# Protocols for the Paradigm in Healthcare

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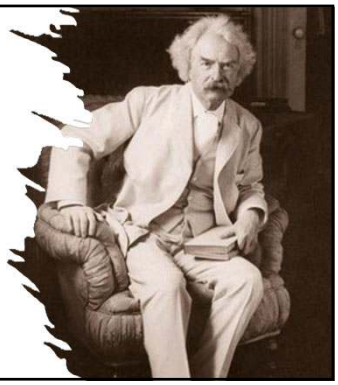
The two important days in your life are the day you were born and the day you find out why.

*Mark Twain*



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# HEALTHSPAN vs. LIFESPAN

What's the difference?

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## Hallmarks of aging

- Inflammation
- Mitochondrial dysfunction
- Microbiome
- Fascia injuries
- Telomere shortening
- Epigenetic damage
- Immune health/resilience
- Zombie/senescent cells
- Loss of muscle mass
- Disrupted nutrient sensing:
  - Insulin signaling
  - mTOR pathway
  - AMPK
  - Sirtuins
- Compromised autophagy

Adapted from the International Health Symposium, NYC 2023

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## Biomarkers for longevity

- IL-1β
- IL-6
- IL-8
- TNF-α
- C-reactive protein
- Hemoglobin A1C
- ApoE-4
- Blood pressure

**Ranking Biomarkers of Aging by Citation Profiling and Effort Scoring**. *Front Genet*, 21 May 2021;12

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## Biomarkers for longevity

- LP(a)
- Uric acid
- Body composition
- Telomere length
- Vo2 Max
- Max grip strength
- Mitochondrial dysfunction:
  - MDA, ROS
  - SOD, GPx

**Ranking Biomarkers of Aging by Citation Profiling and Effort Scoring**. *Front Genet*, 21 May 2021;12

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**MANAGE** **MODULATE**


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## Care for managing chronic inflammation

- Low GI diet
- Reduce saturated fat (trans fat)
- Increase Omega 9 and 3 fats
- Increase fruits and vegetables with Mediterranean diet concept
- Increase soluble/insoluble fiber/prebiotics
- Green and black tea polyphenols
- Vitamin B, C, D, E, zinc, selenium, magnesium
- Pro-resolving mediators
- Remove food sensitivities

Adapted from Dr. Jeff Bland, International Health Symposium, NYC 2023

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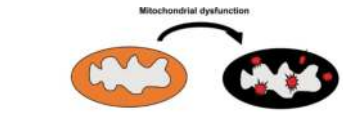
## Consequences of mitochondrial dysfunction




| | |
|---|---|
| Mitochondrial metabolism | Dysfunctional mitochondria |
| Redox homeostasis | Oxidative stress |
| ATP production | Decreased ATP levels |
| Respiration | Dysfunctional OXPHOS |
| Biogenesis | Altered mitochondrial biogenesis |
| Calcium homeostasis | Calcium imbalance |
| Cellular growth | Cell death |

**Mitochondria in skin health, aging, and disease**. *Cell Death & Disease*, *11*(6), 1-14

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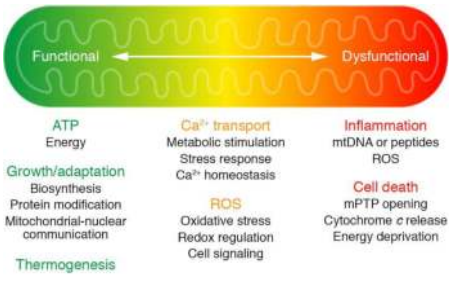
## Overview of mitochondrial function in health and disease




**Mitochondrial dysfunction in pathophysiology of heart failure.** *Journal of Clinical Investigation*, 20 Aug 2018;128

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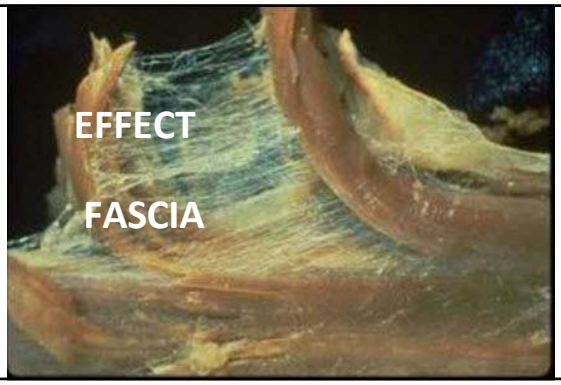
## Longevity of centenaries reflected by gut microbiome with youth-associated signatures

*"…centenarians displayed youth-associated features in the gut microbiome characterized by an over-representation of a Bacteroides-dominated enterotype, increase in species evenness, enrichment of potentially beneficial Bacteroidetes and depletion of potential pathobionts."*

S Pang, X Chen, Z Lu, *et al.* **Longevity of centenarians is reflected by the gut microbiome with youth-associated signatures.** *Nat Aging*, 6 April 2023

12

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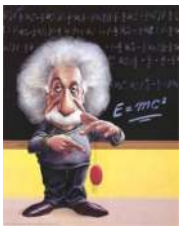
## Key

Extracellular matrix — the fascial system is the largest system in the body and is the only system that touches every other system

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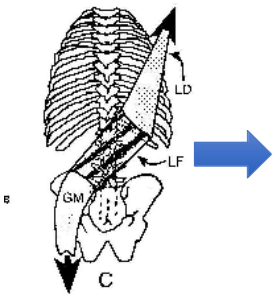


ACUTE/CHRONIC PAIN

PROLONGED FASCIAL CONTRACTION

MUSCULOSKELETAL PAIN

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# IT'S ALL CONNECTED

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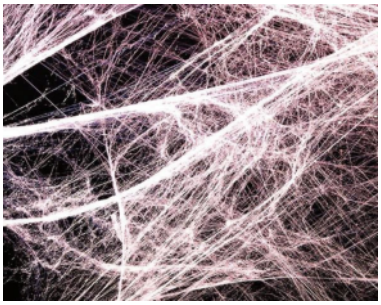
## Fascia

- Living matrix
- Full-body "wetsuit"
- Connective tissue
- Sheath in the body
- Below skin and above muscle
- Lymph nodes live in fascia
- Nerves are in fascia
- Our sensory organ
- Meridians in fascia
- Accounts for 20% of body mass



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## Back pain/fascia

- Fascia plays role in pain
- Interconnected system
- Transfer one region to another
- Ability to slide
- Plays role in back pain
- Without pain slide 75%
- With pain reduced to 50%

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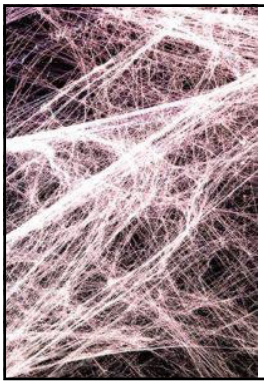

## Nutrients for fascia healing

- Collagen
- Glucosamine/chondroitin sulfate
- Bioflavonoids
- Vitamin C
- SOD
- Zinc
- Hops
- Magnesium
- Sulforaphane

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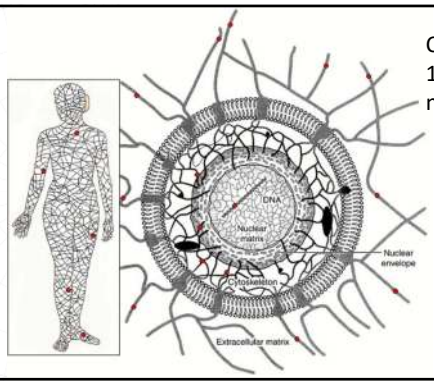


Connective tissue is 1000 X faster than nerve impulses

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*"The key to longevity is turning on the health switches; the MASTER switch is a robust immune system".*

Dr. Rob Silverman

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## Immunity is key to longevity

- New study from Tufts Medical Center and Boston U. School of Medicine – helping to answer question
- Centenarians possess a unique immune cell composition and activity, giving them a highly functional immune system and allowing them to live longer

https://www.medicalnewstoday.com/articles/scientists-may-have-found-the-immunity-secret-to-living-to-100
TT Karagiannis, TW Dowrey, C Villacorta-Martin, et al. **Multi-modal profiling of peripheral blood cells across the human lifespan reveals distinct immune cell signatures of aging and longevity.** *eBio Medicine*, 31 Mar 2023

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## Mastering the Longevity Code: "Immune Resilience" Is Key to Resisting Disease and Living Longer

- Ground-breaking research study introduces concept of "immune resilience"
- Term represents ability to withstand/bounce back from infections and inflammatory stressors
- Using novel metrics – quantified the varying degrees of immune resilience among individuals
- Findings – not solely age-dependent and can affect lifespan/health outcomes

Ahuja, S.K., Manoharan, M.S., Lee, G.C. *et al.* Immune resilience despite inflammatory stress promotes longevity and favorable health outcomes including resistance to infection. *Nat Commun* **14**, 3286 (2023). https://doi.org/10.1038/s41467-023-38238-6

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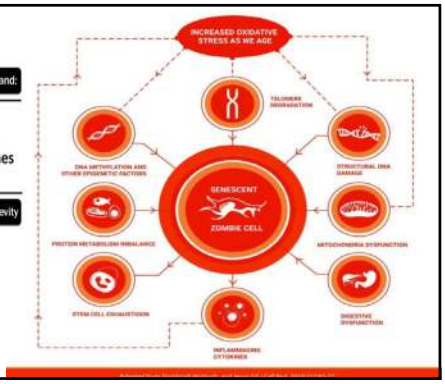
**Senescent cells** accumulate with normal aging and:

- Impede Organ Function
- Create Chronic Inflammation
- Emit Protein-Destroying Enzymes
- Shorten Healthy Lifespan

**Removing Senescent Cells Confers Healthy Longevity**

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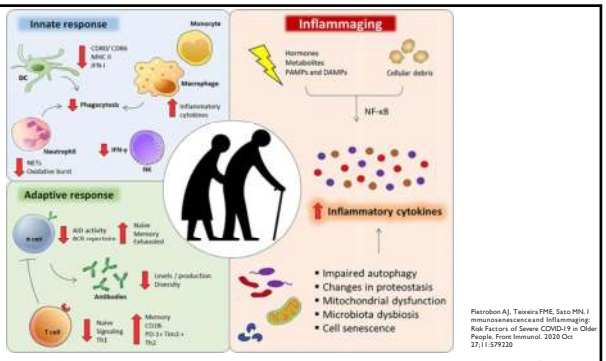


Pietrobon AJ, Teixeira FME, Sato MN. Immunosenescence and Inflammaging: Risk Factors of Severe COVID-19 in Older People. Front Immunol. 2020 Oct 27;11:579220

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## Avoiding sarcopenia

- 1-2% muscle lost each year after age 40
- May lose 25% muscle mass by 65
- Less muscle mass leads to inability to efficiently dispose of glucose
- Animal protein has BCAA, leucine, iso-leucine, and valine
- Micronutrients supporting protein synthesis:
  - Vitamin C, K, Ca, Zn, Mg
  - Omega-3 FA
  - HMB – "anti-catabolic" agent

https://www.nutraingredients.com/Article/2023/08/14/Sports-nutrition-for-sarcopenia-the-missed-opportunity

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## MUSCLE MASS
– organ of longevity

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## Switches of aging

AMPK – activated protein kinase:

