Precision Longevity: Personalizing Nutrition and Supplementation through DNA Testing:

Presented by Dr. Lynn Toohey, PhD Nutrition

drtooheynutriwest@gmailcom

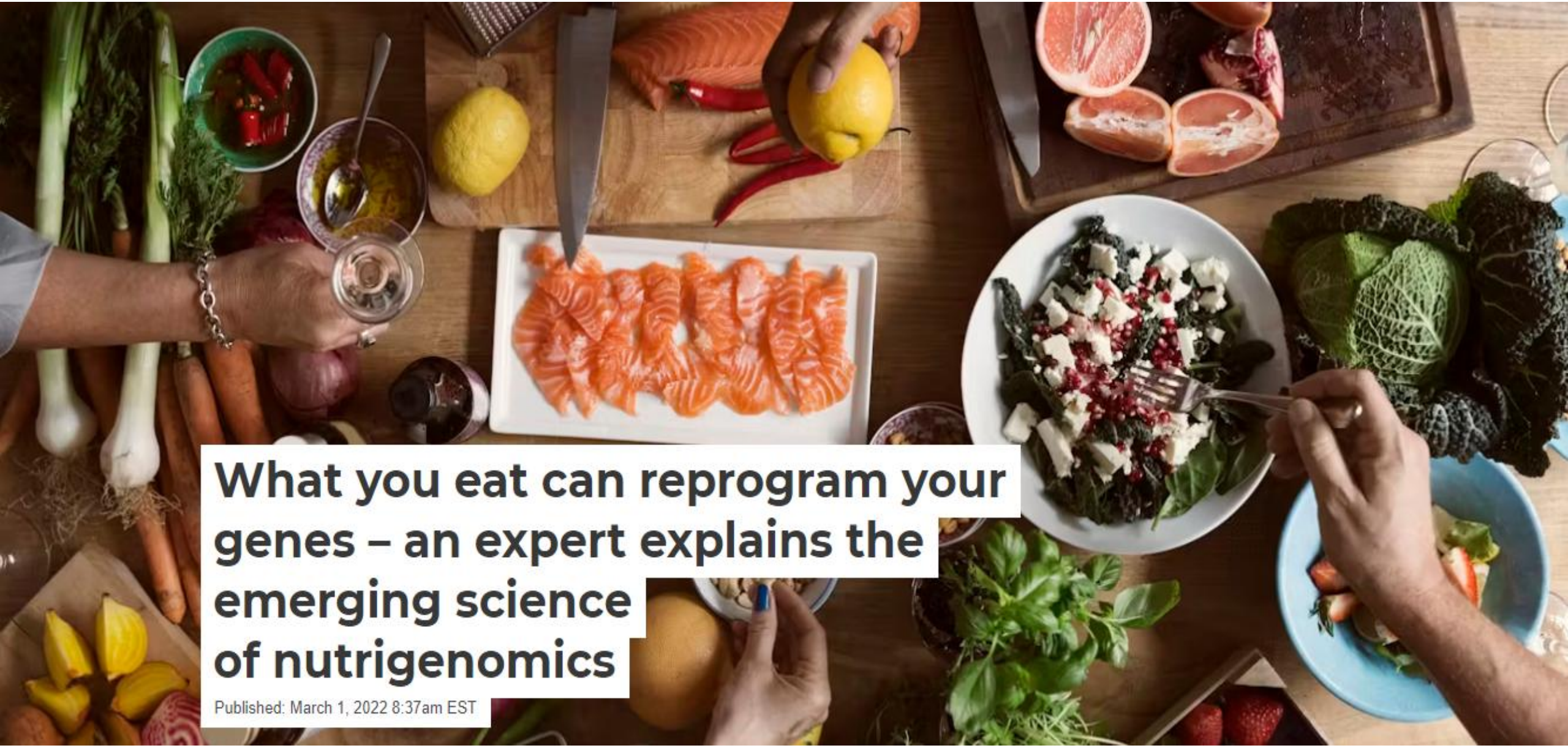
Cellular Senescence

“Exploring protocols for improved longevity and quality of life.”

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



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

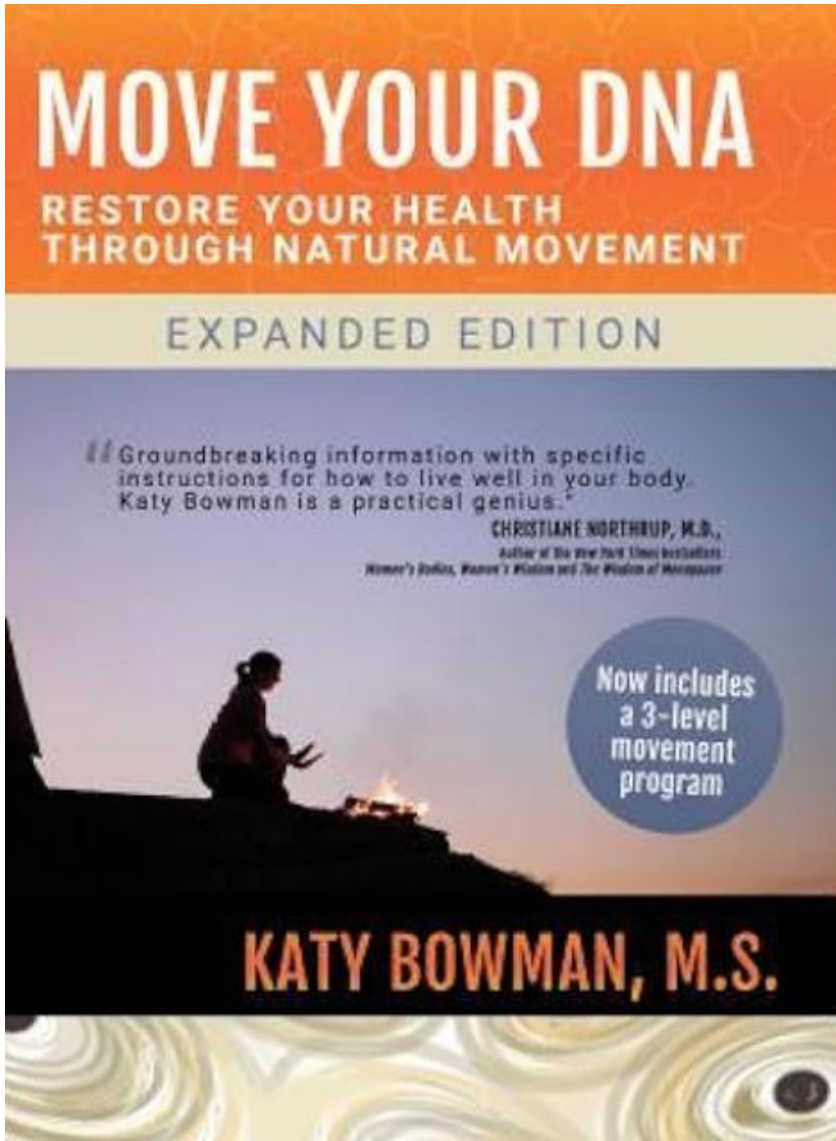
Published: March 1, 2022 8:37am EST

Food also "talks" to our genome -

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

Move your DNA – DNA can Reflect Movement Ability

- DNA can either allow or impede movement; knowing your genetic variants allows personalization
- Outcomes depend on epigenetic manipulation
- Analyze your raw DNA data and get a comprehensive report from www.FHEcloud.com – email if interested!
- drtooheynutriwest@gmail.com; 720-470-1934



Eg. Senescent cells impede mobility and quality of life; some SNPs are protective

Hamann *et al. Immunity & Ageing* (2020) 17:7
https://doi.org/10.1186/s12979-020-00176-y

Immunity & Ageing

SHORT REPORT Open Access

First evidence for STING SNP R293Q being protective regarding obesity-associated cardiovascular disease in age-advanced subjects – a cohort study

Lutz Hamann[1*], Malgorzata Szwed[2], Malgorzata Mossakowska[3], Jerzy Chudek[4] and Monika Puzianowska-Kuznicka[2,5]

rs7380824

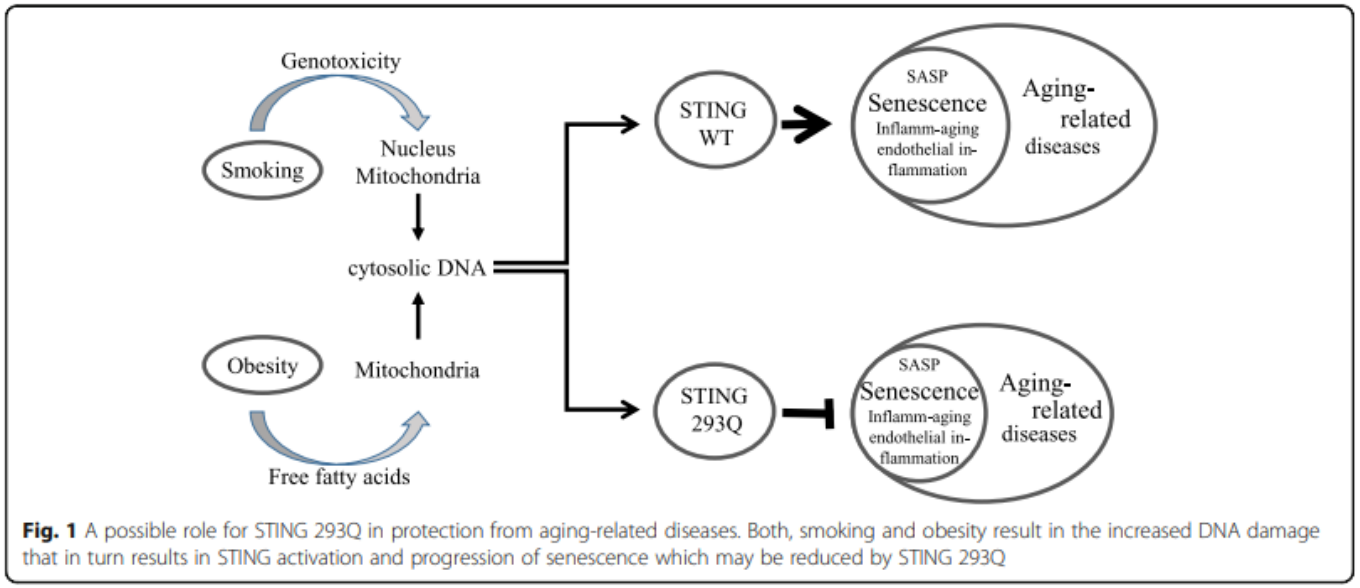


Fig. 1 A possible role for STING 293Q in protection from aging-related diseases. Both, smoking and obesity result in the increased DNA damage that in turn results in STING activation and progression of senescence which may be reduced by STING 293Q

Sting SNPs are protective

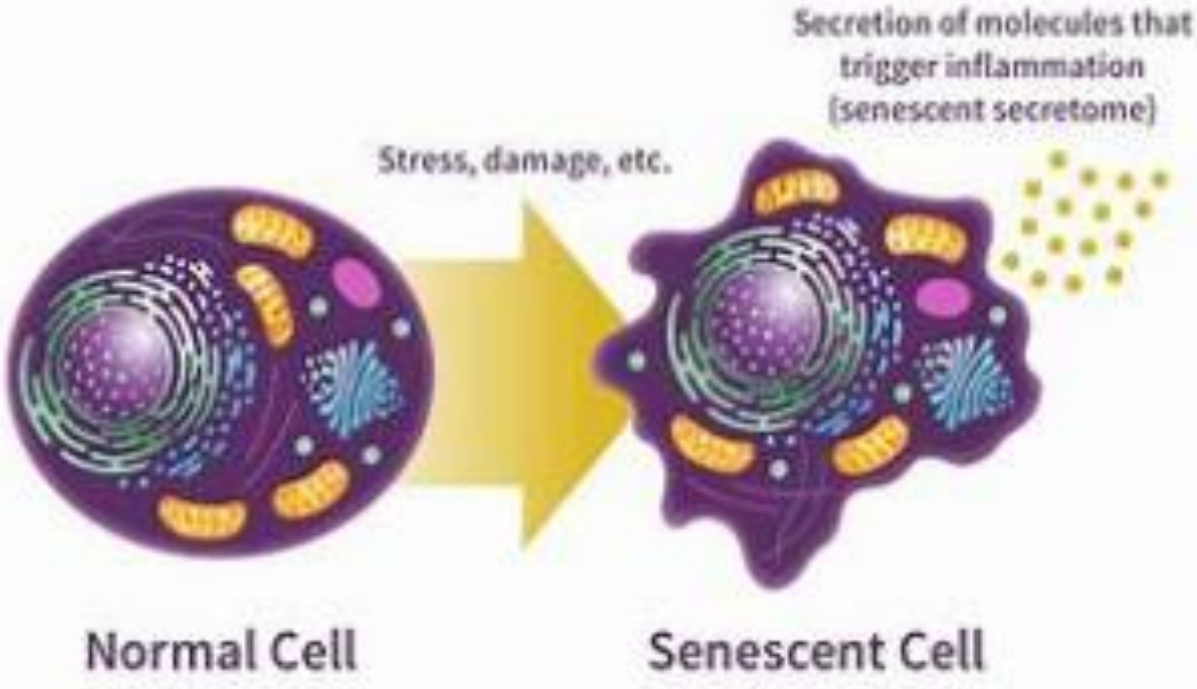
- "The STING (TMEM173) R293Q refers to variant where arginine (R) is replaced by glutamine (Q). This causes a protein change in the STING protein. The gene is closely tied to senescent cell biology because STING senses DNA fragments in the body that activate STING, which induces interferon, NF-κB and other inflammatory cytokines such as IL-6 and TNF-α. Activated STING keep senescent cells inflammatory rather than silent.
- A homozygous variant at R293Q (rs7380824) creates a loss-of-function of the STING protein which can impact inflammatory expression. Benefits of the variant can be lower risk of chronic inflammatory signaling and lower risk of autoimmunity, neuroinflammation, and reduced endothelial inflammation.
- In short, **STING drives the inflammatory output of senescent cells."**

Diet and Lifestyle for the STING SNP

- Lifestyle factors that influence senescent cells.
- A diet full of antioxidant foods can reduce DNA damage, which triggers senescence.
- Smoking increases senescence, so absence of tobacco is recommended.
- Chiropractic, through increased circulation and lymphatic transport, along with effects on stress reduction, decreased inflammation and decreased cytokine production, optimizes the environment to more easily clear senescent cells.
- Movement, exercise, caloric restriction, toxin removal, and hyperbaric oxygen are all environmental protocols that are utilized to reduce formation of, and improve removal of, senescent cells.
- The short list of nutrients and products are N-acetyl cysteine, Quercetin Quercetin-S, Resveratrol, curcumin and sulforaphane.

Definition:

- **What is cellular senescence, and why is it so important to clear senescent cells from the body to optimize health?**

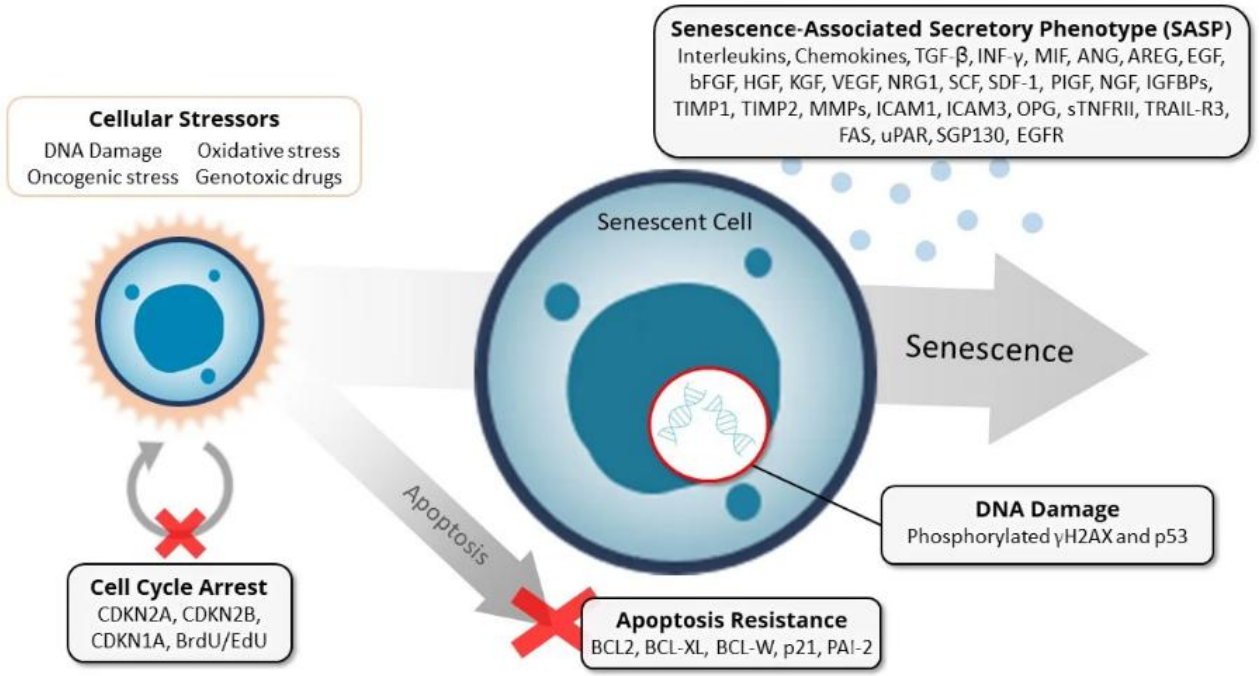


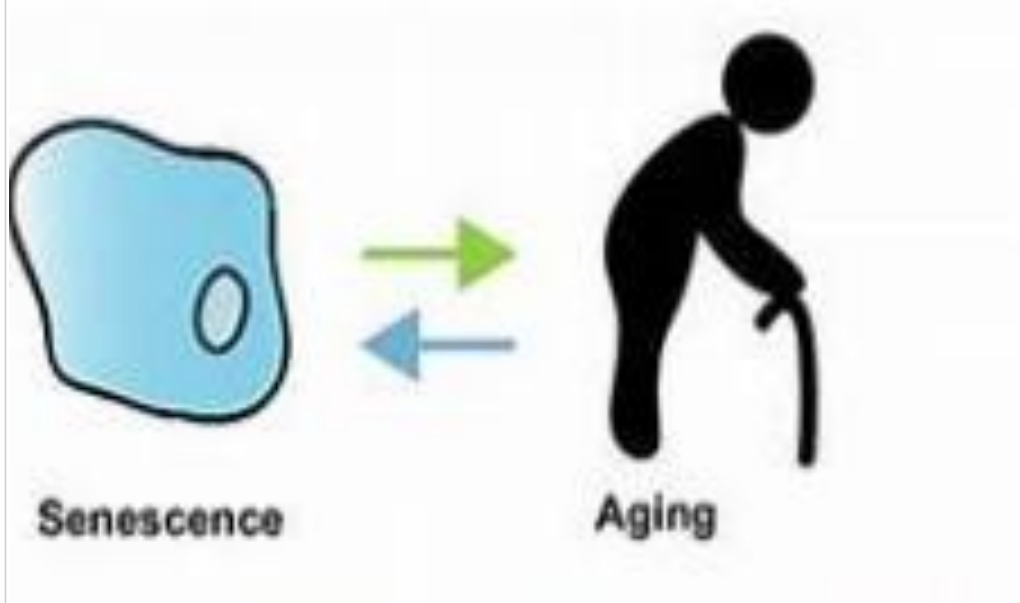
- Cellular senescence is a phenomenon characterized by the cessation of cell division.

- Age decreases the ability to clear these cells; since they don't die, and can't be cleared efficiently, they accumulate.

- This accumulation causes a hypersecretory state and release of harmful chemicals collectively known as SASP (senescence-associated secretory phenotype).

Senescent cells secrete inflammatory chemicals that promote aging and ill-health





SASP: Senescence-associated secretory phenotype:

May 2025 American Chiropractor article: Cellular Senescence – Why we need to pay attention *by Dr. Lynn Toohey*

Pro-inflammatory secretions:

Cytokines
Chemokines
Growth factors
Proteases
Lipids
Extracellular matrix components

Toxins increase senescence

- Please email: drtooheynutriwest@gmail.com

for the 2 hr. video presented to the Oregon Chiropractic Association in 2025

For further info on Senescent Cells and protocols to clear them

How Toxins Are Aging Us

By Lynn Toohey, PhD

Intuitively, we know that toxins can't be good for optimal functioning of our cells, but how exactly do they contribute to aging?

In May 2025, *The American Chiropractor* published my article titled "Cellular Senescence: Why we need to pay attention." Senescent cells lose the ability to divide, but they continue to accumulate and release what's known as SASP — senescence-associated secretory phenotype — and their inflammatory cytokine production is a hallmark of aging.

Toxins are known to add to the accumulation of senescent cells. Toxins infiltrate our bodies and disrupt the delicate balance of all cellular functions, resulting in a downward spiral of inflammation, oxidation, tissue/DNA damage, impaired detox and enzymatic reactions, and cellular dysfunction.[1]

Unfortunately, the SASP secretions that ooze from senescent cells only increase toxicity. So, what can we do about this toxic load? Reducing exposure is one way, and detoxing the body of these toxins is another.

