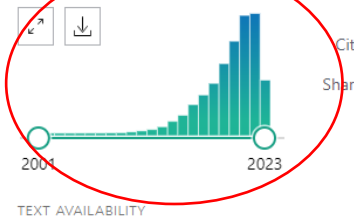
RESULTS BY YEAR



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ARTICLE ATTRIBUTE

- Associated data

ARTICLE TYPE

- Books and Documents
- Clinical Trial
- Meta-Analysis

1 Cite Share

Human gut **microbiota**/microbiome in health and diseases: a review.

Gomaa EZ.

Antonie Van Leeuwenhoek. 2020 Dec;113(12):2019-2040. doi: 10.1007/s10482-020-01474-7. Epub 2020 Nov 2.

PMID: 33136284 Review.

Gut **microbiota** is highly diverse and harboring trillions of microorganisms in human digestive system. ...In addition, many therapeutic strategies of gut **microbiota** aimed at modulating and restoring of the intestinal ecosystem balance have been surveyed....

2 Cite Share

Microbiota in health and diseases.

Hou K, Wu ZX, Chen XY, Wang JQ, Zhang D, Xiao C, Zhu D, Koya JB, Wei L, Li J, Chen ZS.

Signal Transduct Target Ther. 2022 Apr 23;7(1):135. doi: 10.1038/s41392-022-00974-4.

PMID: 35461318 Free PMC article. Review.

Depending on the localized regions, **microbiota** can be classified into gut, oral, respiratory, and skin **microbiota**. ...Then, we highlight the pathogenesis of **microbiota dysbiosis** in disease development and progression, primarily associated with dysregul ...

3 Cite Share

The human gut **microbiota**: Metabolism and perspective in obesity.

Gomes AC, Hoffmann C, Mota JF.

Gut Microbes. 2018 Jul 4;9(4):308-325. doi: 10.1080/19490976.2018.1465157. Epub 2018 May 24.

PMID: 29667480 Free PMC article. Review.

The gut **microbiota** has been recognized as an important factor in the development of metabolic

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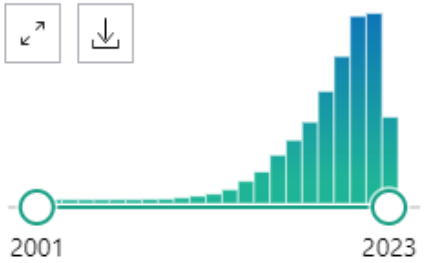
RESULTS BY YEAR



Review > EBioMedicine. 2023 Apr;90:104527. doi: 10.1016/j.ebiom.2023.104527.
Epub 2023 Mar 22.

Gut microbiota and its metabolites in depression: from pathogenesis to treatment

Lanxiang Liu [1], Haiyang Wang [2], Xueyi Chen [3], Yangdong Zhang [4], Hanping Zhang [4], Peng Xie [5]

Affiliations + expand

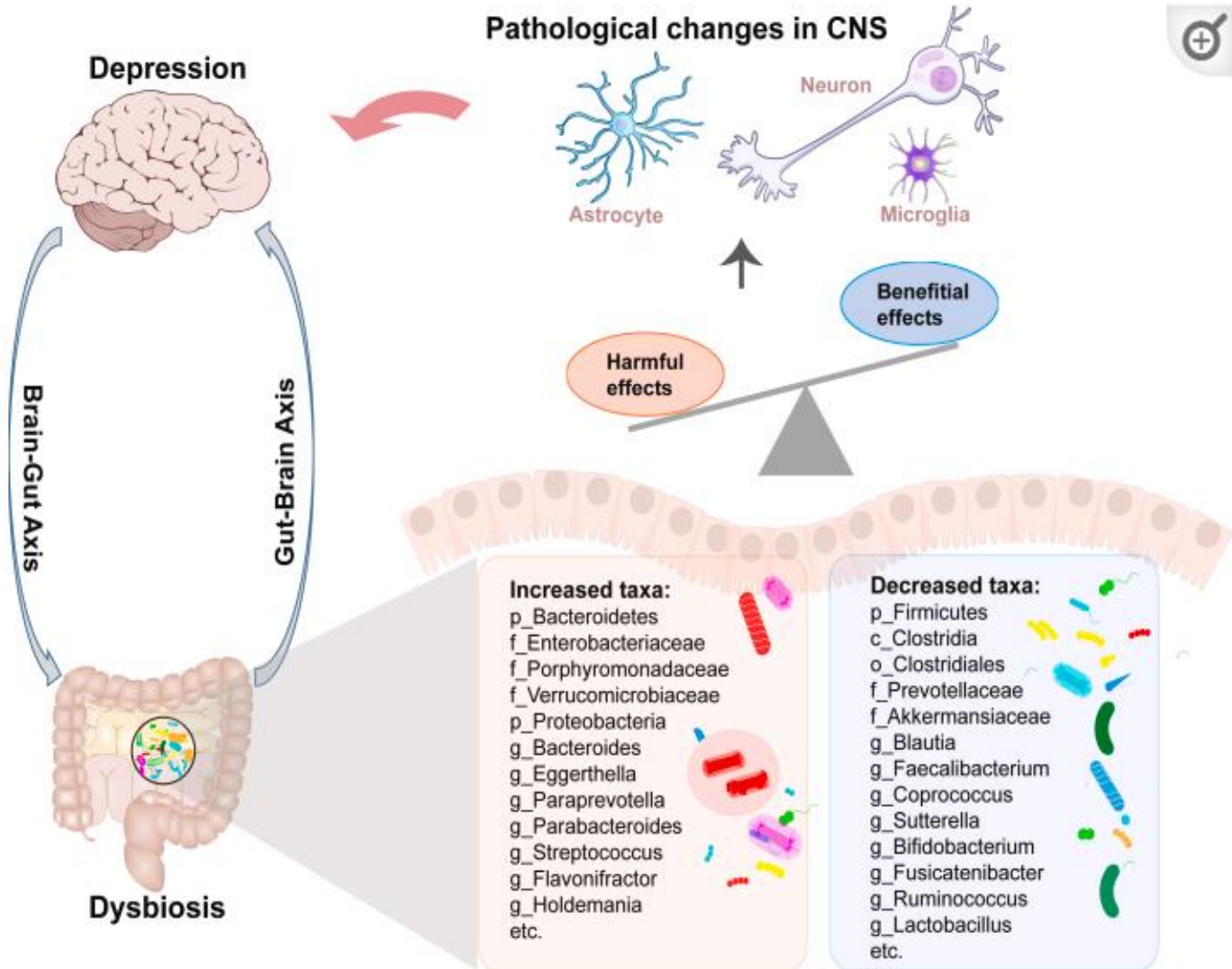
PMID: 36963238 PMCID: PMC10051028 DOI: 10.1016/j.ebiom.2023.104527

