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The One Health Concept: The Central Role of the Microbiome in an Interconnected World

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Disclosures

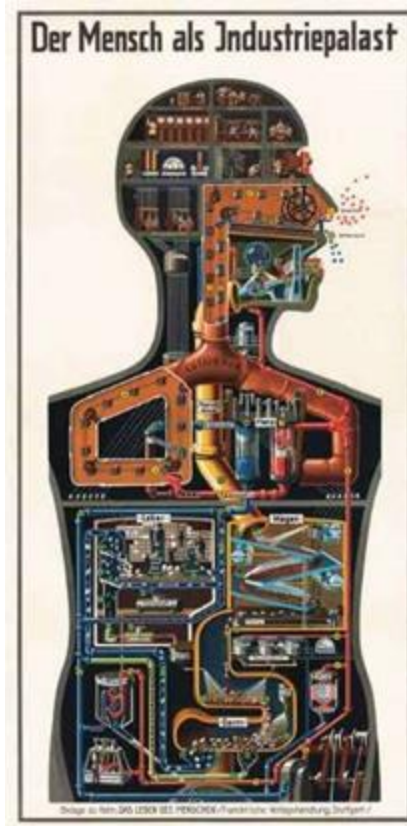
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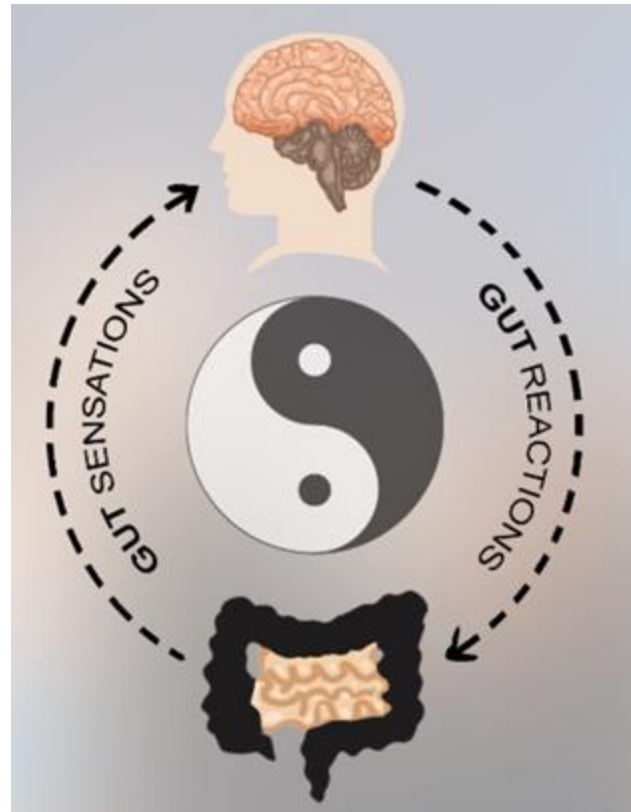
Overview

- The One Health Concept
- The Brain Gut Microbiome System 101
- A Holistic View of Brain and Gut
- Take home message

The 85 Year Journey From a Steam Engine Model to an Integrative View of Brain Gut Interactions and the One Health Concept



Fritz Kahn, 1926



Gut feelings: the emerging biology of gut-brain communication

[Emeran A. Mayer](#)

[Nature Reviews Neuroscience](#) 12, 453–466 (2011) | [Cite this article](#)



Progress in Brain Research, 2000

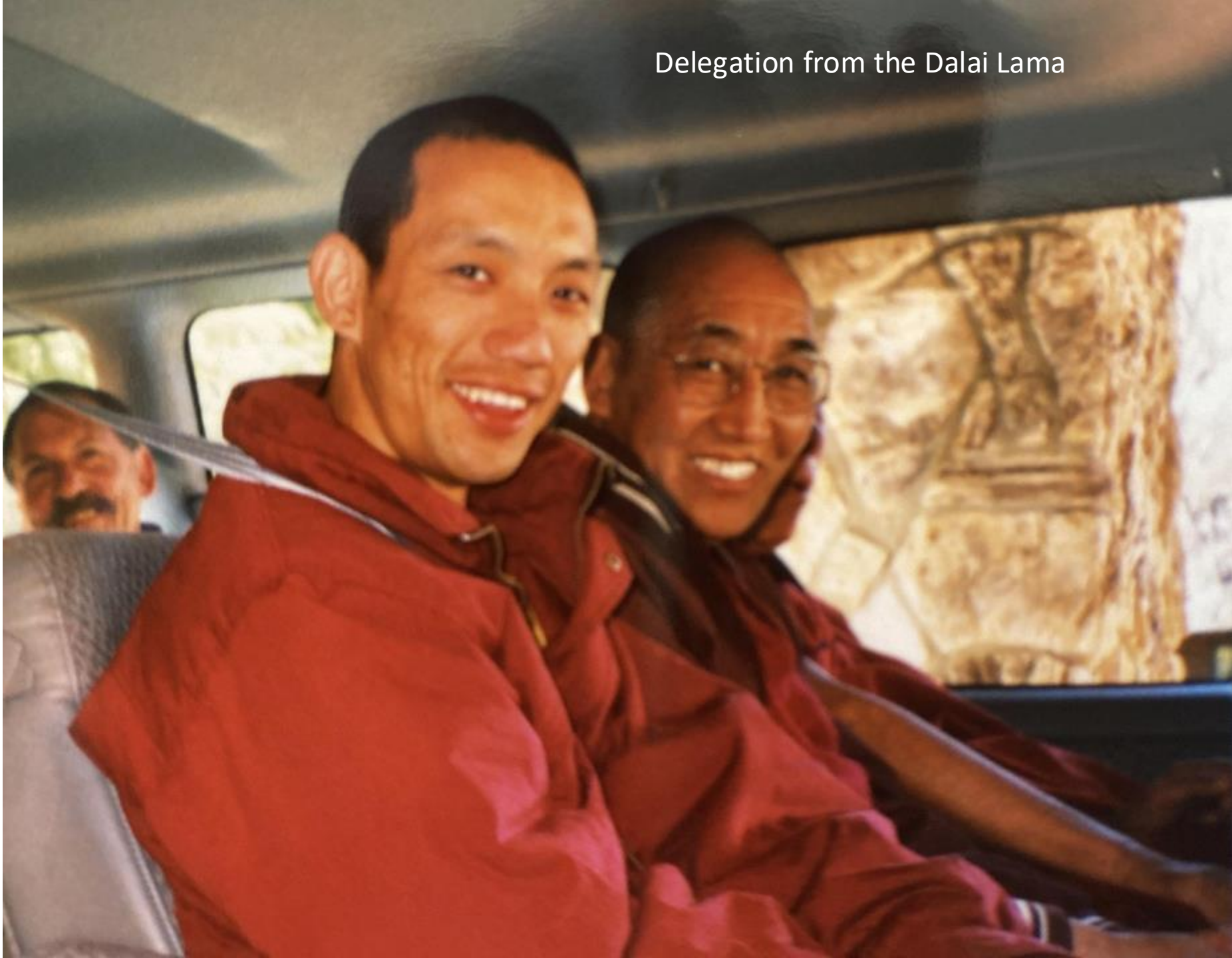


Cliff Saper, PhD and John Furness



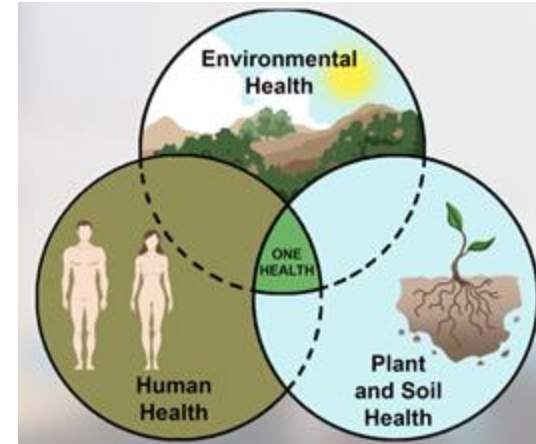
Ernest Rossi, PhD, Jon Kabat-Zinn, Ester Sternberg, Bruce McEwen and Charles Nemeroff

Delegation from the Dalai Lama



The One Health Concept

- The "One Health" concept is a collaborative, multi-disciplinary approach that recognizes the interconnectedness of mind and body, and of human, animal, and environmental health.
- It emphasizes that the health of each domain is interdependent and that many health challenges, including brain gut microbiome disorders can be better understood and addressed through an integrated, multidimensional approach.
- The microbiome is a central linking factor across these systems



Microbes Don't Just Live in our Gut: they are the most Ancient and Universal Ecosystem

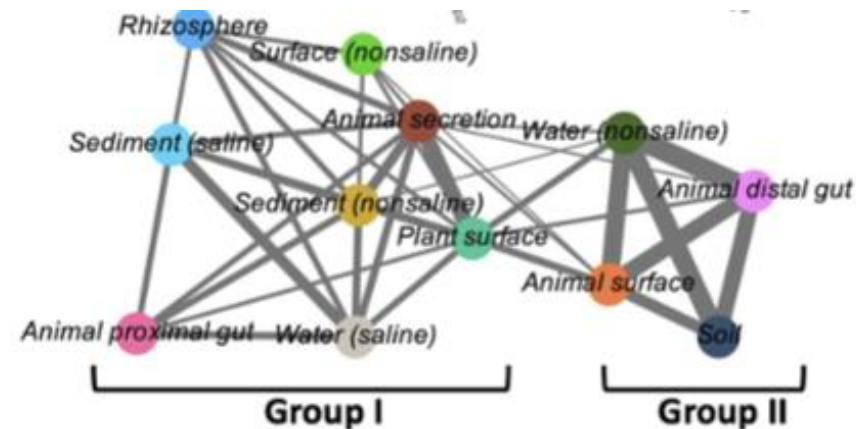
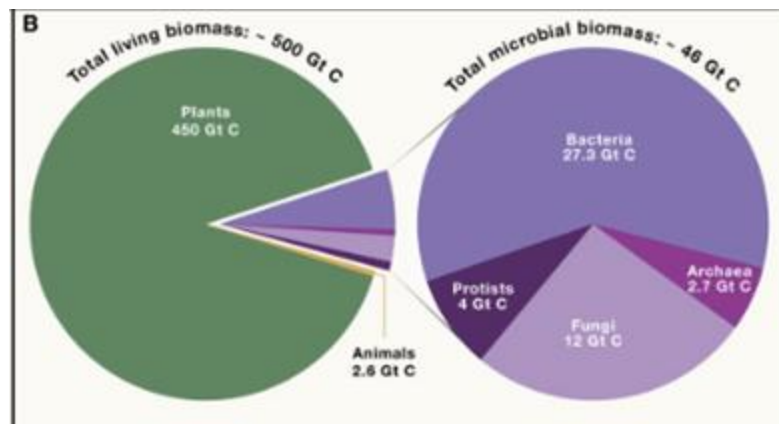
- Microbes inhabit every part of the planet.
- They play crucial roles in the health of humans, animals, plants, soil, and marine environments
- Shared principles of ecosystems: diversity, richness, resilience, adaptation
- The microbiome serves as a keystone for ecosystem health



Ma et al. Microbiome (2020)

The Planetary Microbiome

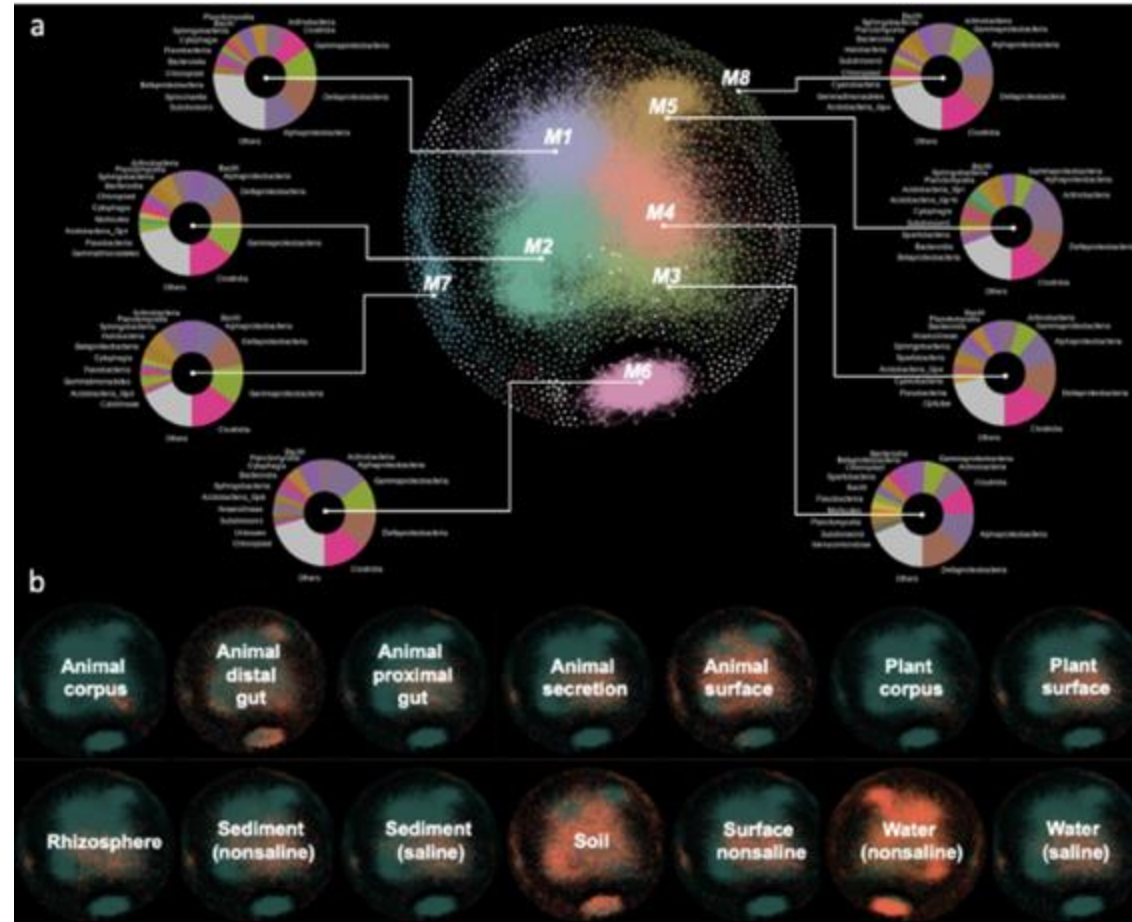
- There are five nonillion (1 followed by 54 zeros) bacteria in the Earth's ecosystem, including the ones found in living beings
- Microbes are the oldest and most abundant lifeform on the planet (>4 B years)
- Microbes are the second biggest biomass on earth (70 G tons, 15% of global) only surpassed by plants



