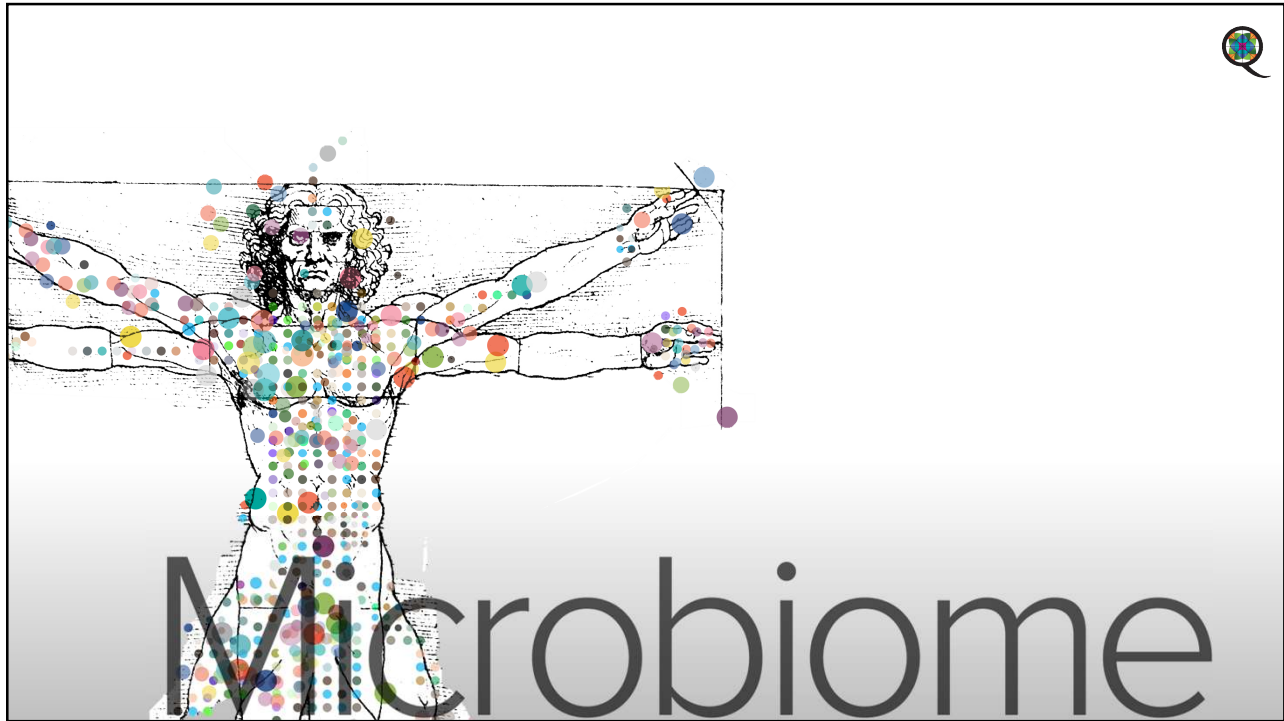


MARTHA'S QUEST



Parkinson's and the Gut Microbiome

By Martha Carlin



Microbiome

Microbiome
IN NUMBERS

100 Trillion The human body has more microbes than there are stars in the Milky Way.

95% of our microbes is located in the GI tract.

150:1 The genes in your microbiome outnumber the genes in our genome by about 150 to one.

>10,000 Number of different microbial species that researchers have identified living in and on the human body.

1.3X You have more microbes than human cells.

2kg The gut microbiota can weigh up to 2kg.

90% It is thought that 90% of disease can be linked in some way back to the gut and health of the microbiome.

5:1 Viruses:Bacteria in the gut microbiota.

2.5 The number of microbes would circle the earth 2.5 times if laid end to end.

Each individual has a unique gut microbiota, as personal as a fingerprint.

APC
Microbiome
Ireland
Interfacing Food & Medicine

The microbiome is more medically accessible and manipulable than the human genome.

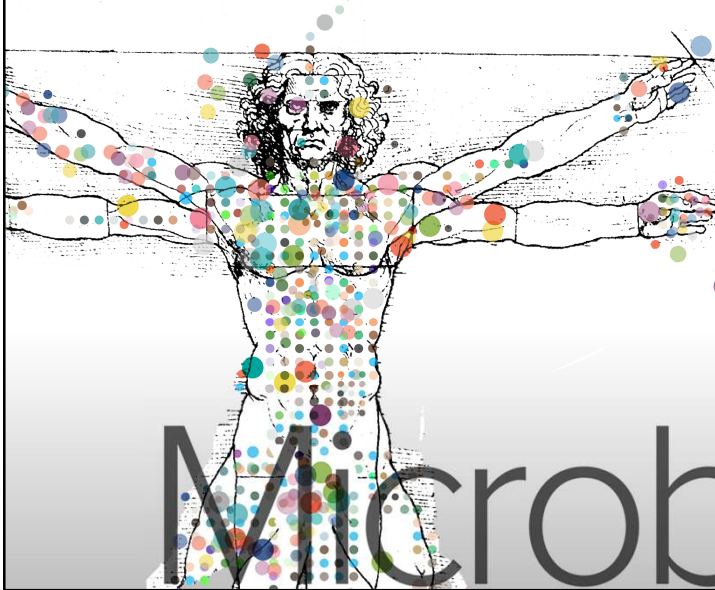
By The Numbers :