Free PMC article

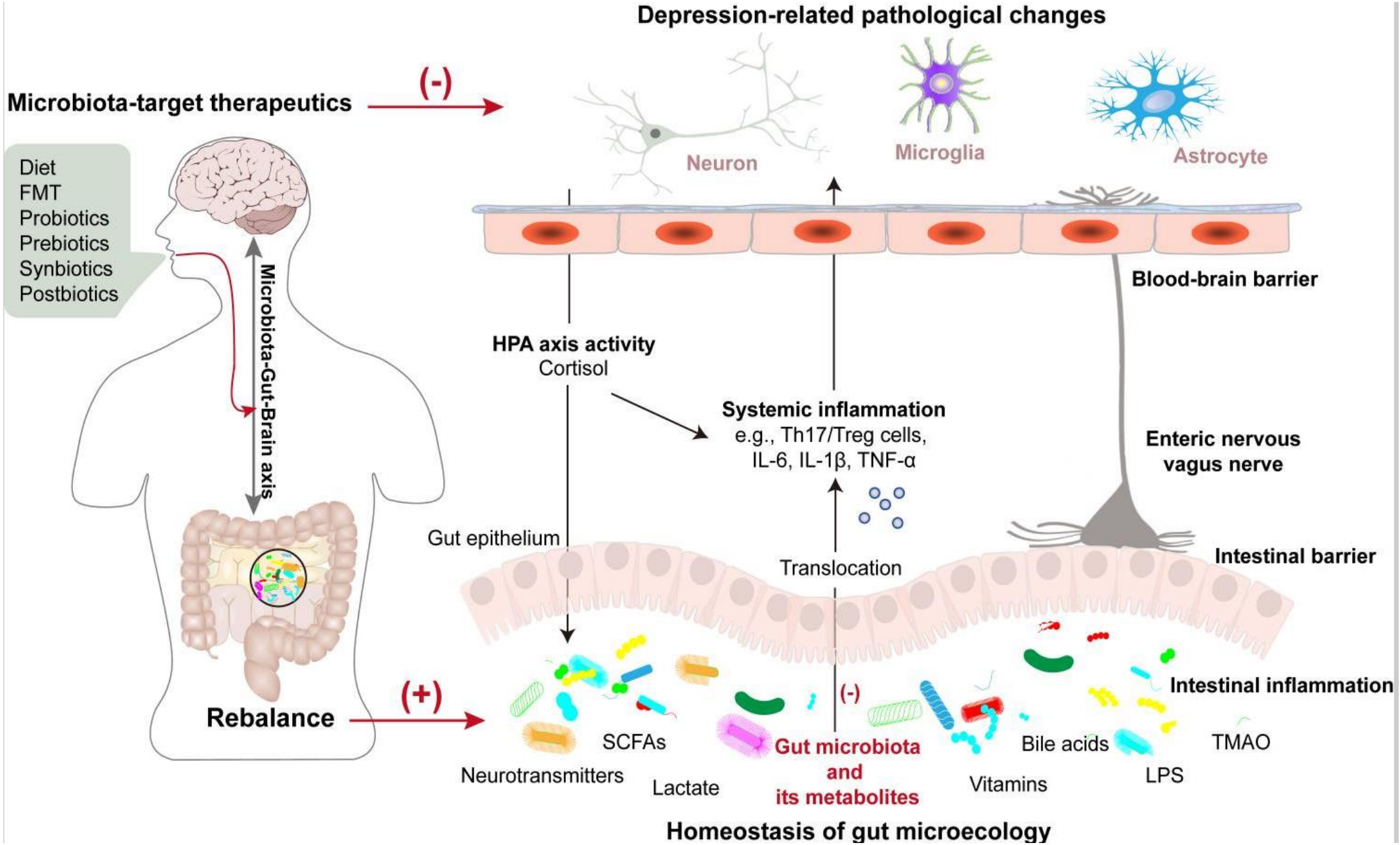
Abstract

Major depressive disorder is one of the most disabling mental disorders worldwide. Increasing preclinical and clinical studies have highlighted that compositional and functional (e.g., metabolite) changes in gut microbiota, known as dysbiosis, are associated with the onset and progression of depression via regulating the gut-brain axis. However, the gut microbiota and their metabolites present a double-edged sword in depression. Dysbiosis is involved in the pathogenesis of depression while, at the same time, offering a novel therapeutic target. In this review, we describe the association between dysbiosis and depression, drug-microbiota interactions in antidepressant treatment, and the potential health benefits of microbial-targeted therapeutics in depression, including dietary interventions, fecal microbiota transplantation, probiotics, prebiotics, synbiotics, and postbiotics. With the emergence of microbial research, we describe a new direction for future research and clinical treatment of depression.

Keywords: Depression; Gut microbiota; Metabolites; Microbial-targeted therapeutics; Pathogenesis.



The association between dysbiosis and central pathological changes during the development of depression. CNS, Central nervous system.


Depression-related pathological changes
Microbiota-target therapeutics
(-)
Diet
FMT
Probiotics
Prebiotics
Synbiotics
Postbiotics
Microbiota-Gut-Brain axis
Neuron
Microglia
Astrocyte
Blood-brain barrier
HPA axis activity
Cortisol
Systemic inflammation
e.g., Th17/Treg cells,
IL-6, IL-1β, TNF-α
Enteric nervous
vagus nerve
Gut epithelium
Translocation
Intestinal barrier
Rebalance
(+)
(-)
Intestinal inflammation
SCFAs
Neurotransmitters
Lactate
Gut microbiota
and
its metabolites
Bile acids
Vitamins
LPS
TMAO
Homeostasis of gut microecology

Review > Front Cell Infect Microbiol. 2023 Apr 25;13:1147687. doi: 10.3389/fcimb.2023.1147687. eCollection 2023.

Gut microbiota and cardiac arrhythmia

Hongxuan Fan [1], Xuchang Liu [2], Zhaoyu Ren [1], Xiaoning Fei [3], Jing Luo [1], Xinyu Yang [1], Yaya Xue [1], Fenfang Zhang [4], Bin Liang [1]

Affiliations + expand

PMID: 37180433 PMCID: PMC10167053 DOI: 10.3389/fcimb.2023.1147687

Free PMC article

Abstract

One of the most prevalent cardiac diseases is cardiac arrhythmia, however the underlying causes are not entirely understood. There is a lot of proof that gut microbiota (GM) and its metabolites have a significant impact on cardiovascular health. In recent decades, intricate impacts of GM on cardiac arrythmia have been identified as prospective approaches for its prevention, development, treatment, and prognosis. In this review, we discuss about how GM and its metabolites might impact cardiac arrhythmia through a variety of mechanisms. We proposed to explore the relationship between the metabolites produced by GM dysbiosis including short-chain fatty acids(SCFA), Indoxyl sulfate(IS), trimethylamine N-oxide(TMAO), lipopolysaccharides(LPS), phenylacetylglutamine(PAGln), bile acids(BA), and the currently recognized mechanisms of cardiac arrhythmias including structural remodeling, electrophysiological remodeling, abnormal nervous system regulation and other disease associated with cardiac arrythmia, detailing the processes involving immune regulation, inflammation, and different types of programmed cell death etc., which presents a key aspect of the microbial-host cross-talk. In addition, how GM and its metabolites differ and change in atrial arrhythmias and ventricular arrhythmias populations compared with healthy people are also summarized. Then we introduced potential therapeutic strategies including probiotics and prebiotics, fecal microbiota transplantation (FMT) and immunomodulator etc. In conclusion, the GM has a significant impact on cardiac arrhythmia through a variety of mechanisms, offering a wide range of possible treatment options. The discovery of therapeutic interventions that reduce the risk of cardiac arrhythmia by altering GM and metabolites is a real challenge that lies ahead.

Keywords: GM; cardiac arrhythmia; mechanism; metabolites; review.

GUT MICROBIOTA AND CARDIAC ARRHYTHMIA

There is a lot of proof that gut microbiota (GM) and its metabolites have a significant impact on cardiovascular health. In recent decades, intricate impacts of GM on cardiac arrythmia have been identified as prospective approaches for its prevention, development, treatment, and prognosis. In this review, we discuss:

- explore the **relationship** between **the metabolites produced by GM dysbiosis** including short-chain fatty acids(SCFA), Indoxyl sulfate(IS), trimethylamine N-oxide(TMAO), lipopolysaccharides(LPS), phenylacetylglutamine(PAGln), bile acids(BA)
  and the currently recognized mechanisms of cardiac arrhythmias including structural remodeling, electrophysiological remodeling, abnormal nervous system regulation

- **how GM and its metabolites differ and change in atrial arrhythmias and ventricular arrhythmias populations compared with healthy people**

- introduce **potential therapeutic strategies including probiotics and prebiotics, fecal microbiota transplantation (FMT) and immunomodulator**

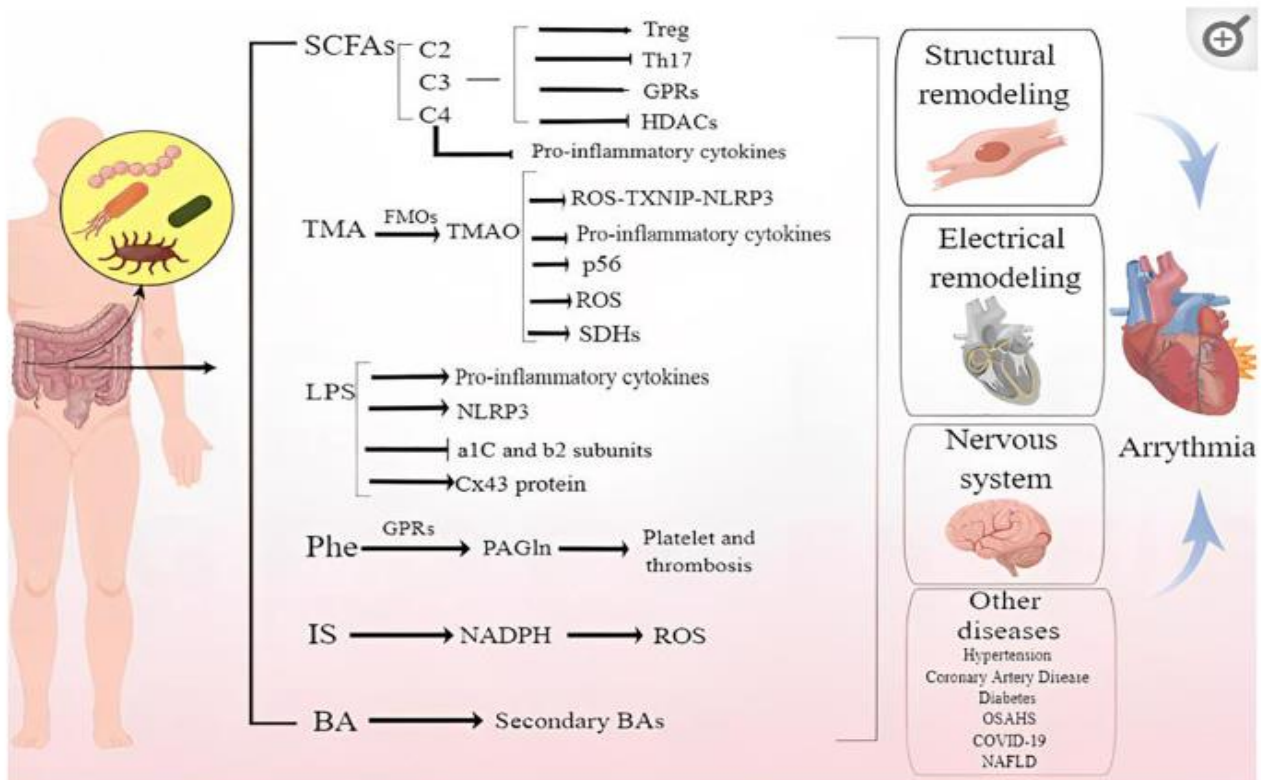
frontiers in Cellular and Infection Microbiology

PMC full text:

Front Cell Infect Microbiol. 2023; 13: 1147687.

