Bringing Out the Best in Your DNA for:

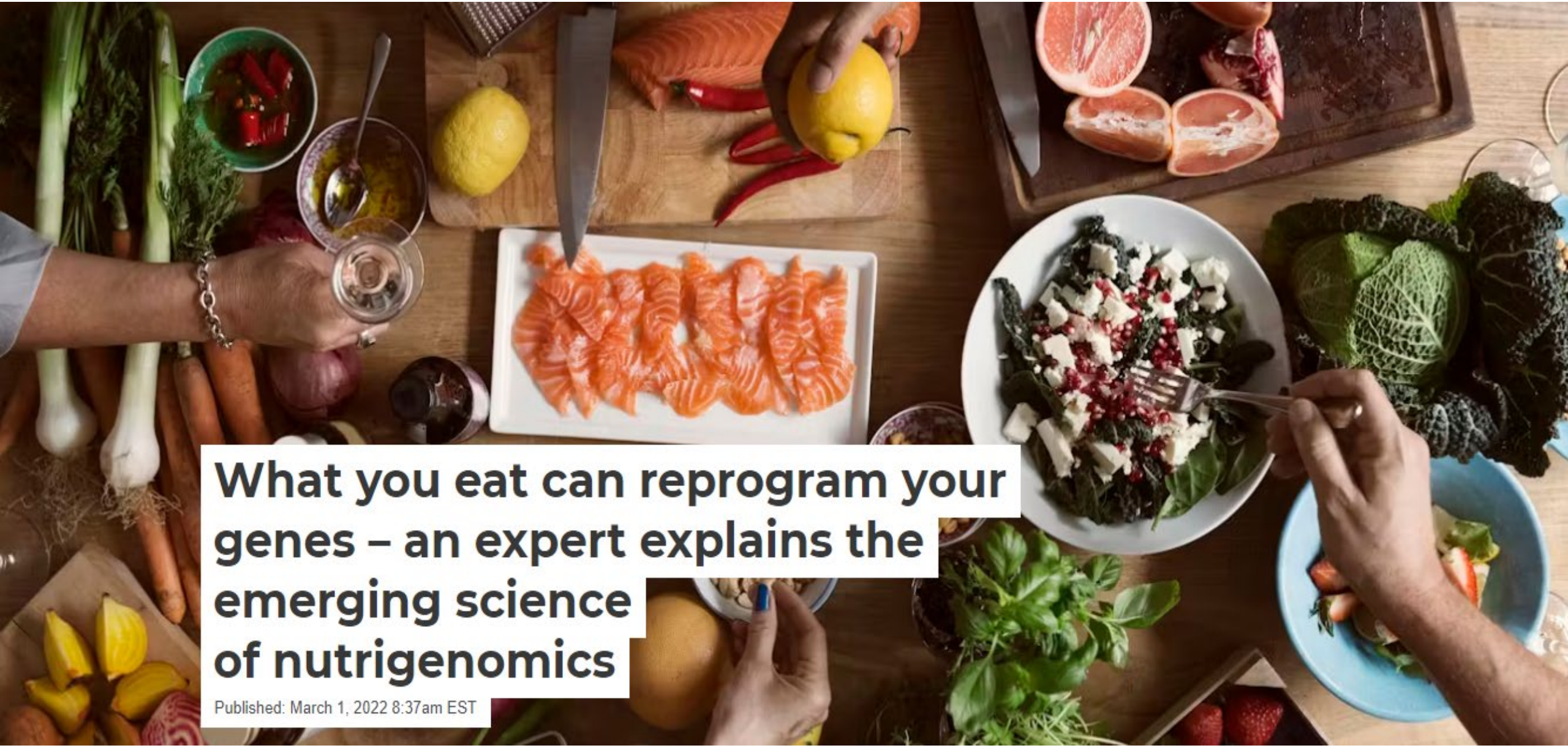
# Longevity & Bones

*Presented by Dr. Lynn Toohey, PhD Nutrition*

## Genetics vs Epigenetics

**“Eating, Supplementing, Exercising and Adjusting for your genes”**

**Recognition – Analysis - Support**



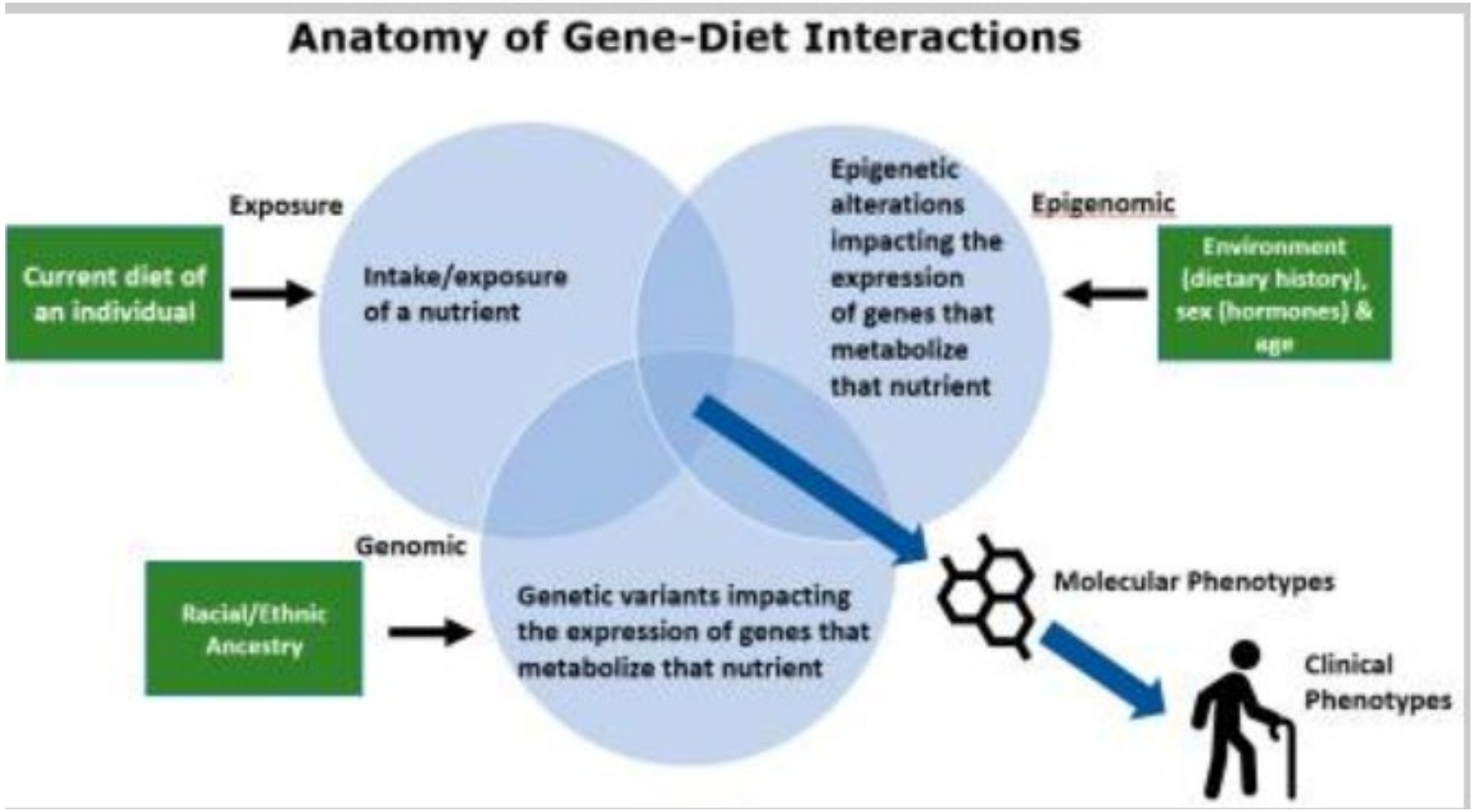
# What you eat can reprogram your genes – an expert explains the emerging science of nutrigenomics

Published: March 1, 2022 8:37am EST

# Food also "talks" to our genome -

- the genetic blueprint that directs the way the body functions down to the cellular level.

# Genotype to Phenotype



# Richard Morgan 93


**“Four-time world champion in indoor rowing, with the aerobic engine of a healthy 30- or 40-year-old and the body-fat percentage of a whippet.”**

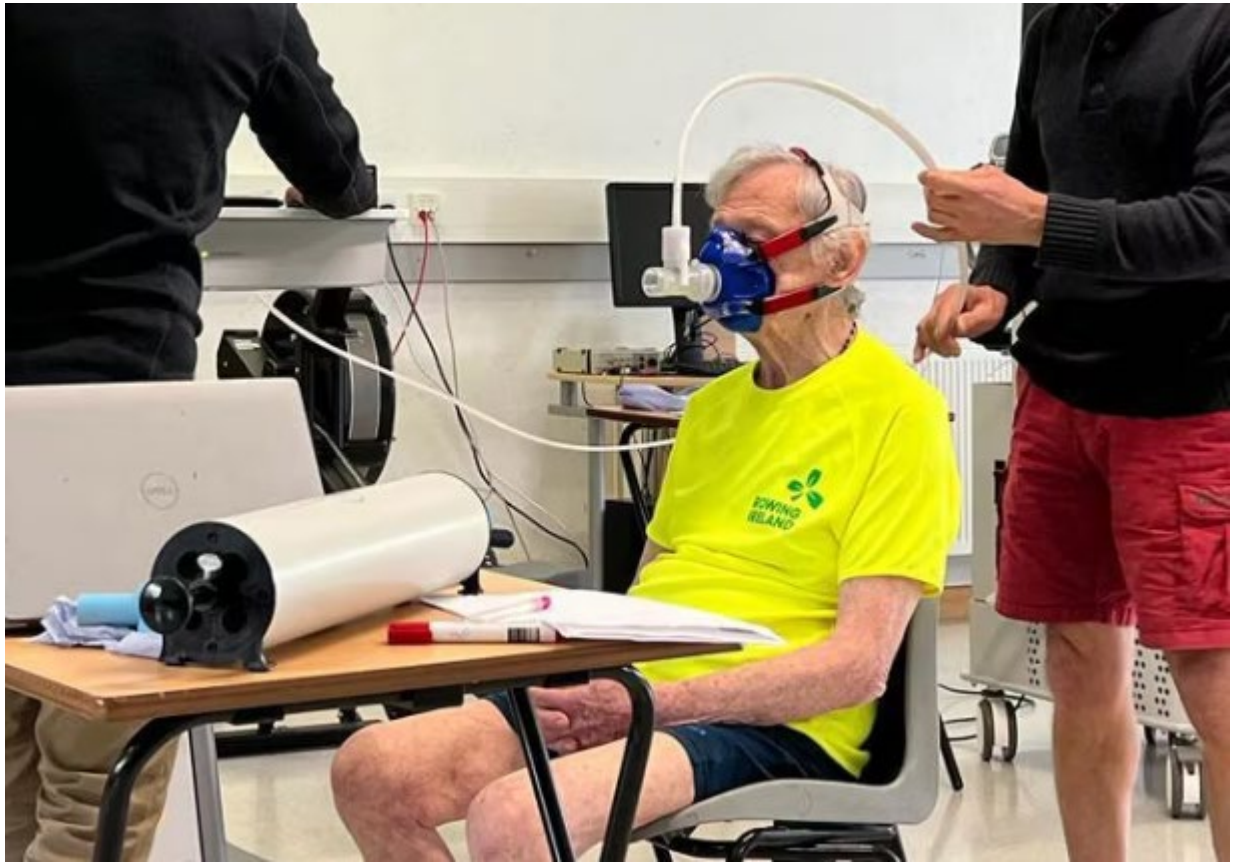
# Do we quit exercising because we get old, or…

- Subject of a new case study, published in the Journal of Applied Physiology; looked at training, diet and physiology (Daly LS, Van Hooren B, Jakeman P.J Appl Physiol. 2023 Dec 1;135(6):1415-1420.)
- A nonagenarian with the heart, muscles and lungs of someone less than half his age
- A onetime baker and battery maker with creaky knees who didn't take up regular exercise until 70s

# Are declines in muscle mass normal and inevitable or due in a big part to a lack of exercise?

- Fitness routine began later in life
- Has now rowed the equivalent of almost 10 times around the globe and has won four world championships
- So what, the researchers wondered, did his late-life exercise do for his aging body?

# Highest Heart Rate on Record for Age



His heart rate also headed toward this peak very quickly, meaning his heart was able to rapidly supply his working muscles with oxygen and fuel.

# Exercise Routine:

- **Consistency:** Every week, he rows about 30 kilometers (about 18.5 miles), averaging around 40 minutes a day.

- **A mix of easy, moderate and intense training:** About 70 percent of these workouts are easy, with Morgan hardly laboring. Another 20 percent are at a difficult but tolerable pace, and the final 10 at an all-out, barely sustainable intensity.

- **Weight training:** Two or three times a week, he also weight-trains, using adjustable dumbbells to complete about three sets of lunges and curls, repeating each move until his muscles are too tired to continue.

- **A high-protein diet:** He eats plenty of protein, his daily consumption regularly exceeding the usual dietary recommendation of about 60 grams of protein for someone of his weight.

# Not Everyone has to Row

# Conclusion:

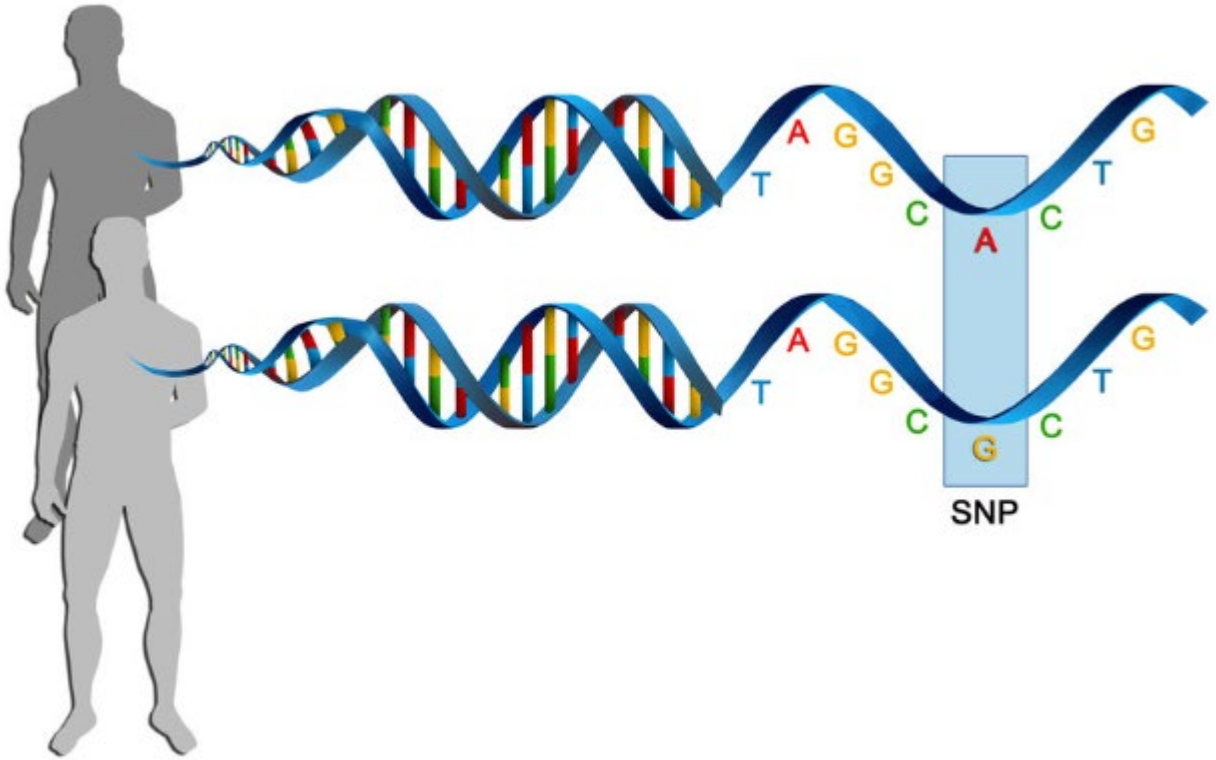
- The human body maintains the ability to adapt to exercise at any age.

- “Morgan probably had some **genetic advantages” - genetic SNPs (single nucleotide polymorphisms) can be manifested differently with environmental changes**).

- SNPs is the fancy expression for “gene variants”.

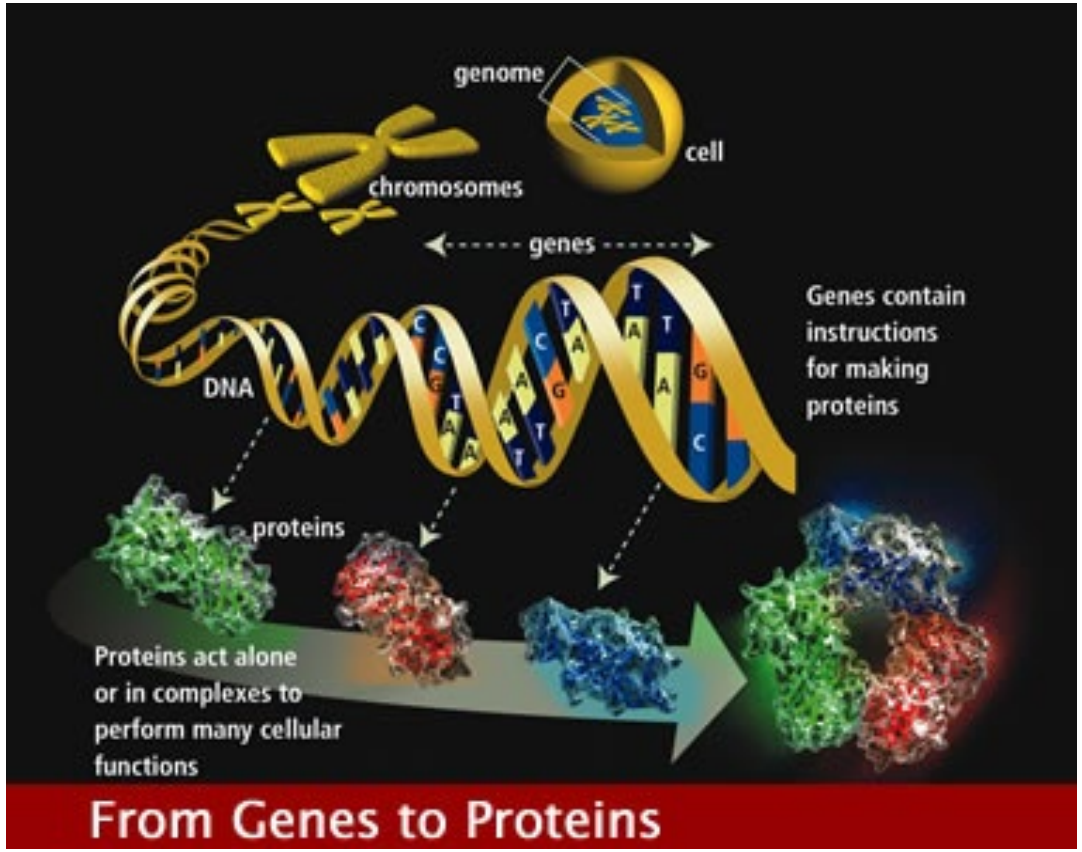
# Genetic variants (SNPs)

- A **single-nucleotide polymorphism** (**SNP**) is a substitution of a single nucleotide that occurs at a specific position in the genome



# Genetic Variants

- Inherited changes in the genetic codes that may have an effect on the functioning of the corresponding enzyme
- (SNiPS) **Single nucleotide polymorphisms** (Minor changes in DNA base pairs that affect the function of the corresponding enzyme)
- **Heterozygous variants**-Only one of your inherited alleles are a variation from normal, reduces activity by approximately 30%
- **Homozygous variants**-Both of your inherited alleles are variants from normal, reduces activity of enzyme by approximately 70%


genome
cell
chromosomes
genes
DNA
Genes contain instructions for making proteins
proteins
Proteins act alone or in complexes to perform many cellular functions
From Genes to Proteins

# AncestryDNA

- Will give Genetic SNiP's
- Cost-$59-$99 (depends on sale)
- Painless-Saliva
- Results in about 4-6 weeks
- Only have to do once!
- Must plug into secondary site for more info (Geneticgenie.org, MTHFRSupport.com, FHEval etc.)
- Preferred over 23andme because they test for more SNPs and 23andme has security problems

# DNA Raw Data

Each line corresponds to a single SNP. For each SNP, we provide its identifier (an rsid or an internal id), its location on the reference human genome, and the genotype call oriented with respect to the plus strand on the human reference sequence.

| •# rsid | chromosome | position | genotype |
|---|---|---|---|
| •rs12564807 | 1 | 734462 | AA |
| •rs3131972 | 1 | 752721 | AG |
| •rs148828841 | 1 | 760998 | CC |
| •rs12124819 | 1 | 776546 | AA |
| •rs115093905 | 1 | 787173 | GG |
| •rs11240777 | 1 | 798959 | GG |
| •rs7538305 | 1 | 824398 | AC |
| •rs4970383 | 1 | 838555 | AC |
| •rs4475691 | 1 | 846808 | CC |
| •rs7537756 | 1 | 854250 | AA |
| •rs13302982 | 1 | 861808 | GG |
| •rs55678698 | 1 | 864490 | CT |
| •i6019299 | 1 | 871267 | CC |

| Cannabinoid Pathway | | | | |
|---|---|---|---|---|
| SNP ID | SNP Name | Risk Allele | Your Alleles | Your Results |
| rs4328262 | VDR C18167A | G | GG | +/+ |
| rs3782905 | VDR C37648G | C | CG | +/- |
| rs2189480 | VDR C39987A | T | GG | -/- |
| rs3847987 | VDR C48238068A | A | CC | -/- |
| rs757343 | VDR C48239675T | T | CC | -/- |
| rs2107301 | VDR C48245T | A | AG | +/- |
| rs2238136 | VDR C48277713T | T | CT | +/- |
| rs11574027 | VDR C48287373A | A | CC | -/- |
| rs7299460 | VDR C48296268T | T | CC | -/- |
| rs2239184 | VDR C59232T | A | GG | -/- |
| rs739837 | VDR C65594A | G | GG | +/+ |
| rs2228570 | VDR Fok | A | AG | +/- |
| rs3890733 | VDR G14442A | T | CC | -/- |
| rs12717991 | VDR G44689A | T | CT | +/- |
| rs1540339 | VDR G46489A | T | CT | +/- |
| rs2239185 | VDR G48244559A | A | GG | -/- |
| rs11168267 | VDR G48251542A | A | GG | -/- |
| rs886441 | VDR G48262964A | G | AA | -/- |
| rs10783218 | VDR G48272743A | A | GG | -/- |
| rs2254210 | VDR G48273714A | A | AG | +/- |
| rs11168287 | VDR G48285414A | G | GG | +/+ |
| rs4334089 | VDR G48286015A | G | GG | +/+ |
| rs4237855 | VDR G48287203A | A | GG | -/- |
| rs11574026 | VDR G48288246A | A | GG | -/- |
| rs11168293 | VDR G48293716T | G | GG | +/+ |
| rs4760655 | VDR G48294131A | G | GG | +/+ |
| rs7975232 | VDR G64978T | A | CC | -/- |
| rs2229828 | VDR S198S | A | GG | -/- |
| rs2239186 | VDR T34405C | G | AA | -/- |
| rs3819545 | VDR T38809C | G | AG | +/- |
| rs11574115 | VDR T412I | A | GG | -/- |
| rs34189316 | VDR T416T | A | GG | -/- |
| rs2239181 | VDR T47866G | C | AA | -/- |
| rs2239182 | VDR T48255411C | C | CT | +/- |
| rs11168275 | VDR T48272275C | C | TT | -/- |
| rs2248098 | VDR T50459C | G | AA | -/- |
| rs11574129 | VDR T66512C | G | AA | -/- |
| rs4760658 | VDR T7329C | G | AA | -/- |
| rs731236 | VDR TAQ | A | AA | +/+ |

# FHEval

| SNIP | rsiD | Risk Allele | Your Allele | Results | Category | Kinesiology Challenge |
|---|---|---|---|---|---|---|
| AANAT | rs11077820 | T | TT | ++ | Sleep | Serotonin |
| ACAT1 | rs3741049 | A | GG | -- | Cardiovascular/Energy | Pyruvate, Glucose, Acetyl Co A, Cholesterol, Lactic Acid, Ethanol |
| ACE | rs4343 | G | AG | -+ | Cardovascular | Angiotensin I |
| ADIPOQ | rs17366568 | A | AG | +- | Obesity/Appetite | Adiponectin |
| ADH1B | rs1229984 | A | CC | -- | Detox/Alcohol | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs2238151 | T | CT | -+ | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs4648328 | T | CT | -+ | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs441 | C | CT | +- | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs968529 | C | CC | ++ | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs4646778 | A | AC | +- | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs671 | A | GG | -- | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs16941667 | T | CC | -- | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |

# One of the most common and most studied SNPs

## MTHFR

- Interferes with the conversion of folic acid to methylfolate (active form) which leads to a functional deficiency of folic acid.
- C677T variant in the MTHFR gene influences susceptibility to migraines with aura. Migraine, with and without aura is a prevalent and complex neurovascular disorder that may also be affected by genetically influenced hyperhomocysteinaemia. BMC Medicine 2004
- **Kinesiology Challenge**: Homocysteine

# Longevity -The health of elderly individuals is closely linked to their protein intake and the abundance of intestinal microbiota

- Deng L. J Sci Food Agric. 2023 Sep;103(12):5949-5957.

# Protein Powder – hydrolyzed proteins:

- **Immunomodulatory activity**
- **Hypoallergenic**
- **“Protein hydrolysates attenuate pro-inflammatory gene expression.”**
- **Epigenetic modification of gene manifestation**
- (Food Chem. 2017 Jun 1;224:320-328. Immunomodulatory activity of protein hydrolysates derived from Virgibacillus halodenitrificans SK1-3-7 proteinase. Toopcham T, et al.)

# Microscopic Focus on One Microbiota Function

- Enteroendocrine cells make GLP-1 (glucagon-like peptide).
  - Secreted in response to food, especially high protein.
- GLP-1 regulates insulin secretion and blood sugar levels, important for longevity prospects.
- GLP-1 is also associated with numerous regulatory and protective effects.
- GLP-1 agonists (drugs) are the rage right now.

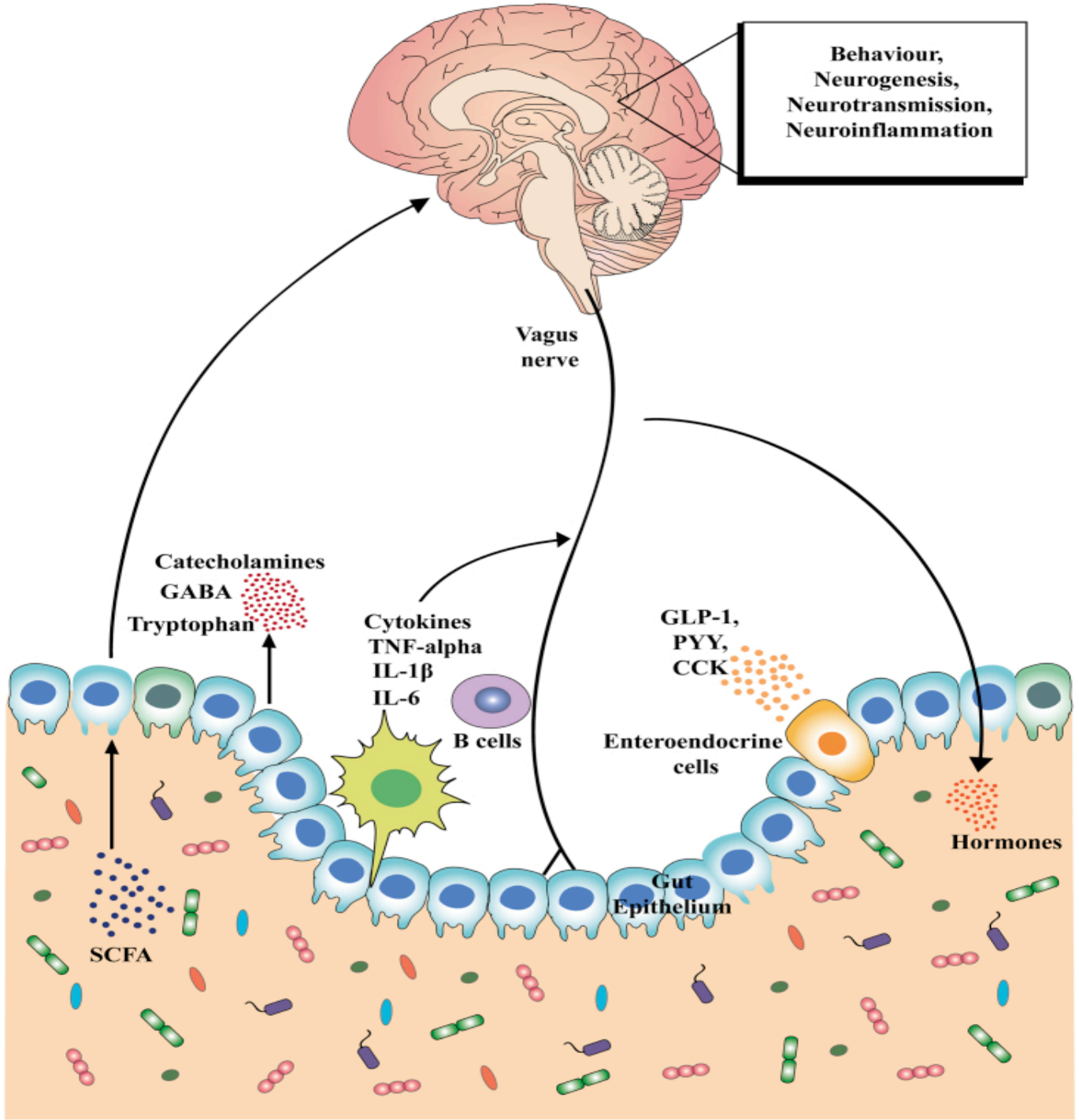
# GLP-1R is a gene for the GLP-1 receptor

- **GLP-1R SNPs**

- **rs10305420**: Associated with glycemic response and weight response to exenatide (forerunner to Ozempic)
- **rs7903146**: Associated with the response to exogenous GLP-1
- **rs10010131**: Associated with the response to exogenous GLP-1
- **rs151290, rs2237892, and rs2237895**: Associated with altered endogenous GLP-1 secretion

- A genetic test reveals whether someone carries a susceptibility for decreased activity for these gene variants.

