



# THE ULTIMATE LONGEVITY CONFERENCE



*The Science & Strategies Behind Extending Lifespan*

**DUBLIN, IRELAND & ONLINE  
SATURDAY, 21ST SEPTEMBER 2024**



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ROUNTREE**



**DR. OLIVIA  
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ABDEL-HADI**

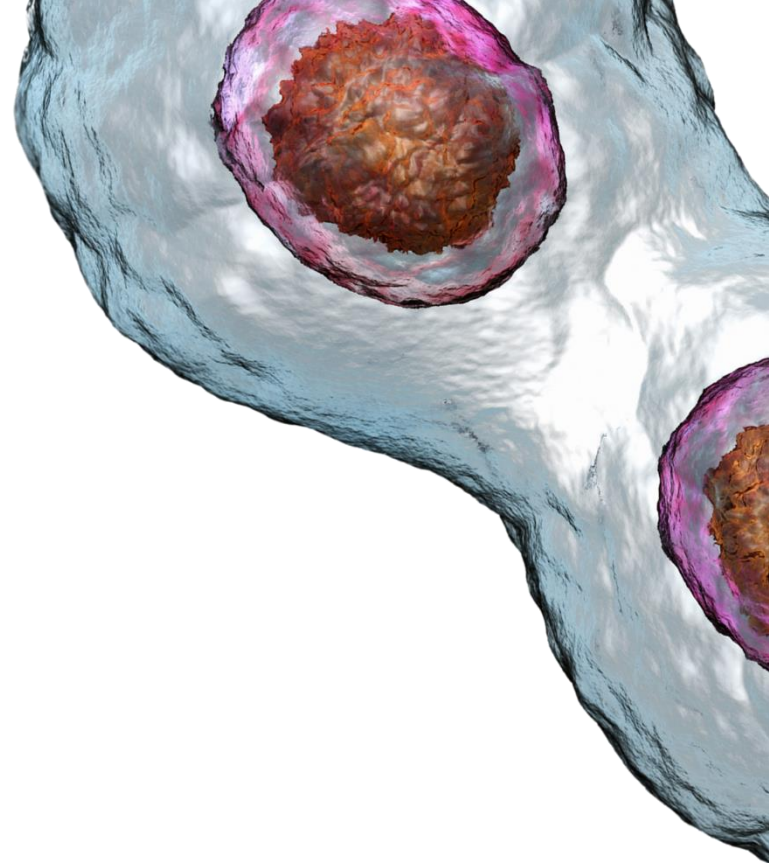
THE ULTIMATE  
**LONGEVITY**  
**CONFERENCE**

The Science & Strategies Behind Extending Lifespan

Pioneering Longevity:  
New Discoveries and  
Timeless Therapies

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Dr. Olivia Lesslar BIR, MBBS



# About

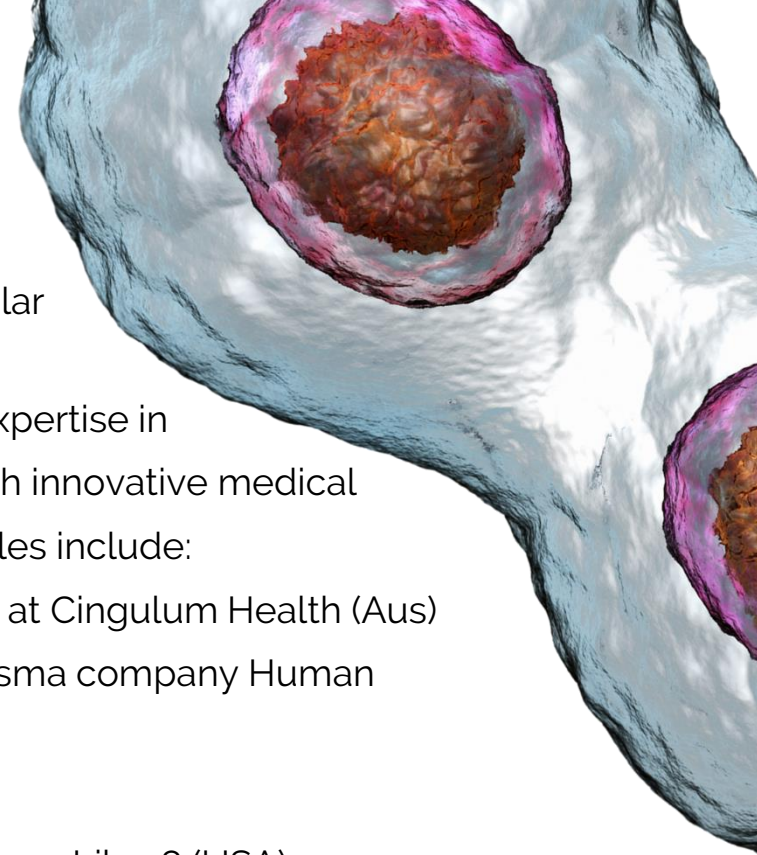
Dr Olivia Lesslar BIR, MBBS    @drolivialelesslar