- Regulates amount of energy
- A nutrient and energy sensor
- Maintains energy homeostasis

Stimulate AMPK:

- ALA
- Berberine
- Omega-3
- Resveratrol
- IF
- High-intensity exercise
- Caffeine

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## Switches of aging

- Sirtuins – protect cell from damage:
  - Repair
  - Reduce inflammation
  - Boost memory
  - Impaired mitochondrial health
- Stimulated by:
  - NMN-NAD
  - EGCG
  - Turmeric
  - Resveratrol
  - Quercetin
  - Exercise
  - IF
  - EVOO
  - Coffee

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## Switches of aging (cont'd)

- mTOR – central processing unit that makes all complex decisions relating to cellular growth
- Signal for growth rather than survival

- Balance/dim:
  - Resveratrol
  - Quercetin
  - Zinc
  - Melatonin
  - Omega-3 fatty acids
  - Curcumin
  - Coffee
  - IF
  - Vitamin D
  - Keto diet

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## Switches of aging
(cont'd)

- More Sirtuins
- Less mTOR
- More AMPK


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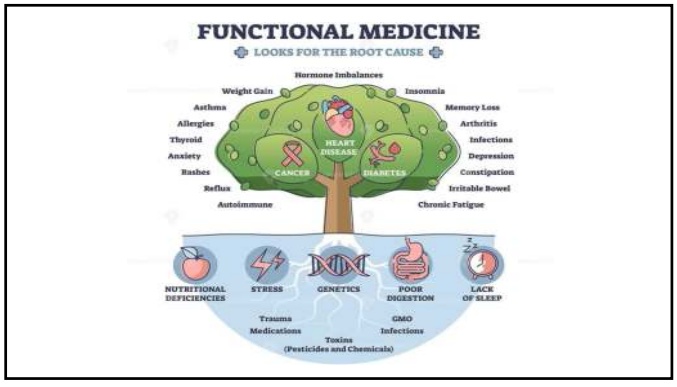


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Concept

**N-of-1**

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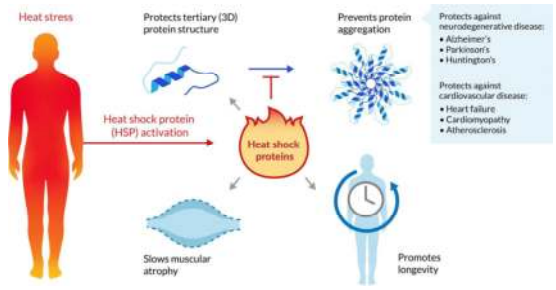
## Heat shock proteins provide protection against cellular stress




**Sauna use as a lifestyle practice to extend healthspan**. *Experimental Gerontology*, 15 Oct 2021;154:111509

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## Cold-shock protein

- Reserve proteins released from liver – dumped into the bloodstream:
  - Anti-inflammatory
  - Support wound-healing
  - Increase muscle repair
  - Increase protein synthesis
  - Increase free radical oxygenation
  - Comes from cold water immersion – 50-59ºF, 5 mins.

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# Importance of Sleep

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Natural Sleep Foundation:

- 35% of adults less than 7 hours of sleep
- 30% have frequent insomnia
- Lack of sleep damages immune system
- They have bidirectional relationship

Even one night of inadequate sleep can damage the immune system

Sleep/brain

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Video courtesy of Laura Lewis / Boston University

*The red waves show blood oxygenation in the brain, followed by blue waves of cerebrospinal fluid.*

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## Key Nutrients for Sleep

- Vitamin B6 (as pyridoxal 5'-phosphate)
- Taurine
- 5-HTP (L-5-Hydroxy-Tryptophan)
- Passionflower, lemon balm ,Hops & valerian
- L-Theanine
- Calcium & magnesium
- MELATONIN

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## Dr. Rob's leading-edge nutrients for longevity

- Fisetin
- EGCG
- Spermidine
- Luteolin
- 2-HOBA
- PEA
- BPC-157

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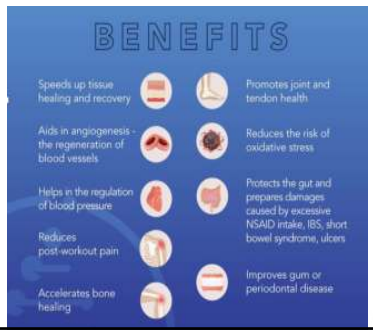
## What is BPC-157?

A peptide referred to as **"Wolverine" supplement** – amazing healing capabilities

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## Could Non-Thermal Laser (NTL) be the answer for longevity?

- Non-invasive
- No downtime
- No pain
- Short treatment time
- Pain-relieving properties
- Decreases swelling
- Improves blood flow
- Enhances energy production
- Optimizes mitochondrial function
- Anti-inflammatory
- Immune boosting properties
- Promotes stem cell production
- Decreases stress hormones
- Neuroprotective
- Down-regulates stress responses in brain
- Accelerates wound-healing
- Upregulates collagen production
- Fat loss
- Cellulite reduction
- Skin conditions

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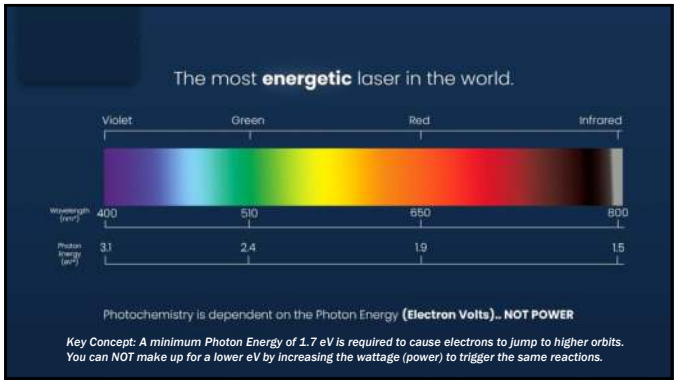


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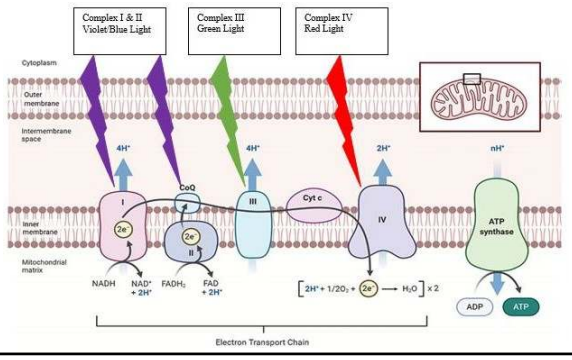


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Mesenchymal Stem Cells Synergize with 635, 532, and 405 nm Laser Wavelengths in Renal Fibrosis: A Pilot Study

635nm
Mitochondrial Activity
Proliferative activity
Production of IL-10

405nm
Reduction of Apoptotic cells on fibrous tissues
Improved breakdown of scar tissue due to high eV

532nm
Reduction of TGF-B
Biggest stimulation of stem cells

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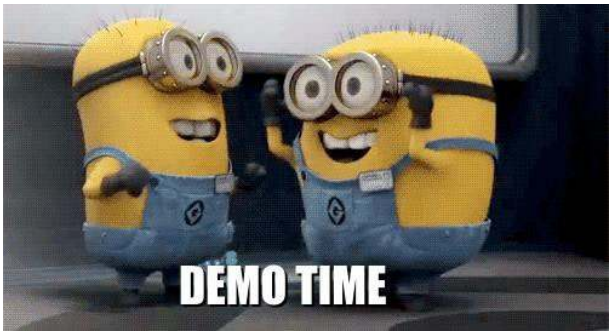


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# Rebalance

## the nervous system

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## As simple as 1, 2, 3

- Point and shoot – static positioning of the patient and laser
- passive – doctor moves patient and moves laser
- Active – patient moves limb and doctor moves laser

**Bonus**

Laser cerebellum for brain up-regulation (laser "locomotor lock-in")

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## Laser "Locomotor Lock-In"

- Resets NMS in 3D motion
- 4, 9, 33, 60
- Facilitated bodies global integration
- 5 sec. eyes open, 5 sec. eyes closed
- Cross-crawl: right arm – left leg, left arm – right leg
- Aim posterior midline-spine
- Repeat pointing at brain

1) Violet 405 Nm – directly over spinal cord
2) Red 635 Nm – over adjacent nerve roots
3) Both lights - cerebellum

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## Scar

- EVRL: 8,25,42,279
- Simultaneously with:
  - Myofascial release – directional
  - Instrument-assisted soft-tissue mobilization
  - Percussor

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## Vagus nerve demo

The perfect 10


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## Dr. Rob's longevity hacks

1) Nutrition – food "Food is medicine"
2) Dramatically reduce sugar, starch, processed foods intake
3) Exercise – incorporate resistance training
4) Sleep
5) Health detectables
6) Meditate
7) Intermittent fasting
8) Supplements
9) Purpose/mission/community
10) Hormesis - hot and cold exposure
11) Low-level-laser

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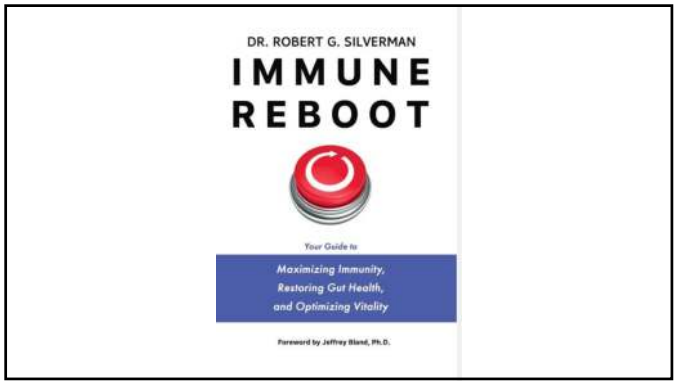


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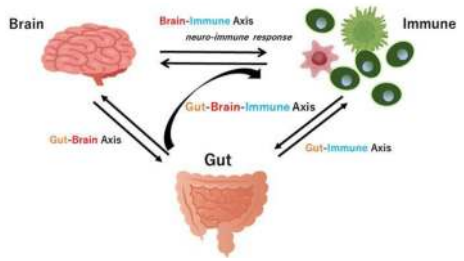
Hypothetical schematic overview and appearance of gut-brain axis cross-talk between the brain and the gut (intestine/colon) in addition to the brain-immune axis and the gut-immune axis




Gut microbiota could modulate the effects of neuro-immune responses and memory traces via the gut-brain-immune axis in schizophrenia. *Explor Neuroprot Ther.* 2022;2:74–86

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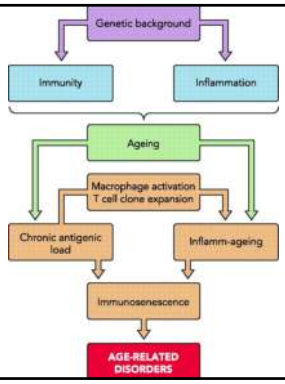
Effect of genetic background and aging on immune system




Aging of the Immune System as a Prognostic Factor for Human Longevity. *Physiology, 2008*

