

The Gut-Brain Continuum, Revelations on the Role of the Microbiome in the Structure and Function of the Neuroendocrine System



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Biomic Sciences

Disclosure

- Founder and CEO of Biomic Sciences
- Founder and President of M Clinic, Charlottesville, VA
- My clinical practice, basic science operations, and our research group's discoveries, experience, and products produce my income
- I am not paid by any third-party companies or organizations for my presentation or educational efforts here
- John Gildea, PhD Molecular Biology and Genetics - UVA
Chief Science Advisor, Biomic Sciences
- Luis Matavelli, MD/PhD
- William Vitalis, Director of Esoteric Sciences, Biomic Sciences




1st World Epidemics – Gut/Brain Source??

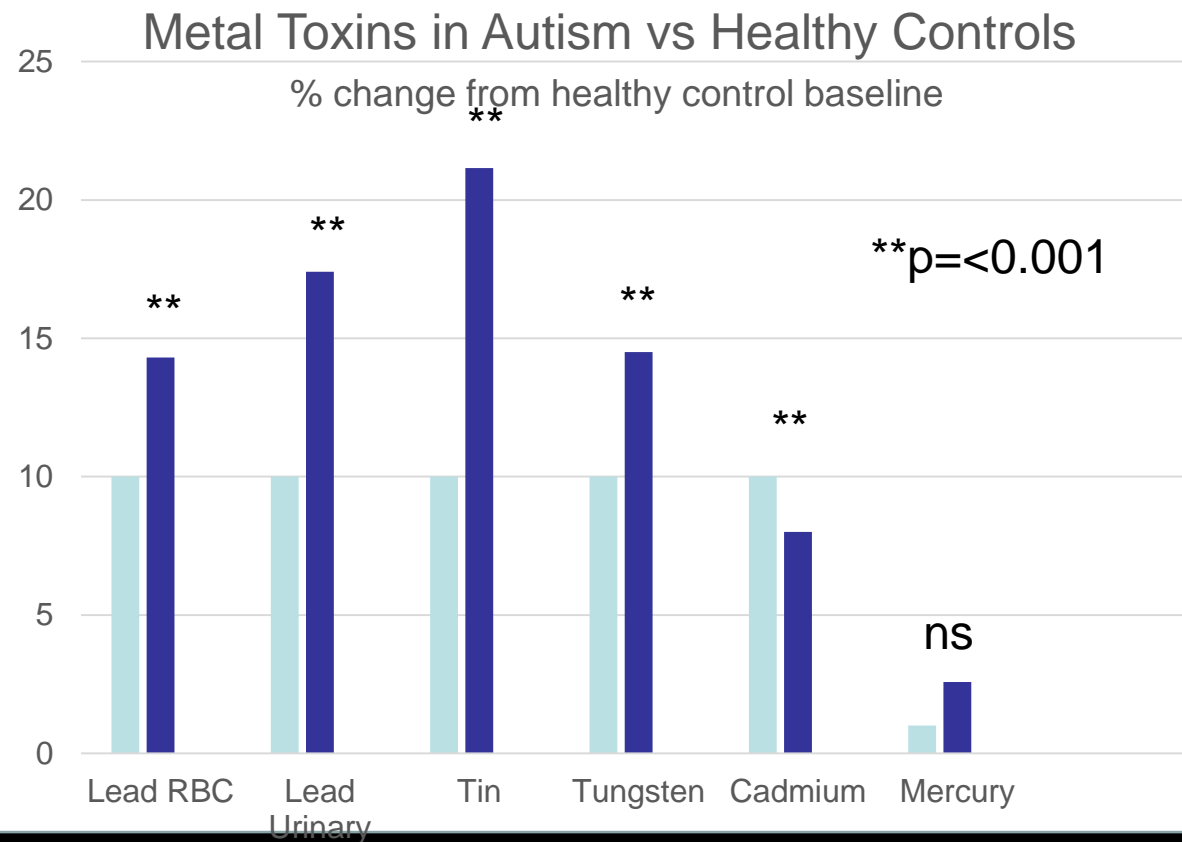
- Autism 1:36
- Attention Deficit 1:10 (70% medicated)
- Asthma 1:10
- Allergy 1:4
- Diabetes 1:4
- Obesity 1:3
- Major Depression 1:2
- Cancer 1:2
- Dementia 1:1

Toxicological Status of Children with Autism vs. Neurotypical Children and the Association with Autism Severity

Authors

Authors and affiliations

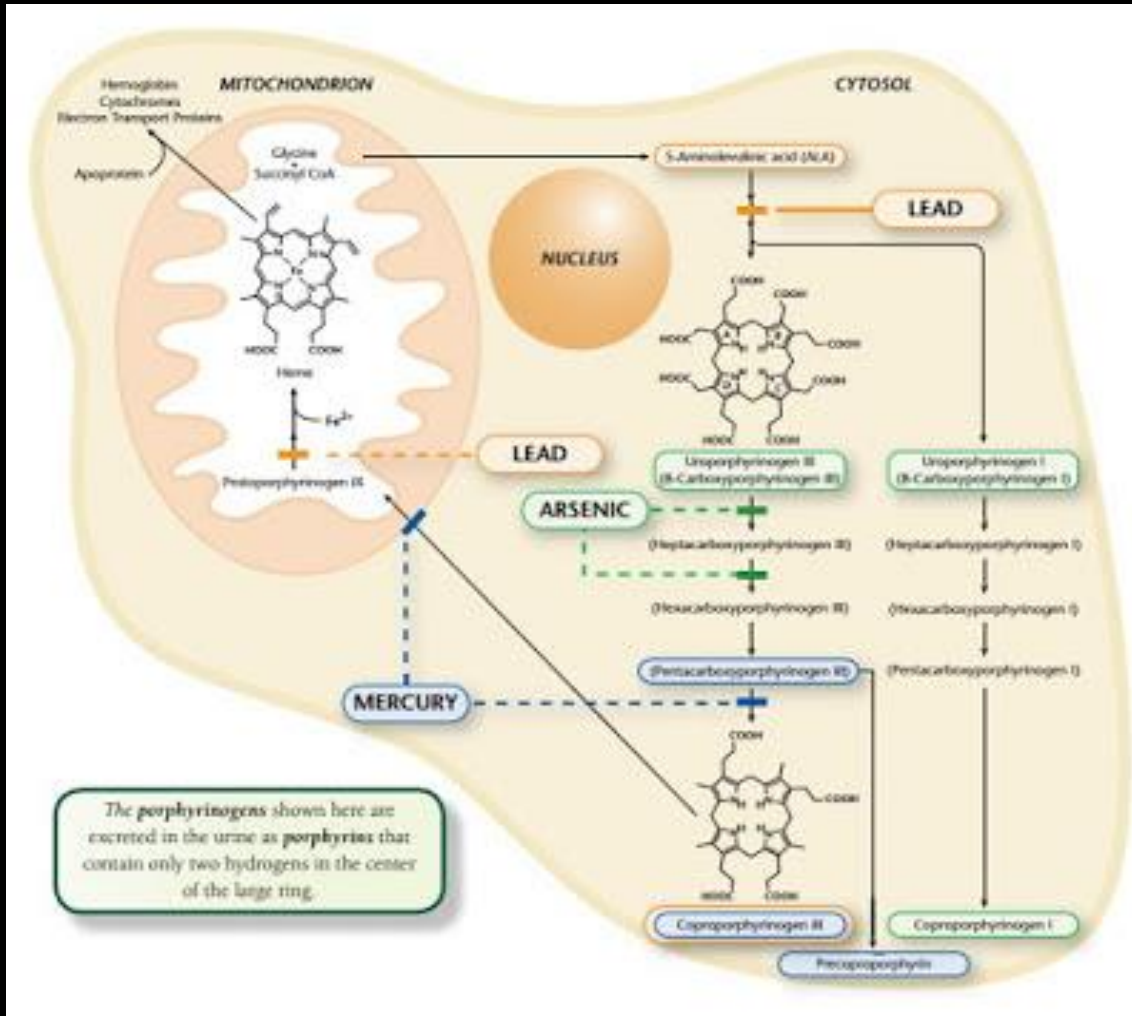
James B. Adams , Tapan Audhya, Sharon McDonough-Means, Robert A. Rubin, David Quig, Elizabeth Geis, Eva Gehn, Melissa Loresto, Jessica Mitchell, Sharon Atwood, Suzanne Barnhouse, Wondra Lee



Subjects: 55 children with autism ages 5-16 years compared to 44 controls of similar age and gender

Altered urinary porphyrins and mercury exposure as biomarkers for autism severity in Egyptian children with autism spectrum disorder.

Khaled EM¹, Meguid NA², Bjørklund G³, Gouda A⁴, Bahary MH⁵, Hashish A², Sallam NM², Chirumbolo S⁶, El-Bana MA⁷




Three groups:

- ASD (40),
- Unaffected Siblings (20)
- Unrelated unaffected controls (40),
 - Mothers with ASD children had a significantly higher number of mercury containing amalgams vs healthy control mothers
 - Mercury related porphyrins were elevated in the Autistic vs Unaffected controls
 - Unaffected siblings had no significant difference in porphyrins than the non-related health controls

Gut Microbiome and ASD-Related Toxicity

- Detoxification Human Genes:
 - The MTHFR genes produces the MTHFR enzyme family
 - 40 to 60 percent of the US population has one or more MTHFR mutations
- 90% of the enzymatic work done in the body is performed by bacteria alone, fungi and yeasts in addition to this!
- Methylation and oxidation detoxification can be done through bacteria, fungi, and yeast
- Methylation of Mercury, Tin, and other metals produces more reactive/volatile compounds that can be cleared

Microbiota Transfer Therapy alters gut ecosystem and improves gastrointestinal and autism symptoms: an open-label study

Dae-Wook Kang[†], James B. Adams[†], Ann C. Gregory[†], Thomas Borody, Lauren Chittick, Alessio Fasano, Alexander Khoruts, Elizabeth Geis, Juan Maldonado, Sharon McDonough-Means, Elena L. Pollard, Simon Roux, Michael J. Sadowsky, Karen Schwarzberg Lipson, Matthew B. Sullivan ✉, J. Gregory Caporaso ✉ and Rosa Krajmalnik-Brown ✉ 

[†] Contributed equally

Microbiome 2017 5:10 | DOI: 10.1186/s40168-016-0225-7 | © The Author(s). 2017

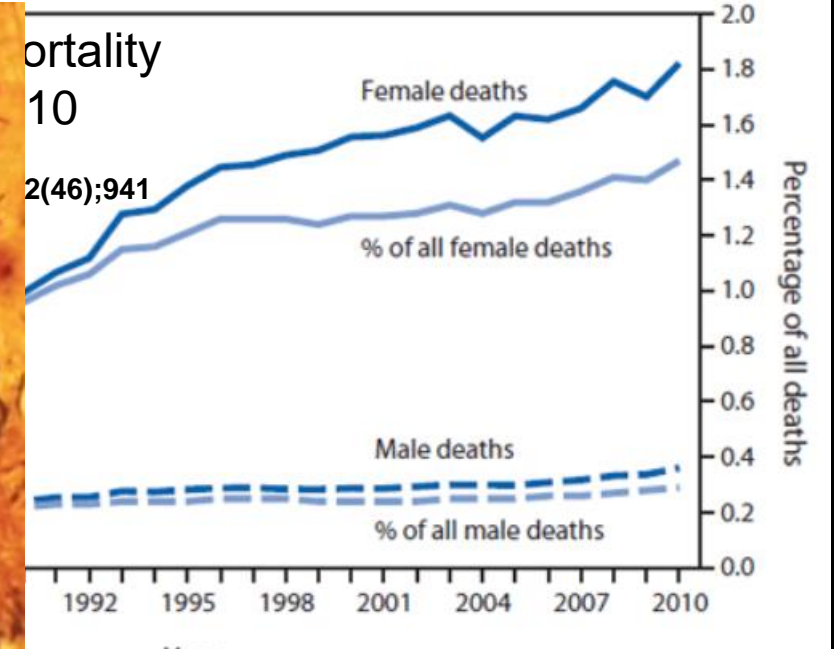
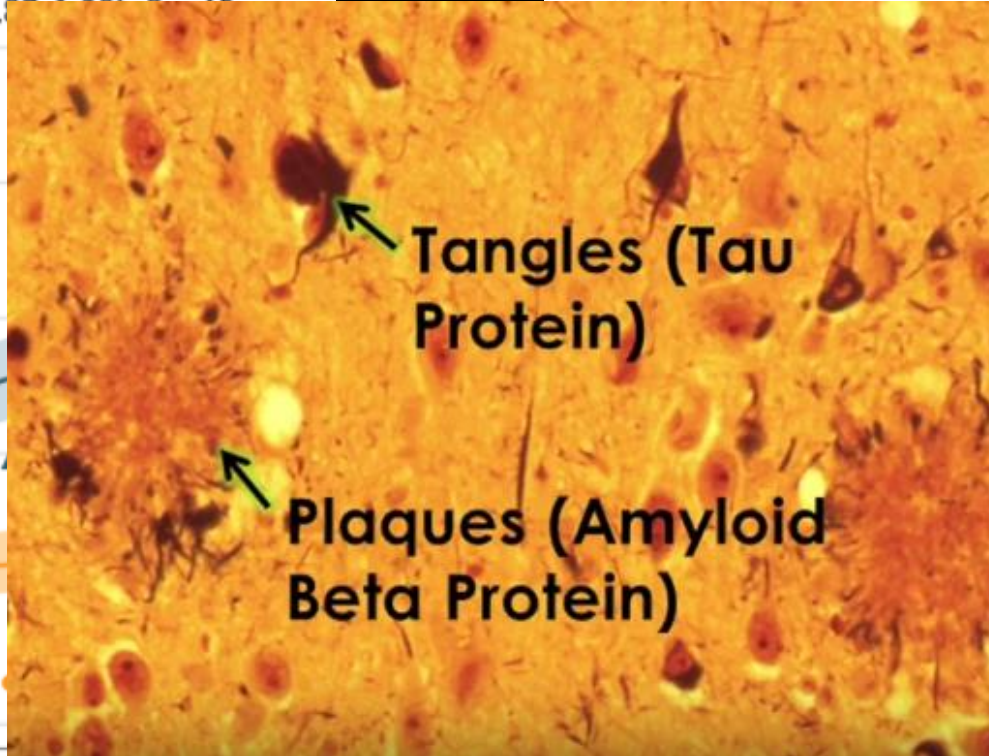
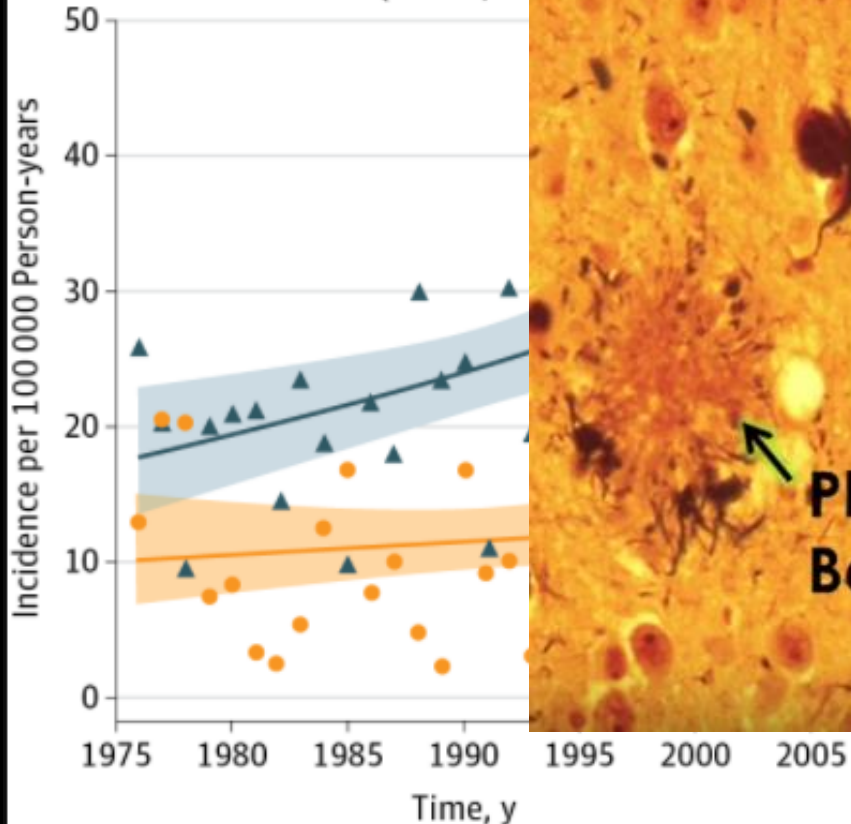
- 18 ASD children
- Oral vancomycin for 2 weeks
- One-day, high dose FMT (fecal microbial transplant)
 - Encapsulated – two arms oral vs rectal
- Followed by low dose maintenance daily FMT for 14 days