- Microbes make up 70% of marine biomass

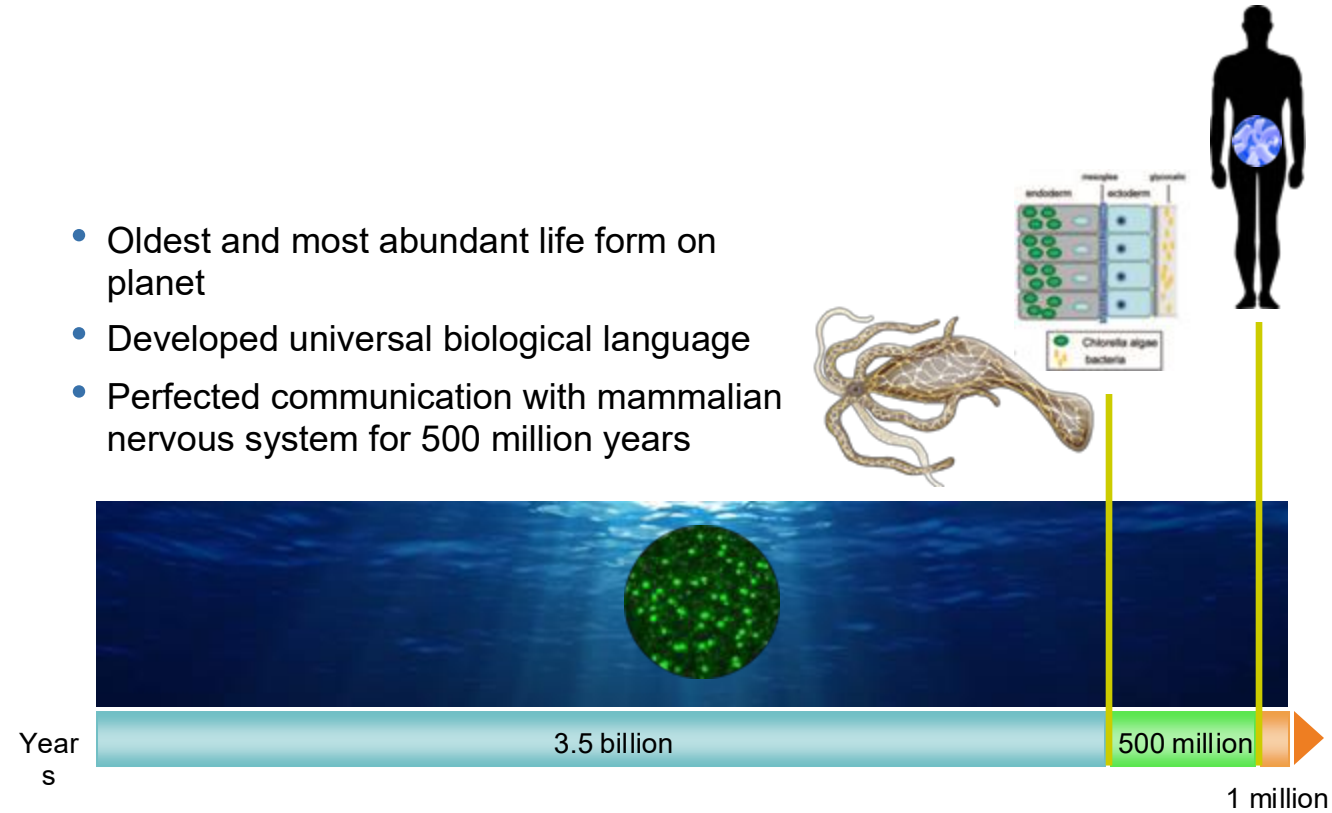
The Interconnectedness of the Planetary Microbiome

- Earth microbial co-occurrence network from:
 - 23,595 samples and 12,646 exact sequence variants
 - from 14 environments in the Earth Microbiome Project dataset.
- *Microbiomes of various environments were clustered into two groups,*
- *Clusters bridged by the microbiomes of plant and animal surface.*

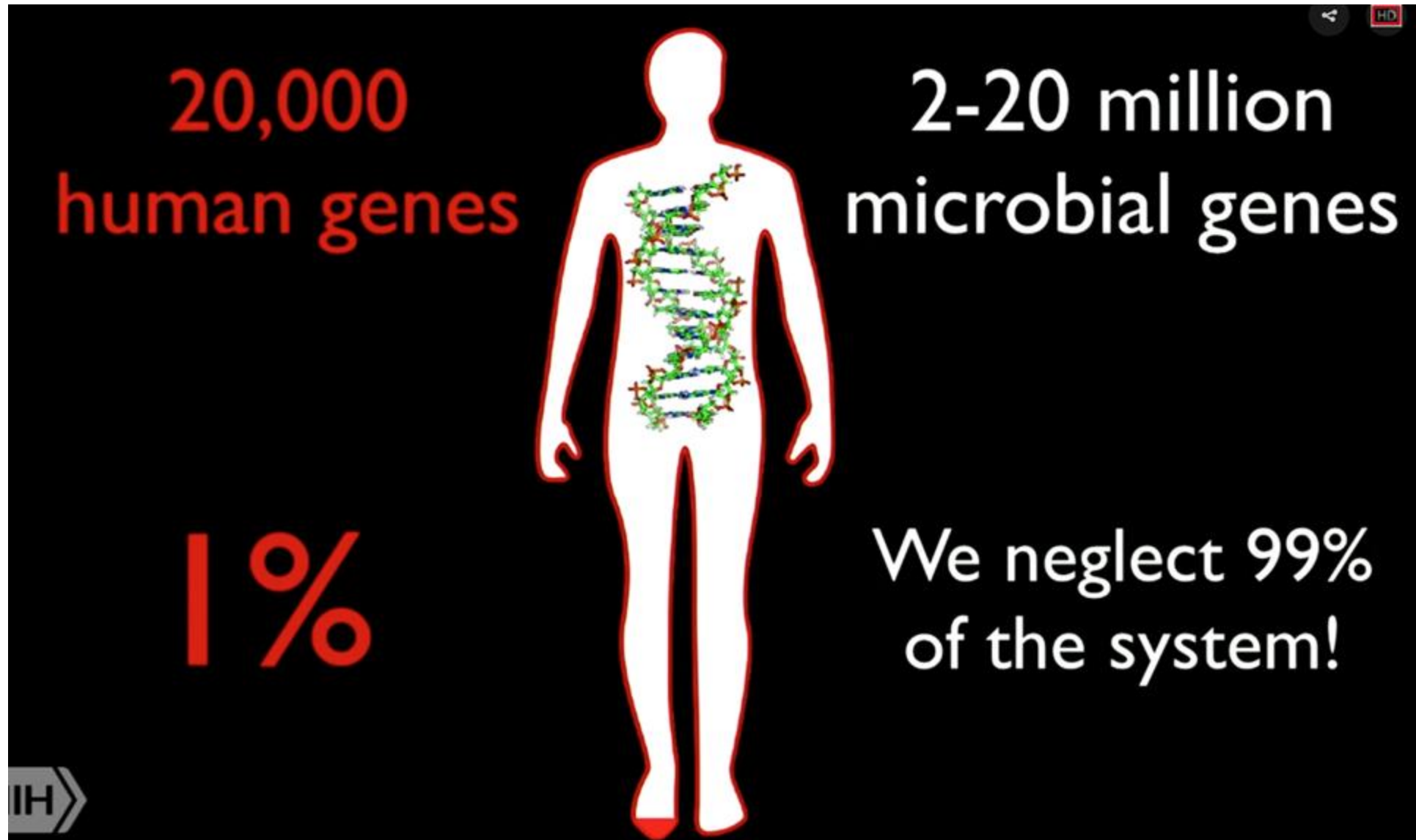


The Origin Story of the Human Gut Microbiome with the Brain

- Oldest and most abundant life form on planet
- Developed universal biological language
- Perfected communication with mammalian nervous system for 500 million years



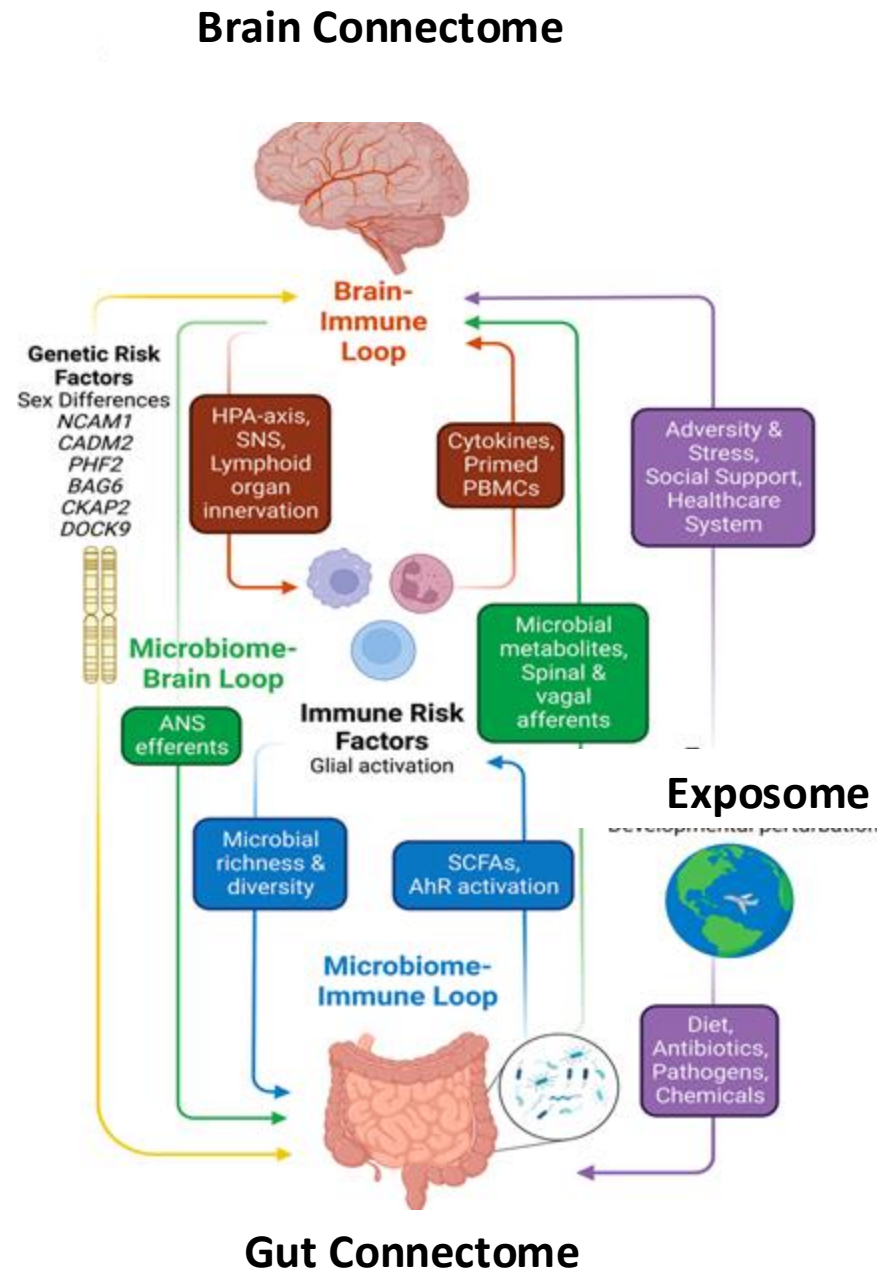
The Human Microbiome – We Are Only Scratching On the Surface



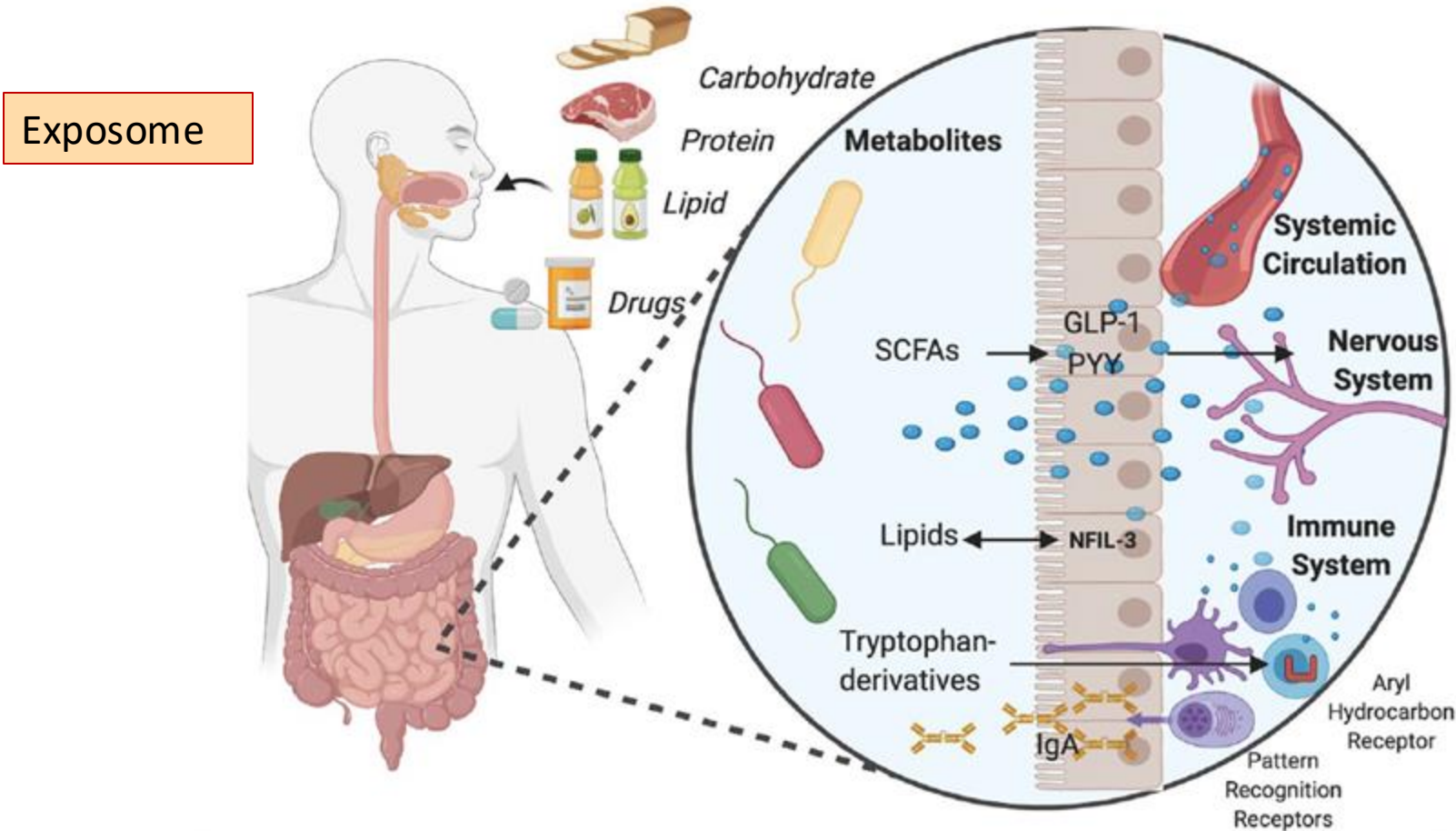
Presented by Dr. R. Knight at NIH Emerging Themes symposium, August 16-18, 2017