Dr Olivia is an Australian medical doctor with an expertise in psychoneuroimmunology. She holds positions with innovative medical practices and companies internationally. These roles include:

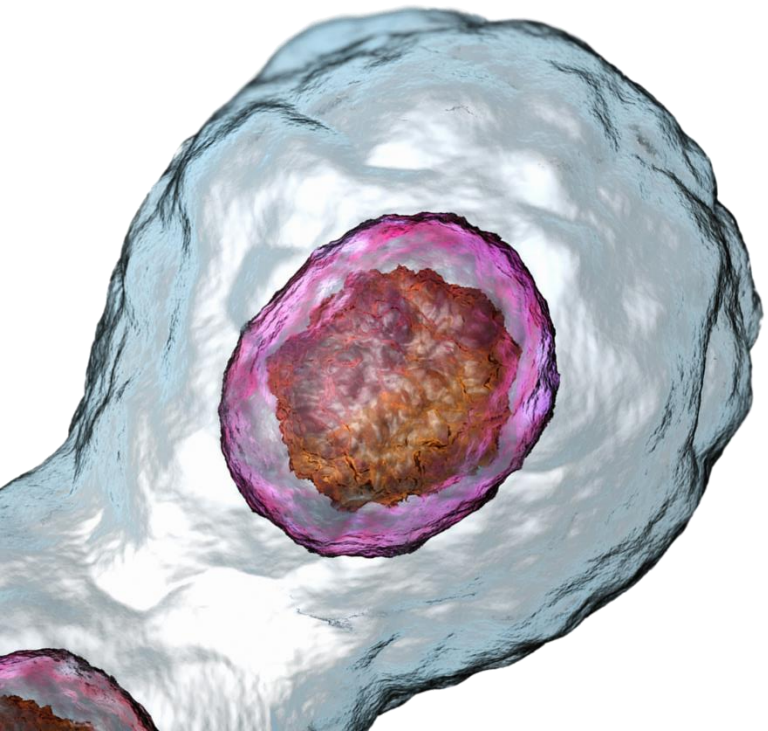
- Director of Functional and Longevity Medicine at Cingulum Health (Aus)
- Chief Medical Advisor at cold atmospheric plasma company Human Regenerator (UK)
- Chief Medical Officer at Atlas (Aus)
- Medical Director at mind-body sciences company Liber8 (USA)
- Chief Medical Officer at L'evive Labs (Malaysia)
- Medical Director of Veteran Peace (USA)
- Vice-President of Women in Defence Security Alliance (Fin)
- Science Director at Sens.ai neurotechnology (Can).

Dr Olivia is affiliated with longevity clinics LifeSpan Medicine LA, Wellgevity UK, and Everest Health Washington DC. Dr Olivia is an Adjunct Senior Lecturer with Griffith University's National Centre for Neuroimmunology and Emerging Diseases (Aus), and a faculty lecturer at the Geneva College of Longevity Science. She is a Trustee of the British College of Functional Medicine.