Reducing exposure: To reduce toxic exposure, we have to be aware of what is entering our bodies so that we can eliminate or mitigate the exposure. There are many toxic exposures, but two that are worth mentioning here to increase awareness are a toxin that some believe is because of the major exposure we endure — air pollution[2] — and another is one of the most insidious that has come to light in recent years — microplastics.[3]

Air pollution (specifically traffic exhaust):

Air pollution is an established health concern and one of the principal causes of premature mortality globally, with vehicle traffic as a leading contributor. Being inside our cars does not protect us from traffic pollution; in fact, many agree that surprisingly large effects result from breathing fumes inside the car.

According to the World Health Organization, short- and long-term exposure to air pollution has been linked to a wide range of health problems, including cardiovascular, lung issues, weight problems, etc.

Microplastics and nanoplastics (MNPs):

The World Wildlife Foundation conducted research that concluded that the average human consumption of plastic in one week is equivalent to eating a credit card. Another group, known as the Environmental Working Group, estimates that one person consumes 12 plastic shopping bags a year.

Regardless of the estimates, one thing is clear — plastic is finding its way into our bodies, organs, arteries, and brains. Obvious sources are plastic bags, cups, water bottles, and to-go containers (should never be used to heat or freeze), as well as more unexpected items, such as polyester clothing and synthetic carpet fibers.[3]

"This also pointed to the fact that we have a daily exposure to plastic that is tied to our toxic exposure from traffic pollution — our own cars!"

Microplastics and nanoplastics (MNPs) act as cell senescence inducers by promoting mitochondrial dysfunction, impairing autophagy, and activating DNA damage responses, exacerbating cellular aging. Increased senescence of reproductive cells and transfer of MNPs/induced damages from parents to offspring in animals further corroborate the transgenerational health risks of the tiny particles.[4]

Scientists from the University of Toulouse, France, recently studied plastic particles 10 micrometers or less — the width of a cotton fiber. They discovered that the highest measurements of microplastic particles were inside cars, suggesting people inhale even more in total than previously estimated. This also pointed to the fact that we have a daily exposure to plastic that is tied to our toxic exposure from traffic pollution — our own cars!

The median amount of microplastics in a car cabin's air measured 2,238 microplastic particles per cubic meter, compared to a median of 523 microplastics per cubic meter in a typical indoor residential environment. Of these particles, 94% were smaller than 10 micrometers.[5]

The reason for the large spike inside cars compared to other environments could be due to the limited ventilation in vehicles, suggesting that car air filters might be a good idea. Combining the results of microplastics in traffic (inside car) with previous studies of microplastics in indoor air, researchers estimated that someone's daily exposure to these smaller particles from air could be roughly 68,000 particles, hundreds of times more than previous estimates.

SASP

- **Cellular senescence is a state of terminal growth arrest associated with the upregulation of different cell cycle inhibitors, mainly p16 and p21, structural and metabolic alterations, chronic DNA damage responses, and**
- **a hypersecretory state known as the senescence-associated secretory phenotype (SASP).**

- **The SASP is the major mediator of the paracrine effects of senescent cells in their tissue microenvironment and of various local and systemic biological functions.**
  - Wang, B. *et al.* The senescence-associated secretory phenotype and its physiological and pathological implications. *Nat Rev Mol Cell Biol* **25**, 958–978 (2024).

Senescence and Ill-health

- Narasimhan A, et al(October 2021). "Role of Cellular Senescence in Type II Diabetes". *Endocrinology*. **162** (10).
- Childs BG, et al. (December 2015). "Cellular senescence in aging and age-related disease: from mechanisms to therapy". *Nature Medicine*. **21** (12): 1424–1435.
- Wyld L, et al. (July 2020). "Senescence and Cancer: A Review of Clinical Implications of Senescence and Senotherapies". *Cancers*. **12** (8): e2134.
- Chen MS, et al. Senescence mechanisms and targets in the heart. Cardiovasc Res. 2022 Mar 25;118(5):1173-1187.
- Hudson HR, et al. Senescent brain cell types in Alzheimer's disease: Pathological mechanisms and therapeutic opportunities. Neurotherapeutics. 2025 Apr;22(3):e00519.
- Wong GC, & Chow KH. DNA Damage Response-Associated Cell Cycle Re-Entry and Neuronal Senescence in Brain Aging and Alzheimer's Disease. J Alzheimers Dis. 2023;94(s1):S429-S451.
- Li, K., et al. Cellular senescence and other age-related mechanisms in skeletal diseases. *Bone Res* **13**, 68 (2025).

- Boyajian J.L. et al. Microbiome and human aging: Probiotic and prebiotic potentials in Longevity, skin health and cellular senescence. Nutrients. 2021, 13, 4550.

Review:

- ”In this review, we outline the cellular senescence and other age-related mechanisms in developing **skeletal conditions, including osteoporosis, intervertebral disc degeneration, osteoarthritis, rheumatoid arthritis… and ankylosing spondylitis**, with the aim of comprehensively understanding their detrimental effects on the aged skeleton and screening the potential targets for **anti-aging therapy within the skeletal system.”**
  - Li, K., et al. Cellular senescence and other age-related mechanisms in skeletal diseases. *Bone Res* **13**, 68 (2025).

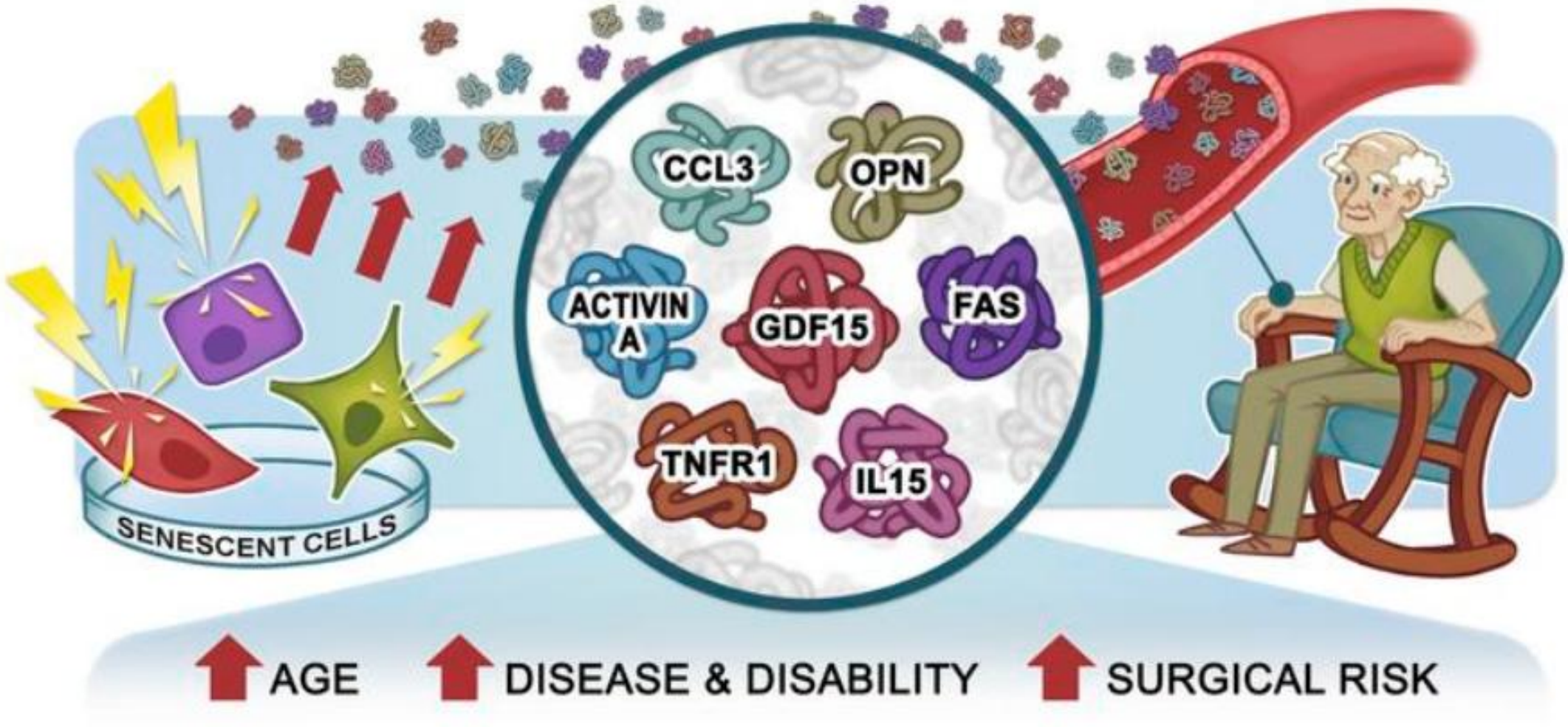
Produced by senescent cells, the senescence-associated secretory phenotype (SASP) is a potential driver of age-related dysfunction

- We tested whether circulating concentrations of SASP proteins reflect age and medical risk in humans.
- A community-based sample of people aged 20–90 years (retrospective cross-sectional) was studied to test associations between circulating SASP factors and chronological age.
- A subset of this cohort aged 60–90 years and separate cohorts of older adults undergoing surgery for severe aortic stenosis (prospective longitudinal) or ovarian cancer (prospective case-control) were studied to assess **relationships between circulating concentrations of SASP proteins and biological age (determined by the accumulation of age-related health deficits) and/or postsurgical outcomes.**
- Marissa J. Schafer, et al. The senescence-associated secretome as an indicator of age and medical risk. *JCI Insight.* 2020;5(12):

SASP proteins were positively associated with age, frailty, and adverse post-surgery outcomes.

- 7 SASP factors composed of growth differentiation factor 15 (GDF15), TNF receptor superfamily member 6 (FAS), osteopontin (OPN), TNF receptor 1 (TNFR1), ACTIVIN A, chemokine (C-C motif) ligand 3 (CCL3), and IL-15 predicted adverse events markedly better than a single SASP protein or age.

- Our findings suggest that the circulating SASP may serve as a clinically useful candidate biomarker of age-related health and a powerful tool for interventional human studies.


CCL3
OPN
ACTIVIN A
GDF15
FAS
TNFR1
IL15
SENESCENT CELLS
AGE
DISEASE & DISABILITY
SURGICAL RISK

How do you clear senescent cells?

- **Known interventions that reduce senescent burden include:**

- **<u>Nutritional Supplements</u>**
- **Exercise**
- **Caloric restriction**
- **Immune surveillance**
- **Decreased inflammation/toxicity**
- **HBOT**
- **Detoxing especially through circulatory and lymphatic transport**
- **<u>Chiropractic</u>**

Hyperbaric Oxygen

- **HBOT may induce significant senolytic effects including significantly increasing telomere length and clearance of senescent cells in the aging populations (35 adults).**

- *Hachmo Y, et al. Hyperbaric oxygen therapy increases telomere length and decreases immunosenescence in isolated blood cells: a prospective trial. Aging (Albany NY). 2020 Nov 18;12(22):22445-22456.*

NAC – N-Acetyl Cysteine

- Studies suggest that NAC is **one of the most efficient SASP nutrients to support anti-senescence and all of the associated secretions from SASP.**

- **NAC raises glutathione**

- In fact, it is suggested that **NAC can even support estrogen deficiency-induced bone loss by a) inhibiting oxidative stress and b) inhibiting DNA damage, and c) by inhibiting SASP.**
  - *Zhou X, et all. Suppression effect of N-acetylcysteine on bone loss... Am J Transl Res. 2020 Mar 15;12(3):731-742.*

Detoxification:
(ranging from a supplement to a program)

- Quercetin, curcumin, resveratrol, quercetin, sulforaphane (organic broccoli sprouts), probiotics, quality protein powder, quality hi-potency fish oil (molecularly distilled and pharmaceutical grade, hi EPA/DHA content), Milk thistle (80% silymarin), green tea extract, dandelion, burdock root, cordyceps, mushroom glycans, apigenin, ergothioneine, beets, etc.

Nutritional components as mitigators of cellular senescence in organismal aging: a comprehensive review.

- With a renewed focus on cellular senescence, emerging studies demonstrate that both primary and secondary nutritional elements such as **carbohydrates, proteins, fatty acids, vitamins, minerals, polyphenols, and probiotics** can influence multiple aspects of cellular senescence.

- Diwan B, Sharma R. Food Sci Biotechnol. 2022 Jun 18;31(9):1089-1109.

Nutritional Components

- "**polyphenols such as quercetin** have already shown promising clinical results in alleviating SC burden and improving age-related pathologies (Hickson et al., 2019).

- …**probiotics** can be useful in mitigating cellular senescence and aging

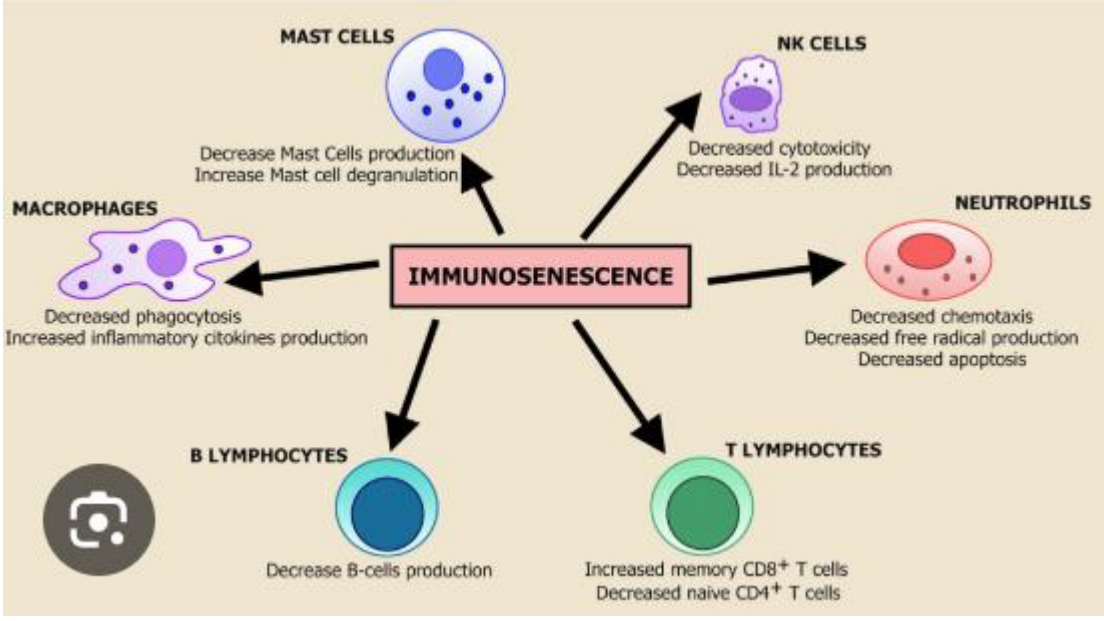
- …it appears that the observed anti-cellular senescence effects of **dietary constituents, including phytomolecules such as quercetin,** could be mediated through the **modulation of the gut microbiota** composition in vivo (Saccon et al., 2021).

Flavonoids for SASP Support:

Vegetable flavonoids, ie: quercetin, apigenin, spirulina, chlorella **spinach, asparagus, parsley, broccoli, broccoli sprouts (which are generally 4% sulforaphane), watercress, carrot, beet, inulin, etc.**

Flavonoids reduce mast cells -> senescent cells

- Mast cells (MCs) undergo age-related changes, including increased accumulation and a shift toward a pro-inflammatory, senescent phenotype
- Senescence decreases mast cells; with age mast cells->senescent cells



Flavonoids in top 3 for inflammation (esp. brain)
- reduce mast cell inflammation

- "Appropriate preventive measures early in life or corrective measures are discussed…"

- such as: fecal microbiota transplantation, probiotics and **flavonoids (quercetin esp.)**
    - Gut-Microbiota-Brain Axis and Its Effect on Neuropsychiatric Disorders With Suspected Immune Dysregulation. Anastasia I. Petra et al. Purpose 2015; 37 (5):984–995.

Flavonoid Luteolin "**potent mast cell blocker**" (in broccoli, carrots, parsley, peppermint, olive oil, dandelion (Is a Subtype of Autism an Allergy of the Brain? Clin ther 2013 May; 35(5):584-91.)

Quercetin also blocks mast cells

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.)

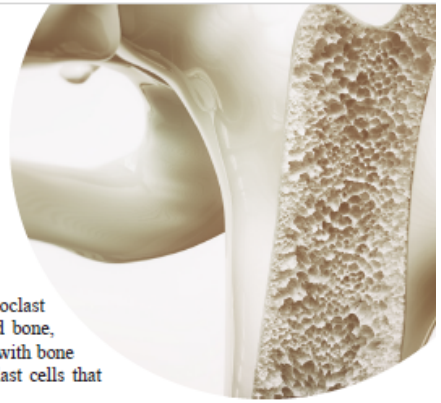
American Chiropractor Jan 2024

CLINICAL EXCELLENCE

Fighting Back Against Osteoporosis

Including natural stem cell support

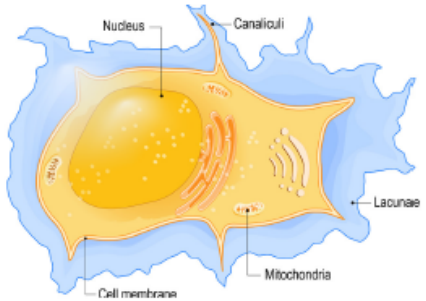
by Lynn Toohey, PhD



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 percentage of dead osteocytes in bone increases with age from less than 1% at birth to 75% after age 80. Reducing the number of osteocytes "leads to faster bone aging and affects the balance of the different cell types required for healthy bone and bone marrow growth."[1]



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, the vitamin C-treated group displayed an increase in the expression of osteoblast differentiation genes, including genes for type I collagen. Vitamin C reduced the expression of osteoclast differentiation genes. Researchers believed that their study was 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.[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.

“Cellular senescence is particularly intriguing as it reflects a cellular state that encompasses and integrates the other biological aging hallmarks:” (Apl 2025)

- “genomic instability
- telomere attrition
- epigenetic alterations
- loss of proteostasis
- altered macroautophagy
- mitochondrial dysfunction
- aberrant nutrient sensing
- stem cell exhaustion
- altered intercellular communication
- dysbiosis
- chronic inflammation.”

Hudson HR, Sun X, Orr ME. Senescent brain cell types in Alzheimer's disease: Pathological mechanisms and therapeutic opportunities. Neurotherapeutics. 2025 Apr;22(3):e00519.

Dietary and Supplemental Health

- **Sulforaphane -** cruciferous vegetables like broccoli and Brussels sprouts, sulforaphane **activates detoxification pathways that reduce senescence markers.**
  - Rajendran, P., et al. (2011). "Sulforaphane and its role in chronic diseases." *Advances in Nutrition*, 2(5), 383-392.

- Named by researchers as having **senolytic activity that can reduce SASP.**

- Some of the other nutrients mentioned along with sulforaphane by those researchers for senolytic activity included **quercetin, curcumin, and resveratrol.**
  - *Malavolta M, et al. Inducers of Senescence, Toxic Compounds, and Senolytics: The Multiple Faces of Nrf2-Activating Phytochemicals… Mediators Inflamm. 2018 Feb 12;2018:4159013.*

Apigenin

- Found in relatively very high quantities in dried parsley – 4500mg/100 gm (the next highest food source is **chamomile** at 500mg/100gm).

- Apigenin is a powerful biochemical that has been identified as one of the nutrients with the **ability to suppress SASP** and resulting **paracrine effects to proximal cells**

  Perrott KM, et al. Apigenin suppresses the senescence-associated secretory phenotype and paracrine effects... Geroscience. 2017 Apr;39(2):161-173.

Perrott, K. M., Wiley, C. D., Desprez, P.-Y. & Campisi, J. **Apigenin suppresses** the senescence-associated secretory phenotype and paracrine effects on breast cancer cells. GeroScience 39, 161–173 (2017).

Product	Apigenin (milligrams per 100 grams)
Dried parsley	4500[5]
Chamomile	300–500
Parsley	215.5
Celery hearts, green	19.1
Rutabagas, raw	4

Senescence and Skin:

- **Cellular senescence is an intrinsic aging process that has been recently associated with microbial imbalance.**

- **Skin is a common site of deposition.**

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.