# Enteroendocrine cells release GLP-1



# Pitfalls of the Ozempic Craze and Natural Support for GLP1 (Upcoming TAC article on Natural Approaches to Ozempic)

- Exenatide(forerunner to Ozempic) generated this headline close to 20 years ago: "Diabetes drug made from lizard spit approved." Newsweek April 29th 2005.

- **Side effects:**
- GI upset/nausea
- If patients go off these drugs, rapid return of lost weight can be expected - there is still an insufficient amount of GLP1 circulating in the body.

# Glutamine

- **Glutamine:** major fuel source for the enteroendocrine cells.
- Scientific evidence that **glutamine** increases GLP1
  - Badole,L. et al.  Oral l-glutamine increases active GLP-1 (7-36) amide secretion and improves glycemic control… Chemico-Biological Interactions. 2013. 203 (2):530-541.

- **Glutamine** positively affects weight balance.
  - Laviano A, et al. Glutamine supplementation favors weight loss in nondieting obese female patients. A pilot study. Eur J Clin Nutr. 2014 Nov;68(11):1264-6.

# More nutrients to support a health intestinal lining

- Zinc
- Alpha lipoic acid
- Ginkgo biloba
- Probiotics
- Prebiotics like Jerusalem artichoke

# Probiotics

- In 2021, “The role of probiotics in reducing body mass index and weight as well as changing the visceral abdominal fat area, waist and hip circumference” was demonstrated in 14 clinical trials included in a systematic review.
  - Tomé-Castro XM, et al. Probiotics as a therapeutic strategy in obesity and overweight: a systematic review. Benef Microbes. 2021 Feb 24;12(1):5-15.

# Clinical trial Pre- and Probiotics

- Three groups: 1) diet (low carbohydrate and low calorie), 2) prebiotics, and 3) probiotics.
- Only the prebiotic and probiotic group showed a significant decrease in fat mass and a significant increase in muscle strength.
- Results also showed a significant decrease in insulinemia and HOMA-IR (measures insulin resistance and beta cell function) in the prebiotic group compared to the diet-alone group, and the probiotic group showed a significant decrease in fasting blood glucose compared to the diet alone group.
- A significant improvement in sleep quality was noted in the prebiotic group, with a significant decrease in depression, anxiety and stress in all three groups. All in all, results confirmed a positive effect for pre- and probiotics for weight support.
  - Ben Othman R, et al. A clinical trial about effects of prebiotic and probiotic supplementation on weight loss, psychological profile and metabolic parameters in obese subjects. Endocrinol Diabetes Metab. 2023 Mar;6(2):e402.

# Certain Foods will Raise GLP-1

- **Eggs –** high in protein; egg whites are particularly beneficial. Associated with lower post-meal blood glucose levels, reduced hunger, decreased food intake and overall satisfaction with a meal.

- **Nuts –** A 2016 research review suggests that almonds and pistachios increase GLP-1 levels through their protein, fiber, and healthy fat content. Fiber in the nuts slows digestion, leading to a gradual release of glucose into the bloodstream and a corresponding increase in GLP-1 secretion. Healthy fats in nuts can improve insulin sensitivity, which further supports the release of GLP-1.

**Eggs can raise HDL**

DiMarco DM, et al. Intake of up to 3 Eggs per Day Is Associated with Changes in HDL Function and Increased Plasma Antioxidants in Healthy, Young Adults. J Nutr. 2017 Mar;147(3):323-329.

# GLP-1 raising foods continued

- **Monounsaturated fats**
- Monounsaturated fats,

ie olive oil, avocados etc.  stimulate GLP-1 release.

- Regular consumption of an olive oil-enriched diet increased GLP-1 secre
lower glucose levels, increased glucose-stimulated insulin secretion, enha
glucose tolerance, decreased weight gain and improved insulin sensitivity
- Avocados additionally increase peptide YY (appetite regulating)

while reducing insulin levels.

# Vision & Skin

- Bodnaruc, A.M., *et al.* Nutritional modulation of endogenous glucagon-like peptide-1 secretion: a review. *Nutr Metab (Lond)* **13**, 92 (2016).

# High fiber foods

- High fiber foods like **cruciferous vegetables** (broccoli, cauliflower, brussel sprouts, cabbage etc), **beets, avocados, oats** etc. slow digestion, gradually releasing glucose into the bloodstream and triggering release of GLP-1. When the fiber is fermented by gut bacteria, it produces short-chain fatty acids (SCFAs) like acetate, propionate, and **butyrate** which simulate GLP-1 release.

- One study conducted in Jakarta, Indonesia, found that **consuming vegetables before carbohydrates significantly affected glucose and GLP-1** levels in individuals with type 2 diabetes, especially 60 minutes after eating.

# GLP-1 Spices

- Healthful digestive spices include ginger, turmeric, peppermint and cinnamon. Use as condiments, teas or supplements.

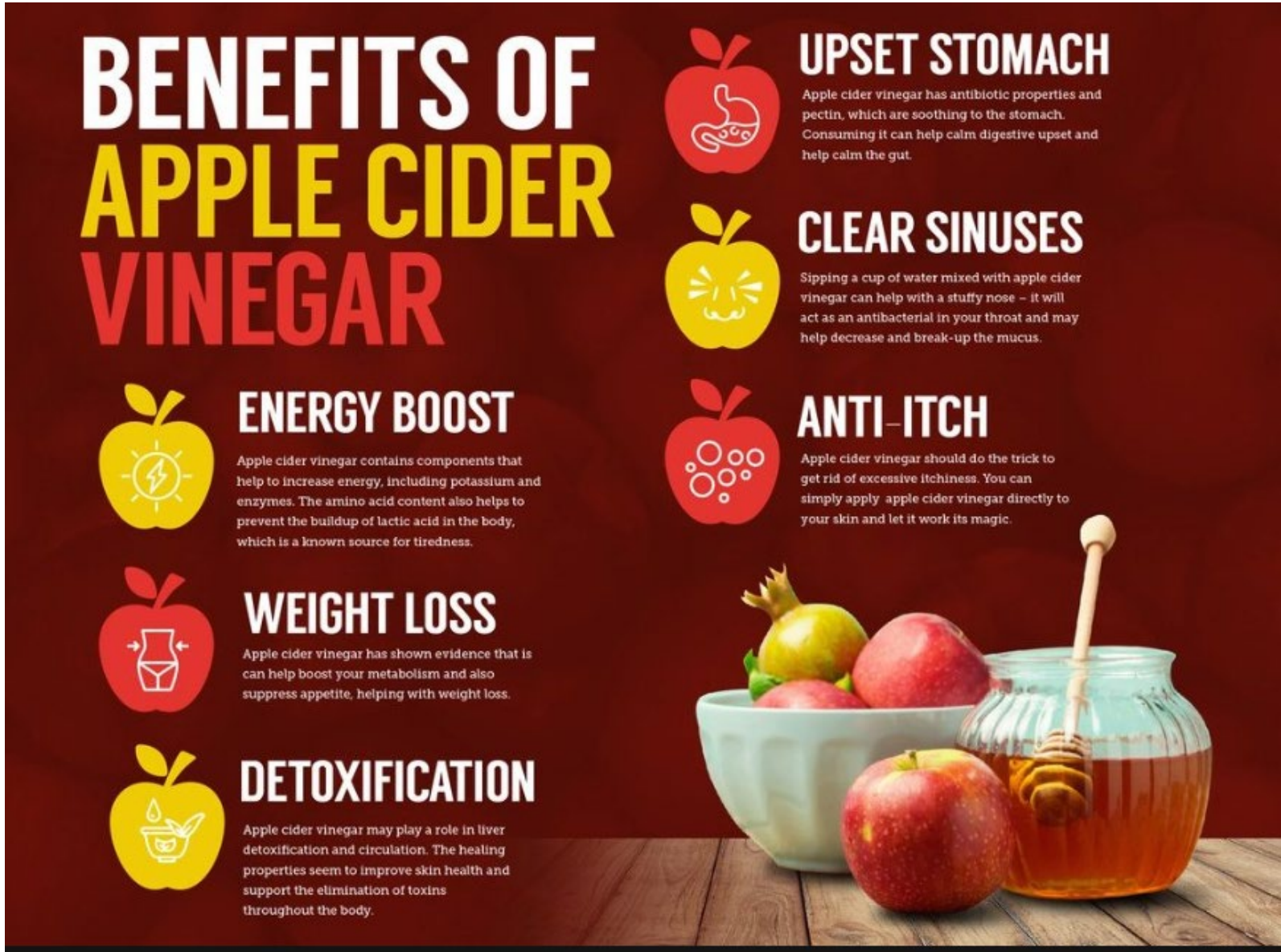
# Prebiotic Foods to raise GLP-1

- Artichoke hearts are high fiber, nutritious, and also good as prebiotics.

- Other good prebiotic foods are mushrooms, onions, leeks, asparagus, bananas and garlic.

# Fermented foods

- Fermented foods like sauerkraut and pickles, yogurt and kefir if not dairy restricted, and raw apple cider vinegar.



# Allulose:

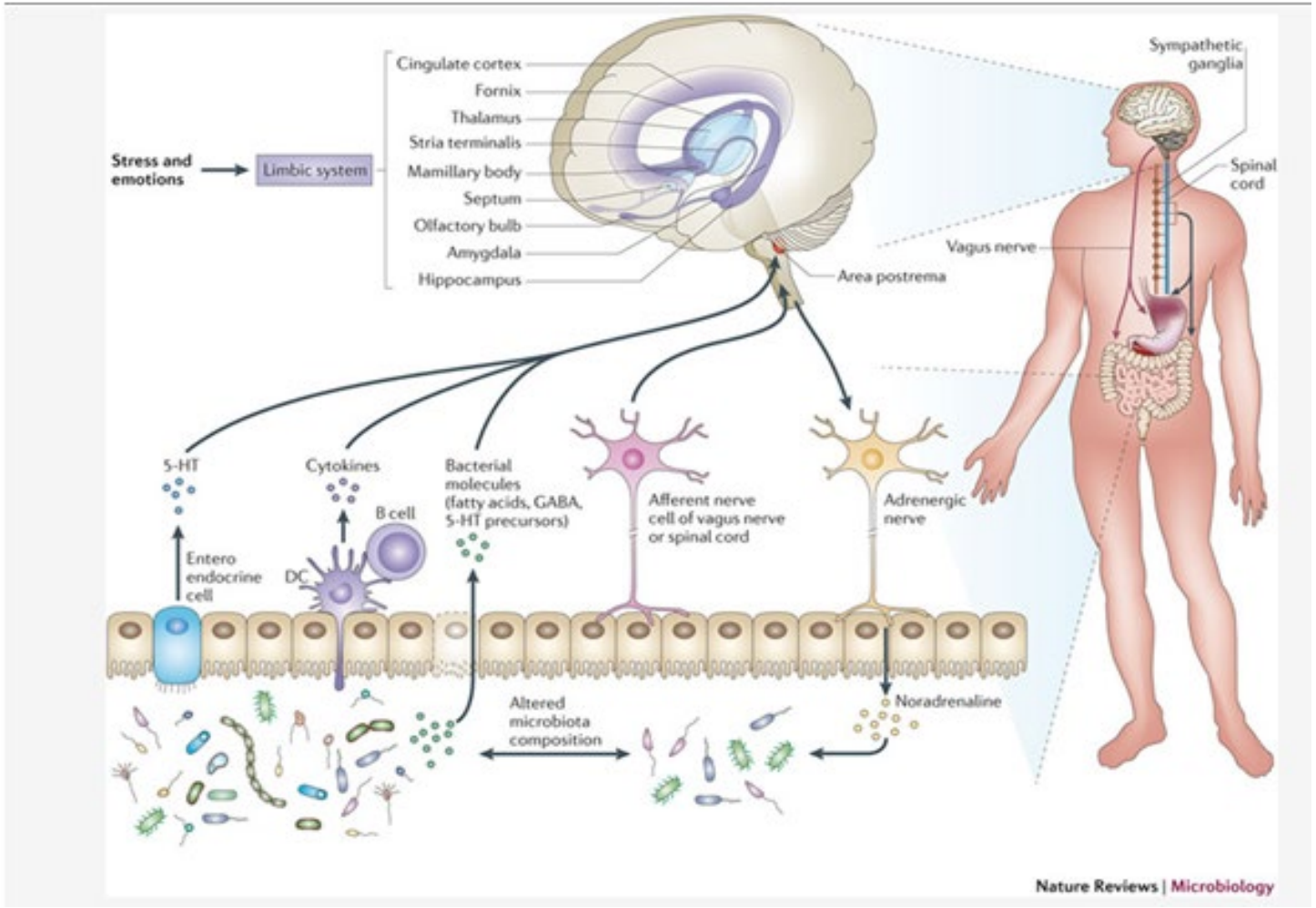
- Oral administration of the non-calorie sweetener, D-allulose induces GLP-1 release, activates vagal afferent signaling, reduces food intake and promotes glucose tolerance.
- Our results identify D-allulose as prominent GLP-1 releaser that acts via vagal afferents to restrict feeding and hyperglycemia. Furthermore, when administered in a time-specific manner, chronic D-allulose corrects arrhythmic overeating, obesity and diabetes, suggesting that chronotherapeutic modulation of vagal afferent GLP-1R signaling may aid in treating metabolic disorders.
- *Iwasaki Y, et al. GLP-1 release and vagal afferent activation mediate the beneficial metabolic and chronotherapeutic effects of D-allulose. Nat Commun. 2018 Jan 9;9(1):113.*

# GLP-1 Stimulators

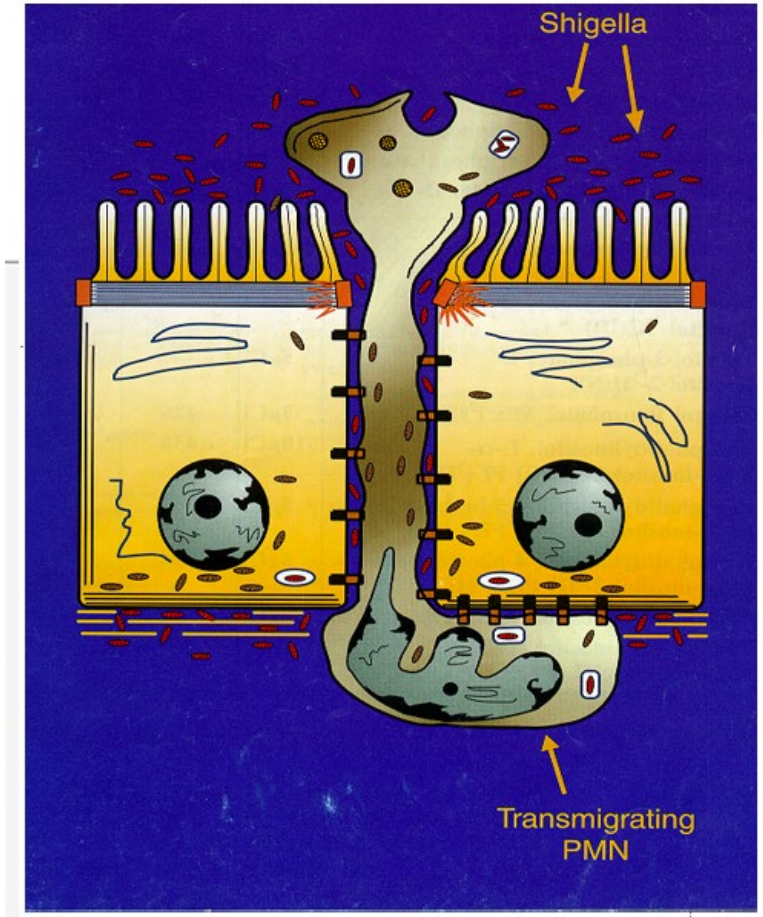
- Highly important for all those carrying the gene variant for the GLP-1 receptor.

- **rs10305420**: Associated with glycemic response and weight response to exenatide (forerunner to Ozempic)
- **rs7903146**: Associated with the response to exogenous GLP-1
- **rs10010131**: Associated with the response to exogenous GLP-1
- **rs151290, rs2237892, and rs2237895**: Associated with altered endogenous GLP-1 secretion

# SNS alters secretions & genetic signaling of the Microbiota




*Collins, SM. Et al. Nature Reviews Microbiology* **10**, 735-742 (November 2012) The interplay between the intestinal microbiota and the brain




Bacterial strains residing in the gut can lead to neurodegeneration. Invading pathogens, ie *M. leprae*, can cause demyelination and nerve damage. Magur, A et al.

**Inflammation preceded invasion**

# The interplay between the intestinal microbiota and the brain

- "The **vagal dependence of probiotic effects** on the brain contrasts sharply with…

- …the vagal independence of the behavioral changes that are induced by destabilization of the microbiota, indicating that gut bacteria communicate with the brain by diverse mechanisms."

- *Collins, SM. Et al. Nature Reviews Microbiology* **10**, 735-742 (November 2012) The interplay between the intestinal microbiota and the brain

# M-G-B (microbiota-gut-brain) Axis regulation by the microbiome

Foster JA et al. Stress & the gut-brain axis: Regulation by the microbiome. Neurobiology of Stress 2017, 7:124-136

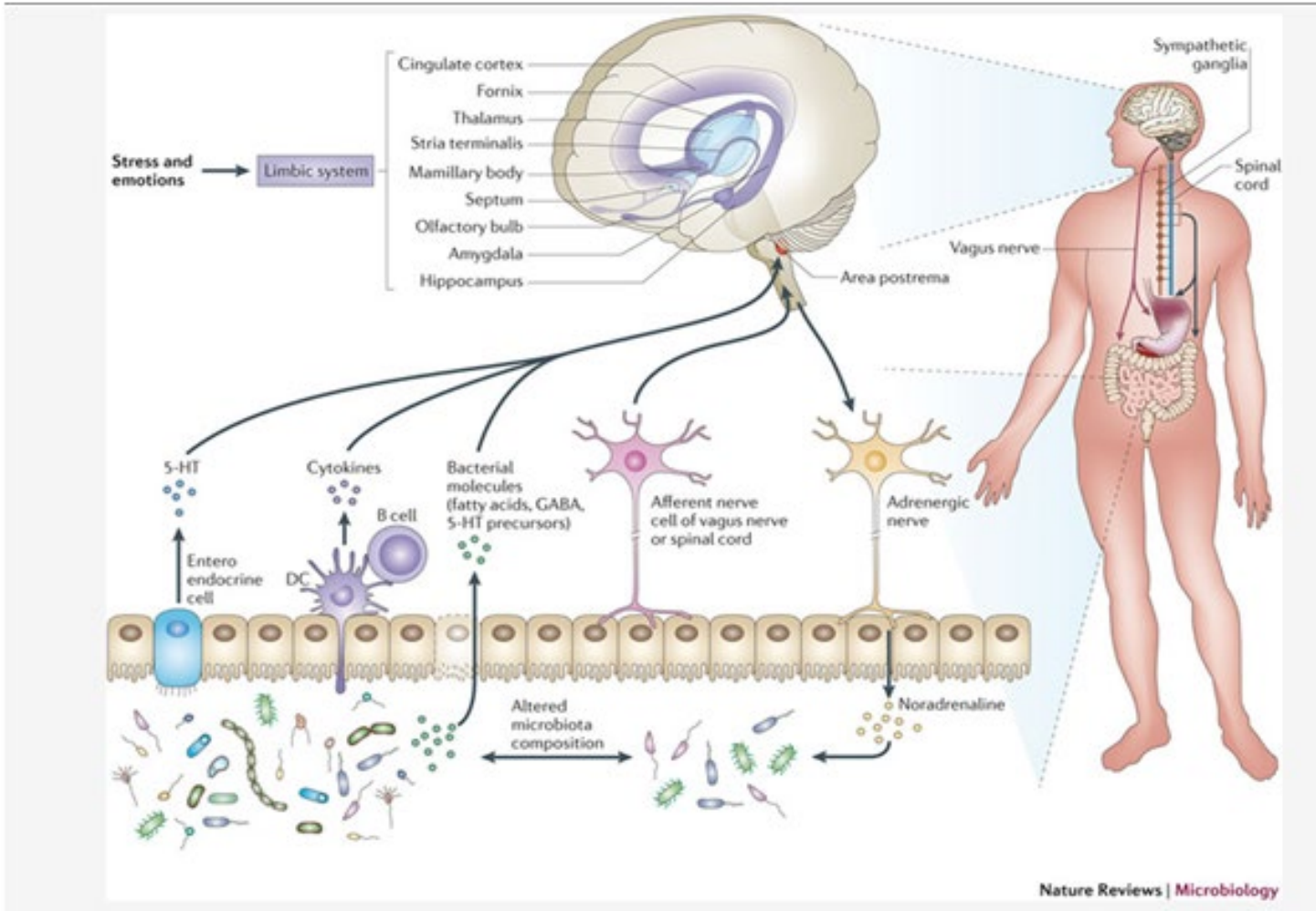
- Key communication pathways of the microbiota–gut–brain axis.

  - 1. Activation of the **vagus nerve**
  - 2. **NT production** norepinephrine,(5-HT (serotonin), dopamine, GABA γ-aminobutyric acid, AcH, tryptophan metabolism
  - 3. **Enteroendocrine signaling** from gut epithelial cells (e.g., CCK, GLP-1, Neuropeptide Y, PYY, somatostatin, VIP, oxytocin, CRF, pancreatic polypeptide, and other peptides)
  - 4. **Immune cell production** (cytokines i.e. TNF alpha, Interleukins, antibodies i.e. SIgA)
  - 5. Production of **microbial antigens** that recruit immune B cell responses
  - 6. Production of **microbial metabolites** (i.e. short-chain fatty acids [**SCFAs**])

# Axis regulation by the microbiome –
## The vagal connection

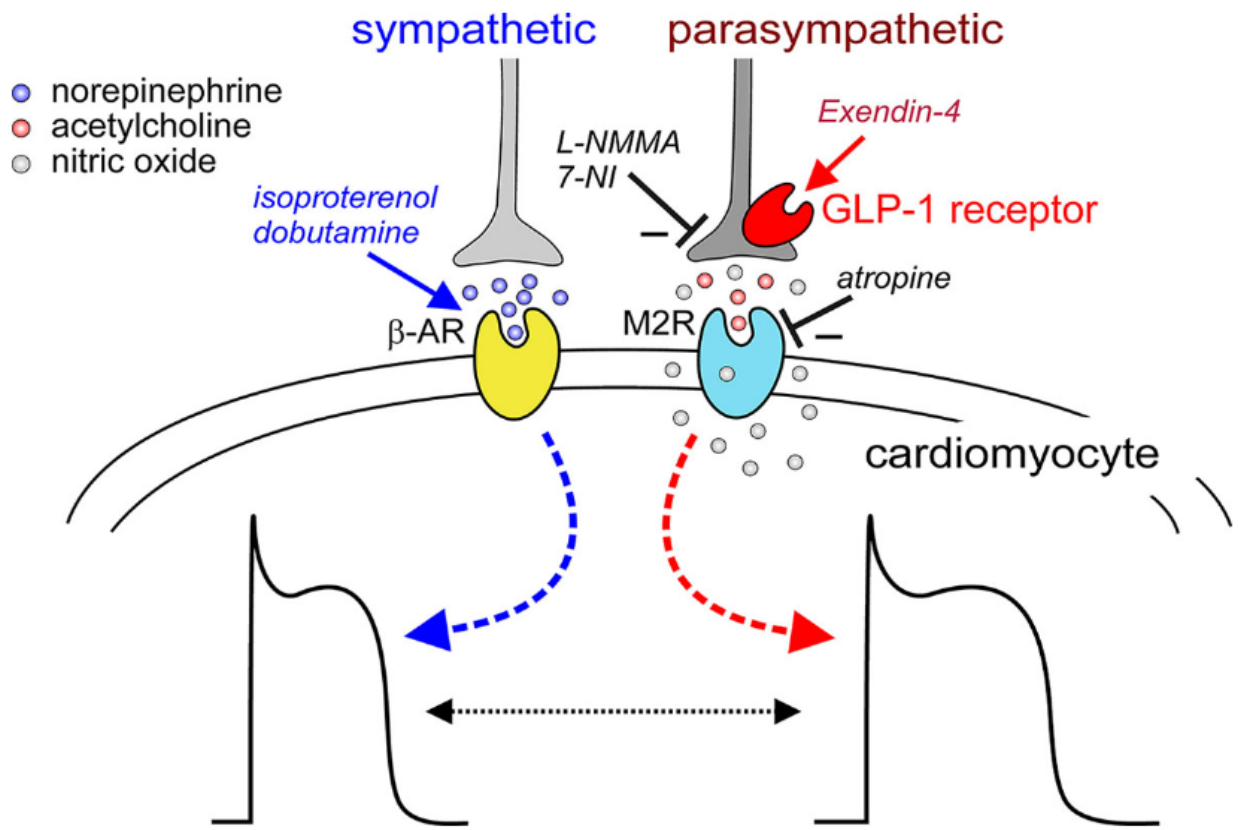
# Chiropractic Stimulation of the Vagus Nerve

- Increased secretion of anti-inflammatory acetylcholine
- Affects microbiota genetic composition in a good way
- Vagus nerve reads the microbiota



# Chiropractic Stimulation of Heart Circulation:

Ang, R et al. Modulation of Cardiac Ventricular Excitability by GLP-1 (Glucagon-Like Peptide-1). Arrhythmia and Electrophysiology. 2018. 11:10 .




- **Epigenetic stimulation of the GLP-1 R**

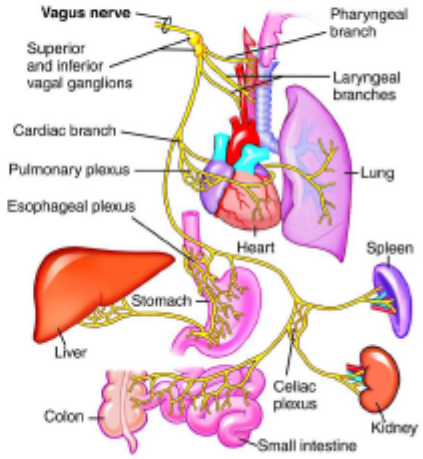
- GLP-1 receptor activation opposes sympathetic effects on cardiac ventricular excitability and reduces ventricular arrhythmic potential.

- These effects are indirect, mediated by acetylcholine and nitric oxide, and can be explained by facilitated release of these signaling molecules from the ventricular terminals of cardiac vagal neurons.

# Vagal Stimulation affects GLP-1R (SNP) and secretion of GLP-1:

## Vagal Projections

- Stomach
- Pancreas
- Small intestine
- Liver
- Gall bladder
- Large intestine
- Kidney
- Heart
- Lungs
- Pharynx
- Larynx




## Vagal Signals

- Functionally vagal signals:
  - Reduce heart rate
  - Constrict bronchi
  - Increase bronchial secretions
  - Increase peristalsis
  - Modulates intestinal blood flow
  - Activates enzyme release
  - Increase secretions in the stomach, intestines, and pancreas
  - Decreases inflammation
  - Modulates immune system

GB1 is acupuncture activator point for acetylcholine

Nutrients for AcH and vagal dysfunction: Choline,phosphatidyl choline, alpha-glycerylphosphoryl choline, CDP choline, methyl folate, probiotics.