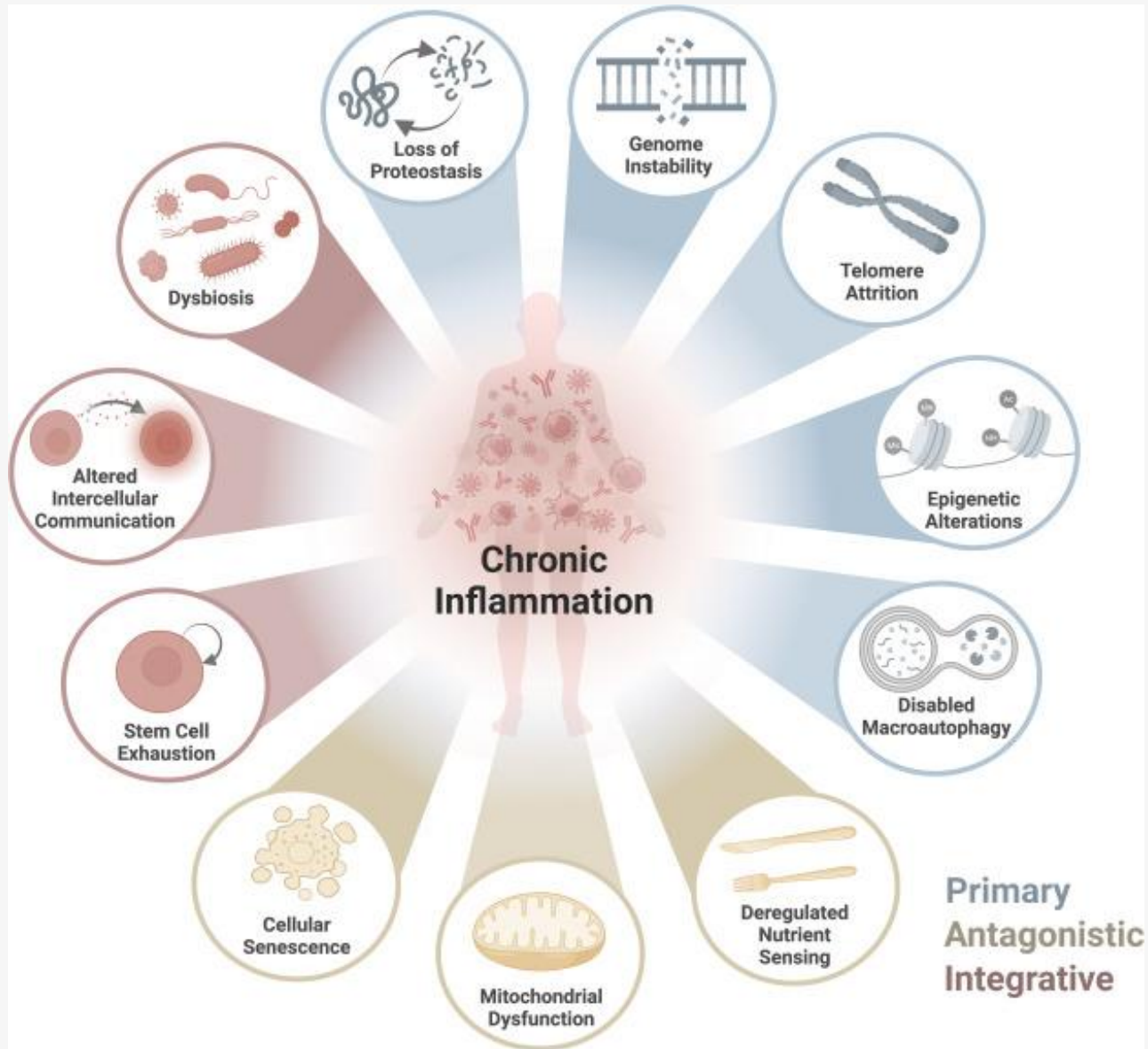
Our attitudes to life purpose, wellness, salugenesis, and longevity (extended lifespan) are philosophical discussions. How you feel about death and what aging means to you determines what you do and how you tackle the 'now' in anticipation of the future. What are your beliefs about disease and aging, and the propensity of the body to heal? What drives your quest for a longer (presumably, healthier) life?

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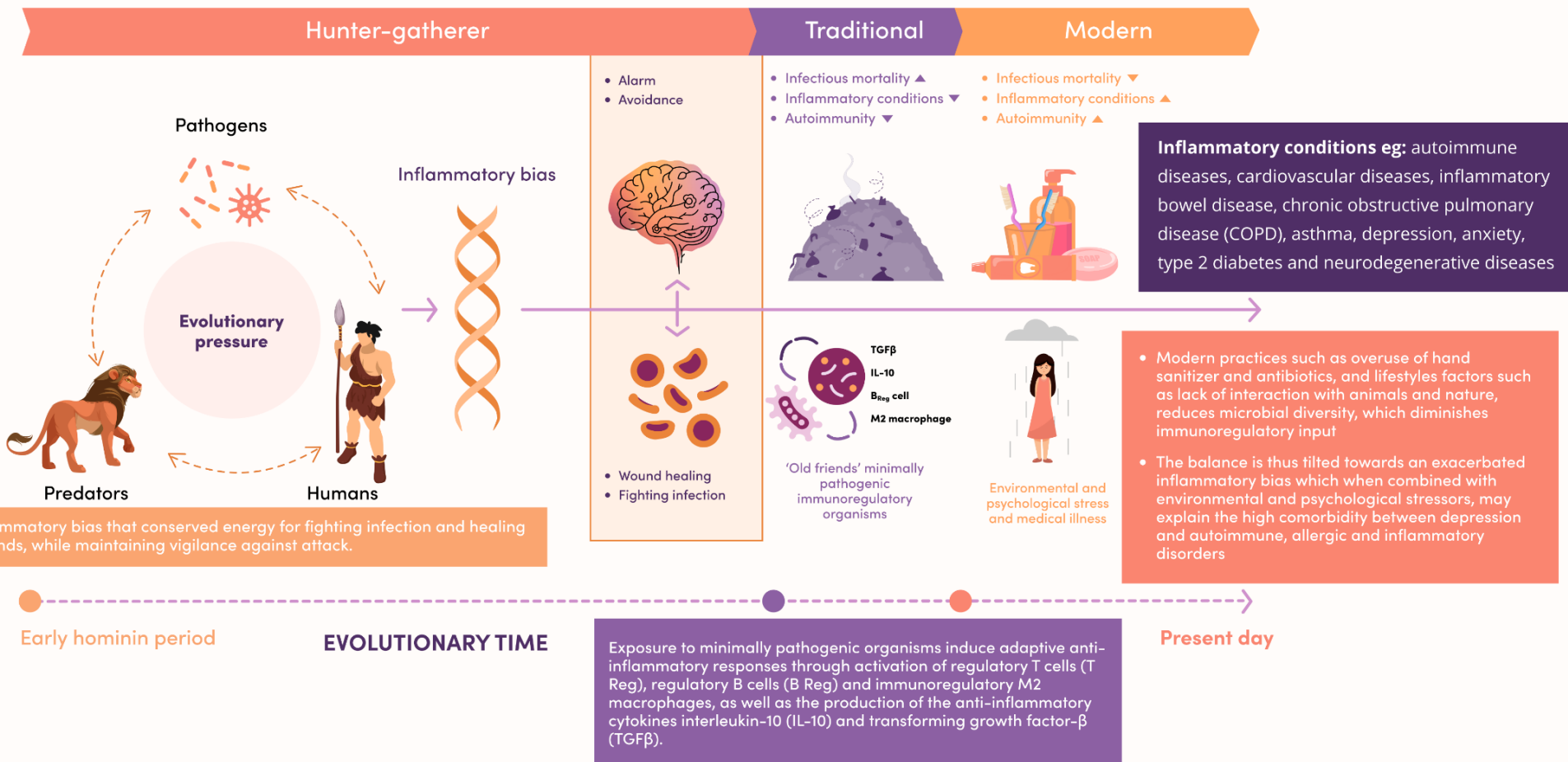
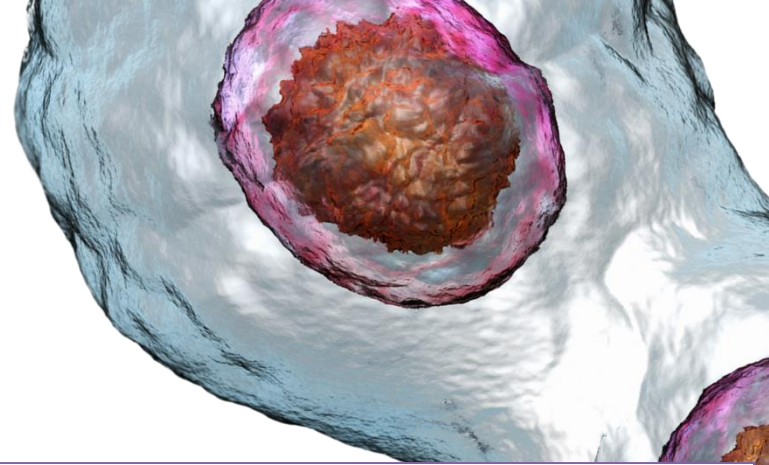