- 90% of disease can be connected in some way to the microbiome
- 1.3X more microbes than human cells
- 150:1 microbial genes to human genes
- 100 Trillion microbes in and on your body

<https://worldmicrobiomeday.com/resources/>

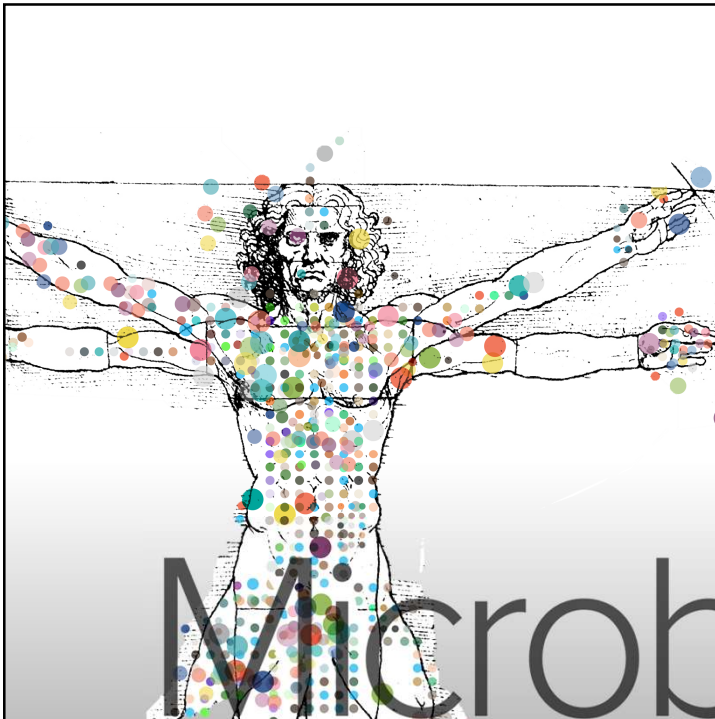
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Some of the Gut Microbiome Functions Are:



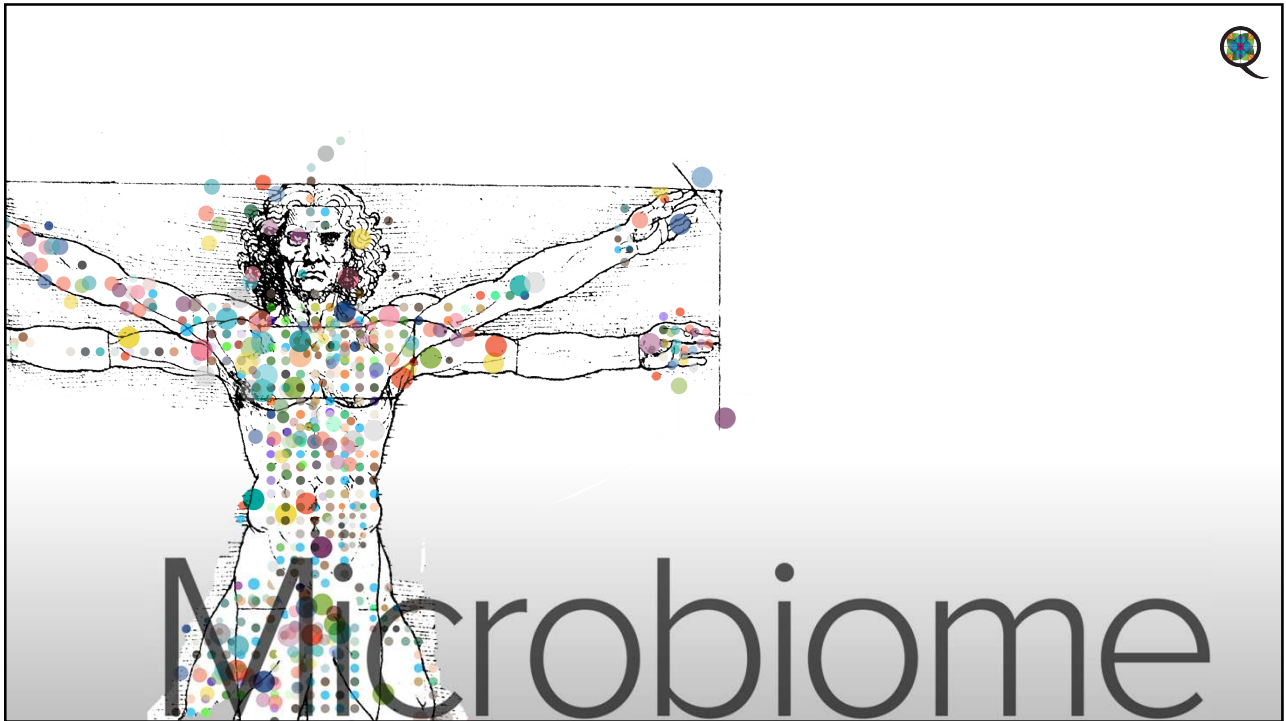
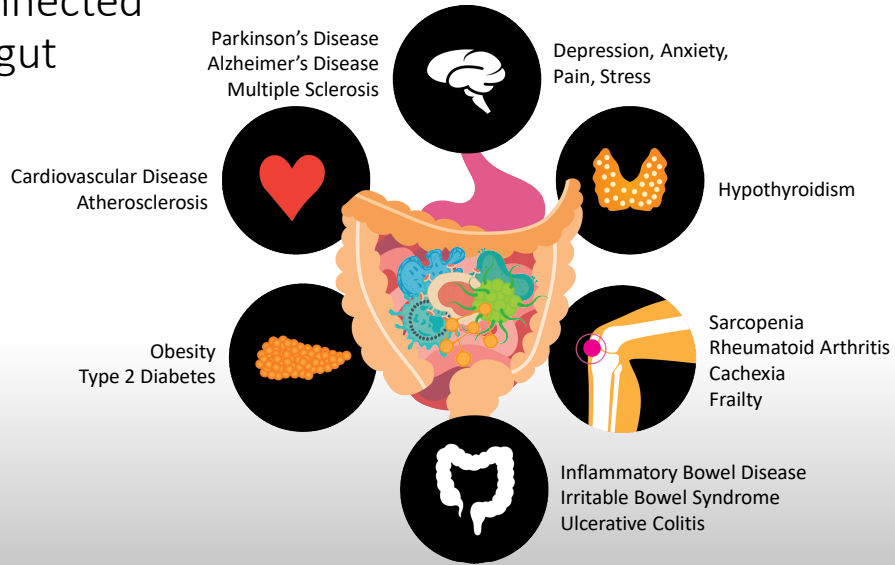
- Production of some vitamins – B vitamins and Vitamin K
- Immune system development
- Digesting food (fiber) that hasn't been broken down in the stomach
- Helping us combat harmful microorganisms – intestinal barrier
- Key to proper digestive functioning