Incidence of Neurodegenerative Injury Adults

D Parkinson disease, all ages

Men: RR = 1.24 (95% CI, 1.08-1.43); $P = .003$

Women: RR = 1.09 (95% CI, 0.97-1.22); $P = .12$

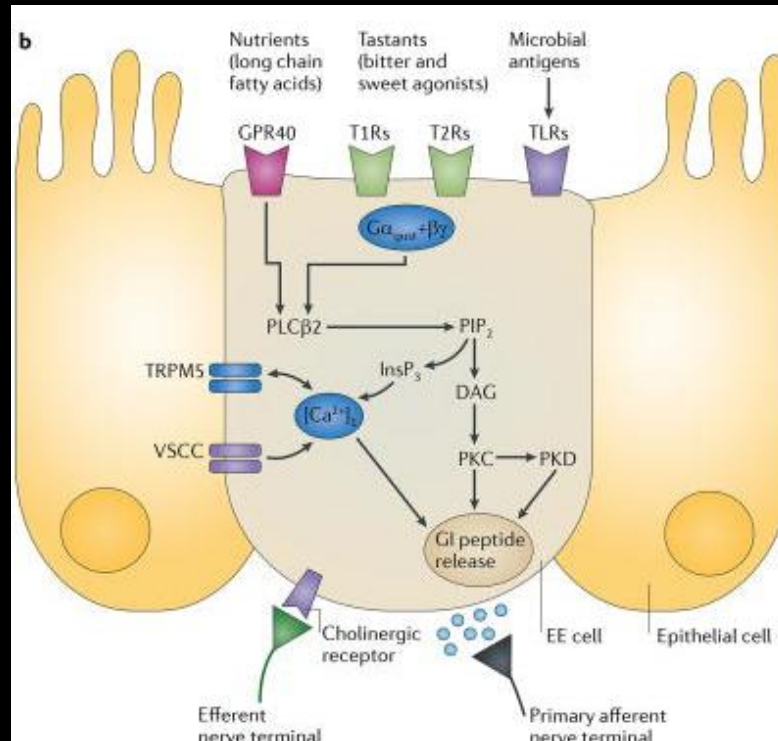
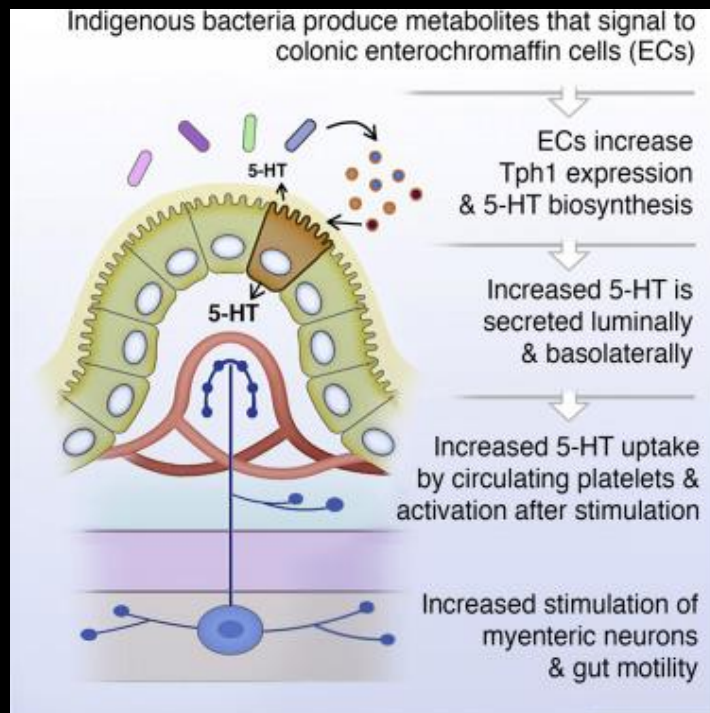


Gut/Brain Postulate

- With a loss of microbiome we lose our ability to detoxify the organic and inorganic compounds
 - Mitochondrial oxidation and damage
 - Poor enzymatic antioxidant function
 - Glutathione lockdown
 - Methylation dysfunction
 - Unregulated Protein Synthesis and Protein Misfolding
 - 26 human proteins now recognized to be able to result in amyloid production

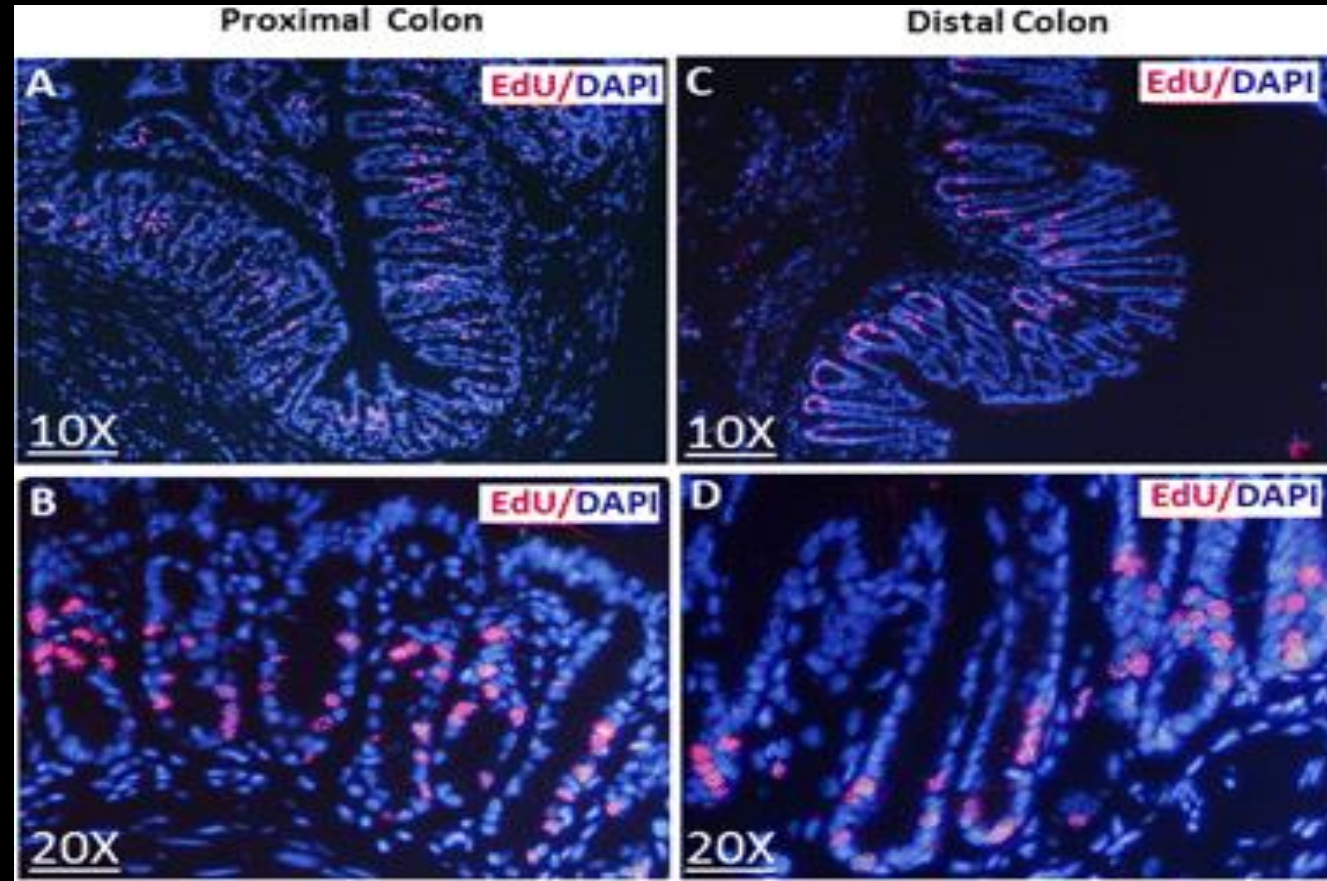
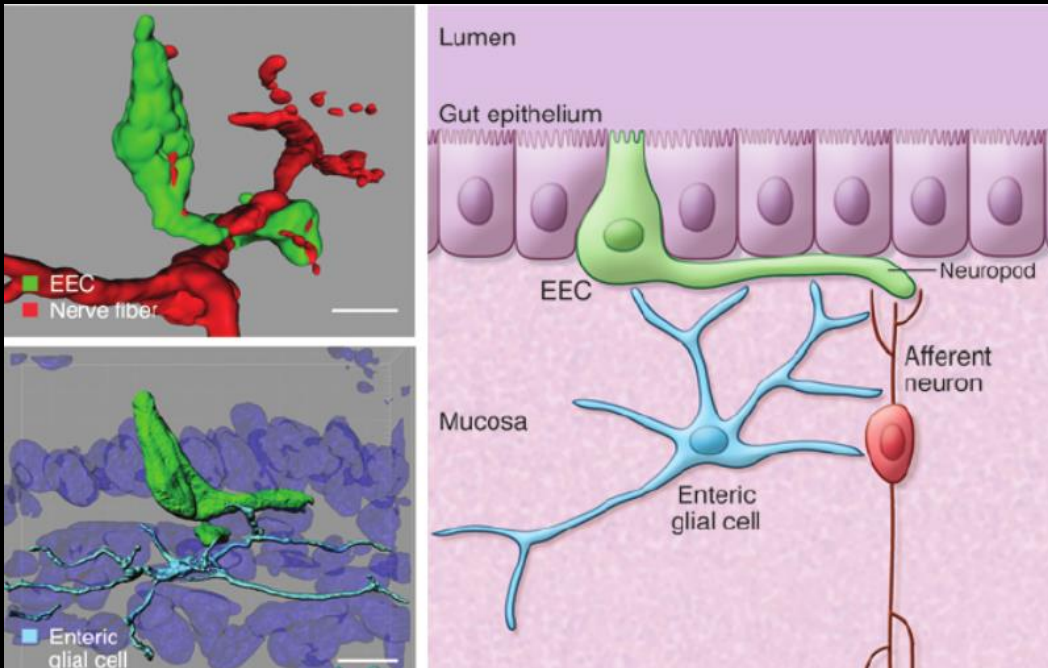
Gut/Brain Connection or is the Gut the Brain?

- Sensory enteroendocrine cell (EEC) in the gut epithelium produce as much as 50% of the dopamine and 90% of the serotonin in the body



Gut Epithelium and the Human Nervous System

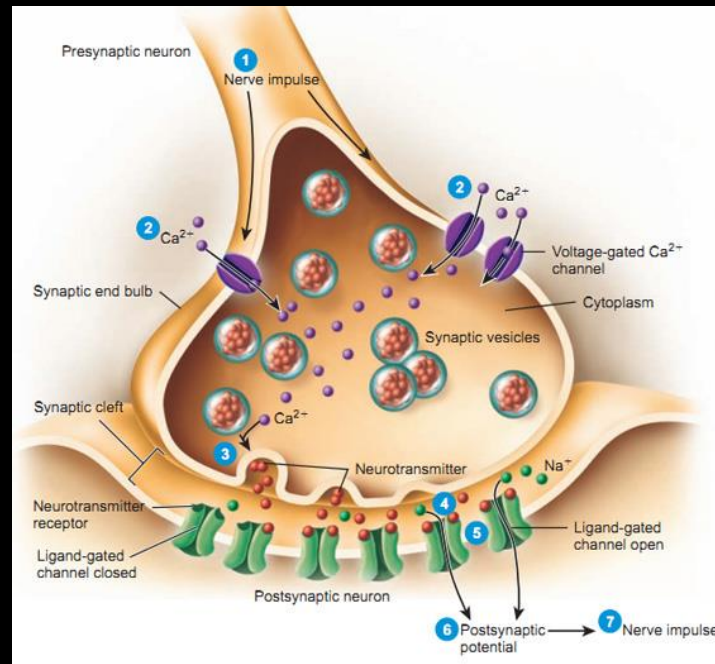
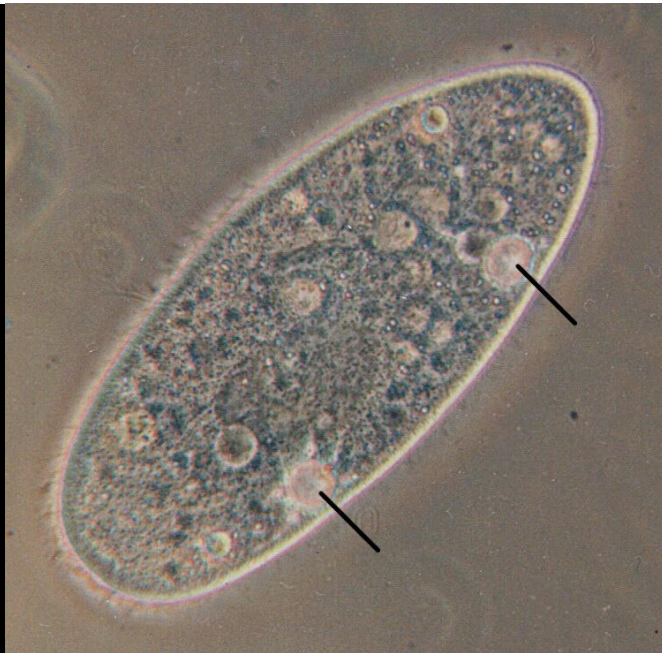
- Sensory enteroendocrine cell (EEC) in the gut epithelium can be seen extending a neuropod to connect with an underlying nerve



Serotonin Production Dependent on Vacuole Forming Bacteria on the EEC

Indigenous Bacteria from the Gut Microbiota Regulate Host Serotonin Biosynthesis

Yano, Jessica M. et.al. *Indigenous Bacteria from the Gut Microbiota Regulate Host Serotonin Biosynthesis*. Cell, 2015;161 (2):264-276



Serotonin Production from Enteric Endocrine Cells is Dependent on the Presence of Vacuole Forming Bacteria

Indigenous Bacteria from the Gut Microbiota Regulate Host Serotonin Biosynthesis

Yano, Jessica M. and Yu, Kristie and Donaldson, Gregory P. and Shastri, Gauri G. and Ann, Phoebe and Ma, Liang and Nagler, Cathryn R. and Ismagilov, Rustem F. and Mazmanian, Sarkis K. and Hsiao, Elaine Y. (2015) *Indigenous Bacteria from the Gut Microbiota Regulate Host Serotonin Biosynthesis*. Cell, 161 (2). pp. 264-276. ISSN 0092-8674. PMCID PMC4393509

Antibiotic Use Increases Risk of Depression and Anxiety

- MDD increase 23-56%
- Anxiety increase 17-44%

[J Clin Psychiatry](#). 2015 Nov;76(11):1522-8. doi: 10.4088/JCP.15m09961.