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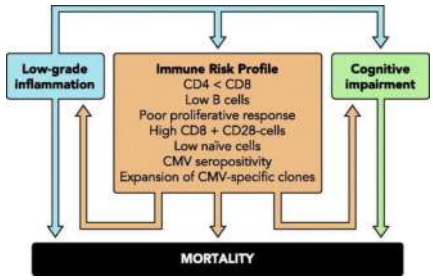
## Interplay between the IRP, low grade inflammation, and cognitive impairment in mortality




Aging of the Immune System as a Prognostic Factor for Human Longevity. *Physiology, 2008*

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## "You are only as young as your immune system"


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## The immune system provides 3 levels of defense against disease-causing organisms

| 1 | 2 | 3 |
|---|---|---|
| **BARRIERS** | **INNATE IMMUNITY** | **ACQUIRED IMMUNITY** |
| *Prevent entry* | *General defense* | *Specific defense* |
| • Skin & mucus membranes<br>• Stomach acid & digestive enzymes<br>• Beneficial bacteria that live in the colon (the gut microbiota) | • WBCs, called neutrophils & macrophages, engulf & destroy foreign invaders & damaged cells | • WBCs called T lymphocytes (T cells) target & destroy infected or cancerous cells<br>• WBC's called B lymphocytes (B cells) & plasma cells produce antibodies that target & destroy infected or cancerous cells |

Innate vs. acquired immunity

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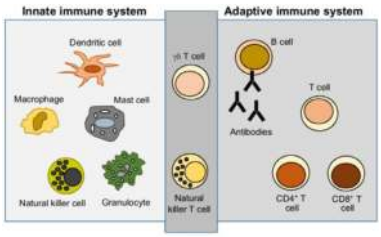
## Cells of the innate and adaptive immune systems




**Genetically modified T cells in cancer therapy: Opportunities and challenges**. *Disease models & mechanisms*. April 2015;8(4):337-350

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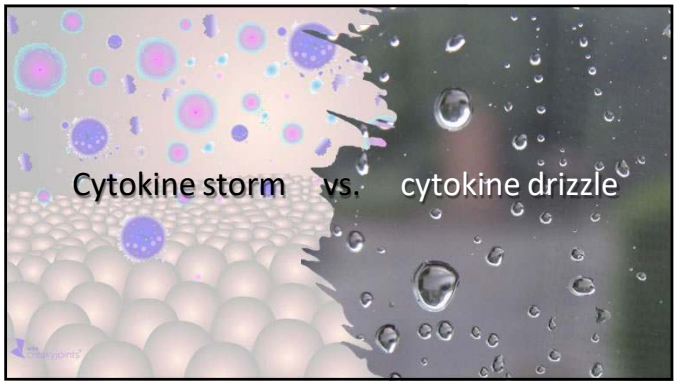


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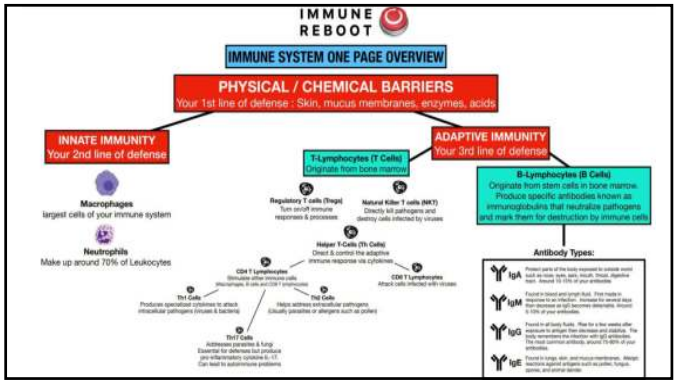


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## Normal Immune Response to Infection


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## Immune Response to Infection


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## Immune imprinting (original antigenic sin)

A phenomenon in which the body preferentially repeats its immune response to the first variant it encountered, despite being alerted to a new variant

**Immune Imprinting and Protection against Repeat Reinfection with SARS-CoV-2.** *N Engl J Med*, 3 Nov 2022; 387:1716-1718

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## Are Our Immune Systems Stuck in 2020?

You never forget your first time with SARS-CoV-2

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## Immune imprinting/long-COVID

- MIT and Harvard
- 112 patients – neurological long-COVID symptoms:
  - Inflammation of brain with cognitive deficits
- Found:
  - Underwhelming antibodies to COVID
  - Overwhelming antibody response to other coronaviruses

**Findings** suggest – immune imprinting can cause neurological long-COVID

M Spatola, N Nziza, WY Jung, et al. **Neurologic sequalae of COVID-19 are determined by immunologic imprinting from previous Coronaviruses**. *medRxiv* 2022.11.07.22282030

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## Accelerated biological aging in COVID-19 patients

- Accelerated epigenetic aging associated with risk of SARS-CoV-2 infection and developing severe COVID-19
- Accumulation of epigenetic aging from COVID-19 may contribute to post COVID-19 syndrome among survivors

X Cao, W Li, T Wang, T. *et al*. **Accelerated biological aging in COVID-19 patients.** *Nat Commun*, 19 April 2022;13(2135)

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## Telomere shortening/COVID-19

**Results:**

- Show a consistent biological age increase in post-COVID-19 population
- Significant telomere shortening parallels this finding in post-COVID-19 cohort compared with COVID-19-free subjects
- ACE2 expression was decreased in post-COVID-19 patients compared with COVID-19-free population

Mongelli A, Barbi V, Gottardi Zamperla M, et al. **Evidence for Biological Age Acceleration and Telomere Shortening in COVID-19 Survivors**. *Int J Mol Sci*. 2021;22(11):6151

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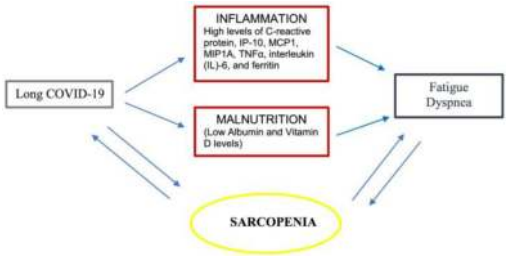
## Interaction between COVID-19 and sarcopenia




**Sarcopenia as potential biological substrate of long COVID-19 syndrome: prevalence, clinical features, and risk factors.** *J Cachexia Sarcopenia Muscle*, 14 June 2022;13(4):1974-82

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## Influence of nutritional intakes in Japan and the US on COVID-19 infection

- COVID cases - 12.1 X higher in the US than Japan
- Death - 17.4 X higher in the US than Japan
- Prevalence of obesity:
  - American men – 7.4 X greater
  - American women – 10 X greater

**Diet**

- 1.5 X more saturated fat, less EPA/DHA consumed in the US than in Japan
- US consumes more: beef 396%, sugar and sweeteners 235%
- Japan more: fish 44.3%, rice 11.5%, tea 54.7%

Kagawa Y. **Influence of Nutritional Intakes in Japan and the United States on COVID-19 Infection**. *Nutrients*. 2022 Feb 1;14(3):633

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## Functional medicine/post COVID

- APEC report adds to growing body of evidence that functional medicine (FM) can help with COVID prevention, treatment, and recovery
- FM can help patients develop enhanced immunity to better resist COVID
- Life interventions – critical add

https://www.apec.org/publications/2023/07/project-report-of-integrative-medicine-(im)-and-covid-19-care

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## Preventing long-COVID

Decrease incidence of long-COVID with healthy lifestyle including:

- Healthy weight
- Never smoker
- Moderate alcohol consumption
- High-quality diet
- 7-9 hrs. of sleep
- At least 150 mins. per week of physical activity

Wang S, Li Y, Yue Y, et al. **Adherence to Healthy Lifestyle Prior to Infection and Risk of Post–COVID-19 Condition**. *JAMA Intern Med.* 2023;183(3):232–241

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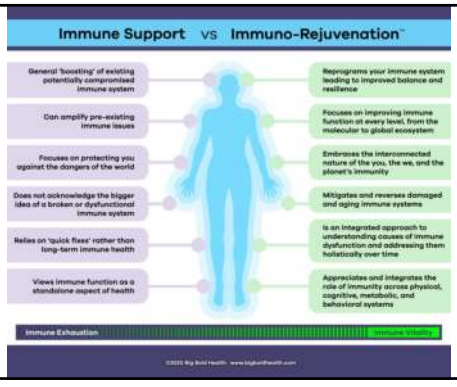


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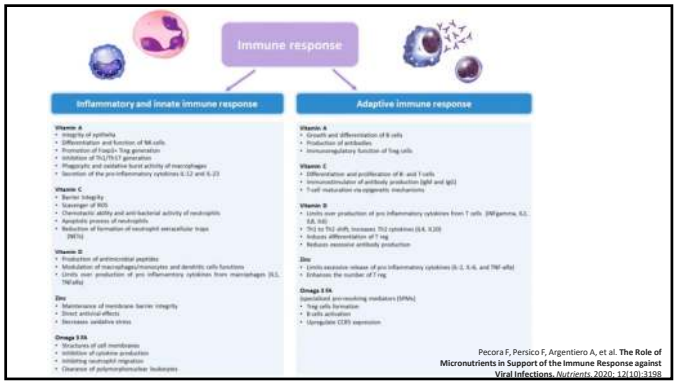
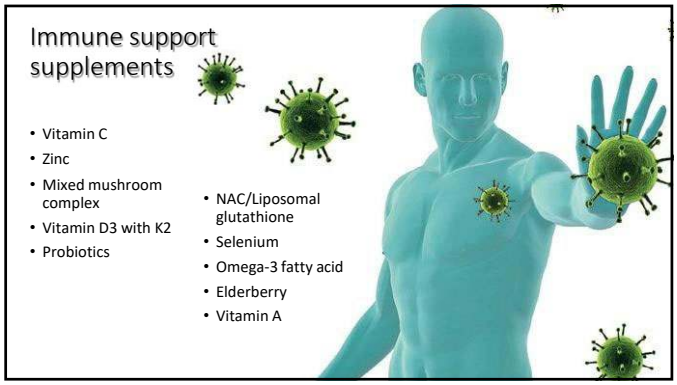



Pecora F, Persico F, Argentiero A, et al. **The Role of Micronutrients in Support of the Immune Response against Viral Infections.** *Nutrients.* 2020; 12(10):3198

76

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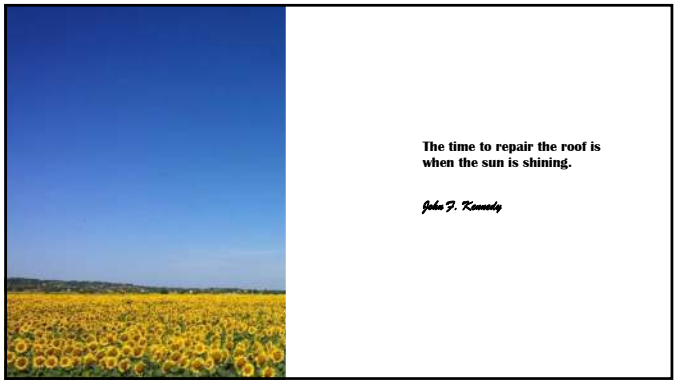


**The time to repair the roof is when the sun is shining.**

*John F. Kennedy*

78

What activates innate immune cells?