# Inflammaging

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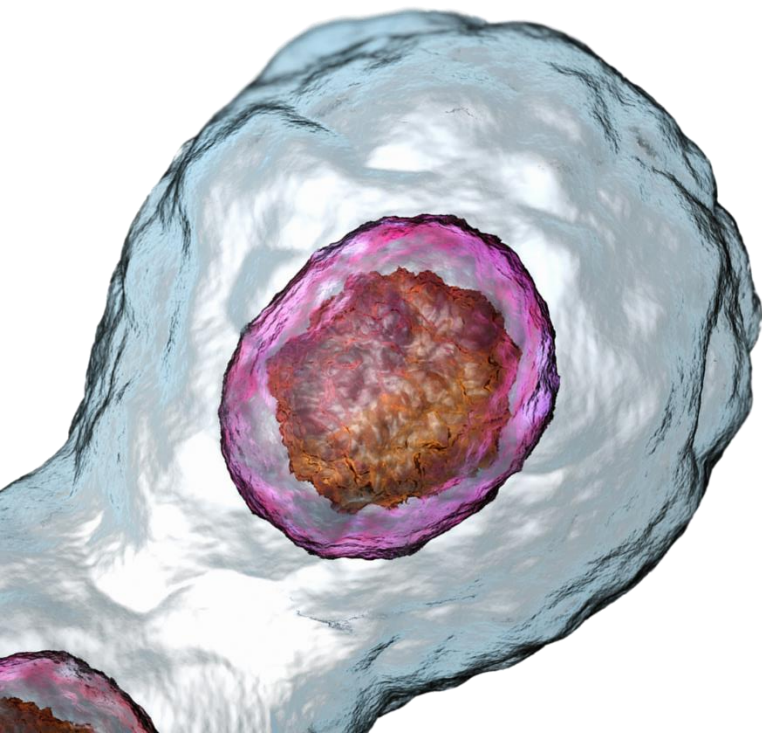