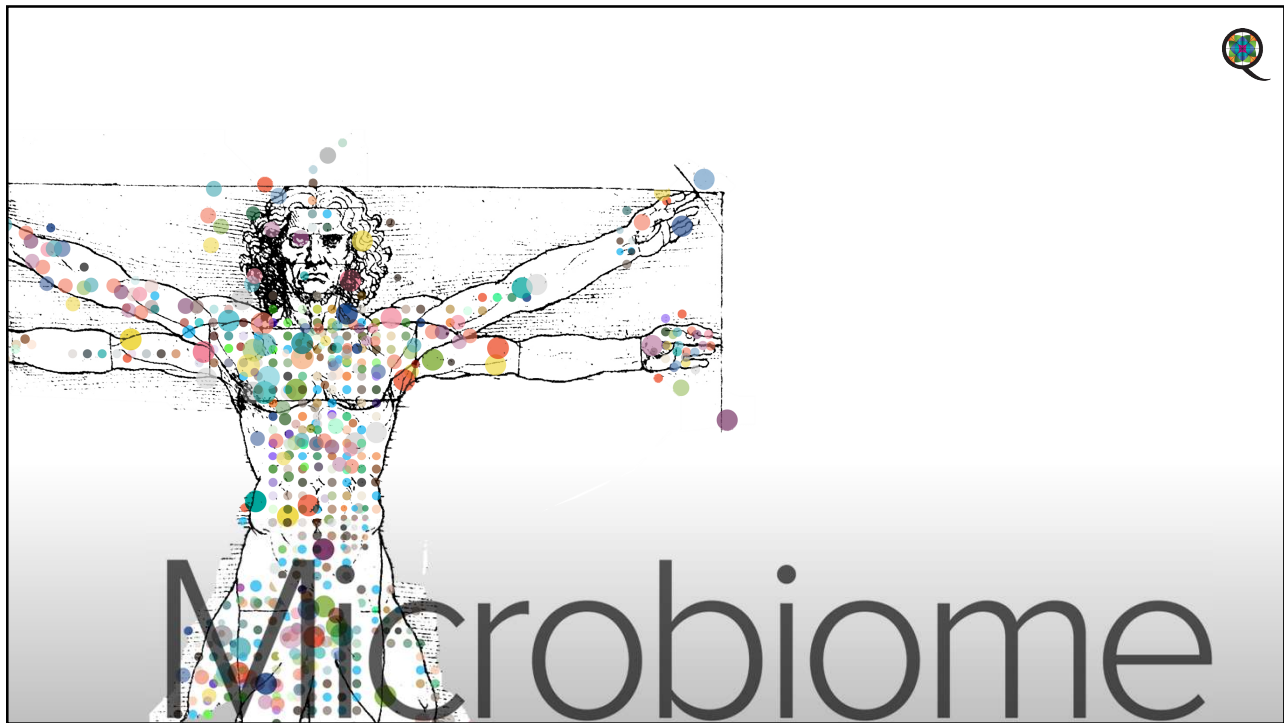
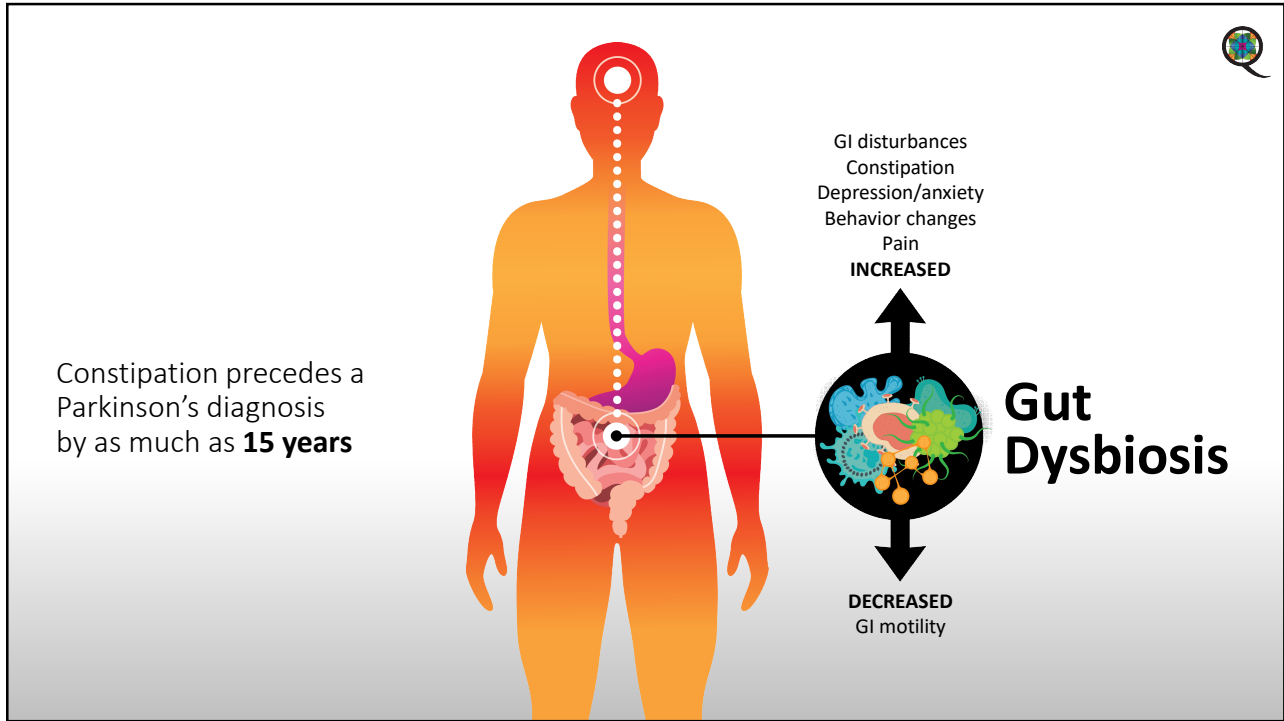
Microbiome