Published online 2023 Apr 25. doi: 10.3389/fcimb.2023.1147687

Figure 1



Demonstrates the mechanism by that gut microbiota and metabolites cause arrhythmia.

Review > Nat Rev Nephrol. 2023 Mar;19(3):153-167. doi: 10.1038/s41581-022-00654-0.
Epub 2023 Jan 11.

The gut microbiome and hypertension

Joanne A O'Donnell [# 1], Tenghao Zheng [# 1], Guillaume Meric [2], Francine Z Marques [3 4]

Affiliations + expand

PMID: 36631562 DOI: 10.1038/s41581-022-00654-0

Abstract

A large body of evidence has emerged in the past decade supporting a role for the gut microbiome in the regulation of blood pressure. The field has moved from association to causation in the last 5 years, with studies that have used germ-free animals, antibiotic treatments and direct supplementation with microbial metabolites. The gut microbiome can regulate blood pressure through several mechanisms, including through gut dysbiosis-induced changes in microbiome-associated gene pathways in the host. Microbiota-derived metabolites are either beneficial (for example, short-chain fatty acids and indole-3-lactic acid) or detrimental (for example, trimethylamine N-oxide), and can activate several downstream signalling pathways via G protein-coupled receptors or through direct immune cell activation. Moreover, dysbiosis-associated breakdown of the gut epithelial barrier can elicit systemic inflammation and disrupt intestinal mechanotransduction. These alterations activate mechanisms that are traditionally associated with blood pressure regulation, such as the renin-angiotensin-aldosterone system, the autonomic nervous system, and the immune system. Several methodological and technological challenges remain in gut microbiome research, and the solutions involve minimizing confounding factors, establishing causality and acting globally to improve sample diversity. New clinical trials, precision microbiome medicine and computational methods such as Mendelian randomization have the potential to enable leveraging of the microbiome for translational applications to lower blood pressure.

THE GUT MICROBIOME AND HYPERTENSION

A large body of evidence has emerged in the past decade supporting a role for the gut microbiome in the regulation of blood pressure.

The gut microbiome can regulate blood pressure through several mechanisms,

Microbiota-derived metabolites are either **beneficial** (for example, short-chain fatty acids and indole-3-lactic acid) **or detrimental** (for example, trimethylamine N-oxide),
can activate several downstream signalling pathways via G protein-coupled receptors or through direct immune cell activation.
Moreover, dysbiosis-associated **breakdown of the gut epithelial barrier can** elicit systemic inflammation and **disrupt intestinal mechanotransduction**.

These alterations activate mechanisms that are traditionally associated with blood pressure regulation, such as the renin-angiotensin-aldosterone system, the autonomic nervous system, and the immune system.

Review > Antioxidants (Basel). 2023 Apr 3;12(4):866. doi: 10.3390/antiox12040866.

Is the Gut Microbiome Implicated in the Excess Risk of Hypertension Associated with Obstructive Sleep Apnea? A Contemporary Review

Sanah S Munir [1], Fatima H Sert Kuniyoshi [1 2], Prachi Singh [3], Naima Covassin [1]

Affiliations + expand

PMID: 37107242 PMCID: PMC10135363 DOI: 10.3390/antiox12040866

Free PMC article

Abstract

Obstructive sleep apnea (OSA) is a highly prevalent sleep disorder and an established risk factor for cardiovascular diseases, including hypertension. The pathogenesis of elevated blood pressure (BP) in OSA is multifactorial, including sympathetic overdrive, vascular aberrations, oxidative stress, inflammation, and metabolic dysregulation. Among the mechanisms potentially involved in OSA-induced hypertension, the role of the gut microbiome is gaining increasing attention. Perturbations in the diversity, composition, and function of the gut microbiota have been causally linked to numerous disorders, and robust evidence has identified gut dysbiosis as a determinant of BP elevation in various populations. In this brief review, we summarize the current body of literature on the implications of altered gut microbiota for hypertension risk in OSA. Data from both preclinical models of OSA and patient populations are presented, and potential mechanistic pathways are highlighted, along with therapeutic considerations. Available evidence suggests that gut dysbiosis may promote the development of hypertension in OSA and may thus be a target for interventions aimed at attenuating the adverse consequences of OSA in relation to cardiovascular risk.

Keywords: cardiovascular disease; gut dysbiosis; gut microbiome; hypertension; hypoxia; obstructive sleep apnea; short-chain fatty acids; sleep fragmentation.

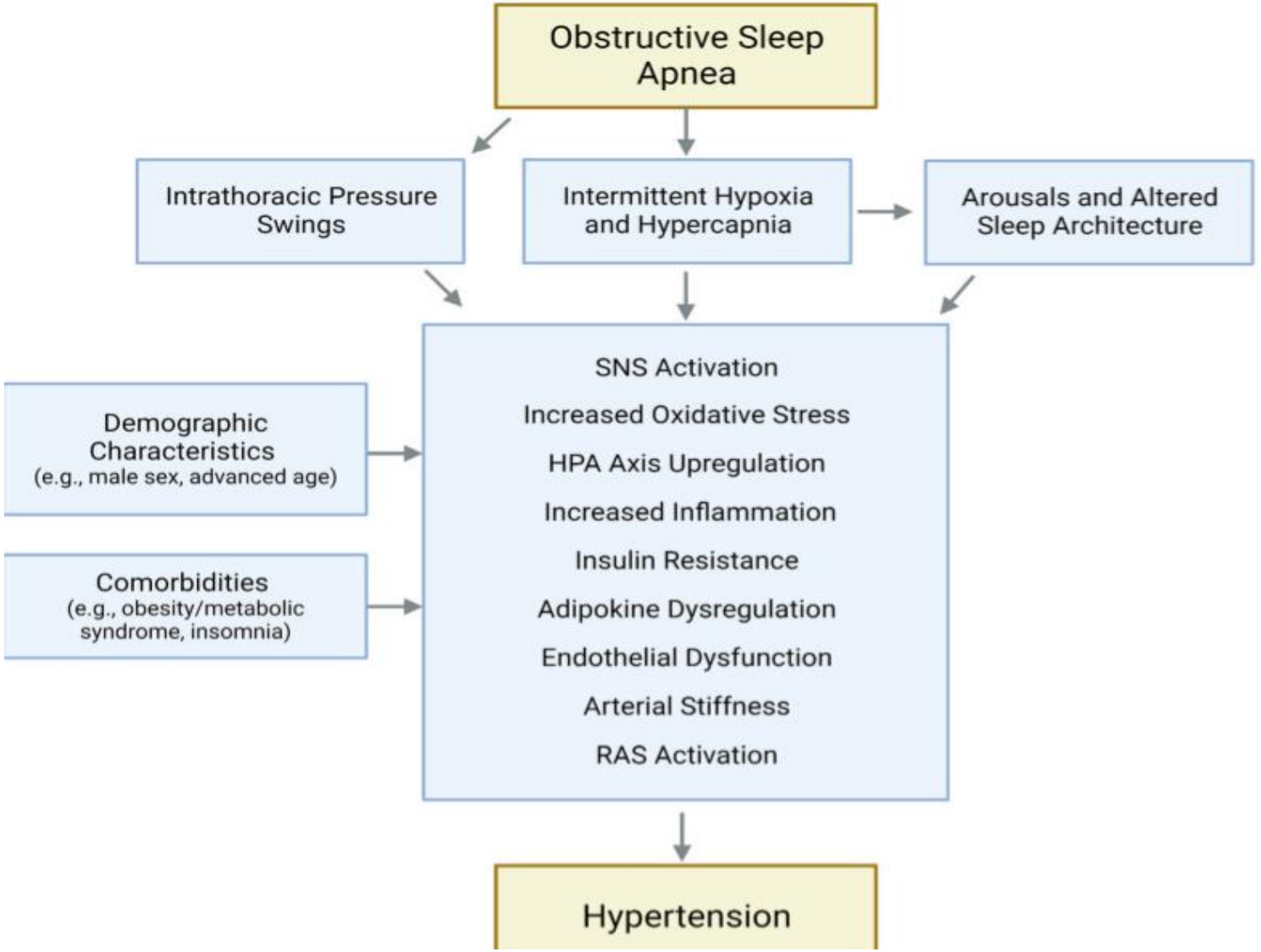


Figure 1 Pathophysiology of hypertension in obstructive sleep apnea. HPA—hypothalamic–pituitary–adrenal; RAS—renin–angiotensin system; SNS—sympathetic nervous system.