# Upper cervical adjustments

Upper Cervical Adjustments Stimulate Vagal Sensory Nerves

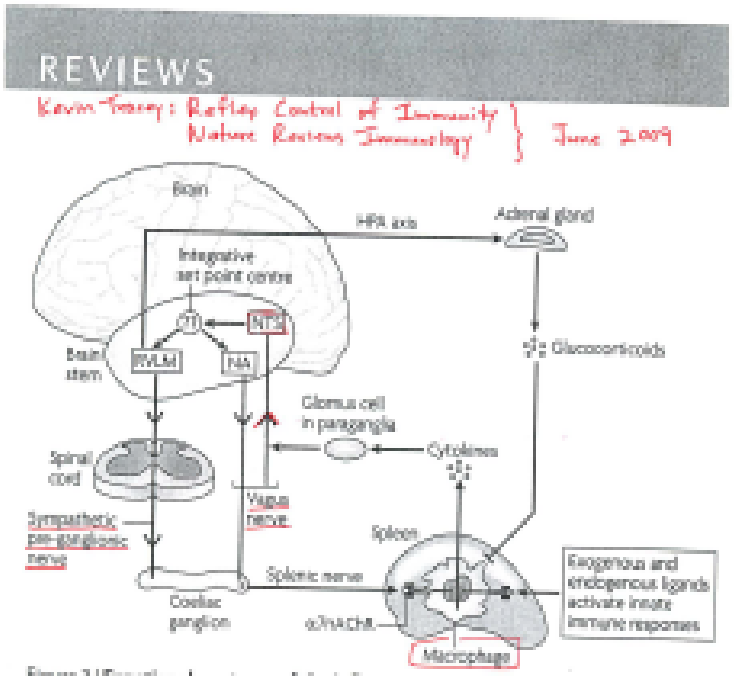


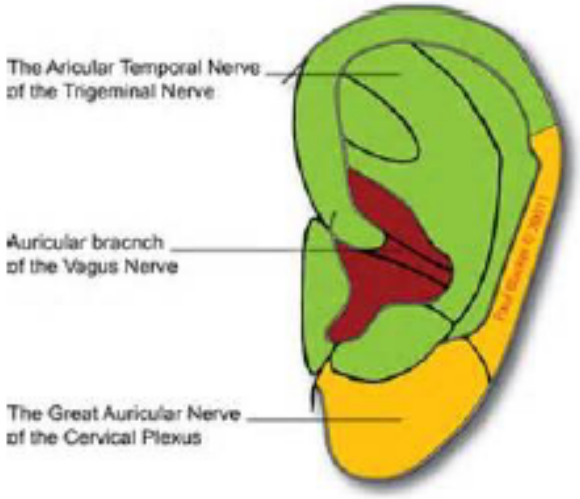

Figure 3 | **Functional anatomy of the inflammatory reflex.** Afferent (sensory) neural signals to the brain stem are relayed by the vagus nerve to the nucleus of the solitary tract/nucleus tractus solitarius (NTS). Polysynaptic relays then connect to the outflow centres of the autonomic nervous system, the rostral ventrolateral medullary (RVLM) sympathoexcitatory neurons and the vagal motor neurons in the nucleus ambiguus (NA) and the dorsal vagal motor nucleus. Outflow arrives at the coeliac ganglion from either the vagus nerve or the preganglionic efferent nerves, which originate in the sympathetic

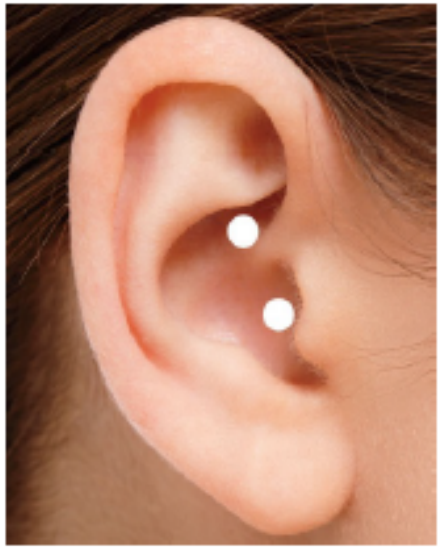
# Structural Correction Vagal Immune
# TL = therapy localized; VRP =visceral referred pain area

## Structural Correction Vagal Immune Modulation

1. Vagal point TL in sternal notch facilitates visceral related muscles
2. Pinching heart and/or lung VRP's inhibits globally
    a. Ventral vagal complex/nucleus ambiguous dysfunction
3. Pinching digestive organ VRP's inhibits globally
    a. Dorsal vagal complex/dorsal motor nucleus dysfunction
4. Treat individual VRP's with cranial faults, segmentally, IRT or DTR

## Sites of Electrical Stimulation



# Vagal Correction Sites

**Correction exercises for vagal dysfunction:**

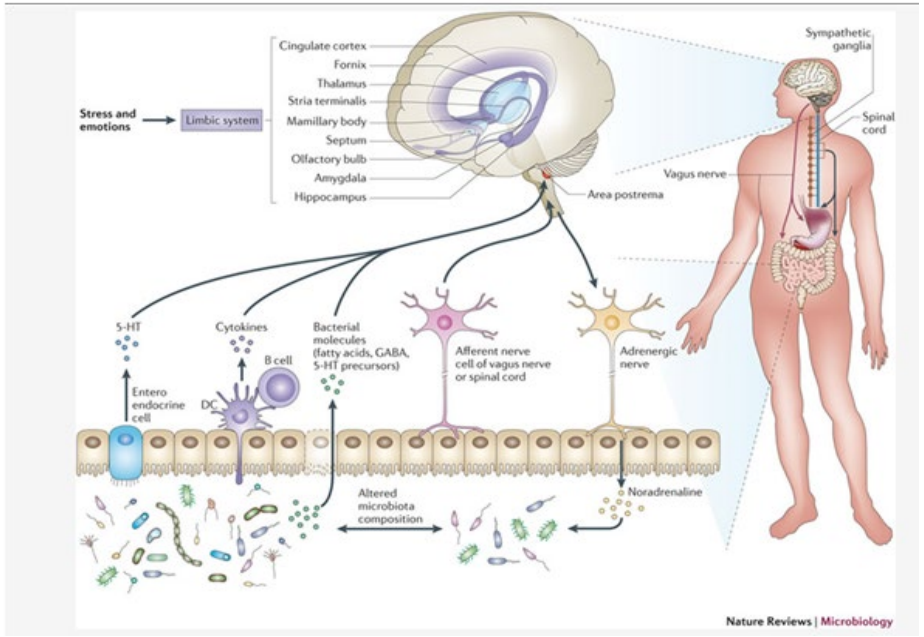
- Vagus: gargling, rub abdomen, abdominal pressure, humming, or repeating sound "OM" (Vagus nerve innervates vocal cords)
- Slow rhythmic diaphragmatic breathing
- Meditation, especially loving kindness meditation
  - Normally have patient perform activity three times a day for as many weeks as it takes to correct dysfunction

“The vagus nerve participates in the direct communication between bacteria and the brain”

Intestinal microbiota impact sepsis associated encephalopathy via the vagus nerve pp. 98–104 Li, Suyan. Neuroscience letters , 2018, Vol.662, p.98-104 (RS)

“FMT can change intestinal microbiota in sepsis patients”

↑ good bacteria ↓ bad




Vagus nerve is a key mediator between intestinal microbiota and SAE

# FMT diabetic female mice received FMT From healthy male mice

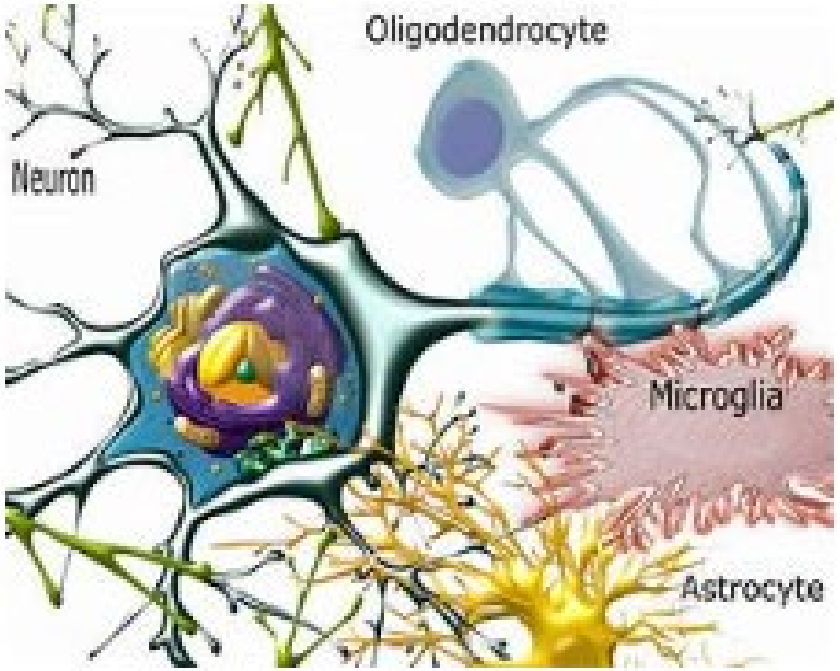
Wang H, et al. Promising Treatment for Type 2 Diabetes: Fecal Microbiota Transplantation Reverses Insulin Resistance and Impaired Islets. Front Cell Infect Microbiol. 2020 Jan 17;9:455

- FMT was used to rebuild the gut microbiota of diabetic mice.
- Fasting blood glucose, oral glucose tolerance tests, and HbA1c levels were monitored, while the hypoglycemic effects of FMT were also observed.
- Insulin levels, HOMA-IR, HOMA-IS, and HOMA-β were calculated.
- Insulin resistance and pancreatic islet β-cells were improved after FMT treatment.
- Inflammatory response decreased following FMT treatment.
- FMT inhibited the β-cell apoptosis.
- Here, the **effect of FMT** on hypoglycemia in **type 2 diabetes** was addressed by **improving insulin resistance and repairing impaired islets**, thereby providing a potential treatment strategy for type 2 diabetes.

# FMT Treatment

- **FMT - better spatial memory**
- **Less EEG abnormalities**
- **Significantly attenuated levels of IL-1β, IL-6, TNF-α, and decreased number of Iba-1 positive microglia in the cortex**
- **Beneficial effects of FMT were reversed by VGX.**

- **FMT regulates the cholinergic anti-inflammatory pathway in cerebral cortex through intestinal microbiota.** **(Li S. et al. 2019 Sep;31(9):1102-1107.)**

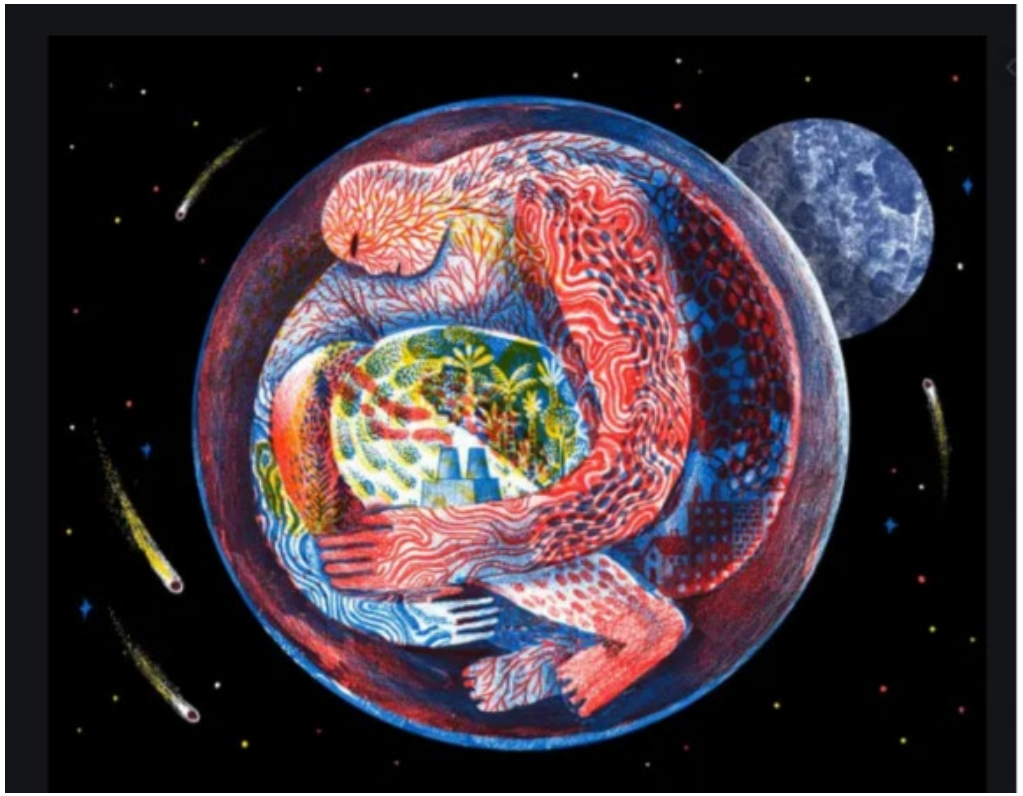


# Effect on genes

- **After FMT, several genes remained overexpressed**

- **“After the addition of vitamin C, which has positive effects in several aspects, to the fecal microbiota transplantation, in the intestinal tissues, the genes that were highly expressed after the fecal microbiota transplantation effectively reduced their expression”.**
  - Huang X, et al.The effect of FMT and vitamin C on immunity-related genes in antibiotic-induced dysbiosis in mice. PeerJ. 2023 May 11;11:e15356

# The Shaping of our DNA begins in the Womb



- Both positive and negative influences start affecting our DNA manifestation before birth

# PFOA was the environmental (epigenetic) influence on DNA of twin mice


- Slide courtesy of Brandon Lundell, DC

# Low Doses BPA resulted in over 7,000 DEGs (differentially expressed genes)

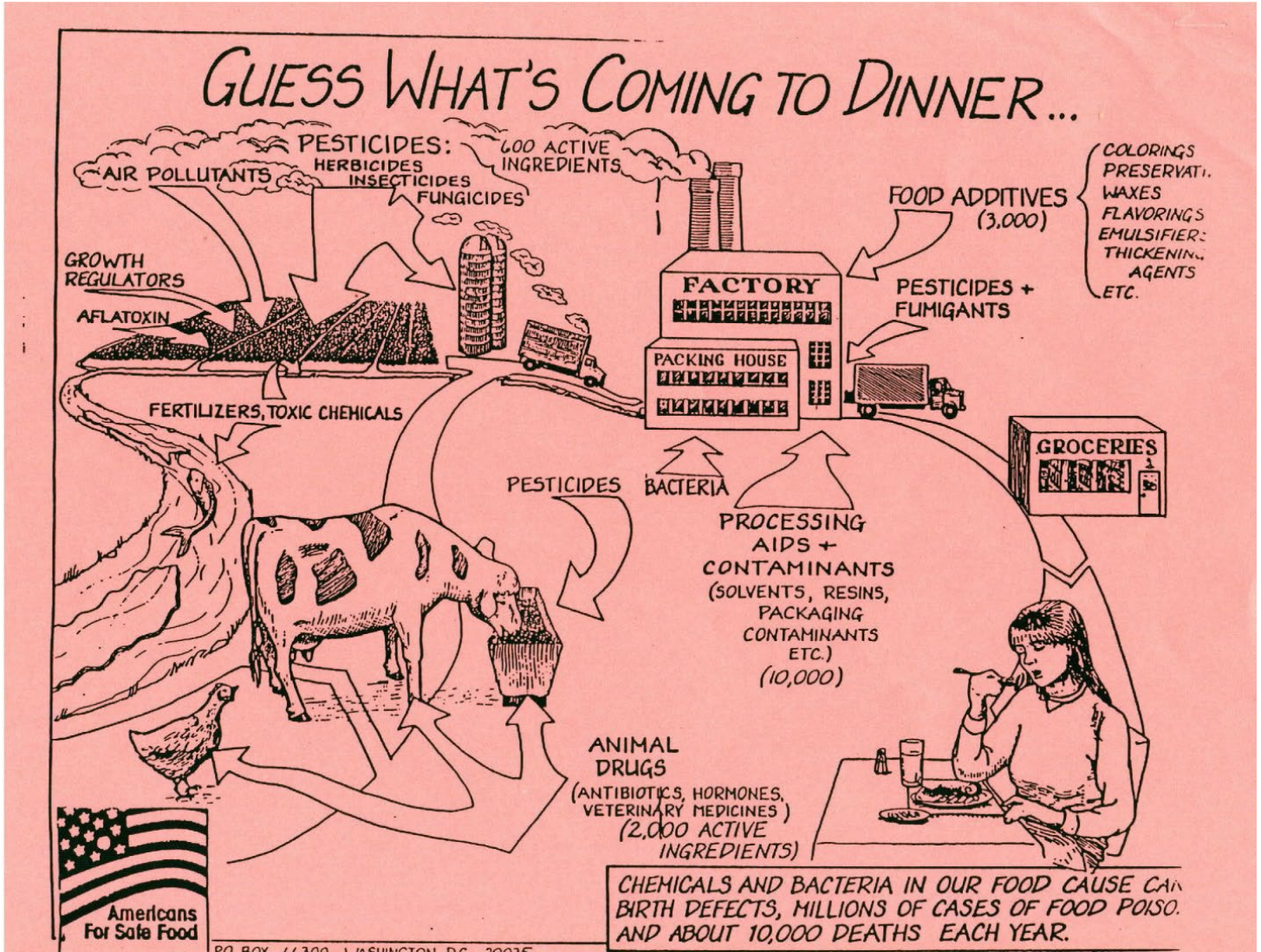
- “In the recent years the influence of xenoestrogens on oncogenes, specifically in relation to breast and prostate cancer has been the subject of considerable study”

- “The **expression** of transcripts encoding **nuclear hormone receptors** as well as histone and DNA methylation, modifying enzymes were **significantly perturbed by exposure to BPA**”
  - Curr Genomics. 2019 May;20(4):260-274. **Genome-Wide Analysis of Low Dose Bisphenol-A (BPA) Exposure in Human Prostate Cells.** Renaud L. et al.

# Stop eating plastic…

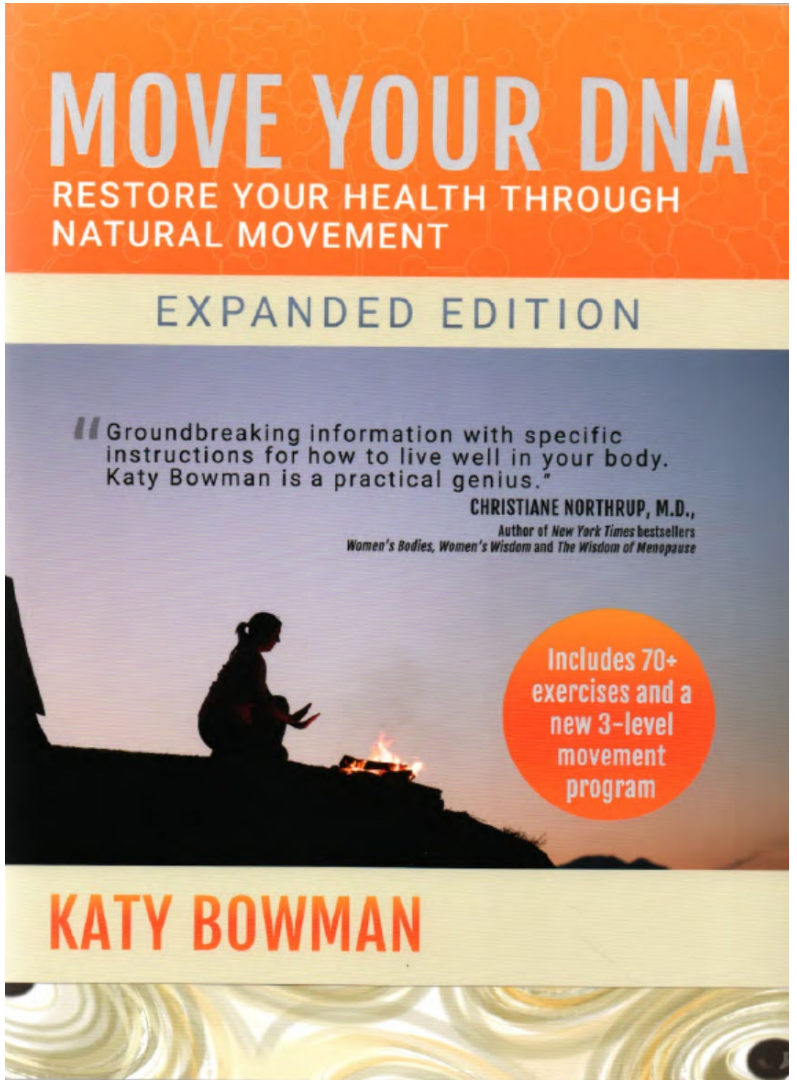
- **Every week we eat – on average: one lego brick;**
- **Every year a dinner plate (100,000 tiny pieces of plastic);**
- **Every decade a lifebuoy**.

# Toxic Influences Affect our Genome Expression



# Mechanobiome

An important positive epigenetic factor for healthy outcomes



*Review*

# Microbiome and Human Aging: Probiotic and Prebiotic Potentials in Longevity, Skin Health and Cellular Senescence

**Jacqueline Lena Boyajian, Merry Ghebretatios, Sabrina Schaly, Paromita Islam and Satya Prakash ***

Biomedical Technology and Cell Therapy Research Laboratory, Department of Biomedical Engineering, Faculty of Medicine, McGill University, 3775 University Street, Montreal, QC H3A 2B4, Canada; jacqueline.boyajian@mail.mcgill.ca (J.L.B.); merry.ghebretatios@mail.mcgill.ca (M.G.); sabrina.schaly@mail.mcgill.ca (S.S.); paromita.islam@mail.mcgill.ca (P.I.)

* Correspondence: satya.prakash@mcgill.ca

**Abstract:** The role of the microbiome in human aging is important: the microbiome directly impacts aging through the gastrointestinal system. However, the microbial impact on skin has yet to be fully understood. For example, cellular senescence is an intrinsic aging process that has been recently associated with microbial imbalance. With age, cells become senescent in response to stress wherein they undergo irreversible growth arrest while maintaining high metabolic activity. An accumulation of senescent cells has been linked to various aging and chronic pathologies due to an overexpression of the senescence-associated secretory phenotype (SASP) comprised of proinflammatory cytokines, chemokines, growth factors, proteases, lipids and extracellular matrix components. In particular, dermatological disorders may be promoted by senescence as the skin is a common site of accumulation. The gut microbiota influences cellular senescence and skin disruption through the gut-skin axis and secretion of microbial metabolites. Metabolomics can be used to identify and quantify metabolites involved in senescence. Moreover, novel anti-senescent therapeutics are warranted given the poor safety profiles of current pharmaceutical drugs. Probiotics and prebiotics may be effective alternatives, considering the relationship between the microbiome and healthy aging. However, further research on gut composition under a senescent status is needed to develop immunomodulatory therapies.



**Citation:** Boyajian, J.L.; Ghebretatios, M.; Schaly, S.; Islam, P.; Prakash, S. Microbiome and Human Aging: Probiotic and Prebiotic Potentials in Longevity, Skin Health and Cellular Senescence. *Nutrients* **2021**, *13*, 4550.

# Points of the article:

- Cellular senescence is an intrinsic aging process that has been recently associated with microbial imbalance.
- With age, cells become senescent in response to stress.
- Undergo irreversible growth arrest while maintaining high metabolic activity.

# Points of the article (cont'd)

- **An accumulation of senescent cells has been linked to various aging and chronic pathologies**
  - **Due to an overexpression of SASP (senescence-associated secretory phenotype) comprised of: pro-inflammatory cytokines, chemokines, growth factors, proteases, lipids and extracellular matrix components.**
  - **Hypersecretory state**
- **Undergo irreversible growth arrest while maintaining high metabolic activity.**

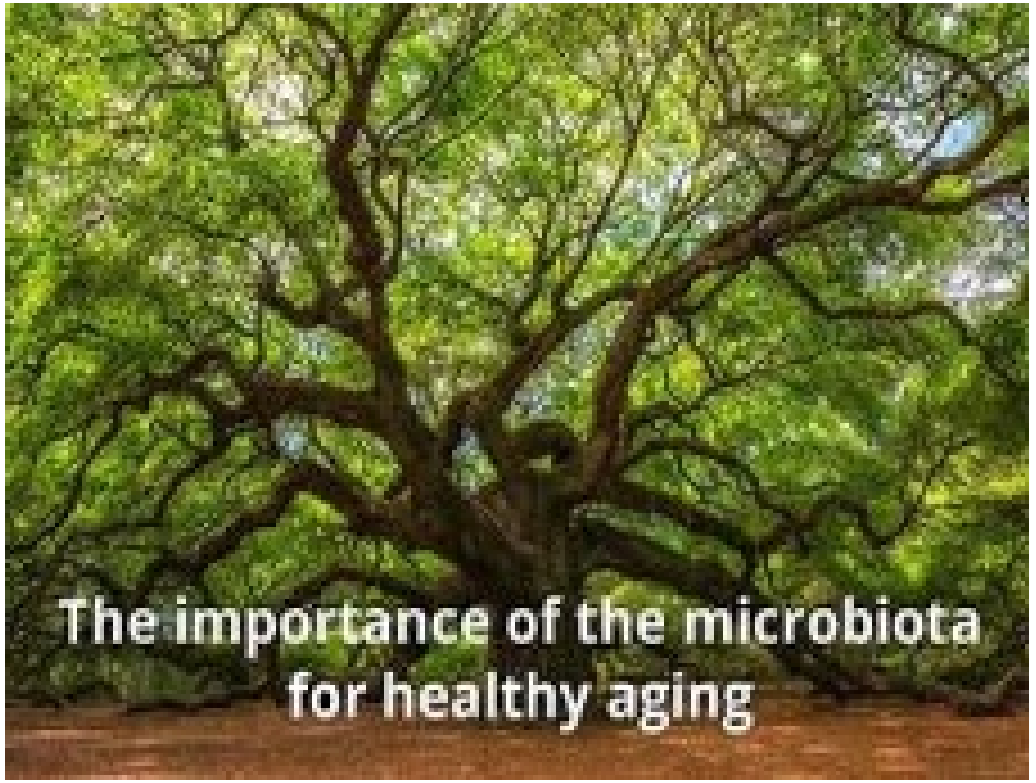
- **Skin a common site of accumulation**

- **The gut microbiota influences cellular senescence and skin disruption through the gut-skin axis and secretion of microbial metabolites.**

- **Metabolomics can be used to identify and quantify metabolites involved in senescence.**
  - **Metabolomics is the scientific study of chemical processes involving metabolites, the small molecule substrates, intermediates, and products of cell metabolism.**

# Conclusion:

“**Probiotics and prebiotics** may be effective alternatives, considering the relationship between the **microbiome and healthy aging**.”



# Probiotics can counteract negative effects of sleep loss

- In addition, it indicates that **probiotic supplementation** can represent a viable strategy to **counteract oxidative stress and inflammation related to sleep loss**, thus possibly limiting its negative consequences on health and well-being.

- Perturbed blood levels of peptide hormones, including **ghrelin, leptin, and glucagon like peptide 1 (GLP-1)**
  - Zheng Y et al. 2023

# Sleep - Critical for Glymphatic Toxin Drainage Removal of B-amyloid Helps Longevity Prospects

## Sleep

| | | | | | | |
|---|---|---|---|---|---|---|
| AANAT | rs11077820 | T | CC | -- | Sleep | Serotonin |
| CLOCK | rs1801260 | G | AG | -+ | Sleep | |
| CLOCK | rs11932595 | G | AG | -+ | Sleep | |
| CLOCK | rs6832769 | G | AG | -+ | Sleep | |
| CLOCK | rs13113518 | C | TT | -- | Sleep | |

**COMT:** (Catechol-O-Methyl Transferase) The COMT enzyme helps break down neurotransmitters and maintain appropriate levels of these neurotransmitters in the brain. Mutations in the COMT gene can lead to high levels of dopamine, norepinephrine (noradrenalin) and epinephrine (adrenalin). High levels of dopamine have been associated with intelligence, however high levels can lead to more difficulty with attention and increased levels of irritation, anxiety and anger. COMT variants have also been shown to be implicated in anxiety, novelty seeking behavior, aggression, and personality imbalance.
In addition, COMT variants have also been shown to be associated with estrogen dominant conditions including free radical attack due to the decreased breakdown of the catechol estrogens.

**Variants are associated with:**

- Anxiety
- Lack of attention
- High cortisol
- High insulin
- High estrogen
- Insomnia
- Depression
- Liver detox difficulty
- Chronic skin problems
- Weight imbalance
- Mental imbalance
- Thyroid imbalance

**Dietary and Lifestyle**
Avoiding stress is a big help for this pathway. If you have a homozygous variant here, breaking down stress hormones is especially difficult for you. This makes you more susceptible to anxiety, especially after a traumatic event. Learning to incorporate rest and stress reduction activities is especially important here. Meditation can be very beneficial, and avoiding caffeine and stimulants is helpful as well.
**Lab Test:** Neurotransmitter and Hormone testing- Adrenaline, Noradrenaline, Cortisol, Dopamine, Estrogens

**Kinesiology Challenge**

| | | | | |
|---|---|---|---|---|
| Adrenaline | Noradrenaline | Estrogens | Cortisol | Dopamine |
| Insulin | | | | |

**Nutrients**

| | | | | |
|---|---|---|---|---|
| Magnesium | Manganese | Minerals | Boron | Calcium synergistic blends |
| Thyroid support | Iodine | Inositol | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| COMT | rs4680 | A | AA | ++ | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs6269 | G | AA | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs4633 | T | TT | ++ | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs737865 | G | AA | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs769224 | A | AG | +- | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs2239393 | G | AA | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs1544325 | A | AA | ++ | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs4646316 | T | TC | +- | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs174699 | C | TT | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs9332377 | T | CC | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs165599 | A | AG | +- | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs5993883 | T | TT | ++ | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs4646312 | C | TT | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |
| COMT | rs737866 | C | TT | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrog Dopamine, Insulin |

| | | | | | | |
|---|---|---|---|---|---|---|
| MAO-A | rs1137070 | C | CC | ++ | Brain Chemistry | Serotonin, Dopamine, Norepineph Tryptophan, 5HTP |
| MAO-A | rs6323 | T | TT | ++ | Brain Chemistry | Serotonin, Dopamine, Norepineph Tryptophan, 5HTP |

# Nutritional help for perpetual wheels turning

- Taurine
- Theanine
- Chamomile
- Magnolia officinalis (bark)
- GABA (gamma amino butyric acid)
- Riboflavin 5-phosphate

# Longevity/aging/memory genes

- APOE e4 is the principle risk gene for late-onset AD

- **Metabolic enhancement for neurodegeneration - (MEND)...**Bredesen DE et al. Aging (Albany NY). 2016 Jun;8(6):1250-8. **Reversal of cognitive decline in Alzheimer's disease.**

- Reversal of cognitive decline in patients with early Alzheimer's disease or its precursors, MCI (mild cognitive impairment) and SCI (subjective cognitive impairment).
  - (James BD, et al. Contribution of Alzheimer disease to mortality in the United States. Neurology. 2014;82:1045–50.[PMC free article] [PubMed]

# MEND and APOE e4 SNPs

- Patients who had had to discontinue work were able to return to work, and those struggling at work were able to improve their performance. The patients, their spouses, and their co-workers all reported clear improvements.

- Results from quantitative MRI and neuropsychological testing

- **Ten patients with cognitive decline, nine ApoE4+ (five homozygous and four heterozygous) and one ApoE4-**, who were treated with the MEND protocol for 5-24 months.

- **“The magnitude of the improvement is unprecedented.”**

# Implications:

- **Phenotype of the gene (SNP) most associated with Alzheimer's risk is malleable and greatly influenced by lifestyle**

- **Greatest efficacy of improvement may be amongst heterozygous and homozygous carriers of APOEe**

# MEND and Nutritional Connections to Cognition

- MEND was not the first study to show relationships between nutrition (ie **fish oil, methylation with B vitamins, designer cholines, curcumin, vitamin D** etc.) and brain/memory/cognitive improvement.

- Success depends on genetics/epigenetics

# *A tidbit on TBI and APOE e4

- We conclude that the **ApoE ε4 allele** confers a risk of **poor outcome following TBI**

- Meta-analysis demonstrated higher odds of a favorable outcome following TBI in those not possessing an ApoE ε4 allele compared with ε4 carriers and homozygotes.

- McFadyen CA, et al. Apolipoprotein E4 Polymorphism and Outcomes from Traumatic Brain Injury: A Living Systematic Review and Meta-Analysis. *J Neurotrauma*. 2021;38(8):1124-1136.

# OAS SNP (decreased interferon) can increase risk for Alzheimer’s

- Magusali N, et al. A genetic link between risk for Alzheimer's disease and severe COVID-19 outcomes via the OAS1 gene. *Brain*. 2021;144(12):3727-3741.

# OAS1 and Alzheimer's

- The single nucleotide polymorphisms rs1131454(A) and rs4766676(T) are associated with Alzheimer's disease, and rs10735079(A) and rs6489867(T) are associated with severe COVID-19, where the risk alleles are **linked with decreased OAS1 expression**.

- Collectively, our data support a link between genetic risk for Alzheimer's disease and susceptibility to critical illness with COVID-19 centered on SNPs of OAS1 showing decreased interferon, a finding with potential implications for future treatments of Alzheimer's disease and COVID-19, and development of biomarkers to track disease progression.
  - Magusali N, et al. 2021

# CDP-choline - Jasielski P, et al. **Application of Citicoline in Neurological Disorders: A Systematic Review**. Nutrients. 2020 Oct 12;12(10):3113.