Microbiome

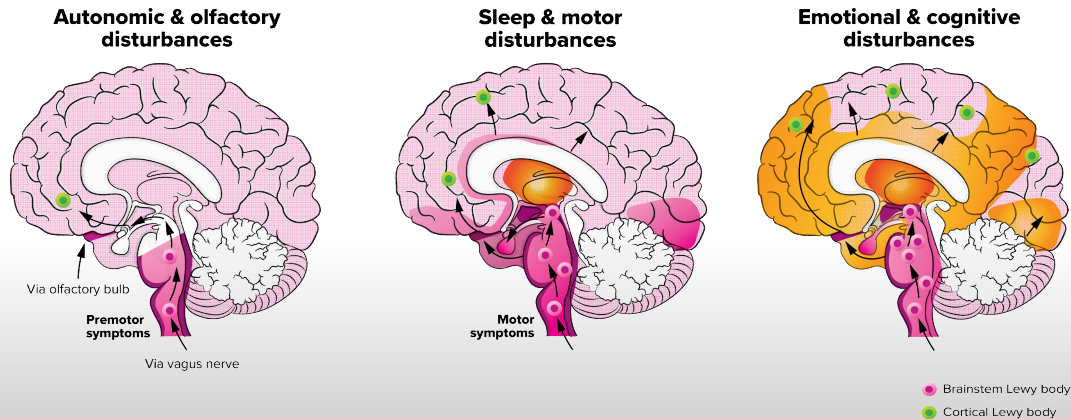
Many diseases
are connected
to the gut





Braak's Hypothesis – 2003 – Staging Parkinson's Disease

Braak's hypothesis states that sporadic PD is caused by a pathogen that enters the body *via* the nasal cavity, and subsequently is swallowed and reaches the gut, initiating Lewy pathology (LP) in the nose and the digestive tract



Filip Scheperjans, MD, PhD
Published the first key Microbiome Research

2014

RESEARCH ARTICLE

Gut Microbiota Are Related to Parkinson's Disease and Clinical Phenotype

Filip Scheperjans, MD, PhD,^{1*} Velma Aho, MSc, BA,² Pedro A. B. Pereira, MSc,² Kaisa Koskinen, PhD,² Lars Paulin, MSc,² Eero Pekkonen, MD, PhD,¹ Elena Haapaniemi, MD, PhD,¹ Seppo Kaakkola, MD, PhD,¹ Johanna Eerola-Rautio, MD, PhD,¹ Marjatta Pohja, MD, PhD,¹ Esko Kinnunen, MD, PhD,³ Kari Murros, MD, PhD,¹ and Petri Auvinen, PhD²