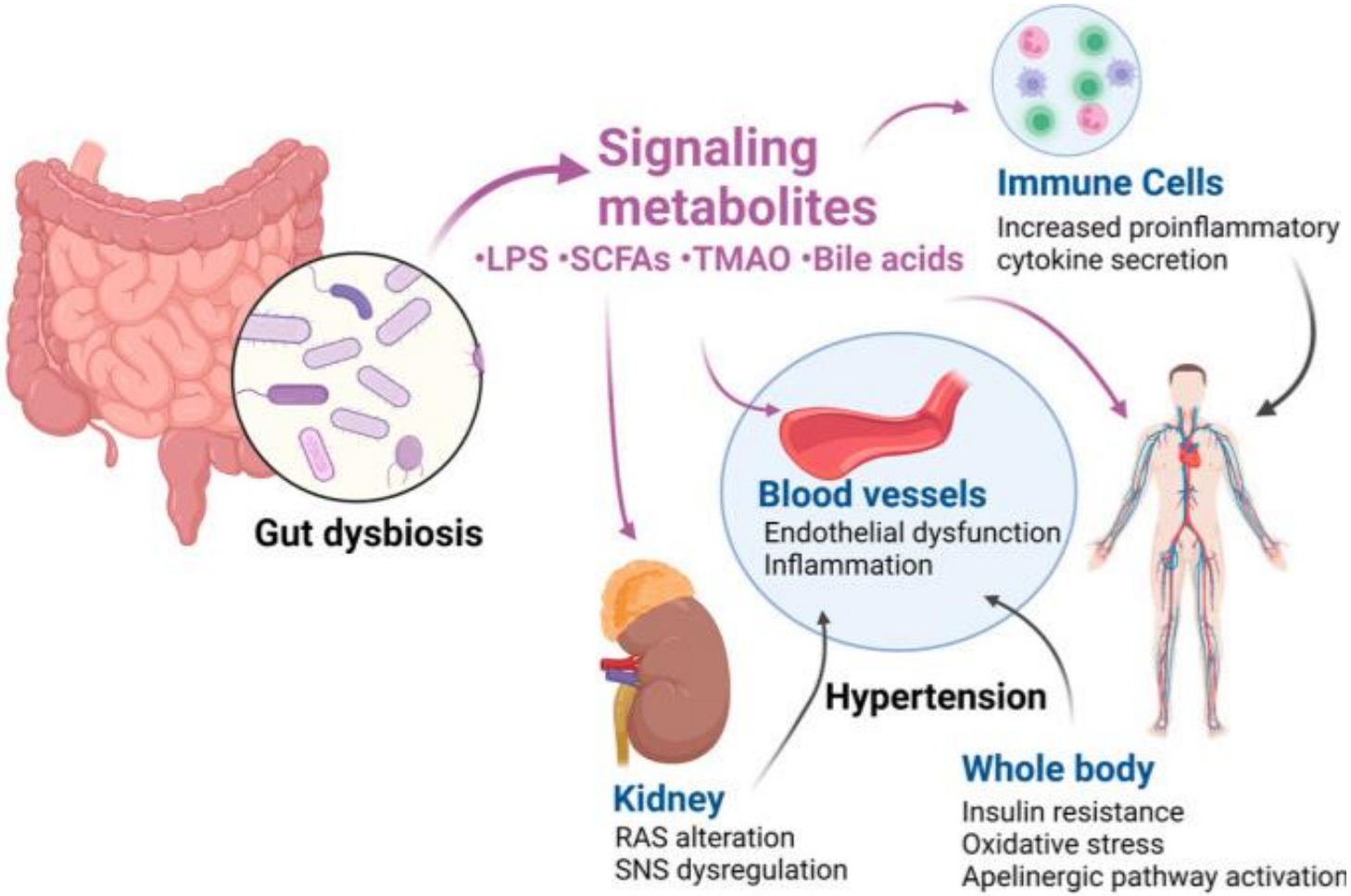


Figure 2 Proposed pathway through which perturbations in the gut microbiome may cause hypertension via altered signaling metabolites. **LPS—lipopolysaccharide**; **RAS—renin–angiotensin system**; **SCFA—short-chain fatty acids; SNS—sympathetic nervous system; TMAO—trimethylamine N-oxide.**

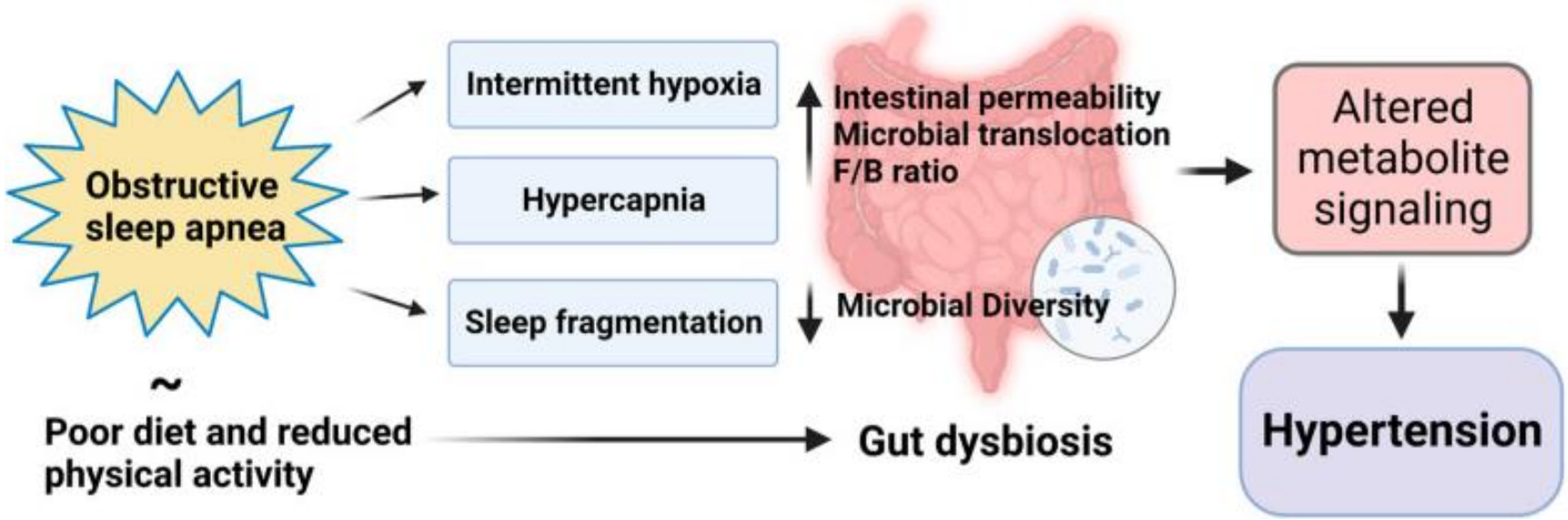


Figure 3 Schematic highlighting the interplay between obstructive sleep apnea and gut microbiome in altering metabolite signaling and facilitating the development of hypertension.
F/B—Firmicutes-to-Bacteroidetes ratio

Interactions between NSAIDs, opioids and the gut microbiota – Future perspectives in the management of inflammation and pain

Zoltán S Zádori [1], Kornél Király [2], Mahmoud Al-Khrasani [2], Klára Gyires [2]

Affiliations + expand

PMID: 36473615 DOI: 10.1016/j.pharmthera.2022.108327

Free article

Abstract

The composition of intestinal microbiota is influenced by a number of factors, including medications, which may have a substantial impact on host physiology. Nonsteroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics are among those widely used medications that have been shown to alter microbiota composition in both animals and humans. Although much effort has been devoted to identify microbiota signatures associated with these medications, much less is known about the underlying mechanisms. Mucosal inflammation, changes in intestinal motility, luminal pH and bile acid metabolism, or direct drug-induced inhibitory effect on bacterial growth are all potential contributors to NSAID- and opioid-induced dysbiosis, however, only a few studies have addressed directly these issues. In addition, there is a notable overlap between the microbiota signatures of these drugs and certain diseases in which they are used, such as spondyloarthritis (SpA), rheumatoid arthritis (RA) and neuropathic pain associated with type 2 diabetes (T2D). The aims of the present review are threefold. First, we aim to provide a comprehensive up-to-date summary on the bacterial alterations caused by NSAIDs and opioids. Second, we critically review the available data on the possible underlying mechanisms of dysbiosis. Third, we review the current knowledge on gut dysbiosis associated with SpA, RA and neuropathic pain in T2D, and highlight the similarities between them and those caused by NSAIDs and opioids. We posit that drug-induced dysbiosis may contribute to the persistence of these diseases, and may potentially limit the therapeutic effect of these medications by long-term use. In this context, we will review the available literature data on the effect of probiotic supplementation and fecal microbiota transplantation on the therapeutic efficacy of NSAIDs and opioids in these diseases.