Antibiotic exposure and the risk for depression, anxiety, or psychosis: a nested case-control study.

[Lurie I](#)^{1,2}, [Yang YX](#), [Haynes K](#), [Mamtani R](#), [Boursi B](#).

Author information

Abstract

OBJECTIVE: Changes in the microbiota (dysbiosis) were suggested to increase the risk of several psychiatric conditions through neurologic, metabolic, and immunologic pathways. Our aim was to assess whether exposure to specific antibiotic groups increases the risk for depression, anxiety, or psychosis.

METHOD: We conducted 3 nested case-control studies during the years 1995-2013 using a large population-based medical record database from the United Kingdom. The study included 202,974 patients with depression, 14,570 with anxiety, and 2,690 with psychosis and 803,961, 57,862, and 10,644 matched controls, respectively. Cases were defined as individuals aged 15-65 years with any medical Read code for depression, anxiety, or psychosis. Subjects with diagnosis-specific psychotropic prescriptions > 90 days before index date were excluded. For

Bacterial Biofilms Function as Electrical Conduits for long Distance Signaling

Ion channels enable electrical communication in bacterial communities

Arthur Prindle, Jintao Liu, Munehiro Asally, San Ly, Jordi Garcia-Ojalvo & Gürol M. Süel

[Affiliations](#) | [Contributions](#) | [Corresponding author](#)

Nature **527**, 59–63 (05 November 2015) | doi:10.1038/nature15709

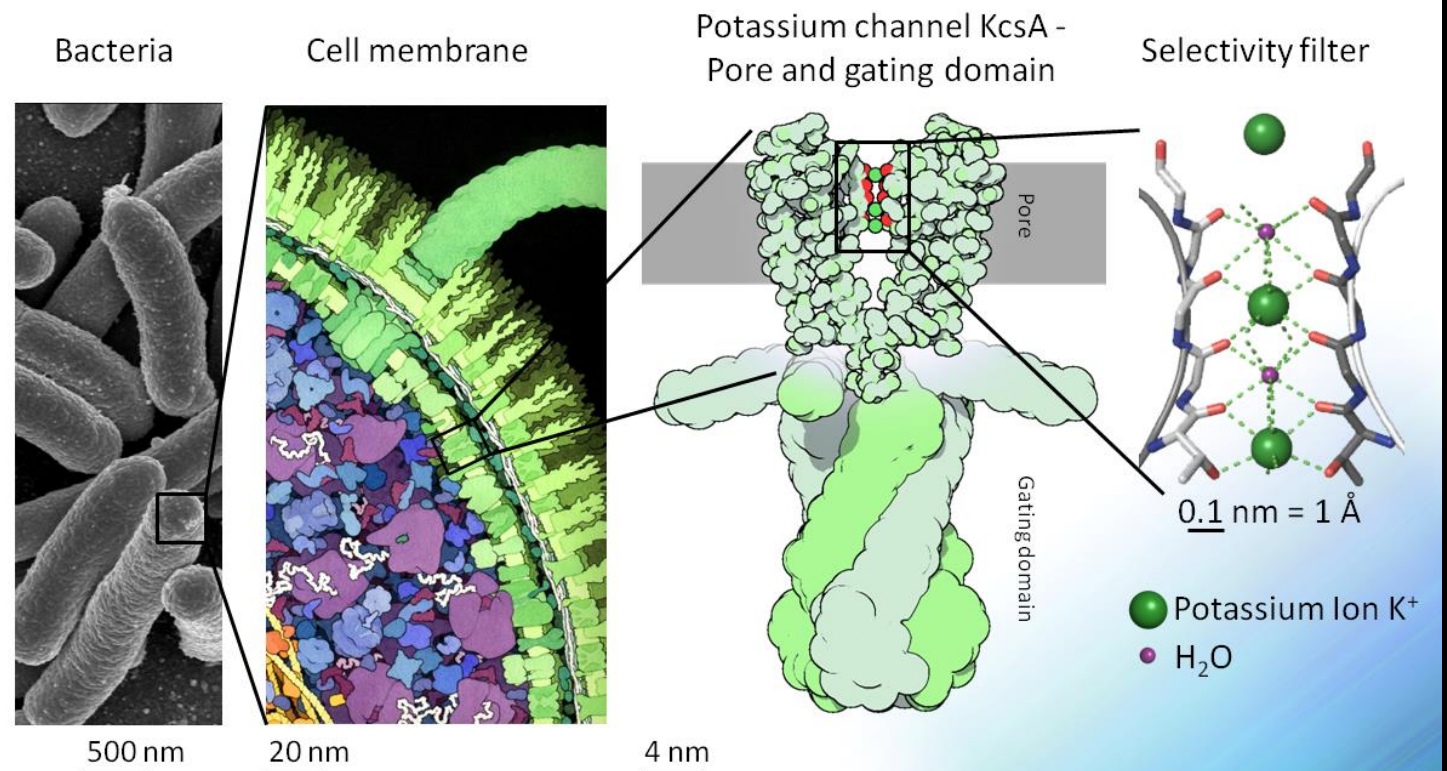
Received 16 June 2015 | Accepted 10 September 2015 | Published online 21 October 2015

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Abstract

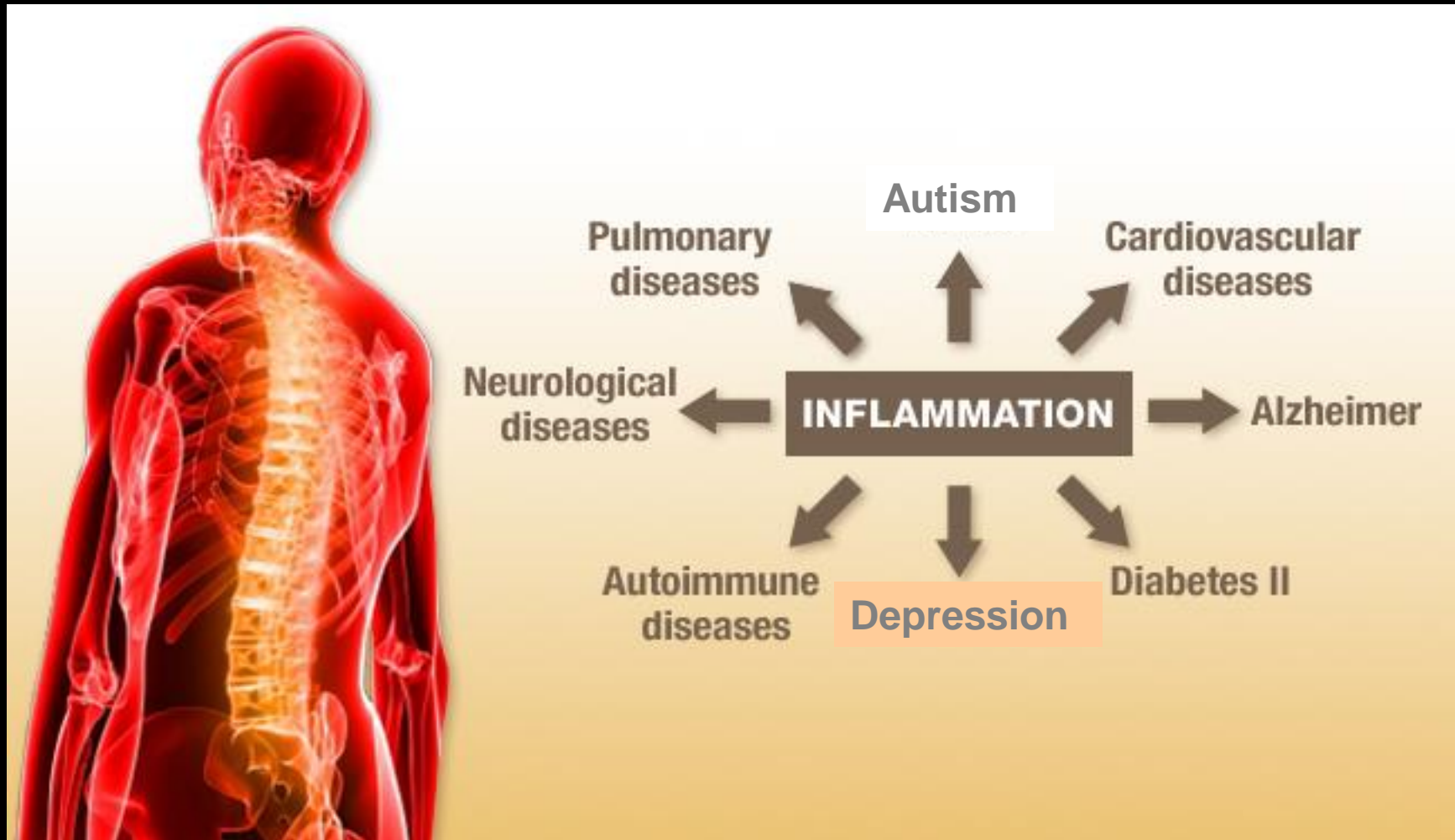
[Abstract](#) • [References](#) • [Author information](#) • [Extended data figures and tables](#) • [Supplementary](#)

The study of bacterial ion channels has provided fundamental insights into the structure of neuronal signalling; however, the native role of ion channels in bacteria has remained elusive. Here we show that ion channels conduct long-range electrical signals within bacterial biofilms through spatially propagating waves of potassium. These waves result from a positive feedback loop, in which a metabolic trigger induces release of intracellular potassium, which in turn depolarizes neighbouring cells. Propagating through the biofilm, this wave of depolarization coordinates metabolic states among cells in the interior and periphery of the biofilm. Deletion of the potassium channel abolishes this response. As predicted by a mathematical model, we further show that spatial propagation can be hindered by specific perturbations to potassium channel gating. Together, these results demonstrate a function for potassium channels in bacterial biofilms, and provide a prokaryotic paradigm for active, long-range electrical signalling in cellular communities.



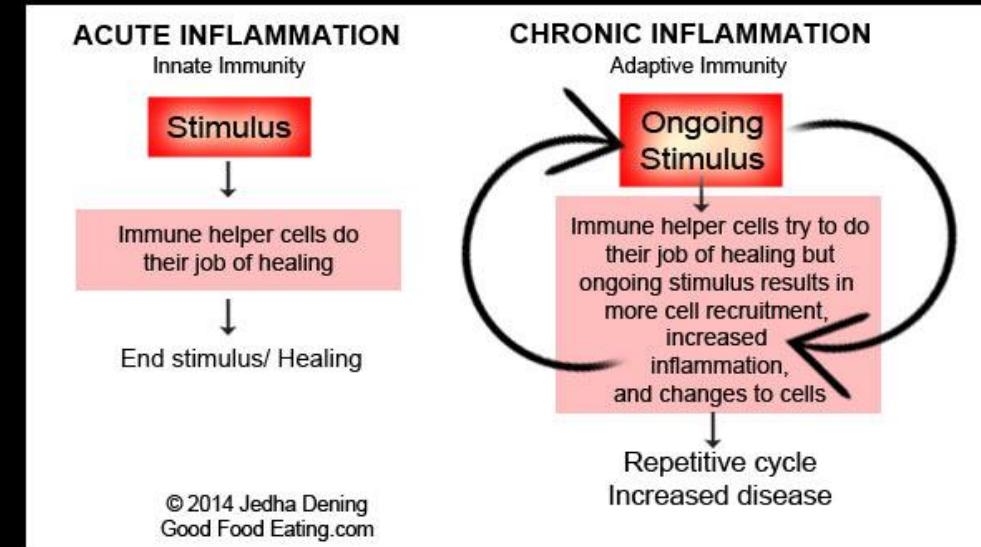
Credit: Rocky Mountain Laboratories, NIAID, NIH and David S. Goodsell

Inflammation is the root of all chronic disorder and disease



Oxidative Stress

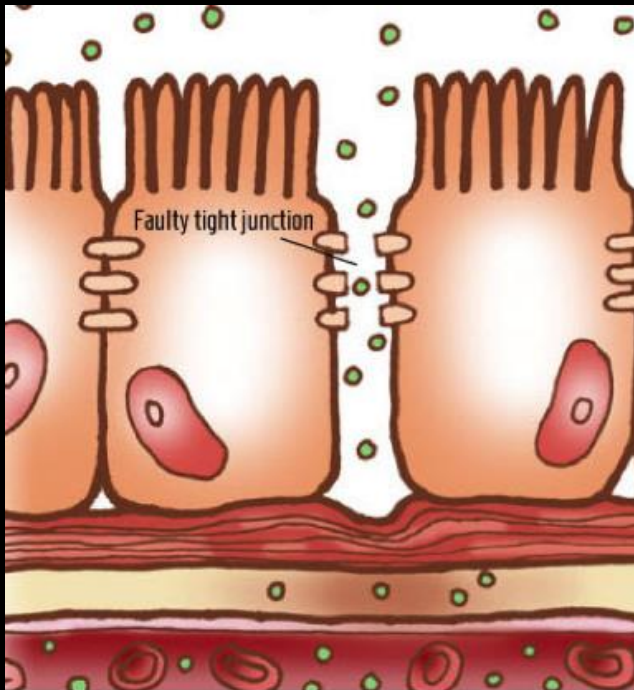
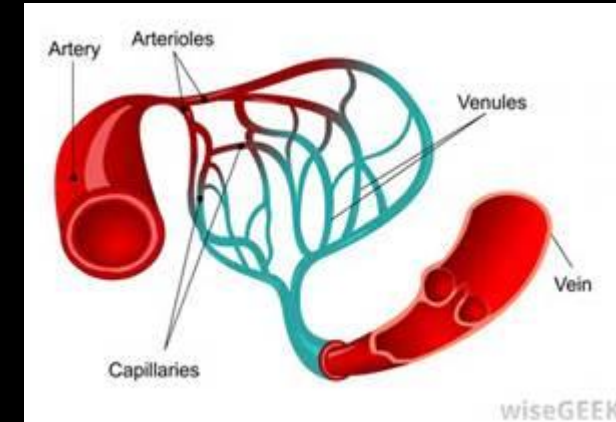
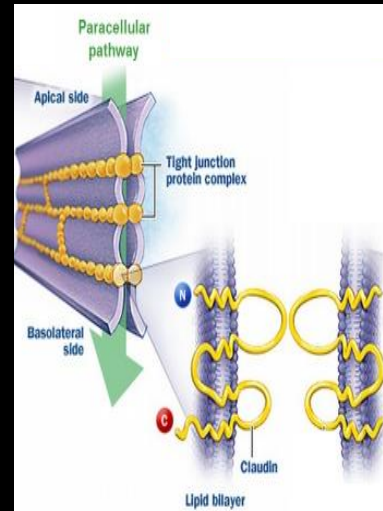
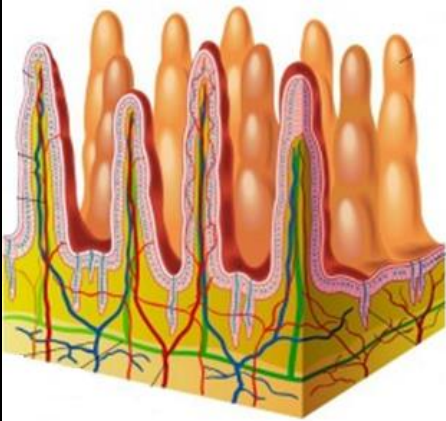
- Acute inflammation = health, regeneration, longevity
 - Injury Repair
 - Infection control
- Chronic inflammation
 - Oxidative stress = positive charge/acid
 - Shutdown/overwhelm of the antioxidant system