Exposure to
molecular patterns

79

## Did you know…

Most innate immune cells are initially in a dormant, resting state; they require multiple signals (e.g. pro-inflammatory cytokines) to become fully activated

80

## Let's Talk

Recognize the possible rise in autoimmunity and increased inflammatory status following recovery from COVID-19 infection

81

## Autoimmunity – hallmark of post-COVID syndrome

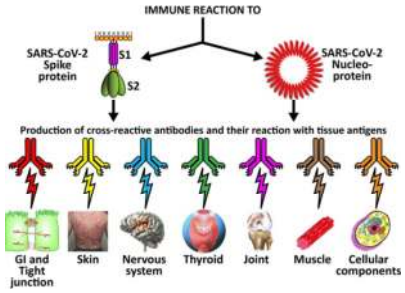
- Autoimmunity – emerged as a characteristic of post-COVID syndrome (PCS)
- Latest autoimmunity and poly autoimmunity found in 83% and 62% of patients, respectively

**Conclusion:** autoimmunity is characteristic of PCS, and latent autoimmunity correlates with humoral response to SARs-CoV-2

Rojas M, Rodríguez Y, Acosta-Ampudia Y, et al. **Autoimmunity is a hallmark of post-COVID syndrome**. *J Transl Med*. 2022 Mar 16;20(1):129

82

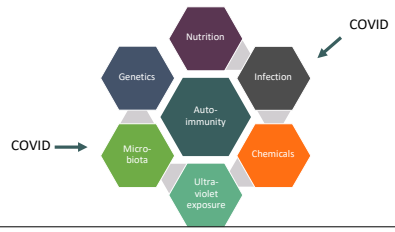
## Possible relationship between SARS-CoV-2 proteins and autoimmune target proteins




Vojdani A, Vojdani E, Kharrazian D. *Front Immunol*. 19 Jan 2021;11:3679

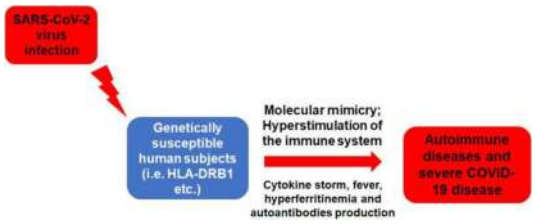
83

## What is the trigger for autoimmunity?




84

## The development of autoimmune diseases following SARS-CoV-2 infection




Halpert G, Shoenfeld Y. **SARS-CoV-2, the autoimmune virus.** *Autoimmun Rev.* 2020;19(12):102695. doi:10.1016/j.autrev.2020.102695

85

## Long-COVID

Study from long-COVID patients

- Long-COVID – a complex, multi-faceted disease that requires comprehensive, personalized and systemic approach to treatment

Davis HE, McCorkell L, Vogel JM, Topol EJ. **Long COVID: major findings, mechanisms and recommendations.** *Nat Rev Microbiol.* 2023 Mar;21(3):133-146

86



## Long-COVID numbers could be underestimated

- Researchers found significant proportion of patients in their study who had never tested positive for COVID-19 but were having symptoms of long-COVID, showed evidence of immune responses consistent with previous exposure
- 41% of these individuals had immune response consistent with SARS-CoV-2 exposure

ZS Orban, L Visvabharathy, GS Perez Giraldo, et al. **SARS-CoV-2–Specific Immune Responses in Patients With Postviral Syndrome After Suspected COVID-19,** *Neurol Neuroimmunol Neuroinflamm,* Nov 2023;10(6):e200159

87

New research suggest people who had COVID-19 – more likely to develop hypertension, even with no prior history of high-blood pressure

V Zhang, M Fisher, W Hou, et al. **Incidence of New-Onset Hypertension Post–COVID-19: Comparison With Influenza.** *Hypertension*, 21 August 2023

88

## COVID effect on the liver

SARS-CoV-2 infects liver, stimulating glucose production and contributing to severe form of COVID-19

E Barreto, AS Cruz, et al. **COVID-19-related hyperglycemia is associated with infection of hepatocytes and stimulation of gluconeogenesis.** *Proceedings of the National Academy of Sciences*, 15 May 2023;120(21):e2217119120

89

## Thyroid dysfunction may linger a year after severe COVID-19

American Thyroid Association (ATA) 2022 Annual Meeting, oral abstract 12, 21 Oct 2022

90

## Long COVID: disrupted sleep, fatigue common months after infection

- After recovery from COVID-19:
  - 41.3% of patients reported at least moderate sleep disturbances
  - 8% described severe sleep issues
  - More than two-thirds of patients (67.2%) reported moderate fatigue
  - Anxiety linked to increased long-COVID sleep disruption

CPena Orbea, B Lapin, I Katzan, et al. **0735 Sleep Disturbances in Post-Acute Sequelae of COVID-19 (PASC).** *Sleep*, June 2022;45(1):A321

91

## Post acute sequelae of COVID-19 at 2 years

- People who have been infected with COVID have greater risk of many long-term health conditions, including:
  - Diabetes
  - Lung problems
  - Fatigue
  - Blood clots
  - GI disorders
  - M/S disorders

B Bowe, Y Xie, Z Al-Aly. **Postacute sequelae of COVID-19 at 2 years**. *Nat Med*, 21 August 2023

92

## Biological changes of people post-COVID

- Disturbances in circulatory function:
  - Destruction of enzyme that is cellular receptor for the virus
- Ongoing state of inflammation in the body:
  - Immune system typically not returned to pre-COVID state
  - Abnormalities in T cell function
  - High rate of autoantibody function
- Mitochondrial distress/dysfunction
- Gut microbiome – maybe first:
  - Loss of diversity
  - Loss of anti-inflammatory organism
  - Increased level of inflammatory-reducing microbes
  - Increased leaky gut occurrence

93

## Acute blood biomarkers predict cognitive deficits 6 & 12 months post-COVID

- Data from 1,837 adults hospitalized with COVID-19
- Found 2 blood biomarkers – elevated fibrinogen and D-dimer linked to cognitive deficits
- A separate vs. study involving 17,911 patients corroborated findings – D-dimer specific for COVID-19 cognitive issues

M Taquet, Z Skorniewska, A Hampshire, A. *et al.* **Acute blood biomarker profiles predict cognitive deficits 6 and 12 months after COVID-19 hospitalization**. *Nat Med*, 31 Aug 2023

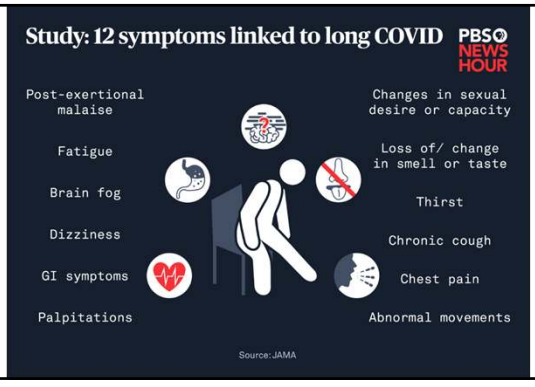
94

## WOW!!

Estimates have long-COVID costing the US economy $3.7 trillion and growing

CNBC

95



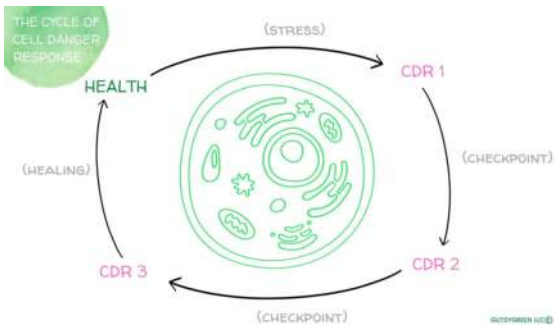

96

## Cell danger response (CDR)

- CDR – complex innate defense by our individual cells to danger/cellular threat
- Our cells must maintain certain level of energy for cellular homeostasis
- If drop in energy – our mitochondria senses as threat
- Results in mitochondria changing primary function from energy production to cell defense
- Switch called cell danger response

Naviaux RK. **Metabolic features of the cell danger response.** *Mitochondrion.* 2014 May;16:7-17

97




https://www.gutsygreen.com/blog/how-mitochondrial-dysfunction-and-cell-danger-response-lead-to-chronic-illness

98

## Long COVID and Epstein-Barr Virus (EBV) reactivation



- 185 randomly selected COVID-19 patients
- 30.3% developed long-COVID
- Of those, 66.7% long COVID subjects versus 10% control subjects – positive for EBV reactivation
- Reactivation of EBV may occur early in COVID-19 infection cycle

**Conclusion:**

Many long COVID symptoms may not be direct result of SARs-CoV-2 virus but may be result of COVID-19 inflammation-induced EBV reactivation

Gold JE, Okyay RA, Licht WE, Hurley DJ. **Investigation of Long COVID Prevalence and Its Relationship to Epstein-Barr Virus Reactivation**. *Pathogens.* 2021 Jun 17;10(6):763

99

## COVID long-hauler panel

- IL-2
- IL-4
- IL-6
- IL-8
- IL-10
- IL-13
- GM-CSF
- SCD40L
- CCL3
- CCL4
- CCL5
- TNF-alpha
- IFN-gamma
- VEGF
- Long Hauler Index

Radiance Diagnostics

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## Long COVID Protocol

- Gut health
- Mitochondrial support
- Immune activation
- Manage and modulate inflammation:
  - Obesity
  - Blood-sugar
  - Anti-inflammatory status

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## Long COVID Protocol

- Improve mitochondrial function (decrease fatigue)
  - NMN makes NAD: 200 mg/day
  - B vitamins: 60 mg/day
  - CO-Q 10: 300 mg/day
  - Acetyl-L-Carnitine: 1000 mg/day
  - ALA: 600 mg/day
  - Glutathione: 500 mg/day
  - Magnesium: 200 mg/day
  - Zinc: 40 mg/day
  - Selenium: 200 mcg/day
  - Vitamin C: 2000 mg/day
- Immune activation – mushrooms: reishi, maitake, lion's mane, chaga, shiitake

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## Long COVID Protocol (cont'd)

- Lifestyle:
  - Diet:
    - Intermittent fasting (mitophagy)
    - GI carbs
    - No processed carbs
    - Good fats and AA
  - Sleep and exercise
- Low-level laser – electro-magnetic transfer of energy
- Detox – remove toxins

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## Exerkines/long-COVID/Longeivty

- Exerkines – signaling moieties released during exercise and affect multiple organ systems
- Released from skeletal muscle, brown adipose tissue, white adipose tissue, neurons, heart, and liver
- Exerkines via molecular signals and pathways attenuate effects of COVID-19 and long-COVID on organ systems:
  - CV system
  - Respiratory system
  - Nervous system
  - COVID-19
  - Long-COVID
  - Organ damage
  - Immune system

G Torres, D Constantinou, P Gradidge, et al. **Exercise is the Most Important Medicine for COVID-19**. *Current Sports Medicine Reports*, August 2023;22(8):284-289

105

## Omicron protocol/Eris(EG.5)

- D3 5000 with K2
- Melatonin
- Astaxanthin
- Curcumin
- quercetin
- Zinc
- NAC
- pro resolving mediators
- L. rhamnosus
- L. plantarum
- Resveratrol
- NAD+

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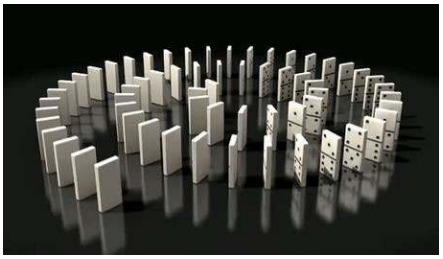