The Brain Gut Microbiome Immune System

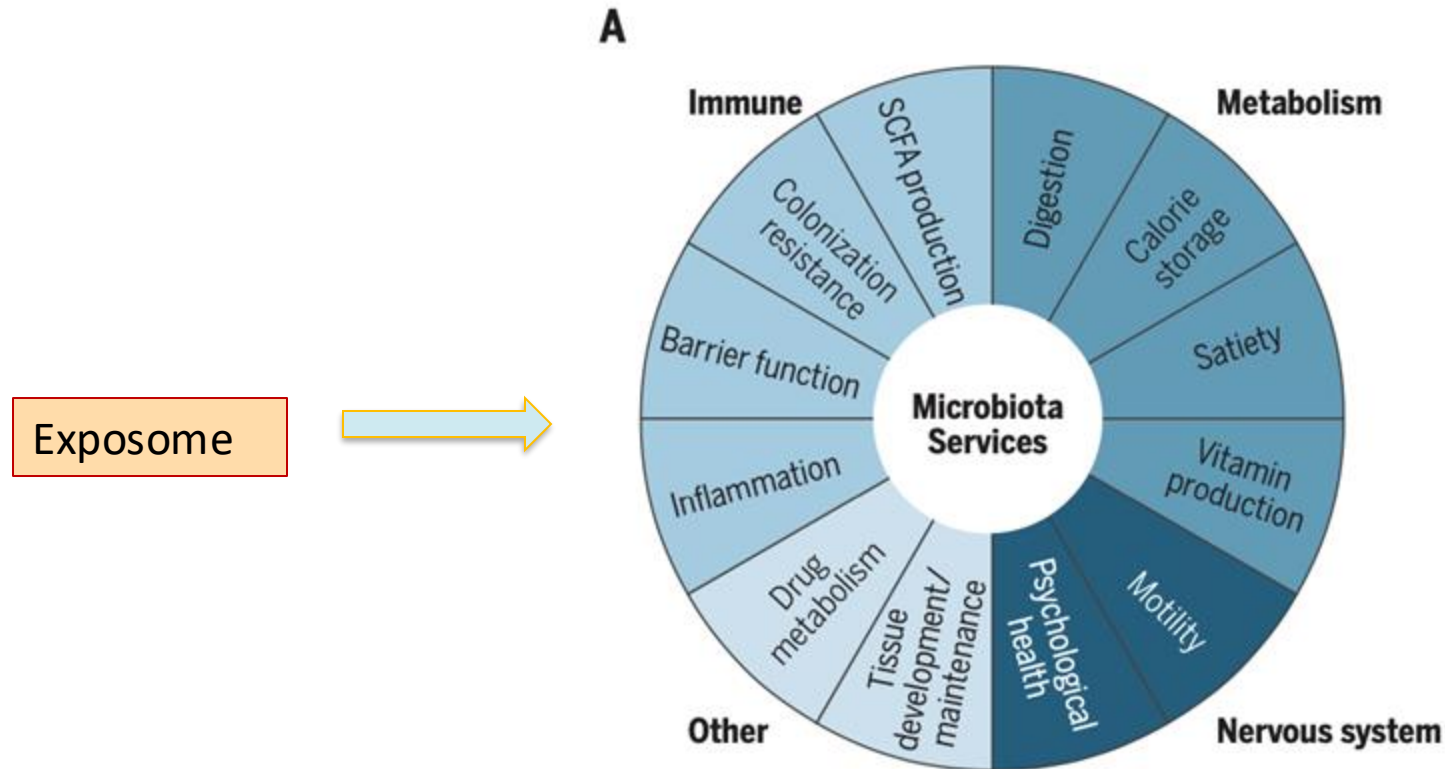
The brain, gut, microbiome and immune system are interconnected via multiple bidirectional communication loops. This BGM systems receives input from interoceptive bodily signals and from the exposome.



The Microbiome Translates Food Components into Thousands of Biologically Active Metabolites Circulating throughout the Body, Including the Brain

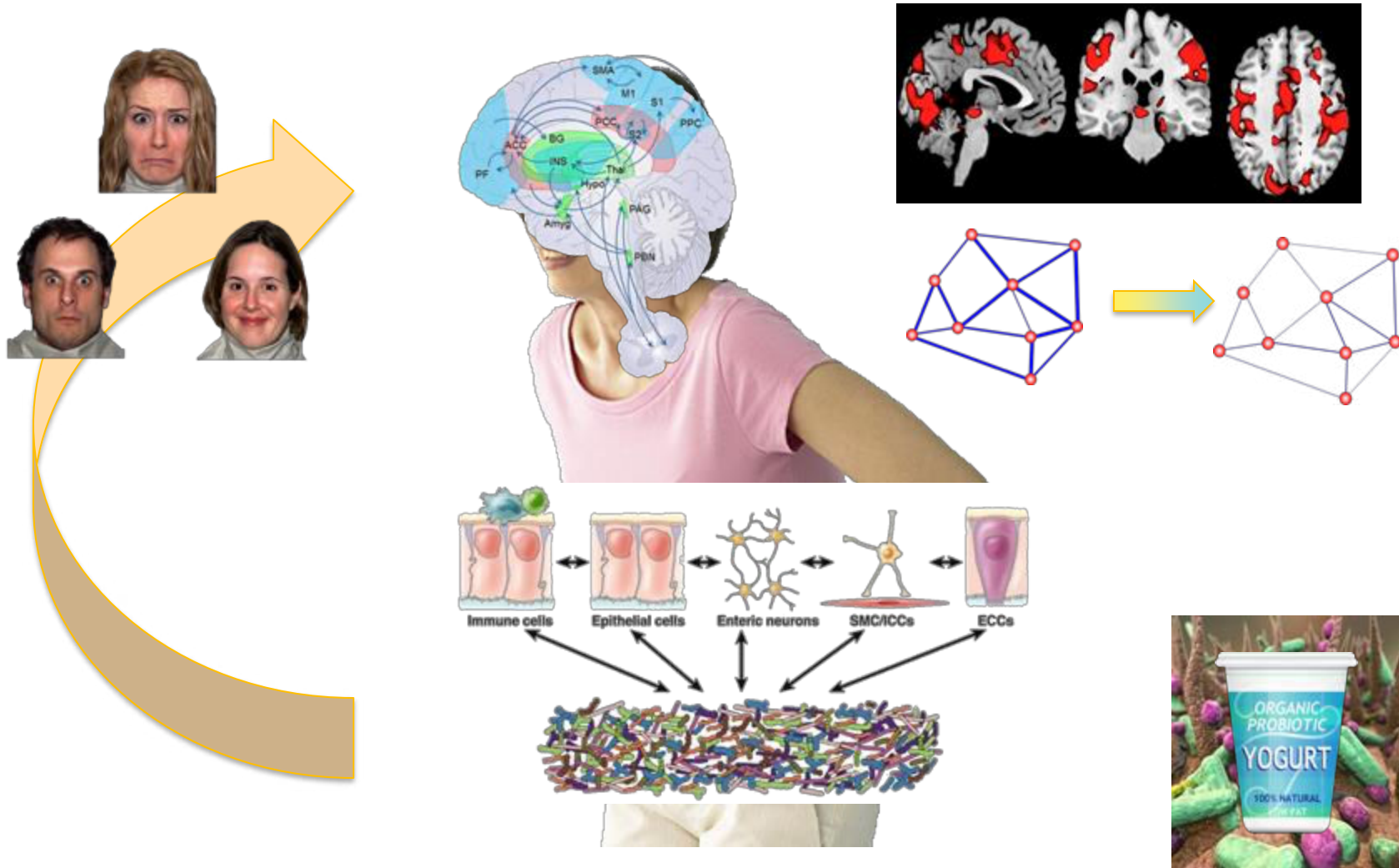


The Gut Microbiome is a Key Interface between the Exposome And Our Immune, Nervous Systems & Metabolism