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

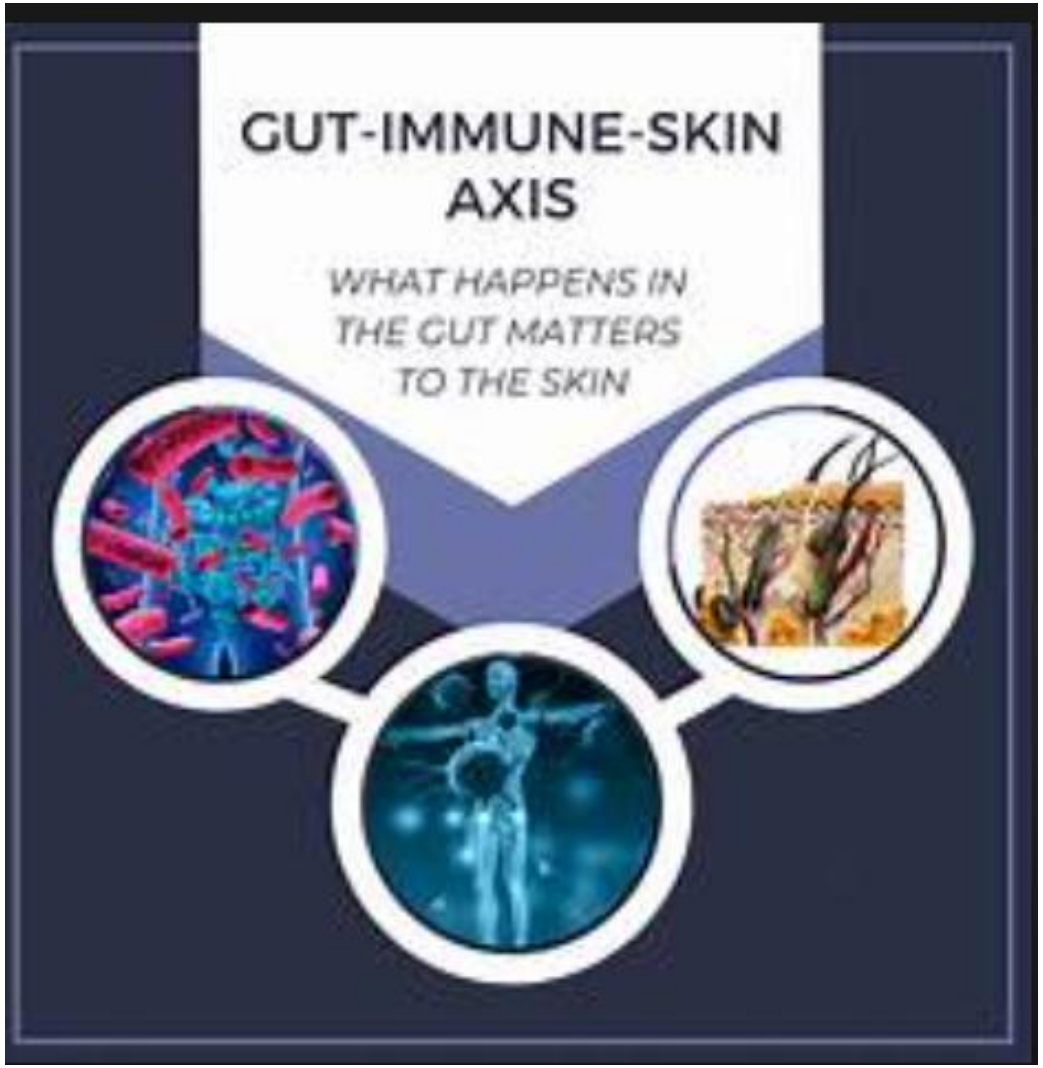
- "Mushrooms are proven to possess anti-allergic, anti-cholesterol, anti-tumor, and anti-cancer properties.

- **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

Gut-Skin Axis

- The gut microbiota influence skin disruption through the gut-skin axis and secretion of microbial metabolites

- SASP secretions follow microbial imbalance



“Probiotics and Prebiotics May Be Effective Alternatives…”

- “Novel anti-senescent therapeutics are warranted, given the poor safety profile of current pharmaceutical drugs.”
  - Microbiome Review

- Variety of Probiotics is Important

How does Chiropractic Clear SASP

- Chronic **sympathetic dominance** increases:
  - Oxidative stress
  - DNA damage
  - Pro-inflammatory signaling → senescence

- Improved **parasympathetic (vagal) tone** is associated with:
  - Reduced inflammatory cytokines (IL-6, TNF-α)
  - Better immune surveillance

- ➞ Less inflammatory signaling = **less induction of senescence**, and potentially **better immune-mediated clearance**.

Chiropractic decreases inflammatory cytokines

- Sixty-four subjects
- Single thoracic adjustment
- **Decreased inflammatory cytokines**
- *Tiodorczyk-Injevan, J.A. Spinal Manipulative Therapy Reduces Inflammatory Cytokines…Manipulative and Physiological Therapeutics. Jan 2006. 29(1):14-21.*

March 28, 2020

> *"Medicine is the study of disease and what causes man to die. Chiropractic is the study of health and what causes man to live."*[1]
>
> – ATTRIBUTED TO BJ PALMER, DC
> PHC FOUNDER OF THE INTERNATIONAL CHIROPRACTORS ASSOCIATION

[1] One of our sage members provided that this quote was actually from Clarence S. Gonstead, DC, who made significant contributions to the field. The quote is widely attributed to Dr. Palmer, however; we wish to note that it may have originally been a statement from Dr. Gonstead.

International Chiropractors Association (cont'd)

- "Evidence existed in the eight studies which found that spinal manipulation influences various biomarkers typically identified as ones **not only involved in pain perception/modulation** but also play an important role in **inflammation, tissue healing and immune response**."

- The nervous system has *biological connections* with immune regulation

International Chiropractors Association (cont'd)

- **"They concluded, basic science studies support chiropractic theory that spinal subluxation and spinal manipulation impact neurologic function. In addition, the interdependence of nervous, endocrine, and immune systems has been discussed here.**

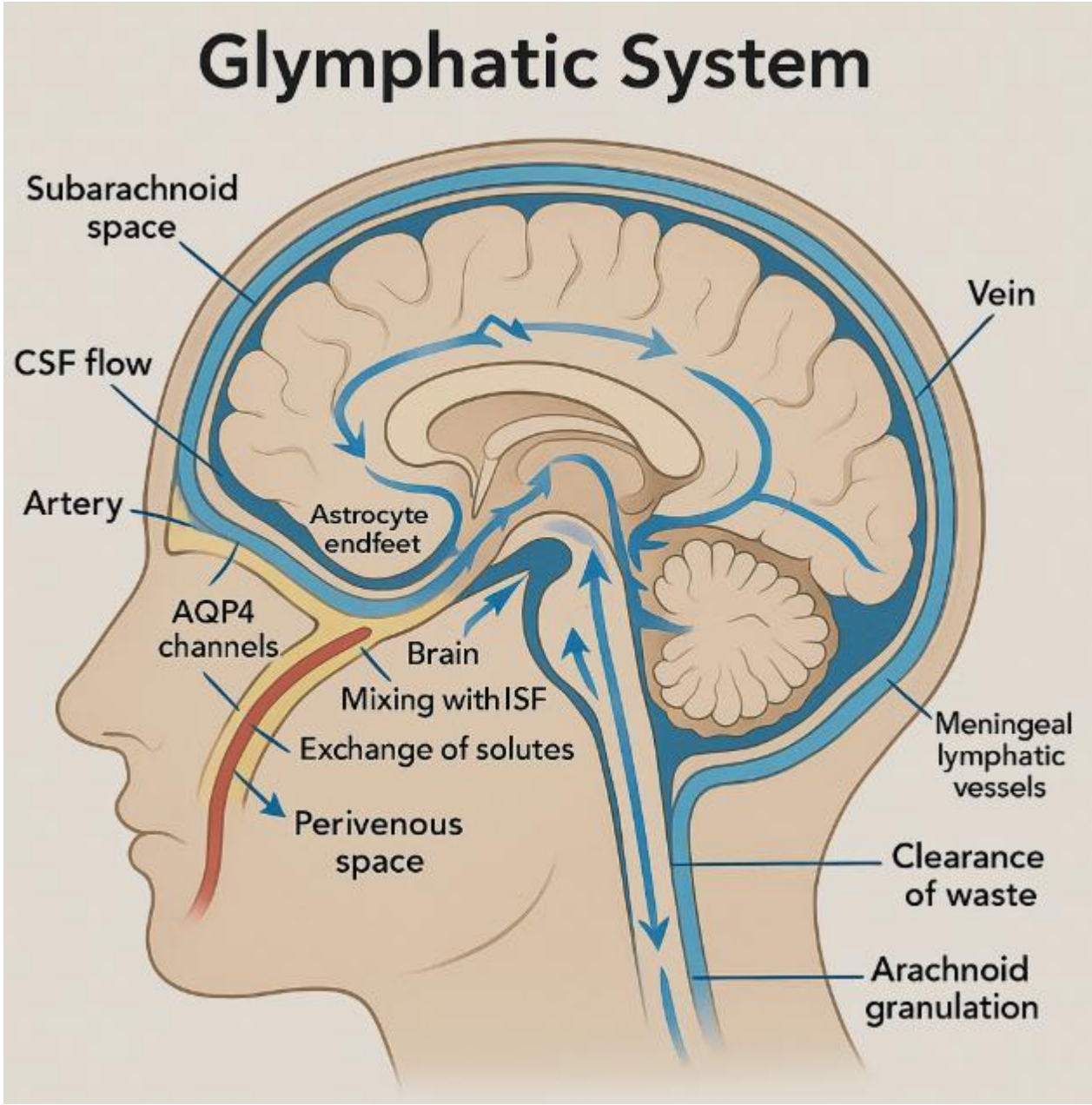
- **These studies suggest mechanisms by which spinal influences may mediate a clinically significant impact on immune function".**

Chiropractic improved lymphatic and glymphatic flow

- Movement of the spine and rib cage affects:

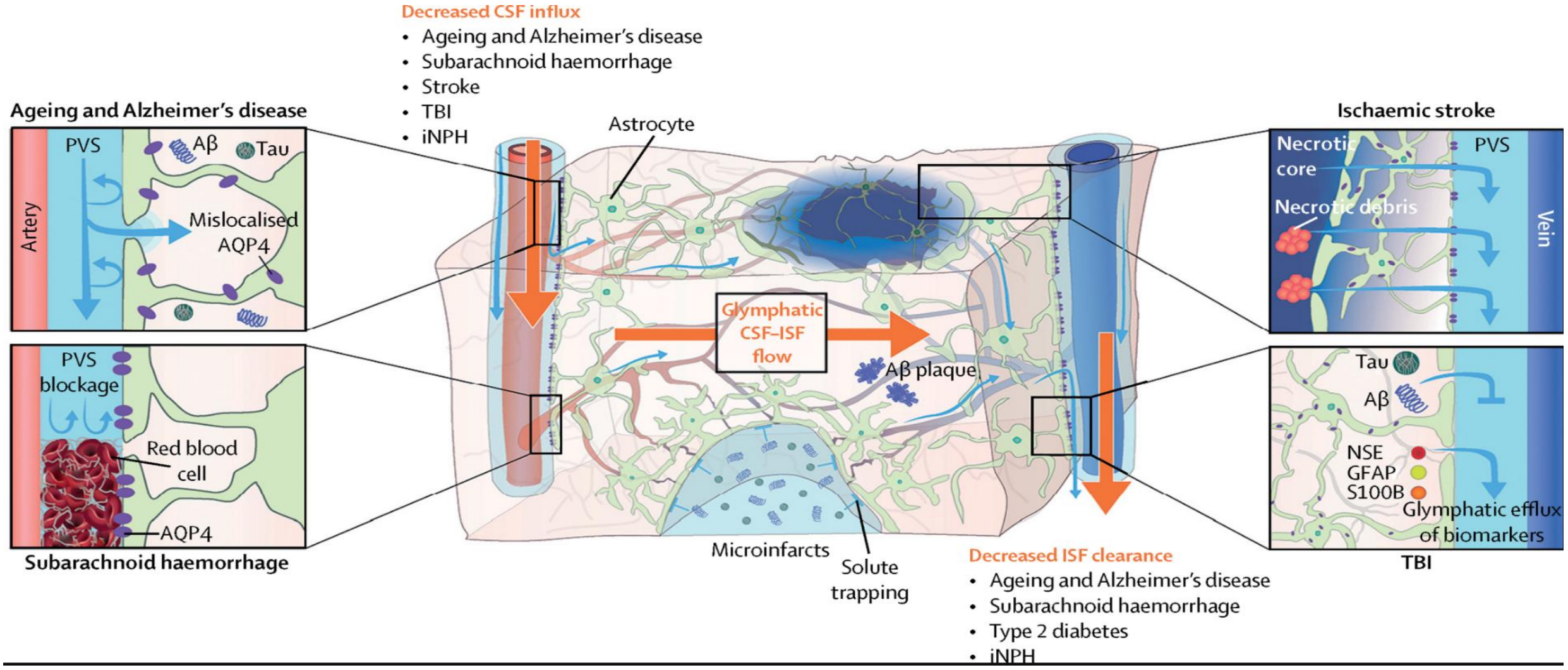
- Thoracic duct flow
- Cervical **lymphatic drainage**
- **Glymphatic clearance**
  - (especially upper cervical mobility)

- The glymphatic system is a brain-wide waste clearance pathway that functions primarily during sleep. It uses cerebrospinal fluid (CSF) to wash away neurotoxic waste, such as amyloid-beta, particularly during non-REM (N3) slow-wave sleep. During sleep, brain cells shrink by up to 60%, reducing resistance and allowing more efficient.



Sleep - Critical for Glymphatic Toxin Drainage

Removal of B-amyloid & Toxins Helps Longevity Prospects



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

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 COMT, MAO, GAD

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

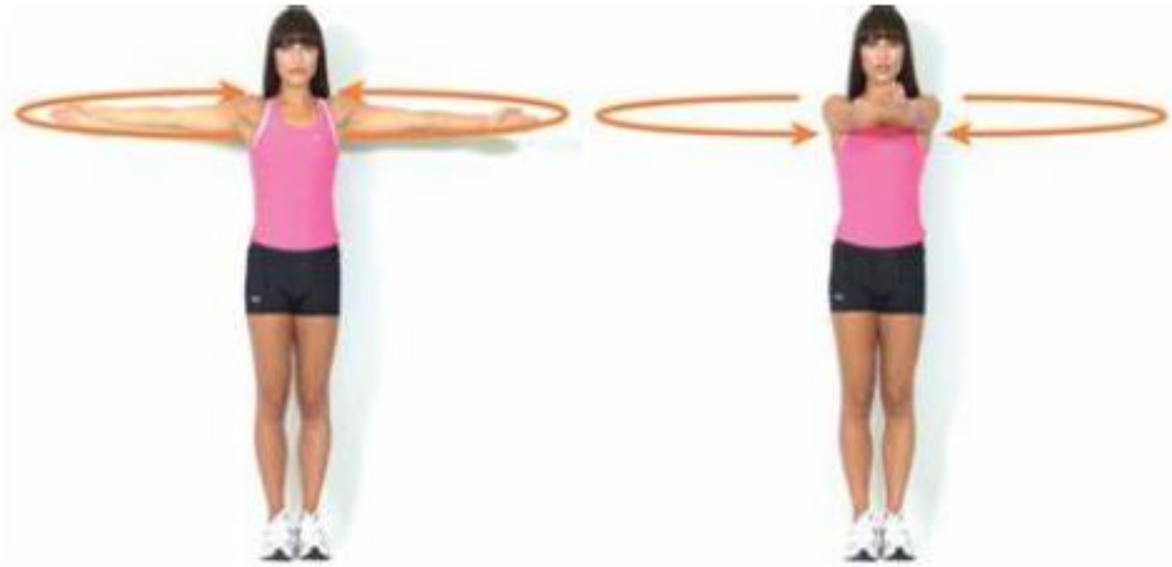
Chiropractic optimizes the immune environment that clears SASP

- Several studies show short-term immune changes after spinal manipulation, including:

- Increased natural killer (NK) cell activity
  - (primary in clearing senescent cells)
- Changes in cytokine profiles
- Improved leukocyte responsiveness

Movement increases Detox

- Better mechanical motion = **better waste removal**
- **Intensity does not necessarily equal improved results**



Reduction of chronic mechanical and neurogenic inflammation

- Joint dysfunction, altered afferent signaling, and muscle hypertonicity can sustain:
- Local and neurogenic inflammation
- Elevated cortisol and catecholamines

- ➞ By reducing chronic nociceptive input, **chiropractic** may **lower ongoing senescence signaling**.

Chiropractic, Stress and the HPA axis

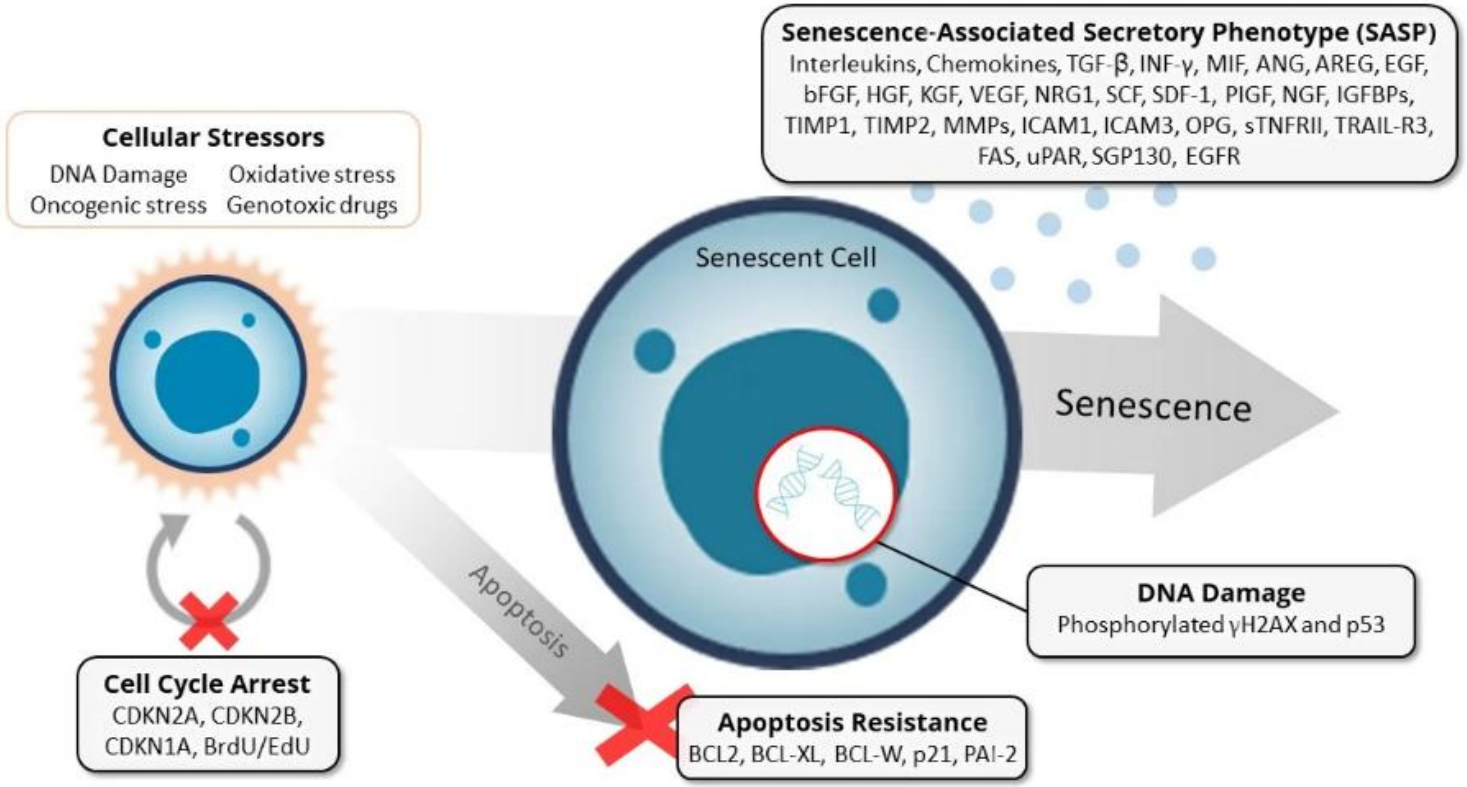
- **Chronic Stress causes:**

- Accelerated senescence via telomere shortening
- Impaired autophagy
- Mitochondrial damage

- **Chiropractic Care is associated with:**
- Better movement
- Reduced perceived stress
- Lower cortisol
- Improved sleep and HRV
- Stress reduction that results in slower senescence accumulation

Movement decreases stress!