chronic inflammation = loss of communication

Intercellular Tight Junctions

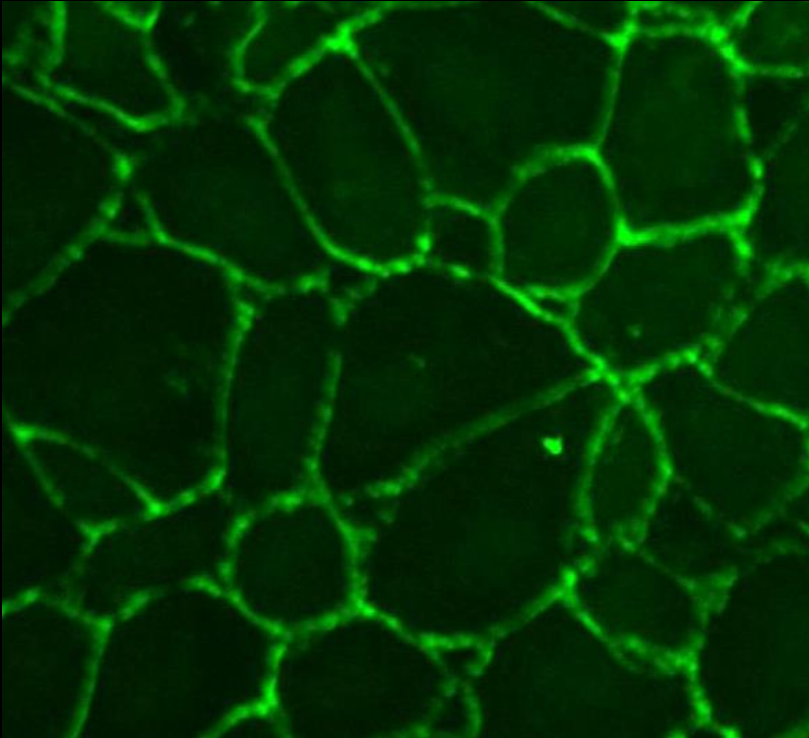
Firewalls of Defense



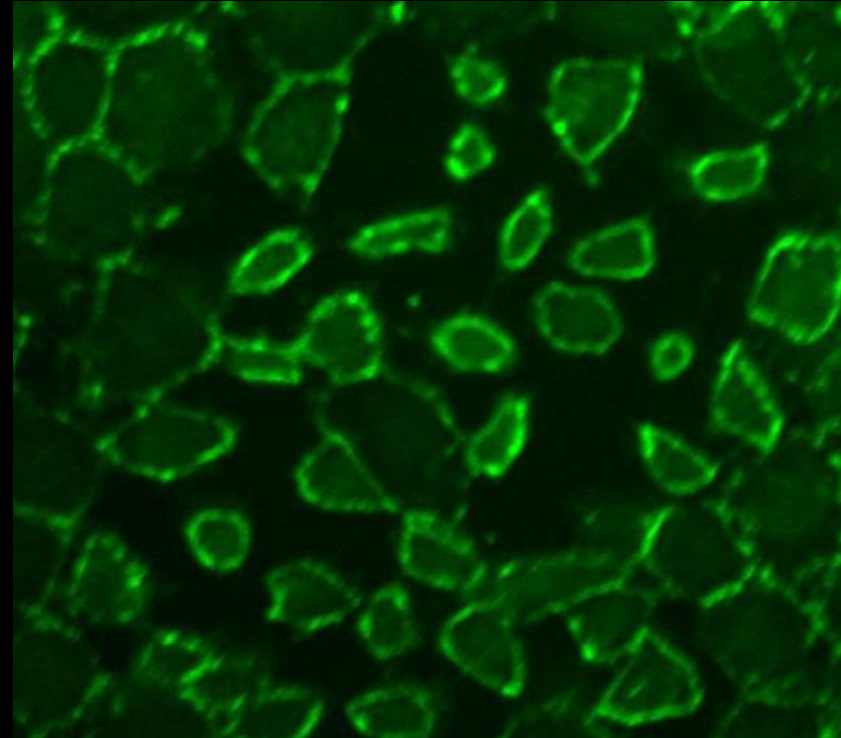
Glyphosate Tight Junction Imaging

CONTROL

IEC-6 Small intestine membrane

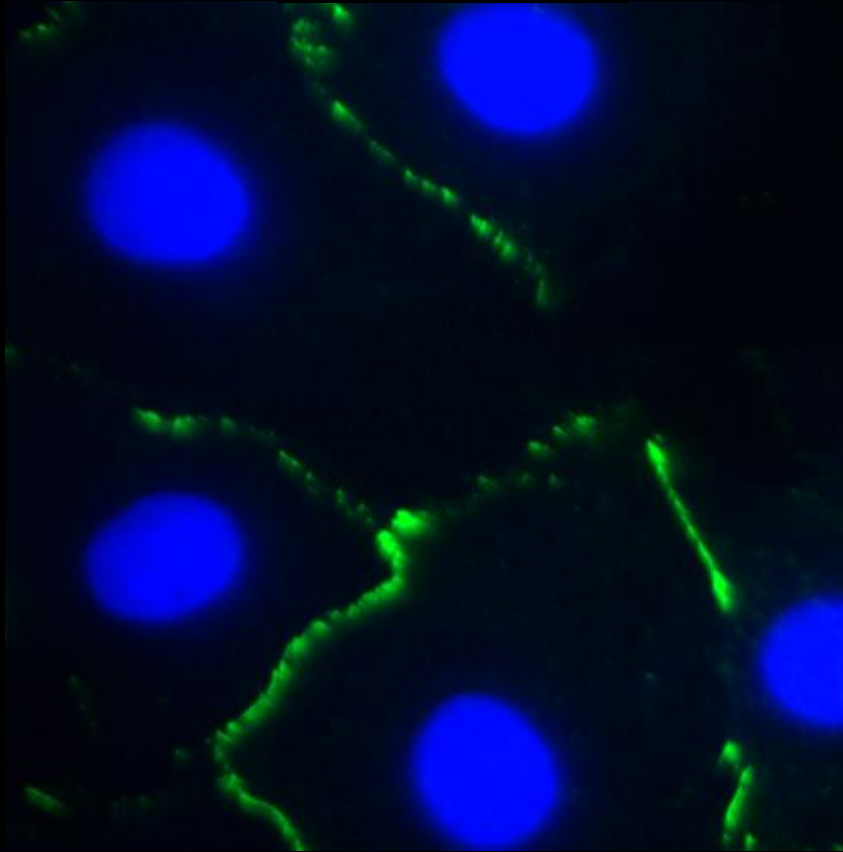


GLYPHOSATE 20 ppm, 16 minutes

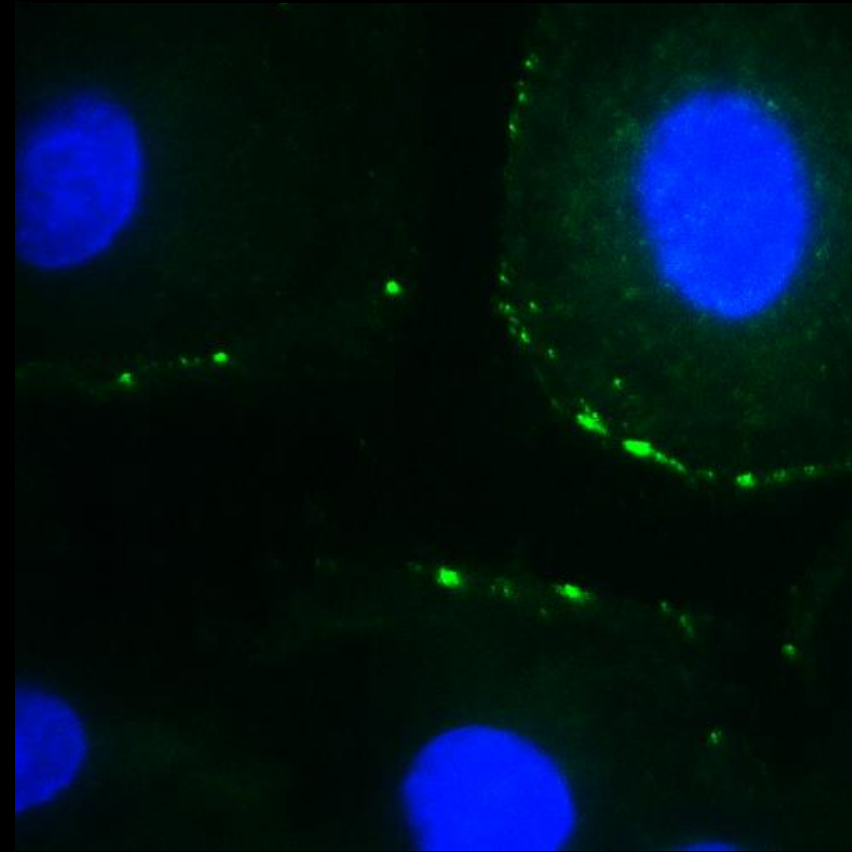


Gliadin (Gluten) Tight Junction Imaging

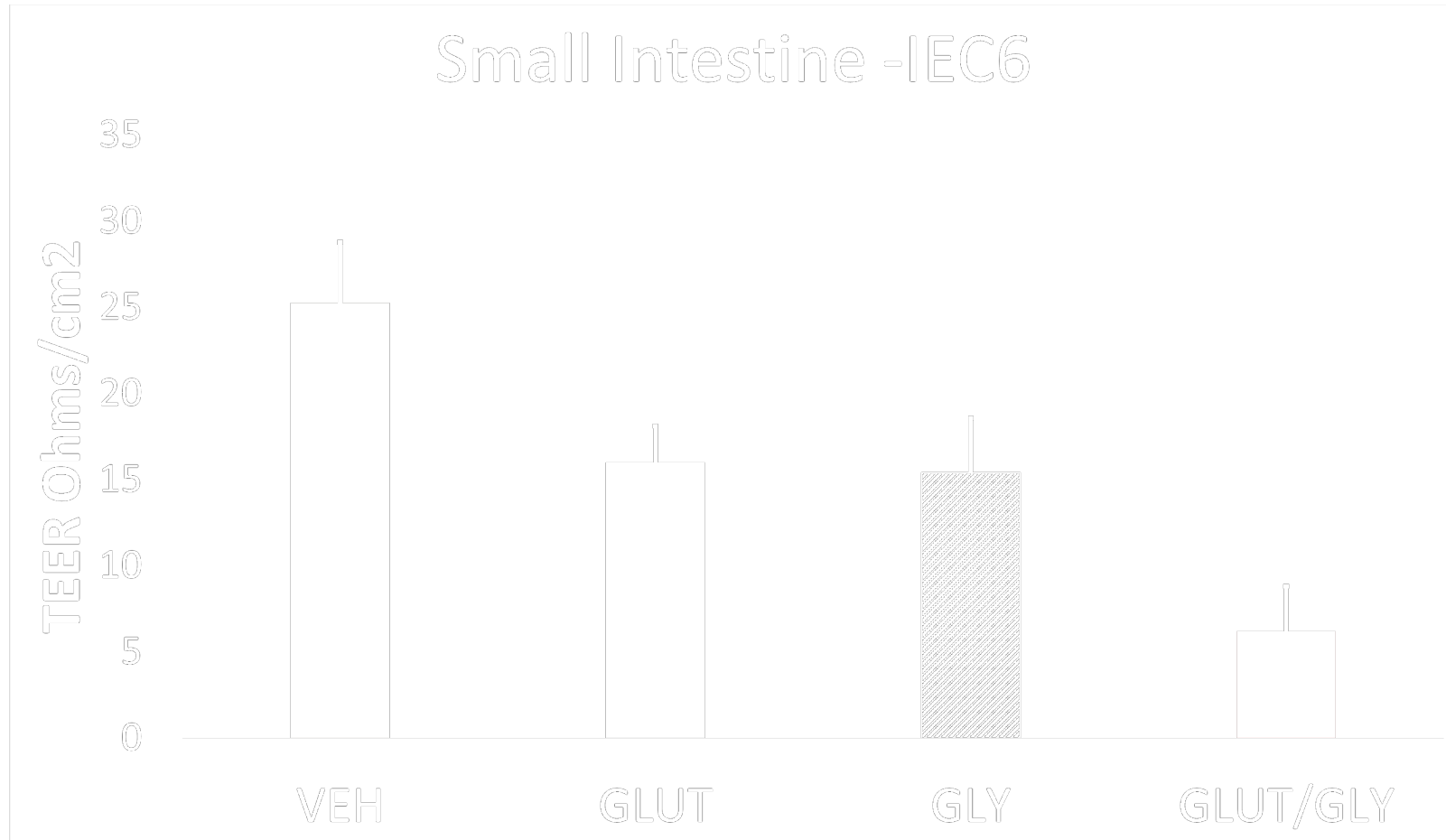
CONTROL



Gliadin in 1 slice of pizza



Functional Gut Barrier



Mechanism of Glyphosate/Gliadin Synergy and Bacterial Protection

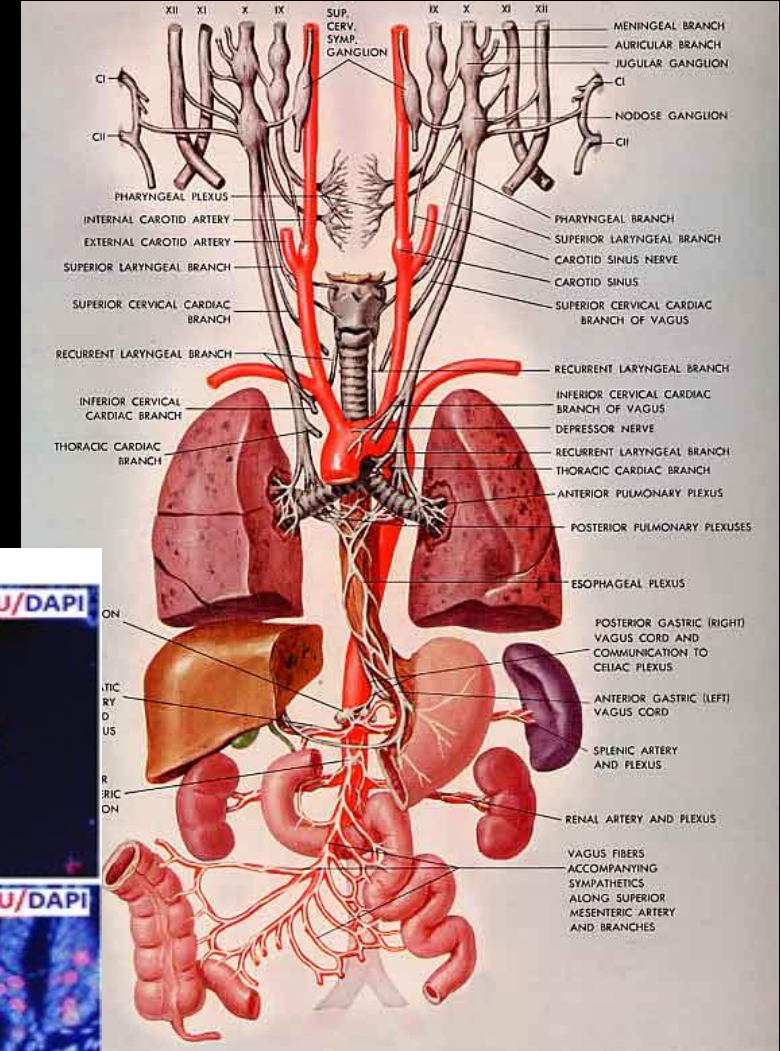
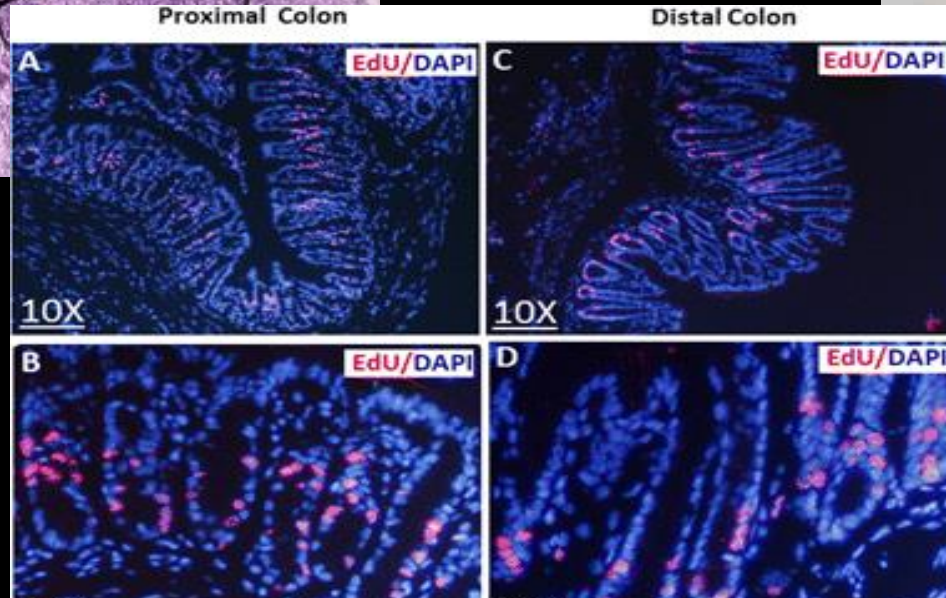
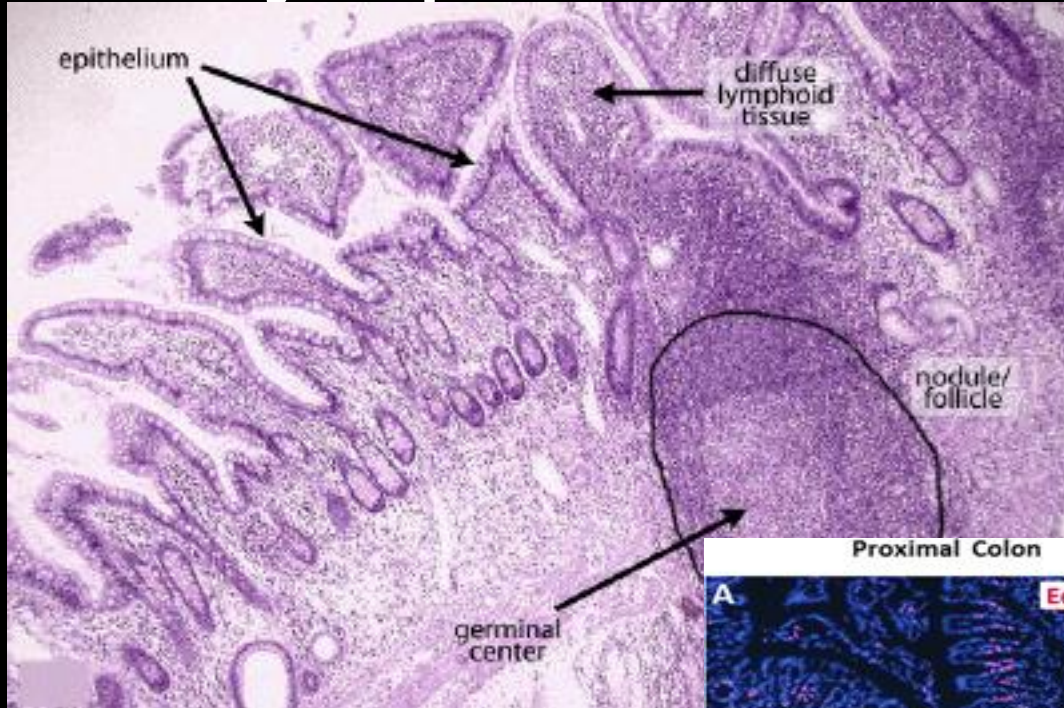
- Glyphosate exposure upregulates CXCR3 receptors at the gut epithelium
- Gliadin binds CXCR3 receptors to trigger Zonulin production
- Zonulin Occludins Toxin (ZOT) pathway degrades tight junctions
- Bacterial Metabolites from Terrahydrite block CXCR3 upregulation and increase DPP4 enzyme block on ZOT pathway

Symptoms of Gluten Sensitivity

- Mental fatigue, also known as “brain fog”
 - Neuromuscular fatigue, weakness
 - Abdominal pain
 - Major Depression
 - Headache
-
- After one year of strict gluten-free diet 85% of NCGS patients still report symptoms

Leaky Gut or Leaky Brain?

Sympathetic Nervous System Overload



Gut/Brain Postulate

- Loss of Microbiome Leads to Loss of Our Macro-membrane Integrity and System Wide Immune Overwhelm Results
 - Chronic Inflammation in the GALT
 - Sympathetic dysregulation of the Vagus Nerve throughout the intestines
 - Direct CNS insult from disruption of the Sinonasal/Brain and Blood Brain Barriers
 - The Glial Cell Systems Are Overwhelmed

Shikimate pathway purpose