107

## COVID tied to increased risk for Alzheimer's (AD) and Parkinson's disease (PD)

- 43,262 individuals with positive COVID test
- 876,356 without positive COVID test
- After 12 months:
  - 3.4 x AD in COVID positive group vs negative group
  - 2.2 x PD diagnosis within first 12 months in COVID positive individuals compared with negative people

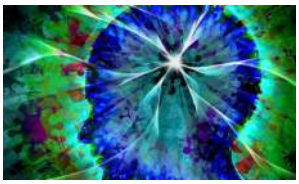
P Zarifkar, C Peinkhofer, ME Benros, D Kondziella. **Frequency of Neurological Diseases After COVID-19, Influenza A/B and Bacterial Pneumonia**. *Front Neurol*, 23 June 2022

108

## Association of COVID-19 with Alzheimer's disease

**Conclusion:**

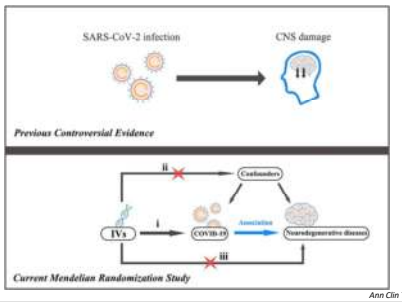
Older adults with COVID-19 – significantly increased risk for new diagnosis of Alzheimer's disease with highest risk in people age ≥85 and in women



Wang L, Davis PB, Volkow ND, et al. **Association of COVID-19 with New-Onset Alzheimer's Disease**. *J Alzheimers Dis*. 2022;89(2):411-14

109

## COVID-19 and the risk of Alzheimer's disease, amyotrophic lateral sclerosis, and multiple sclerosis




*Ann Clin Transl Neurol*, 02 November 2022

110

## SARS-CoV-2 drives NLRP3 inflammasome activation in human microglia

- Interaction of virus and microglial directly induced robust inflammasome activation
- Therefore – increased vulnerability to developing neurological symptoms akin to Parkinson's disease in COVID-19 infected individual

EA Albornoz, AA Amarilla, N Modhiran, N. *et al.* **SARS-CoV-2 drives NLRP3 inflammasome activation in human microglia through spike protein**. *Mol Psychiatry*, 1 Nov 2022

111

## Long COVID symptoms linked to effects on vagus nerve

Most long COVID subjects with vagus nerve dysfunction symptoms had range of structural and/or functional alterations in their vagus nerve, including:

- nerve thickening
- trouble swallowing
- symptoms of impaired breathing

**Conclusion:**

"Our findings so far thus point at vagus nerve dysfunction as a central pathophysiological feature of long COVID."

EurekAlert!: "Pilot study suggests long COVID could be linked to the effects of SARS-CoV-2 on the vagus nerve."

112

## Vagus nerve/long-COVID

**Conclusion:**

Study suggests – non-invasive stimulation of the auricular branch of the vagus nerve of tVNS treatment is possible therapeutic modality for treating long-COVID

BH Natelson, M Blate, T Soto. **Transcutaneous Vagus Nerve Stimulation in the Treatment of Long Covid-Chronic Fatigue Syndrome**, *medRxiv* 2022.11.08.22281807

113

## Vagus nerve inflammation contributes to dysautonomia in COVID-19

**Conclusion:**

SARs-CoV-2 induces vagus nerve inflammation followed by autonomic dysfunction when contributing to critical disease courses and might contribute to dysautonomia observed in long COVID

Woo, M.S., Shafiq, M., Fitzek, A. *et al.* **Vagus nerve inflammation contributes to dysautonomia in COVID-19**. *Acta Neuropathol*, 15 July 2023;146:387–394

114

## Vagus nerve dysfunction in post-COVID-19 condition

**Findings:**

Most prevalent symptoms:

- Cognitive dysfunction 83%
- Dyspnea 80%
- Tachycardia 80%
- Patients showed thickening and hyperechogenic vagus nerve in neck ultrasounds

G Llados, M Massanella, et al. **Vagus Nerve Dysfunction in the Post-COVID-19 Condition**. Preprints in *The Lancet*, 19 Jun 2023

115

## VAGUS NERVE NUTRITIONAL SUPPORT

| Function |
|---|
| Vagally-mediated probiotics |
| Short-chain fatty acids (butyric acid) - direct effect on afferent sensory firing |
| Fiber – increases GLP-1 |
| Increase bile acid flow |
| Omega-3 fatty acids – increases HRV |
| L-citrulline – increases HRV |
| Time-restricted eating (TRE) |
| Sleep more |

*Metabolism*. 2012 Sept;61(9):1312-20. Epub 2012 Mar 24
*Mol Metab*. 2014 Sept;3(6):595-607. Epub 2014 Jun 27

116



## Immune Reboot Hacks

Avoid certain foods:

- GPS
- DNA
- Follow an anti-inflammatory diet
- Control your glycemic load
- Detect or avoid food sensitivities
- Environmental overload

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## Immune Reboot Hacks (cont'd)

Make clean-eating a priority:

- Organic
- Wild SMASH fish
- Plant-based diet
- Fruits and vegetables
- Grass-fed meats
- High fiber
- Nuts and seeds
- Chicken soup
- Snack - organic dark chocolate
- Herbals - ginger, turmeric
- Bone broth
- Appropriate fluid intake
- Organic coffee, tea
- Oils – EVOO, avocado, macadamia nut
- Mushrooms - shiitake, reishi, chaga, turkey tail, maitake, oyster, lion's main

- Include nuts, avocado, olive oil in your diet
- Oleic acid from these foods stimulate SIRT1 – the defense enzyme

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## Immune Reboot Hacks (cont'd)

- Consider a time-restrictive eating (intermittent fasting) - fast for 12-16 hours
- Get sufficient sleep - aim for 7-8 good quality hours
- Home exercise plan
- Chiropractic care
- Low level laser therapy
- Modify stress
- Support your immune system

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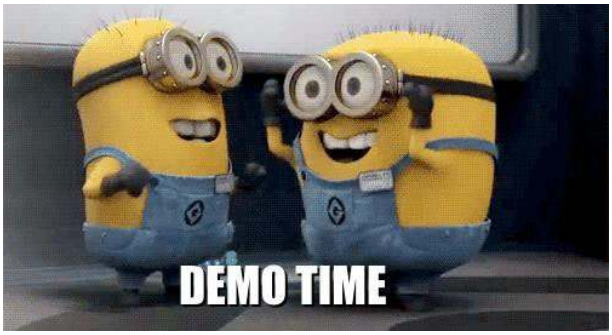


121

## Gut protocol – FX635/405
## 4,4,9,26,9,26

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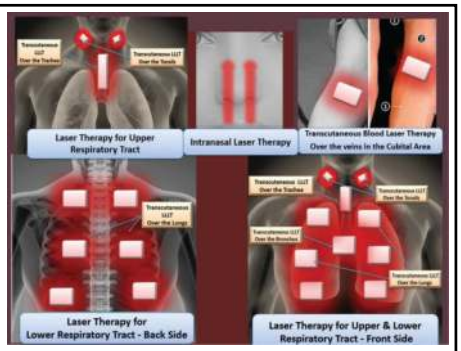
## Long COVID Demo




Mokmeli S, Vetrici M. **Low level laser therapy as a modality to attenuate cytokine storm at multiple levels, enhance recovery, and reduce the use of ventilators in COVID-19**. *Can J Respir Ther*. 23 July 2020;56:25-31

123

## Omicron Eris protocol – EVRL/GVL 1,30,1,30

- Nasal sinus (L & R)
- In mouth (L & R)
- Trachea region
- Upper primary bronchus (L & R)
- Mid-secondary bronchus (L & R)
- Lower tertiary bronchus (L & R)
- Bronchioles (L & R)
- Vagus nerve (L & R)
- Phrenic nerve
- Full gut sweep

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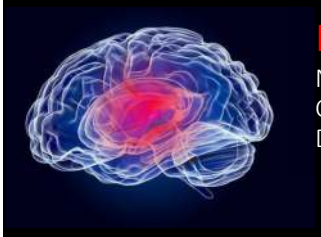
## Immune rejuvenation/resilience

- FX635/405 – gut
- Gut positioning – middle arm
- Outside arms in lung field
- GVL – cervical region

Immune setting: 10-20-40-73 (465-728)

125



## Neural Reboot

Nutritional Protocols for Concussion/Neurodegenerative Diseases

126

## THE BRAIN

is the most nutrient dependent, energy dependent and toxin and stress vulnerable organ

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## BRAIN STATS

- 75% water
- 60% fat
- 80 billion neurons – average
- 1,000 trillion connections between brain cells and cortex
- Takes up to 20% of blood and $O_2$ in your body
- 60% white matter
- Feels no pain

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## Concussion

- Head injury from direct or indirect forces with or without LOC leading to symptoms immediately after injury or for weeks or months after injury
- May or may not lead to Traumatic Brain Injury
- Symptoms may vary but have been called Post-Concussion Syndrome

129

## New concussion rules

**New study:**

Athletes who recover more slowly from concussion may be able to return to play with additional month of recovery beyond the typical recovery time

TW McAllister, SP Broglio, BP Katz, et al. on behalf of Concussion Assessment, Research and Education (CARE) Consortium. **Characteristics and Outcomes of Athletes With Slow Recovery From Sports-Related Concussion, A CARE Consortium Study.** *Neurology* Apr 2023, 100 (14) e1510-e1519

130

## Concussion

- A mismatch between demand and supply of energy to the cell
- Cells struggle to operate at their normal efficiency
- Energy problem happens, different systems in brain can be decompensated and that decompensation of certain systems are exemplary of concussion

**Key:**

- Where is aberrant signal coming from?
- What system is decompensated?
- Apply the right treatment to the problem

The Drive, Peter Attia Podcast #263

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## Signs & symptoms of concussion

**Signs of concussion:**

- Loss of consciousness
- Confusion
- Balance issues
- Vomiting

**Symptoms of concussion:**

- Dizziness
- Fogginess/feeling detached
- Feeling one step behind
- Light/noise sensitivity
- Nausea
- Fatigue
- Blurred/double/fuzzy vision
- Headache
- Post-traumatic/retrograde amnesia
- Loss of memory before/after injury

The Drive, Peter Attia Podcast #263

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## Symptom on the field that best predicts a longer recovery from concussion

Dizziness is 6X more predictive than any other symptoms

The Drive, Peter Attia Podcast #263

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## Pathways

- Vestibular system mediate the sympathetic nervous system:
  - Heart rate increases
  - Increased cortisol
- Rest only makes brain injury worse because the way to treat vestibular problem is by retraining it

The Drive, Peter Attia Podcast #263

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## Dr Collins 6 Types of Concussions


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## TBI

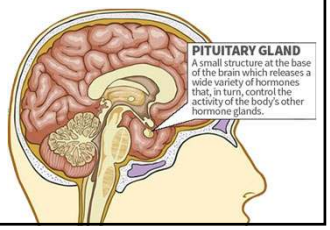
- BIAFAC – brain injury associated fatigue and altered cognition
- TBI injury impairs:
  - Hormone production
  - Sleep
  - Cognition
  - Memory
  - Intestinal health