Chiropractic reduces cellular stressors that cause SASP



The short version for patients:

- Genetics and lifestyle combine to determine how we handle **Zombie cells** – cells that are not quite alive and not quite dead, but they **release inflammatory substances that age us and cause disease.**

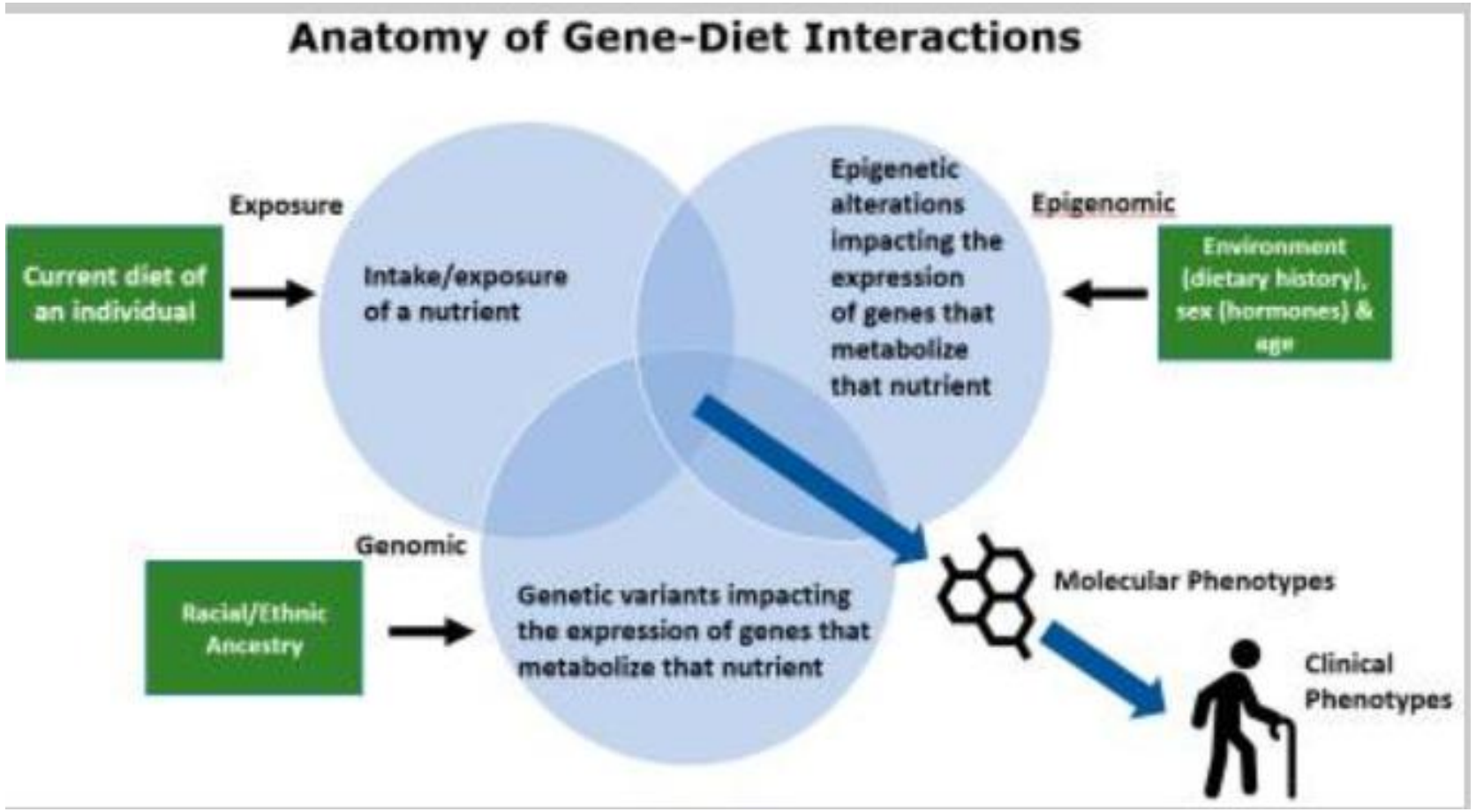
- To fight zombie cells:
- **Nutritional Supplements**
- **Exercise**
- **Caloric restriction**
- **Immune surveillance**
- **Decreased inflammation**
- **HBOT**
- **Detoxing especially through circulatory and lymphatic transport**
- **<u>Chiropractic</u>**


ZOMBIE CELLS
HOW TO GET RID OF THEM

Additional nutrient/supplement recommendations

- Sulforaphane
- Curcumin
- Resveratrol
- Green tea
- Apigenin
- NAC
- Probiotics & Prebiotics
- Hypoallergenic protein
- Fish oil
- Mushroom glycans
- Ergothioneine
- Milk thistle
- Silymarin
- Dandelion
- Burdock root
- Glutathione
- Beet
- Alpha lipoic acid
- Liver glandular

Genotype to Phenotype



Richard Morgan 94

“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.”

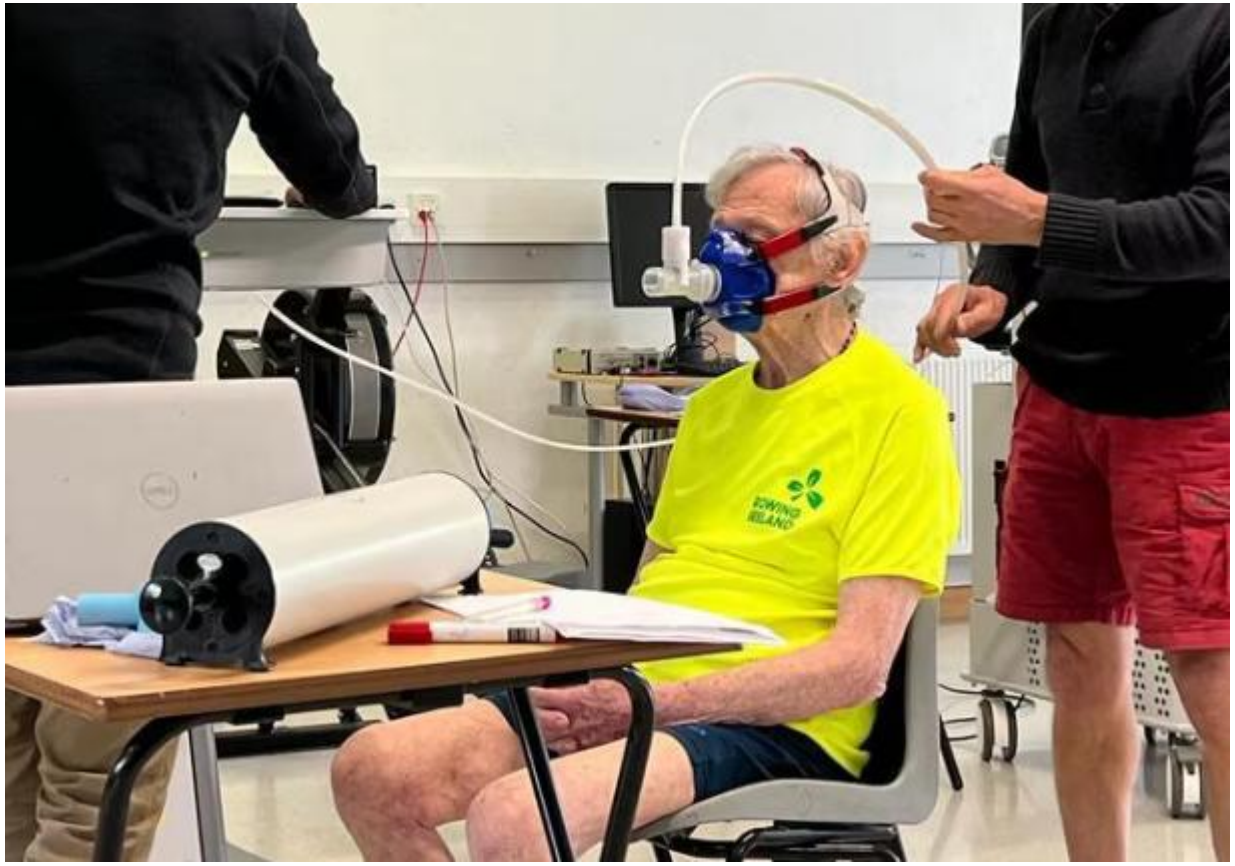
Do we quit exercising because we get old, or…

- 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 with creaky knees who didn't take up regular exercise until 70s

Are declines in muscle mass normal and inevitable or due mostly 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:

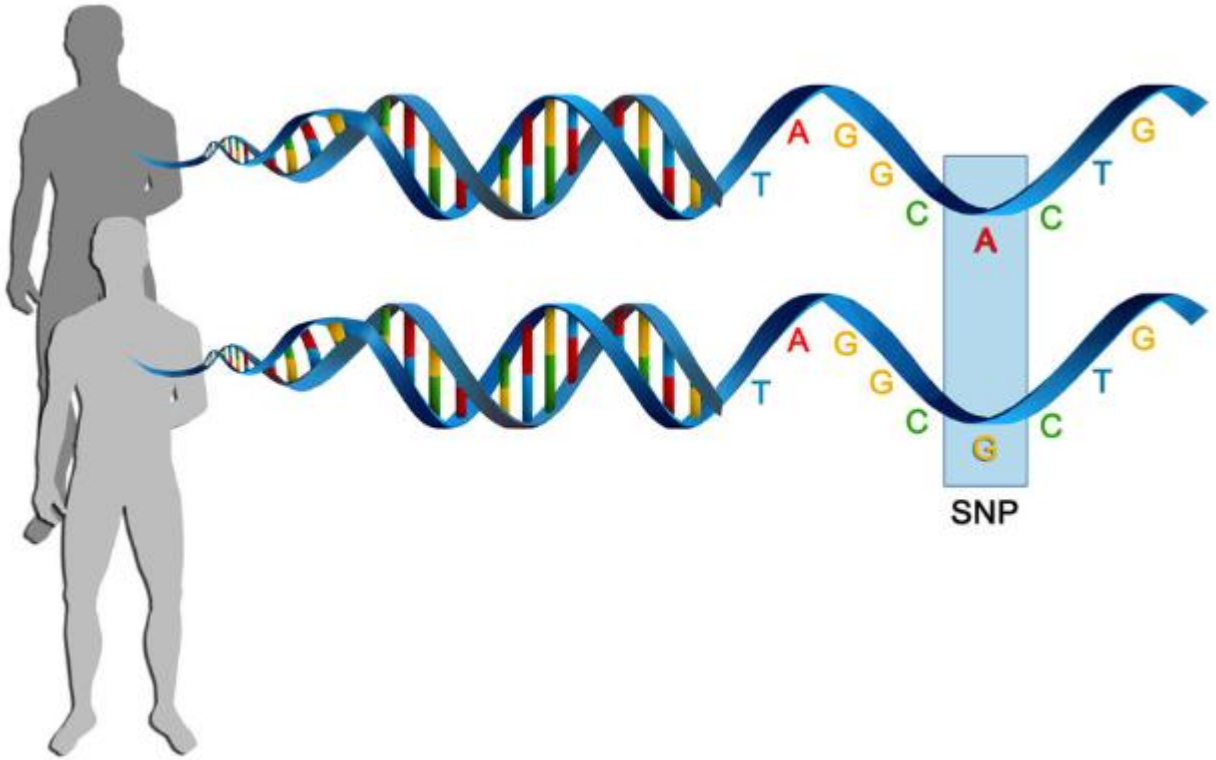
- The human body maintains the ability to adapt to exercise at any age.

- “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”.

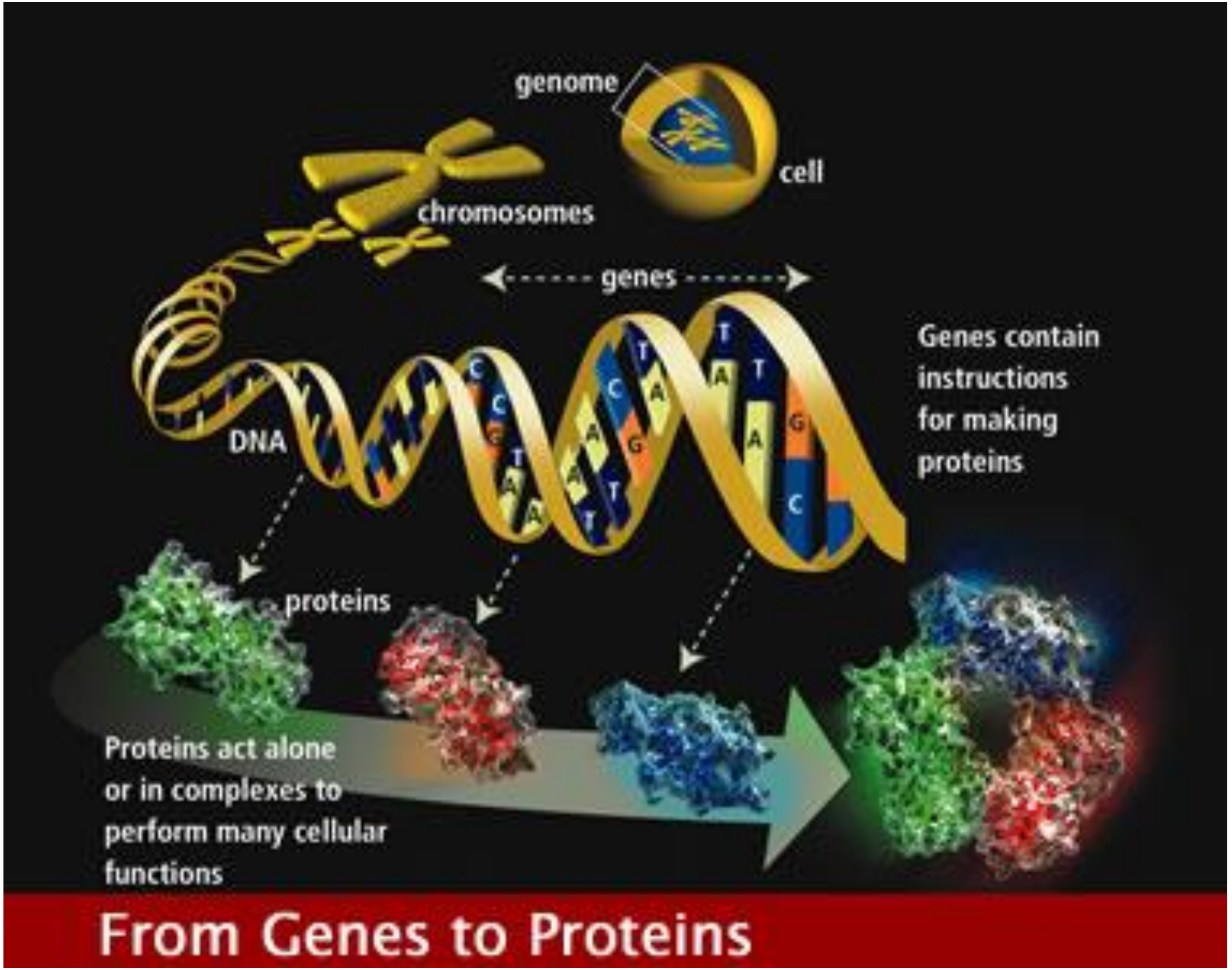
Genetic variants (SNPs)

- 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% (estimate)
- **Homozygous variants**-Both of your inherited alleles are variants from normal, reduces activity of enzyme by approximately 70% (estimate)


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 (eg.)

- **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 (FHEval, Geneticgenie.org, MTHFRSupport.com, 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

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

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	+/+

Alimoradi *et al. Virology Journal* (2022) 19:48
https://doi.org/10.1186/s12985-022-01782-6

Virology Journal

RESEARCH Open Access

SNPs of ACE1 (rs4343) and ACE2 (rs2285666) genes are linked to SARS-CoV-2 infection but not with the severity of disease

Nahid Alimoradi[1], Moein Sharqi[2], Dena Firouzabadi[3,4], Mohammad Moein Sadeghi[1], Mohammad Iman Moezzi[1] and Negar Firouzabadi[1*]

ACE2 - **Genome-wide analysis provides genetic evidence that ACE2 influences COVID-19 risk and yields risk scores associated with severe disease**

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) enters human host cells via angiotensin-converting enzyme 2 (ACE2) and causes coronavirus disease 2019 (COVID-19).
- Here, through a genome-wide association study, we identify a variant rs190509934
- Downregulates *ACE2* expression by 37% and reduces the risk of SARS-CoV-2 infection by 40%, providing human genetic evidence that ACE2 expression levels influence COVID-19 risk.
- We also replicate the associations of six previously reported risk variants, of which four were further associated with worse outcomes in individuals infected with the virus (*LZTFL1*, MHC, *DPP9* and *IFNAR2*).
- Lastly, we show that common variants define a risk score that is strongly associated with severe disease

FHEval

ACE: (Angiotensin Converting Enzyme) This enzyme converts angiotensin I to angiotensin II. Angiotensin II causes blood vessels to constrict, which can result in arterial pressure imbalance. This enzyme also stimulates production of aldosterone, which triggers the absorption of salt and water by the kidneys. The increased amount of fluid in the body can also imbalance arterial pressure. Proper balanced pressure during fetal development is critical for development of the kidneys. Mutations in the ACE gene are the most common cause of non-homeostatic kidney

function, the inability to produce urine (anuria), and low arterial pressure imbalances.

Mutations in this enzyme are also related with anxiety and learning/memory imbalance. ACE variants have also been linked to imbalance when it comes to age-related memory function.

Increased ACE activity can also throw off mineral balance in the body due to decreased excretion of sodium in the urine and increased excretion of potassium in the urine, provided the kidneys are functioning properly. This subsequent decreased potassium can also lead to fatigue and decreased energy production. Symptoms of genetic variants in the ACE enzyme can also include anxiety and non-homeostatic blood clotting.

Increased pressure on the CBS pathway can increase the conversion of angiotensin I to Angiotensin II which can lead to arterial pressure imbalance. Pathways need to be balanced with nutrients to maintain healthy arterial pressure.

ACE variants are associated with:

ACE variants are associated with:

- Anxiety
- Fatigue
- Low potassium

And non-homeostatic function of:

- Arterial pressure
- Blood clotting
- Blood sugar
- Kidney
- Learning/Memory
- Heart

Diet and Lifestyle Recommendations: Increase potassium-containing foods in the diet including beans, dark leafy greens, potatoes, squash, yogurt, fish, avocados, mushrooms, and bananas.

Kinesiology Challenge Vial:

- Angiotensin I

Analysis of the ACE SNP

- Definition of the SNP and information on its function
- Dietary and Lifestyle recommendations
- Nutrient and Supplement recommendations
- Kinesiology challenges and Suggested Lab Tests

Recognition, Analysis, Support

Nutrient Support Recommendations:

- Potassium
- Kidney support
- Molybdenum
- Riboflavin

CBS: (Cystathione Beta Synthase) This enzyme converts homocysteine to cysteine and glutathione. The variant is an *upregulation* defect; CBS regulates the enzymes that help to convert homocysteine into glutathione, a major antioxidant. Mutations in the CBS genes will produce more sulfur end products from the methylation cycle. In particular, individuals who have the CBS (+/+, or +/-) the homozygous or heterozygous variants may want to limit intake of sulfur-containing foods (like garlic, and supplements, such as MSM) as well as medications (like DMPS.) Even cruciferous vegetables contain sulfur. Both the CBS homozygous and heterozygous mutations also have a higher risk for ammonia detoxification issues. This mutation can also indirectly affect an enzyme called G6PDH, which has negative effects on blood sugar metabolism, red blood cell formation, and blood vessel stability, leading to easy bruising, bleeding, and broken blood vessels along with vascular imbalances.

Variants are associated with low energy, brain fog, headaches, blood sugar imbalance, immune attack, anxiety, and insomnia (from increased cortisol). This defect can also lead to a depletion of SAMe (S-adenosyl-methionine, the major methyl donor) and a subsequent increase in histamine in the body.

It has also been observed that BH4 can also become depleted with a CBS upregulation. BH4 helps regulate neurotransmitters and mood. COMT +/+ and or VDR -/- individuals will have higher dopamine and BH4 levels and may get ill less frequently, but will be more sensitive to methyl cycle intermediates, which could increase dopamine too much, causing irritability/erratic behavior. For other mutations (such as MTHFR A1298C), chronic immune assaults and aluminum can also lead to low BH4 levels. Lack of BH4 can lead to mast cell degranulation and issues with mast cell activation.

Variants are associated with:

- Low vitamin B12 (It gets drained too quickly)
- Overload of detox pathways
- Food and chemical sensitivity
- Sulfite sensitivity
- Dairy intolerance (xanthine oxidase deficiency)
- Alcohol intolerance
- Ammonia build up
- Heavy metal toxicity
- Anxiety
- Chronic immune attack
- Chronic discomfort
- Depression/mood issues
- Leaky gut
- Fatigue
- Increased cortisol
- Non-homeostatic nerve function and brain fog

Note: When utilizing methyl donors, it is a good idea to integrate synergy and make sure that blocked pathways, such as CBS, are cleared. Methylation is a good thing, and it will increase detoxification, so you want to make sure your detox pathways are clear to get rid of the waste, toxins, and metals getting dumped. Other synergistic nutrients, such as N-acetyl cysteine (which detoxifies metals and toxins), will help cover these "blocked pathways". Green tea can also be helpful. Identify other "blocked" pathways where there is a genetic variant, and concentrating on the nutrition for that blocked pathway will relieve pressure there. CBS will do its job of detoxifying efficiently and gently. If there is also a SUOX SNiP, it is very important that this pathway get balanced (molybdenum supplementation may be necessary).

Diet and Lifestyle Recommendations:

Be aware of sulfur containing foods such as garlic, onions, and cruciferous vegetables (broccoli, cauliflower, kale etc.) until the pathway is cleared. Avoid sulfites in foods (preservatives).