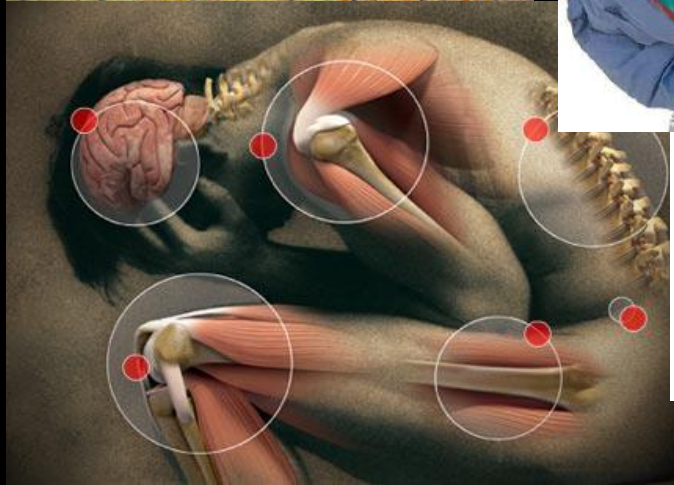
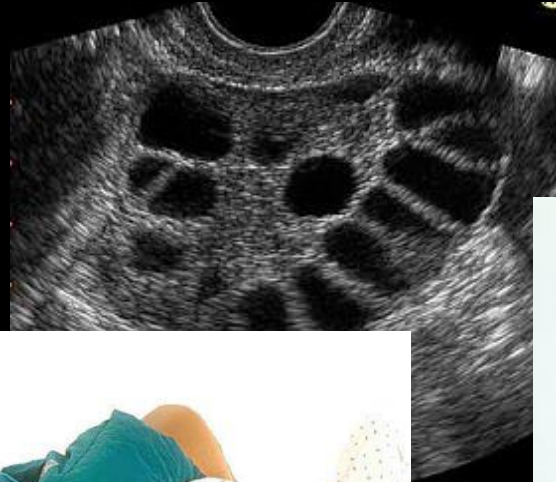
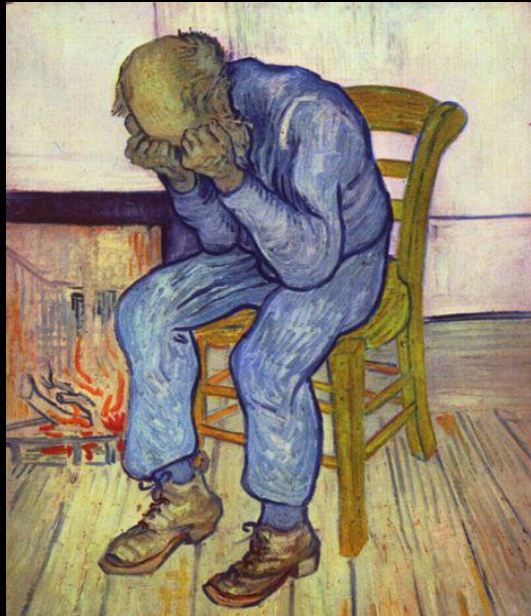
- Produces the aromatic amino acids
 - Phenylalanine
 - Tyrosine
 - Tryptophan
 - The aromatic amino acids are used in the synthesis of proteins and, in plants, fungi, and bacteria, give rise to a number of other specialized metabolites, such as phenylpropanoids and alkaloids

Alkaloids – Bacteria and Plant Based Medicine for the Ages

- Alkaloids have a wide range of pharmacological activities pertinent to the CNS
 - antiADHD (e.g. ephedrine)
 - cholinomimetic (e.g. galantamine)
 - vasodilatory (e.g. vincamine)
 - analgesic (e.g. morphine)
 - antihyperglycemic activities (e.g. piperine)

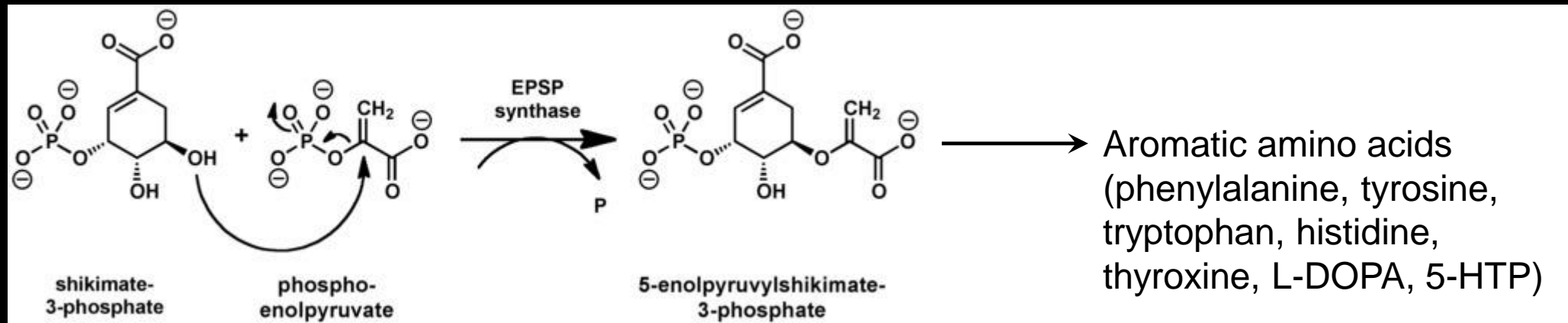


US Ranks 49th in Health Outcomes; Why Can't We Heal?



Thy Food Was Thy Medicine

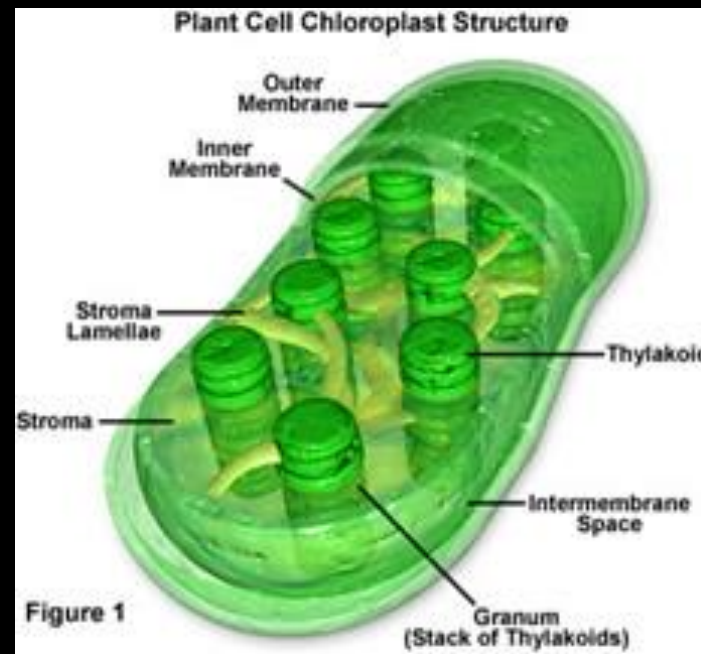
- Glyphosate inhibits the activity of the enzyme 5-enolpyruvyl shikimate 3-phosphate synthase (EPSPS)



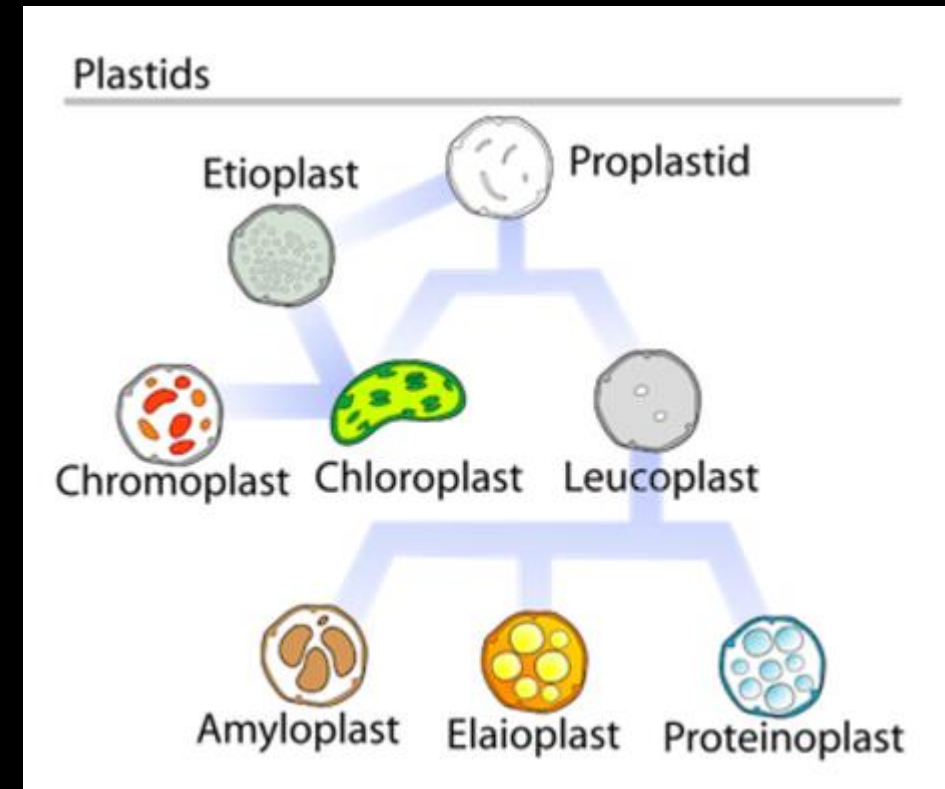
- This metabolic pathway exists in plants, fungi, and bacteria, but not in animals (Kishore & Shah 1988)

Plant Plastids

- Double Membrane Organelles in Bacteria, Fungi, and Plants



J Schmid, M Amrhein. Molecular organization of the shikimate pathway in higher plants. *Phytochemistry*. Volume 39, Issue 4, July 1995, Pages 737-749, July 1995, Pages 737-749



Alkaloids

- Alkaloids have a wide range of pharmacological activities including
 - Anti-parasite (e.g. quinine)
 - antiasthma (e.g. ephedrine)
 - anticancer (e.g. homoharringtonine)
 - cholinomimetic (e.g. galantamine)
 - vasodilatory (e.g. vincamine)
 - antiarrhythmic (e.g. quinidine)
 - analgesic (e.g. morphine)
 - antihyperglycemic activities (e.g. piperine)