¹Department of Neurology, Helsinki University Central Hospital, and Department of Neurological Sciences, University of Helsinki, Helsinki, Finland
²Institute of Biotechnology, DNA Sequencing and Genomics Laboratory, University of Helsinki, Helsinki, Finland
³Department of Neurology, Hyvinkää Hospital, Hyvinkää, Finland

Scheperjans Microbiome work expanded



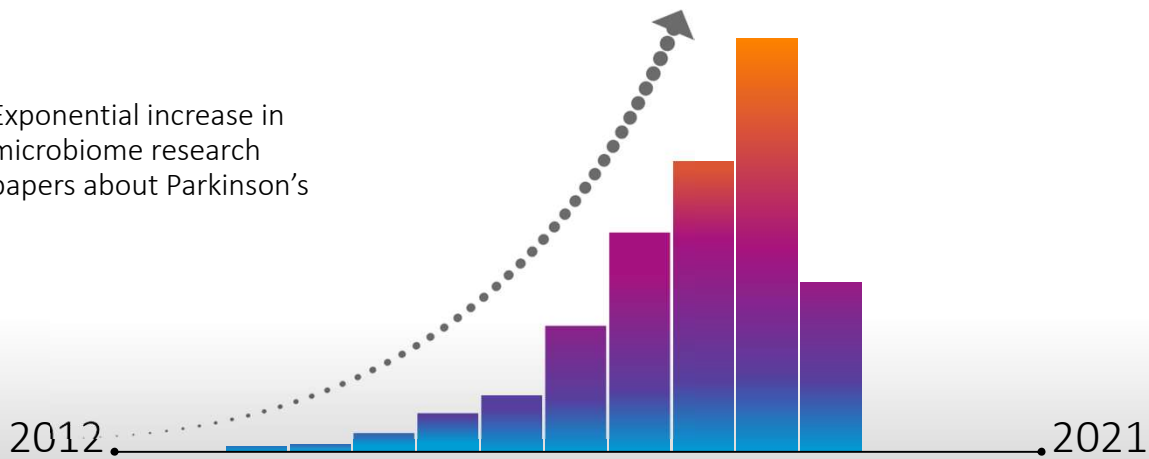
The collage features three articles:

- Editorial:** "The Prodomal Microbiome" by Filip Scheperjans, MD, PhD. Published in *Movement Disorders*, Official Journal of the International Parkinson and Movement Disorder Society.
- Research Article:** "Antibiotic Exposure and Risk of Parkinson's Disease in Finland: Nationwide Case-Control Study" by Tuomas H. Mertsalmi MD, Eero Pekkonen MD, PhD, Filip Scheperjar. Published in *Movement Disorders* on November 18, 2019.
- Research Article:** "Gut Microbiota, 10¹³ new pieces in the Parkinson's disease puzzle" by Scheperjans, Filip¹. Published in *Euro Movement Disorders* in December 2019.
- Research Article:** "Relationships of gut microbiota, short-chain fatty acids, inflammation, and the gut barrier in Parkinson's disease" by Veima T. E. Aho^{1,2*}, Madelyn C. Houser^{1,4}, Pedro A. B. Pereira^{1,5,6}, J. Vici¹, Hertzberg¹, Petri Auvinen¹, Malu G. Tarney¹, and Filip Scheperjans^{1,7}. Published in *Molecular Neurodegeneration*.

Many Parkinson's Researchers Joined the Search for Answers



Exponential increase in microbiome research papers about Parkinson's



From PubMed 2021

Quarterly summaries of research <https://www.marthasquest.com>

PD Microbiome Research expanded the connections

2012-2021

npj | Parkinson's Disease
REVIEW ARTICLE OPEN
Is LRRK2 the missing link between inflammatory bowel disease and Parkinson's disease?
 Mary K. Herrick¹ and Malu G. Tansey^{1*}

Links that implicate the gastrointestinal system common, PD shares several similarities with hypothesized to contribute to PD neuropath contributors to IBD. Variants in LRRK2 have 2 studied intensely in

Griffiths and Muzumdar Genome Medicine
 https://doi.org/10.1186/s13075-018-0909-9 (2018) 19:98

COMMENT Open Access
Emerging evidence linking the gut microbiome to neurologic disorders
 Jessica A. Griffiths¹ and Sarkis K. Mazmanian^{1*}

Editorial summary
 The gut microbiome contributes to the development and function of the immune, metabolic, and nervous systems. Furthermore, commensal bacteria modulate symptoms and pathology in mouse models of neuropsychiatric and neurodevelopmental diseases. Uncovering mechanisms that are utilized by the microbiome to mediate gut-brain connections may provide novel opportunities to target therapies to the brain and immune system development [6]. These early colonizers are instrumental during development in educating the immune system, metabolizing nutrients, and influencing complex behaviors. One example of the impact of early colonization is illustrated by differences in cognitive scores between infants born via cesarean section and vaginally born children [6]. The lower scores of children born via cesarean section may result from differences in early gut colonization by microbes from the mother's skin (cesarean) or vagina (natural birth), re-