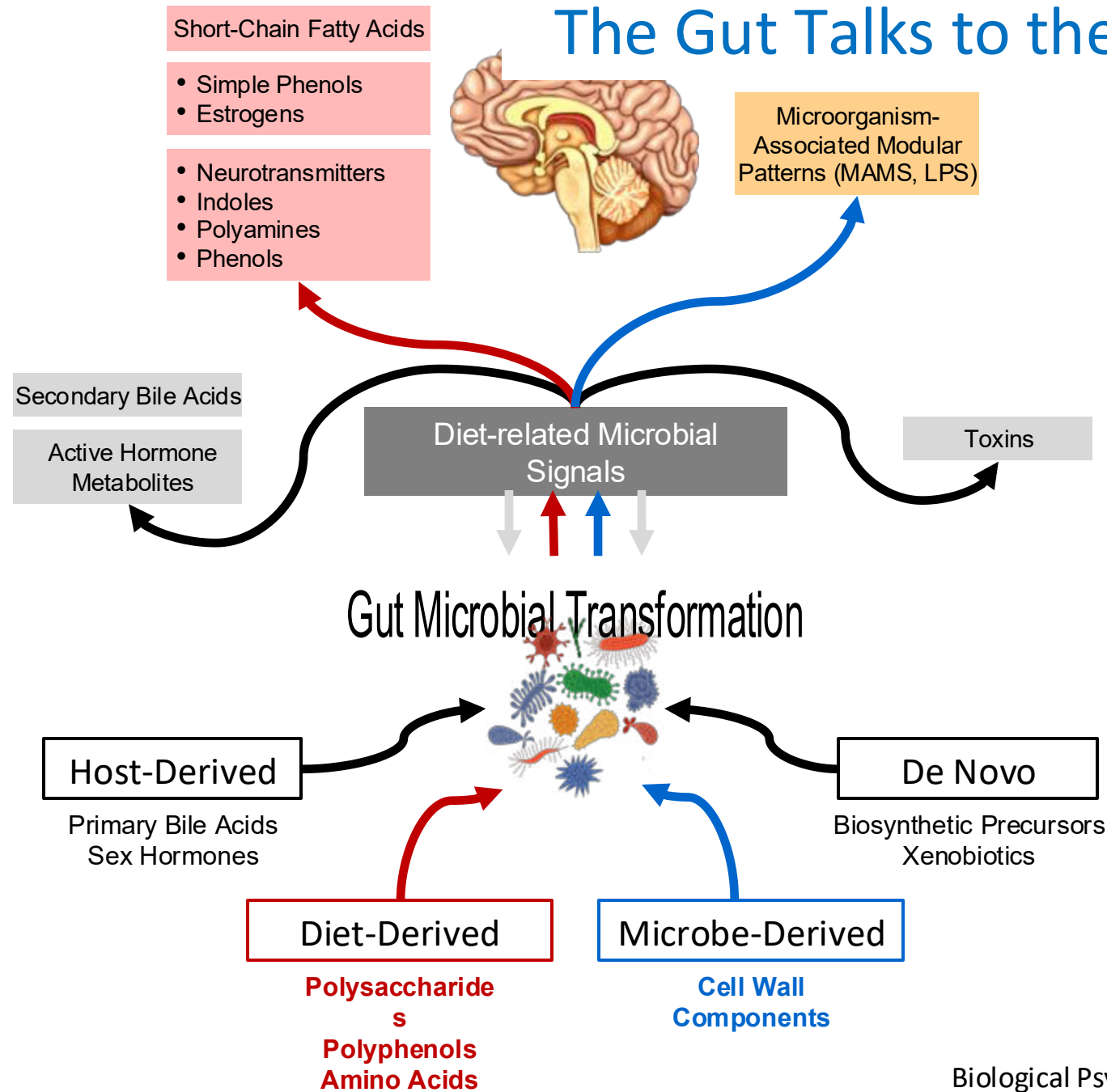


Courtesy of E. Sonnenburg

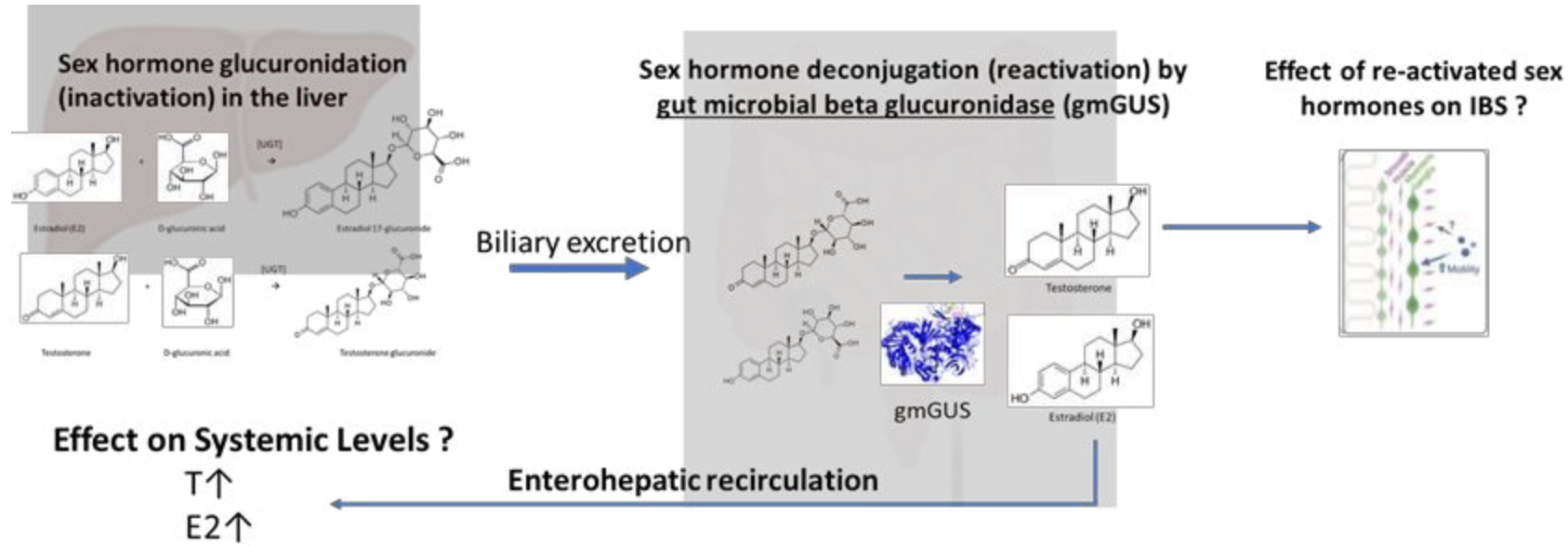
Microbes in the Gut Can Talk to the Brain



The Gut Talks to the Brain



The Gut Microbiome Influences Systemic Estrogen Levels



- Estrogen glucuronides formed in the liver are secreted with the bile into the small intestine
- Gut microbes in the ileum convert some of these metabolites into absorbable molecules
- These reabsorbed estrogen molecules increase the estrogen levels in the systemic circulation

The Gut and its Microbiome Are a Mirror Image of our Emotions

Psychosocial
Stress

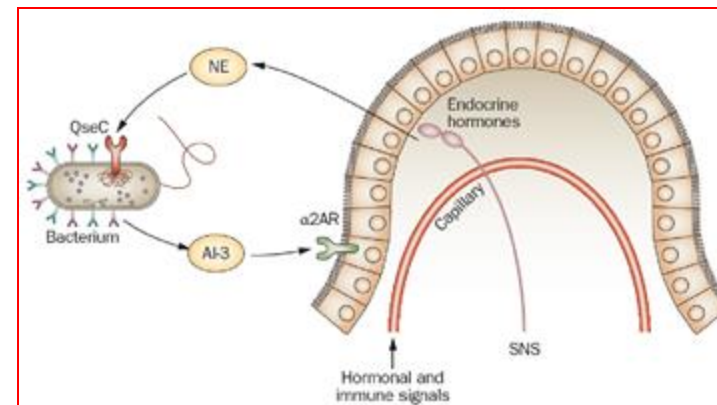
Anxiety, fear
Anger
Sadness



Changes of the microbial habitat:

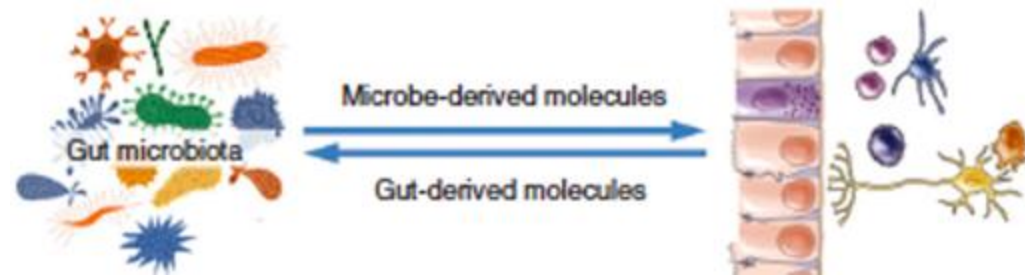
- Regional GI motility and transit
- Intestinal fluid and mucus secretion (biofilm?)
- Gastric/bile acid secretion
- Paneth cell secretion (antimicrobials)
- **Enteroendocrine cell function**
- Intraintestinal pH
- **Immune modulation**
- Epithelial & blood brain barrier permeability

Changes in microbial behavior:



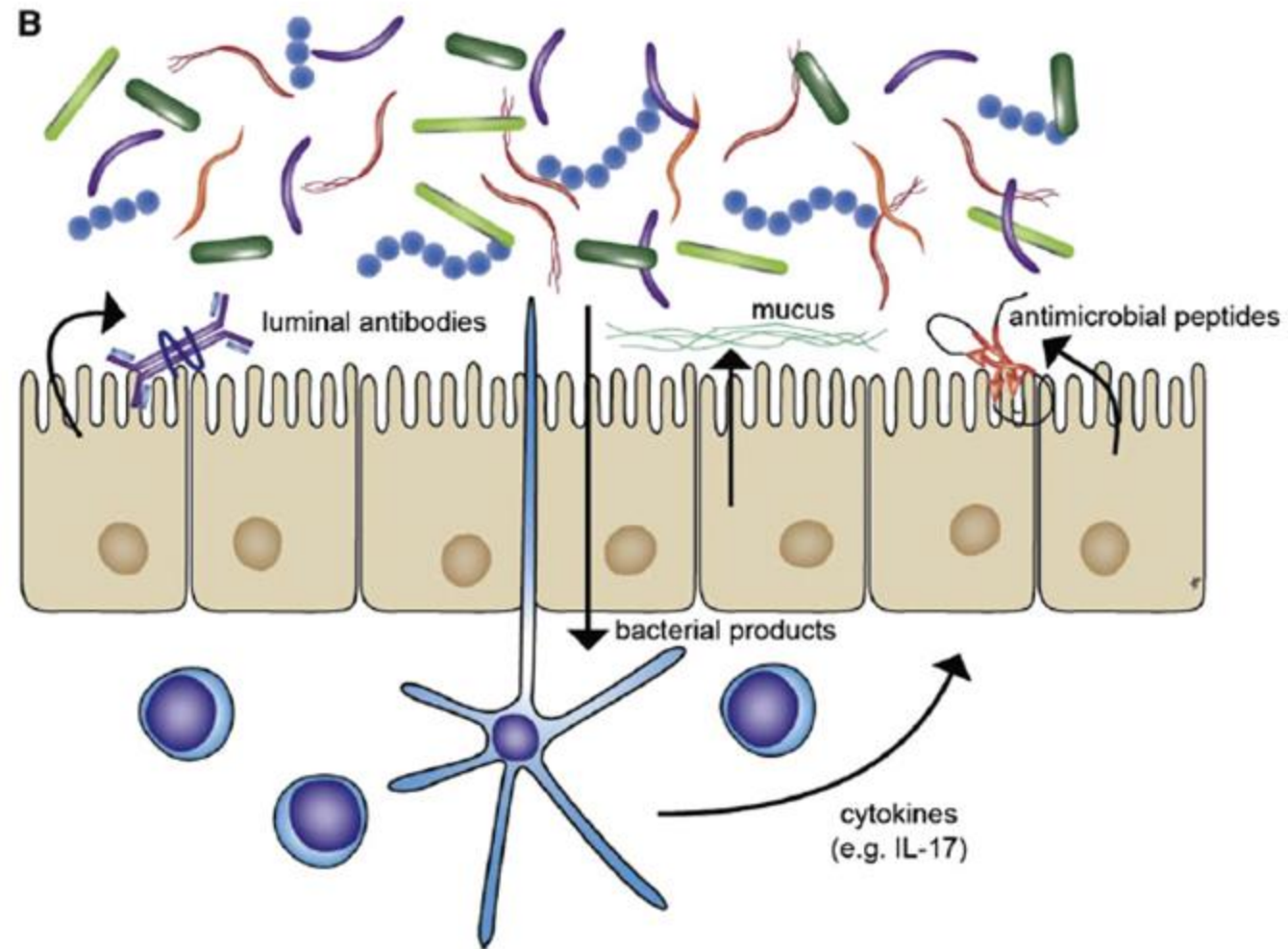
What Has Gone Wrong in the Human Microbial Ecosystem?

Traditional Symbiotic Relationship of Gut Microbiome and Gut Connectome



Symbiotic relationship between ancient gut microbiome with human GI tract over a 1 M years

Multiple Bidirectional Interactions of Gut Associated Immune System with Gut Microbiome



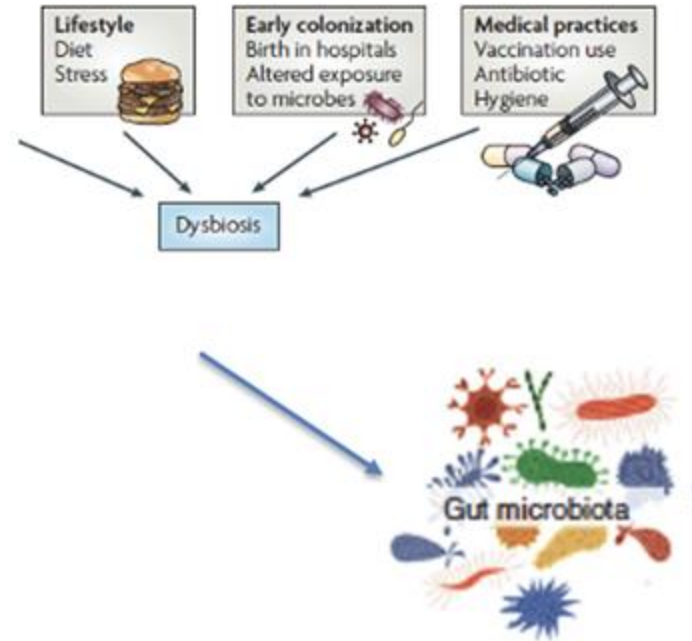
Vulnerability of the Industrialized Microbiota

One world, One Health

- As people increasingly move to cities, their lifestyles profoundly change.
- The shift of recent generations from rural, outdoor environments to urbanized and industrialized settings has profoundly affected our biology and health.
- The signals of change are seen most strikingly in the reduction of commensal microbial taxa and loss of their metabolic functions.
- The extirpation of human commensals is a result of bombardment by new chemicals, foodstuffs, sanitation, and medical practices.

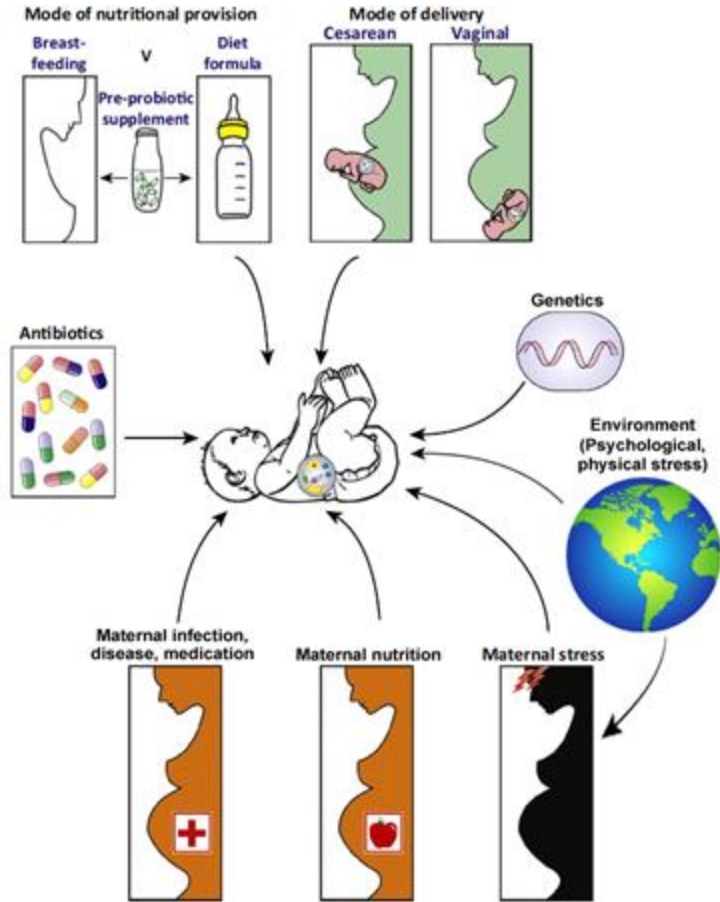
Rapid Adaptation of the Gut Microbiome to Changing Exposome during past 75 Years

Dramatic changes of exposome during past 75 years

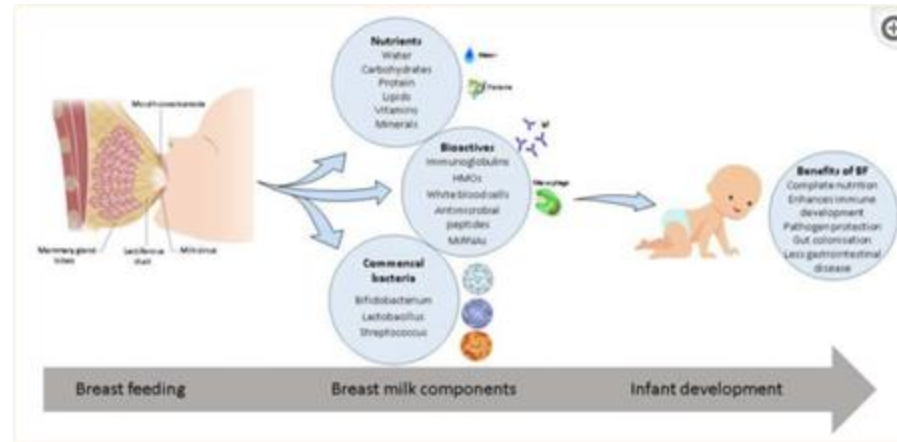


Rapid (days)
adaptation of relative
abundances, diversity
and function to
changing exposome