- **Citicoline (CDP choline)** is a chemical compound involved in the synthesis of cell membranes. Research on the use of citicoline is conducted in neurology, ophthalmology, and psychiatry.
- Accessible databases were searched for 47 articles regarding citicoline use in neurological diseases. Citicoline has been proven to be a useful compound in **preventing dementia progression** and reversing adverse changes. It improves prognosis after stroke. In a model of nerve damage and neuropathy, citicoline **stimulated nerve regeneration** and **lessened pain.**
- Citicoline has a wide range of effects and could be an essential substance in the treatment of many neurological diseases. Its **positive impact on learning and cognitive functions among the healthy population** is also worth noting.
- This systematic review showed citicoline has a **wide range of uses in neurological conditions.** **Citicoline also improved memory and other cognitive functions among healthy volunteers.** Citicoline, depending on its application, can be **considered both as a dietary supplement and as a medicine**.

# Jasielski P. et al. 2020 More mechanisms CDP choline

- Citicoline is an **intermediary for phosphatidylcholine** in neuronal cell membrane.

- Neuroprotective properties – greater availability of PC may stimulate the repair and regeneration of damaged cell membranes of neurons.

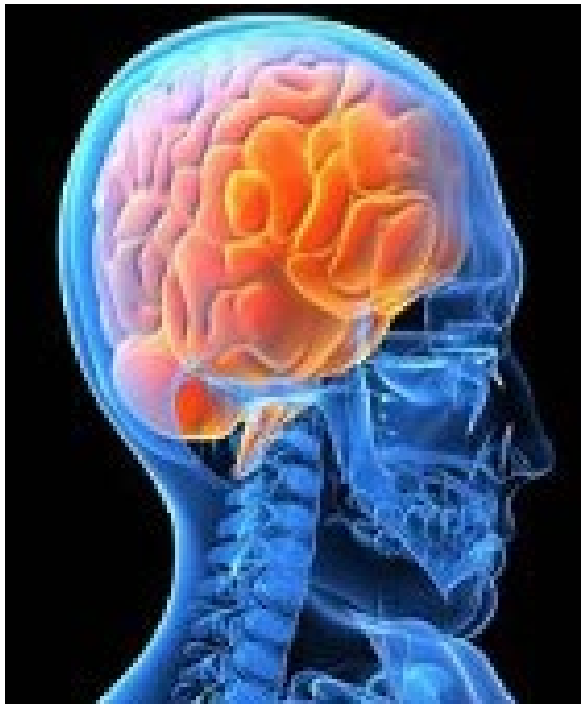
- Another likely mechanism of action is to **block inflammation** by inhibiting phospholipase A2. Citicoline improves brain functions and stunts cognitive deficits.

Concluding, it was proved that citicoline is beneficial in the **regeneration of neurons**, can **increase levels of neurotransmitters**, and has a positive **impact on cognitive functions**. Moreover, it can be an additional therapy for **depression and mood regulation**.

# CDP benefits – addt'l resources


- Synoradzki K. & Grieb P. Citicoline: A Superior Form of Choline? *Nutrients.* 2019;11:1569.
- Blusztajn J.K. & Slack B.E., Mellott T.J. Neuroprotective Actions of Dietary Choline. *Nutrients.* 2017;9:815.
- Gareri P., et al. The Citicholinage Study: Citicoline Plus Cholinesterase Inhibitors in Aged Patients Affected with Alzheimer's Disease Study. *J. Alzheimer's Dis.* 2017;56:557–565.
- Gandolfi S.A., et al. Cytidine 5′-Diphosphocholine (Citicoline): Evidence for a Neuroprotective Role in Glaucoma. *Nutrients.* 2020;12:793. (calls CDP choline a neuroprotective drug (NPD)
- Seifaddini R., et al. The Effects of Citicoline on Cerebrovascular Hemodynamic Status in Ischemic Stroke Patients. *J. Kerman Univ. Med. Sci.* 2017;24:480–486.
- Trimmel H., Majdan M., Wodak A., Herzer Z., Csomor D., Brazinova A. Citicoline in Severe Traumatic Brain Injury: Indications for Improved Outcome: A Retrospective Matched Pair Analysis From 14 Austrian Trauma Centers. *Wien Klin Wochenschr.* 2018;130:37–44

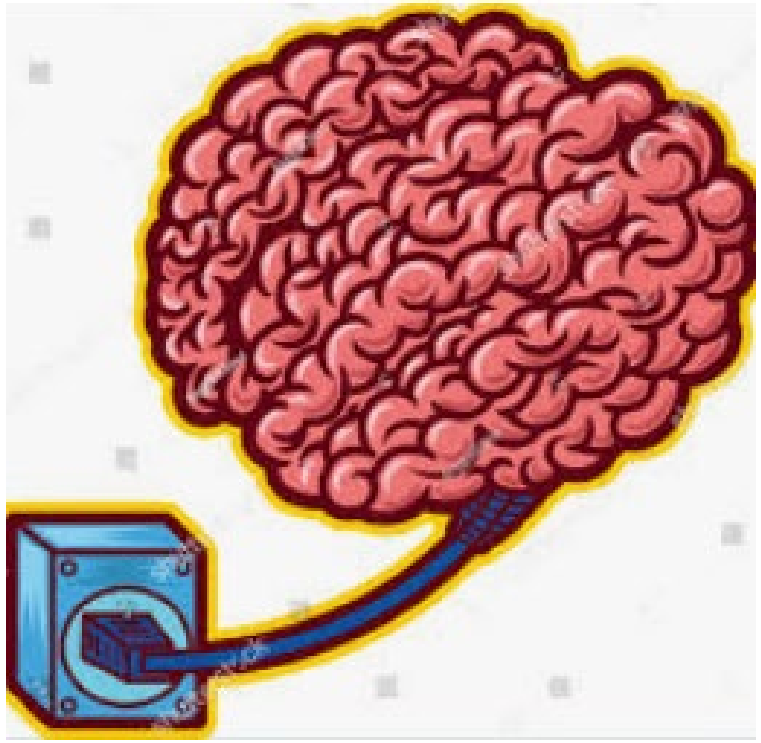
# Alpha GPC



- Alpha-GPC) is a derivative of phosphatidylcholine known to support the parasympathetic nervous system.

- Alpha-GPC demonstrated benefit for patients in a number of clinical studies conducted on the brain and maintenance of brain function.

- “being impressed not only with results but in lack of side effects,it was recommended that it is desirable to reconsider **alpha glycerylphosphocholine (Alpha GPC)**… for the maintenance of brain function”
  - (Scapicchio PL. Revisiting choline alphoscerate profile: a new, perspective, role…Int J Neurosci. 2013 Jul;123(7):444-9.)



# FHEval Report - SNP detection leading to support with nutrients:

- **APOE:** (Apolipoprotein E) The APOE gene provides instructions for making a protein called apolipoprotein E. This protein combines with fats to form lipoproteins. These molecules package cholesterol and other fats and carry them through the bloodstream. Maintaining normal levels of cholesterol is essential for heart and blood vessel health. The APOE e4 allele may also be associated with an earlier onset of non-homeostatic memory function. This allele is associated with amyloid plaques in the brain tissue of affected people.
- 
- There are at least three slightly different versions (alleles) of the APOE gene. The major alleles are called e2, e3, and e4. The most common allele is e3, which is found in more than half of the general population. In general, E2 carriers are associated with low LDL cholesterol and low incidence of vascular imbalances. In contrast, E4 carriers are prone to high LDL cholesterol,
- 
- **Diet and Lifestyle Recommendations:** Low-fat diets can help in the presence of this genetic variant.
- 
- **Kinesiology Challenge Vials:**
- Cholesterol
- 
- **Product Support Recommendations:**
- Complete Brain Charge
- Complete Omega-3 Essentials 2:1
- 
- **Nutrient Support Recommendations:**
- Phosphatidyl Choline
- Essential Fatty Acids

# Fish Oil & Alzheimers

- McGrattan AM, et al. 2019 (Nutrition & Brain Health)

- **Review of randomized clinical trials:** Vlachos GS & Scarmeas N. Dietary interventions in mild cognitive impairment and dementia. Dialogues Clin Neurosci. 2019 Mar;21(1):69-82.

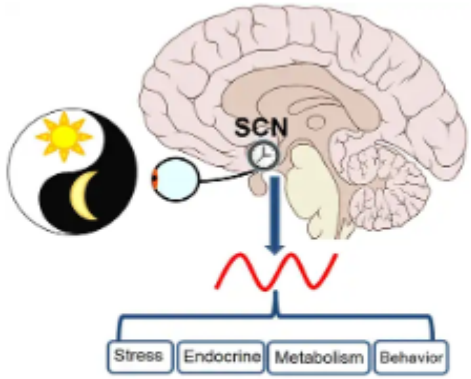
- Zhang Y, et al. Intakes of fish and polyunsaturated fatty acids and mild-to-severe cognitive impairment risks: **a dose-response meta-analysis of 21 cohort studies**. Am J Clin Nutr. 2016 Feb;103(2):330-40.

# Vitamin D improves cognitive function

- “Daily oral vitamin D supplementation (800 IU/day) for 12 months may **improve cognitive function and decrease Aβ-**related biomarkers in elderly patients with AD.”
  - Jia J, Hu J, Huo X, Miao R, Zhang Y, Ma F. Effects of vitamin D supplementation on cognitive function and blood Aβ-related biomarkers in older adults with Alzheimer's disease: **a randomized, double-blind, placebo-controlled trial**. J Neurol Neurosurg Psychiatry. **2019** Dec;90(12):1347-1352

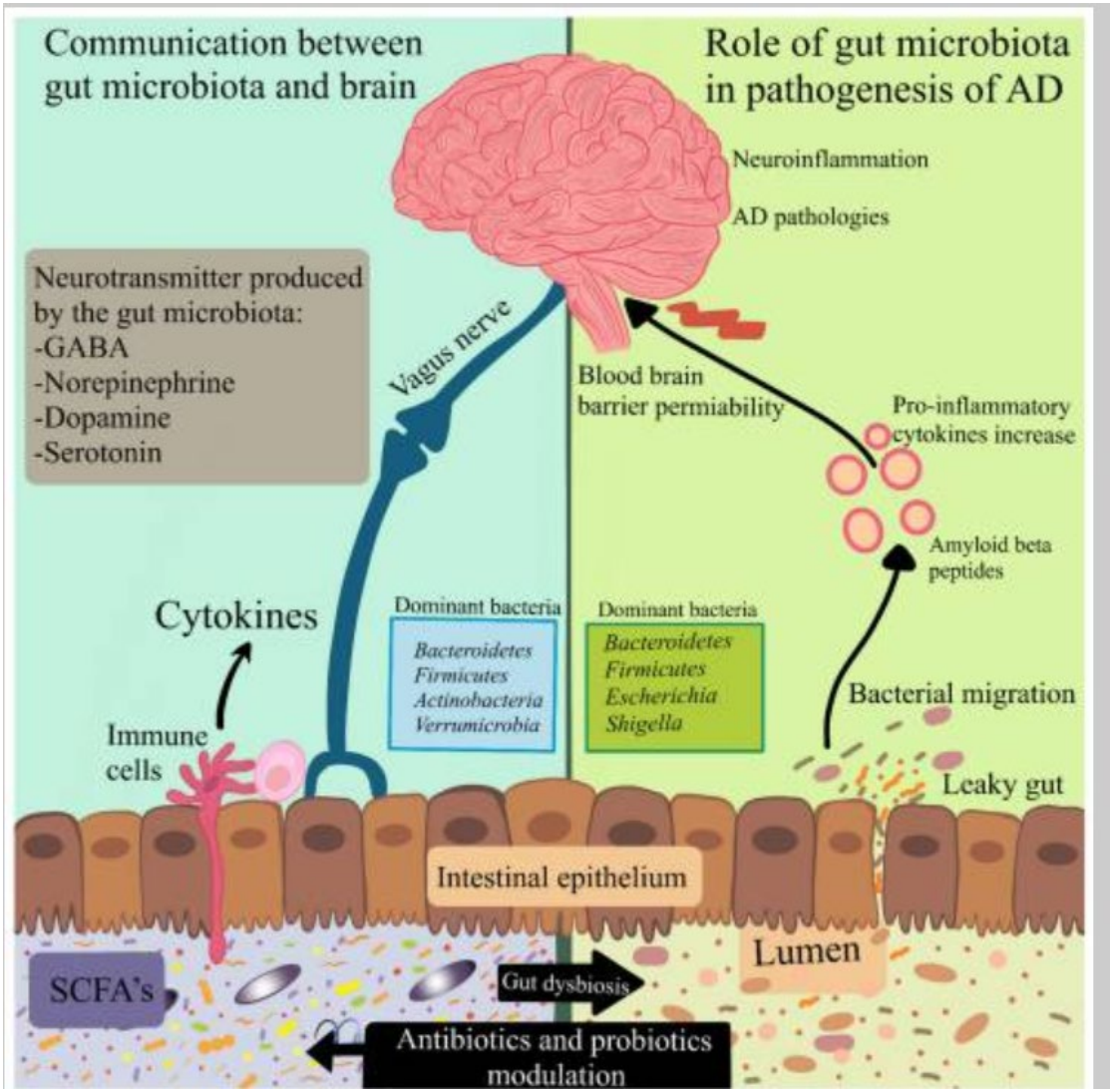
“Observations support multiple mechanisms by which vitamin D can act against **neurodegenerative processes**.”

Landel V, et al. Vitamin D, Cognition and Alzheimer's Disease: **The Therapeutic Benefit is in the D-Tails**. J Alzheimers Dis. 2016 May 11;53(2):419-44.




Sunlight, as it turns out, is the primary regulator of the SCN, and can help to synchronize our circadian rhythm, leading to better sleep and overall health.

# Probiotic Supplementation and the Brain

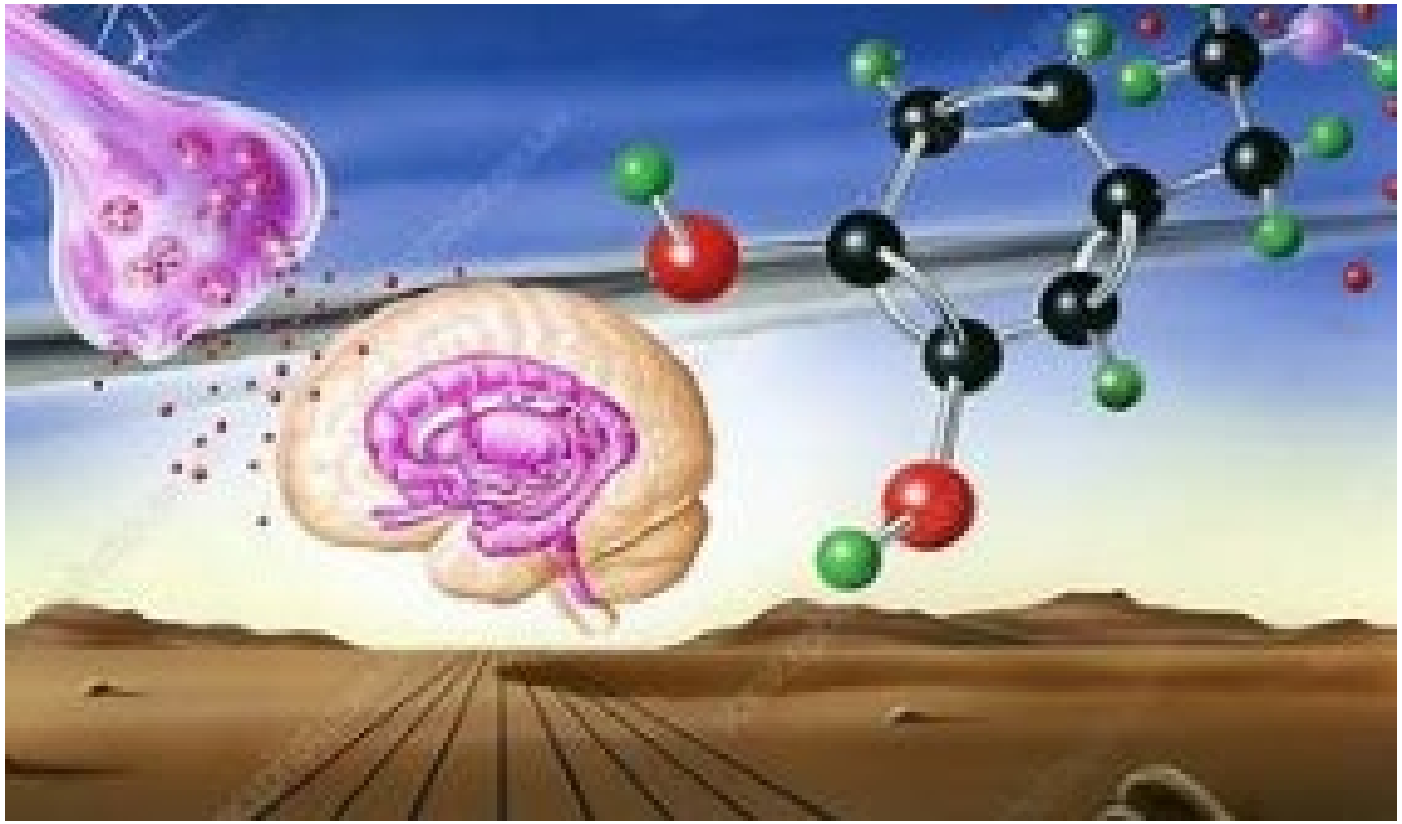



- "Our study provides direct support to the growing evidence that **probiotics can attenuate oxidative stress and inflammation in the brain and at the systemic level via the gut-brain axis."**
  - Zheng Y, et al. Probiotics Supplementation Attenuates Inflammation and Oxidative Stress Induced by Chronic Sleep Restriction. Nutrients. 2023 Mar 21;15(6):1518.

# SIRT1 – Suspected pathway for Probiotics & Alzheimer's

- Antioxidant and neuroprotective effects in Alz.

- Suspected pathway: activating the silencing information regulator 2 related enzyme 1 (SIRT1) pathway
  - Zheng Y et al. 2023



- Research shows that **alteration in gut microbial diversity and defects in gut brain axis are linked to AD**.

- **Probiotics are known to be one of the best preventative measures against cognitive decline in AD.**

- Numerous in vivo trials and **recent clinical trials have proven the effectiveness of selected bacterial strains in slowing down the progression of AD.**

- It is proven that **probiotics modulate the inflammatory process, counteract with oxidative stress, and modify gut microbiota.**
  - **Naomi, R. et al. Nutrients 2022**

nutrients

MDPI

*Review*

# Probiotics for Alzheimer's Disease: A Systematic Review

Ruth Naomi [1], Hashim Embong [2], Fezah Othman [3], Hasanain Faisal Ghazi [4], Nithiyah Maruthey [5] and Hasnah Bahari [1,*]

- (Nutrients 2022, 14, 20)

- "The results evidenced in this study help to clearly illustrate the **relationship between probiotic supplementation and AD**.

- Thus, this systematic review will help identify novel therapeutic strategies in the future as **probiotics are free from triggering any adverse effects in human body."**

# Synbiotics: Probiotics + Prebiotics

- Some research focuses on specific genus and species

- Scientists recommend for general health a good **Variety** of species from Lactobacillus and Bifidus as the critical factor

- Addition of **Prebiotics** is helpful: Provides dietary substrate for probiotics. **EG: Jerusalem artichoke, beets, rose hips, mushrooms**
  - Prebiotics are non-digestible fiber compounds that are degraded by gut microbiota and are often lacking in the standard American diet.

# Mushrooms - Prebiotics

- **Mushrooms are a great source of prebiotics because they contain a variety of polysaccharides:**
- **Chitin, galactans, xylans, hemicellulose, β and α-glucans, & mannans**

# Reishi - high in prebiotics

- Gut microbiota
- Adaptogenic
- Stress response
- Mental clarity
- Immune system
- Soothe body and mind before a quality night’s sleep
- Digestion
- Overall well-being and weight

# Maitake, Shiitake, Lion's Mane, Coriolus Versicolor, Cordyceps…

- "Mushrooms are proven to possess anti-allergic, anti-cholesterol, anti-tumor, and anti-cancer properties.

- Mushrooms act as a prebiotics to stimulate the growth of gut microbiota, conferring health benefits to the host."
  - Jayachandran M, et al. 2017. A Critical Review on Health Promoting Benefits of Edible Mushrooms through Gut Microbiota. Int J Mol Sci. 2017 Sep 8;18(9):1934

# Ergothioneine (high in mushrooms) for Longevity

# **Is ergothioneine the longevity vitamin?** (Longevity Nutrients part I) American Chiropractor Feb 2024

- Ergothioneine - an amino acid found mainly in mushrooms as a dietary source, but not many other sources contain substantial amounts. It is called the longevity vitamin by reputable researchers, including RB Beelman et al., who noted in the Journal of Nutritional Sciences (Cambridge)…
- "***we believe that ergothioneine is a 'longevity vitamin' that is limited in the American diet"***[1]
- "limited intake of ergothioneine in the diet may compromise long-term health and life expectancy", and therefore should be considered a conditionally essential amino acid/vitamin.

# Sources

- **Shiitake, maitake and oyster mushroom** are particularly high in ergothioneine and are considered a good food and supplement source for this aging support nutrient.

- A cross-sectional study involving over 600 participants reported on the potential role of mushrooms and their bioactive compounds to contribute to neuronal and cognitive health.

- Participants who consumed more than two portions of mushrooms a week had the best association with cognitive/neuronal support and lack of dysfunction

# Longevity Synergy

- While ergothioneine appears to be a powerhouse longevity nutrient, it is not the only one, and synergy with other longevity nutrients is recommended for optimal healthy aging.
  - Synergistic Longevity Nutrients - Feb. & March issues 2024 American Chiropractor “Longevity Part and Part II”

# Other Longevity Nutrients

- Dr. Bruce Ames lists several of these nutrients at the top of his list, such as **ergothioneine.** Other evidence led Dr. Ames to classify **taurine** as a conditional vitamin, stating that other conditional vitamins should include **lipoic acid, co-q-10, and carnitine**. Dr. Ames explains that aside from essential vitamins and minerals needed for survival, there are dietary biochemicals that are putative longevity nutrients, and that list includes: **pyrroloquinoline quinone (PQQ) lutein, zeaxanthin, lycopene** and **astaxanthin.**

# Longevity References:


- Beelman RB, et al. Is ergothioneine a ‘longevity vitamin’ limited in the American diet?’ J Nutr Sci. 2020 Nov 11;9:e52
- 3Priscilla S, et al. 2022. Ergothioneine Mitigates Telomere Shortening under Oxidative Stress Conditions, Journal of Dietary Supplements, 19:2, 212-225; Han Y, et al. The current status of biotechnological production and the application of a novel antioxidant ergothioneine. Crit Rev Biotechnol. 2021 Jun;41(4):580-593.
- Feng, L. et al. The Association between Mushroom Consumption and Mild Cognitive Impairment: A Community-Based Cross-Sectional Study in Singapore J of Alzheimer’s Disease 2019; 68(1):197-203.
- Ames BN. Prolonging healthy aging: Longevity vitamins and proteins. Proc Natl Acad Sci U S A. 2018 Oct 23;115(43):10836-10844

# Probiotics and TBI – Aging Well Means Pain-Free

- **Probiotics may be a therapeutic strategy for treating traumatic brain injury (TBI) because they can reduce inflammation and improve clinical prognosis.**

- Probiotics can also help with neurological disorders by **producing short-chain fatty acids, neurotransmitters, and they have anti-inflammatory properties**.

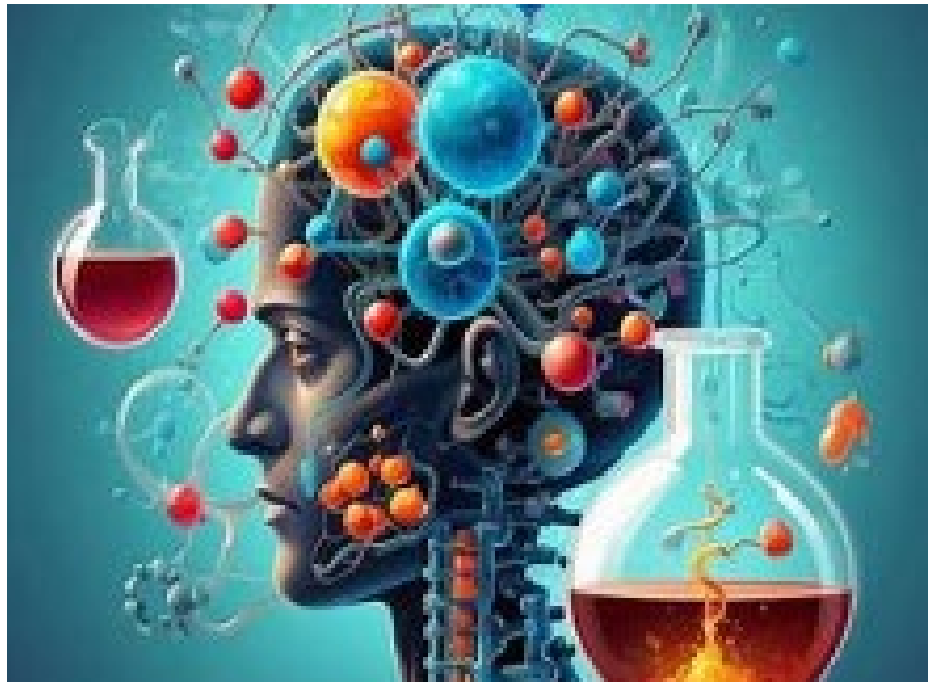
- "Therapeutic strategies such as FMT and **probiotics may offer a neuroprotective benefit by targeting the dysregulated gut-microbiota-brain axis and restoring the gut microbiota to a healthier profile."**
  - Zhu CS, et al. A Review of Traumatic Brain Injury and the Gut Microbiome: Insights into Novel Mechanisms of Secondary Brain Injury and Promising Targets for Neuroprotection. Brain Sci. 2018 Jun 19;8(6):113

# LA increases neuronal survival

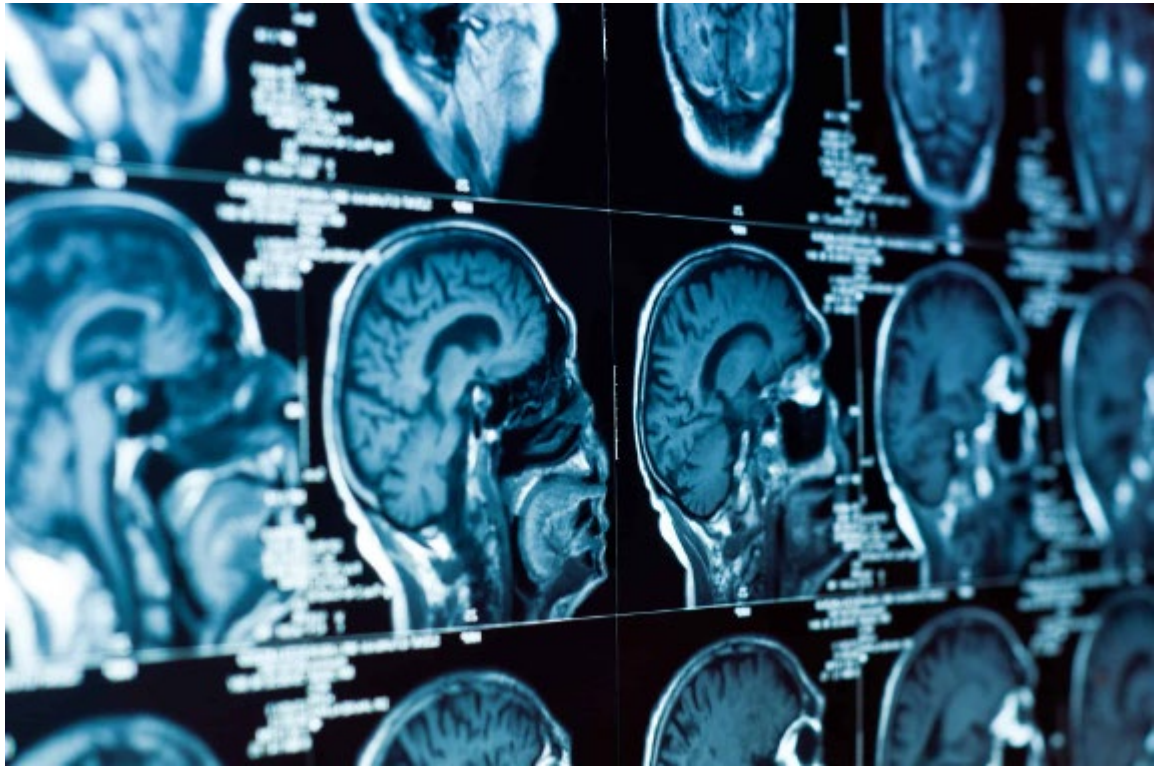
Author links open overlay panel [redacted]

- “Studies have shown that probiotics can have neuroprotective effects after neurotraumatic events. For example, one study found that **Lactobacillus acidophilus** (LA) administration **reduced sensorimotor deficits and increased neuronal survival after TBI.” –** Lactobacillus acidophilus exerts neuroprotective effects. Journal of Nutrition 2019; 149(9).

- “Probiotics combined with early enteral nutrition could **reduce serum levels of ET-1, CRP, and IL-6, IL-10, and TNF-α,** and could thus **improve the recovery of patients with severe TBI. ”**
    - Wan G, Wang L, Zhang G, Zhang J, Lu Y, Li J, Yi X. Effects of probiotics combined with early enteral nutrition on endothelin-1 and C-reactive protein levels and prognosis in patients with severe traumatic brain injury. J Int Med Res. 2020 Mar;48(3):300060519888112



# MRI scan – adjustments reduce pain and improve brain chemistry



- EasternOklahomaChiropractic.com

# Quality of life in longevity

## Prebiotics and probiotics for depression and anxiety: A systematic review and meta-analysis of controlled clinical trials.

- Liu RT, Walsh RFL, Sheehan AE. Neurosci Biobehav Rev. 2019 Jul;102:13-23.

- Meta-analysis of 34 controlled clinical trials evaluating the effects of prebiotics and probiotics on depression and anxiety.