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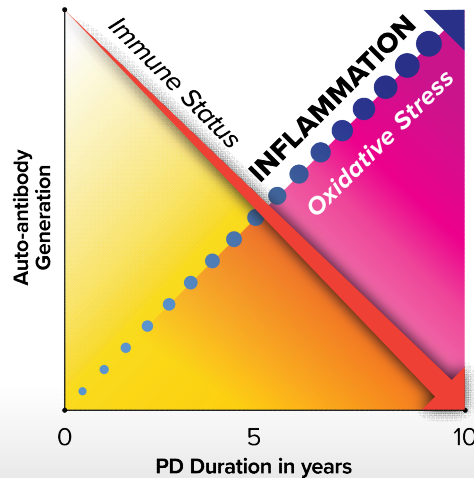
Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease
 Timothy R. Sampson^{1*}, Justine W. Debaty², Taren Thron¹, Stefan Jansson¹, Gauri G. Shastri¹, Catherine E. Schretter¹, Sandra Rocha¹, HeeJin¹, Ali Keshevarajan¹, Katharina M. ...

A gut bacterial amyloid promotes α -synuclein aggregation and motor impairment in mice
 Timothy R. Sampson^{1*}, Collin Challin¹, Neha Jain^{1*}, Anantayai Moleysenka¹, Mark S. Ladinsky¹, Gauri G. Shastri¹, Taren Thron¹, Brittany D. Newsham¹, Iliana Horvath¹, Justine W. Debaty², Stefan Jansson¹, Rob Knight¹, Pernilla Wittung-Stafshede³, Viviana Gradinaru⁴, Matthew Chapman⁵, Sarkis K. Mazmanian^{1*}

The gut microbiome in neurological disorder
 John C. Open, Kenneth D. Woodson, Kiana Saitoh, Ibrahim Peterson, Timothy C. Olson

Summary
 Research into the role of the gut microbiome in modulating brain function has revealed a bidirectional relationship between the gut and the brain. Increasing clinical and preclinical evidence in animal models of neurodegenerative disorders, including Alzheimer's disease and Parkinson's disease, and studies in mouse models of neurodegenerative disorders are beginning to suggest that the gut microbiome may be a key susceptibility factor for neurodegenerative diseases. However, the mechanisms contributing to the pathophysiology of such diseases. However, the composition of the gut microbiome is highly variable and personalized medicine approaches are often difficult to apply. Systems biology approaches are beginning to provide novel opportunities to target therapies to the

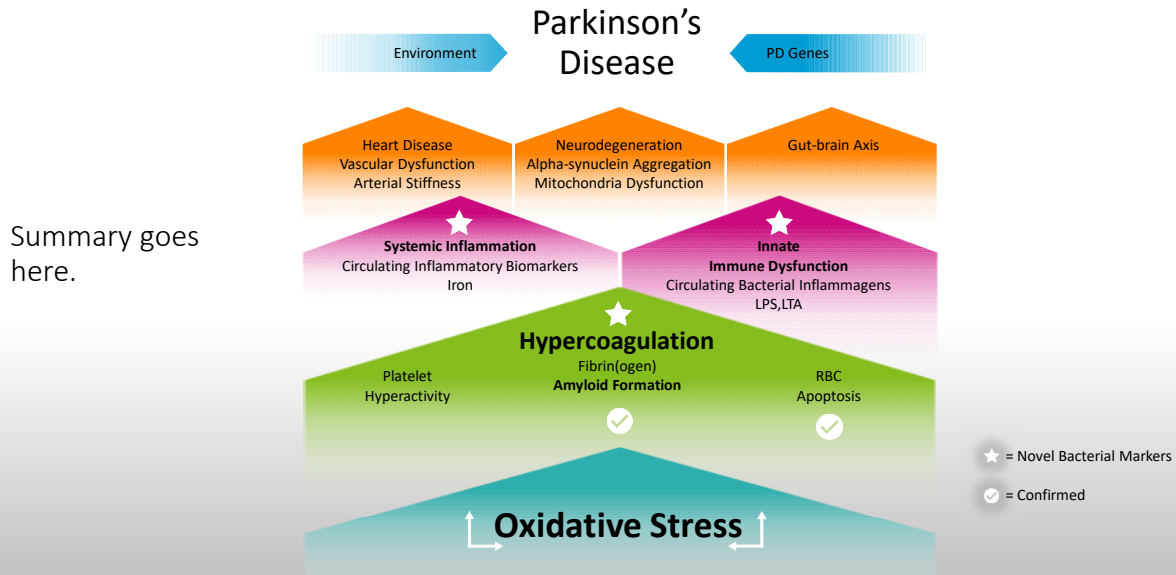
Inflammation



Inflammation feeds oxidative stress.