# Inflammatory Bias



# Blood Biomarkers

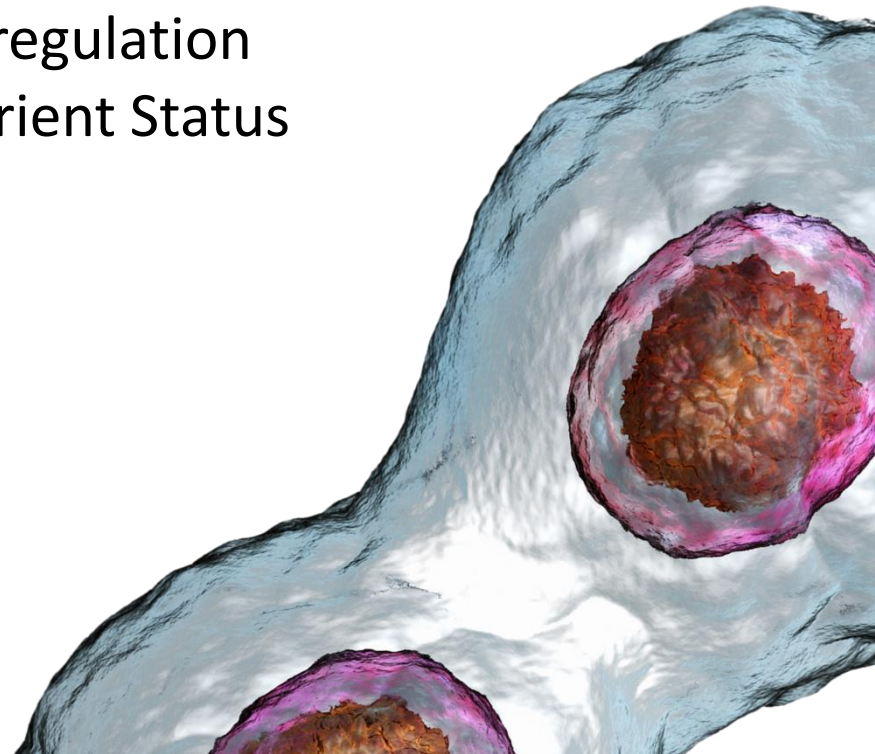
(of Aging and Inflammation...)



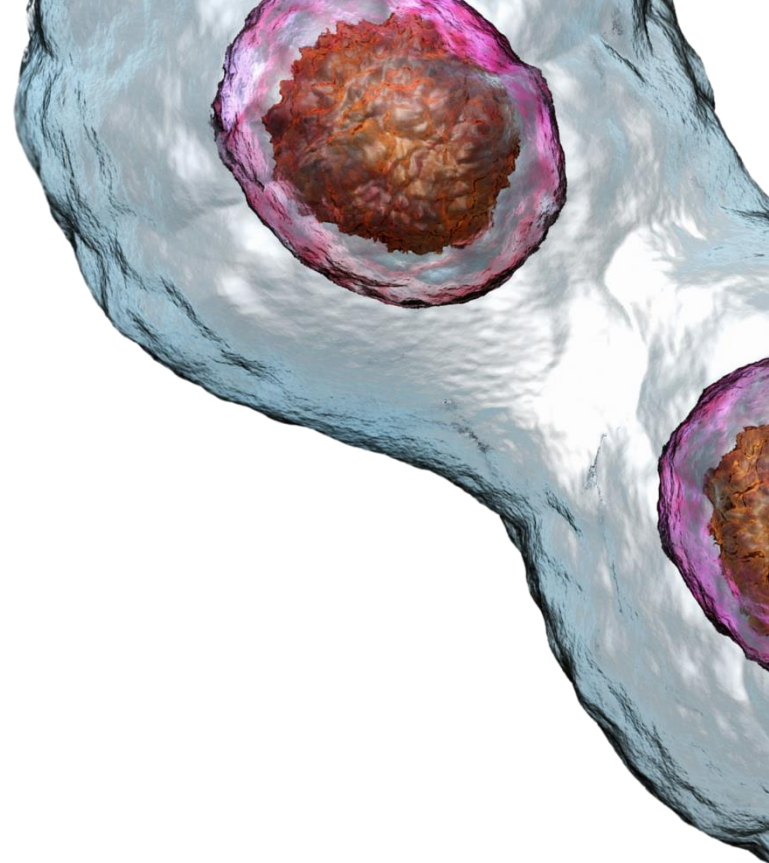
hs-CRP, ESR, IL-1, IL-6, IL-8, histamine, tryptase, TNF- $\alpha$ , Fibrinogen, Procalcitonin, Serum Amyloid A, WBC, Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), Monocyte-to-HDL Cholesterol Ratio (MHR), Soluble CD40 Ligand (sCD40L), GlycA, Myeloperoxidase (MPO), Lipoprotein-Associated Phospholipase A2 (Lp-PLA2), Adiponectin, Galectin-3, Soluble Urokinase Plasminogen Activator Receptor (suPAR), Homocysteine, Pentraxin 3 (PTX3), ox-LDL, TMAO, Uric Acid, F2-Isoprostanes, matrix metalloproteinases (MMPs): MMP-1 (Collagenase-1), MMP-2 (Gelatinase A), MMP-3 (Stromelysin-1), MMP-7 (Matrilysin), MMP-8 (Collagenase-2), MMP-9 (Gelatinase B), MMP-12 (Macrophage Metalloelastase), MMP-13 (Collagenase-3), MMP-14 (Membrane-Type 1 MMP), MMP-19, Heat Shock Proteins: eHSP60,  $\sim$ HSP70, HSP90, eHSP27, eGRP78...