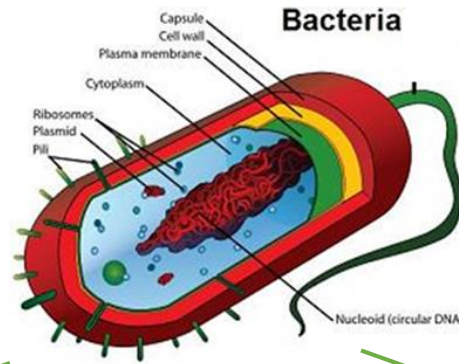
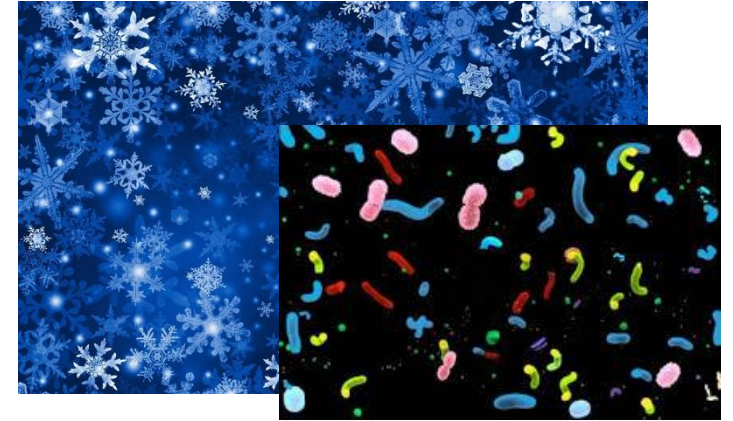
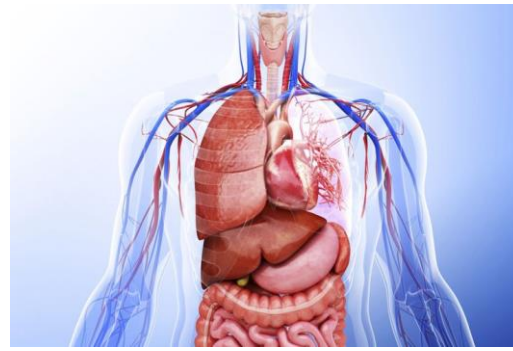
Gut/Brain Postulate #4

- Loss of the Microbiome Leads to a Loss of the production of neuro-modulatory alkaloid medicinal components of our food
 - Loss of sensory integration
 - Poor sleep quality
 - IBS
 - Migraine
 - MDD
 - Anxiety
 - Chronic Pain

Glyphosate's Legacy

- Destroys the ecosystem of bacteria, fungi, and parasites in the soil
- Eliminates nutrient delivery to our plants, sick crops require more chemical fertilizer, pesticides, herbicides
- Eliminates microbiome diversity and number in the gut of human and animals consuming the chemical in food and water
- Loss of microbiome genomics leads to a loss of genomic regulation of the Human genome
- Erodes the tight junctions in the gut, vascular, blood brain barriers triggering chronic inflammatory cascade
- ECM disruption enabling spirochete foothold in the epithelial and endothelial layers?
- Eliminates the medicinal alkaloids from our food chain



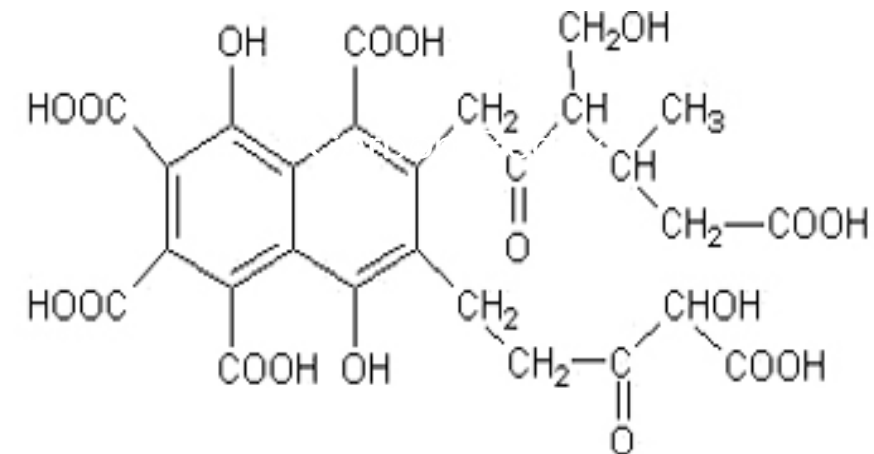
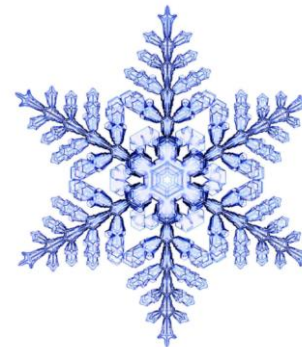


FAT

SUGAR

PROTEIN

MICRONUTRIENTS



Why Not Probiotics??

Cell

ARTICLE | VOLUME 174, ISSUE 6, P1406-1423.E16, SEPTEMBER 06, 2018

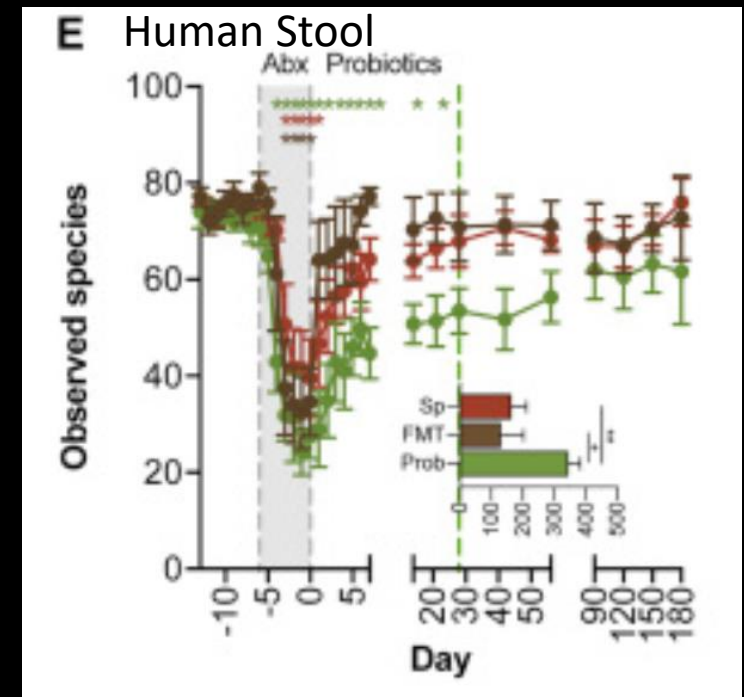
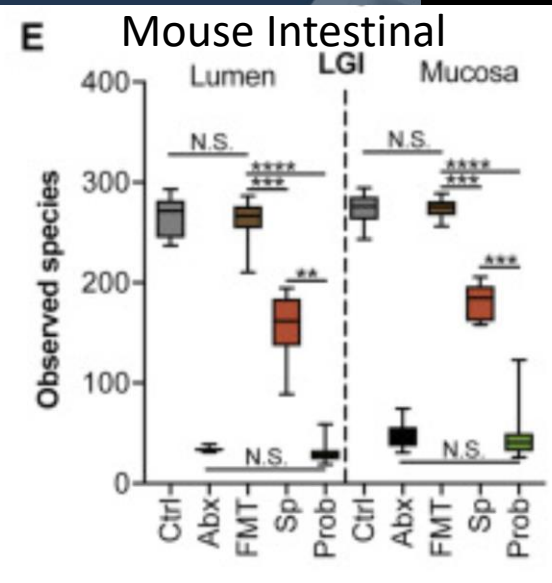
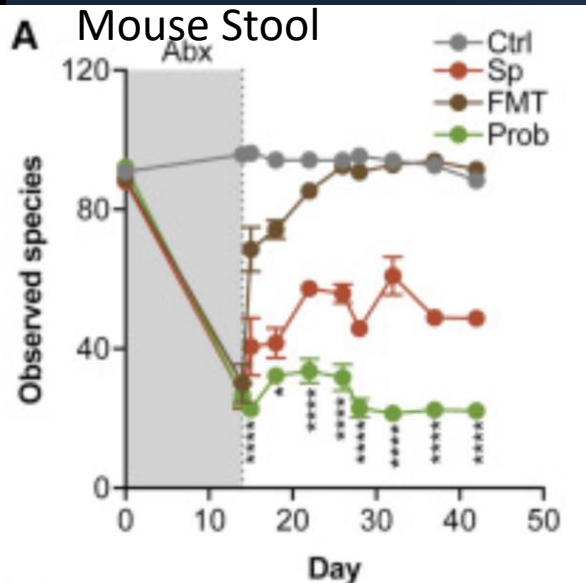
Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT

Jotham Suez¹¹ • Niv Zmora¹¹ • Gili Zilberman-Schapira¹¹ • ... Zamir Halpern¹² ✉ •

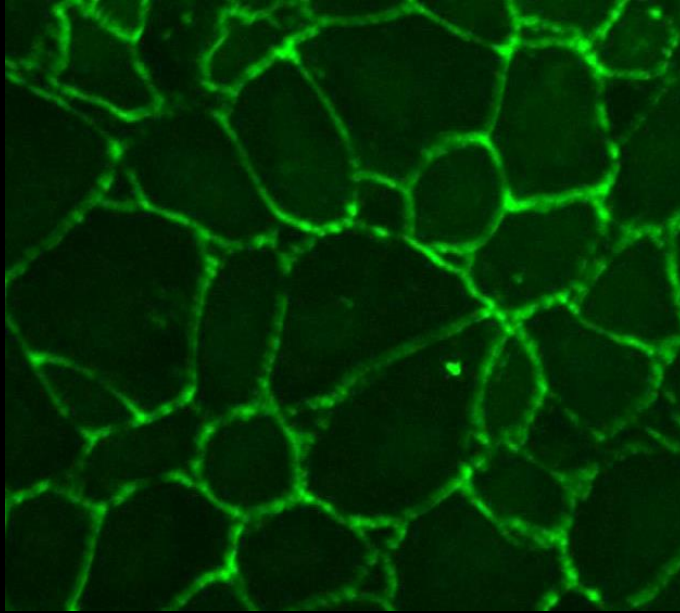
Eran Segal¹² ✉ • Eran Elinav^{12, 13} ✉ • Show all authors • Show footnotes

DOI: <https://doi.org/10.1016/j.cell.2018.08.047> • [Check for updates](#)

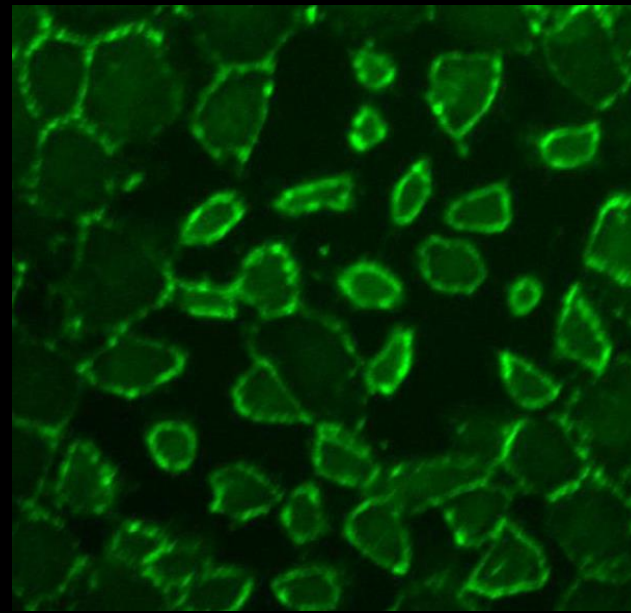
- Probiotic admin prevents post-antibiotic recovery of native microbiome for 6 months or more!!



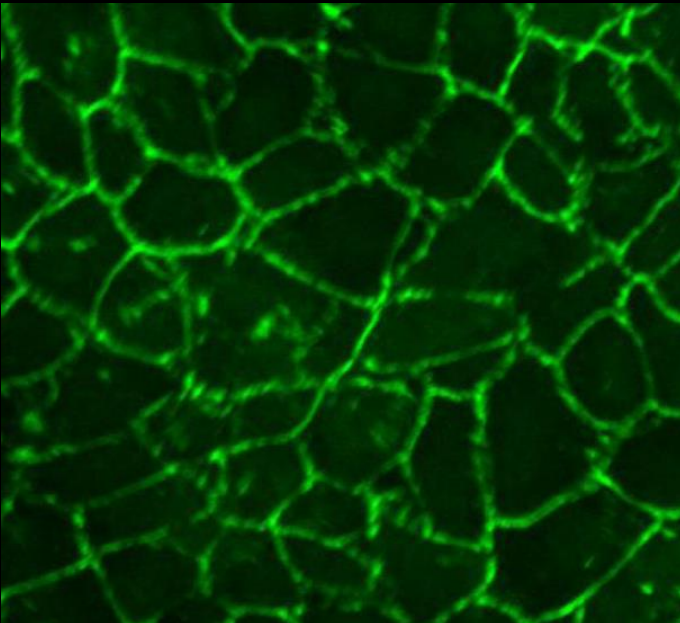
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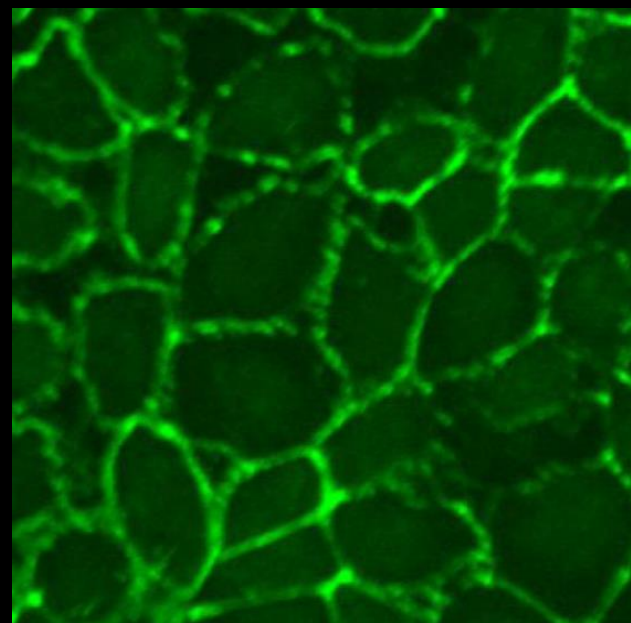
GLYPHOSATE