Kinesiology Challenge Vials:

- Ammonia
- Toxic Metals
- Taurine
- Cortisol
- Sulfates/sulfites
- Angiotensin II
- Chemicals/hydrocarbons
- Homocysteine
- Methyl Donors (SAMe, TMG, DMG)
- Lactose

Nutrient Support Recommendations:

- Pantothenic Acid
- Niacin
- Manganese
- Heavy metal detox support
- Zinc
- Careful of vitamin B6!! (It speeds up this pathway)
- Supplementation with molybdenum to stimulate SUOX - high doses may be necessary. Homogenized dairy products contain xanthine oxidase, which further depletes molybdenum, and should be avoided if molybdenum levels are low.
- GABA may help neutralize excitotoxin activity when there is excessive alpha-keto-glutarate being produced.

OAS1 – Interferon SNP

- Another example of a beneficial SNP (certain rs ID numbers), indicating a person makes optimal levels of interferon

OAS SNPs (some decrease 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

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.

AANAT: (Aralkylamine N-Acetyltransferase) This enzyme is critical in the production of melatonin from serotonin. It controls the night/day rhythm of melatonin production in the pineal gland. Genetic variants are associated with sleep phase imbalance.

There seems to be a link between genetic variability in the AANAT gene with depression.

Dietary and Lifestyle Recommendations: Keeping regular hours for sleeping can help balance this genetic variant. Reduce light in the bedroom and electromagnetic fields near the bed.

Kinesiology Challenge Vial:

- Serotonin

Nutrient Support Recommendations:

- Melatonin

ADIPOQ: This gene is expressed in adipose tissue exclusively. Mutations in this gene are associated with adiponectin deficiency. Decreased adiponectin means less efficient fat burning and less glucose utilization and therefore mutations are associated with non-homeostasis of weight imbalance and blood sugar. The gene is directly involved in the control of fat metabolism and insulin sensitivity. Symptoms include non-homeostasis of blood sugar, insulin, arterial pressure, and triglycerides. This can create chronic complications in the eyes, kidneys, nerves, and blood vessels.

Two particular variants of the ADIPOQ cause cells to make less adiponectin. One variant results in a ~20% decreased adiponectin level and the other results in a ~40% decrease. Up to 26% of the general population carries the variant associated with a 20% decrease in adiponectin and up to 59% carries the variant associated with a 40% decrease in adiponectin.

Diet and Lifestyle Recommendations: For risk variant carriers, avoid excess calorie intake and choose low saturated fats and low-glycemic index foods to help achieve healthy weight and insulin metabolism.

Gene-diet interaction studies show that carriers of these variants respond better to diets high in MUFA (monounsaturated fatty acids) to maintain homeostasis. Monounsaturated fats are found in red meat, nuts and high fat fruits such as olives and avocados. Olive oil is about 75% monounsaturated fat while sunflower oil contains as much as 85% monounsaturated fat. Canola oil, cashews, avocado oil, macadamia nut oil, grapeseed oil, peanut oil, sesame oil, corn oil, popcorn, oatmeal, almond oil, sunflower oil, and hemp oil contain MUFA's. Avoid allergens and eat organically for best results.

Kinesiology Challenge Vials:

- Adiponectin

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

TBI – Roadblocks to Longevity & Well-Being

- **Brain Injury reduces the capacity to function optimally**

- **Without optimal brain function, mobility, cognition, everyday tasks can be limited**

*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.

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.**

Implications:

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

- **Greatest efficacy of improvement may be amongst heterozygous and homozygous carriers of APOEe (*explains variance in improvement)**

- 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 Bredeson's MEND protocol for 5-24 months.

- **"The magnitude of the improvement is unprecedented."**

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

- 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]

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.)

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.

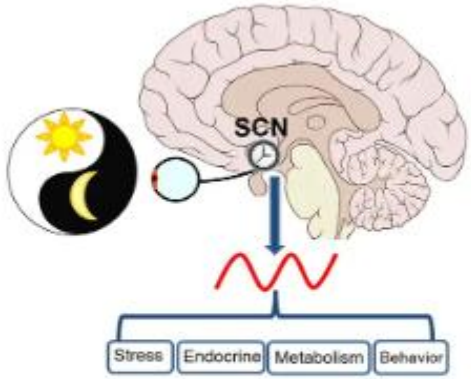
- Zhang Y, et al. Intakes of fish and polyunsaturated fatty acids and mild-to-severe cognitive impairment risks: **a dose-response meta-analysis of 21 cohort studies**. Am J Clin Nutr. 2016 Feb;103(2):330-40.

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

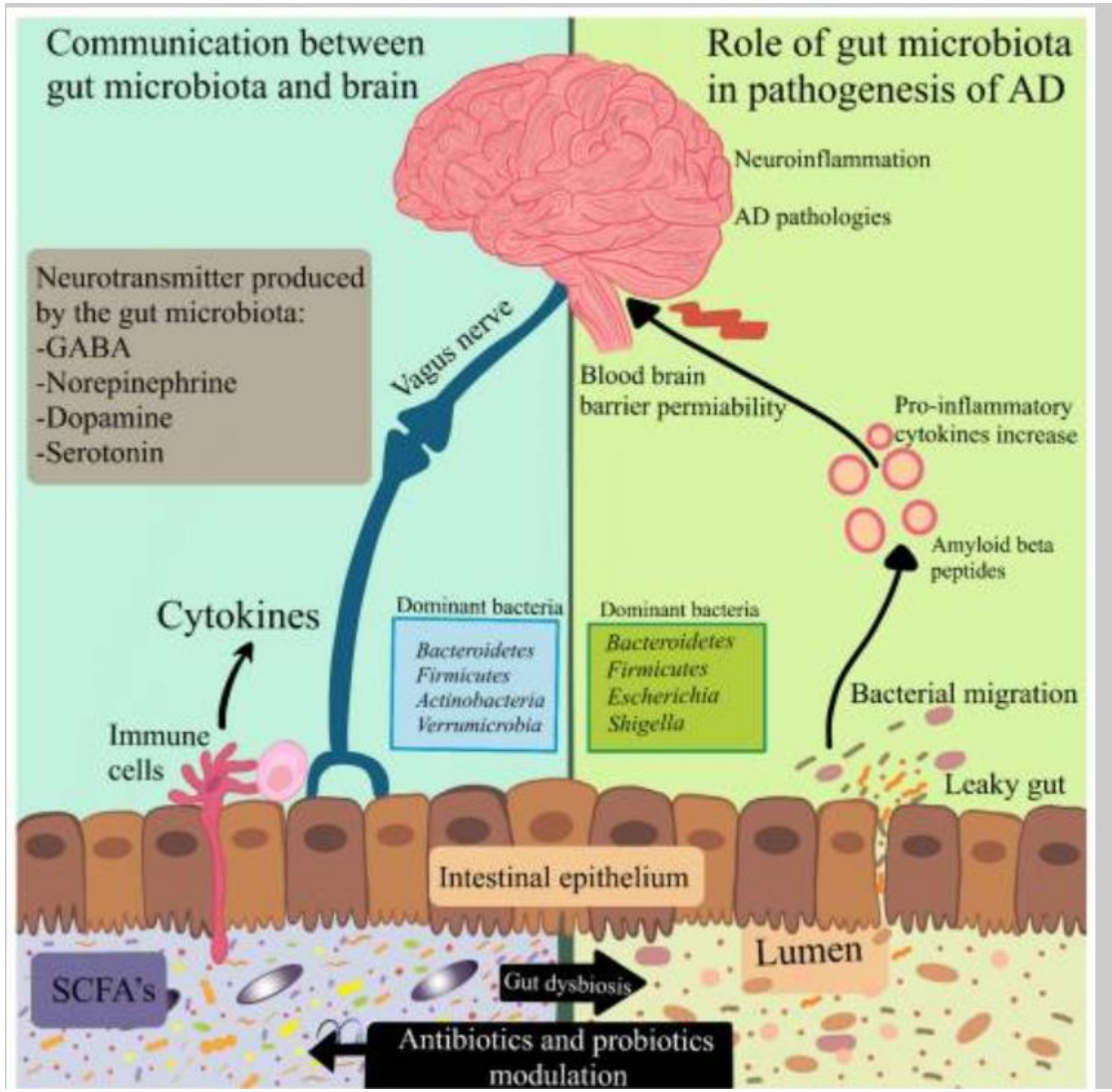
“Observations support multiple mechanisms by which vitamin D can act against **neurodegenerative processes**.”

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.

- 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**

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

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.

Why GSH SNPs are important for TBI

- GSH (glutathione)is hugely important for TBI protection, and also for recovery.
- Patients with GSH SNPs are impaired in their ability to utilize GSH for recovery
- Patients with GSH SNPs need Xtra help when it comes to having glutathione substrates and optimizing their GSH metabolism

Glutathione SNPS

- **GPx1:** (Glutathione Peroxidase) is an enzyme whose main function is to support cells so that they are strong against oxidative damage. It reduces lipid hydroperoxides to alcohols and reduces free hydrogen peroxide to water.
- Genetic variants have been associated with dysfunction in the digestive tract and skin pigmentation. Lower plasma glutathione peroxide levels have been seen in patients with non-homeostatic nerve health and blood sugar levels. Glutathione peroxidase and superoxide dismutase polymorphisms may play a role in the development of celiac.
- **Diet and Lifestyle recommendations:** Ginger has been shown to increase the activity of SOD and GPX. Brazil nuts are high in selenium as are fish, grass fed meats, and turkey. Increasing levels of antioxidant rich foods would be highly beneficial for this genotype.
- **Kinesiology Challenge Vials:**
- H2O2
- Lipid peroxide
- **Nutrient Support Recommendations:**
- Ginger
- Zinc
- Selenium

Surgical Neurology International

OPEN ACCESS

For entire Editorial Board visit : http://www.surgicalneurologyint.com

Editor: James I. Ausman, MD, PhD University of California, Los Angeles, CA, USA

Review Article

Diminished brain resilience syndrome: A modern day neurological pathology of increased susceptibility to mild brain trauma, concussion, and downstream neurodegeneration

Wendy A. Morley, Stephanie Seneff[1]

Thionetic Nutrition, Richmond Hill, ON L4C 7T3, Canada, [1]Spoken Language Systems Group, Computer Science and Artificial Intelligence Laboratory, MIT, Cambridge MA 02139 USA

E-mail: Wendy A. Morley - wendy@thioneticnutrition.com; *Stephanie Seneff - Seneff@csail.mit.edu
*Corresponding author

Received: 11 December 13 Accepted: 31 March 14 Published: 18 June 14

This article may be cited as:
Morley WA, Seneff S. Diminished brain resilience syndrome: A modern day neurological pathology of increased susceptibility to mild brain trauma, concussion, and downstream neurodegeneration. Surg Neurol Int 2014;5:97.
Available FREE in open access from: http://www.surgicalneurologyint.com/text.asp?2014/5/1/97/134731

Additional Nutrients for TBI

- **Curcumin** normalized brain-derived neurotrophic factor levels, and improved motor and learning performance in animals exposed to TBI.[86]
- **Sulforaphane** was shown to improve blood–brain barrier integrity,[87] reduce cerebral edema and improve cognition in a rodent model of TBI.[88]
- **Resveratrol** has been shown to reduce ROS, suppress excitotoxicity, and reduce inflammation in a controlled cortical impact model of TBI.[89]
- **Resveratrol** also reduced lipid peroxidation, decreased TBI lesion size, and specifically protected astrocytes after experimental TBI.[90]
- Ansari and colleagues showed that different types of **antioxidants** are depleted at various time points following mild TBI.[92] Therefore, targeting mild TBI with different types of antioxidants may be a **viable approach to treatment.**
  - **Luckwold, B et al. Nutri. Neuroscience 2016**

TBI, Sulforaphane, Curcumin & Resveratrol

▸ Nutr Neurosci. Author manuscript; available in PMC: 2019 Feb 1.

Published in final edited form as: Nutr Neurosci. 2016 Oct 5;21(2):79–91. doi: 10.1080/1028415X.2016.1236174

Supplements, nutrition, and alternative therapies for the treatment of traumatic brain injury

Brandon P Lucke-Wold [1,2,†], Aric F Logsdon [2,†], Linda Nguyen [2], Ahmed Eltanahay [3], Ryan C Turner [1], Patrick Bonasso [2], Chelsea Knotts [1], Adam Moeck [4], Joseph C Maroon [5], Julian E Bailes [6], Charles L Rosen [1]

Probiotics and TBI –

- **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

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.)

The Microbiome and Healthy Aging:

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

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.

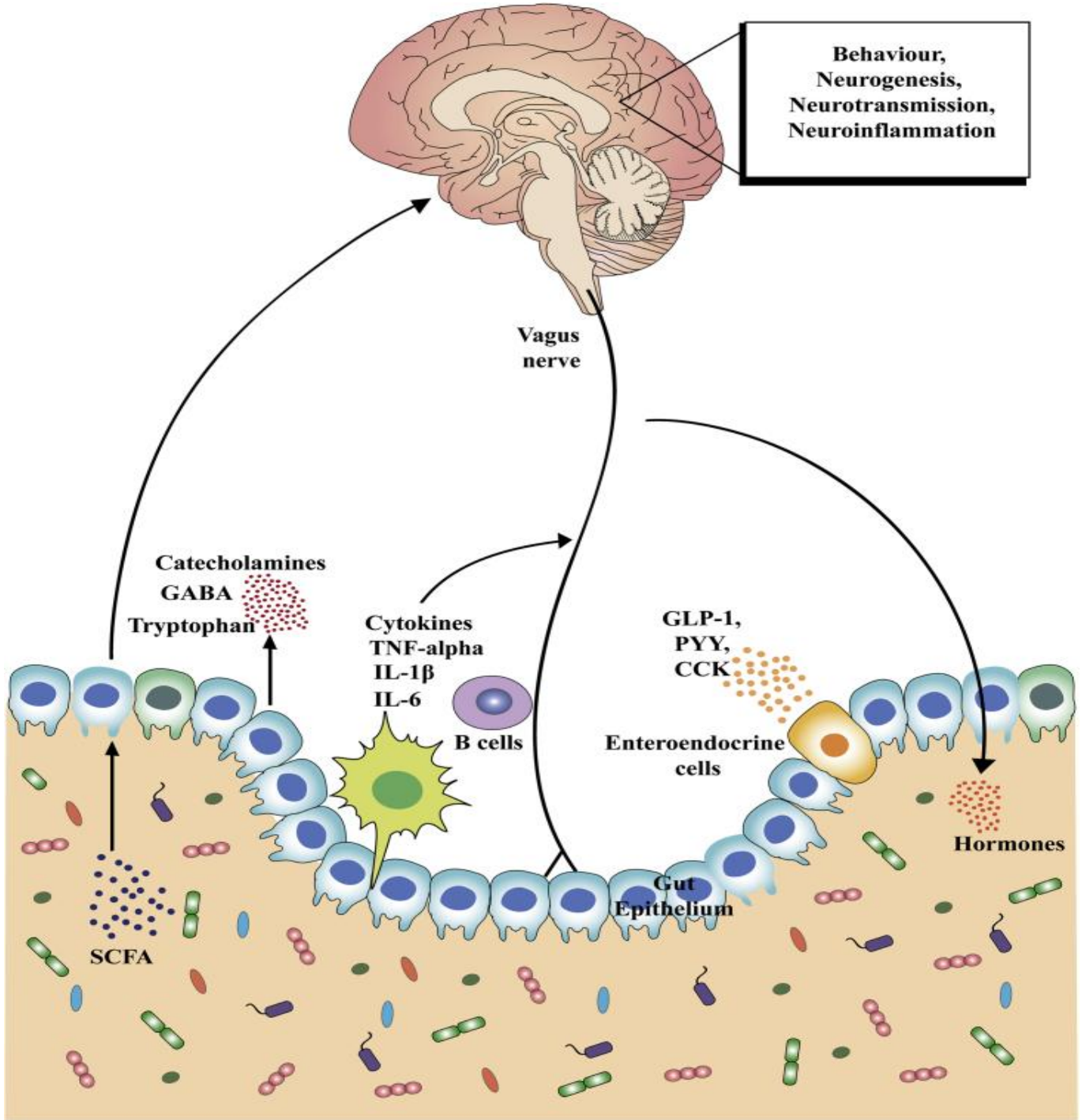
GLP-1R is a gene for the GLP-1 receptor

- **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.

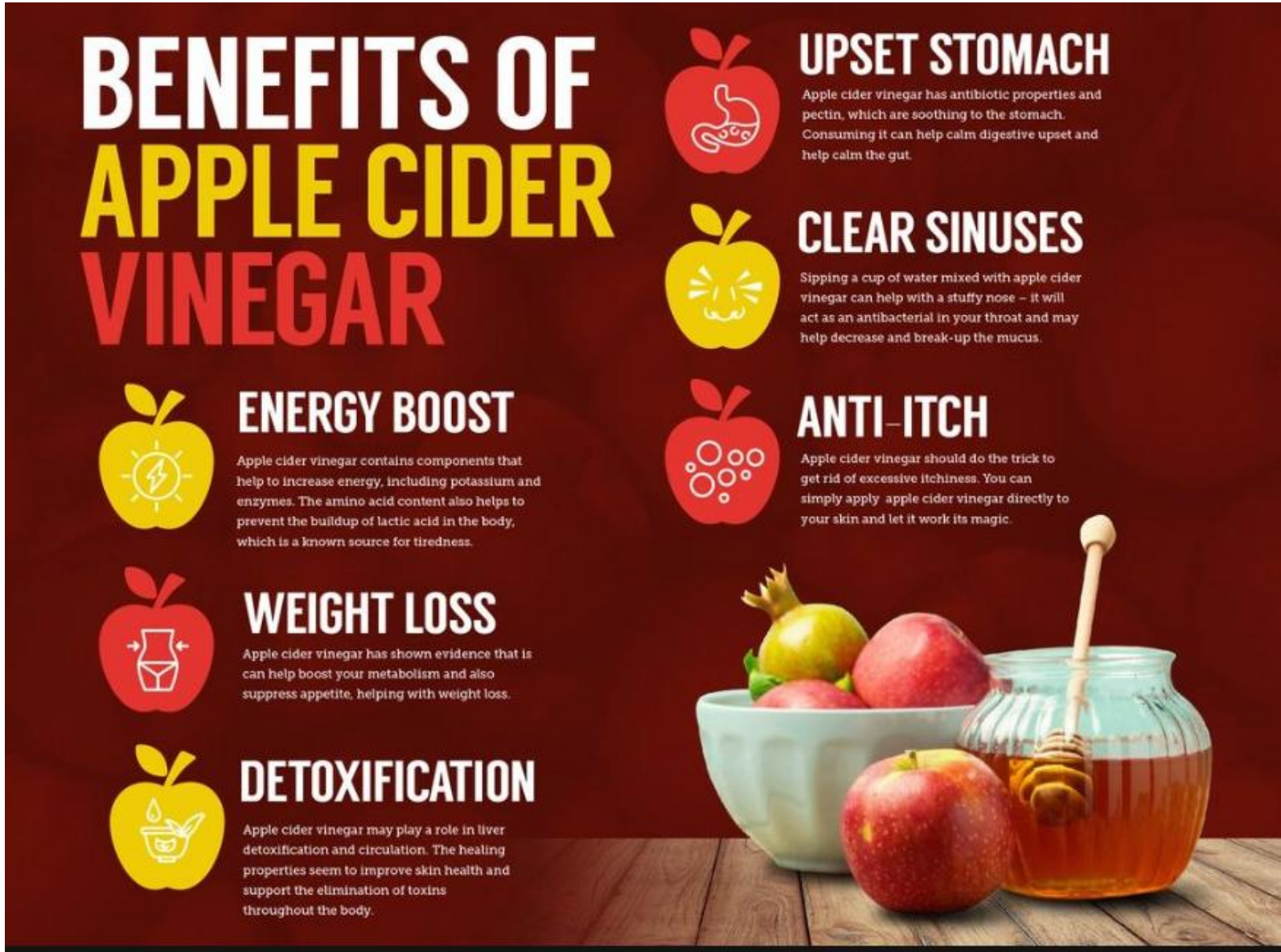
Prebiotic Foods to raise GLP-1

- 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:

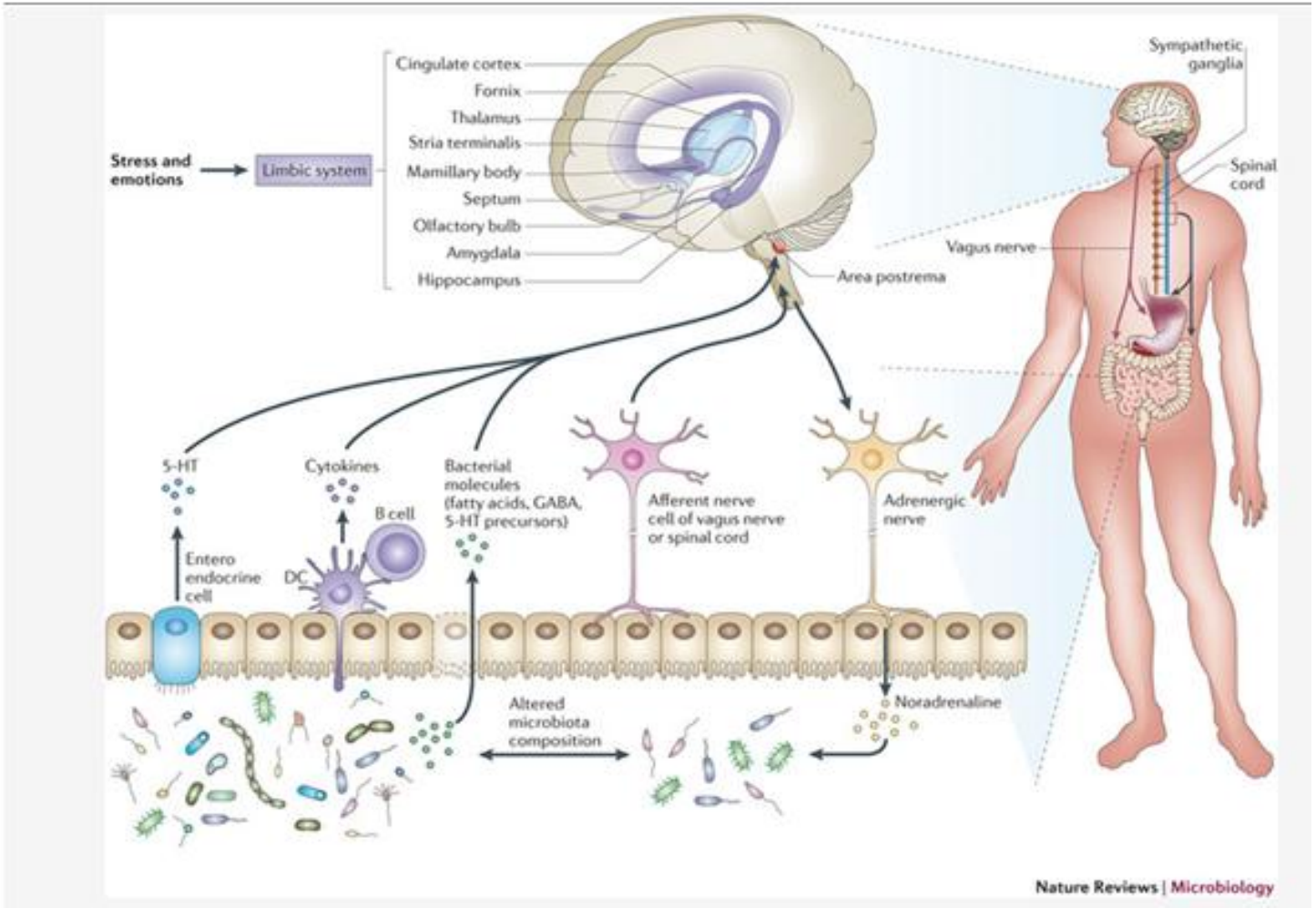
- Oral administration of the non-calorie sweetener, D-allulose induces GLP-1 release, activates vagal afferent signaling, reduces food intake and promotes glucose tolerance.
- Our results identify D-allulose as prominent GLP-1 releaser that acts via vagal afferents to restrict feeding and hyperglycemia. 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

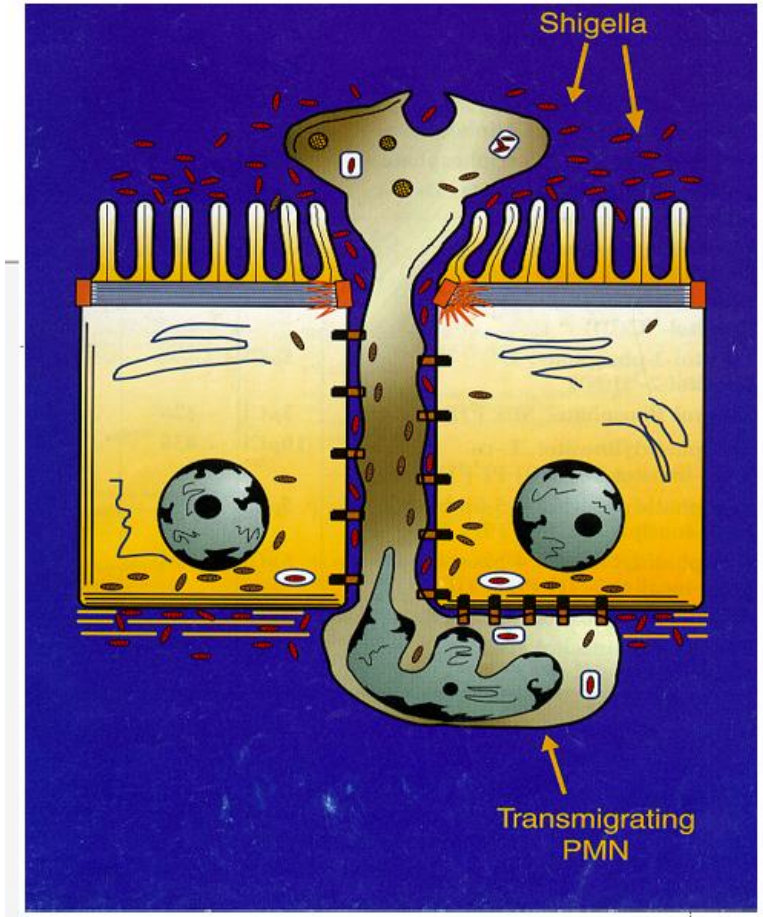
- Highly important for all those carrying the gene variant for the GLP-1 receptor.

- **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

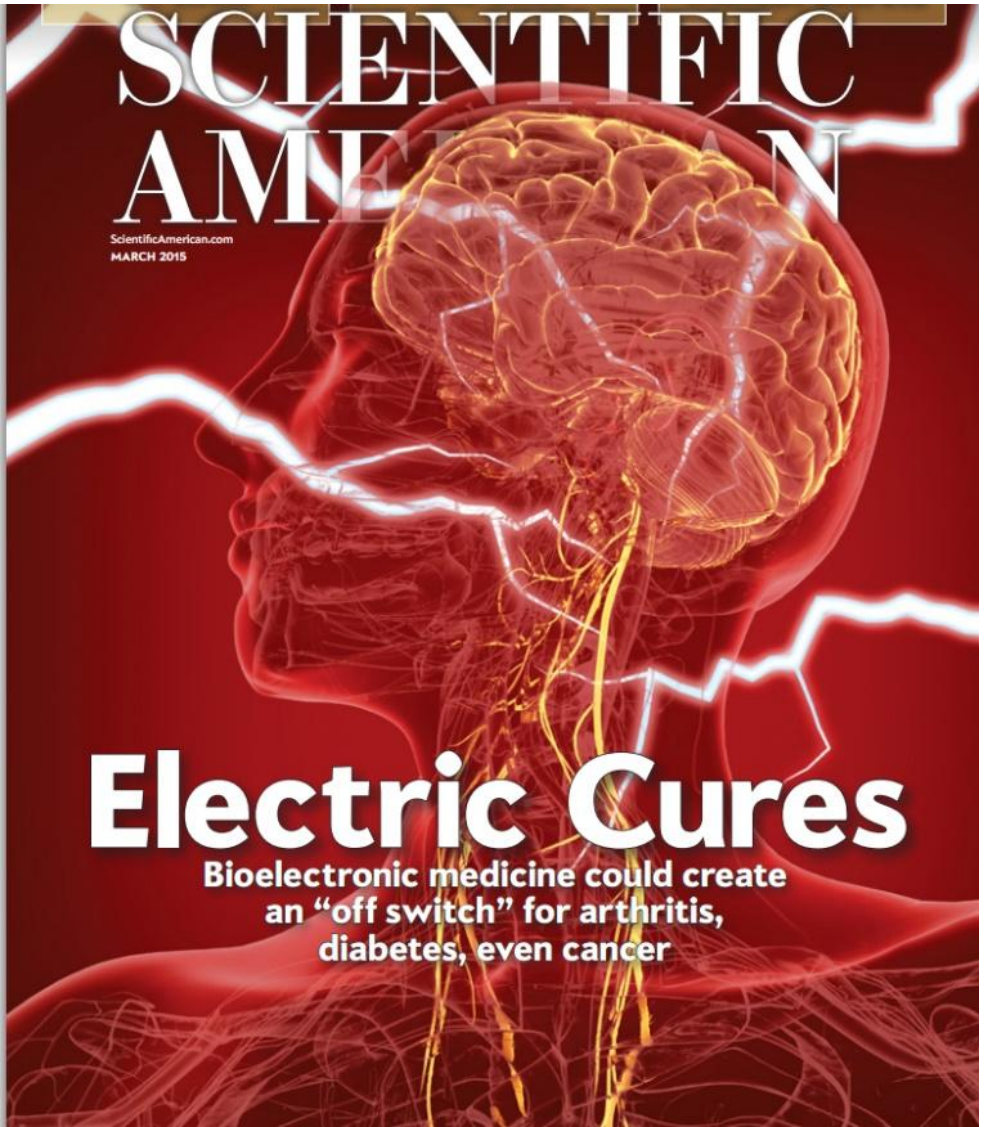
M-G-B (microbiota-gut-brain) Axis regulation by the microbiome

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.

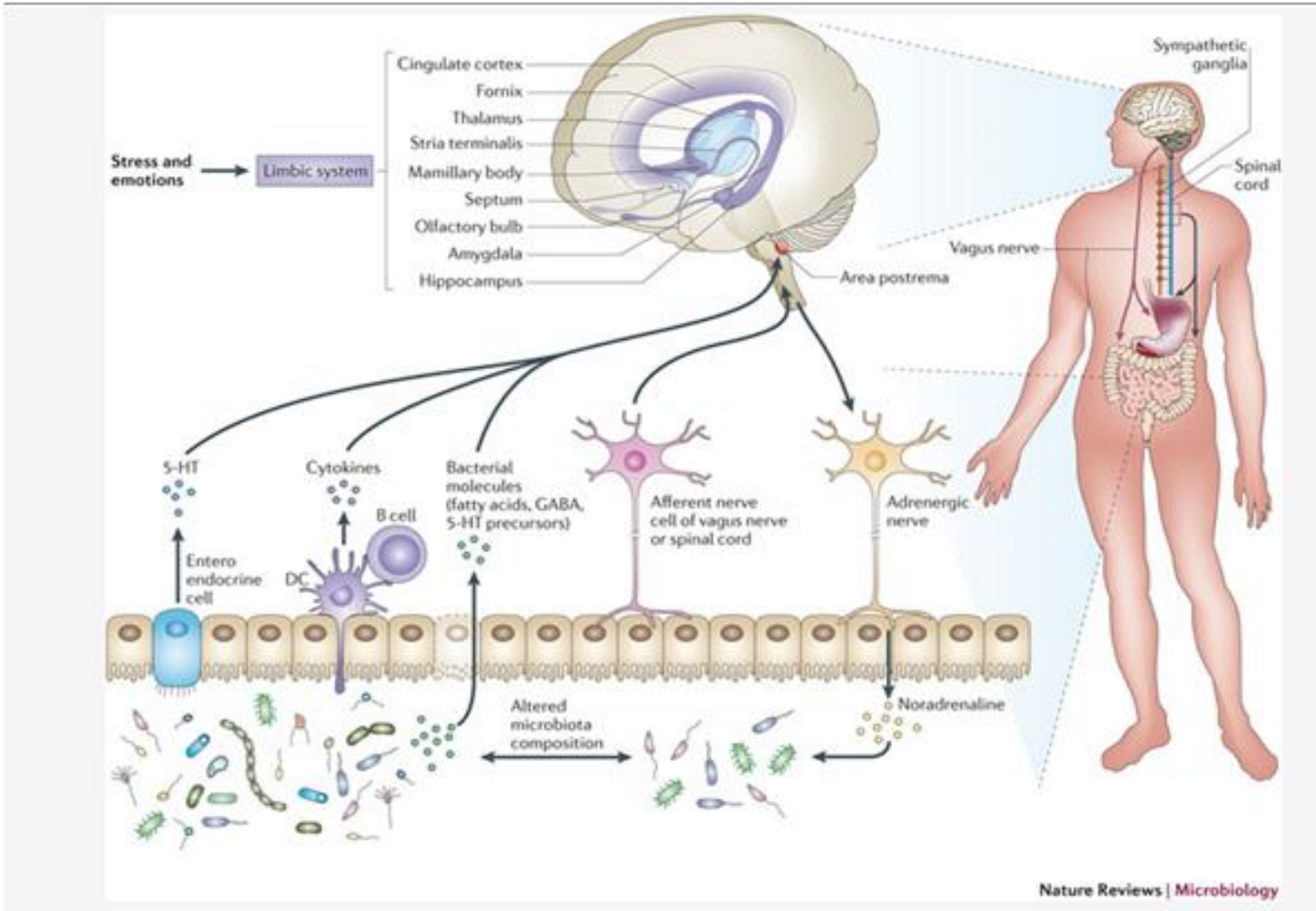
  - 1. Activation of the **vagus nerve**
  - 2. **NT production** norepinephrine,(5-HT (serotonin), dopamine, GABA γ-aminobutyric acid, AcH, tryptophan metabolism
  - 3. **Enteroendocrine signaling** from gut epithelial cells (e.g., CCK, GLP-1, Neuropeptide Y, PYY, somatostatin, VIP, oxytocin, CRF, pancreatic 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



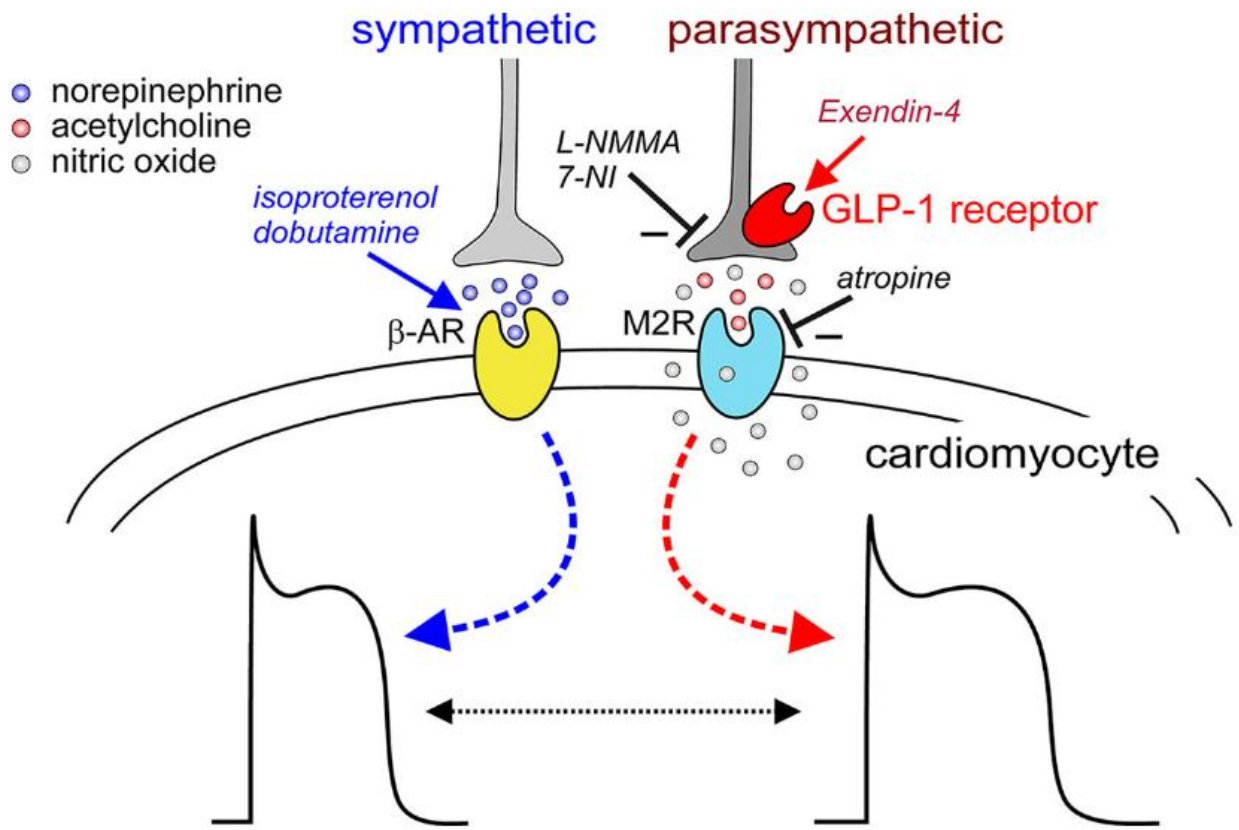
Chiropractic Stimulation of the Vagus Nerve

- 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 .

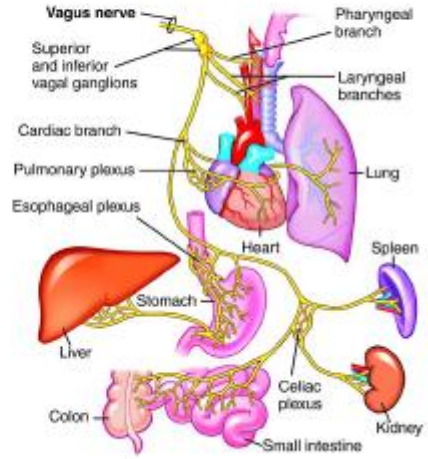


- **Epigenetic stimulation of the GLP-1 R**
- GLP-1 receptor activation opposes sympathetic effects on cardiac ventricular excitability and reduces ventricular arrhythmic potential.
- These effects are indirect, mediated by acetylcholine and nitric oxide, and can be explained by facilitated release of 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

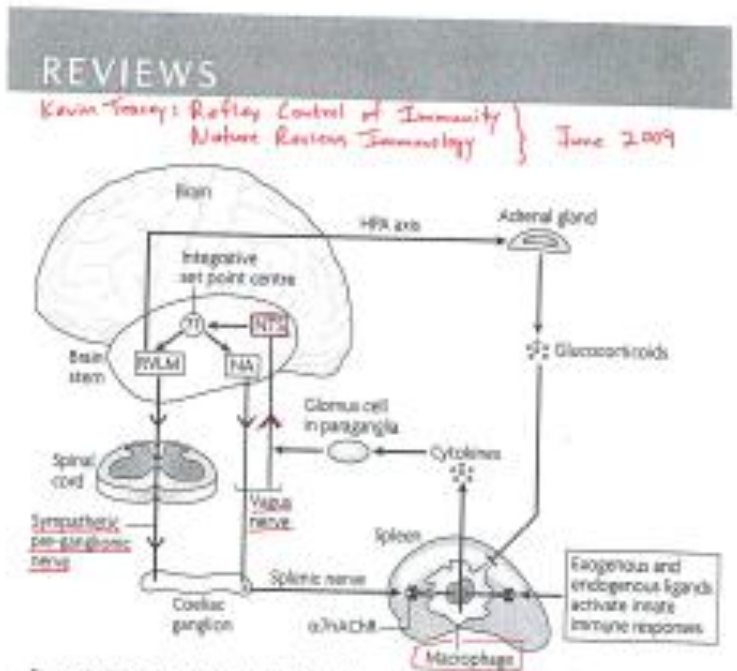
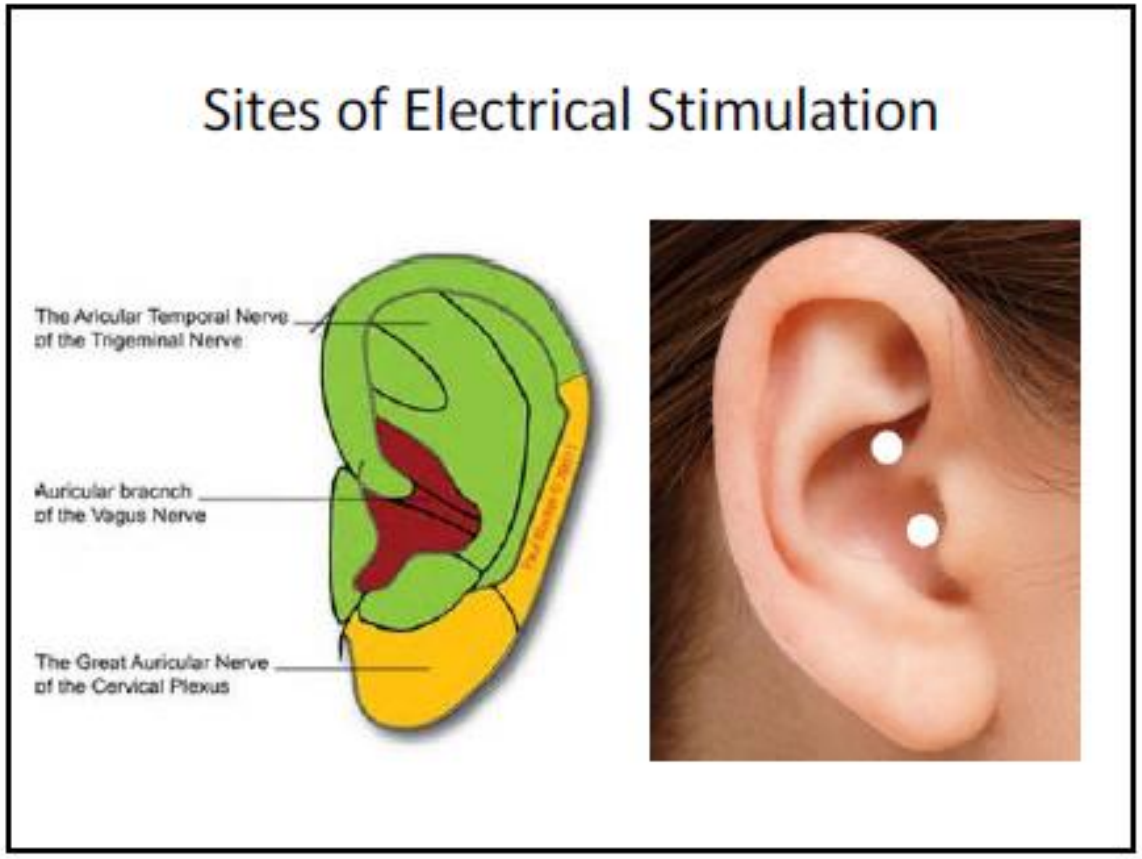