# “My Tests are Normal”

1. Subclinical or Low-Grade Inflammation
2. Inflammation in Specific Tissues or Compartmentalisation
3. Timing and Episodic Nature of Inflammation
4. Differences in Individual Immune Responses
5. The Type of Tests Used
6. The Influence of Medications and Lifestyle Factors
7. Inflammation Resolution and Dysregulation
8. Impact of Nutrition and Micronutrient Status







# Biomarkers:

- Blood
- Physical/ Functional
- Cognitive

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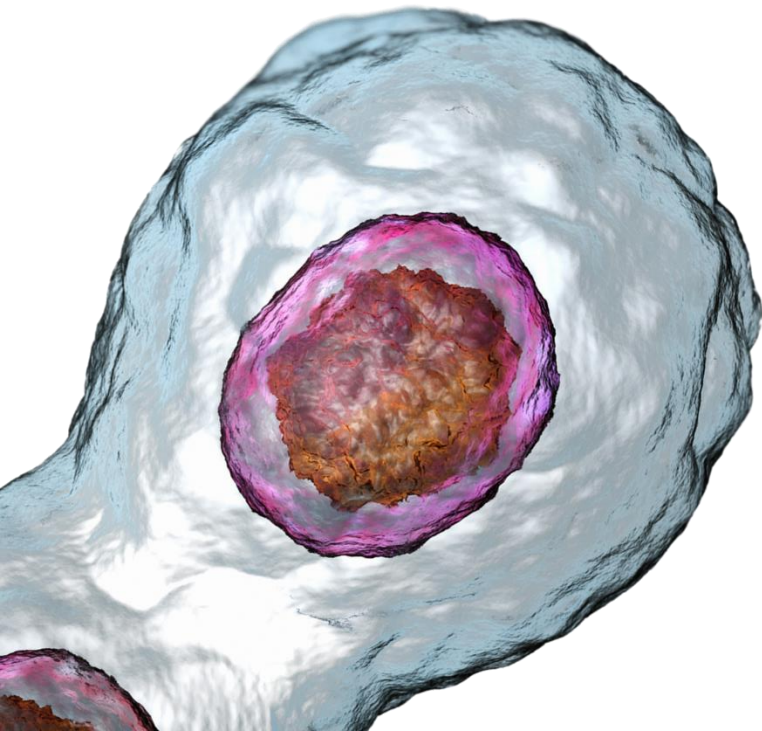
Dr. Olivia Lesslar BIR, MBBS

NTOI



# Biomarkers

Standard blood tests,  
Newer insights



**Neutrophil-to-Lymphocyte Ratio:** a higher NLR is a marker of systemic inflammation and is associated with worse outcomes in conditions like cancer, cardiovascular diseases, and infections.

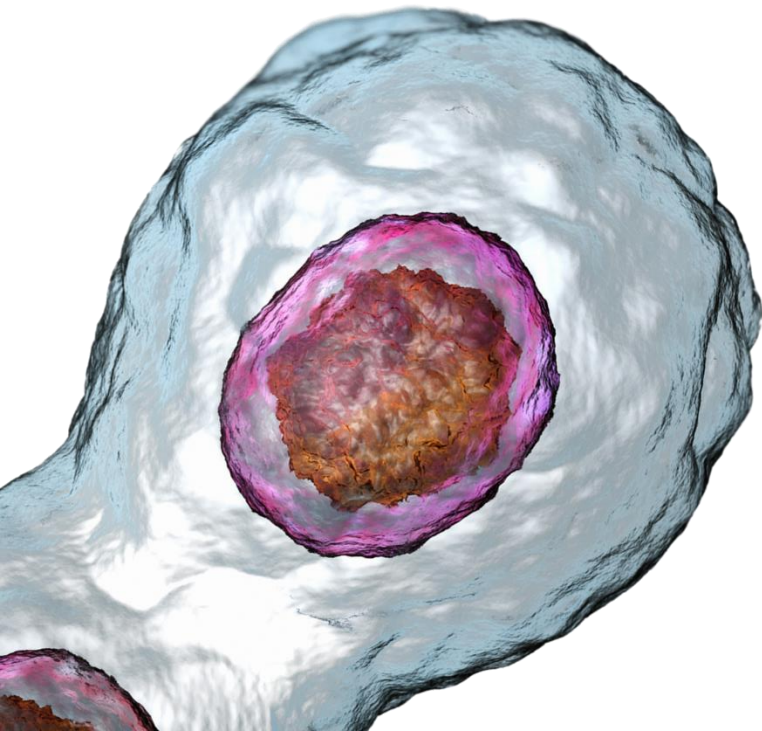
**Platelet-to-Lymphocyte Ratio:** associated with inflammation and is used as a prognostic marker in cardiovascular diseases, cancers, and chronic inflammatory conditions.