Early Programming of Gut Microbiome



Prenatal Programming



Postnatal Programming

Lyons et al, Nutrients 2020

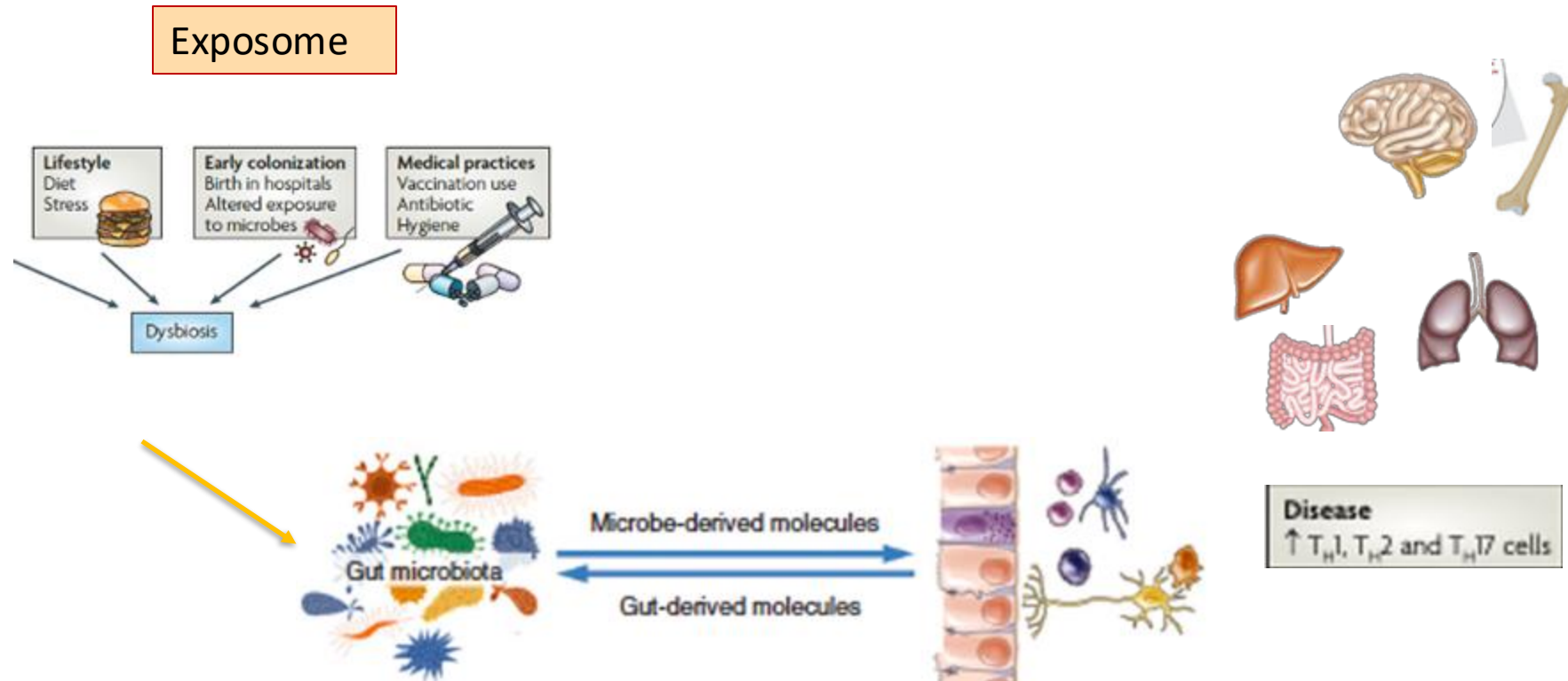
Jasarevic & Bale, 2019

Antibiotic Consumption by the Numbers

- >73 billion doses worldwide yearly
- 258 million courses (833/1000) in USA (2010):
- 2.7 courses by age 2; 10.9 courses by age 10



Poor Gut Health Can Have Widespread Effects on the Body



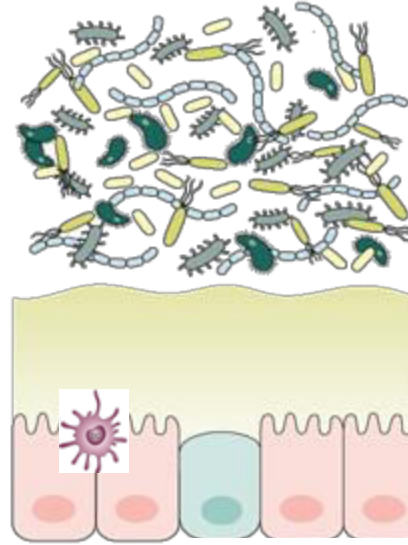
Healthy Diet

- Complex carbohydrates
- High fiber
- ☐ Fiber degradation
- ☐ Gut microbiome diversity
- ☐ Abundance of mucus-stimulating microorganisms
- ☐ Prevotella abundance

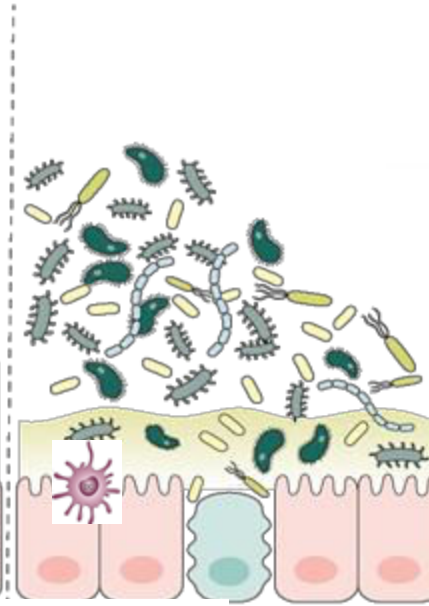
☐ Mucus thickness

Intact gut barrier

Healthy Gut



“Leaky” Gut



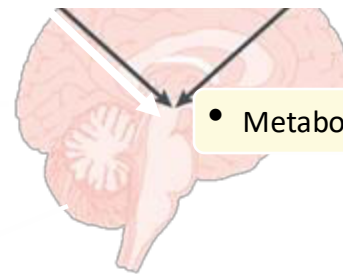
Chronic Stress

Western diet

- Refined carbohydrates, sugar
- High fat
- Low fiber
- ☐ Fiber degradation
- ☐ Gut microbiome diversity
- ☐ Abundance of mucus-stimulating microorganisms
- ☐ Prevotella abundance

☐ Mucus thickness

☐ Gut barrier



• Metabolic endotoxemia

Increased genetic risk

Metabolic syndrome

Osteoporosis

NAFLD

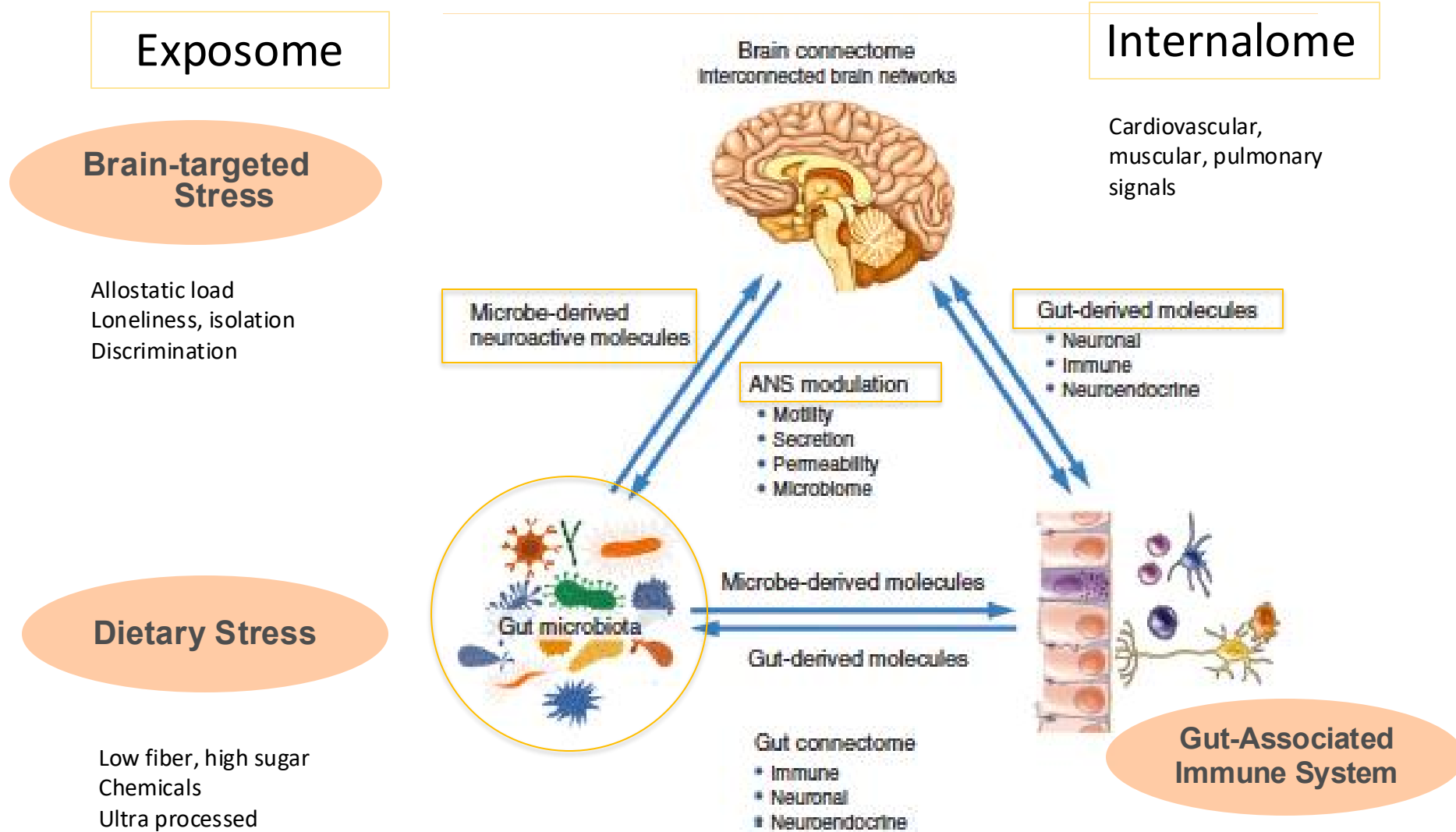
Colon cancer

Depression

Cognitive decline (AD)

Parkinson's Disease

Systems View of the Effects of Chronic Stress on Brain Gut Microbiome Interactions



The Detrimental Effects of Combined Chronic Psychological and Dietary Allostatic Load on Health Mediated by the Gut Microbiome

Increasing allostatic load is associated with:

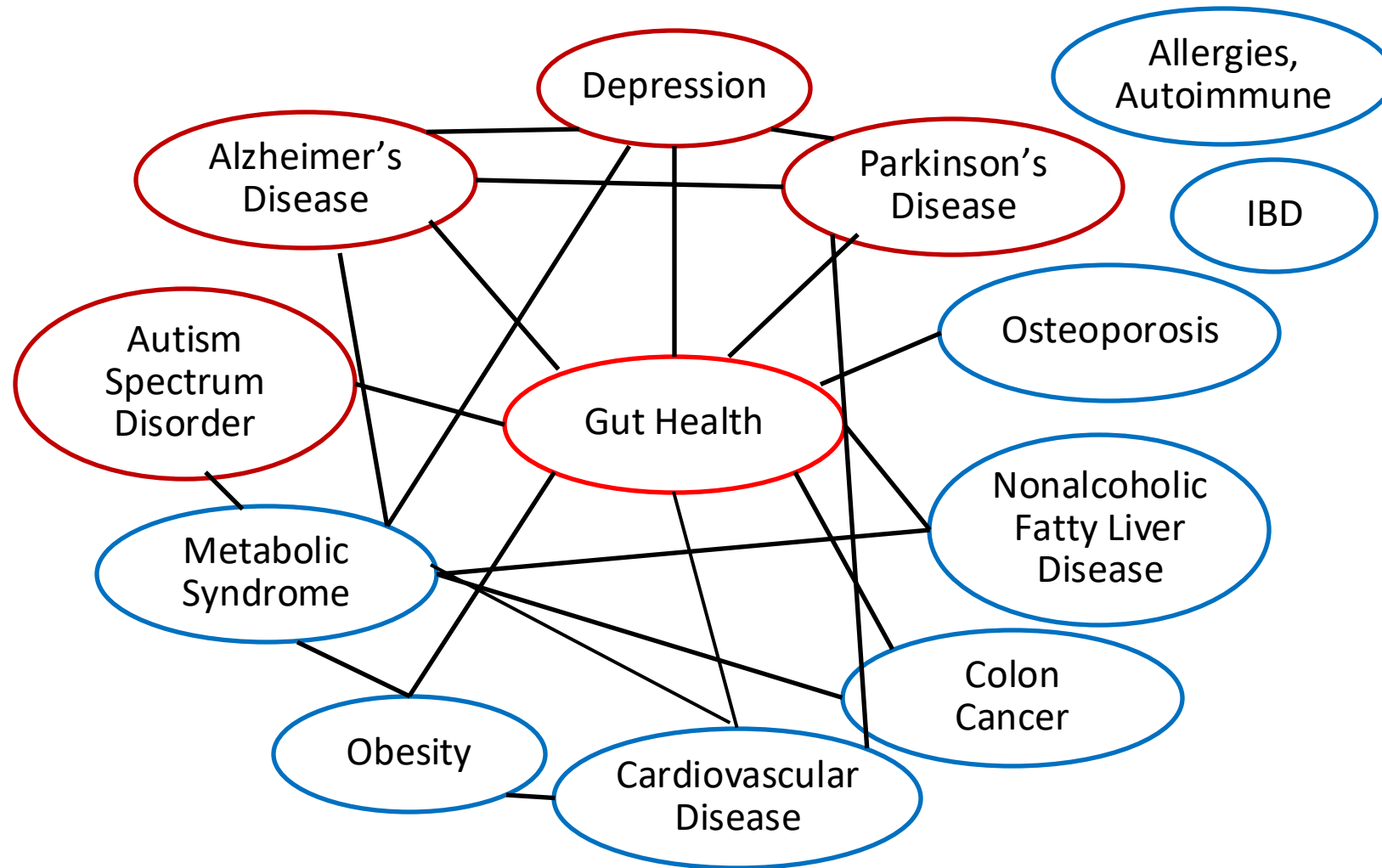
- Gut microbiome alterations
- Chronic systemic immune activation**
- Alterations in the body's metabolism
- Negative effects on many organ systems
- Structural and functional brain changes
- Chronic Non-infectious disease