Inflammation

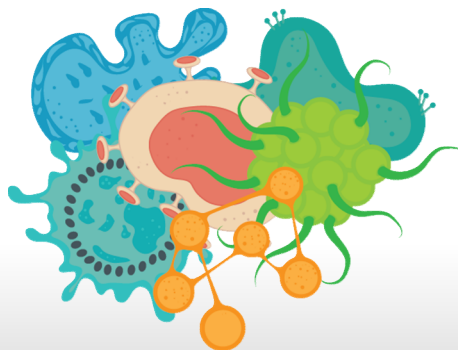
Oxidative stress



Organisms with connection to PD or PD-like symptoms =
Neisseria, Toxoplasma, Mycobacterium avium paratuberculosis



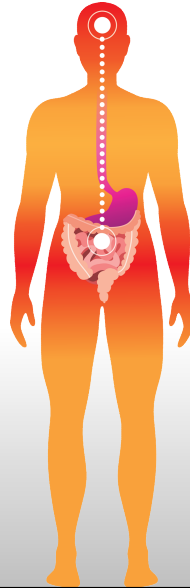
Martha add paper titles here



Ways Microbes impact PD pathology



- Forms pores (holes) in the gut lining
- Enables release of light chain (amyloid)
- Light chain catalyzes blockage of neurotransmitter release



Bacterial Protein Toxins:

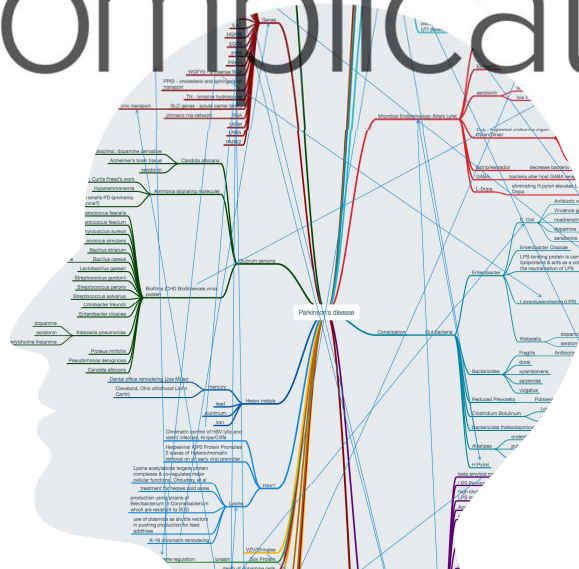
- Deaminase Toxins: Rho GTPase
- Enterotoxin
- Shiga Toxin (E.coli)
- Cholesterol Dependent Cytolysin
- Vacuolating Toxins
- Botulinum Toxin

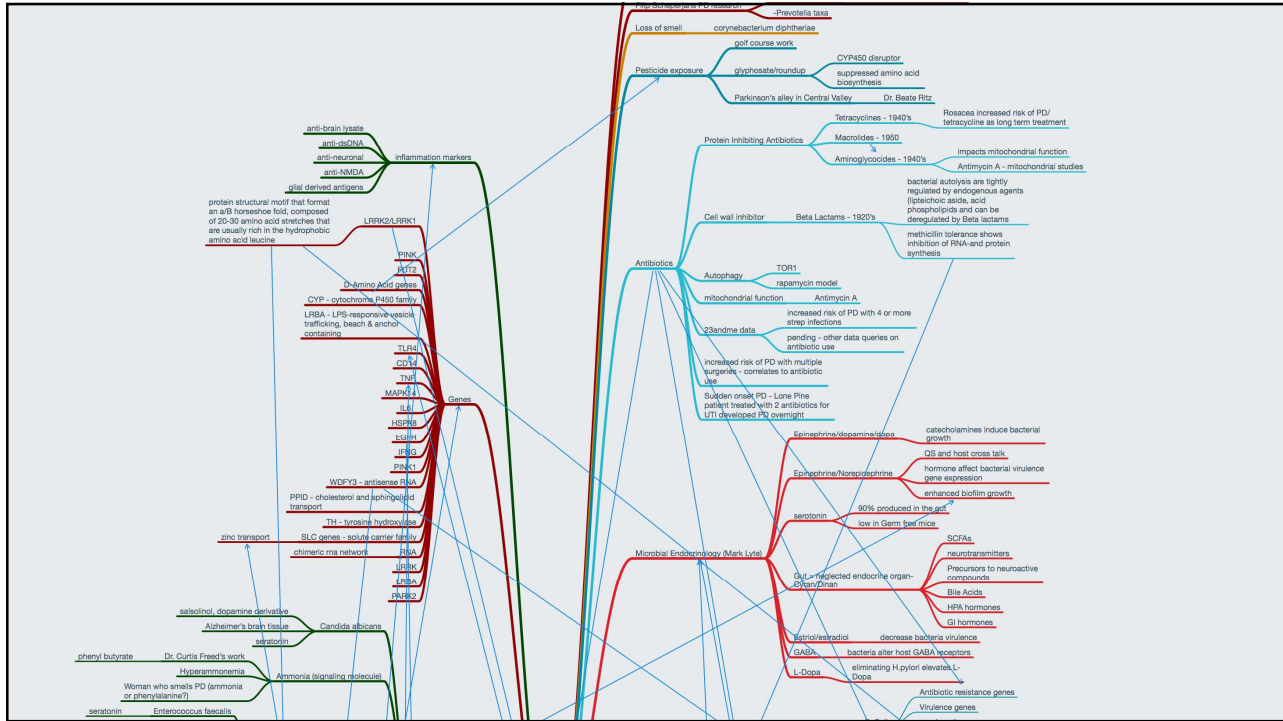
Slowed Speed of Transit: Constipation leads to toxin build up