**Monocyte-to-HDL Cholesterol Ratio:** reflects systemic inflammation and has been linked to cardiovascular diseases and metabolic syndrome.

**Triglyceride-to-HDL Cholesterol Ratio (TG/HDL):** A high TG/HDL ratio is strongly associated with insulin resistance, metabolic syndrome, and increased cardiovascular risk. It reflects an imbalance in lipid metabolism and is considered a useful predictor of heart disease.

# Biomarkers

Standard blood tests,  
Newer insights



**Cystatin C:** This marker provides a more accurate assessment of kidney function, especially in people with muscle mass variations (e.g., athletes, elderly) where creatinine levels can be misleading.

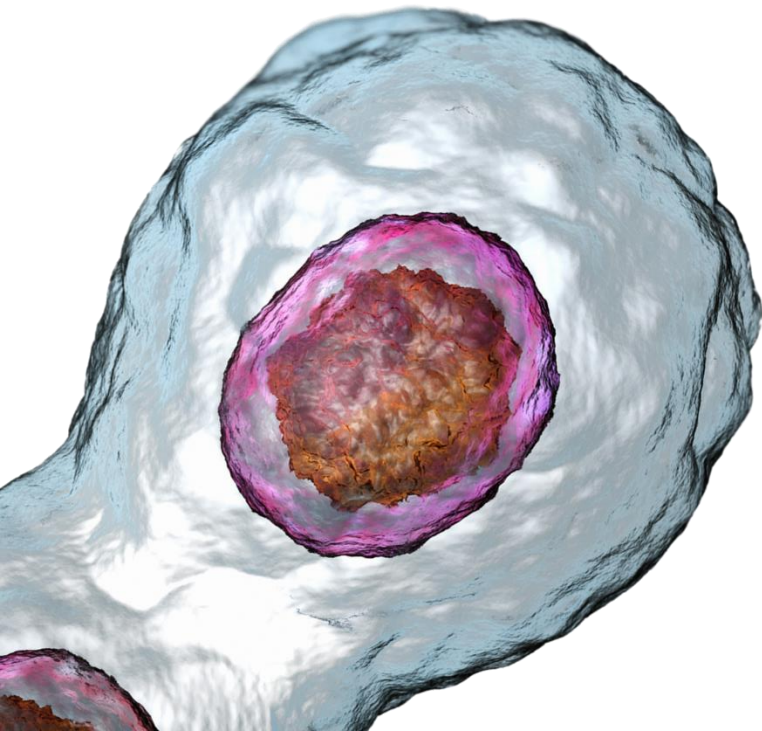
**BUN-to-Creatinine Ratio:** A high ratio can indicate dehydration, heart failure, or protein catabolism, while a low ratio might suggest liver disease or malnutrition.

**Hepcidin:** Hepcidin is a peptide hormone primarily produced by the liver that controls the absorption, distribution, and storage of iron by regulating the activity of ferroportin, a protein that exports iron from cells into the bloodstream. High hepcidin levels can also impact the absorption and utilization of zinc and copper due to competition at the transport level.

**Vitamin D-to-PTH Ratio:** Instead of relying on vitamin D levels alone, the ratio helps assess how well the body is compensating for low vitamin D. If PTH is high despite normal calcium, it signals functional vitamin D deficiency.

# Biomarkers

## Newer insights



**GlycA:** increased levels of this composite signal (glycosylation of several acute phase proteins) derived from NMRS of serum/ plasma have been linked to cardiovascular risk, metabolic syndrome, and overall mortality.

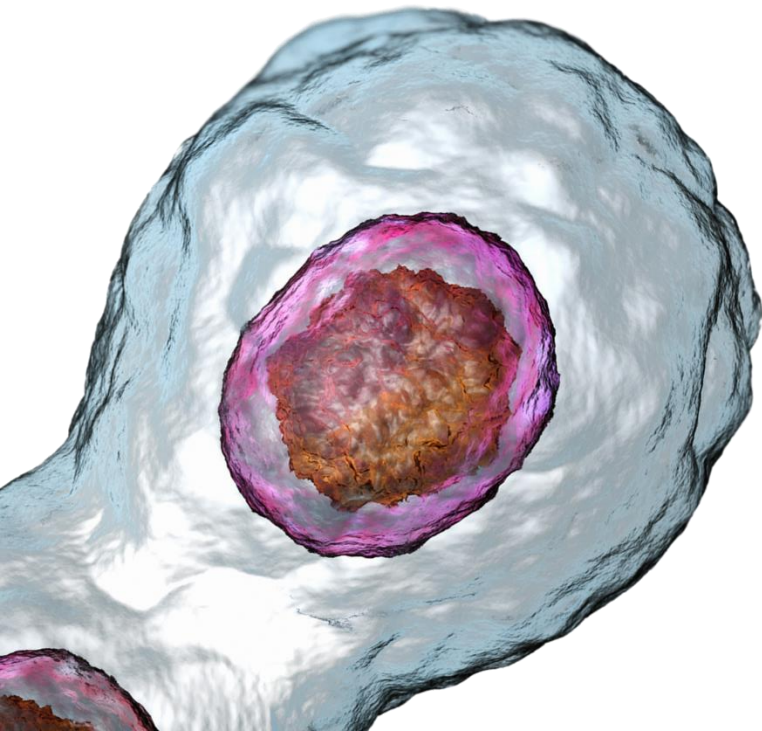
**F2-Isoprostanes:** High levels of F2-isoprostanes in blood/ urine indicate oxidative damage to cells and tissues, contributing to diseases like cancer, CVD, and neurodegeneration.