Increased risk for Chronic Non-Infectious Diseases:

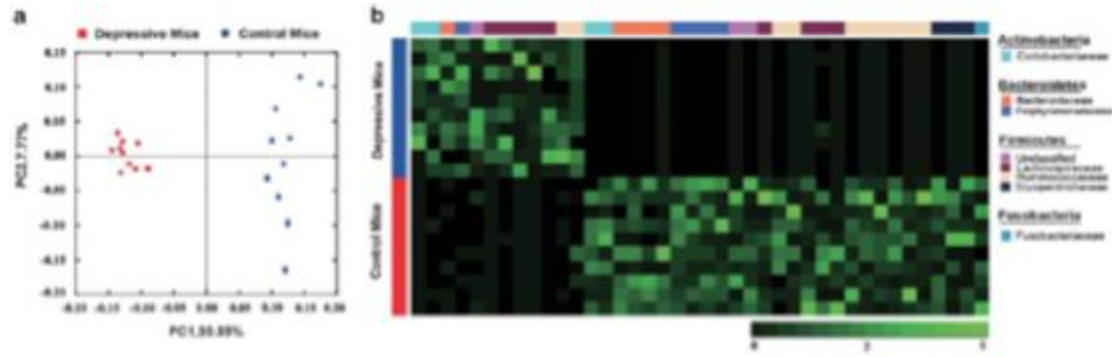
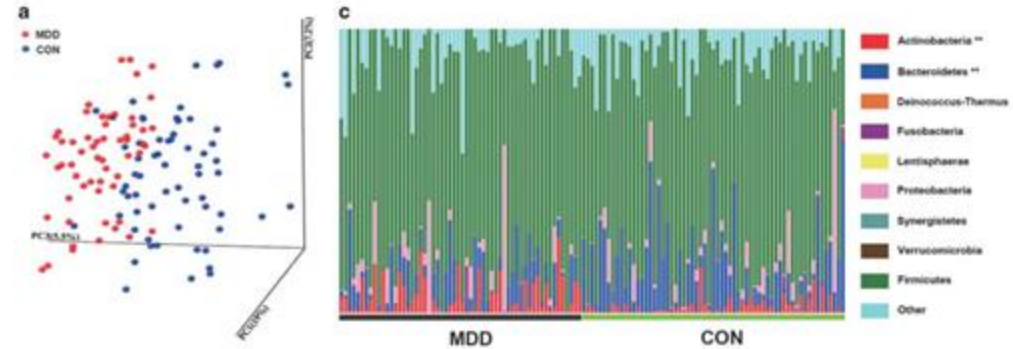
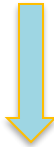
- Obesity
- Metabolic syndrome
- Hypertension
- Cardiovascular disease
- Chronic pain
- Cognitive Decline
- Depression
- Cancer

Gut Health is at the Center of the Chronic Non-Communicable Disease Network



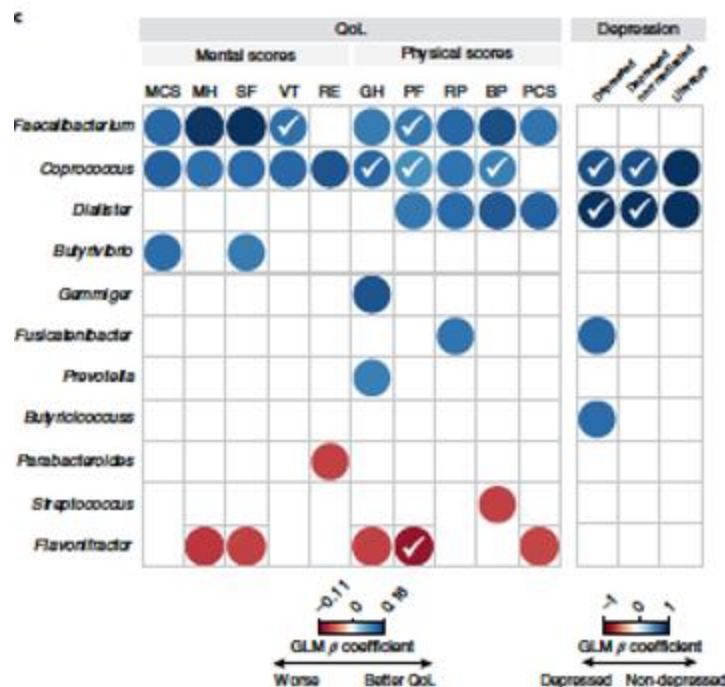
Depression:

Fecal Microbial Transfer of Altered Gut Microbiota from Patients with Major Depressive Disorder to GF Mice



The neuroactive potential of the human gut microbiota in quality of life and depression

Mireia Valles-Colomer^{1,2}, Gwen Falony^{1,2}, Youssef Darzi^{1,2}, Etti F. Tigchelaar³, Jun Wang^{1,2}, Raul Y. Tito^{1,2,4}, Carmen Schiweck⁵, Alexander Kurilshikov³, Marie Joossens^{1,2}, Cisca Wijmenga^{3,6}, Stephan Claes^{5,7}, Lukas Van Oudenhove^{7,8}, Alexandra Zhernakova³, Sara Vieira-Silva^{1,2,9} and Jeroen Raes^{1,2,9*}



- Butyrate-producing *Faecalibacterium* and *Coprococcus* bacteria were associated with higher QoL indicators.
- Gut–brain module analysis of faecal metagenomes indicated a potential role of microbial GABA production in depression.
- Together with *Dialister*, *Coprococcus* spp. were also depleted in depression

Gut Microbiome Alterations in Depression

nature communications



Article

<https://doi.org/10.1038/s41467-022-34502-3>

Gut microbiome-wide association study of depressive symptoms

Received: 28 May 2021

Accepted: 26 October 2022

Published online: 06 December 2022

Djawad Radjabzadeh¹, Jos A. Bosch ^{2,3}, André G. Uitterlinden ^{1,4},
Aeilko H. Zwinderman⁵, M. Arfan Ikram ⁴, Joyce B. J. van Meurs¹,
Annemarie I. Luik ⁴, Max Nieuwdorp ⁶, Anja Lok ⁷, Cornelia M. van Duijn ^{4,8},
Robert Kraaij ¹  & Najaf Amin ^{4,8} 

Thirteen microbial taxa, including genera Eggerthella, Subdoligranulum, Coprococcus, Sellimonas, Lachnospiraceae, Hungatella, Ruminococcaceae, Lachnospiraceae, Eubacterium and family Ruminococcaceae were associated with depressive symptoms.

“These bacteria are known to be involved in the synthesis of glutamate, butyrate, serotonin and gamma amino butyric acid (GABA), which are key neurotransmitters for depression”

SCIENTIFIC REPORTS



OPEN

Long-term benefit of Microbiota Transfer Therapy on autism symptoms and gut microbiota

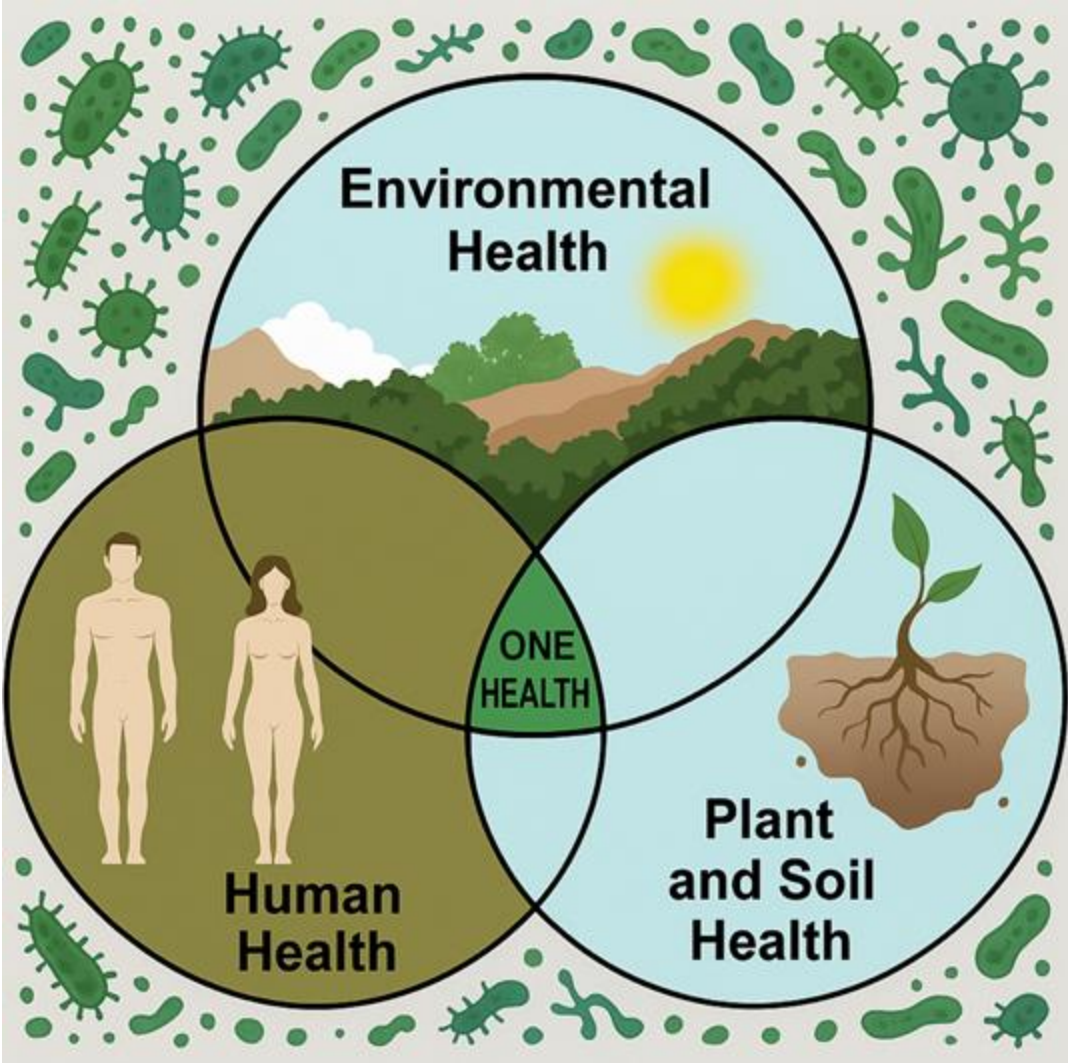
Received: 3 December 2018

Accepted: 5 March 2019

Published online: 09 April 2019

Dae-Wook Kang^{1,2,8}, James B. Adams³, Devon M. Coleman³, Elena L. Pollard³,
Juan Maldonado^{1,2}, Sharon McDonough-Means⁴, J. Gregory Caporaso^{5,6} &
Rosa Krajmalnik-Brown^{1,2,7}

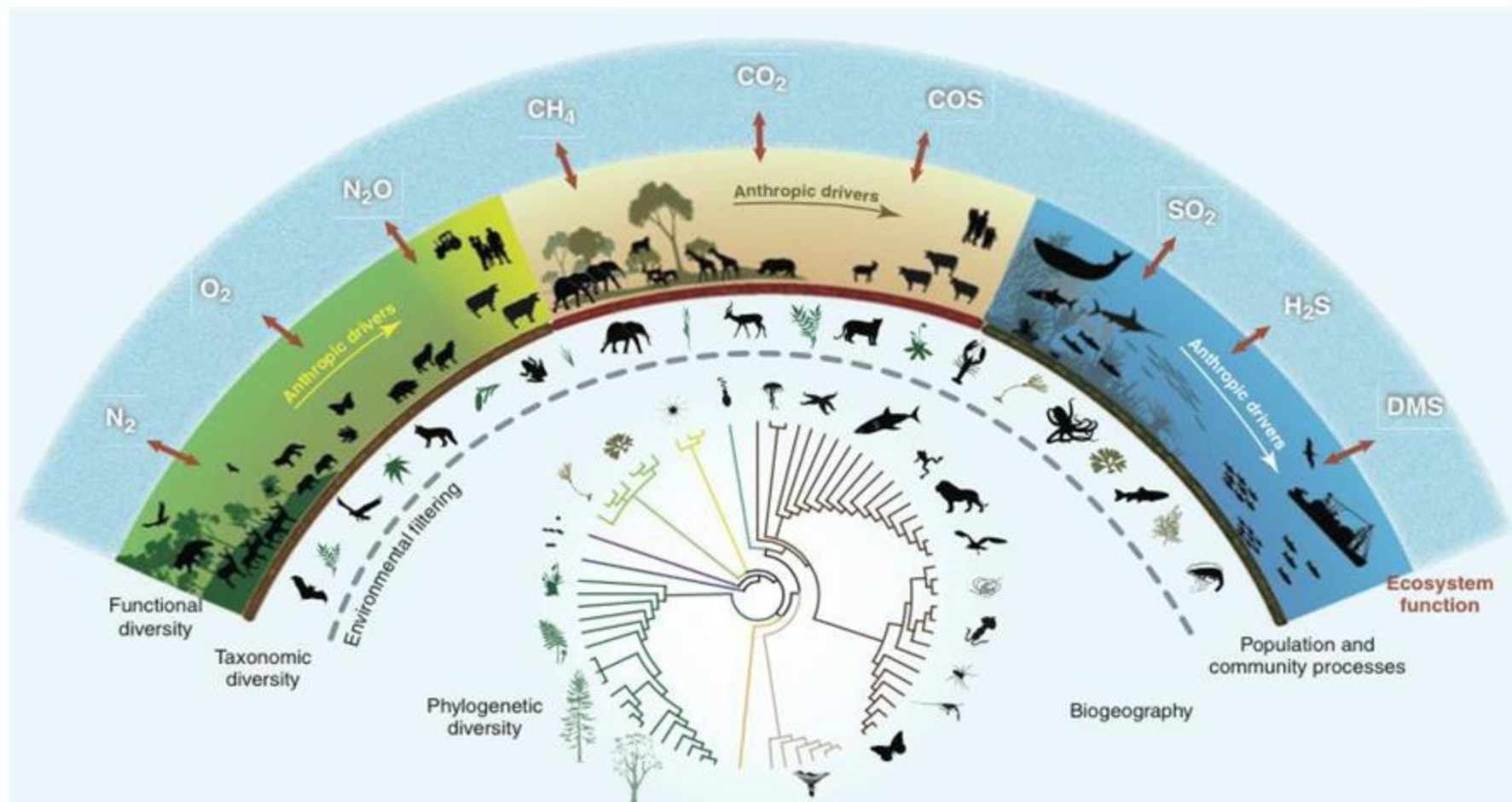
The Planetary Microbiome Connects Different Domains of Health



The Functions of Biological Diversity in an Age of Extinction

Shahid Naeem,^{1*} J. Emmett Duffy,² Erika Zavaleta³

www.sciencemag.org SCIENCE VOL 336 15 JUNE 2012



Courtesy from F. DeClerck

Plant Health & Human Food Supply in the Age of Extinction

* Since the 1900s, some 75% of plant genetic diversity has been lost as farmers worldwide have left their multiple local varieties and landraces for genetically uniform, high-yielding varieties.