*Journal of Neurotrauma*, Jan. 2020
Neurosciencenews.com, Jan. 21, 2020

136

## Pituitary dysfunction after concussion

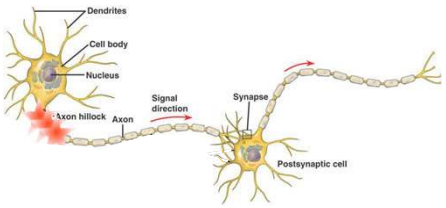
- % of pituitary varies with type of concussion
- GH is most common hormone lost
- Then ACTH, Fsh and LH then TSH
- Genetic predisposition and autoimmunity have a role




*Endocrine News.* June 1, 2015;305-42

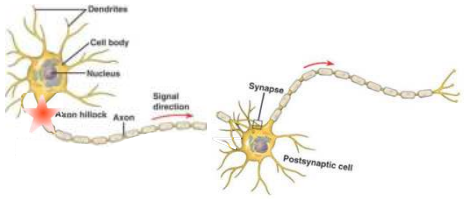
137

## Normal Communication Between Neurons



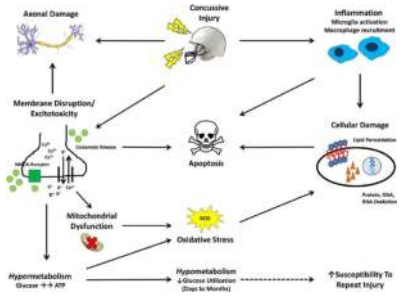

138

## Concussion injury causes shearing (tearing) of neurons and disrupts communication




139

## Molecular cascade of events after a mild traumatic brain injury




Erin Cernkovich Barrett et al. *Adv Nutr* 2014;5:268-77

140

## Concussion update

- TBI has two mechanisms of cell death:
  - Direct axonal death
  - Neuronal inflammation (most common) – can persist for more than a decade and chemically affect neighboring neurons

Rank K, Ramos G, Addie C, et al. *Role of exercise and dietary supplementation in attenuation of traumatic brain injury in American football. Sport Exerc Med Open J.* 2019; 5(1): 5-10. doi: 10.17140/SEMOJ-5-168

141

## Why increased incidence of concussion?

Diminished brain resilience syndrome:

Modern-day neurological pathology of increased susceptibility to mild brain trauma, concussion, and downstream neurodegeneration

*Surgical Neurology International* 2014, June 14

142

## Diminished Brain Resilience Syndrome

- **Modern environment:** Toxicant exposure, nutrient-deficient foods, unhealthy omega 3:6 ratio in diet
- **Altered physiology:** Disruption of gut flora/liver function/CYP enzymes
- **Diminished brain resilience:** Nutrient functional deficiencies, reduced protection against impact damage
- **Neurological pathology:** Increased susceptibility to concussion, reduced ability to heal spontaneously from uncomplicated single concussion

*Surgical Neurology International*, 2014. 5:97

143

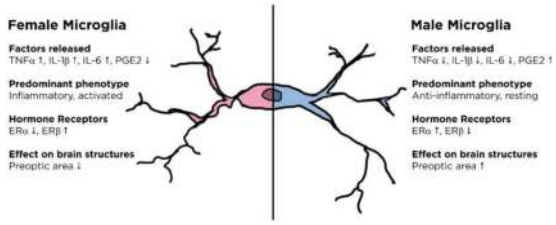
## Women's Brains May Have Tougher Time Recovering From Concussion

- Female athletes suffer concussions at higher rate than male athletes playing similar sports
- Women have weaker muscles in the neck – a factor in how head injures affect them
- "Withdrawal hypothesis": If woman suffers a concussion in the premenstrual phase when progesterone levels are naturally high, an abrupt drop in progesterone after injury produces a kind of withdrawal – either contributes to or worsens post concussive symptoms like headache, nausea, dizziness and trouble concentrating

Broglio, S., Ellemberg, D. Apr 28, 2015, *Radiology* online,
*Journal of Head Trauma Rehabilitation* Dec. 2010, p.2255-60, *J of Head Trauma Rehab* Nov. 13, 2013

144

## Gender-related disparities in microglial function




*Int J Mol Sci.* 2017 Mar;18(3):561

145

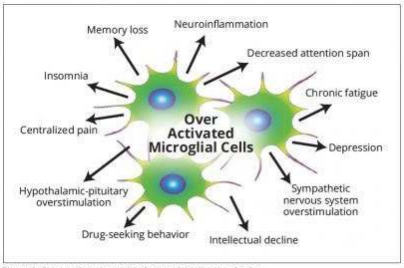
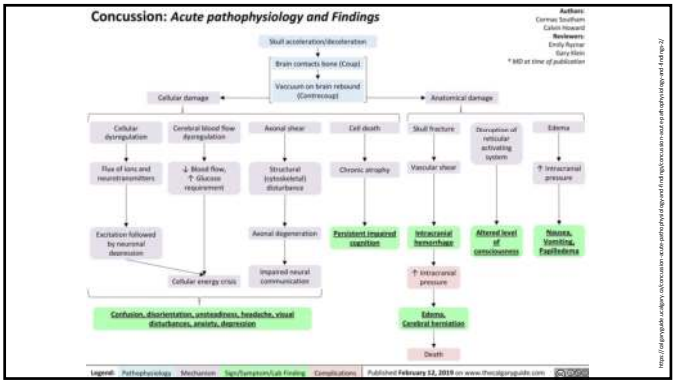


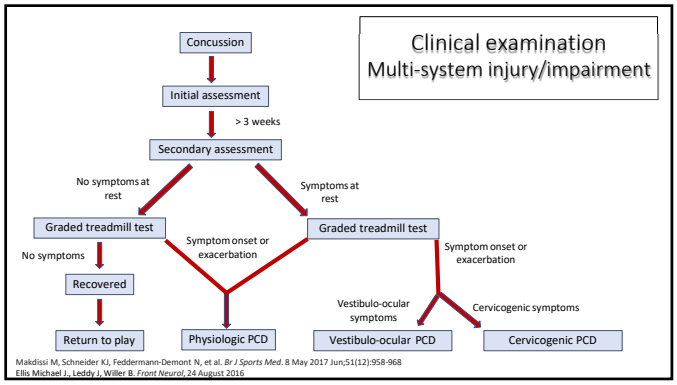

**Figure 2.** Some pathologic results of microglial cell overactivation.

https://www.practicalpainmanagement.com/resources/clinical-practice-guidelines/clinical-diagnosis-centralized-pain-age-icd-10

146




147




148

## Active and targeted treatments may enhance recovery after concussion

*Neurosurgery*, Oct. 2016

149

## Dr. Rob's Concussion Protocol

Multisystem approach:

- Musculoskeletal system
- Balance
- Visual disturbances
- Laser
- Nutrition support

150

## Effect of the Suboccipital Musculature on Symptom Severity and Recovery after Mild Traumatic Brain Injury (TBI)

**Conclusion:** In mild TBI, the rectus capitis posterior minor is the only suboccipital muscle associated with symptom severity and poor outcomes

Fahkran S, et al. *Am J of Neuroradiology*. 2016

151

## C-spine in patients with post-concussion symptoms

- The C/S may contribute to persistent post-concussion symptoms
- Physical exam is important to identify those with a cervicogenic component
- **Pain on manual segmental testing a key feature of a cervicogenic component**
- **Neck treatment appears to benefit neck-related persistent post-concussion symptoms**

Kennedy E, Duinn D, et al. **Clinical characteristics and outcomes of treatment of the cervical spine in patients with persistent post-concussion symptoms: A retrospective analysis.** *MusculoskeletalScience and Practice*, June 29, 2017;91-98

152

## Why the eyes…

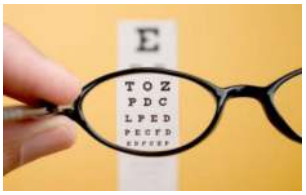
- 70% of our brain – dedicated to vision in some fashion
- 80% of all sensory goes through the eyes
- 90% of individuals who have concussion demonstrates one or more ocular difficulties
- 40% of individuals will have ocular difficulties longer than 3 months

*Training and Conditioning*, Aug/Sept. 2019

153

## Impairments

- Blurred or fluctuating vision
- Double vision
- Eye-tracking deficits
- Light sensitivity
- Reduced cognitive abilities
- Balance difficulties/dizziness

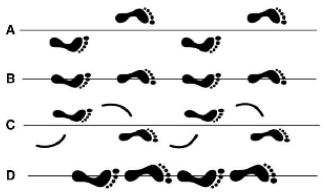



*Training and Conditioning*, Aug/Sept. 2019

154

## Concussion – Tandem gait

**Results:** Tandem gait is a clinically feasible assessment that can be performed by a single clinician, and thus has considerable potential implications for concussion management




*Sports Health*. July/August 2017:305-11

155

156

## Proprioception

- Concussion patients went through 8 weeks of intensive balance training
- Researchers noticed structural changes in portions of the subjects' cerebellums and improvements in balance and postural control

*NeuroImage: Clinical*, 2015;7:240-50

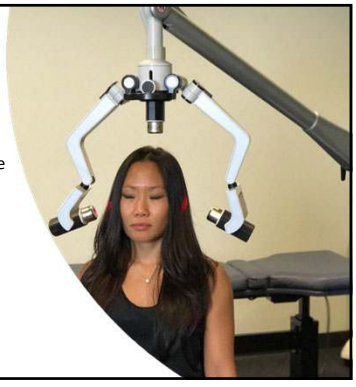
157

## Gaze stabilization

158

## Is Transcranial Laser Therapy effective in acute phase recovery post TBI?

Low level laser therapy (LLLT) effective in reduction of pain, swelling and inflammation Chung. Ann *Biomed*, 2012, improves cerebral circulation Tian. *Lasers Surg Med* 2016 and may "significantly improve neural function, decreased lesion volume, augment cell proliferation and even protect the brain against neuronal damage." Xuan W, et al. *Transcranial LLLT improves neurological performance in TBI in mice*, PlosOne



159

## Is Transcranial Laser Therapy efficacious in acute phase recovery post TBI?

- Low Level Laser therapy improves neurological performance in TBI (PLoS One, 2013)
- Treatment can stimulate growth of new nerve tissue (Xuan W, et al. *Transcranial LLLT enhances learning, memory, and neuroprogenitor cells after TBI in mice*, J Biomed Opt, 2014 Oct(10);19)
- Also been shown to modulate oxidative stress and nitric oxide production (Manchini. PLoS One, 2014. Chen. PLoS One, 2011)
- LLLT down-regulates pro-inflammatory microglial cytokine expression (Song, 2012)

160

## Is Transcranial Laser Therapy efficacious in acute phase recovery post TBI? (cont'd)

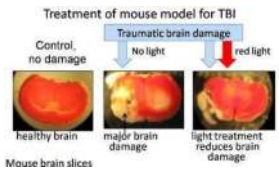
- 635 nm LLLT modulates NF-kB signaling pathways (Lim, 2013)
- Laser shown to mitigate cell apoptosis (Moreira, 2011)
- Transcranial Laser Therapies researched in stroke injury (Naeser, 2011and Lampl 2007) and in clinical trials (Stemer, 2010)
- LLLT improves cognitive deficits and inhibits microglial activation after controlled cortical impact in mice (*J Neurotrauma*, 2012 Jan 20)

161

## Proof lasers heal the brain

Study from Israel, Dr. Oron found:

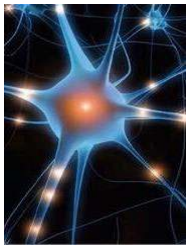
- Laser on mice with traumatic brain injuries had far fewer neurological deficits 5 days later than control groups
- And size of injury 30 days later was significantly smaller




A. Oron, et al. Low level laser therapy applied transcranially to mice following traumatic brain injury, *J of Neurotrauma*, 2007, 24:651-56

162

"LLLT suppressed pro inflammatory cytokine expression of IL-1b and IL-6…LLLT elevated production of Immediate Early Responsive Gene X-1 in injured brain. The protective effect of LLLT may be ascribed to enhanced ATP production and selective modulation of pro inflammatory mediators."