# CDP-Choline benefits


- Synoradzki K. & Grieb P. Citicoline: A Superior Form of Choline? *Nutrients.* 2019;11:1569.
- Blusztajn J.K. & Slack B.E., Mellott T.J. **Neuroprotective** Actions of Dietary Choline. *Nutrients.* 2017;9:815.
- Gareri P., et al. The Citicholinage Study: Citicoline Plus Cholinesterase Inhibitors in Aged Patients Affected with Alzheimer's Disease Study. *J. Alzheimer's Dis.* 2017;56:557–565.
- Gandolfi S.A., et al. Cytidine 5′-Diphosphocholine (Citicoline): Evidence for a **Neuroprotective** Role in Glaucoma. *Nutrients.* 2020;12:793. (calls CDP choline a neuroprotective drug (NPD)
- Seifaddini R., et al. The Effects of Citicoline on Cerebrovascular Hemodynamic Status in Ischemic Stroke Patients. *J. Kerman Univ. Med. Sci.* 2017;24:480–486.
- Trimmel H., Majdan M., Wodak A., Herzer Z., Csomor D., Brazinova A. Citicoline in **Severe Traumatic Brain Injury: Indications for Improved Outcome**: A Retrospective Matched Pair Analysis From 14 Austrian Trauma Centers. *Wien Klin Wochenschr.* 2018;130:37–44

# Alpha GPC Benefits

**Cognitive improvement in mild to moderate Alzheimer's dementia after treatment with the acetylcholine precursor alpha GPC: a multicenter, double-blind, randomized, placebo-controlled trial.** Clin Ther. 2003 Jan;25(1):178-93. Moreno, M.

The first attempts to treat patients with Alzheimer's disease (AD) involved the cholinergic-precursor loading approach. Despite encouraging early results, well-controlled clinical trials did not confirm a clinical utility of cholinergic precursors such as choline and lecithin (phosphatidylcholine) in AD.

A total of 261 patients (132 in the CA group, 129 in the placebo group) were enrolled in the study.

## CONCLUSION:

## The results of this study suggest the clinical usefulness and tolerability of alpha GPC in the treatment of the cognitive symptoms of dementia disorders of the Alzheimer type.

# Take Home Messages:

- Supplementation with designer cholines (**CDP-choline, Alpha GPC-choline**) can increase cholinergic activity and release of acetylcholine

- Increased cholinergic activity is correlated with decreased inflammation, increased brain activity, neuroprotection

- **Chiropractic + Supplementation can result in optimal outcomes for Life in Our Years (healthy aging).**

# Gene SNPS Correlated with Longevity

- **FOXO3**: “FOX03- A Major Gene in Longevity” was the title of a research paper focusing on aging aspects (Gerontology. 2015; 61(6): 515–525),

- **APOEe**: has long been associated with memory

- **MnSOD**:  Manganese super oxide dismutase (MnSOD) is a manganese dependent gene responsible for scavenging the highly reactive superoxide radical, thereby offering antioxidant properties important for longevity.

# Gene SNPS Correlated with Bones

- SNPs of genes ***COL11A1, VEGF, GDF5*, and IL-8**, etc., have been associated with **OA**.
  - Wang T, et al. Single Nucleotide Polymorphisms and Osteoarthritis: An Overview and a Meta-Analysis. Medicine (Baltimore). 2016 Feb;95(7):e2811.

- Gene polymorphisms showed different levels of association with increased risk of OA.

- Some polymorphisms **may be specific to OA subtypes (hip-, knee-, or hand-OA) and ethnic groups**
  - Eg. SNP rs7639618 of DVWA gene is associated with a significantly increased risk of knee OA in Asians.

# Meta-analysis - 9500 OA cases and 9365 controls in 7 studies relating to SNP rs7639618

- Over 50 SNPs from different genes have been shown to be associated with either hip OA, or knee OA, or both.

- SNP rs7639618 of DVWA, increased knee OA risk was observed in all genetic models analyzed.

# Gene SNPS Correlated with OP/Bone Stem Cells

- Role of **USP7** - **regulating self-renewal and differentiation** of human bone marrow derived mesenchymal stromal cells
  - Stromal cells can become connective tissue cells of any organ; contribute to tissue repair

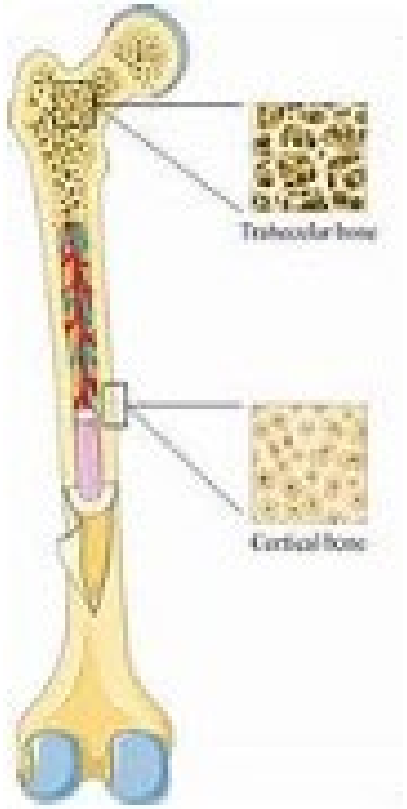
- Directly required during the early stages of **osteogenic, adipogenic, and chondrogenic differentiation** of hBMSCs.

- Furthermore, **USP7 is an upstream regulator** of the self-renewal regulating proteins **SOX2 and NANOG** in hBMSCs
  - Kim YJ, et al. Deubiquitinating Enzyme USP7 Is Required for Self-Renewal and Multipotency of Human Bone Marrow-Derived Mesenchymal Stromal Cells. Int J Mol Sci. 2022 Aug 4;23(15):8674.

# Exploring Factors for Stem Cell Growth

- Examine the **effects of aging on MSC growth** and how **MSC's can convert to fat cells without support.**
- Discover what **foods and supplements** encourage stem cell growth.
- **Chiropractic** adjustment and the effect on the vagus nerve **stimulates MSC** (mesenchymal stem cells), the multipotent stem cells found in bone marrow that make and repair skeletal tissues.

- **TAC Jan 2024:  Fighting Back Against Osteoporosis**



# Differentiation – the genetic explanation

- **How Stem Cells Turn into Bone and Fat**

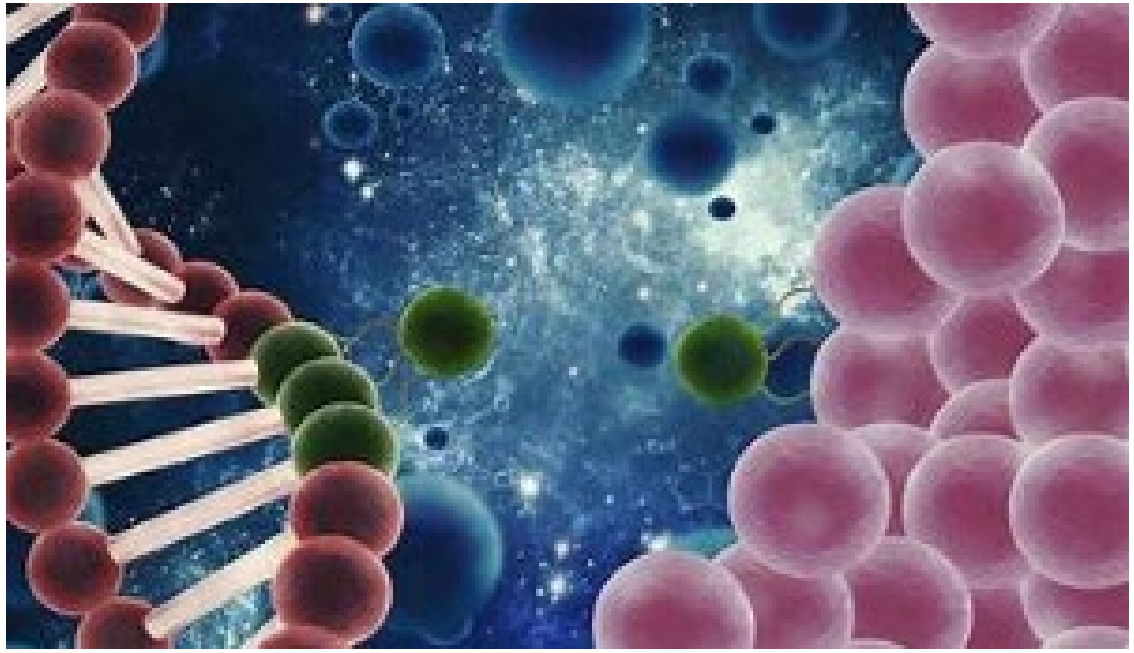
  Arjun, D. M.D. N Engl J Med June 5, 2019;380:2268-2270

How a single MSC generates cells of completely different phenotypes has been a mystery. A recent study by Rauch et al. provides some clues that have ramifications for our understanding of obesity and disorders of bone mineralization.

Rauch A, et al. **Osteogenesis depends on commissioning of a network of stem cell transcription factors that act as repressors of adipogenesis**. *Nat Genet* 2019; 51: 716–27.

# Genetic Explanation

- Undifferentiated MSC resemble the osteoblast more than the adipocyte. Most of the **gene-expression machinery was already turned on**; hence, morphing into an osteoblast required amplification of gene networks that were already active.



In contrast, differentiation into an adipocyte involved the expression of a completely new set of genes along with silencing of genes that were active in the undifferentiated MSC. **How Stem Cells Turn into Bone and Fat**

# Bottom Line:

**“Thus, the hurdles or the genetic barriers that the MSC must overcome to become an adipocyte are far greater than those it must overcome to become an osteoblast.”**

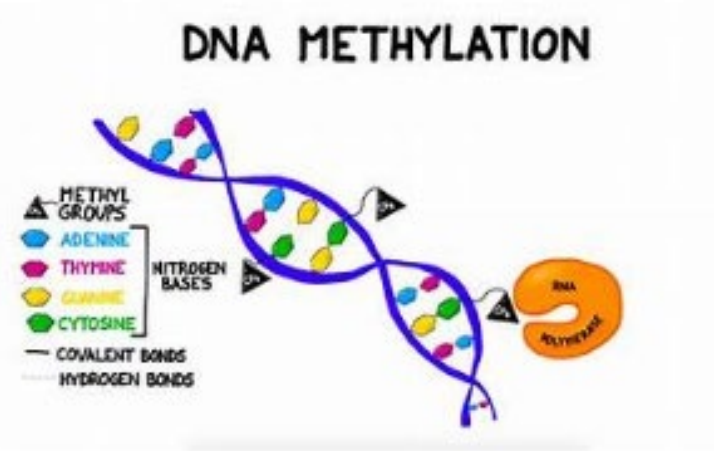
How Stem Cells Turn into Bone and Fat

# Genetic Explanation of Differentiation and Expression (cont'd)

- **SNPs that disrupt enhancer function or gene-expression networks** driving the adoption of adipogenic or osteogenic fates could cause or **affect the phenotype**.

- Delay in **fracture healing** could be caused by the inability or **malfunction of gene networks** to efficiently drive MSCs to adopt osteogenic cell fates.
  - **How Stem Cells Turn into Bone and Fat**

# Genetic & Epigenetic



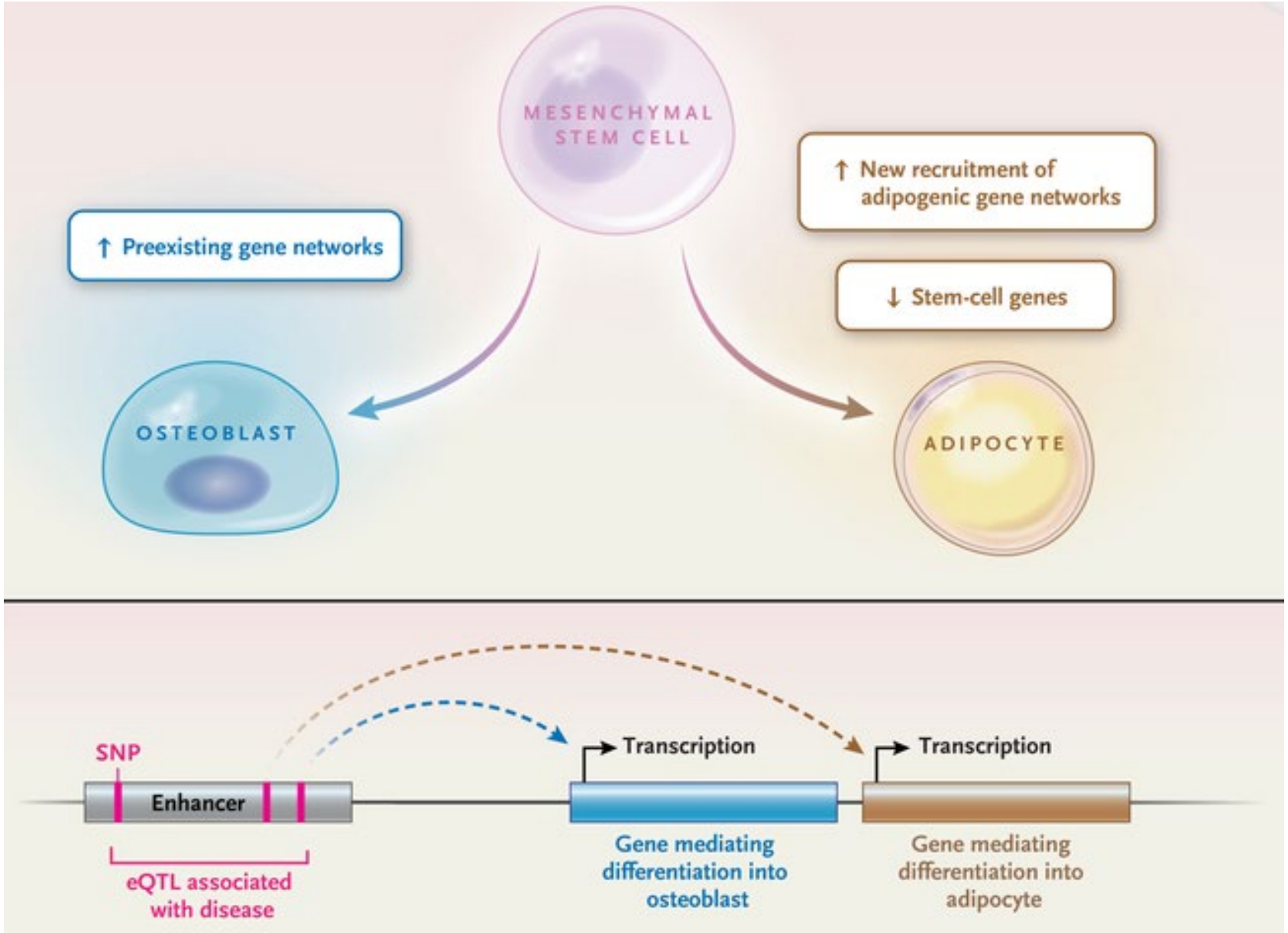

- Mesenchymal stem cells differentiate into the osteoblast lineage by activating different signaling pathways, including the **Wnt pathway**.

- Recent data indicate that bone remodeling processes are also epigenetically regulated by processes such as **DNA methylation**
  - Oton-Gonzalez L, et al. Genetics and Epigenetics of Bone Remodeling and Metabolic Bone Diseases. Int J Mol Sci. 2022 Jan 28;23(3):1500.

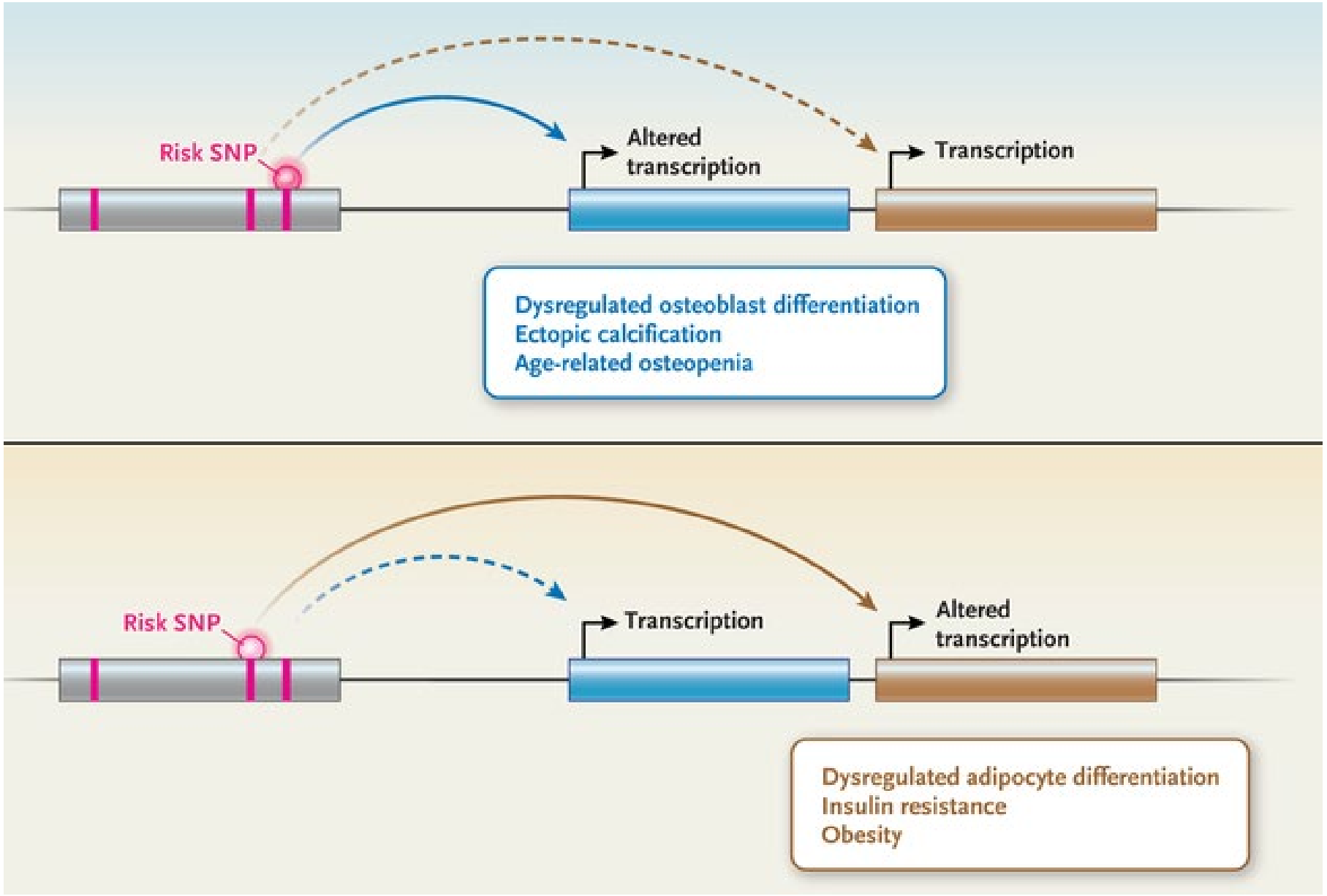
- Epigenetic influences like **vitamin C upregulate Wnt**

# Methylation Factors:

- SAM-e
- 5-MTHFolate
- Methylcobalamin
- P-5-P
- N-Acetyl Cysteine
- Sulforaphane – **“Molecule with Nutrigenomic Properties”** - Houghton CA. Sulforaphane: Its "Coming of Age" as a Clinically Relevant Nutraceutical in the Prevention and Treatment of Chronic Disease. Oxid Med Cell Longev. 2019 Oct 14;2019:2716870 and **“potent epigenetic modulator of methylation”** (Eur J Nutr. 2021 Feb;60 (1):147-158.)
- Curcumin- Fabianowska-Majewska K, et al. Curcumin from Turmeric Rhizome: **A Potentia**l **Modulator of DNA Methylation** Machinery in Breast Cancer Inhibition. Nutrients. 2021 Jan 23;13(2):332.




- **How Stem Cells Turn into Bone and Fat**


Risk SNP
Altered transcription
Transcription
Dysregulated osteoblast differentiation
Ectopic calcification
Age-related osteopenia
Risk SNP
Transcription
Altered transcription
Dysregulated adipocyte differentiation
Insulin resistance
Obesity

# Osteoporosis SNPs

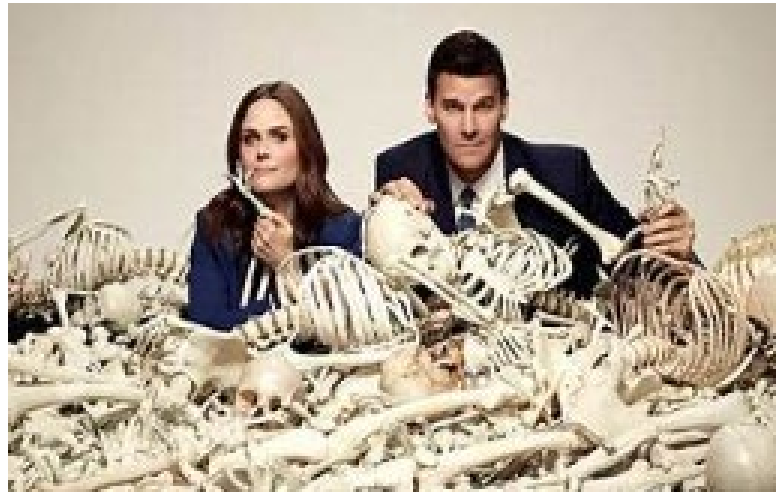
- **Mutations in more than 15 genes** have been implicated in the pathogenesis of osteoporosis.

- These genes largely comprise regulators of bone metabolism, including local regulators of bone metabolism and bone matrix components, as well as **cell receptors and calciotrophic hormones.**

- Among them, Vitamin (1, 25-dihydroxyvitamin) D receptor (**VDR**), estrogen, and androgen receptors and the Collagen type I α (COLIA1) gene have been the most extensively investigated
  - Oton-Gonzalez L, et al. 2022

# VDR SNP receptive to calcium & vitamin D

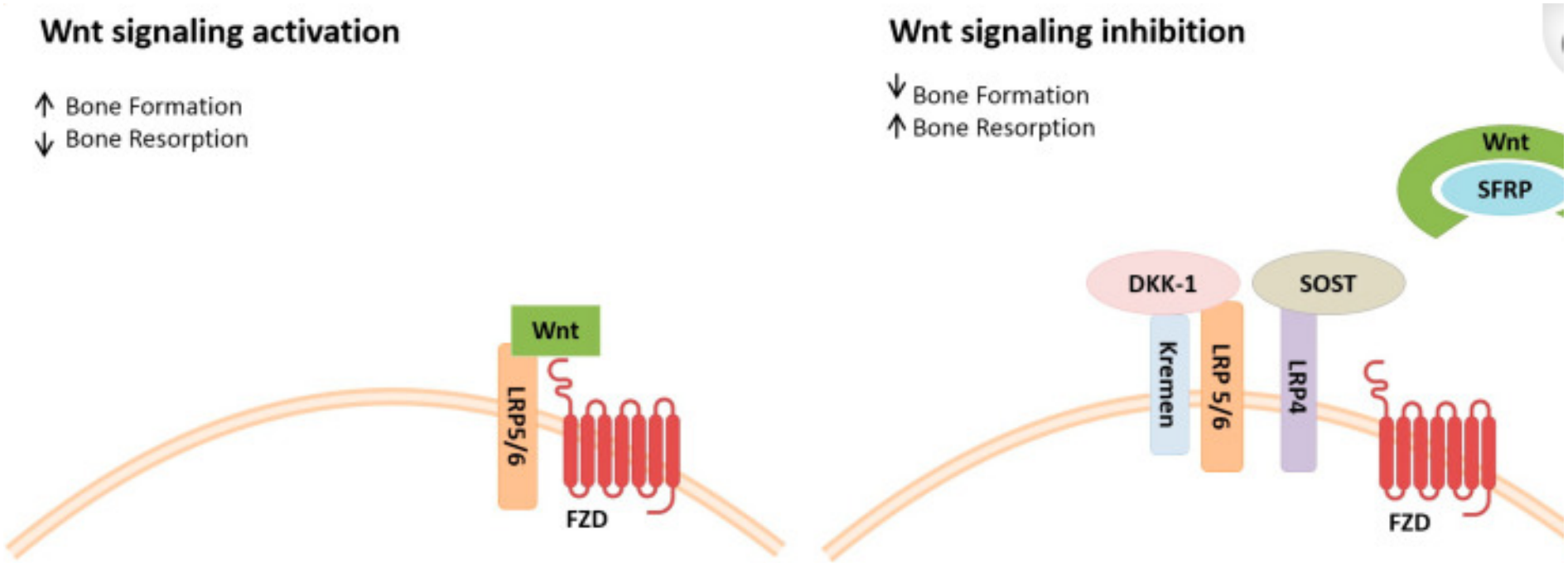
- Morrison et al., in 1994, first identified polymorphisms in the 3′ region of the VDR, which have been linked to **low ostecalcin levels and an increased risk of osteoporotic fracture**.



- Overall, related to up to **75% of the genetic effect on bone mineral density.**

- However, the relationship between VDR-3′ genotype and bone mineral density may be **modulated by high vitamin D and calcium intake**
  - Oton-Gonzalez L, et al. 2022

# LRPS – SNP for High Bone Mass




**Mutations that lead to Wnt pathway activation**

**Loss of function mutations**

**SOST** Sclerosteosis, type 1

**LRP4** Sclerosteosis, type 2

**SFRP4** Pyle's disease

**Gain of function mutations**

**LRP5** High bone mass

**Mutations that lead to Wnt pathway inhibition**

**Loss of function mutations**

**LRP5** Osteoporosis-pseudoglioma syndrome

**Wnt1** Early-onset osteoporosis

Osteogenesis imperfecta

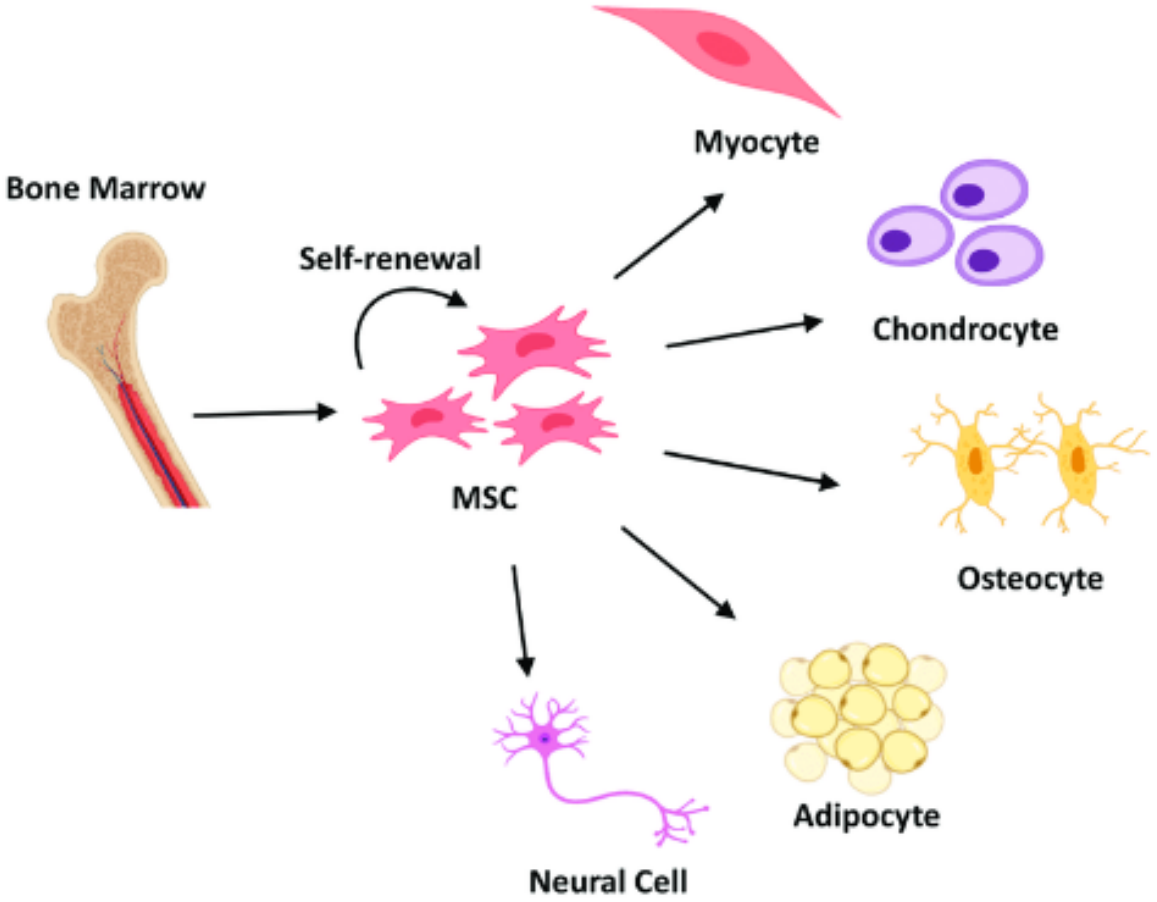
# Environmental Epigenetic Factors

- **Aging and obesity** induce **adipocyte accumulation** in the bone marrow
- Impairs **hematopoietic and osteogenic regeneration**
- More specifically, **aging inhibits** the **osteogenesis** (age-related osteopenia)
- Whereas a **high-fat diet promotes adipogenic expansion.**

- **Opposite of aging: Promoting Longevity**
- **Opposite of high fat diet: Healthy Smart Eating**

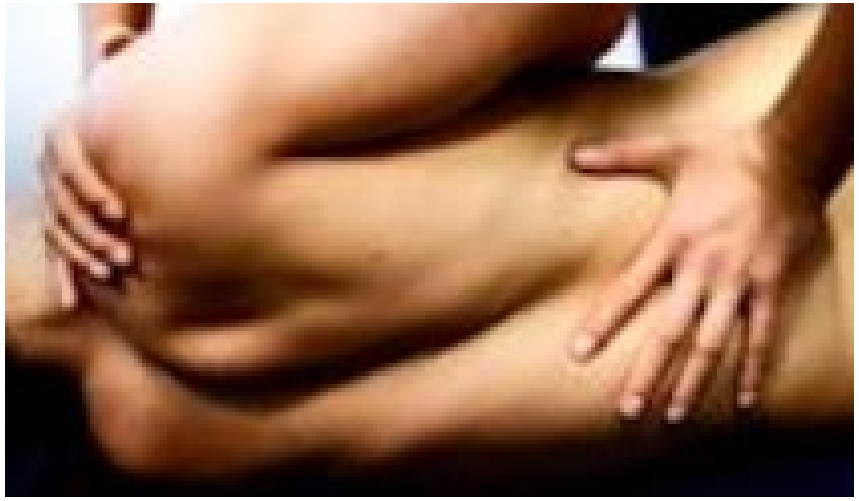
# Take Home Message:

- Knowing genetic SNPs offers insight into propensity for low BMD
- Acting on knowledge of epigenetic factors can help the outcome
- Many longevity factors are good for differentiation of MSCs into osteogenic cells (good for bones).
- Everything good for the bones is good for improving the quality of life in later years