* 30 percent of livestock breeds are at risk of extinction; six breeds are lost each month.

* Today, 75 percent of the world's food is generated from only 12 plants and five animal species.

* Of the 4 percent of the 250 000 to 300 000 known edible plant species, only 150 to 200 are used by humans. Only three - rice, maize and wheat - contribute nearly 60 percent of calories and proteins obtained by humans from plants.

* Animals provide some 30 percent of human requirements for food and agriculture and 12 percent of the world's population live almost entirely on products from ruminants.

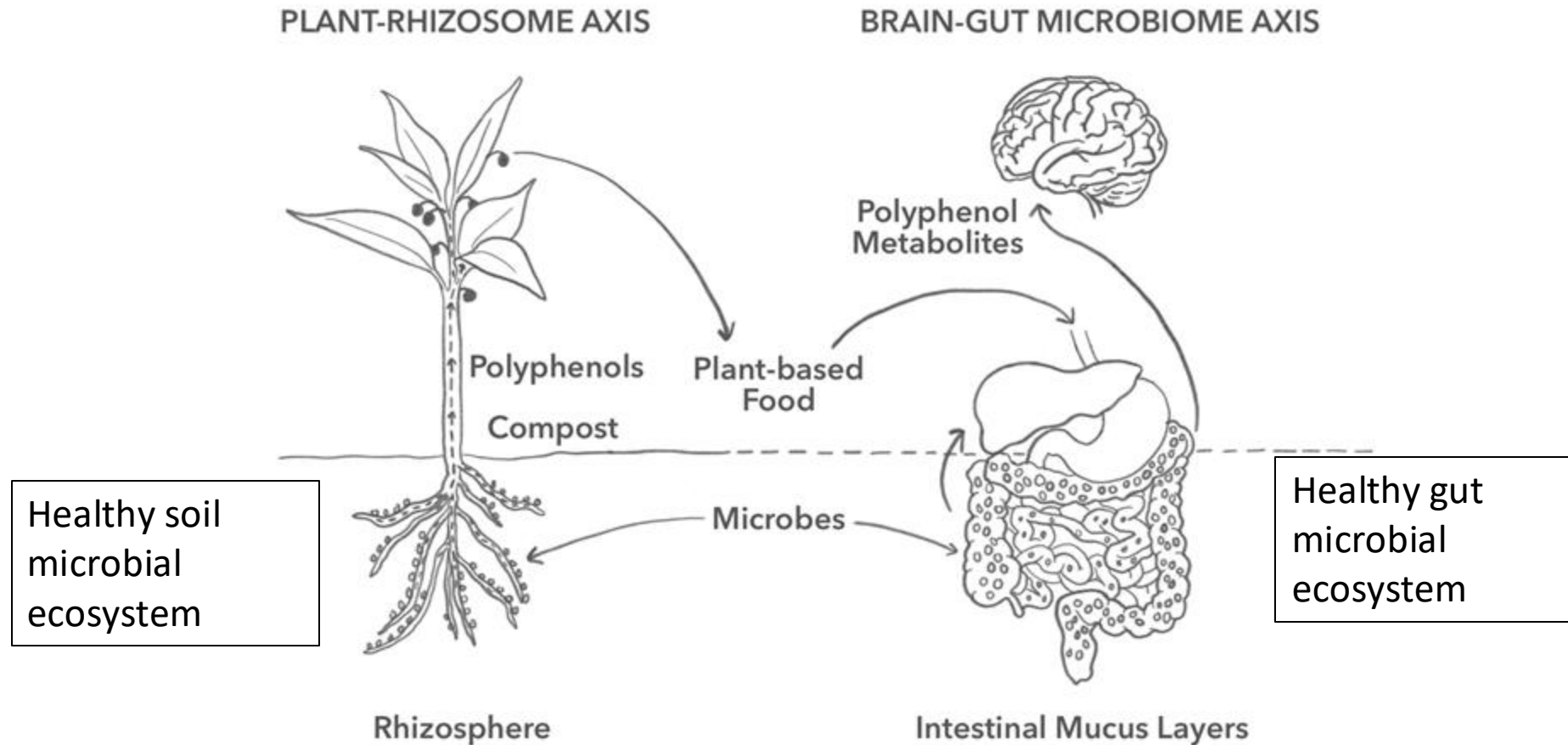
Animal Health & the Microbiome

- Livestock and companion animals depend on healthy gut microbiota
 - Dysbiosis in pigs, calves and chickens associated with Intestinal inflammation and mortality and treated with antibiotics
- Influences disease resistance, growth, and welfare
- Zoonotic interface: role of microbial ecosystems in pandemics

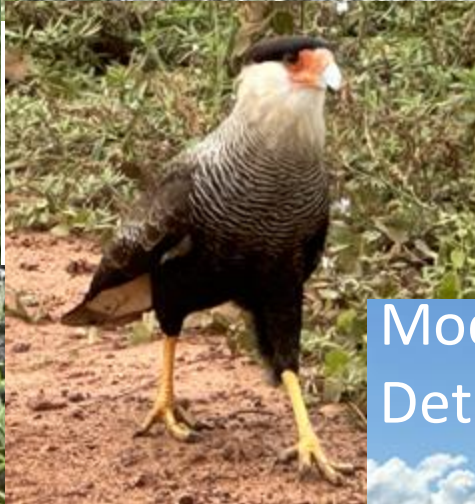
Plant & Soil Microbiomes

- Rhizosphere microbiome: nutrient cycling, disease suppression, stress resilience
- Impacts of pesticides, herbicides, monocultures, climate change
- Role of regenerative agriculture

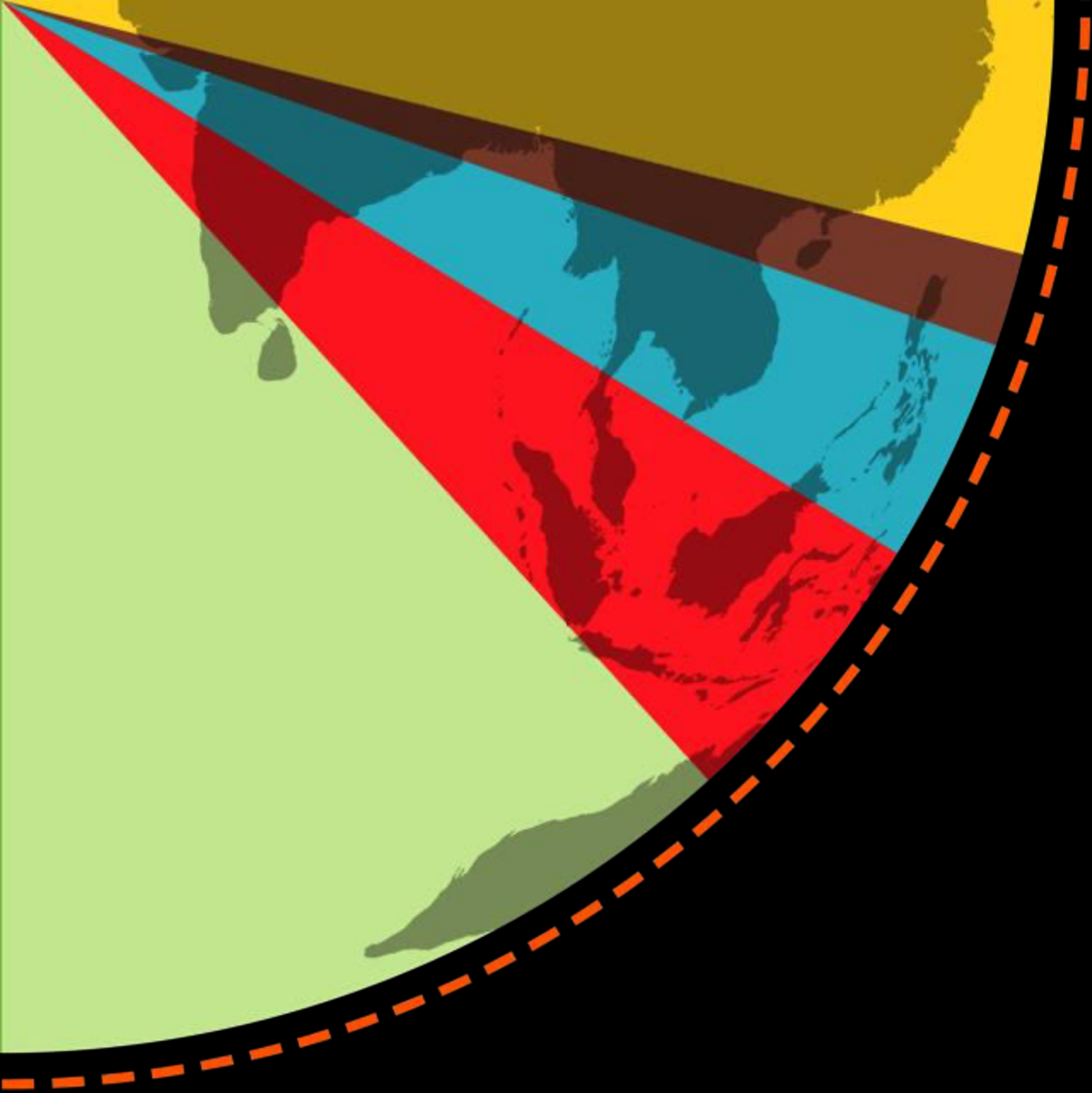
The Close Connection Between Soil Health and the Health of the Gut Microbial Ecosystems



**1 gram of soil harbors
10 trillion (10^{10}) microbial cells
10 000 different microbial species**



Modern Food Production is Detrimental for the Planet



The EAT-Lancet
Commission on
Healthy
Diets From
Sustainable Food
Systems

Food Planet Health



Our Food in the Anthropocene: Healthy Diets From Sustainable Food Systems

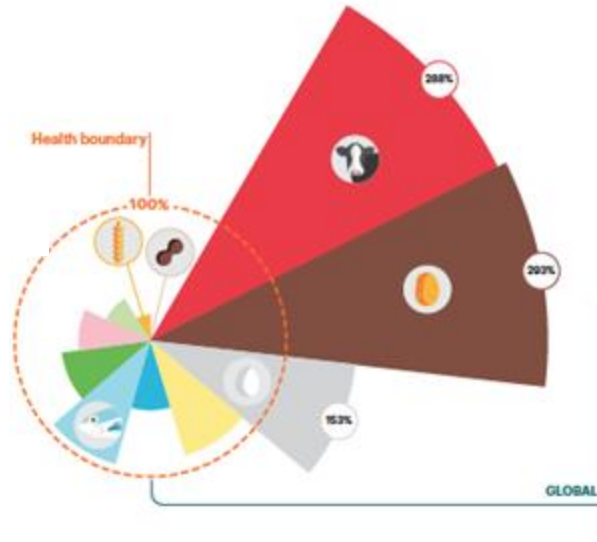


Prof. Walter Willett MD
Harvard T.H. Chan School of Public Health

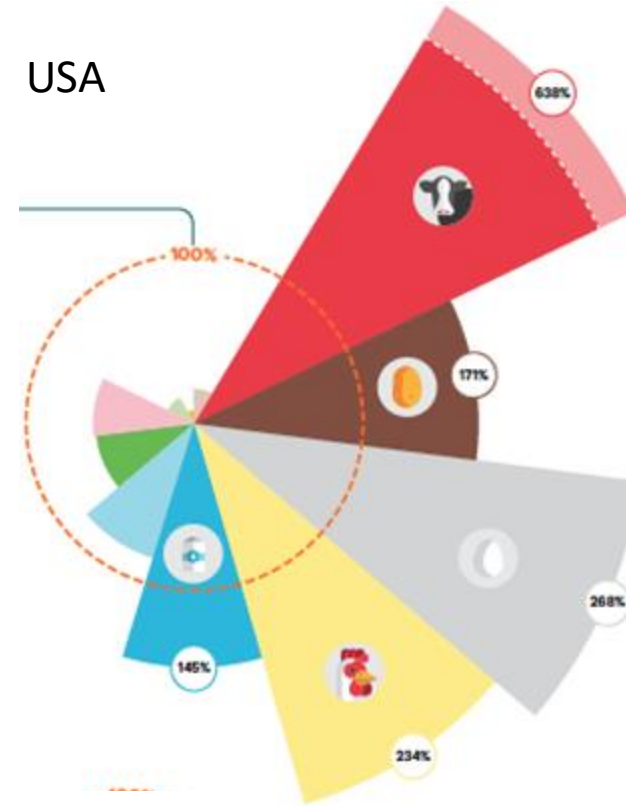
“Transformation to healthy diets by 2050 will require substantial dietary shifts. Global consumption of fruits, vegetables, nuts and legumes will have to double, and consumption of foods such as red meat and sugar will have to be reduced by more than 50%. A diet rich in plant-based foods and with fewer animal source foods confers both improved health and environmental benefits.”