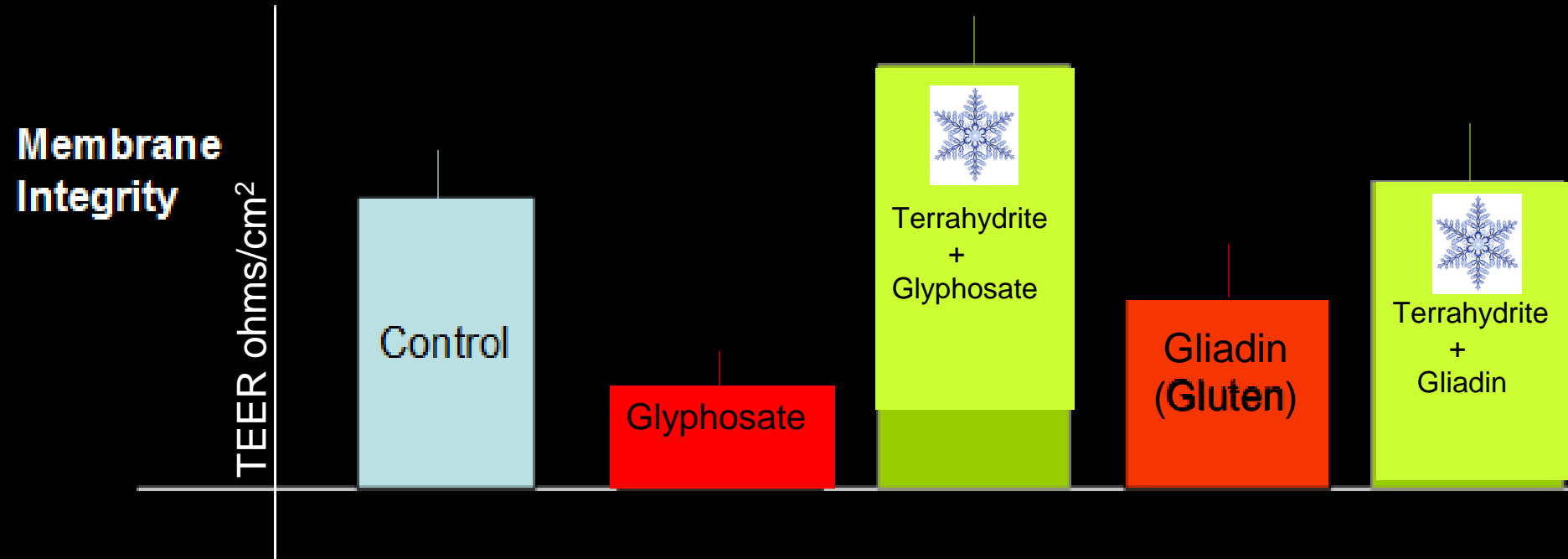
Terrahydrite



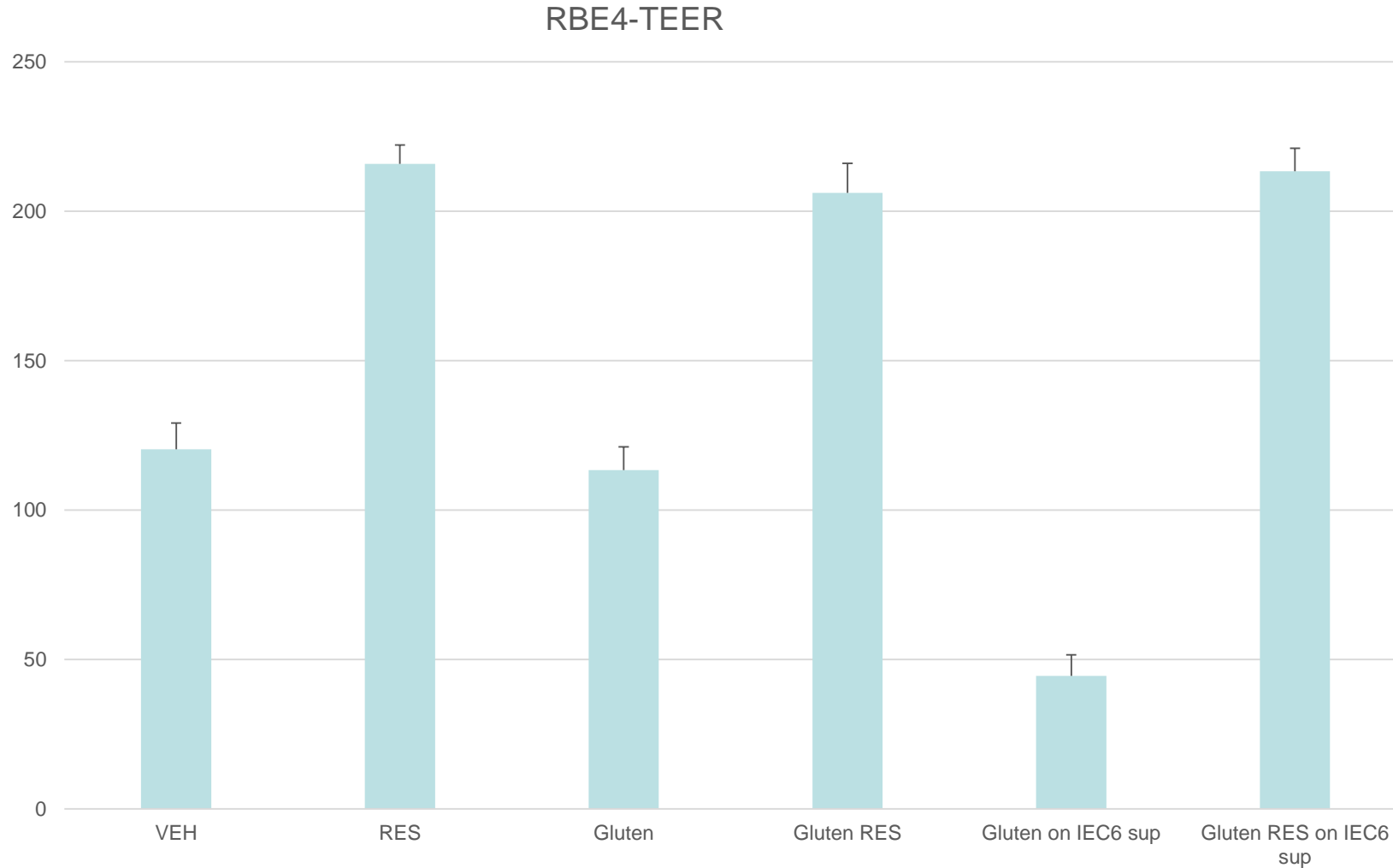
GLYPHOSATE and Terrahydrite



Bacterial Communication Protects The Gut Barrier System

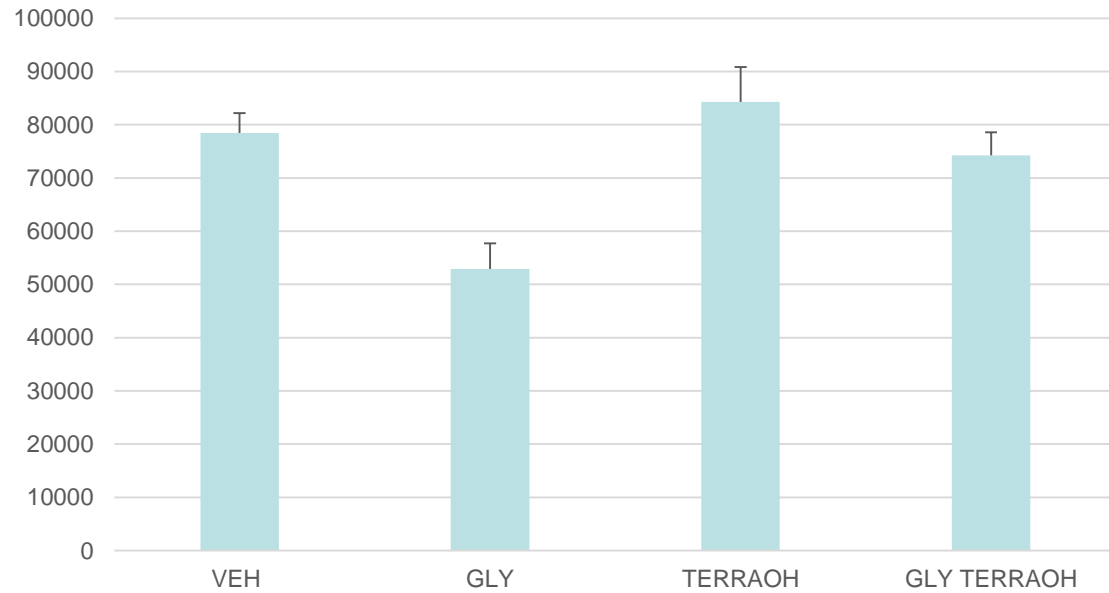


The Role of Terrahydrite in The Blood Brain Barrier

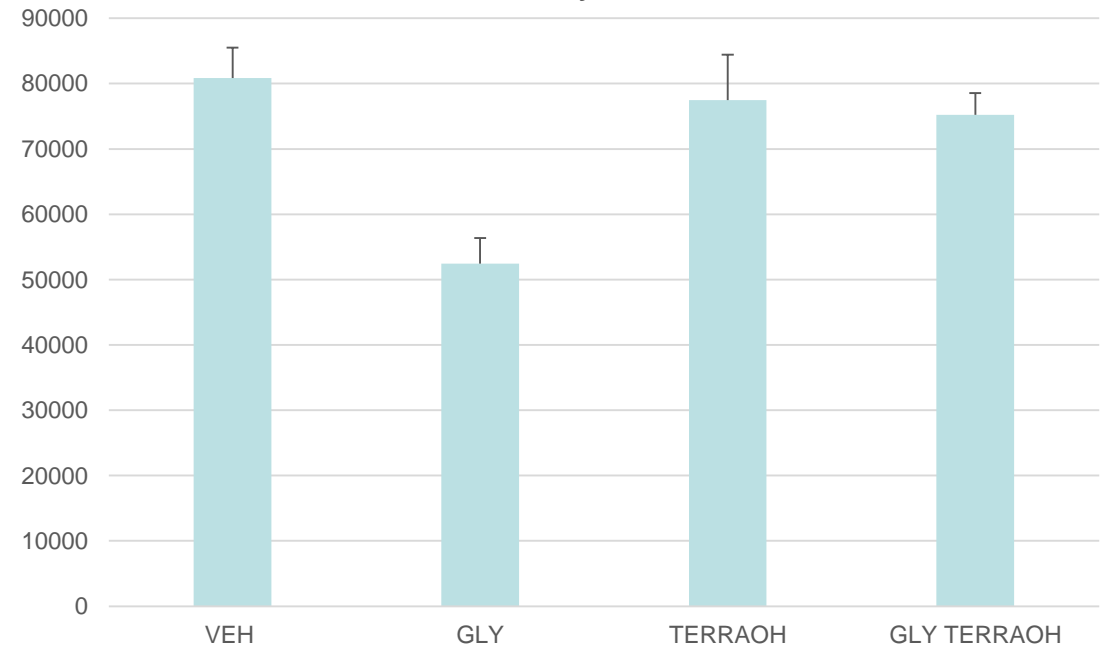


Terrahydrite Maintains Intestinal DPP4 Enzyme Production With or Without Glyphosate Injury