Keywords: Microbiota; Neuropathic pain; Nonsteroidal anti-inflammatory drugs (NSAIDs); Opioids; Rheumatoid arthritis; Spondyloarthritis.

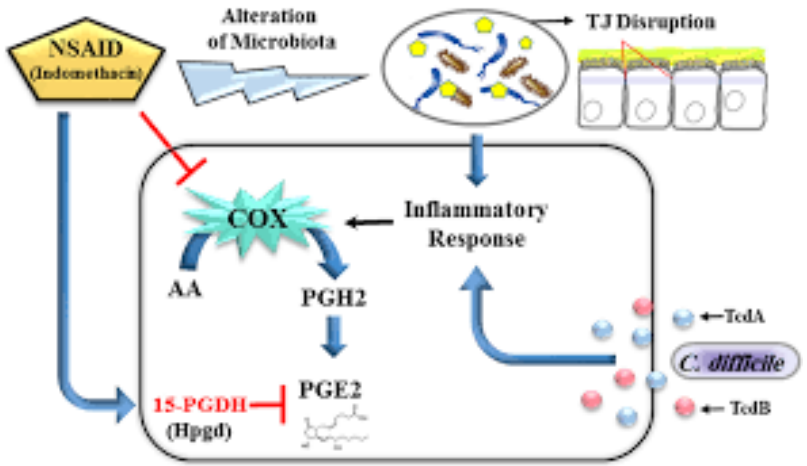
INTERACTIONS BETWEEN NSAIDS, OPIOIDS AND THE GUT MICROBIOTA - FUTURE PERSPECTIVES IN THE MANAGEMENT OF INFLAMMATION AND PAIN

Nonsteroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics are among those widely used medications that **have been shown to alter microbiota composition** in both animals and humans.

UNDERLYING MECHANISMS TO NSAID- AND OPIOID-INDUCED DYSBIOSIS:

- **Mucosal inflammation**
- **changes in intestinal motility**
- **luminal pH and bile acid metabolism**
- **direct drug-induced inhibitory effect on bacterial growth**

In addition, **there is a notable overlap between the microbiota signatures of these drugs** and certain diseases in which they are used, such as **spondyloarthritis (SpA), rheumatoid arthritis (RA) and neuropathic pain associated with type 2 diabetes (T2D).**



The aims of the review are threefold.

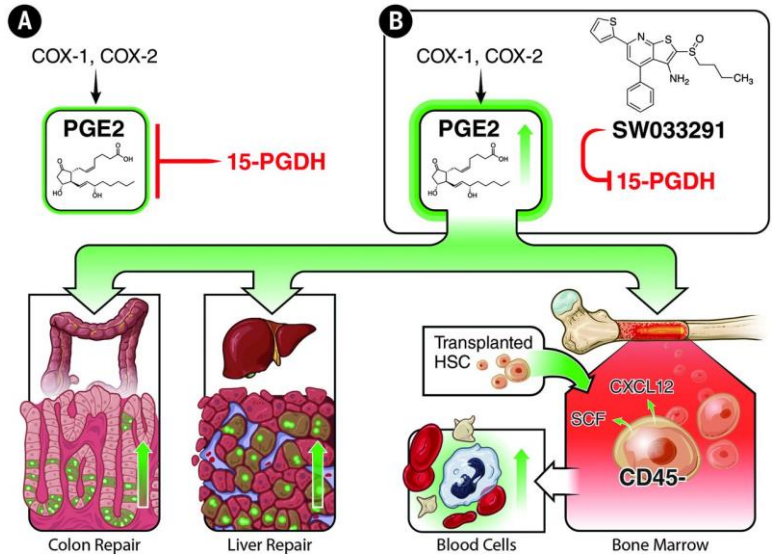
1. provide a comprehensive up-to-date summary on the bacterial alterations caused by NSAIDs and opioids.
2. review the available data on the possible underlying mechanisms of dysbiosis.
3. review the current knowledge on gut dysbiosis associated with SpA, RA and neuropathic pain in T2D,

We posit that drug-induced dysbiosis may contribute to the persistence of these diseases, and may potentially limit the therapeutic effect of these medications by long-term use.

In this context, we will review the available literature data on the effect of probiotic supplementation and fecal microbiota transplantation on the therapeutic efficacy of NSAIDs and opioids in these diseases.

NSAID-induced dysbiosis has been investigated primarily in the context of gut damage (enteropathy) whereas opioid-induced dysbiosis in the development of opioid analgesic tolerance and opioid-induced sepsi

The connection between drugs and intestinal bacteria is bidirectional. That is, not only drugs shape the composition of gut microbiota, but also **dysbiosis can change** the pharmacokinetics of drugs. **Opioid-induced dysbiosis has been shown to decrease the enterohepatic recirculation of morphine, which lowered its bioavailability and reduced gradually its efficacy as an analgesic agent**. Likewise, gut dysbiosis after antibiotic treatment caused significant alterations in the metabolism of indomethacin and decreased its half-life, which reduced its inhibitory effect on cyclooxygenase enzymes

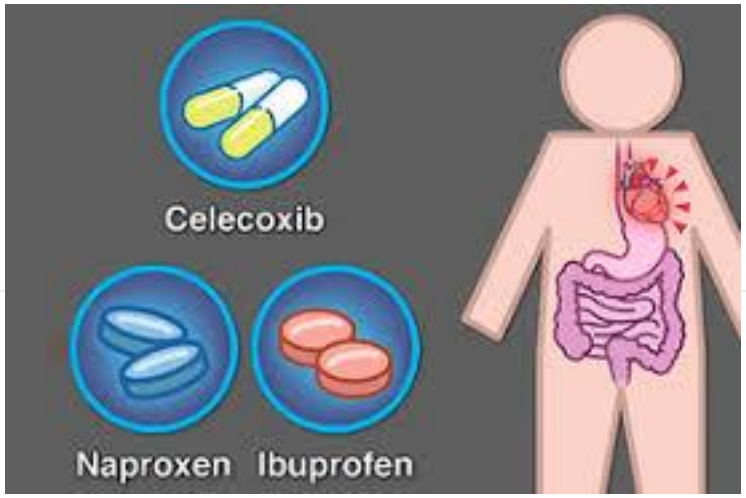


	Wistar rat	10 mg/kg, 1 to 4 times, 12 h apart	24 and 48 h	ileum	↑ Gram–negatives*	Reuter et al., 1997
diclofenac	Wistar rat (40-wk old)	4 mg/kg, twice a day for 2 wk	2 wk	ileum	↑ *Proteobacteria*, *Bacteroidetes* ↓ *Firmicutes*, *Lactobacillus*	Colucci et al., 2018

	Wistar rat	100 mg/kg, 1 to 4 times, 12 h apart	24 and 48 h	ileum	no effect	Reuter et al., 1997
acetylsalicylic acid 	C57BL/6 mouse (AOM+DSS-treated), or $Apc^{Min/+}$ mouse	400 or 1200 mg/L, for 80 d /C57BL/6/ or 84 d /$Apc^{Min/+}$ /	80 or 84 d	feces	↑ *Lactobacillus* (*L. reuteri, L. gasseri, L. johnsonii*), *Bifidobacterium* (*B. pseudolongum, B. breve, B. animalis*), *Faecalibacterium rodentium* ↓ *Alistipes finegoldii* and *Bacteroides fragilis* (high-dose acetylsalicylic acid)	Zhao et al., 2020
	Sprague-Dawley rat	10.4 mg/kg once a day for 2 wk	15 d	feces	↑ *Muribaculaceae* (*S24-7*), *Cyanobacteria*, *Melainabacteria* ↓ *Lachnospiraceae*, *Coriobacteriia*, *Eubacteriaceae*, *Streptococcaceae*	Chi et al., 2021

naproxen	Wistar rat	10 mg/kg twice a day for 4 d, or 20 mg/kg for 2 d	48 and 96 h	jejunum	↑ *Bacteroidaceae*, *Enterococcaceae*, *Porphyromonadaceae*, *Enterobacteriaceae* ↓ *Lachnospiraceae*	Blackler et al., 2015
	rat	20 mg/kg, twice a day for 4 d	96 h	cecum	*Proteobacteria* ↑	Syer et al., 2015
celecoxib	$Apc^{Min/+}$ mouse	1000 ppm for 10 wk	10 wk	ileum and feces	↑ *Coriobacteriaceae* (ileum and feces) ↓ *Lactobacillaceae* (ileum), *Bifidobacteriaceae* (feces),	Montrose et al., 2016
ibuprofen	C57BL/6 mouse	50 mg/kg, once a day for 1 week	1 wk	cecum	↑ *Bacteroidetes*, *α,β-Proteobacteria*, *Verrucomicrobia* ↓ *Firmicutes*, *δ,γ-Proteobacteria*, *Deferribacter*	Lu et al., 2018

various NSAIDs (acetylsalicylic acid, ibuprofen, celecoxib, ketorolac, naproxen)	human (155 commu-nity residents with age of ≥18, using different medica-tions)	ND (drug was used within past 30 d)	ND	feces	↑ *Acidaminococcaceae*, *Desulfovibrionaceae*, *Enterococcaceae*, *Erysipelotrichaceae* (in NSAID users vs non-users) ↑*Acidaminococcaceae*, *Enterobacteriaceae*, *Propionibacteriaceae*, *Pseudomonadaceae*, *Puniceicoccaceae*, *Rikenellaceae* (in ibuprofen users) ↑*Acidaminococcaceae*, *Enterobacteriaceae* (in celecoxib users) ↑*Alistipes* (in ketorolac users) changes in *Prevotella*, *Bacteroides*, *Ruminococcaceae*, *Barnesiella* (in acetylsalicylic acid users) changes in *Enterobacteriaceae*, *Bacteroides*, *Alistipes* (in naproxen users)	Rogers & Aronoff, 2016