Figure 3 | **Functional anatomy of the inflammatory reflex.** Afferent (sensory) neural signals to the brain stem are relayed by the vagus nerve to the nucleus of the solitary tract (nucleus tractus solitarius; NTS). Polysynaptic relays then connect to the outflow centres of the autonomic nervous system, 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



Vagal Correction Sites

Correction exercises for vagal dysfunction:

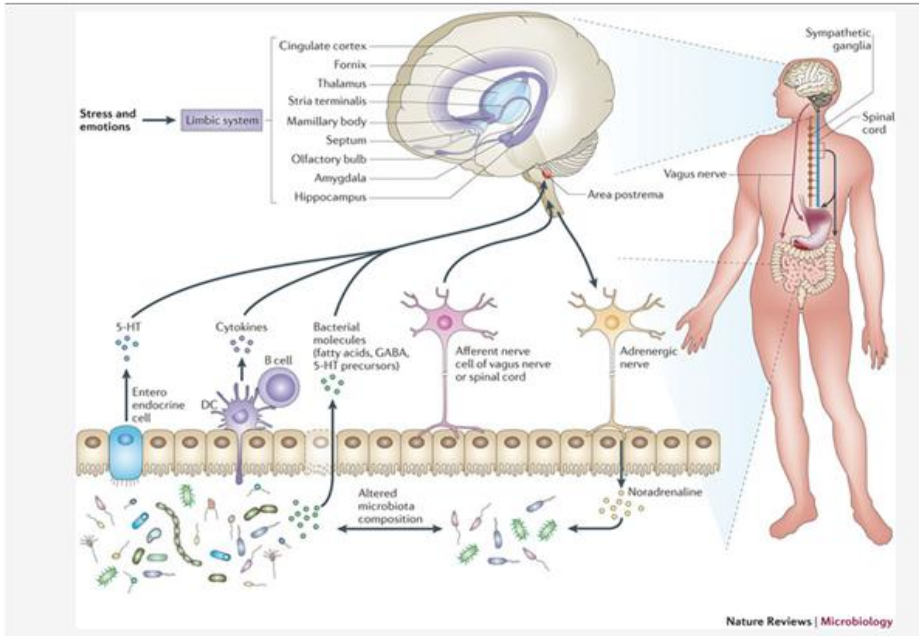
- Vagus: gargling, rub abdomen, abdominal pressure, humming, or repeating sound "OM" (Vagus nerve innervates vocal cords)
- Slow rhythmic diaphragmatic breathing
- Meditation, especially loving kindness meditation
  - Normally have patient perform activity three times a day for as many weeks as it takes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

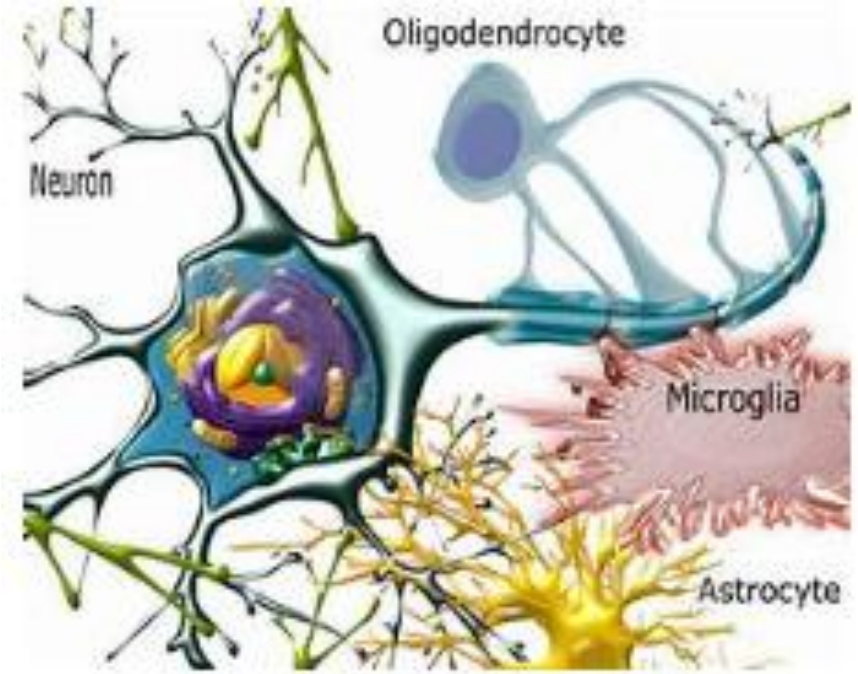
Wang H, et al. Promising Treatment for Type 2 Diabetes: Fecal Microbiota Transplantation Reverses Insulin Resistance and Impaired Islets. Front Cell Infect Microbiol. 2020 Jan 17;9:455

- 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.)**

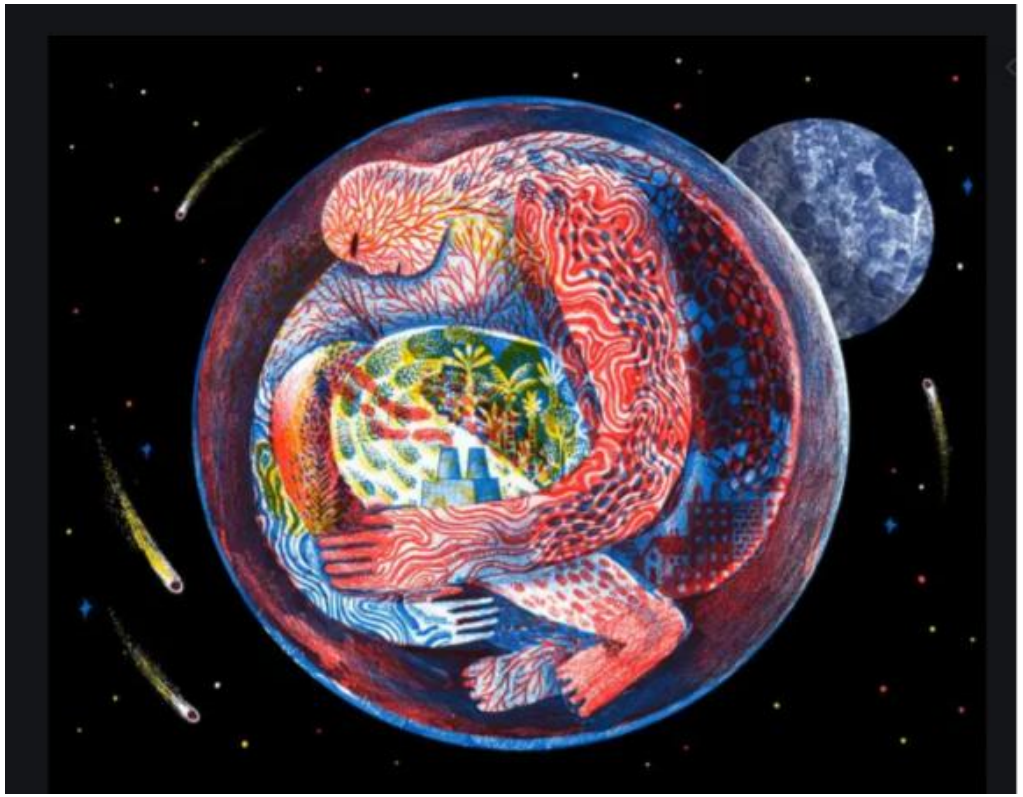


Effect on genes

- **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 were effectively reduced in 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

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

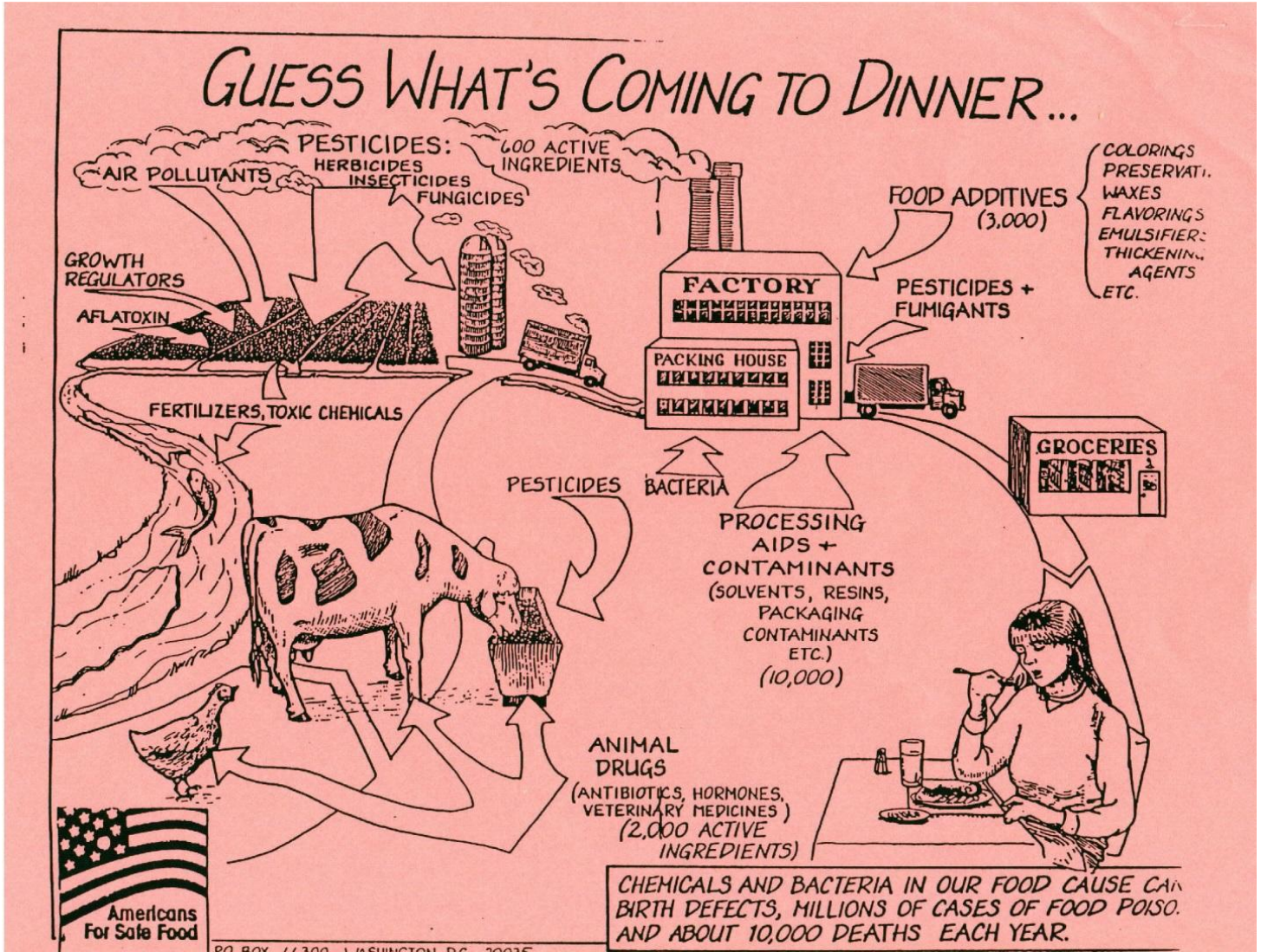
- "In the recent years the influence of xenoestrogens on oncogenes, specifically in relation to breast and prostate cancer has been the subject of considerable study"

- "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



Take Home Messages:

- **Chiropractic + movement + diet + supplementation = optimal epigenetic outcomes for longevity and quality of life**

- **Attention to genetic variations can help personalize diet + supplementation protocols to maximize efficiency of epigenetic contributions**

Supplementation Take Home Messages

- drtooheynutriwest@gmail.com for ideas and protocols for basic supplementation, including multi-vitamin and mineral, probiotics, fish oil, antioxidants, etc.

- NAC (at the very least)for senescent cells

- Personalize the nutritional protocol by testing DNA variants and run them through an analysis program

Thank You!

- **To the NCCA for the invitation and welcome**
- **To Nutri-West Coastal Plains for sponsorship**
- **To the audience for the reception**
- **Keep healthy and vital by paying attention to diet, lifestyle, supplements, chiropractic, and everything mentioned in this presentation to optimize reduced production and increased clearance of senescent cells.**

Extra slides on longevity for further reference:

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

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

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

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

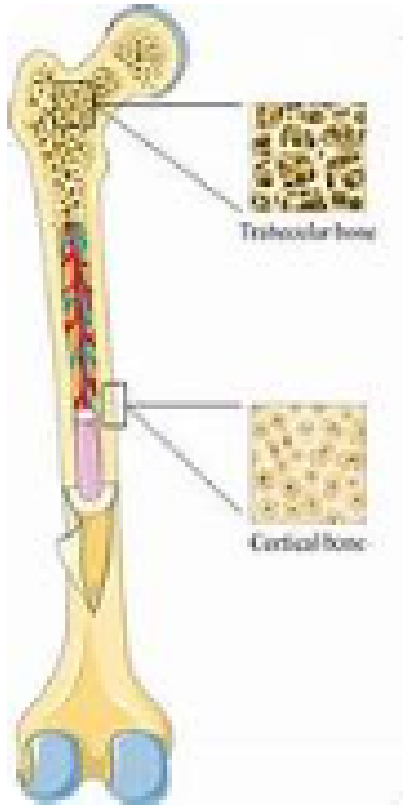
- Directly required during the early stages of **osteogenic, adipogenic, and chondrogenic differentiation** of hBMSCs.

- 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**

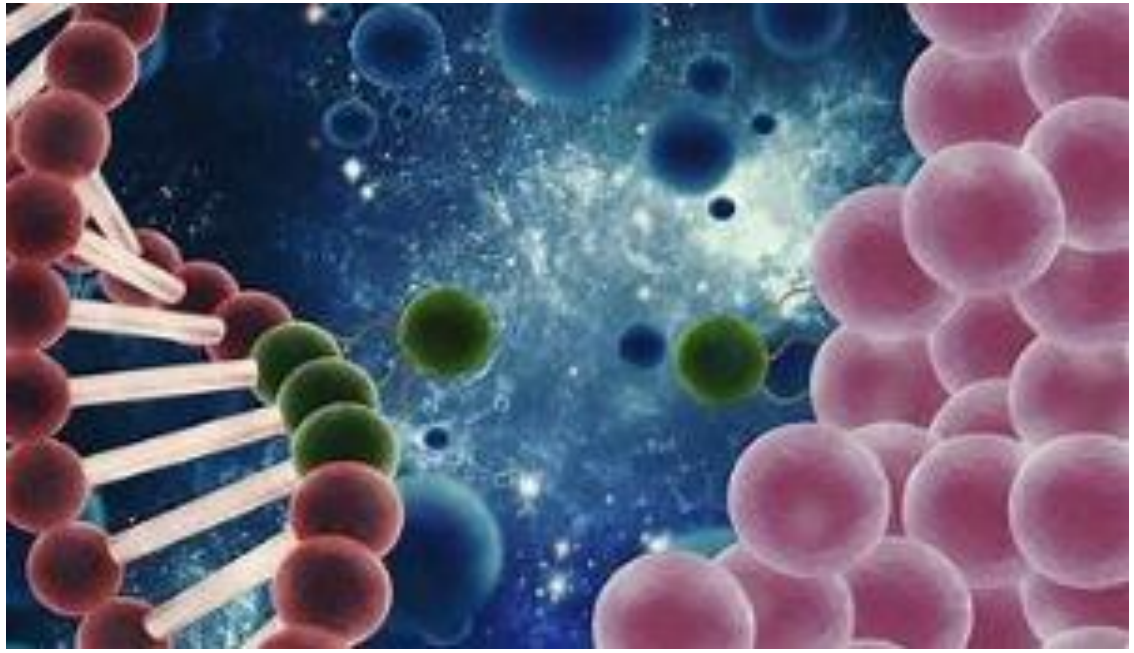
  Arjun, D. M.D. N Engl J Med June 5, 2019;380:2268-2270

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.”

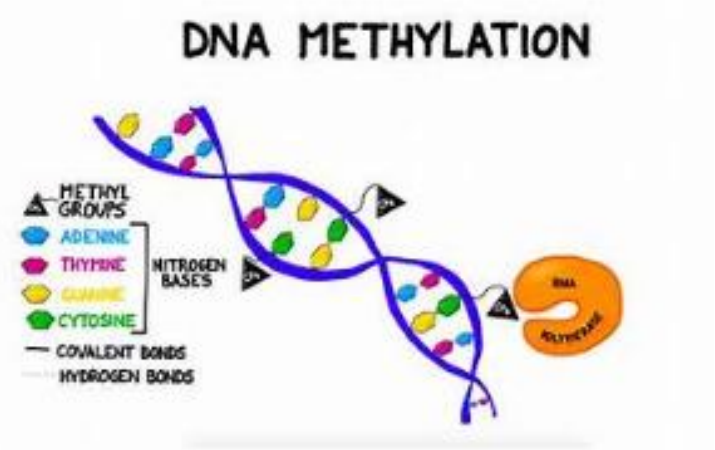
How Stem Cells Turn into Bone and Fat

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



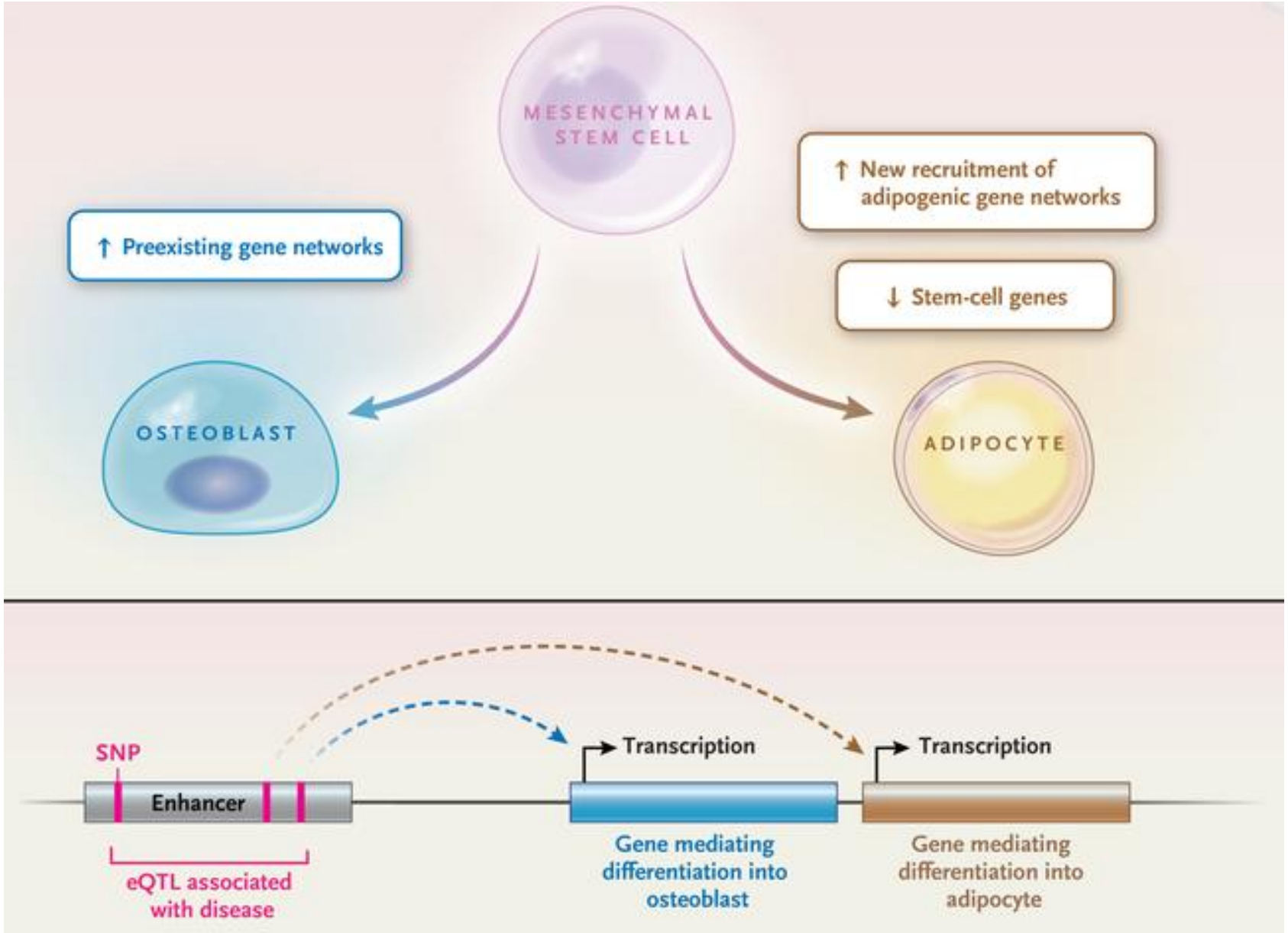
- Mesenchymal stem cells differentiate into the osteoblast lineage by activating different signaling pathways, including the **Wnt pathway**.