Transformation to healthy diets by 2050

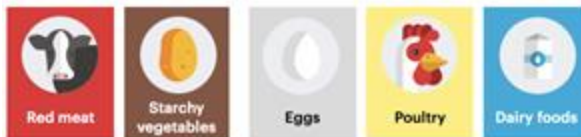
Global



USA



Limited intake



Optional foods

Emphasized foods



Approach 1 Comparative Risk	19%	or	11.1 million adult deaths per year
Approach 2 Global Burden of Disease	22.4%	or	10.8 million adult deaths per year
Approach 3 Empirical Disease Risk	23.6%	or	11.6 million adult deaths per year

Healthy Diet for Humans and the Planet

“Food is the single strongest lever to optimize human health and environmental sustainability on Earth”

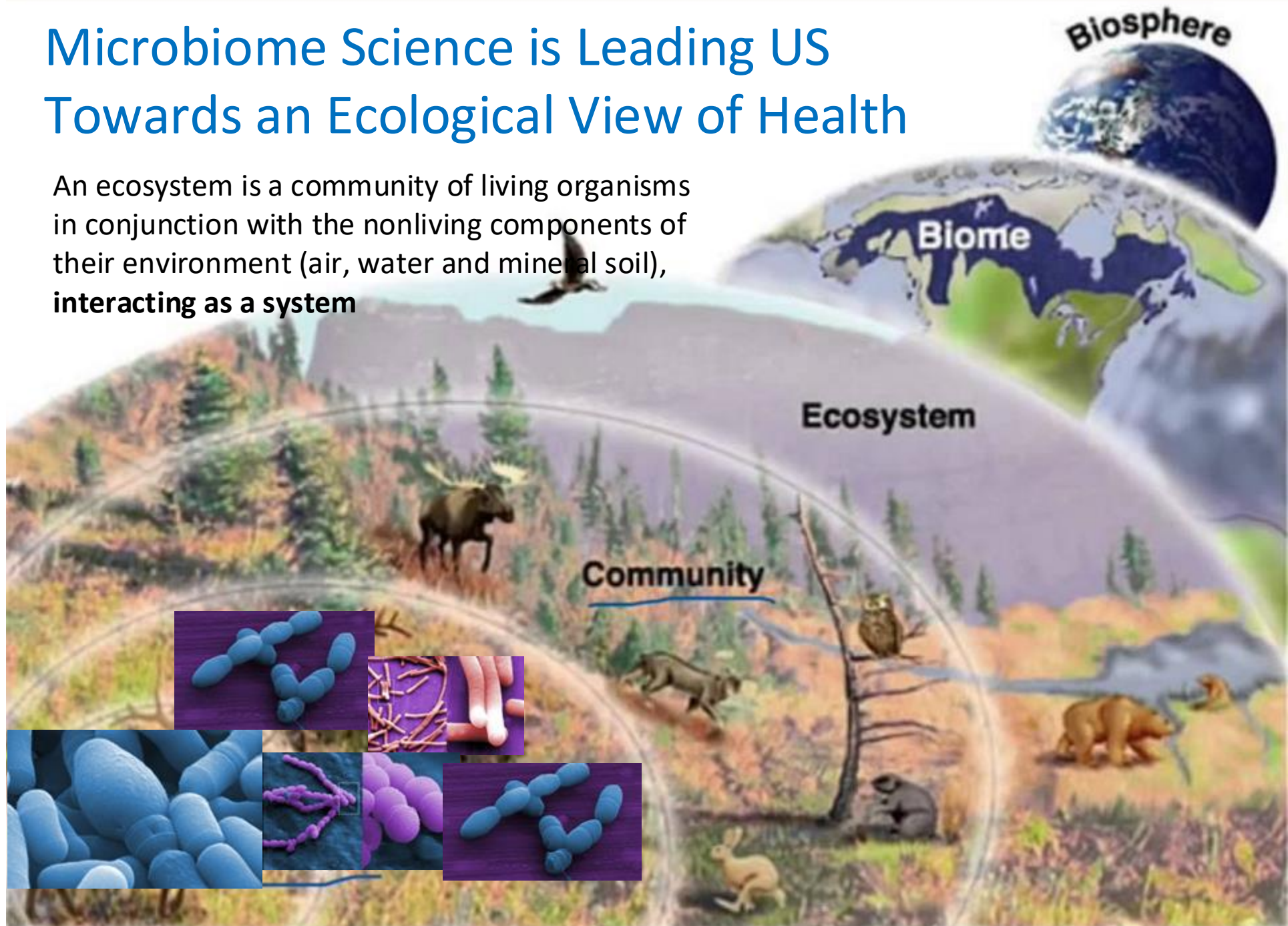


Healthy Diets

2500 kcal/day

Microbiome Science is Leading US Towards an Ecological View of Health

An ecosystem is a community of living organisms in conjunction with the nonliving components of their environment (air, water and mineral soil), **interacting as a system**



Conclusions

- The microbiome with its billions of years of evolution stored in millions of genes is the thread weaving human, animal, plant, and planetary health
- The human gut microbiome has the highest density of microorganisms on the planet and it translates dietary factors and environmental toxins into signals modulating the immune, metabolic and nervous system.
- Major disturbances of the health of our natural ecosystems by how we grow our food, how we interact socially, our exposure to chronic stress and how we treat our gut microbiome during the past 75 years are being translated into different aspects of human health and chronic diseases.

Conclusions

- Ecosystem deterioration and extinction of key players decreasing diversity, and richness is impacting key determinants of human and animal health:
 - Widespread low grade immune system activation
 - Reduced resilience to perturbations by the exposome to natural and pathogenic perturbations leading to reduced resilience
- The understanding and treatment of our most common chronic diseases require a systems biological understanding based on the interconnectedness of multiple ecosystems on planet Earth

Is Microbiome Science Causing a Fundamental Transformation of Our View of Health?



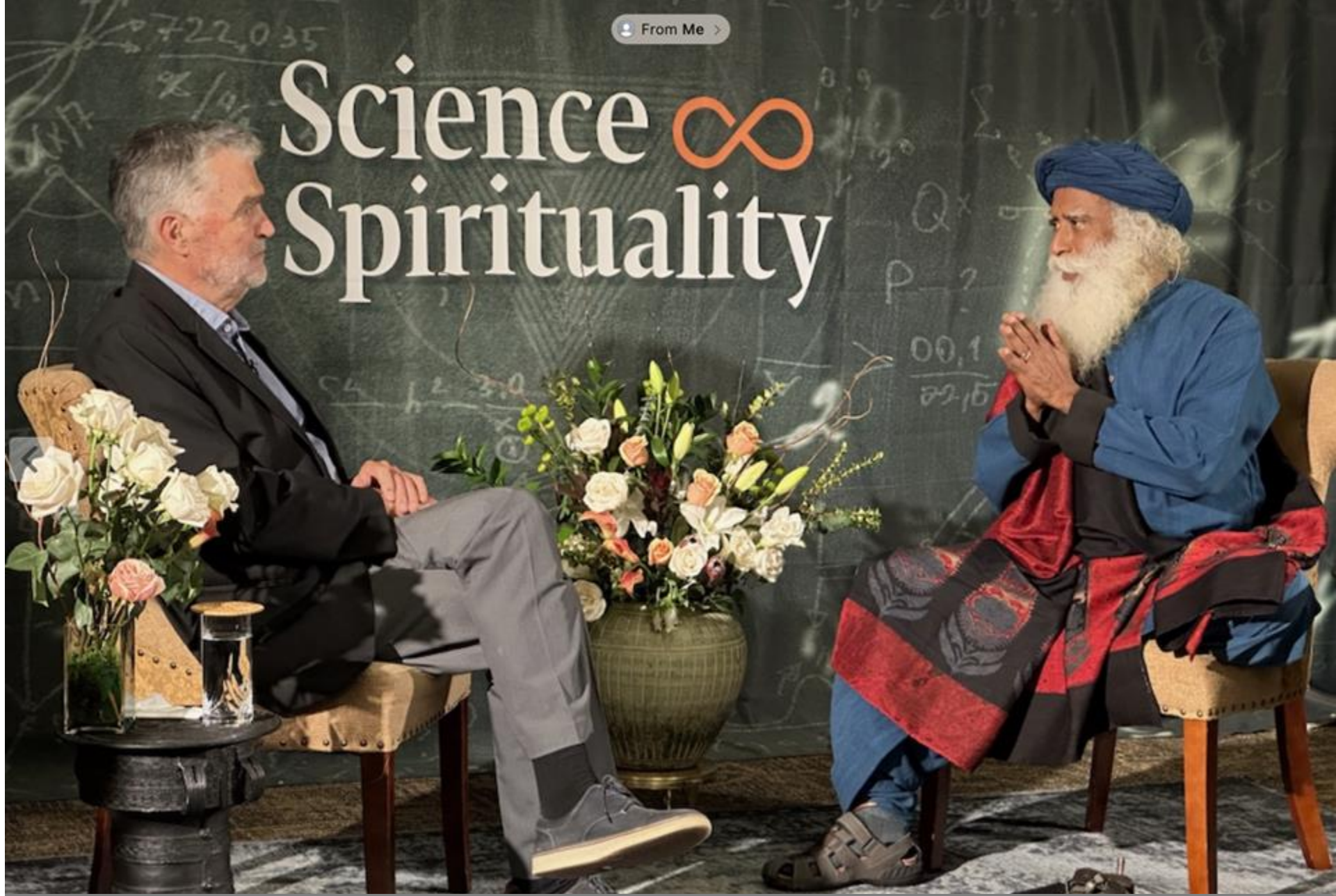
Science is a series of peaceful interludes punctuated by intellectually violent revolutions ... in each of which one conceptual world view is replaced by another..

The Structure of Scientific Revolutions,
Thomas S. Kuhn, 1962



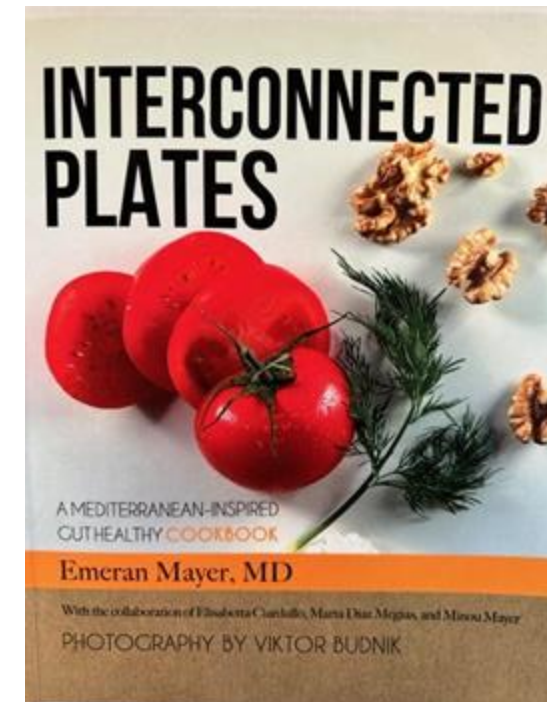
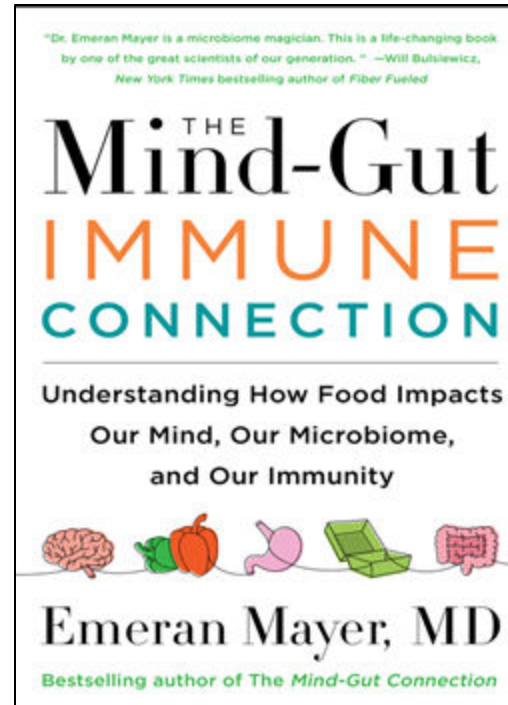
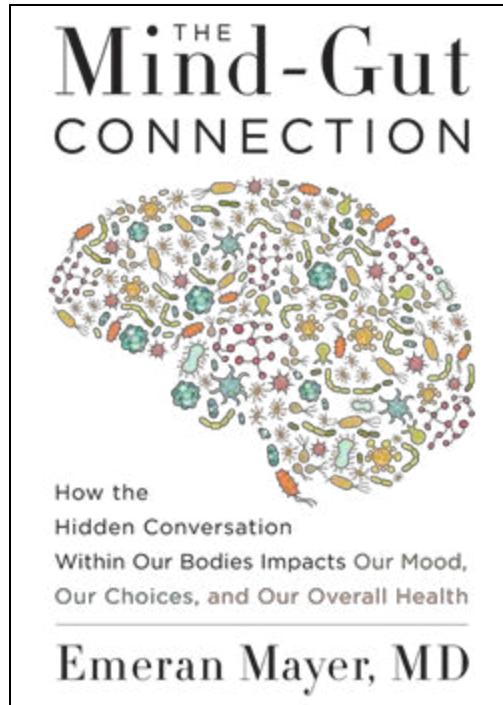
Courtesy of E.
Schadt

Science Spirituality



*Harvard Symposium on Consciousness-
Science, Spirituality and Social Impact, Boston Oct 26-27, 2023*

Thank You!



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