One of the most consistent observations is the expansion of Gram-negative bacteria in response to NSAID treatment. This is mainly due to the enrichment of the phyla *Bacteroidetes* and *Proteobacteria*,

he NSAID-induced overgrowth of *Bacteroides* (or the corresponding higher taxonomic levels *Bacteroidaceae*, *Bacteroidales* or *Bacteroidetes*), in both absolute and relative terms, has been confirmed by several groups, using either the same indomethacin or other drugs, such as diclofenac or naproxen

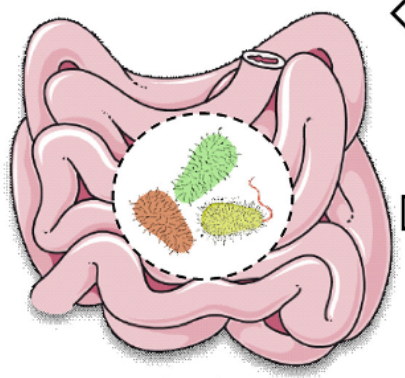
In our recent study, genera belonging to the *Gammaproteobacteria* (*Pantoea*, *Serratia*, *Escherichia-Shigella*, *Enterobacter*, *Rodentibacter*) and *Parasutterella* (a member of *Betaproteobacteria*) increased rapidly after indomethacin treatment,

NSAIDs

↑ *Bacteroides, Prevotella, Akkermansia, Enterobacteriaceae, Enterococcus*

↓ *SFB, Lachnospiraceae Ruminococcaceae*

- Inflammation
- Motility
- Bile acids?
- pH?
- Direct actions?



Gut dysbiosis

Opioids

↑ *Prevotella, Akkermansia, Sutterella, Enterococcus, Erysipelotrichaceae, Allobaculum*

↓ *Lactobacillus, Clostridiaceae Lachnospiraceae, Ruminococcaceae*

↑ *Bacteroides, Prevotella, Akkermansia*

↓ *Faecalibacterium prausnitzii*

* *Proteobacteria, Ruminococcus gnavus, Dialister, Acidaminococcus fermentans*

SpA

↑ *Prevotella, Lactobacillus*

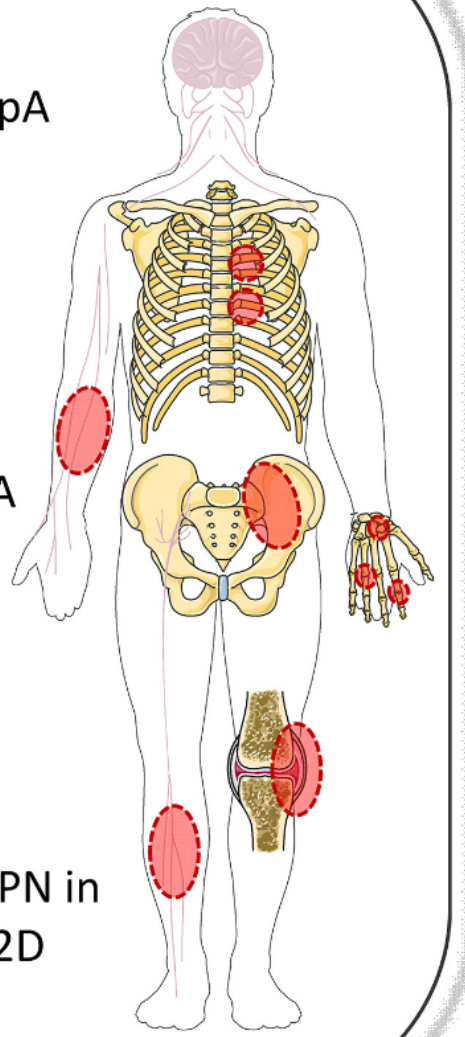
* *Collinsella, Akkermansia, Gammaproteobacteria, Pasteurellales, Anaerobranca zavarzinii, Alloprevotella, Parabacteroides*

RA

↑ *Bacteroidetes, Prevotella*

↓ *Roseburia, Faecalibacterium*

DPN in T2D



Review > Heliyon. 2023 Mar;9(3):e13801. doi: 10.1016/j.heliyon.2023.e13801. Epub 2023 Feb 17.

Decoding the bidirectional relationship between gut microbiota and COVID-19

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Free PMC article

Abstract

From late 2019, whole world has been facing COVID-19 pandemic which is caused by SARS-CoV-2 virus. This virus primarily attacks the respiratory tract and enter host cell by binding with angiotensin 2 converting enzyme receptors present on alveoli of the lungs. Despite its binding in the lungs, many patients have reported gastrointestinal symptoms and indeed, RNA of the virus have been found in faecal sample of patients. This observation gave a clue of the involvement of gut-lung axis in this disease development and progression. From several studies reported in past two years, intestinal microbiome has shown to have bidirectional link with lungs i.e., gut dysbiosis increases the tendency of infection with COVID-19 and coronavirus can also cause perturbations in intestinal microbial composition. Thus, in this review we have tried to figure out the mechanisms by which disturbances in the gut composition can increase the susceptibility to COVID-19. Understanding these mechanisms can play a crucial role in decreasing the disease outcomes by manipulating the gut microbiome using prebiotics, probiotics, or combination of two. Even, faecal microbiota transplantation can also show better results, but intensive clinical trials need to be done first.

Keywords: ACE2; COVID-19; Coronavirus; Gut lung axis; Gut microbiome.