- C. perfringens: perfringolysin O
- C. boltea : BN toxin
- E. Coli: deaminating toxins
- B. thurigiensis: pore forming toxins
- H. pylori: pore forming toxins
- Streptococcus: super antigen A, exotoxins, streptolysin O, streptolysin S

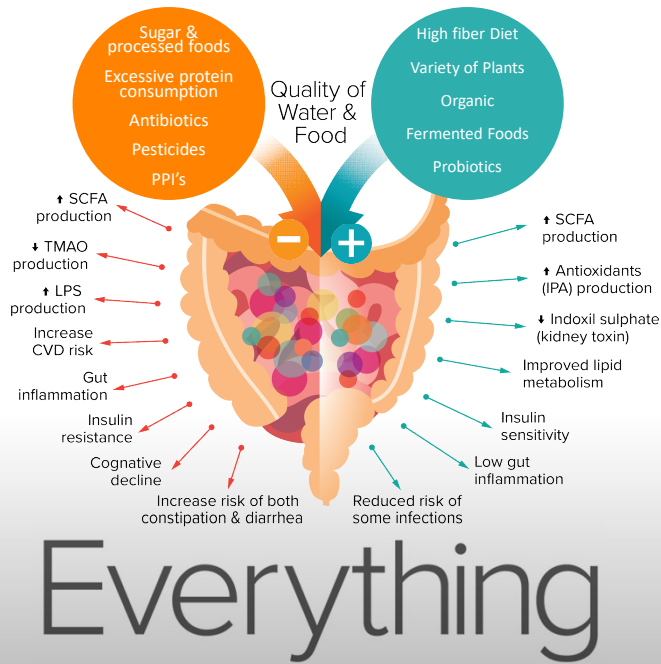
Parkinson's is extremely

Complicated

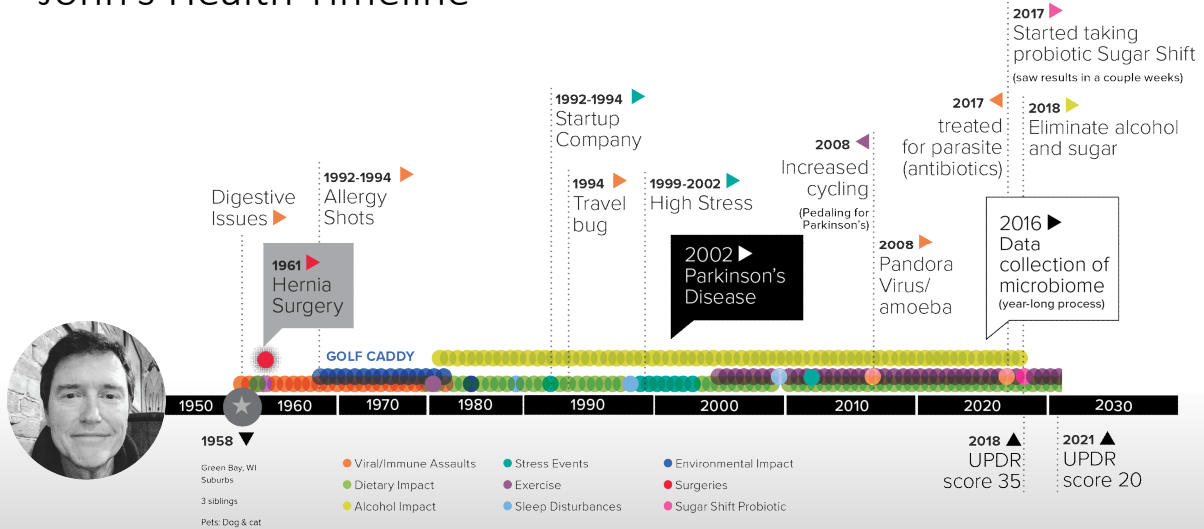




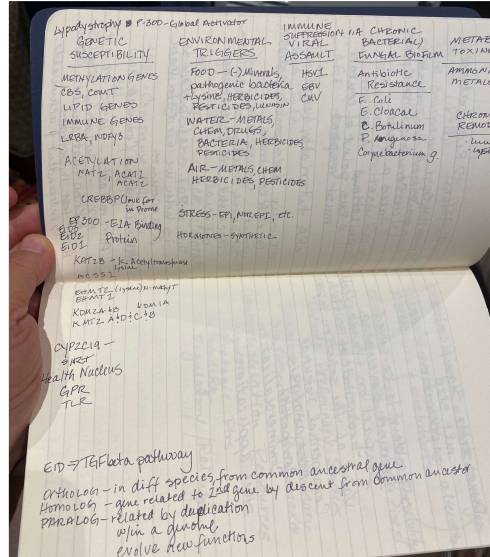
What impacts the Microbiome



John's Health Timeline



Connecting John's health story with the microbiome



What now?



You can make a difference in your health today and every day going forward.

Water • Food (source & quality) • Diet (meat vs. vegetables) • Nutrient Quality (B vitamins and the gut bacteria that make them) • Avoid Sugar • Eat More Fiber • Rest your digestion (periodic fasting/intermittent fasting) • Digestive Enzymes • Exercise • Probiotics

Own your health!

For more information and other resources visit my blog:
www.marthasquest.com

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Let's stay connected.



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