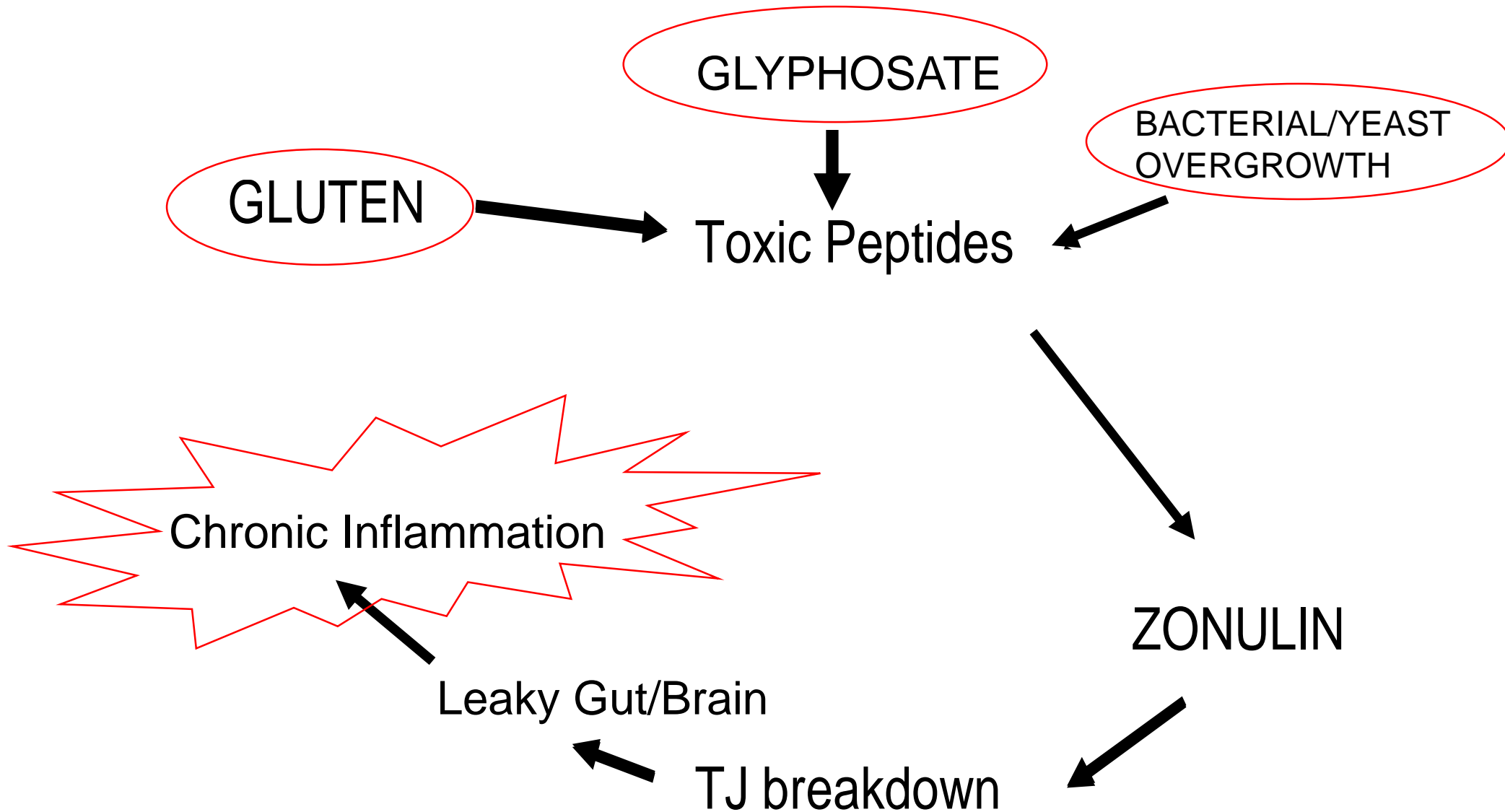
Small Intestine DPP4 Production



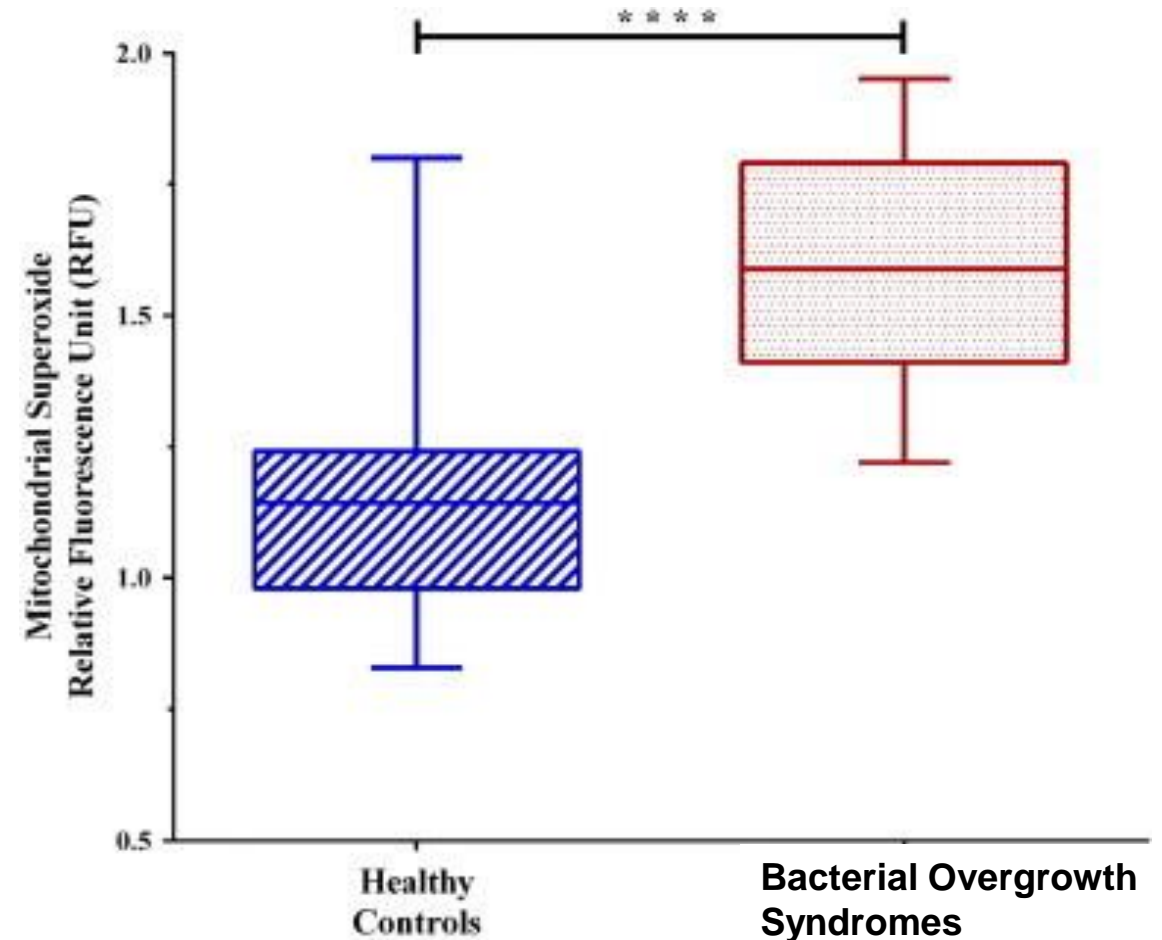
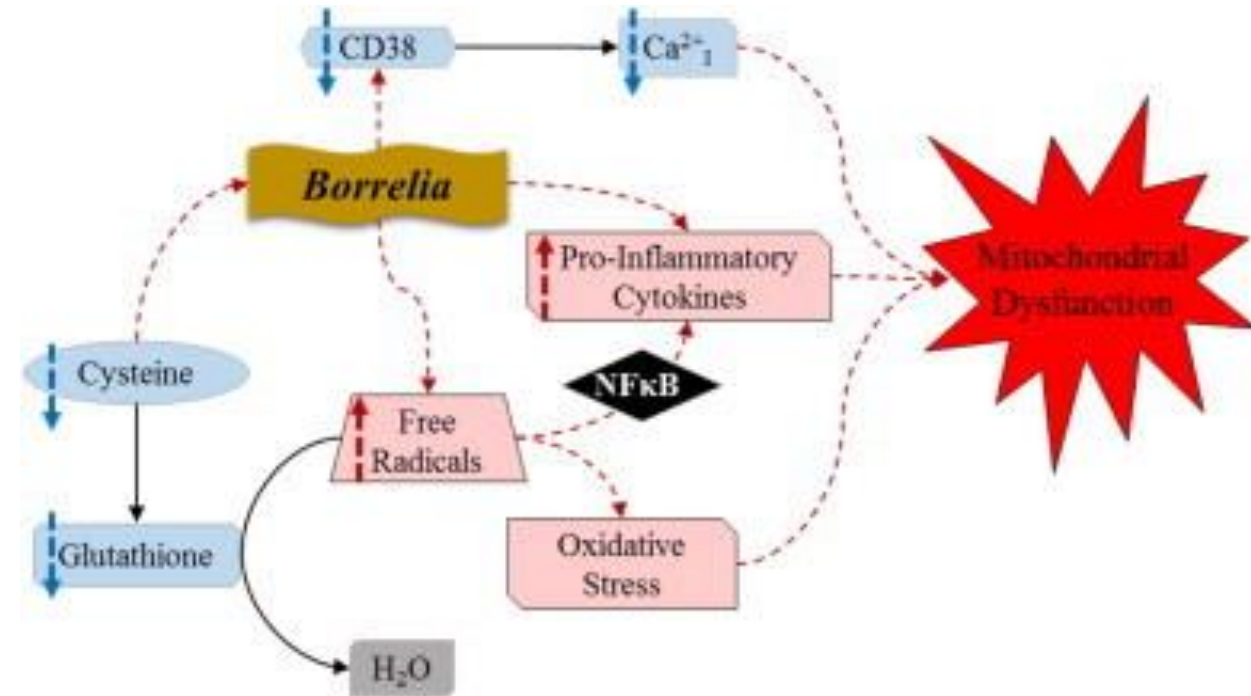
Colon DPP4 Enzyme Production



Acute vs Chronic Inflammatory Balance

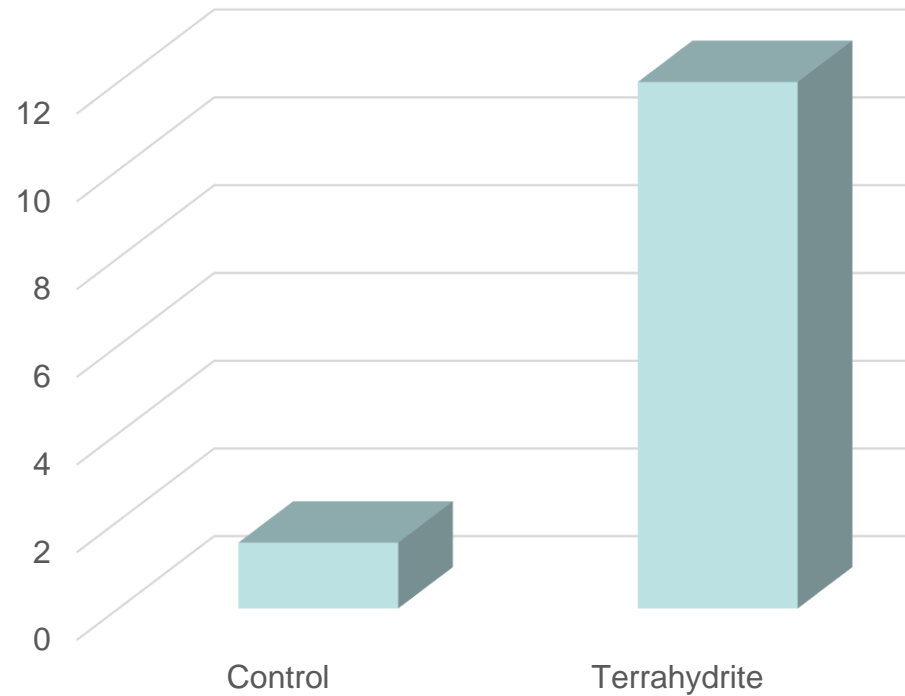


Mitochondrial Dysregulation In Autism



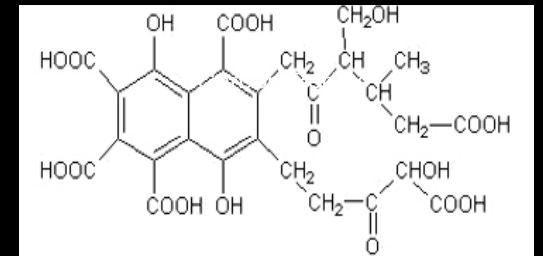
Small Bowel Glutathione Production Response to Terrahydrite

IEC6 and RTC Glutathione Before and 18 hours
after introduction of Terrahydrite

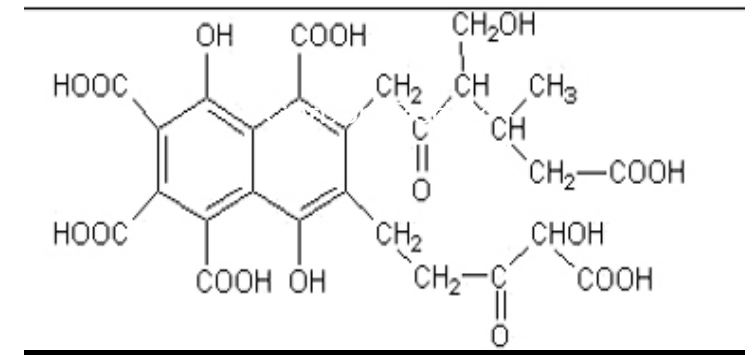


Established Functions of Terrahydrite

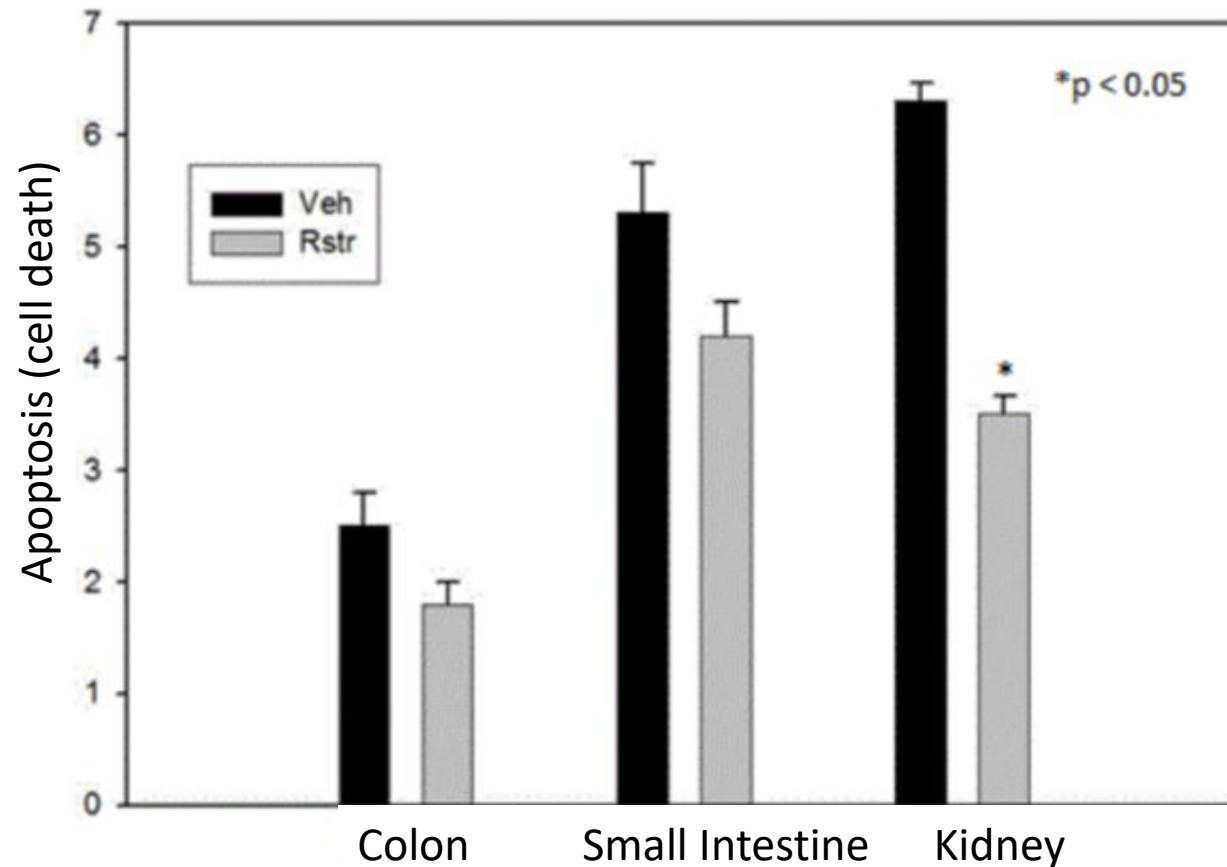
- Nutrient delivery
- Detoxification
- Maintenance of the intelligent gut barrier – tight junctions
- Support for the gap junctions – light / redox signaling
- Regulation of mitochondrial redox potential
- Regulation of antioxidant (glutathione) production
- Expand the microbiome volume for genomic and metabolic support (amino acids, microRNA, alkaloids, etc)



- Bacteria-derived carbon-based molecules are drawn from the massive ecosystem record in the fossil soil of the US desert
 - 60 Million years ago the ecosystem thrived on a level unimaginable today
 - Each species makes its own 'carbon snowflake'
 - Balance the Redox biochemical state
 - Mineral Amino Acid Complexes



Unparalleled Safety in Soil Extract Supplements



Terrahydrite Usage Guidelines

- Typical oral usage is one teaspoon 3X day before or with your meals
- Titrate as needed to 2 ounces three times daily for optimal results
- LYME/AUTISM/SENSITIVE INDIVIDUALS
 - START VERY SLOWLY
 - 3-5 drops under the tongue at bedtime
 - Double usage every week or as tolerated until at optimal results
 - 6-8 hour efficacy
 - Frequent usage can be more effective than higher volumes

Going for the nose

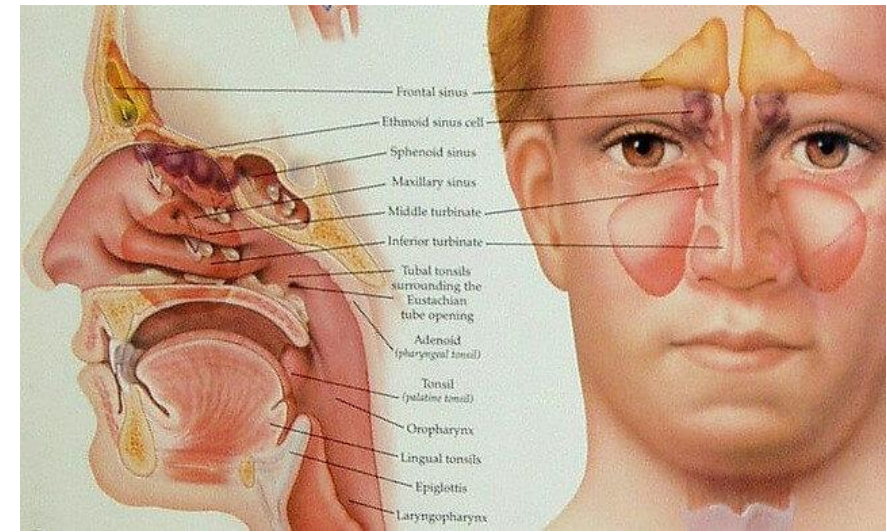
How do you take it?

Twice daily, 2-4 sprays per nostril

As often as needed through the day –
Every hour anyone?

Important before environmental and germ exposures –
Support your naso sinus barriers, the skin!!

SIBO? Go for the Nose – and acidify the stomach (HCl with Betai



Grow Your Medicine

- Soil management can return the medicinal quality of the food
 - Mycelium and Bacterial Management – Composting
 - Permaculture and Biodynamic Farming
 - Buy local, know your farmer – CSA, farmers market, farm to table restaurants
 - Grow Something in your window, yard or otherwise
- Eat crops picked ripe
- Cook your night shade vegetables (potatoes, peppers, egg plant, etc)
- Beware of the new “Organic” Hydroponic Crops!
- No-till organic is key to the future of soil recovery
- Push for labeling laws in all states to match or exceed the EU

So How Do We Heal, How Do We Rise

- Vaginal Birthing as much as possible, Vaginal Swab C-Section
- Breathe Nature – Get Outside
- Grow your own food!
- Grow your garden with your hands, touch the earth and your food that grows in it
- Stand barefoot in the grass soil – nakedness get extra credit
- Eat fermented foods daily
- Hug, kiss and generally celebrate every human, animal and plant that you can touch

The Team That Makes All This Known