- 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.

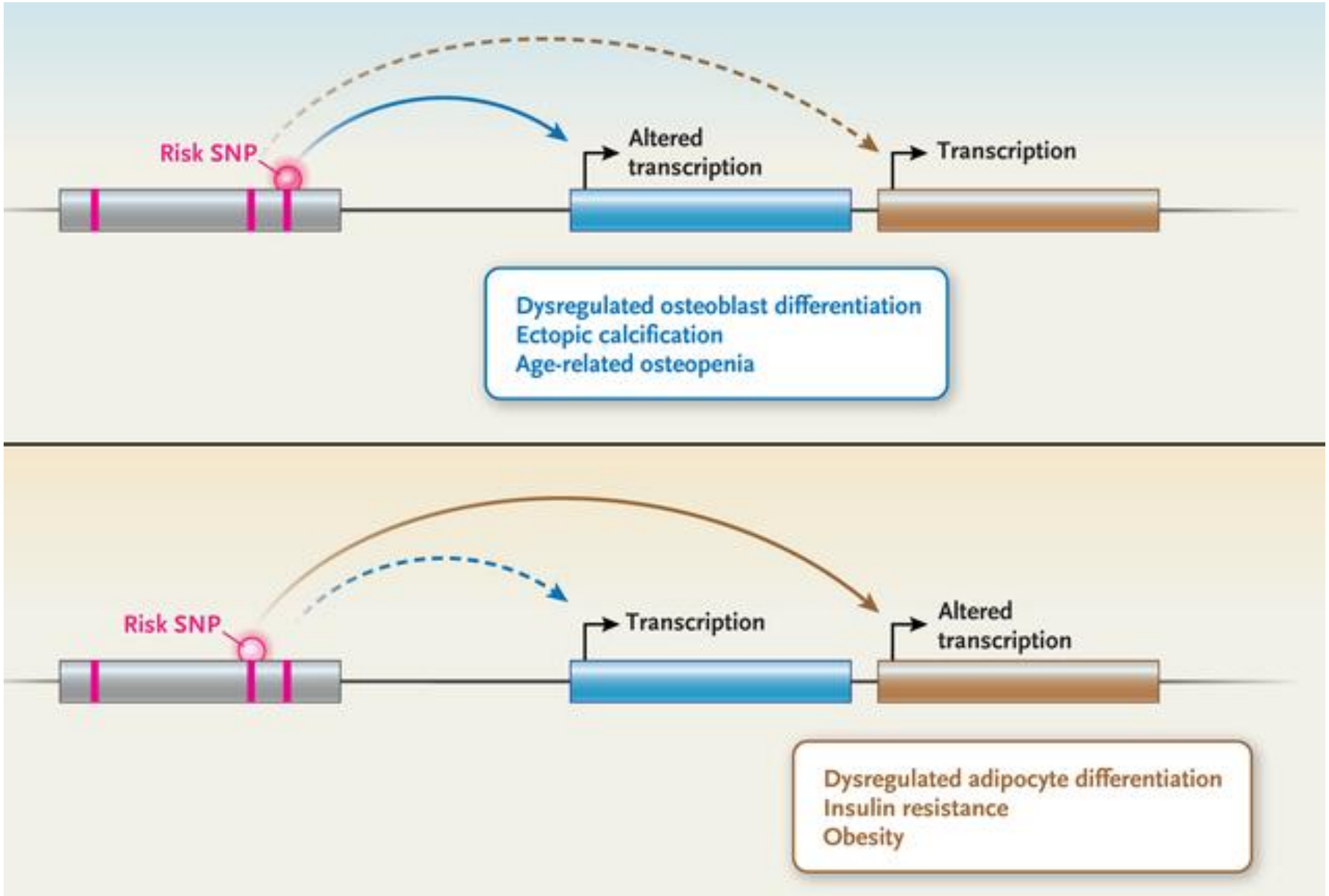
- Epigenetic influences like **vitamin C upregulate Wnt**

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

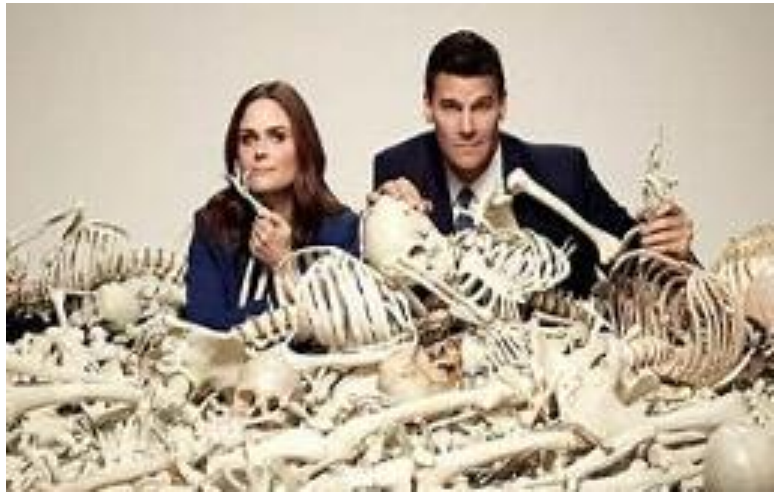
- **Mutations in more than 15 genes** have been implicated in the pathogenesis of osteoporosis.

- 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

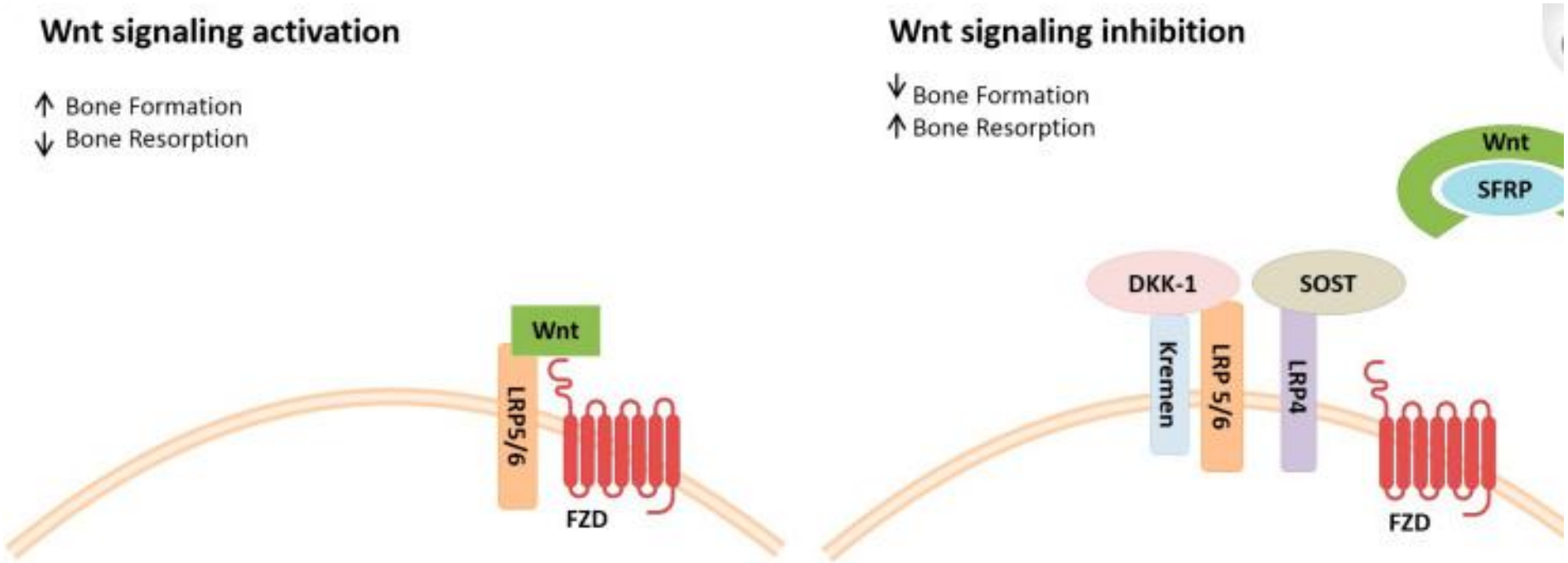
- Morrison et al., in 1994, first identified polymorphisms in the 3′ region of the VDR, which have been linked to **low ostecalcin levels and an increased risk of osteoporotic fracture**.



- 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

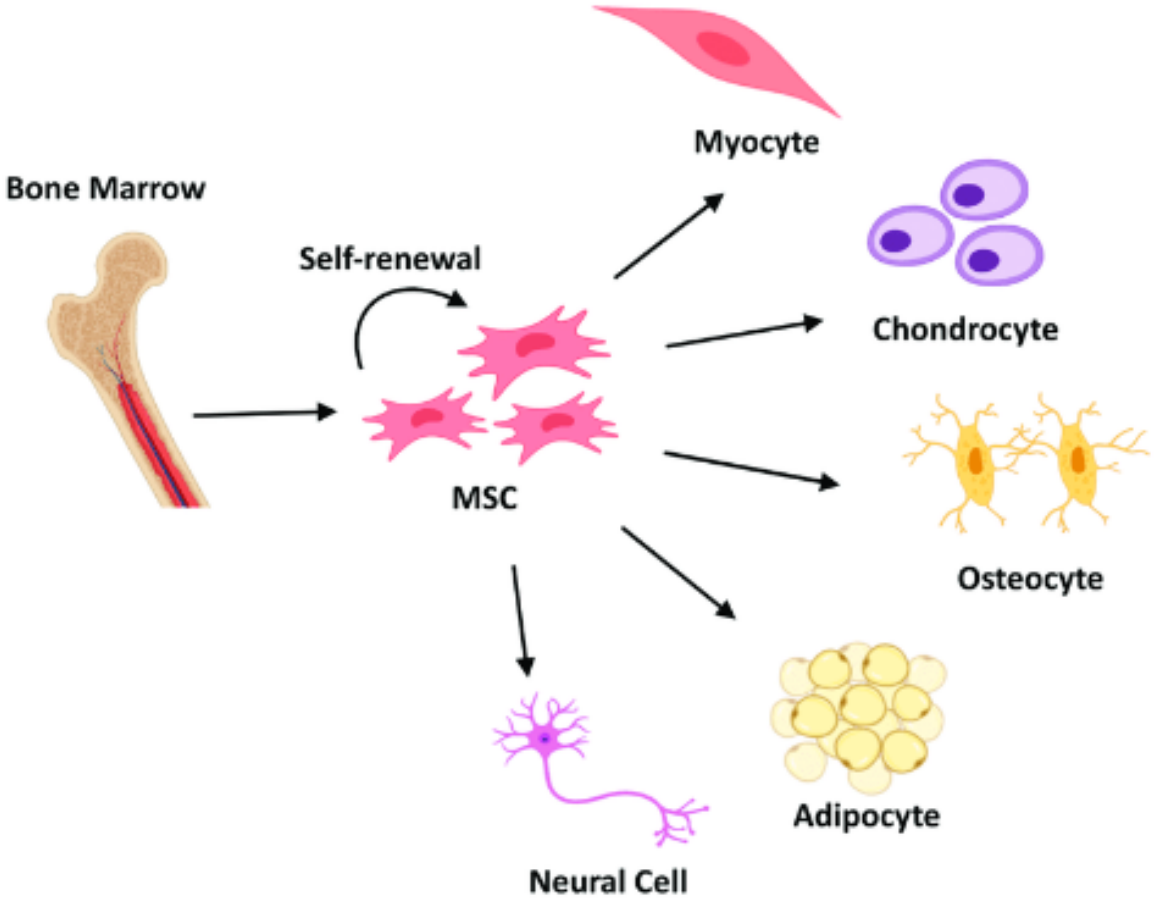
Environmental Epigenetic Factors

- **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.**

- **<u>Opposite of aging: Promoting Longevity</u>**
- **<u>Opposite of high fat diet: Healthy Smart Eating</u>**

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

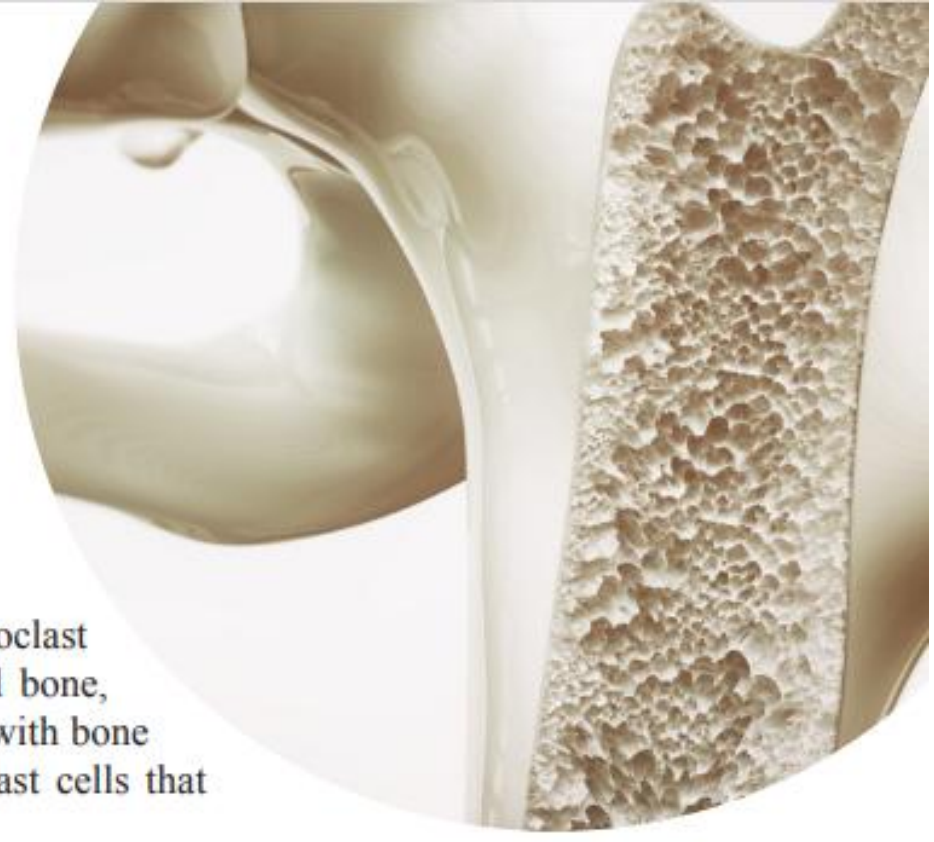
- Diet
- Supplementation
- Chiropractic

CLINICAL EXCELLENCE

Fighting Back Against Osteoporosis

Including natural stem cell support

by Lynn Toohey, PhD



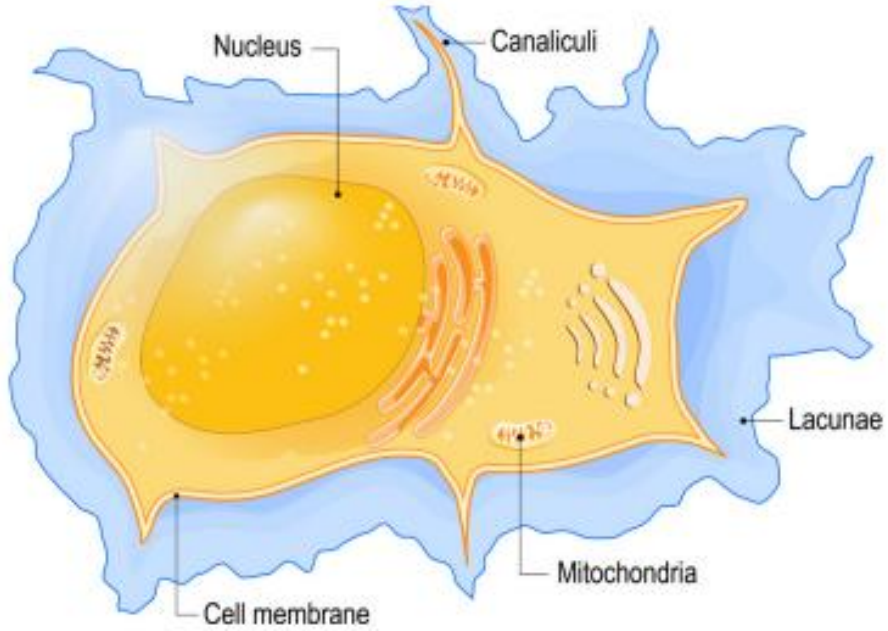
Osteoporosis is when bones become weak and brittle. Osteoclast cells break down bone, and osteoblast cells typically build bone, but with osteoporosis, new bone formation doesn't keep up with bone removal. We hear less about osteocytes, which are osteoblast cells that become embedded in the matrix it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

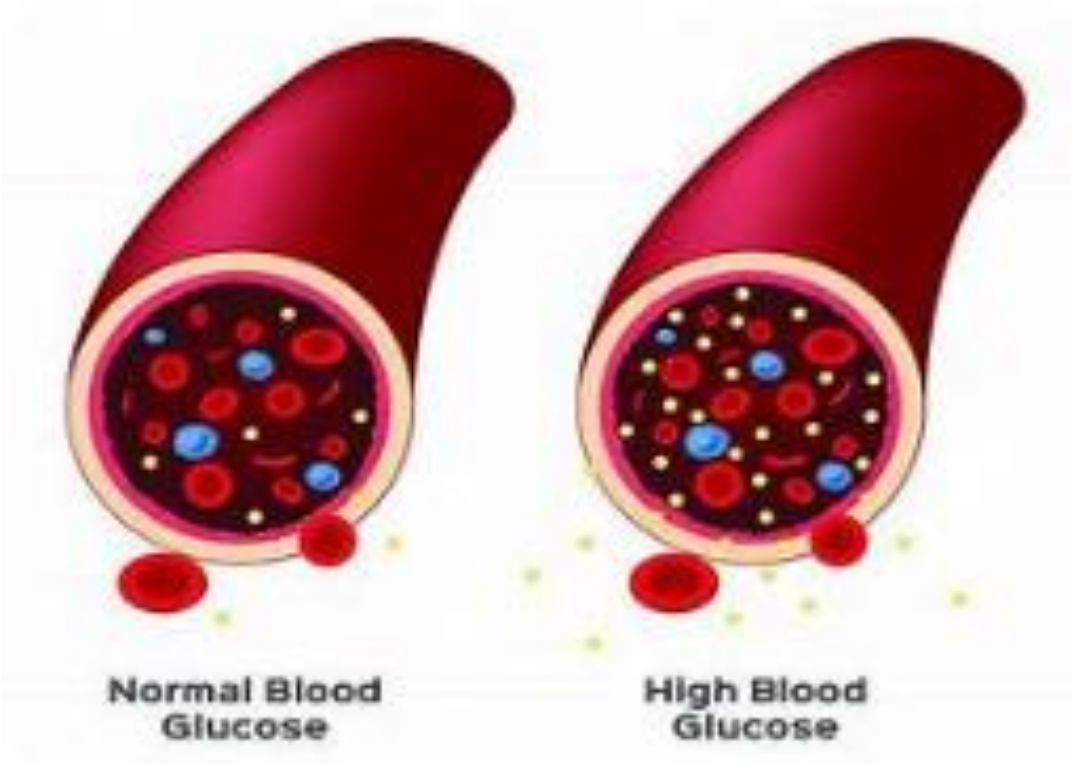
- All the more reason to entertain alternatives such as **curcumin, boswellia, ginger, quercetin, fish oil, melatonin** (see TAC May 2023 article on melatonin and pain), etc.

- 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

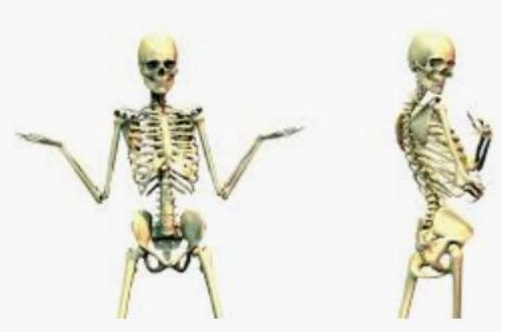
- Electrical or chiropractic stimulation of the vagus nerve has an added benefit of being non-invasive and **overcoming the hurdles of surgical implants that affect migration, proliferation, maturation and integration of the stem cells.**
- Additionally, the vagus nerve also **innervates the thyroid 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**

Thank You!

- **To the NCCA for the invitation and welcome**
- **To Nutri-West for sponsorship**
- **To the audience for the reception**
- **Keep healthy and vital by paying attention to diet, lifestyle, supplements, chiropractic, and everything mentioned in this presentation to optimize reduced production and increased clearance of senescent cells.**