# Factors Affecting Proliferation of MSCs

- Diet
- Supplementation
- Chiropractic

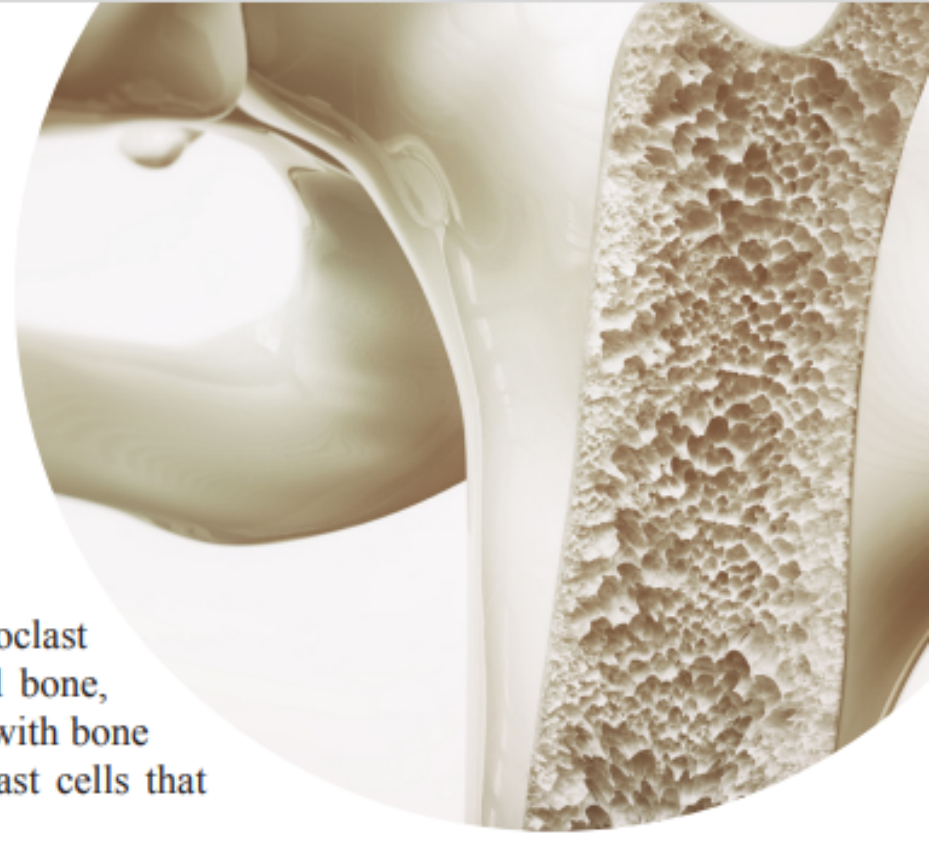


CLINICAL EXCELLENCE

# Fighting Back Against Osteoporosis

## Including natural stem cell support

*by Lynn Toohey, PhD*



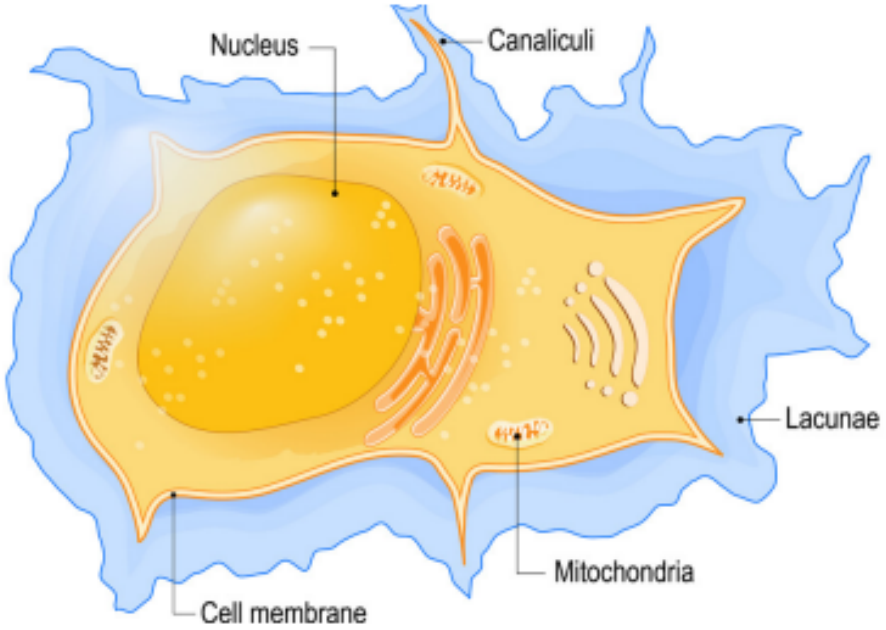
Osteoporosis is when bones become weak and brittle. Osteoclast cells break down bone, and osteoblast cells typically build bone, but with osteoporosis, new bone formation doesn't keep up with bone removal. We hear less about osteocytes, which are osteoblast cells that become embedded in the matrix it has secreted.

**Osteocytes** are the most prevalent cells in bone. They regulate bone mineral deposition, play a large role in bone function (regulating osteoblasts and osteoclasts), bone remodeling, production of nerve growth factors after bone fracture, and can send signals to distant organs (similar to the nervous system), such as the kidneys, to regulate phosphate transport. Without enough phosphorus, bones soften, and muscles weaken.

Osteocytes have received recent attention because of their control over bone signaling, mineral deposition, halting of bone loss, and, of course, their role in building new bone. The encouraging stem cell growth of bone cells. While calcium and vitamin D get all the press when it comes to bone support, the following nutrients are extremely helpful, and some are necessarily synergistic (like vitamin K) for optimal results.

### Osteocyte Specific Support:

**Vitamin C** actually supports bone by several different mechanisms. First, it is a good antioxidant to help go after free radicals that would otherwise destroy osteocytes. In one study that evaluated the effects of vitamin C on osteogenic differentiation, osteoclast formation, and bone microstructure,




**"Since osteocytes do not divide and replicate, it is important to preserve the existing repertoire of cells".**

Osteocytes are derived from the mesenchymal stem cells, some of which differentiate into active osteoblasts (which may further differentiate to osteocytes.). Since osteocytes do not divide and replicate, it is important to preserve the existing repertoire of cells. Free radicals are a big destroyer of osteocytes; therefore, antioxidants are a big preserver of osteocyte cells. Besides preserving existing osteocytes, this article will conclude with the supplements, diet/lifestyle, and alternative methods for

osteoporosis and bone regeneration by promoting osteoblast formation and blocking osteoclastogenesis by their tested molecular pathway intervention.[2]

**Magnesium** has proven to be as important as calcium as a bone nutrient. The balance of magnesium to calcium must be maintained to avoid calcium calcifying or depositing in the arteries. Researchers reported that magnesium and vitamin C supplementation synergistically reduced the apoptosis (cell death) of osteocytes and osteoclast number and increased osteoblast surface. Vitamin C significantly increased a bone formation marker, and the combination significantly decreased a bone resorption marker. Oxidative injury was decreased in bone marrow in the vitamin C/magnesium combination group. "The combination supplementation significantly inhibited osteoclast differentiation potential of marrow cells."[3]

**Vitamin K2** promotes osteoblast-to-osteocyte transition.[4] It is a necessary nutrient to supplement with the more well-known bone nutrients calcium and vitamin D. Vitamin D will increase calcium absorption, but vitamin K2 will support the avoidance of deposition into soft tissue, such as the arteries. In fact, vitamin K2 activates a protein called matrix GLA that removes calcium from soft tissues. Vitamin K also activates osteocalcin, which holds calcium to bone, so it is important for mineralization. It is important to take vitamin K in a combination of vitamin K1, K2-4 and K2-7 to get all the benefits a supplement offers.

**Other nutrients** are listed in a review done by McCarty et al. (2022), where scientists noted, "There is vast pre-clinical

# OP Protocol: Preserve, Protect, Proliferate

- **Vitamin C** – antioxidant, preserve osteocytes and other bone cells; promotes proliferation
  - **Osteocytes:** regulate bone mineral deposition, play a large role in bone function (regulating osteoblasts and osteoclasts), bone remodeling, production of nerve growth factors after bone fracture and they can also send signals out to distant organs

- Study evaluating the effects of vitamin C on osteogenic differentiation, osteoclast formation and bone microstructure, the vitamin C-treated group displayed an **increase in the expression of osteoblast differentiation genes, including genes for type I collagen**.
  - Wnt/β-Catenin/ATF4 Signaling Pathways) (Choi HK, et al. Vitamin C Activates Osteoblastogenesis and Inhibits Osteoclastogenesis via Wnt/β-Catenin/ATF4 Signaling Pathways. Nutrients. 2019 Feb 27;11(3):506.

- Vitamin C **ALSO reduced the expression of osteoclast differentiation genes**. Researchers believed that their study is the first to show the influence of vitamin C on osteoporosis and bone regeneration by promoting osteoblast formation and blocking osteoclastogenesis by their tested molecular pathway intervention

# Magnesium

- As important if not more important than magnesium
- Balance of magnesium to calcium must be maintained to avoid calcium calcifying or depositing into the arteries. Researchers reported that **magnesium and vitamin C** supplementation **synergistically reduced the apoptosis** (cell death) of **osteocytes and osteoclast number, and increased osteoblast surface.**
- Vitamin C **significantly increased a bone formation marker, and the combination significantly decreased a bone resorption marker**.
- **Oxidative injury was decreased** in bone marrow in the vitamin C/magnesium combination group. **"The combination supplementation significantly inhibited osteoclast differentiation potential of marrow cells"**

# Vitamin K2

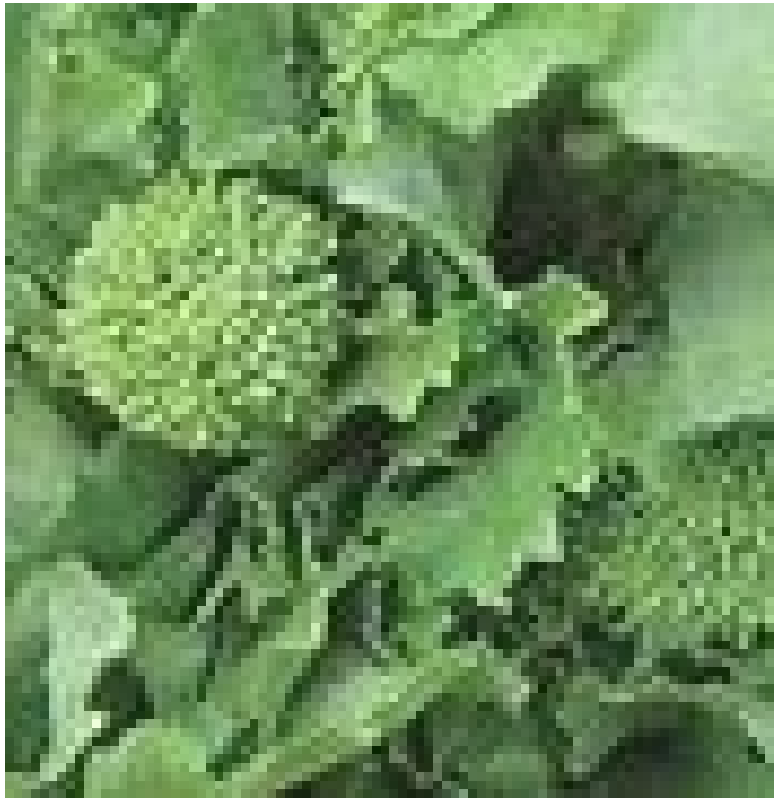
- Promotes **osteoblast-to-osteocyte transition**
- Nutrient that is necessary, like magnesium, to supplement with the more well-known bone nutrients calcium and vitamin D, because vitamin D will increase calcium absorption, but **vitamin K2 will support the avoidance of deposition into soft tissue like the arteries.**
- In fact, vitamin K2 activates a protein called matrix GLA which removes calcium from soft tissues. **Vitamin K also activates osteocalcin, which holds calcium to bone, so it is important for mineralization.**

Several nutrients are listed in a review done by McCarty MF et al. (2022), where the scientists noted that "There is vast pre-clinical literature suggesting that certain nutraceuticals have the potential to aid the preservation of bone mass"

McCarty MF, et al. Targeting Sirt1, AMPK, Nrf2, CK2, and Soluble Guanylate Cyclase with Nutraceuticals: A Practical Strategy for Preserving Bone Mass. Int J Mol Sci. 2022 Apr 26;23(9):4776.

- Some of the listed nutrients mentioned in the review article have mechanisms that affect specifically osteocytes, but all support bone processes.

- They include **taurine, N-acetylcysteine, zinc, potassium, flavonoids (particularly quercetin), biotin, lipoic acid, melatonin, glucosamine sulfate, nicotinamide riboside and sulforaphane** from cruciferous vegetables, as well as vitamins D & K2 and magnesium.



# Stem Cell Support:

- **Diet:** Eat organically to avoid the toxins that impede stem cell growth.
- Blueberries, raspberries, blackberries, **sulforphane-containing** cruciferous vegetables, sprouts, polyphenol/glycan-containing mushrooms, nuts and seeds, turmeric, fish oil, ginger, etc. and all foods high in **vitamin C and D** will all support **stem cell growth.**
- Vitamin D not only supports bone and stem cell growth, it helps differentiate stem cells into osteoblasts and osteocytes, and vitamin C helps differentiation and promotes proliferation.

# Curcumin and Resveratrol

- **Turmeric** – it contains **curcumin**, which can **upregulate bone factors, reduce oxidative stress, and help stem cell function.**

- Foods such as **red and purple grapes** are high in **resveratrol,** which **supports cartilage and helps stem cells differentiate and multiply,** but that it is nearly impossible to get the amount you would need in order to optimize its health benefits through food alone.

# Lifestyle:

- **Alcohol, smoking and exposure to environmental chemicals** all disrupt key pathways in our body's chemistry as it relates to stem cell function.
  - Some may think that toxic chemical exposure is small, but multiply that by the immense amount we get exposed to every day.
- **Aging** is also responsible for the loss of signaling necessary to lay new bone.
- **Antibiotics** can injure stem cells and tendon tissue.
- **Anti-inflammatory steroids** will flip the switch on stem cells and nix new growth.
- **Non-steroidals** like ibuprofen and aspirin will affect stem cell growth to a lesser degree.

# Alternatives:

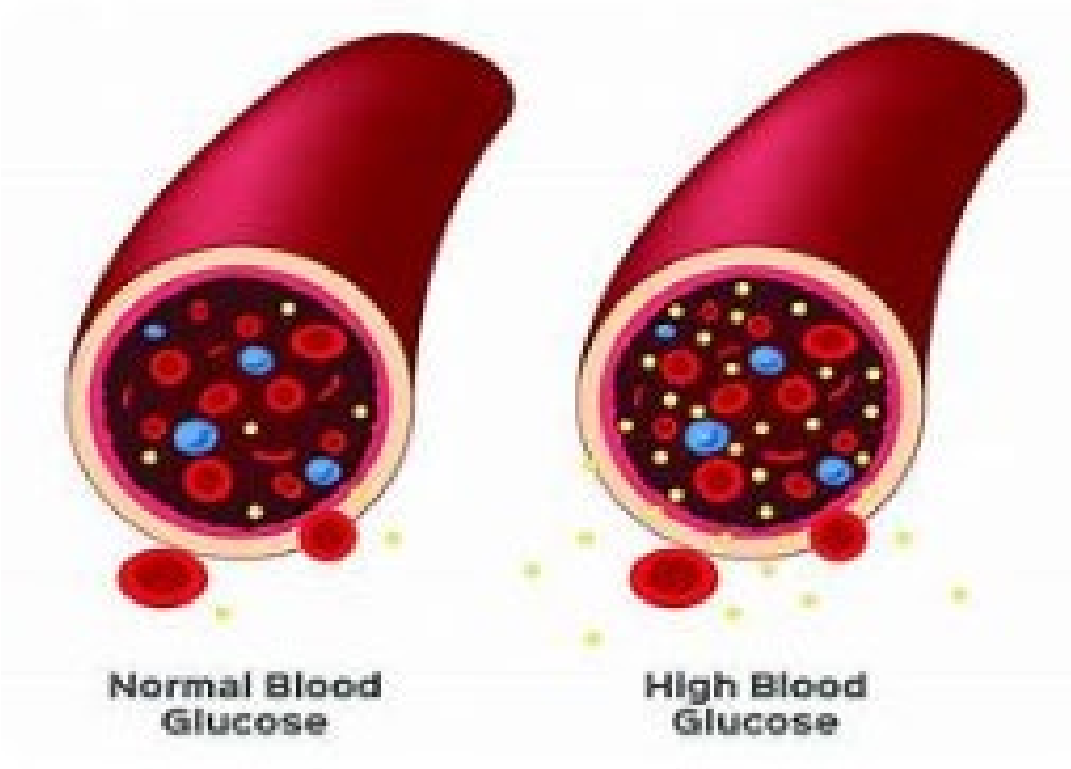
- All the more reason to entertain alternatives such as **curcumin, boswellia, ginger, quercetin, fish oil, melatonin** (see TAC May 2023 article on melatonin and pain), etc.

- Supplementing with **fish oil also helps decreases triglyceride (TG) levels**, and **high TGs slow stem cell growth**.

# High Blood Sugar slows stem cell growth

- **Support for blood sugar:**

- **Chromium**
- **Gymnema sylvestre**
- **Alpha lipoic acid**
- **Benfotiamine**



# Environmental Factors (cont'd)

- **Exercise and weight lifting** will stimulate stem cell growth.
- Short term calorie restriction or **intermittent fasting of 10-12 hours overnight,** (not fasting for days or weeks that depletes nutrient stores), can also be helpful.
- One study concluded that "**improvement of body composition** affects the number of stem/progenitor cells in circulation
  - Mikirova NA, et al. Effect of weight reduction on cardiovascular risk factors and CD34-positive cells in circulation. Int J Med Sci. 2011;8(6):445-52.)

# Chiropractic:


- Chiropractic **stimulates the vagus nervous system**, which stimulates the release of acetylcholine (cholinergic) with many benefits, including the effect on an inflammatory environment
- A study of 21 patients demonstrated that electrical vagus nerve stimulation (VNS) **improved bone mineral density (BMD) in the lumbar spine**
- Researchers concluded that their study "could lead to a **new application for VNS in the treatment of osteoporosis."** Other studies have shown that cholinergic stimulation **could decrease fracture risk**
  - Tamimi I, et al. *Osteoporos Int.* 2018; 29:849–857.

# Chiropractic & Vagal Stimulation

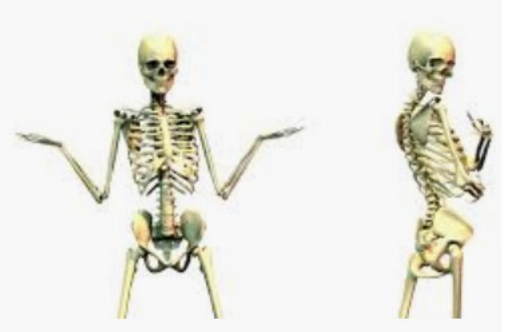

- Electrical or chiropractic stimulation of the vagus nerve has an added benefit of being non-invasive and **overcoming the hurdles of surgical implants that affect migration, proliferation, maturation and integration of the stem cells.**
- Additionally, the vagus nerve also **innervates the thyroid gland and kidneys and potentially contributes to bone remodeling through the regulation of these organs**
  - Baquiran M, Bordoni B. Anatomy, Head and Neck, Anterior Vagus Nerve. *In: StatPearls.* Treasure Island (FL): StatPearls Publishing; 2019.

# Hyperbaric oxygen (HBO) treatment

- Increase stem cell growth after twenty or so treatments
- Therapy that is being observed as helpful support for osteoporosis.
- Bones are controlled by an electrical network of force sensors; physical impact of the foot when walking activates these force sensors and when bone is under pressure, the stem cells that turn into osteoblasts/osteoclasts are stimulated by these sensors.
- HBO is a form of pressure that helps bone formation via osteogenic differentiation of bone marrow stromal cells (BMSCs), which is regulated by Wnt3a/β-catenin signaling
    - Song-Shu et al. Hyperbaric oxygen promotes osteogenic differentiation of bone marrow stromal cells by regulating Wnt3a/β-catenin signaling—An in vitro and in vivo study. Stem Cell Research 2014 Jan. 12 (1):260-274.

- This signaling pathway is also involved in the bone support mechanism of vitamin C.

# BPA is bad for the bones



- BPA also upsets the **microbiome**, which **controls DNA outcomes** and **affects bones**

- “Is it a gut feeling, a feeling in your bones, or both?”

- Research from the journal Aging Clinical and Experimental Research tells us that “**Bone homeostasis is influenced by gut microbiota composition and/or products**. Gut microbiota appears to be a major player in the various determinants of bone health” (2019;31(6):745-751).

# *Healthful exposures vs toxic exposures that affect gene expression*

# Dr. Allomong - respected authority in methylation pathways & DNA variants

- **From Dr. Jared Allomong:** "The most significant new discovery I learned while studying longevity was that most variants in **genetics that impact longevity positively or negatively** have a direct effect on the **ability of cells to cope with stressors."**

- **Good genetic coping skills equals optimal aging.** Supporting the body's natural ability to cope with stress by **decreasing the overwhelming burden of stressors is the best solution to support longevity in the 21st century.**

- **Genes variants in FOXO3 and APOE have the biggest impact** while **mitochondrial inflammation** is another contributor with variants in **MnSOD**."

# Epigenetic stress exposure -DNA methylation stress shows up in 3rd generation

- **Hunger Winter** – diabetes and other health problems showed up in third generations

- Grandmaternal stress during pregnancy and **DNA methylation of the third generation**: an epigenome-wide association study
  - Transl Psychiatry. 2017 Aug 15;7(8):e1202. Serpeloni F. et al.

- “Stress during pregnancy may impact subsequent generations, which is demonstrated by an increased susceptibility to childhood and adulthood health problems in the children and grandchildren.”

# Regrettable Substitutions for BPA

- BPA has been replaced by what the experts call “regrettable substitutions”.
- Many of the efforts to replace chemicals have resulted in so-called “Regrettable Substitutions”, when a chemical with an unknown or unforeseen hazard is used to replace a chemical identified as problematic.
- **Bisphenol A was replaced with Bisphenol S**
- In particular, we focus on how Green Toxicology can offer a way to make better substitutions.
  - Alexandra Maertens, Emily Golden and Thomas Hartung; *ACS Sustainable Chem. Eng.* June 1 2021, 9, 23, 7749–7758

# EPA - Are BPA Substitutes Any Safer Than BPA?

***By Dr.Lynn Toohey***

*Published September 11, 2024*

- The researchers specifically tested the impact of these chemicals on estrogen receptor activity, which if altered could affect the body's endocrine systems, with potentially serious consequences for fetuses, infants and young children.

- The team showed that some of the BPA alternatives were actually **more potent than BPA itself in activating the estrogen receptor.** These findings highlight the need for testing of replacement chemicals prior to their introduction into commerce to demonstrate that they are safer than the chemical being replaced.

# Problems with substitutions:


# Phase I & Phase II

Systemically detox through all seven pathways:

Liver
Colon
Blood
Lungs
Lymph
Skin
Kidney

# The Seven Detoxification Pathways:

**The Liver:** The liver utilizes nutrients such as glutathione to hook onto the toxins, make them water soluble, and eliminate them. Other important nutrients for toxin binding include taurine, glycine, and methionine. Cruciferous vegetables, like broccoli, help the liver detox. As part of the detoxification process, free radicals are generated, and it is imperative to have adequate antioxidant protection. Antioxidants include vitamin C, vitamin E, beta carotene, quercetin, selenium, coenzyme Q 10, taurine and curcumin. Zinc, selenium and glutathione are necessary components for antioxidant enzymes in the body. N-acetyl cysteine has specific antioxidant action in the liver, it protects cells, and it acts as a building block for glutathione. Red beets are very cleansing and have a specific action on the liver (and the bowels). Chlorophyll and dandelion facilitate liver detox, and dandelion has been traditionally utilized to address liver congestion and imbalance of liver and gall bladder.

**The Bowels:** Our colon is sometimes called, "the final elimination pathway". Since it is an elimination pathway for toxins, it is important that this pathway is not obstructed. Inefficient colon elimination results in toxin storage instead of removal. There are many nutrients which can facilitate the optimal functioning of the bowels. Many plant substances are high in fiber, such as beet root, asparagus, and broccoli. Additionally, there are many phytochemicals in these plants that favorably influences detox pathways. Beets provide a good source for the short-chain fatty acids (SCFA's) which maintain the health of the colon. Yellow dock stimulates bile; dandelion can relieve constipation.

**The Blood:** Chlorophyll is the main component of the plant's blood, just as hemoglobin is the main component in human blood. Chlorophyll has long been used for its blood-cleansing properties. Chlorophyll enhances toxin-scavenging activity in the blood. Dandelion purifies the blood by straining and filtering toxins and wastes. Yellow dock is so well-known for its blood-cleansing properties; it is dubbed the "blood purifier"

**The Lungs/Lymph:** Curcumin is important in the detox pathway of the lungs and the lymph; it tones mucus membranes, supports a normal inflammatory response, and facilitates mucous reduction. Quercetin is a powerful flavonoid, which affects histamine release (histamine can cause sneezing, itching, watery eyes, etc.).

**The Skin:** Yellow dock is helpful in skin conditions, especially those caused by blood-borne toxins. Skin problems can be the result of accumulated wastes that are released into the blood; the more aggressive the liver detox, the more of a load that is unleashed and needs to be bound and removed (This is one of the reasons why a gentler, non-fasting, nutrient-supported detox regimen is always recommended!)

**The Kidney:** Dandelion works on four major detox pathways: kidney, blood, liver, and colon. It has the power to stimulate kidney function and the urea detox path, while preserving potassium status. Dandelion is a widely applicable diuretic and liver tonic.

# For Microplastics:

- **Extra Quercetin and N-Acetyl Cysteine**

# Epigenetics + Genetics (SNP's) + Lab testing for manifested genes + Reports (suggestions for lifestyle protocols)

***(Recognition, Analysis, Support)***

- From the **latest research** on health implications for genetic variants, to **analysis of what your genetics mean** and what epigenetic changes you can make to **optimize your DNA and find out how it ties into longevity**…

- Start with **the science and get to the practical application** of producing DNA reports and transforming lifestyles to create the best possible health scenario!

# Genomics in Personalized Nutrition: Can You "Eat for Your Genes"?

- Mullins VA, et al. Genomics in Personalized Nutrition: Can You "Eat for Your Genes"? Nutrients. 2020 Oct 13;12(10):3118.

**Success – genetics & epigenetics**

# Eat for your genes (cont'd)

- **Genome-wide single nucleotide polymorphism (SNP) data** are now quickly and inexpensively acquired, **raising the prospect of creating personalized dietary recommendations based on an individual's genetic variability at multiple SNPs.**

# Recognition, Analysis, Support

- **Recognition**: Patient orders DNA saliva testing kit, and provides inherited SNP information in the way of a "raw data" file, accessible from their website.

- **Analysis**: Patient gives raw data file to the doctor, who then uploads the file into a DNA analysis program, so that the SNPs and their frequency can be analyzed, reported on, and clearly observed.

- **Support**: The detailed Report

# Genome Studies

- Keep in mind when you read a gene study that it was probably taken from a database such as 23andme
- There are privacy alternatives

# Fracture Study used 23andme

- Personal genetics data from **hundreds of thousands of people collected by 23andMe,** Inc.
- Genetic factors for lower BMD were linked to **increased risk of bone fracture**.
- **126 target genes** identified.
- **DAAM2 influences bone density, mineralization, porosity, and strength**.
- The team also highlighted five other genes that preliminary work suggests are **important for BMD and fracture**:
  - **CBX1, WAC, DSCC1, RGCC, and YWHAE.**

# Example SNP Report

- From definition to protocol support with appropriate supplement recommendations.
- SNPs reported by category, i.e. Detox, Brain, etc. are user-friendly
- DNA testing from Ancestry or other institutions
- Alternatives available that protect privacy
- **Automated lab entry helpful**
- **Automated DNA raw data upload helpful** through LabCorp (**Professional Co-Op, free to join**)
- **Example:  COMT SNP**

# **COMT:** (Catechol-O- Methyl Transferase)

- The COMT enzyme helps break down neurotransmitters and maintain appropriate levels of these neurotransmitters in the brain. COMT catalyzes the transfer of the methyl-group from SAM to catecholamine substrates **Mutations in the COMT gene can lead to high levels of dopamine, norepinephrine (noradrenalin) and epinephrine (adrenalin).** High levels of dopamine have been associated with intelligence, however high levels can lead to more difficulty with attention and increased levels of irritation, anxiety and anger. COMT variants have also been shown to be implicated in anxiety, novelty seeking behavior, aggression, and personality imbalance.

- In addition, COMT variants have also been shown to be associated with estrogen dominant conditions including cancer due to the **decreased breakdown of the catechol estrogens.**

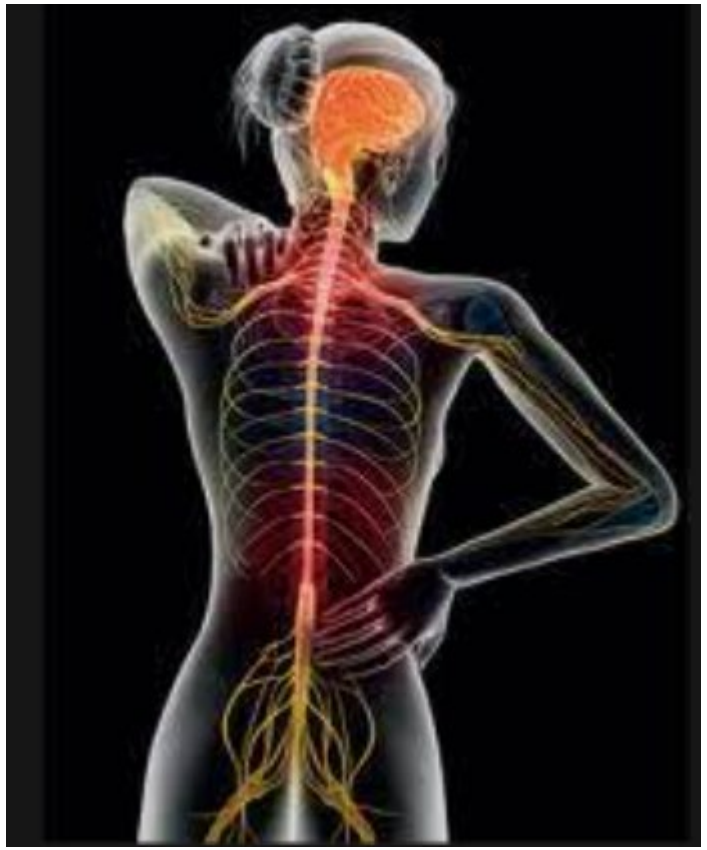
# COMT and Cognition

- **How does COMT affect cognitive function?**
- Although the underlying mechanism for the association between COMT and cognitive function remains unclear, alterations in dopaminergic function is a likely pathway.