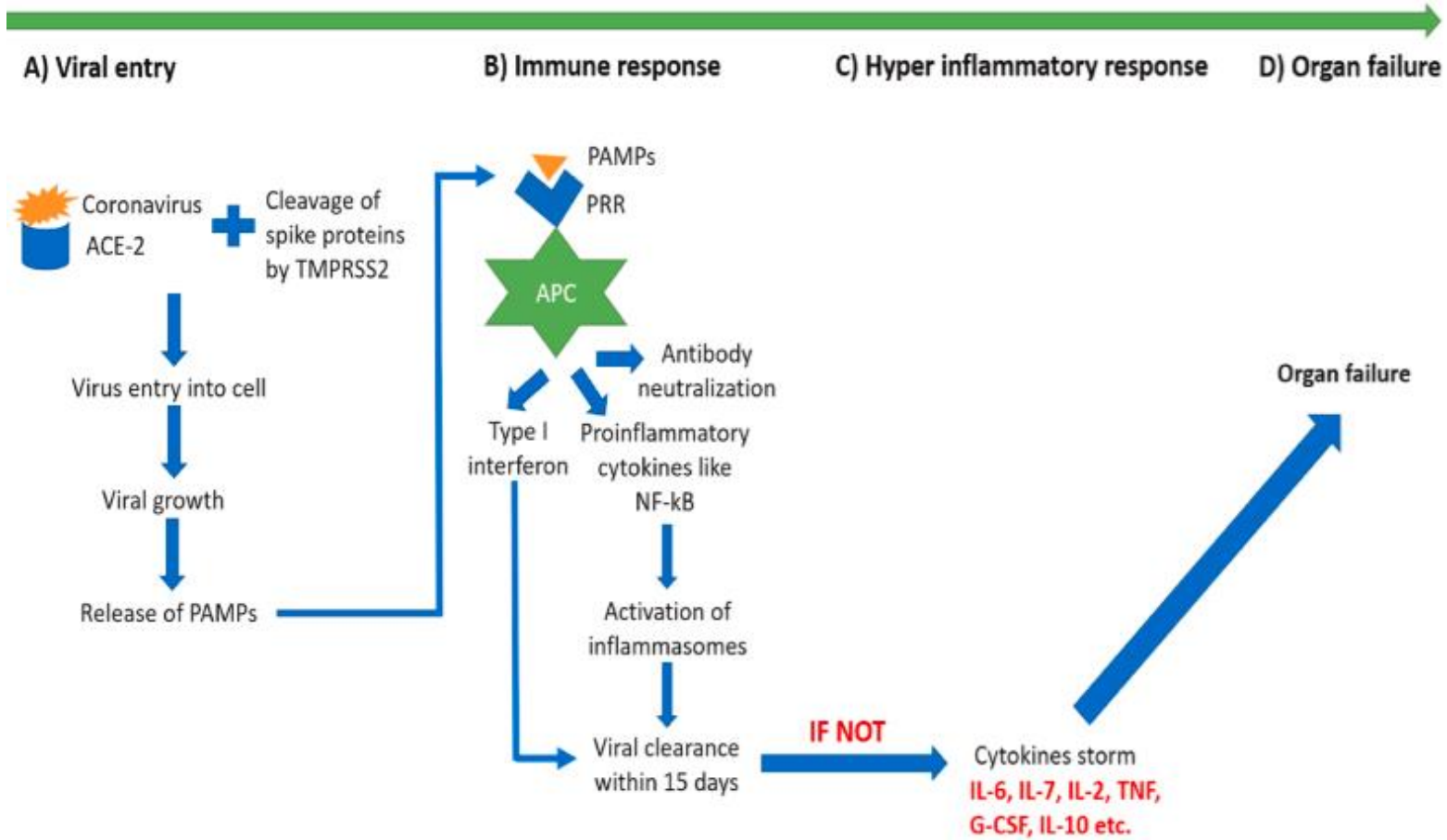

Fig. 1 Mechanism of attack of coronavirus in the human body.

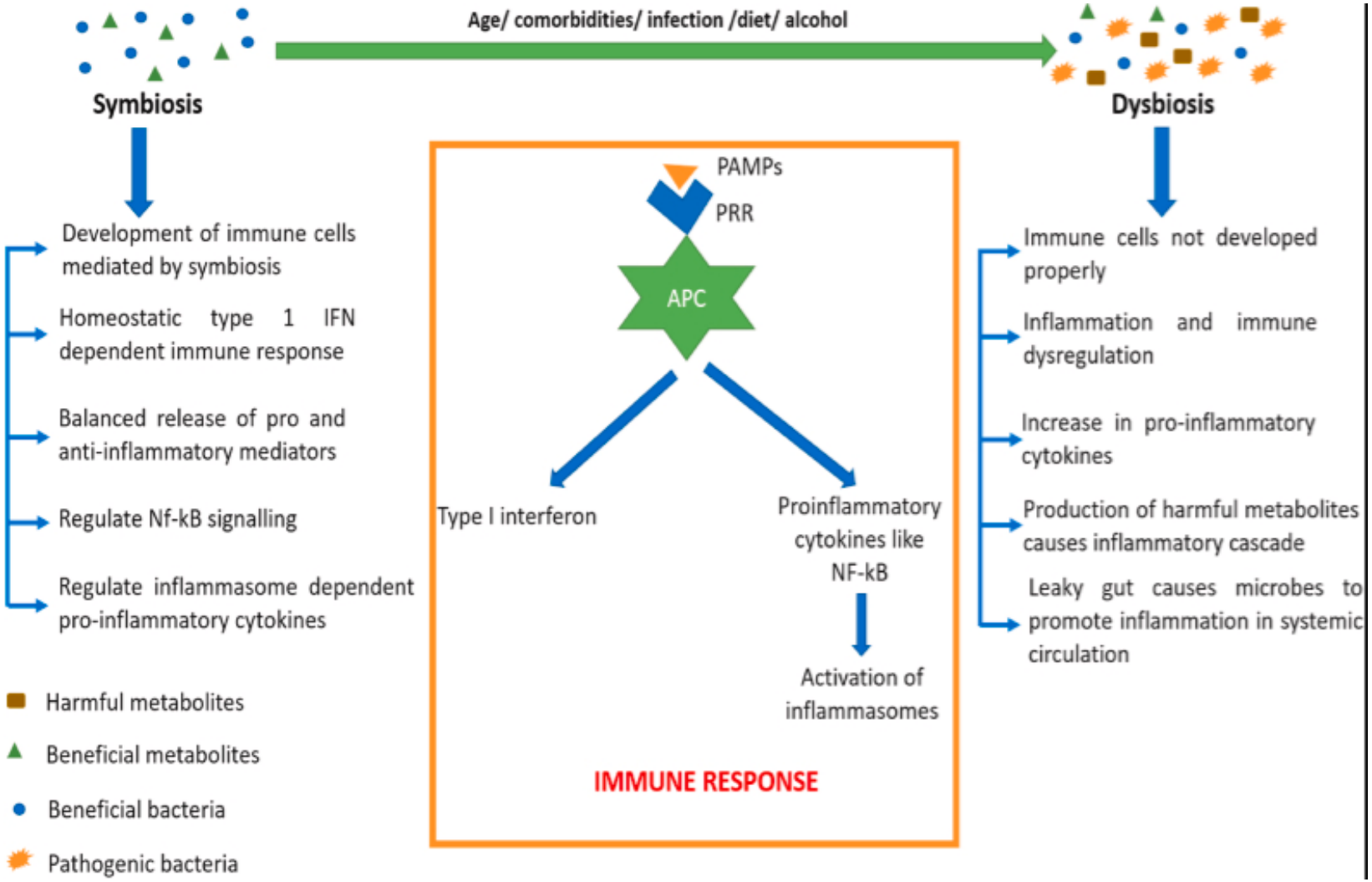

Fig. 2 Interactions of immune system in symbiotic and dys-biotic conditions.

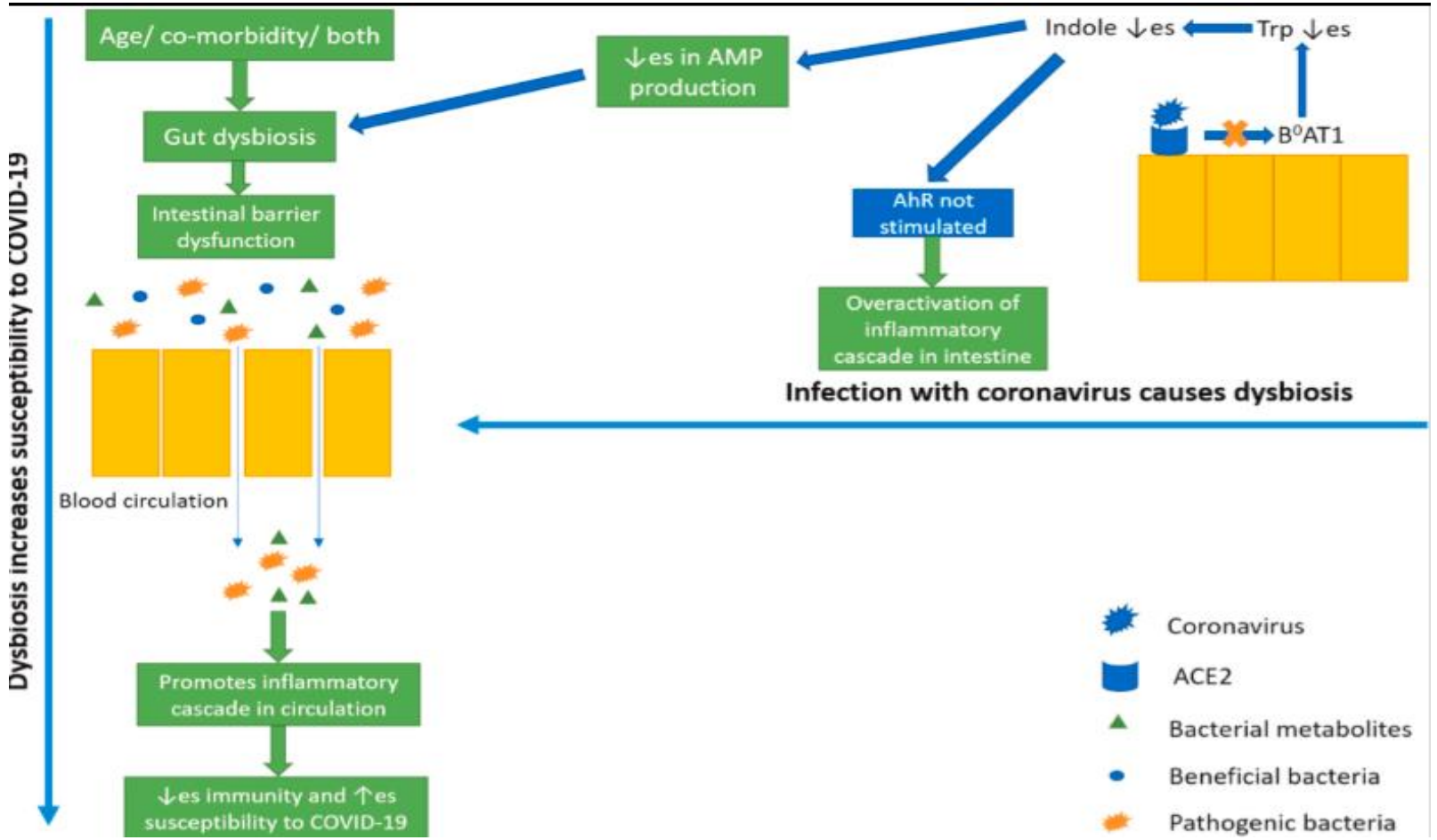

Fig. 3 Bidirectional link of COVID-19 infection and gut dysbiosis (AMP: Antimicrobial peptide, AhR: Aryl hydrocarbon receptor, Trp: Tryptophan.