Low-level Laser effectively prevents second brain injury induced by immediate early response gene X-1 deficiency. Zhang, J *Cereb Blood Flow Metab.* 2014

163

## LLLT for BDNF

**Conclusion:** Benefit of LLLT to the brain is mediated by stimulation of BDNF production, which may in turn encourage synaptogenesis.

LLLT may have applications for neurodegenerative conditions

Xuan W, Agrawal T, huang L, et al. *J Biophotonics*. 2015 Jun;8(6):502-11

Study suggests upregulation of BDNF with LLLT can ameliorate AB-induced neurons loss and dendrite atrophy. Thus, identifying a novel pathway by which LLLT protects against AB-induced neurotoxicity

*J Mol Neurosci* 2013 Aug 14;33(33):13505-17

164

## LLLT post-TBI

LLLT improves:

- Neurological function
- Lessens size of brain lesion
- Reduces inflammation in the brain
- Stimulates formation of new neurons – increase BDNF, synaptogenesis

Thunshelle C, Hamblin MR. **Transcranial Low-Level Laser (Light) Therapy for Brain Injury**. *Photomed Laser Surg*. 2016;34(12):587-598

165

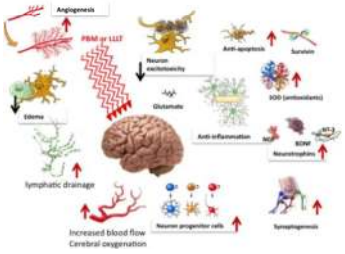
## Photobiomodulation for TBI

- Findings: PBM
  - Reduce swelling
  - Increase antioxidants
  - Decrease inflammation
  - Protect against apoptosis
  - Modulate microglial activation
- Acute TBI found positive effects:
  - Neurological function
  - Learning and memory
  - Reduced inflammation
  - Reduced cell death in brain
  - Upregulate BDNF

Hamblin MR. *J Neurosci Res* 2018 Apr;96(4):731-743. doi: 10.1002/jnr.24190. Epub 2017 Nov 13

166

## Shining light on the head: Photobiomodulation for brain disorders




BBA Clin. 2016 Dec;6:113-124. Published online 2016 Oct 1*Journal of Neuroscience Research*, first published 13 November 2017; 96(4):731-43

167

## Dr. Rob's Laser Concussion Protocol

- ★FX405- 10 minutes. (Fig. A & B – 5 mins each)
  - First 3 weeks: 1,1,1,1,1,1,1,1
  - After 3 weeks: 1,1,1,10,10,20,1,40
  - Chronic (6 months): 1,10,40,60,1,10,40,60
- ★Vagus nerve (GVL)-10,10,10,10
- Nose region for CSF: 60 sec., hard palate open mouth: 30 sec.
- ★2 lasers – use gut-brain reconnection
- 1 laser – use gut protocol

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## Concussion – FX635

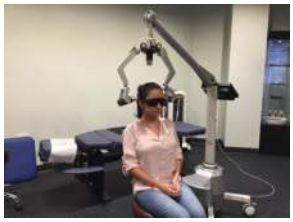

Fig. A

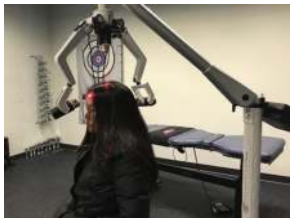

Fig. B

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## Nutritional factors in sports-related concussion

Highlights

- Brain uses 20% of ingested calories and requires more than 40 nutrients
- Concussions cause overconsumption of nutrients by the brain
- Nutritional supplementations reduce deleterious effects of sports-related concussion
- DHA, certain AA and micronutrients, have emerged as potential nutritional strategies
- Gut microbiota – important factor in concussion recovery, pointing to benefit of pro/prebiotics

Walrand S, Gaulmin R, Aubin R, et al. **Nutritional factors in sport-related concussion.** *Neurochirurgie.* 2021 May;67(3):255-258. Epub 2021 Feb 11

170

## Concussion Nutrition Protocol

Feed the concussion

1) **Ketogenic diet:** ketone bodies provide energy for the brain
2) **Creatine:** gives the brain an intense/immediate energy to heal cells
3) **Reduce inflammatory damage** to brain DHA, boswellia, quercetin, ginger, turmeric
4) **Antioxidants:** alpha-lipoic acid
5) **PRM:** resolution of inflammation
6) **Choline:** critical for brain development

"Enhancement of learning and memory by elevating brain magnesium". *Neuron*, Jan. 28, 2010:165-77
"Presynaptic NMDA receptors biology of the NMDA receptor". Boca Raton, FL. CRC Press, 2009
"The effects of nutrients or brain function". *Not Rev Neuroscience*, 2008 Jul:568-78

171

## Concussion Nutrition Protocol (cont'd)
### Feed the concussion

7) **Vitamin D:** neuroprotective
8) **Zinc:** enzyme for CNS
9) **Sulforaphane:** inhibits MMP-9 and activates NRF2
10) **Magnesium:** great weapon against delayed brain injury
11) **Acetyl-L-carnitine:** energizes the brain
12) **Glutathione:** body's #1 intracellular antioxidant
13) **Coffee fruit extract:** increases BDNF
14) **Taurine:** protection against excitotoxicity

"Enhancement of learning and memory by elevating brain magnesium". *Neuron*, Jan. 28, 2010:165-77
"Presynaptic NMDA receptors biology of the NMDA receptor". Boca Raton, FL. CRC Press, 2009
"The effects of nutrients or brain function". *Nat Rev Neuroscience*, 2008 Jul:568-78

172

## Ketogenic protocols for management of TBI

- Many people after TBI have seizures
- Keto diet then makes sense
- Sustainable – low-carb diet with supplemental ketones (ester or salts)
- Glucose ketone (blood glucose and blood ketone levels) index off 1-2:
  - Lower inflammation
  - Provides alternative energy source to brain
- Salt more efficacious than ester
- **Best approach** – salt + MCT oil
- Exogenous ketones provide immediate substrate
- MCT molecule is stimulating ketones to be made in the liver
- MCT (converts to ketones) can cross BBB

*The Drive Podcast* #116, Dr. Dom D'Agostino

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## Gluten/brain inflammation

**Overview:**

- Researchers in New Zealand observed that wheat gluten can cause brain inflammation
- Gluten added to low-/high-fat diet triggered inflammation in the brain's hypothalamic region
- Experts theorize – gluten may elicit inflammatory immune response similar to what people with celiac experience
- Research ties inflammation of nerve cells, to the onset of metabolic disease

**Gluten may cause brain inflammation, mouse study suggests.** *MedicalNewsToday*, 16 August 2023
MZ Rizwan, R Kerbus, K Kamstra, et al. **Dietary wheat gluten induces astro- and microgliosis in the hypothalamus of male mice.** J Neuroendocrinology, 17 July 2023;35(8):e13326

174

## Gluten/brain inflammation (cont'd)

- Addition of gluten to either a low- or high-fat diet "led to a marked increase in the number of microglia and astrocytes in the arcuate nucleus (ARC) of the hypothalamus"
- Gluten-induced hypothalamic inflammation can lead to:
  - Brain damage
  - Bodyweight gain
  - Impaired glucose regulation
- Gluten added to low-fat diet increases C-reactive protein
- Gut microbiota and LPS can enter bloodstream, causing "inflammatory cascade"

**Gluten may cause brain inflammation, mouse study suggests.** *MedicalNewsToday*, 16 August 2023
MZ Rizwan, R Kerbus, K Kamstra, et al. **Dietary wheat gluten induces astro- and microgliosis in the hypothalamus of male mice.** J Neuroendocrinology, 17 July 2023;35(8):e13326

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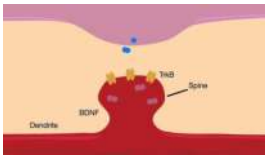
## Brain-derived neurotrophic factor (BDNF)




- Supports branching network of neurons
- Reduces neurodegeneration risk
- Makes neuronal synapses and communication more efficient
- Fertilizer or "Miracle Gro" for brain
- Allows brain cells to "fire together" than "wire together"

Exercise positively impacts BDNF

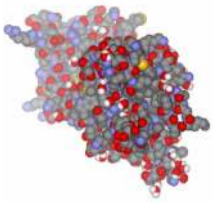
"Physical exercise increases adult hippocampal neurogenesis," *J of Physiology*, Feb. 24, 2016

176

## BDNF

Shows promise as treatment strategy for neurodegenerative disease:

- Lower levels of BDNF present in Parkinson's disease
- Brain BDNF expression is reduced in people with Alzheimer's disease
- Production and transport of BDNF altered in Huntington's disease



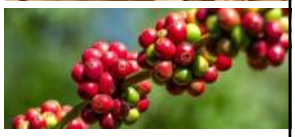
Chen S-D, Wu C-L, Hwang W-C, Yang D-I. **More Insight into BDNF against Neurodegeneration: Anti-Apoptosis, Anti-Oxidation, and Suppression of Autophagy.** *International Journal of Molecular Sciences*. 2017; 18(3):545

177

## WHAT ENHANCES BDNF

- Exercise
- Turmeric
- Low Level Laser Therapy
- Taurine
- DHA
- Alpha-lipoic acid
- *Lactobacillus brevis, Bifidobacterium longum*
- Ketones
- Prebiotics
- Whole coffee fruit extract
- Resveratrol





Etnier JL, Wideman L, Labban JD, et al. *J Sport Exerc Psychol*. 2016 Aug;38(4):331-40

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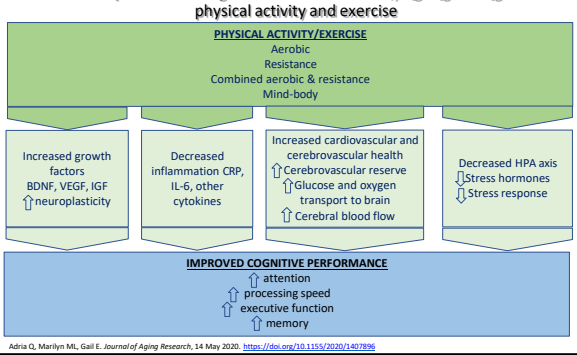
## AEROBIC EXERCISE SOON AFTER CONCUSSION

- Contributes to faster recovery and return to sport, school and work
- Study supports view that aerobic exercise is safe and potentially protective in symptomatic individuals
- Individuals benefit from starting low-impact, aerobic activity as early as 24 hours after injury
- Exercises recommended (minimal head movement):
  - Stationary cycling
  - Elliptical
  - Walking