- Reduced enzyme activity decreases the degradation and increases the concentration of dopamine in the brain, which further enhances cognitive function.

- **COMT (catechol-O-methyltransferase) affects areas of the pre-frontal cortex involved with:**

- **Cognition**
- **Short-term memory**
- **Personality**
- **Behavior**
- **Mood**
- **Emotion, etc.**



- **COMT** even affects **sensitivity to pain.**

# Does COMT predict pain intensity in chronic shoulder pain?

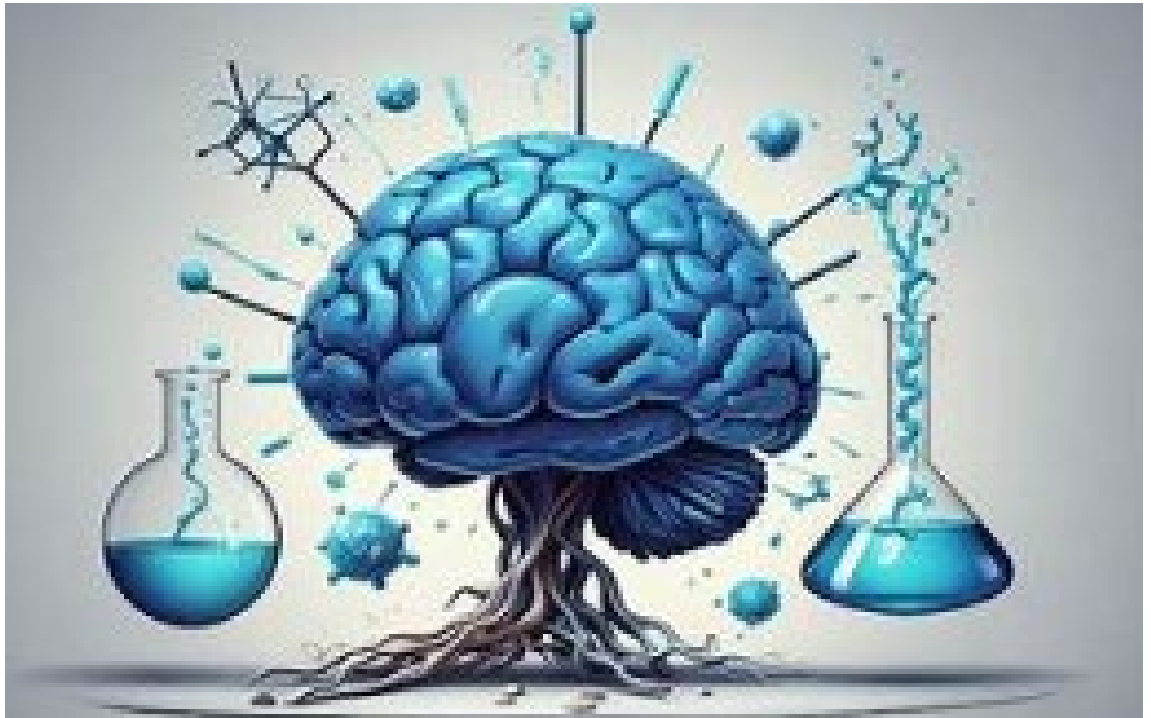
- COMT interacted with pain catastrophizing (a maladaptive cognitive approach to pain characterized by rumination, magnification, and helplessness) to predict pain intensity in patients with chronic shoulder pain.
  - Fillingim RB. Individual differences in pain: understanding the mosaic that makes pain personal. **Pain**. 2017 Apr;158 Suppl 1(Suppl 1):S11-S18.

# **COMT:** (Catechol-O- Methyl Transferase)

- **<u>Dietary and Lifestyle Recommendations:</u>**
- Avoiding stress is a big help for this pathway. If you have a homozygous variant here, breaking down stress hormones is especially difficult for you. This makes you more susceptible to anxiety, especially after a traumatic event. Learning to incorporate rest and stress reduction activities is especially important here. Meditation can be very beneficial, and avoiding caffeine and stimulants is helpful as well.

**Variants are associated with:**

- Anxiety
- Lack of attention
- Weight imbalance
- High cortisol
- High insulin
- High estrogen
- Insomnia
- Depression
- Memory difficulty
- Liver detox difficulty
- Chronic skin problems
- Mental imbalance
- Thyroid imbalance



# **COMT:** (Catechol-O- Methyl Transferase)

- **<u>Product Support Recommendations:</u>**
- Suggestions here

**<u>Nutrient Support Recommendations:</u>**

- Magnesium
- Manganese
- Minerals
- Inositol
- Boron
- Calcium synergistic blends
- Thyroid support
- Iodine

Reduce Stress!

# COMT and Memory

- Amiel Castro R, et al. Pregnancy-related hormones and **COMT** genotype: Associations with maternal working **memory**. Psychoneuroendocrinology. 2021 Oct;132:105361.
- Tamm G, et al. Platelet **MAO** activity and **COMT** Val158Met genotype interaction predicts visual working memory updating efficiency. Behav Brain Res. 2021 Jun 11;407:113255.
- Wang J, et al. Interaction of **COMT** and KIBRA modulates the association between hippocampal structure and episodic **memory** performance in healthy young adults. Behav Brain Res. 2020 Apr 20;384:112550
- Van der Auwera S, et al. Sex effects for the interaction of dopamine related genetic variants for **COMT** and **BDNF** on declarative **memory** performance. Genes Brain Behav. 2021 Jun;20(5):e12737.
- Papenberg G, et al. **COMT** polymorphism and **memory** dedifferentiation in old age. Psychol Aging. 2014 Jun;29(2):374-83.
- O'Donnell KJ, et al. Maternal prenatal anxiety and child **COMT** genotype predict working **memory** and symptoms of ADHD. PLoS One. 2017 Jun 14;12(6):e0177506.

# 20 study systematic review of COMT & brain

- **The influence of COMT rs4680 on functional connectivity in healthy adults: A systematic review (20 studies). Kim Morris et al.** Eur J Neurosci. 2020 Oct;52(8):3851-3878.

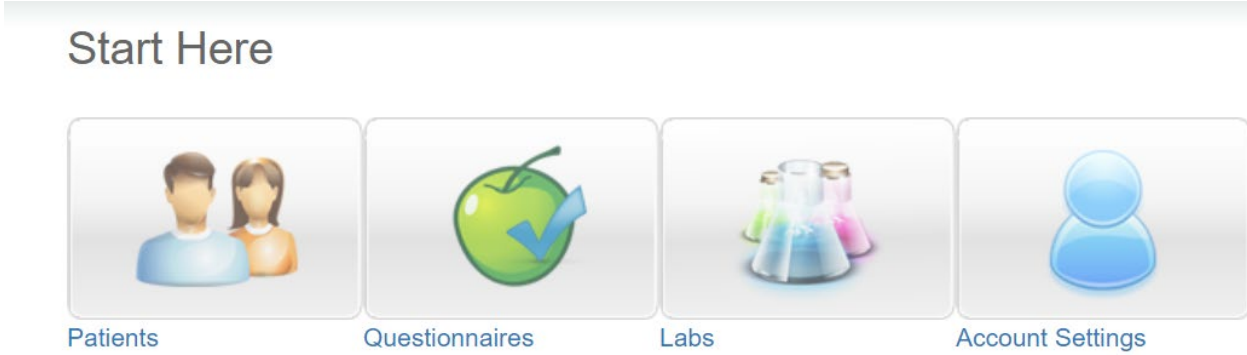
- The Val allele is associated with improved **cognitive flexibility** allowing integration of novel relevant stimuli, and the Met allele allows **improved sustained attention** and targeted **neural processing**, particularly between limbic regions and prefrontal cortex. The most promising brain regions implicated in a **COMT genotype influence on functional connectivity include prefrontal regions, amygdala and hippocampus.**

# Eating For Your Genes:

- **Foods high in magnesium:**
- **Foods high in calcium:**
- **Foods high in manganese and minerals:**


- **Avoid caffeinated beverages**


One example of an analysis program:




Choose patient

Upload the raw data file

Display the report

www.FHEcloud.com

# What to look for in a DNA Report

- Definition – explanation of beneficial vs risk alleles; **links to references** and scientific validation for the physiology, recent discoveries, nutritional research, etc.
- Dietary & Lifestyle – Recommendations for healthy choices regarding eating and navigating a lifestyle that benefits and supports the individual SNPs.
- Nutrient Support – Recommendations for nutritional support for specific SNPs
- Product Support – Recommendations for formulas that support specific SNPs

## Example Report: Viral support gene (blue type indicates links)

**OAS1** Oligoadenylate synthetase (OAS) enzymes play a major role in the **innate immune system.** These enzymes **defend against foreign invaders (viruses)** by acting as sensors. **Interferon** (a major viral signaling protein that is becoming a major buzzword in our current environment) up regulates the OAS enzyme. OAS then signals for a degradation of viral RNA, shutting down host protein synthesis/replication. OAS proteins are also suspected of entering cells with direct activity. OAS may also be involved in removing old tired cells to make room for new healthy ones, and in autophagy (sometimes called our central recycling system), which saves useful components from dying cells, while trashing the junk.
A/G and G/G SNP genotypes of **rs10774671** and **rs2660** may be beneficial for activity of OAS. Having at least one G allele is linked to higher activity, with G/A linked to intermediate activity, and A/A linked to lowest activity **(ref I)(ref II)(ref III).**

**Dietary and lifestyle Recommendations:** Eat a healthy diet that promotes a strong immune system, filled with organic whole foods, including lots of organic greens and colored vegetables. The following dietary sources have nutrients which support the interferon response: Mushrooms are high in glycan content; elderberries are high in ferulic acid, cruciferous vegetables are high in sulforaphane, Broccoli, garlic and onions are good sources of selenium (when grown in soils rich in selenium), as are seafood, liver and Brazil nuts.

Eat adequate amounts of good protein, as most players of the immune system are proteins. Regular exercise is good for the immune system.

**Nutrient Support Recommendations:**

Glucans/glycans; ferulic acid (elderberry); alpha lipoic acid; selenium; N-acetyl cysteine; glucosamine; sulforaphane (ref).

**Product Support Recommendations:**

- Glycan Renew
- Total VR-X
- Total Alpha Lipoic Acid
- Selenium Chelate
- NAC Renew
- Total JT Plus
- Methyl Renew

# Viral Nutraceutical Support

Lynn Toohey, Ph.D

Some viruses, such as the current one we are all dealing with, are known to inhibit the induction of interferon and interferon signaling pathways (Interferons are immune-stimulating compounds that suppress viral attack.) The name interferon is derived from the interference it provides with respect to a virus's ability to infect or replicate. This permits the virus to attack the body while the appropriate immune responses are thwarted. Inappropriate immune responses can lead to an inflammatory "cytokine storm" that causes serious cell damage. My husband, Don Bellgrau, Professor of Immunology, authored a paper on the cytokine storm and interferon, recently accepted by the Scandinavian Journal of Immunology[1]. In dealing with a virus, instead of "boosting the immune system", it makes sense that one would want to target the specific arm of the immune system that is involved with viral activity, namely interferons.

OAS-1 is one of many interferon-inducible genes. Dr. Bellgrau explains OAS-1 as a gene that impairs the ability of viral RNA to replicate, however, gene variants may affect the activity of this gene. It is known that some people have genetic variants and may produce low OAS-1 protein and may face the scenario of poor anti-viral defense. There is a rich scientific literature that indicates this is one reason why some people are more susceptible to damage caused by certain viruses. (More



# The American Chiropractor Jan 2021 p. 16-22

PERSPECTIVE COVID

**"Only 25% of the virus-infected subjects in the NAC group developed symptoms, as contrasted to 79% of those in the placebo group."**

### Genetic Associations

Back to the genetic influences that were alluded to earlier: The A/G and G/G SNP genotypes of rs10774671 and rs2660 (from the previously mentioned OAS1 SNP) may be beneficial for activity of OAS1. Having at least one G allele is linked to higher activity, with G/A linked to intermediate activity, and A/A linked to lowest and possibly impaired activity.[4]

As a general disclaimer on DNA reporting, keep in mind that these DNA reports are based on association studies, which are correlative and are not necessarily causative. In addition, any one genetic variant will typically contribute only a portion to the overall health scenario, and non-genetic factors play a large role in the overall health scenario as well.

The discussion of SNPS (single nucleotide polymorphisms), or genetic variants, and genotypes (ie A/G, GG, etc) is beyond the scope of this article, however the NIH has a Genetic Home Reference Guide with much information that can be found in an internet search.

Again, it makes sense, nutritionally speaking, that we would want to support the immune system specifically with nutrition that is known for targeting interferon and interferon signaling pathways, especially since some may not effectively express their OAS1 gene. That would include support with all of the nutrients listed above for interferon support. Having said that, keep in mind that a genetic variant will typically contribute only a portion to the overall health scenario, and non-genetic factors play a large role in the overall health scenario as well. Therefore, having one or more of these genotypes does not necessarily describe a phenotype. Both 23andme and AncestryDNA provide this information in their raw data, which then can be analyzed after utilizing one of the several program options out there that crunch the raw data into an understandable report.

Dr. Lynn Toohey received her Ph.D. in nutrition (summa cum laude) from CO State University in Ft. Collins, CO. She has lectured to chiropractors, chiropractic associations, and other health professionals across the country and overseas on nutrition-related topics, and has published numerous articles in peer-reviewed journals.

DNA Analysis Report by Category

## Lynn Toohey

Dr. Lynn Toohey
1874 Ridgecrest Way
Highlands Ranch , CO 80129

## Patient

**Patient :** 1

**Date of Analysis:** January 1, 0001
**Gender:** Male
**Age:** 61
**Blood type:** Unknown

PDF Report

### Brain Chemistry

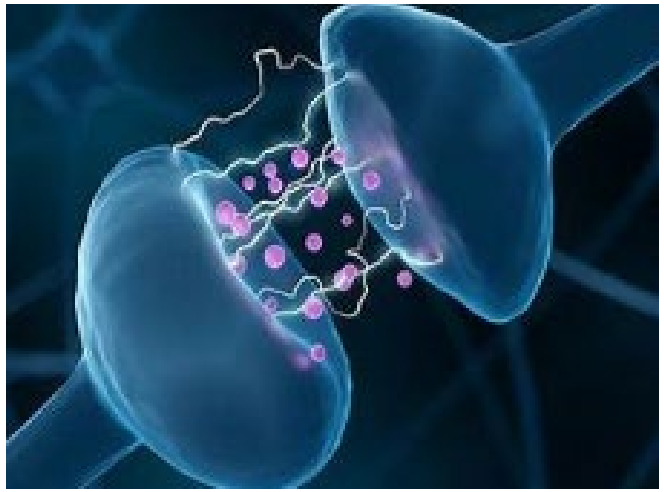
| | | | | | | |
|---|---|---|---|---|---|---|
| CHAT | rs3810950 | A | AG | +- | Brain Chemistry | Choline |
| CHAT | rs8178990 | T | CC | -- | Brain Chemistry | Choline |
| CHAT | rs1880676 | A | AG | +- | Brain Chemistry | Choline |
| CHAT | rs733722 | T | CC | -- | Brain Chemistry | Choline |
| CHAT | rs885834 | A | AA | ++ | Brain Chemistry | Choline |
| CNR1 | rs806368 | C | TT | -- | Brain Chemistry | |
| CNR1 | rs806366 | T | TC | +- | Brain Chemistry | |





| | | | | | |
|---|---|---|---|---|---|
| CNR1 | rs806369 | T | CC | -- | Brain Chemistry |
| CNR1 | rs1049353 | T | TC | +- | Brain Chemistry |
| CNR1 | rs806377 | C | TC | -+ | Brain Chemistry |

# Report by category – e.g. Brain Chemistry



# ChAT

**ChAT:** This enzyme catalyzes the reaction from Choline and acetyl CoA to acetylcholine. Genetic variants are associated with lower acetylcholine levels.

**Variants are associated with:**

- Exercise intolerance





- Muscle fatigue and cramping to muscle imbalance
- Neurological imbalances
- Memory imbalances
- Brain function imbalances

# ChAT (cont'd)

**Dietary and Lifestyle**

Foods high in B Vitamins (high quality meat) are recommended with genetic variants along with increased levels of minerals; including pumpkin seeds in the diet (they are high in zinc) may be helpful.

**Kinesiology Challenge**

Choline

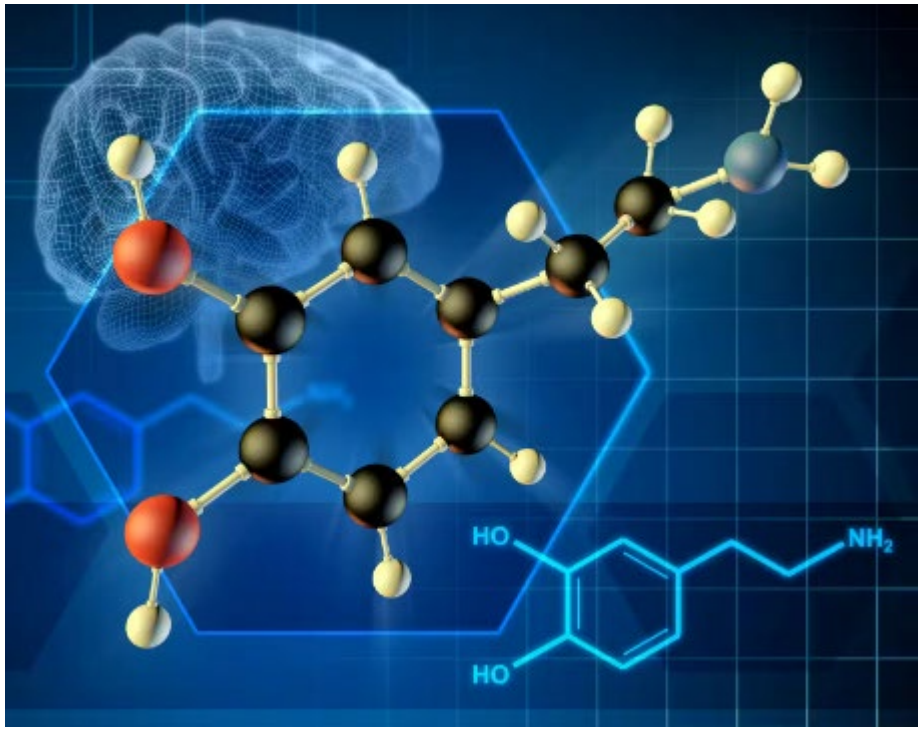
**Nutrients**

Choline
Phosphatidylcholine
Pantothenic acid
Zinc
Methyl B12
Methyl Folate

# Report by category – e.g. Brain Chemistry

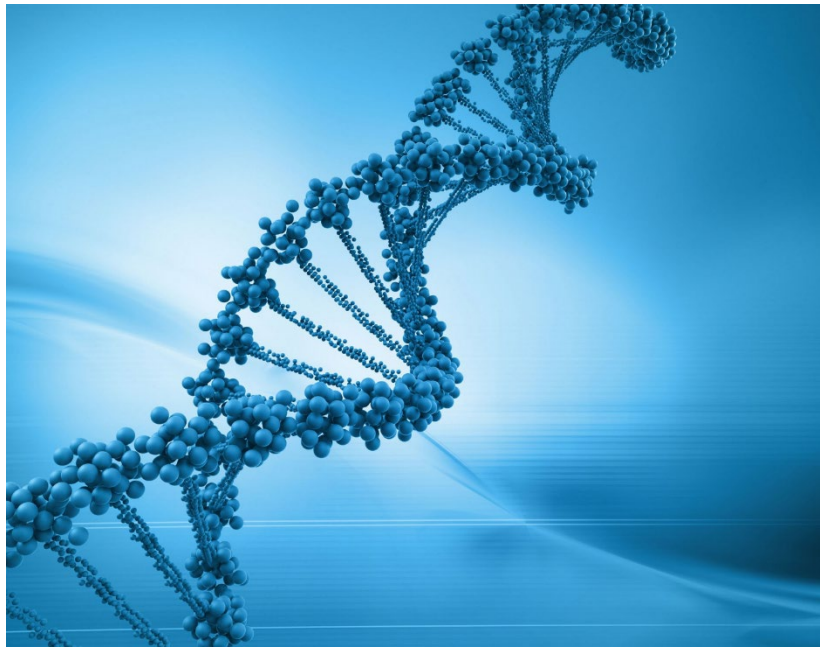
| | | | | | | |
|---|---|---|---|---|---|---|
| COMT | rs4680 | A | AA | ++ | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |
| COMT | rs6269 | G | AA | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |
| COMT | rs4633 | T | TT | ++ | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |
| COMT | rs737865 | G | AA | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |
| COMT | rs769224 | A | AG | +- | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |
| COMT | rs2239393 | G | AA | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |
| COMT | rs1544325 | A | AA | ++ | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |
| COMT | rs4646316 | T | TC | +- | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |
| COMT | rs174699 | C | TT | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |
| COMT | rs9332377 | T | CC | -- | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |
| COMT | rs165599 | A | AG | +- | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |
| COMT | rs5993883 | T | TT | ++ | Brain Chemistry | Adrenaline, Noradrenaline, Estrogens, Cortisol, Dopamine, Insulin |

# Report by category – e.g. Brain Chemistry (cont'd)




| | | | | | | |
|---|---|---|---|---|---|---|
| MAO-A | rs909525 | C | TT | -- | Brain Chemistry | Serotonin, Dopamine, Norepinephrine, Tryptophan, 5HTP |
| MAO-A | rs1137070 | C | CC | ++ | Brain Chemistry | Serotonin, Dopamine, Norepinephrine, Tryptophan, 5HTP |
| MAO-A | rs6323 | T | TT | ++ | Brain Chemistry | Serotonin, Dopamine, Norepinephrine, Tryptophan, 5HTP |
| PNMT | rs876493 | A | AA | ++ | Brain Chemistry | Noradrenalin (Norepinephrine) |

# Getting from DNA data collection to the consult



->

| SNIP | rsID | Risk Allele | Your Allele | Results | Category | Kinesiology Challenge |
|---|---|---|---|---|---|---|
| AANAT | rs11077820 | T | TT | ++ | Sleep | Serotonin |
| ACAT1 | rs3741049 | A | GG | -- | Cardiovascular/Energy | Pyruvate, Glucose, Acetyl Co A, Cholesterol, Lactic Acid, Ethanol, Insulin |
| ACE | rs4343 | G | AG | -- | Cardovascular | Angiotensin I |
| ADH1B | rs1229984 | A | CC | -- | Detox/Alcohol | Ethanol, Aldehyde, Formaldehyde |
| ADH1C | rs1693482 | T | CT | -- | Alcohol | Ethanol |
| ADIPOQ | rs17366568 | A | AG | ++ | Obesity/Appetite | Adiponectin |
| ALDH2 | rs16941667 | T | CC | -- | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs2238151 | T | CT | -- | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs441 | C | CT | ++ | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs4646778 | A | AC | ++ | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs4648328 | T | CT | -- | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs671 | A | GG | -- | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH2 | rs968529 | C | CC | ++ | Detox/Aldehydes | Ethanol, Aldehyde, Formaldehyde |
| ALDH3 | rs72547564 | A | GG | -- | Detox/Aldehydes | Aldehyde, Formaldehyde, Lipid Peroxide |
| ALDH3 | rs72547566 | T | CC | -- | Detox/Aldehydes | Aldehyde, Formaldehyde, Lipid Peroxide |
| ALDH3 | rs72547575 | G | AA | -- | Detox/Aldehydes | Aldehyde, Formaldehyde, Lipid Peroxide |
| APOA2 | rs5082 | C | AA | -- | Obesity/Appetite | Ghrelin |
| APOC1 | rs4420638 | G | AA | -- | Cardiovascular/Brain | Cholesterol |
| APOE | rs429358 | C | TT | -- | | Cholesterol |
| APOE | rs7412 | T | CC | -- | | Cholesterol |
| ARG1 | rs2781666 | T | GT | -- | Cardiovascular | Arginine, Ammonia |
| AVPR1A | rs10784339 | G | GG | ++ | Addictive Behavior | Vasopressin |
| AVPR1A | rs11174811 | G | CC | -- | Addictive Behavior | Vasopressin |
| BCMO1 | rs12934922 | T | AA | -- | Vitamin A absorption | Beta Carotene |
| BCMO1 | rs4889294 | C | TT | -- | Vitamin A absorption | Beta Carotene |
| BCMO1 | rs7501331 | T | CC | -- | Vitamin A absorption | Beta Carotene |
| BHMT | rs3733890 | A | GG | -- | Energy | Trimethylglycine , Glycine , Homocysteine |
| BHMT | rs567754 | T | CT | -- | Energy | Trimethylglycine , Glycine , Homocysteine |
| BHMT | rs651852 | T | CT | -- | Energy | Trimethylglycine , Glycine , Homocysteine |
| BHMT | rs6875201 | G | AA | -- | Energy | Trimethylglycine , Glycine , Homocysteine |

- **Step 1:** Get DNA results from a DNA testing company
- **Step 2:** Upload raw data file into **an analysis program** with a click
- **Step 3:** Utilize the analysis report by consulting with patient for their individualized needs and charge for the consult

**VDR:** (Vitamin D Receptor) Genetic variants in the VDR can interfere with the ability to absorb Vitamin D. Low vitamin D levels are implicated in many non-homeostatic scenarios. The immune system is dependent on adequate Vitamin D levels, therefore variants in the VDR genes can lead to low immune function. In addition, variants are implicated in scenarios where the immune system has lost tolerance.

- Low function of the VDR can lead to low levels of dopamine, serotonin and adrenal hormones. Low levels of these hormones and neurotransmitters can lead to fatigue, non-homeostatic memory function and depression. **Stress** is known to decrease expression of VDR, which is expressed in most tissues of the body. It also regulates intestinal transport of calcium, iron and other minerals. Low expression of the VDR is implicated in bone density issues.

## VDR variants are associated with:

- Low vitamin D Levels
- Loss of self-tolerance
- Bone density issues
- Teeth/jaw issues
- Low dopamine depression and apathy
- Free radical attack
- High blood calcium levels
- Cravings and addictive behavior
- Alopecia
- Proteinuria
- Esophagitis
- Keloids
- Distance sight
- Kidney stones
- Itchy skin

# DNA Report

And non-homeostatic function of:

- Blood sugar
- Spine health and alignment
- Joint health
- Immune health
- Heart health
- Intervertebral discs
- Arterial health
- Colon health
- Syringomyelia
- Prostate health
- Kidney health
- Lung health
- Bone health
- Blood sugar and eye health
- Blood sugar and kidney health
- Endothelium immune response
- Arterial pressure
- Weight balance

# VDR Receptor

**Diet and Nutritional Recommendations:**

- Getting sunlight is the best way to increase VDR activity.

**Kinesiology Challenge Vials:**

- T Cells
- Vitamin D
- Infections (Bacteria, virus etc.)
- Insulin
- L. Dopa
- Lactose
- Phenylalanine
- Tryptophan
- Tyrosine

**Nutrient Support Recommendations:**

- Vitamin K2
- Vitamin A
- Vitamin D
- Magnesium
- Boron
- Calcium
- Manganese

**Product Support Recommendations:**

- Suggestions here

# Eating (organically) for your genes (VDR SNP)

- **Vitamin K2:** Organic, dark leafy greens; many will also be high in calcium
- **Vitamin D**: Mushrooms
- **Vitamin A:** Beef, lamb, liver. Broccoli raab - 3-ounce (85g) serving provides 21% of the daily value. A 205-gram cup of cooked butternut squash offers 127% of the daily value. Cantaloupe melon - each 160-gram cup serving contains 30% of the daily value.

# **Minerals:** Calcium, magnesium, manganese and boron

- **<u>Calcium</u>** (non-dairy sources) found in ***kale*** – one steamed cup packs 177 mg of calcium, while one raw cup delivers 53 mg. ***Bok Choy*** - one cup of the raw plant contains 74 mg of calcium, while one cooked cup offers 158 mg. ***Broccoli*** – chopped raw 43mg, 86mg steamed. Also contains some vitamin A. ***Turnip greens*** one cup steamed supplies almost 200 mg of calcium. An ***orange*** contains 65 mg of calcium. A six-ounce serving of fresh ***salmon (please choose wild, not farmed)*** has about 340 milligrams of calcium. Canned has even more, but probably comes with BP fill in the blank bisphenols. Spinach has oxalic acid, not a good source. **Greens are good sources of Vitamin K2.**
- **Non-dairy alternatives contain a good amount of calcium**
  - (Taking a mineral supplement can be helpful. Only 5-600 mg at a time away from magnesium 2 x day. More at a time will decrease the absorption from food. Upper limit slide next)

# Calcium Upper limits

Table 3: Tolerable Upper Intake Levels (ULs) for Calcium [1]

| Age | Male | Female | Pregnant | Lactating |
|---|---|---|---|---|
| 0–6 months | 1,000 mg | 1,000 mg | | |
| 7–12 months | 1,500 mg | 1,500 mg | | |
| 1–8 years | 2,500 mg | 2,500 mg | | |
| 9–18 years | 3,000 mg | 3,000 mg | 3,000 mg | 3,000 mg |
| 19–50 years | 2,500 mg | 2,500 mg | 2,500 mg | 2,500 mg |
| 51+ years | 2,000 mg | 2,000 mg | | |

# Magnesium

- **Seeds**: Pumpkin (156 mg) or chia seeds (111 mg)
- **Nuts**: Almonds (80 mg) and cashews (74 mg)
- **Greens**: Spinach (78 mg)
- **Protein**: Peanut butter (49 mg) (peanuts are legumes; try almond butter)
- **Seafood**: Salmon (26 mg)
- **Dairy products**: Yogurt (42 mg) and milk (24–27 mg) – again, non-dairy will contain some magnesium
- **Fruits**: Avocados (22 mg) and bananas (32 mg)

# Manganese

- Green leafy veggies
- Oats
- Tea
- Pumpkin seeds
- Cloves and other spices
- Pecans, almonds, peanuts
- Raspberries, strawberries…


# Boron

- Most research shows health benefits from boron when it is consumed at doses of 3 mg/d or more

- A cup of cubed **avocado** will contain around 3.09 mg of boron
- ***Nuts*** - An ounce of almonds has 0.8 mg of boron
- Handful ***raisins*** – almost 1 mg
- ***Peaches, red grapes, dried fruit***
- ***Peas, beans legumes (lectins)***
- 5 fluid ounces of Shiraz Cabernet wine will deliver around 1.29 mg of boron*

- ***Note that this is not an excuse to have 3 glasses of wine to get the recommended amount of boron*** 🍷😜

**Follow up on genetic testing –** Genetic Analysis should always be followed up with other tests and modalities to confirm expression of genes.