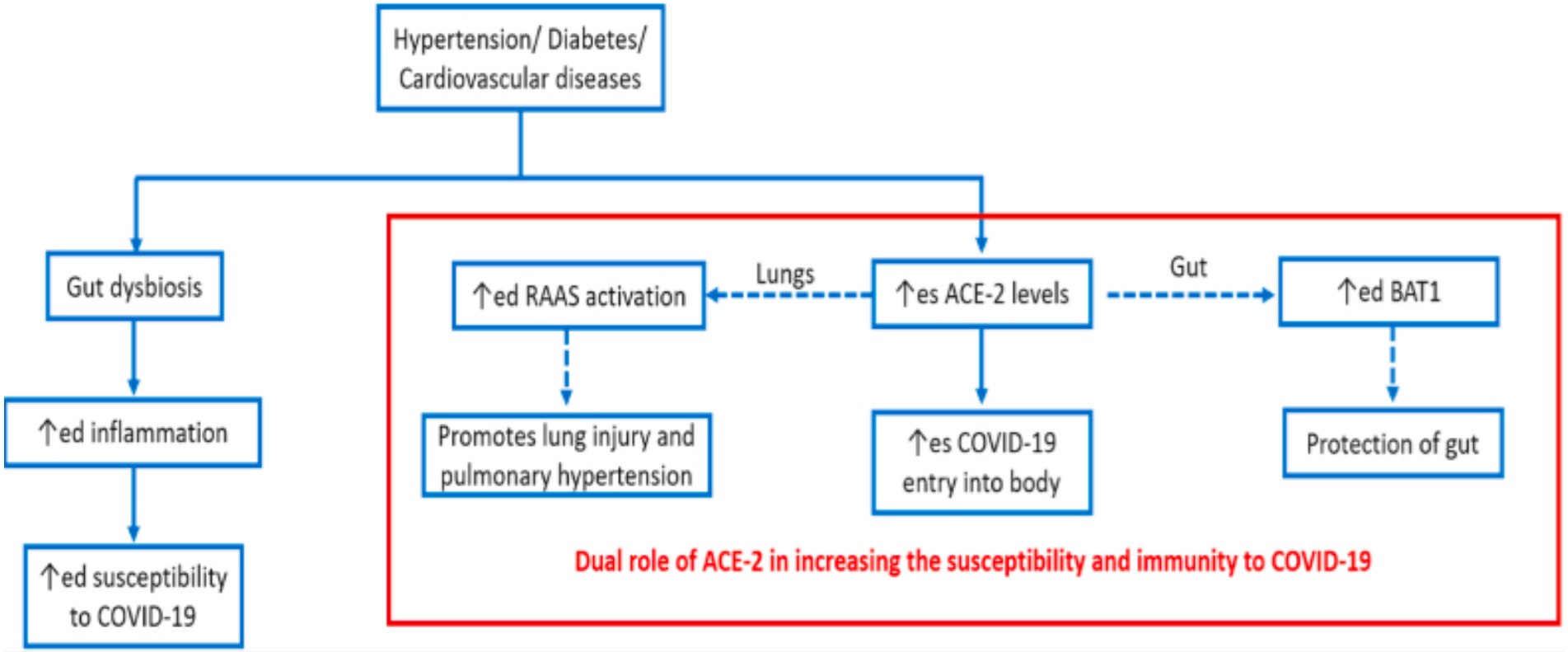

Fig. 4 Probable mechanisms of increase in COVID-19 susceptibility due to presence of associated co-morbidities.

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Gut Microbes Meet Machine Learning: The Next Step towards Advancing Our Understanding of the Gut Microbiome in Health and Disease

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PMID: 36982303 PMCID: PMC10049444 DOI: 10.3390/ijms24065229

Free PMC article

Abstract

The human gut microbiome plays a crucial role in human health and has been a focus of increasing research in recent years. Omics-based methods, such as metagenomics, metatranscriptomics, and metabolomics, are commonly used to study the gut microbiome because they provide high-throughput and high-resolution data. The vast amount of data generated by these methods has led to the development of computational methods for data processing and analysis, with machine learning becoming a powerful and widely used tool in this field. Despite the promising results of machine learning-based approaches for analyzing the association between microbiota and disease, there are several unmet challenges. Small sample sizes, disproportionate label distribution, inconsistent experimental protocols, or a lack of access to relevant metadata can all contribute to a lack of reproducibility and translational application into everyday clinical practice. These pitfalls can lead to false models, resulting in misinterpretation biases for microbe-disease correlations. Recent efforts to address these challenges include the construction of human gut microbiota data repositories, improved data transparency guidelines, and more accessible machine learning frameworks; implementation of these efforts has facilitated a shift in the field from observational association studies to experimental causal inference and clinical intervention.

Keywords: artificial intelligence; dysbiosis; eubiosis; gut microbiome; gut microbiota; health; machine learning; metagenomics; microbiome; omics; supervised learning; unsupervised learning.

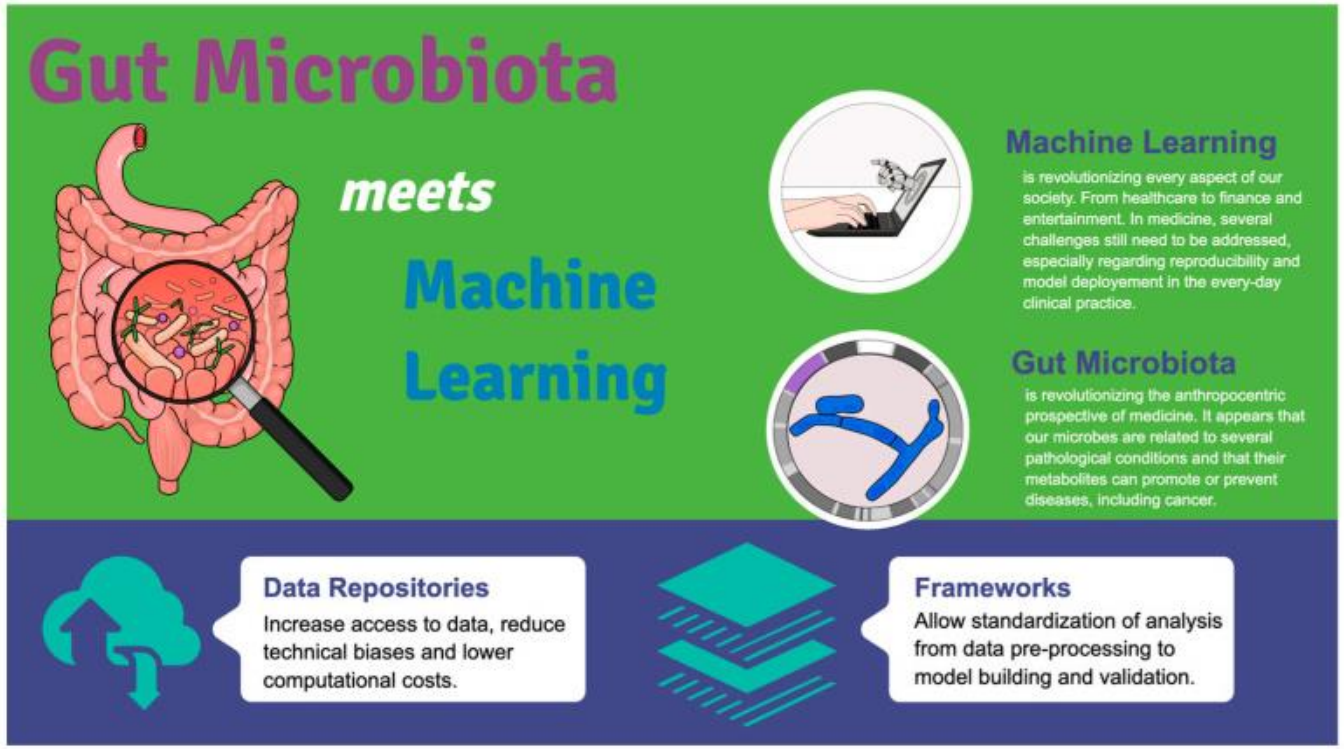

Figure 1 Gut Microbiota meets machine learning. The increasing data availability due to omics analysis has not been followed by the creation of data repositories, guidelines, and analytical frameworks in the past, which resulted in unsatisfactory reproducibility and reliability. **The implementation of such tools has facilitated a shift in the field from observational association studies to experimental causal inference and clinical intervention.**


Non sempre cambiare
equivale a migliorare, ma per
migliorare bisogna cambiare.
Winston Churchill