*PLOS One*. April 18, 2018

179

## Overview of potential biological mechanisms underlying cognitive gains with physical activity and exercise




Adria Q, Marilyn ML, Gail E. *Journal of Aging Research*, 14 May 2020. https://doi.org/10.1155/2020/1407896

180

## Exercise-induced neuroplasticity

**Highlights:**

- Studied structural plasticity after 12 weeks of balance training
- Balance training elicited changes in visual vestibular motion processing areas
- Gray matter changes correlated with balance improvements
- Vestibular networks may contribute to cognitive benefits after physical exercise

Ann-Kathrin R, Brigitte R, Astrid Z, Kirsten H. **Exercise-induced neuroplasticity: Balance training increases cortical thickness in visual and vestibular cortical regions.** *NeuroImage*, 2018;179:471-479

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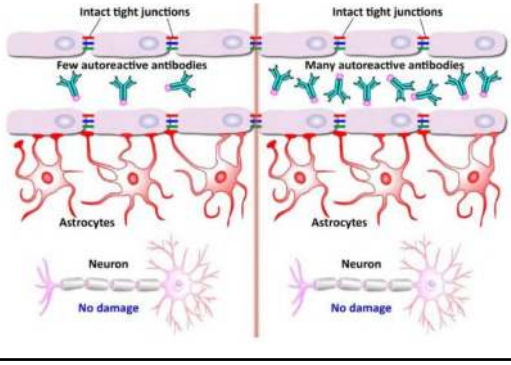


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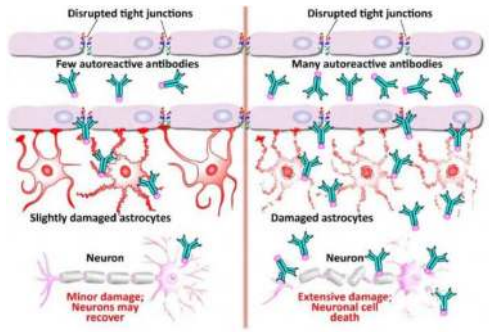


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## CHRONIC BRAIN INFLAMMATION

- Brain cells including microglial cells can produce TNF alpha, IL1b and IL6
- Inflammation – continue to damage brain cells
- Brain injury and disruption of BBB – lead to chronic ongoing brain inflammation and ongoing brain damage from leaky BBB
- **If you take care of patients with head injury you must assess and treat the BBB**

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## POST-CONCUSSION/LEAKY BBB

- Leaky BBB will allow neurotoxins into brain increasing damage from brain injury
- Leaky BBB will not transport nutrients efficiently for brain tissue repair
- Problem compounded if there is also a leaky or excessively permeable intestine
- Microbiome changes after TBI
- Microbiome and bacterial endotoxins can damage brain

Vojdani, A. "Brain-reactive antibodies in traumatic brain injury," *Funct Neurol Rehab Ergon*, 2013;3(203):173-81
Levin, EC., Acharya NK., et al. "Brain-reactive autoantibodies are nearly ubiquitous in human sera and may be linked to pathology in the context of blood-brain barrier breakdown," *Brain Res*, 2010;1345:221-32

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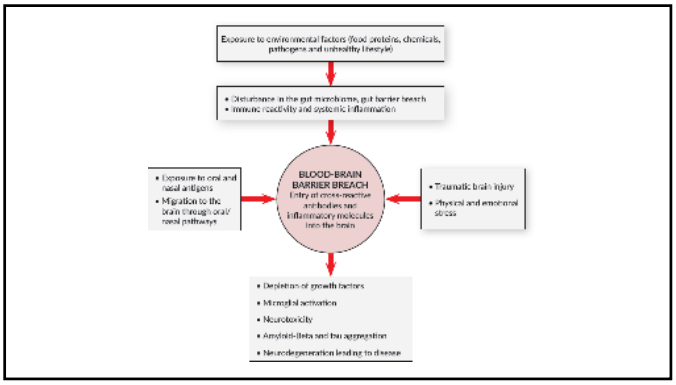


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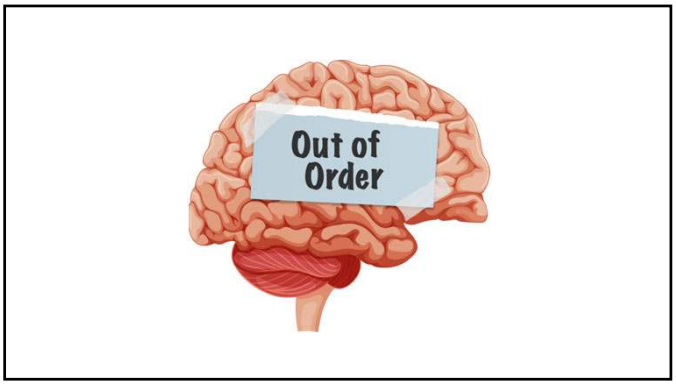


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## Microglia

- **M1** – microglia release inflammatory mediators and induce inflammation and neurotoxicity
- **M2** – microglia release anti-inflammatory mediators and induce anti-inflammatory and neuroplasticity

**Microglia Polarization From M1 to M2 in Neurodegenerative Diseases**. *Front. Aging Neurosci.*, 16 February 2022;14. *Sec. Neuroinflammation and Neuropathy*

189

## Macrophages

- PBM modulates ratio of M1 & M2 macrophage phenotypes, reducing proinflammatory cytokines and chemokines, increasing anti-inflammatory cytokines, thus balance inflammation process

A Liebert, B Bicknell, W Markman, H Kiat. **A Potential Role for Photobiomodulation Therapy in Disease Treatment and Prevention in the Era of COVID-19**. *Aging and disease*, 2020/12/01;1352(11)

190

## Head injuries may lead to early Alzheimer's

- Contact sports that can result in concussions – football – lead to early onset Alzheimer's
- Conclusions drew by looking at post-mortem Alzheimer's cases
- Alzheimer's onset could be "accelerated" by up to 9 years

*Neuropsychology*. Feb 1, 2018

191



*Brain*. Jan. 11, 2017

## Concussion linked to brain changes in people at genetic risk for Alzheimer's

192

## LLLT/Parkinson's disease

Results:

- Statistical significant reduction in VAS for gait and cognitive function were observed
- Gait – 30% improvement
- Cognitive – 38% improvement
- Difficulty with speech lowered by study end

Conclusion:

Data suggest laser therapy may serve as non-invasive instrument for symptom reduction of PD

Erchonia Medical. **The Application of Low-Level Laser Therapy for the Symptomatic Care of Late Stage Parkinson's Disease: A Non-Controlled, Non-Randomized Study**. *Lasers Surg Med* , 22 Sept 2022;185

193

## Photobiomodulation (PBM) in Alzheimer's disease

**Results:**

Studies showed PBM able to reduce inflammatory response, oxidative stress and apoptotic effects generated by amyloid beta and restore mitochondrial function/cognitive behavior

**Conclusion:**

Results indicate PBM maybe be useful tool for treating AD

Cardoso FDS, Lopes Martins RÁB, Gomes da Silva S. **Therapeutic Potential of Photobiomodulation In Alzheimer's Disease: A Systematic Review**. *J Lasers Med Sci*. 2020 Fall;11(Suppl 1):S16-S22

194

## LLLT ameliorates disease progression in a mouse model of Alzheimer's disease (AD)

**Conclusion:** Results suggest use of LLLT as a therapeutic application in progressive stages of AD

*J Mol Neurosci* 2015 Feb; 55(2):430-6

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## LLLT for beta amyloid toxicity

**Conclusion:**

By alleviating a broad spectrum of AB-induced pathology that includes mitochondrial dysfunction, oxidative stress neuroinflammation, neuronal apoptosis, and tau pathology, LLLT represents a new promising therapeutic strategy for AD

196

## Photobiomodulation therapy and Alzheimer's

**Findings:**

Gf (gut flora)-targeted PBM regulates diversity of intestinal flora, which may improve damage caused by AD. Gf-targeted PBM has potential to be noninvasive microflora regulation method for AD patients

Qianqian C, Jinpeng W, Xiaoxi D, et al. **Gut flora-targeted photobiomodulation therapy improves senile dementia in an Aß-induced Alzheimer's disease animal model,** *J of Photochemistry and Photobiology B: Biology*, 2021;216:112152

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**Suit up**

**Study up**

**Speak up**

http://www.biausa.org/brain-injury-children.htm

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Dr. Rob's Mastermind Laser Group on FB

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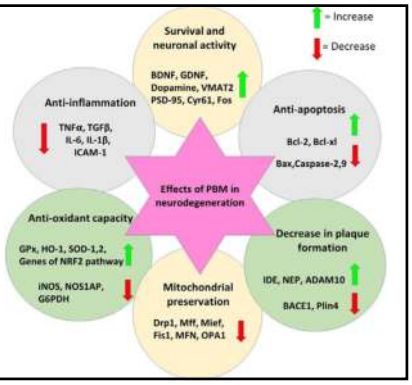
201

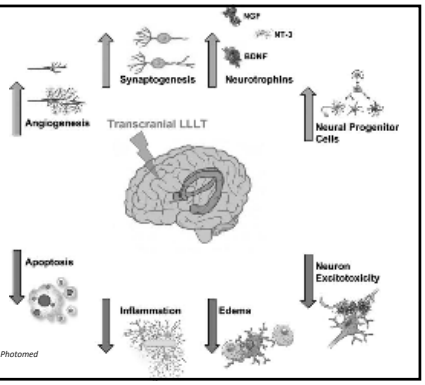
## Overall effects of PBM on genes and proteins playing different roles in neurodegeneration




M Bathini, CR Raghushaker, KK Mahato. **The Molecular Mechanisms of Action of Photobiomodulation Against Neurodegenerative Diseases: A Systematic Review**. *Cell Mol Neurobiol* (2020)

202

## Molecular mechanisms of transcranial LLLT




**Transcranial Low-Level Laser (Light) Therapy for Brain Injury**. *Photomed Laser Surg*. 2016 Dec;34(12):587-598

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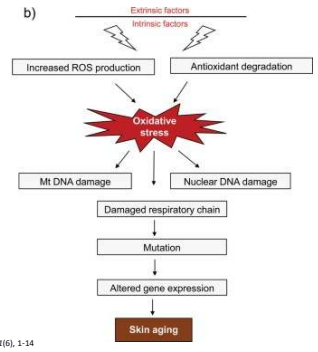
## Mitochondria settings

Dr. Rob's mitochondrial setting: 4,9,16,32

Dr. Rob's skin setting: 5,20,35,112




**Mitochondria in skin health, aging, and disease**. *Cell Death & Disease, 11*(6), 1-14

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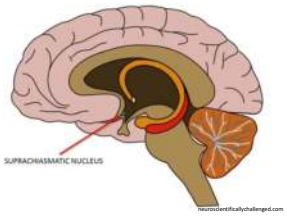
## Suprachiasmatic nucleus (SCN)




**IF protocol:**

- SCN – GVL: 1,5,10,20 – 3 mins.
- Gut – GVL/FX 405, master gut protocol: 4,4,9,26 – 3 mins.

Bilateral structure located in anterior part of hypothalamus. The central pacemaker of the circadian timing system and **regulates most circadian rhythms in the body**

Ma MA, Morrison EH. **Neuroanatomy, Nucleus Suprachiasmatic**. [Updated 2022 Jul 25]. Treasure Island (FL): StatPearls Publishing

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