## Examples:

- Blood labs
- Questionnaires
- Other lab testing (metals, toxicity, hormones, nutrients, mold/fungus, food allergy, neurotransmitters etc.)

# LabCorp Lab Summary

| Description | Result | Rating | Lab Ranges | Optimal | Units |
|---|---|---|---|---|---|
| Magnesium, RBC | 5.20 | Optimal | 4.2-6.8 | 5-7 | |
| Glucose, Serum | 78.00 | Optimal | 65-99 | 75-89 | mg/dl |
| Hemoglobin A1c | 5.40 | Optimal | 4.8-5.6 | 4.7-5.4 | Pct |
| Uric Acid, Serum | 3.80 | Optimal | 2.4-8.2 | 3.5-6 | mg/dl |
| BUN | 17.00 | Optimal | 5-26 | 12-19 | mg/dl |
| Creatinine, Serum | 0.68 | Low | 0.57-1 | 0.7-1.1 | mg/dl |
| eGFR | 95.00 | Optimal | 60-150 | 60-150 | mL/min/1.73m² |
| BUN / Creatinine Ratio | 25.00 | High | 6-25 | 12-18 | Calc |
| Sodium, Serum | 140.00 | | 135-145 | - | mEq/L |
| Potasssium, Serum | 3.80 | | 3.5-5.2 | - | mEq/L |
| Chloride, Serum | 101.00 | Optimal | 97-108 | 100-107 | mEq/L |
| Carbon Dioxide, Total | 27.00 | Optimal | 20-32 | 22-28 | mEq/L |
| Calcium, Serum | 9.60 | Optimal | 8.6-10.2 | 9.2-9.8 | mg/dl |
| Phosphorus, Serum | 3.20 | Optimal | 2.5-4.5 | 3.2-4 | mg/dl |
| Protein Total, Serum | 7.20 | Optimal | 6-8.5 | 6.9-7.5 | g/dl |
| Albumin, Serum | 4.90 | High | 3.6-4.8 | 4-4.7 | g/dl |
| Globulin, Total | 2.30 | Low | 1.5-4.5 | 2.5-3.2 | g/dl |
| A/G Ratio | 2.10 | High | 1.1-2.5 | 1.4-1.8 | Calc |
| Bilirubin, Total | 0.70 | Optimal | 0-1.2 | 0.4-1 | mg/dl |
| Bilirubin, Direct | 0.19 | High | 0.01-0.1 | - | mg/dl |
| Alkaline Phosphatase, Serum | 63.00 | Low | 25-165 | 80-120 | U/L |
| CK, Total | 46.00 | | 29-143 | - | U/L |
| LD, Serum | 135.00 | Optimal | 100-250 | 125-175 | U/L |
| AST (SGOT) | 21.00 | Optimal | 0-40 | 12-27 | U/L |
| ALT (SGPT) | 21.00 | Optimal | 0-40 | 12-27 | U/L |
| GGT | 11.00 | Optimal | 3-55 | 10-30 | U/L |
| Iron Binding Capacity (TIBC) | 332.00 | Optimal | 250-450 | 275-375 | µg/dl |
| UIBC | 221.00 | Optimal | 150-375 | 150-375 | µg/dl |
| Iron, Serum | 111.00 | Optimal | 35-155 | 60-135 | µg/dl |
| Iron Saturation | 33.00 | Optimal | 15-55 | 15-50 | Pct |
| Ferritin, Serum | 92.00 | Optimal | 13-150 | 15-130 | ng/ml |
| Vitamin D, 25 OH, Total | 29.20 | Low | 30-100 | - | ng/ml |

| | | | | | |
|---|---|---|---|---|---|
| Cholesterol, Total | 216.00 | High | 100-199 | 135-195 | mg/dl |
| Triglycerides | 70.00 | Optimal | 0-149 | 30-75 | mg/dl |
| HDL Cholesterol | 91.00 | Optimal | 39-200 | 60-200 | mg/dl |
| VLDL Cholesterol Calc | 14.00 | | 5-40 | - | Pct |
| LDL Cholesterol Calc | 111.00 | High | 0-99 | 0-90 | mg/dl |
| LDL/HDL Ratio | 1.20 | Optimal | 0-3.2 | 0-3 | number |
| C-Reactive Protein, Cardio | 0.20 | | 0-3 | - | mg/L |
| Homocysteine, Plasma | 9.10 | High | 0-15 | 4-7 | number |
| TSH | 3.30 | High | 0.45-4.5 | 1.5-2.9 | mIU/ml |
| Thyroxine (T4) | 9.00 | Optimal | 4.5-12 | 7.5-11 | µg/dl |
| T3 Uptake | 30.00 | Optimal | 24-39 | 27-33 | Pct |
| Free Thyroxine Index | 2.70 | High | 1.2-4.9 | 1-1.4 | µg/dl |
| T-3, Total | 114.00 | Low | 90-200 | 115-185 | ng/dl |
| Triiodothyronine, Free, Serum | 2.70 | | 2-4.4 | - | pg/ml |
| Reverse T3, Serum | 14.90 | | 13.5-34.2 | - | ng/dl |
| T4, Free (Direct) | 1.24 | | 0.82-1.77 | - | ng/dl |
| Thyroid Peroxidase (TPO) Ab | 10.00 | | 0-34 | - | ng/dl |
| Antithyroglobulin Antibodies | 19.00 | | 0-40 | - | ng/dl |
| Sex Hormone Binding Globulin, Serum | 188.80 | High | 18-114 | - | ng/dl |
| RA Latex Turbid. | 11.30 | | 0-13.9 | - | |
| Fibrinogen | 224.00 | | 175-425 | - | mg/dl |
| WBC | 3.30 | Low | 4-10.5 | 5.5-8.5 | $10^3$ c/mm$^3$ |
| RBC | 5.46 | High | 3.8-5.1 | 4.4-5.2 | 10e6 c/µl |
| Hemoglobin | 15.30 | High | 11.5-15 | 13-14.5 | g/dl |
| Hematocrit | 45.60 | High | 34-44 | 37-45 | Pct |
| MCV | 84.00 | Optimal | 80-98 | 83-91 | µm$^3$ |
| MCH | 28.00 | Optimal | 27-34 | 28-31 | pg/cell |
| MCHC | 33.60 | Optimal | 32-35 | 32.5-35 | pg/cell |
| RDW | 15.30 | High | 11.7-15 | 11-13 | Pct |
| Platelets | 215.00 | Optimal | 140-415 | 165-340 | $10^3$ c/mm$^3$ |
| Neutrophils | 35.00 | Low | 40-74 | 45-65 | Pct |
| Lymphs | 55.00 | High | 14-46 | 25-35 | Pct |
| Monocytes | 7.00 | Optimal | 4-13 | 3-7 | Pct |
| Eos | 3.00 | Optimal | 0-7 | 1-3 | Pct |
| Basos | 0.00 | Optimal | 0-3 | 0-1 | Pct |
| Neutrophils (Absolute) | 1.20 | High | 0.002-0.008 | 0.002-0.006 | cells/µl |
| Lymphocytes (Absolute) | 1.80 | High | 0.001-0.005 | 0.002-0.003 | cells/µl |
| Monocyte (Absolute) | 0.20 | High | 0-0.001 | 0-0.001 | cells/µl |
| Eos (Absolute) | 0.10 | High | 0-0 | 0-0 | cells/µl |
| Baso (Absolute) | 0.00 | Low | 0-0 | 0-0 | cells/µl |
| Immature Granulocytes % | 0.00 | | 0-2 | - | Pct |
| Immature Granulocytes (Abs) | 0.00 | | 0-0 | - | cells/µl |
| ESR | 2.00 | Low | 0-45 | 4-14 | mm/hr |

# An example of lab values that do not reflect genetic SNPS – remember epigenetics!

- **24 yr old female homozygous for MTRR tests negative for increased Hcys or SAM**

MTRR / A66G | +/+ | G

*Methylation Profile; plasma*

DOCTOR'S DATA INC.

| PRIMARY & INTERMEDIATE METABOLITES | RESULT/UNIT | | REFERENCE INTERVAL | PERCENTILE 2.5th 16th 50th 84th 97.5th |
|---|---|---|---|---|
| Methionine | **2.8** | µmol/dL | 1.6- 3.6 | |
| Cysteine | **25** | µmol/dL | 20- 38 | |
| S-adenosylmethionine (SAM) | **88** | nmol/L | 86- 145 | |
| S-adenosylhomocysteine (SAH) | **12.4** | nmol/L | 10- 22 | |
| | | | | 68th 95th |
| Homocysteine | **5.9** | µmol/L | < 11 | |
| Cystathionine | **0.01** | µmol/dL | < 0.05 | |

| METHYLATION INDEX | RESULT | REFERENCE INTERVAL | PERCENTILE 68th 95th |
|---|---|---|---|
| SAM : SAH | **7.1** | > 4 | |

- **Another 51 yr old female tested homozygous for MTHFR with no abnormality in Hcys or Sam-e**

| | | | |
|---|---|---|---|
| MTHFR / C677T | | +/+ | T |
| MTHFR / A1298C | -/- | | A |
| MTHFR / 3 | -/- | | C |
| MTR / A2756G | -/- | | A |
| MTRR / A66G | | +/- | Hetero |
| MTRR / H595Y | -/- | | C |
| MTRR / K350A | -/- | | A |
| MTRR / R415T | -/- | | C |
| MTRR / S257T | -/- | | T |
| MTRR / 11 | | +/- | Hetero |
| BHMT / 1 | | +/- | Hetero |
| BHMT / 2 | -/- | | C |
| BHMT / 4 | -/- | | A |
| BHMT / 8 | -/- | | C |
| CBS / C699T | -/- | | C |
| CBS / A360A | | +/- | Hetero |
| CBS / N212N | -/- | | C |
| COMT / V158M | | +/+ | A |
| COMT / H62H | | +/+ | T |
| COMT / 61 | -/- | | G |
| SUOX / S370S | -/- | | C |
| VDR / Taq1 | | +/+ | T |
| VDR / Fok1 | -/- | | C |
| MAO A / R297R | | +/+ | T |
| NOS / D298E | | +/- | Hetero |
| ACAT / 1-02 | -/- | | G |

"+/-" indicates there is one mutation

"+/+" indicates there is a double mutation

# **References and contacts** for programs, labs, tests & lab co-ops mentioned in this lecture:

- Professional Co-Op (free service to chiropractors; discounts lab tests): www.professionalco-op.com

- Doctor's Data (various metabolic/toxicity/nutritional tests): www.doctorsdata.com

- (Genetic/epigenetic test reports; blood lab reports; questionnaires: www.FHEcloud.com or the DNA testing program of your choice

# Doctor's Data

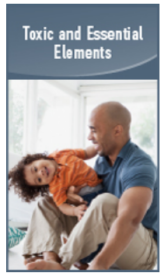
www.doctorsdata.com

- **GI, stool testing, toxic metals, nutrient status, detoxification, environmental exposure, cardiometabolic risk, allergy, immunology, methylation, endocrinology, methylation…**

***Choose any category below/right/above for a detailed overview of the biomarkers included in each profile, as well as collection instructions, CPT codes and more.***

You can also review sample reports to see how Doctor's Data presents results in clear, easy-to-understand formats that detail target ranges and graphically illustrate areas of concern. In addition, tests include result-specific commentary to aid in interpreting the results and determining next steps.

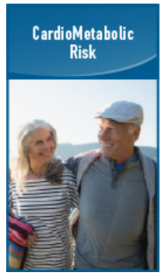

*Identification of about 1,000 bacterial, yeast and parasitic species, including cultures from stool samples and vaginal swabs- dysbiotic bacterial and yeast sensitivities provided*



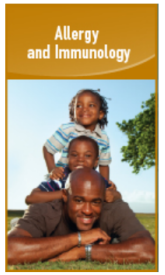

*Hair, urine, fecal and blood tests for comprehensive analysis of element levels*


*Analysis of amino acids, fatty acids, vitamin D, iodine and antagonistic halides provide insight into a vast array of symptoms and sustained conditions*


*Measures of hepatic function, oxidative stress, porphyrins and other markers*




*Complete profiles and oxidized LDL analysis for early identification of risk*




*Serology testing for Celiac disease, non-celiac gluten sensitivity (gliadin) and wheat allergy*


*Easy, minimally invasive collection for testing for Celiac disease and gluten and gliadin sensitivities, vitamin D status and DNA Methylation SNPs*


*Analysis of blood or urine hormones, neuro-biogenic amines and peptides that may affect health, metabolism, mood or behavior.*

| Category | Test | | Result | Units | Normal Range |
|---|---|---|---|---|---|
| **Creatinine (Urine)** | | | | | |
| | Creatinine A (Waking) | Within range | 0.63 | mg/ml | 0.3 - 3 |
| | Creatinine B (Morning) | Within range | 0.72 | mg/ml | 0.3 - 3 |
| | Creatinine C (Afternoon) | Within range | 0.41 | mg/ml | 0.3 - 3 |
| | Creatinine D (Night) | Within range | 0.35 | mg/ml | 0.3 - 3 |
| **Daily Free Cortisol and Cortisone (Urine)** | | | | | |
| | Cortisol A (Waking) | Within range | 43.8 | ng/mg | 18 - 80 |
| | Cortisol B (Morning) | Low end of range | 75.2 | ng/mg | 50 - 200 |
| | Cortisol C (Afternoon) | Above range | 73.6 | ng/mg | 13 - 55 |
| | Cortisol D (Night) | Within range | 14.5 | ng/mg | 0 - 25 |
| | Cortisone A (Waking) | Low end of range | 64.4 | ng/mg | 50 - 140 |
| | Cortisone B (Morning) | Low end of range | 101.7 | ng/mg | 100 - 240 |
| | Cortisone C (Afternoon) | Within range | 90.8 | ng/mg | 40 - 115 |
| | Cortisone D (Night) | Within range | 32.0 | ng/mg | 0 - 70 |
| | 24hr Free Cortisol | Within range | 207.1 | ng/mg | 100 - 310 |
| | 24hr Free Cortisone | Low end of range | 288.9 | ng/mg | 250 - 500 |
| **Cortisol Metabolites and DHEA-S (Urine)** | | | | | |
| | b-Tetrahydrocortisol (b-THF) | Above range | 4440.0 | ng/mg | 1750 - 4000 |
| | a-Tetrahydrocortisol (a-THF) | Within range | 389.0 | ng/mg | 175 - 700 |
| | b-Tetrahydrocortisone (b-THE) | Within range | 3165.0 | ng/mg | 2350 - 5800 |
| | Metabolized Cortisol (THF+THE) | Within range | 7994.0 | ng/mg | 4550 - 10000 |
| | DHEA-S | Low end of range | 122.0 | ng/mg | 30 - 1500 |

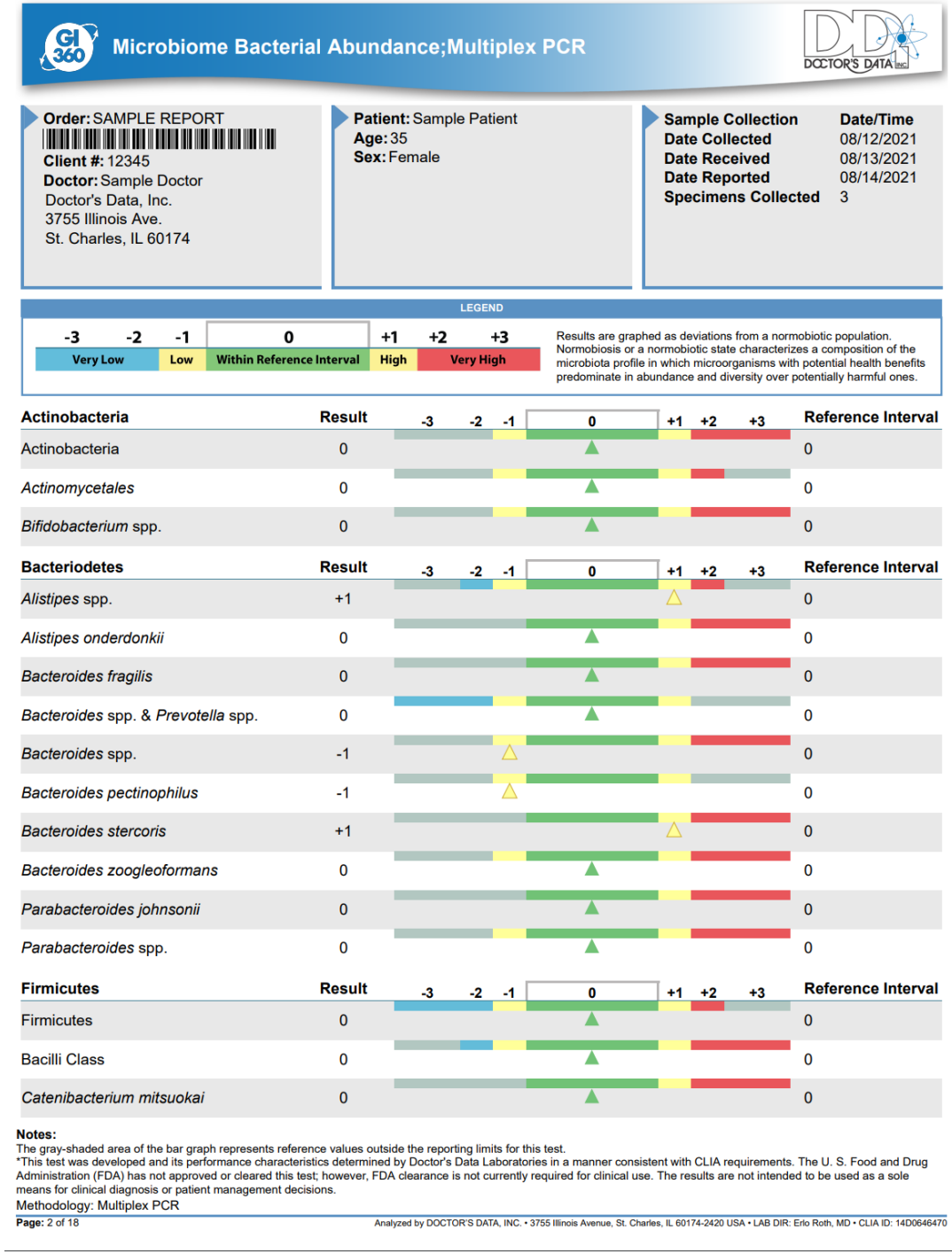
| Category | Test | | Result | Units | Normal Range |
|---|---|---|---|---|---|
| **Progesterone Metabolites (Urine)** | | | | | |
| | b-Pregnanediol | Low end of range | 105.0 | ng/mg | 75 - 400 |
| | a-Pregnanediol | Below range | 11.0 | ng/mg | 20 - 130 |
| **Estrogens and Metabolites (Urine)** | | | | | |
| | Estrone(E1) | Within range | 7.3 | ng/mg | 4 - 16 |
| | Estradiol(E2) | Low end of range | 0.67 | ng/mg | 0.5 - 2.2 |
| | Estriol(E3) | Within range | 3.6 | ng/mg | 2 - 8 |
| | 2-OH-E1 | Within range | 1.56 | ng/mg | 0 - 5.9 |
| | 4-OH-E1 | Within range | 0.31 | ng/mg | 0 - 0.8 |
| | 16-OH-E1 | Within range | 0.85 | ng/mg | 0 - 1.2 |
| | 2-Methoxy-E1 | Within range | 0.68 | ng/mg | 0 - 2.8 |
| | 2-OH-E2 | Within range | 0.13 | ng/mg | 0 - 0.6 |
| | 4-OH-E2 | Low end of range | 0.0 | ng/mg | 0 - 0.3 |
| | 2-Methoxy-E2 | Within range | 0.2 | ng/mg | 0 - 0.8 |
| **Androgens and Metabolites (Urine)** | | | | | |
| | DHEA-S | Low end of range | 122.0 | ng/mg | 30 - 1500 |
| | Androsterone | Low end of range | 896.0 | ng/mg | 500 - 3000 |
| | Etiocholanolone | Within range | 1027.0 | ng/mg | 400 - 1500 |
| | Testosterone | Within range | 53.7 | ng/mg | 25 - 115 |
| | 5a-DHT | Within range | 17.0 | ng/mg | 5 - 25 |
| | 5a-Androstanediol | Low end of range | 46.9 | ng/mg | 30 - 250 |
| | 5b-Androstanediol | Within range | 132.6 | ng/mg | 40 - 250 |
| | Epi-Testosterone | Low end of range | 31.9 | ng/mg | 25 - 115 |

- **Patients's urine hormone profile**

- **More comprehensive testing would offer more insight**

| Neurotransmitter Metabolites | | | | |
|---|---|---|---|---|
| Dopamine Metabolite - (Urine) | | | | |
| Homovanillate (HVA) | Within range | 10.6 | ug/mg | 4.8 - 19 |
| Norepinephrine/Epinephrine Metabolite - (Urine) | | | | |
| Vanilmandelate (VMA) | High end of range | 7.7 | ug/mg | 2.8 - 8 |
| Serotonin Metabolite - (Urine) | | | | |
| 5-Hydroxyindoleacetate (5HIAA) | Within range | 5.7 | ug/mg | 3 - 10 |
| | | | | |
| Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine) | | | | |
| Melatonin* (Waking) | Low end of range | 12.9 | ng/mg | 10 - 85 |
| Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine) | | | | |
| 8-OHdG (Waking) | Within range | 2.3 | ng/mg | 0 - 8.8 |

# Doctor’s Data Microbiome testing



## Microbiome Bacterial Abundance;Multiplex PCR

**Order:** SAMPLE REPORT
**Client #:** 12345
**Doctor:** Sample Doctor
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174

**Patient:** Sample Patient
**Age:** 35
**Sex:** Female

| Sample Collection | Date/Time |
|---|---|
| Date Collected | 08/12/2021 |
| Date Received | 08/13/2021 |
| Date Reported | 08/14/2021 |
| Specimens Collected | 3 |

LEGEND

| -3 | -2 | -1 | 0 | +1 | +2 | +3 |
|---|---|---|---|---|---|---|
| Very Low | | Low | Within Reference Interval | High | Very High | |

Results are graphed as deviations from a normobiotic population. Normobiosis or a normobiotic state characterizes a composition of the microbiota profile in which microorganisms with potential health benefits predominate in abundance and diversity over potentially harmful ones.

| Actinobacteria | Result | Reference Interval |
|---|---|---|
| Actinobacteria | 0 | 0 |
| *Actinomycetales* | 0 | 0 |
| *Bifidobacterium* spp. | 0 | 0 |

| Bacteriodetes | Result | Reference Interval |
|---|---|---|
| *Alistipes* spp. | +1 | 0 |
| *Alistipes onderdonkii* | 0 | 0 |
| *Bacteroides fragilis* | 0 | 0 |
| *Bacteroides* spp. & *Prevotella* spp. | 0 | 0 |
| *Bacteroides* spp. | -1 | 0 |
| *Bacteroides pectinophilus* | -1 | 0 |
| *Bacteroides stercoris* | +1 | 0 |
| *Bacteroides zoogleoformans* | 0 | 0 |
| *Parabacteroides johnsonii* | 0 | 0 |
| *Parabacteroides* spp. | 0 | 0 |

| Firmicutes | Result | Reference Interval |
|---|---|---|
| Firmicutes | 0 | 0 |
| Bacilli Class | 0 | 0 |
| *Catenibacterium mitsuokai* | 0 | 0 |

**Notes:**
The gray-shaded area of the bar graph represents reference values outside the reporting limits for this test.
*This test was developed and its performance characteristics determined by Doctor's Data Laboratories in a manner consistent with CLIA requirements. The U. S. Food and Drug Administration (FDA) has not approved or cleared this test; however, FDA clearance is not currently required for clinical use. The results are not intended to be used as a sole means for clinical diagnosis or patient management decisions.
Methodology: Multiplex PCR


Analyzed by DOCTOR'S DATA, INC. • 3755 Illinois Avenue, St. Charles, IL 60174-2420 USA • LAB DIR: Erlo Roth, MD • CLIA ID: 14D0646470

# Professional Co-Op

- **FREE** discounts.  The discount service is free:  no sign up, no annual fee.

- Their new website makes ordering easy and efficient.

- It's easy to order a panel.  **Professional Co-Op** offers Dr. Brandon Lundell's Standard panel and Deluxe panel. A comprehensive panel retailing for over 2,000 is 265.00 through Professional Co-Op.  They have already negotiated steep discounts for professionals such as yourself

- Excellent customer service and support; **Professional Co-Op** guides you through the lab ordering process so that you are comfortable with it.

- **Disclaimer:**  I have no monetary affiliation with Professional Co-Op or Doctor's Data.  I recommend them strictly because I like working with them because of the tests they offer.

# Professional Co-Op

Professional Co-op Services, Inc.
2700 N. 29th Ave, Suite 106
Hollywood, FL 33020
P: 866.999.4041 F: 866.999.9175
www.ProfessionalCo-op.com

- It doesn't matter if you already have a **LabCorp** account, you can still join **Professional Co-Op**

- www.professionalco-op.com or call 866-999-4041 –

# Eg. Of discount lab pricing for the Deluxe Lundell Panel

- **<u>LabCorp Retail Price:</u>**
- $2,324.00

- **<u>PCS Member Price:</u>**
- $265.00 plus the C**omplete UA (which includes microscopic) for $10. Draw fee = 7.00. Total price 282.00 with draw fee**

# Components of the Comprehensive Blood Test:

- Glucose, Serum
- Hemoglobin A1c
- Uric Acid, Serum
- BUN
- Creatinine, Serum
- Estimated GFR
- BUN/Creatinine Ratio
- Sodium, Serum
- Potassium, Serum
- Chloride, Serum
- Carbon Dioxide, Total
- Calcium, Serum
- Phosphorus, Serum
- Magnesium, RBC
- Protein, Total, Serum
- Albumin, Serum
- Globulin, Total
- A/G Ratio
- Bilirubin, Total
- Bilirubin, Direct
- Alkaline Phosphatase, S
- Creatine Kinase,Total,Serum
- LDH
- AST (SGOT)
- ALT (SGPT)
- GGT
- Iron Bind.Cap.(TIBC)
- UIBC
- Iron, Serum
- Iron Saturation

Ferritin, Serum
Vitamin D, 25-Hydroxy
Cholesterol, Total
Triglycerides
HDL Cholesterol
VLDL Cholesterol Cal
LDL Cholesterol Calc
LDL/HDL Ratio
C-Reactive Protein, Cardiac
Homocyst(e)ine, Plasma
TSH
Thyroxine (T4)
T3 Uptake
Free Thyroxine Index
Triiodothyronine (T3)
Triiodothyronine,Free,Serum
Reverse T3, Serum
T4,Free(Direct)
Sex Horm Binding Glob, Serum
Thyroid Peroxidase (TPO) Ab
Antithyroglobulin Ab
Antinuclear Antibodies, IFA
RA Latex Turbid.
Fibrinogen Activity
CBC, Platelet Count, and Differential:
WBC
RBC
Hemoglobin
Hematocrit
MCV
MCH
MCHC
RDW
Platelets

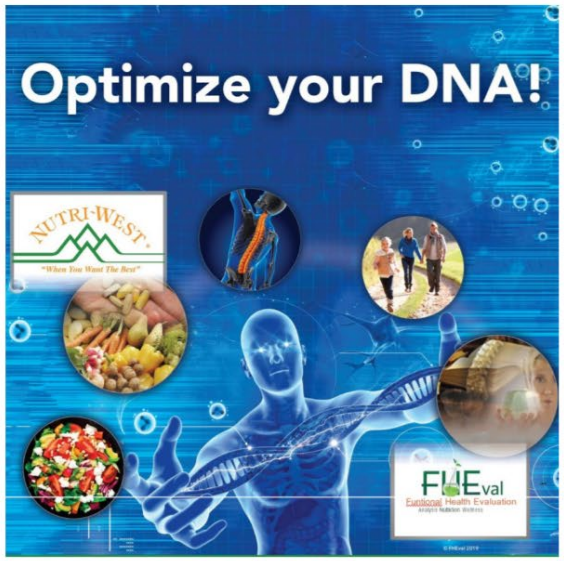
Neutrophils
Lymphs
Monocytes
Eos
Basos
Immature Cells
Neutrophils (Absolute)
Lymphs (Absolute)
Monocytes(Absolute)
Eos (Absolute)
Baso (Absolute)
Immature Granulocytes
Immature Grans (Abs)
NRBC
Hematology Comments:

Urinalysis Gross Exam
Specific Gravity
pH
Urine-Color
Appearance
WBC Esterase
Protein
Glucose
Glucose Reflex
Ketones
Occult Blood
Bilirubin
Urobilinogen,Semi-Qn
Nitrite, Urine
Microscopic Examination
Sedimentation Rate (ESR)

# If you are interested in testing out a DNA analysis program for three FREE months:

- Sign up through website www.FHEcloud.com
- No obligation
- Satisfaction Guaranteed
- 39.00 a month after the **trial period for ALL MAC attendees**

- Also does Blood lab analysis & Questionnaires




**Test your DNA**

**FHEval Analyzes Raw Data**

**Comprehensive Report:**

- **Gene description/fxn**
- **Dietary rec.**
- **Lifestyle rec.**
- **Nutrient rec.**
- **Product support**

**Completely new site www.FHEcloud.com with added info/improved functions, including:**

- **New page display, easy to read results**
- **Each gene links to a reference guide**
- **Links to scientific references**
- **New! Added Viral Support/Immune SNPS**
- **User friendly, even unzips raw data files!**
- **Only $39.00/month, no contracts or sign up fees**

**866-271-8888 - Dr. Lynn Toohey**

**Current users call or email for your temporary password!**

# Conclusion:

- Recognize the genetic contribution to health by **testing DNA raw data**
- Analyze the data through one of the many programs available to **get a report**
- Support healthy aging & bones (and general health) by **utilizing the epigenetic information in the report to modify diet, lifestyle & supplements for the best outcomes.**

# Thank you!

- **MAC for bringing me in as a speaker**
- **Nutri-West for their sponsorship**