**Advanced Lipoprotein Testing:** Smaller, denser LDL particles are more atherogenic and associated with higher cardiovascular risk than larger particles

**Adiponectin:** High adiponectin levels are associated with reduced inflammation, improved insulin sensitivity.

# Biomarkers

## Newer insights



**Insulin-like Growth Factor 1:** Both high and low levels of IGF-1 have been linked to age-related diseases. Balancing IGF-1 is important for reducing cancer risk and promoting healthy aging.

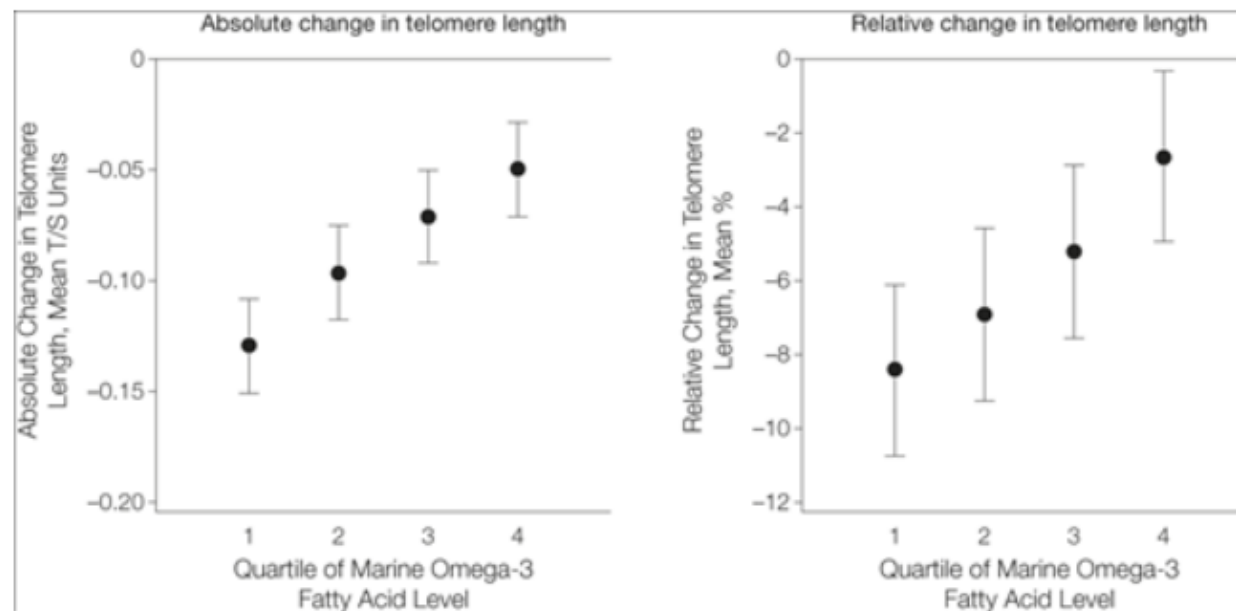
**HOMA-IR:** This index calculates insulin resistance using fasting insulin and glucose levels, offering a more sensitive measure often before blood glucose levels become abnormal.

**TMAO (Trimethylamine N-oxide):** A gut microbiome-derived metabolite. High TMAO levels are linked to increased risk of CVD, particularly atherosclerosis. It reflects microbiome health (a higher ratio of Firmicutes to Bacteroidetes respond more to dietary TMA precursors, which can increase TMAO production).

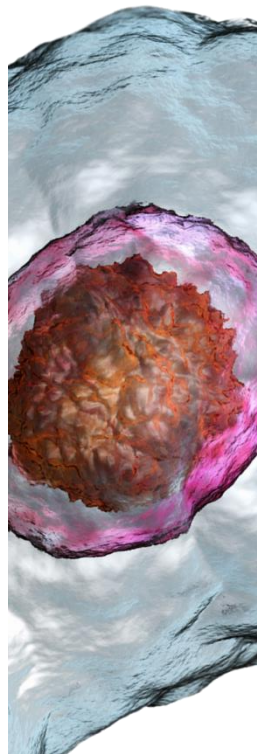
**Biological Age Testing:** DNA Methylation, Immune Age Profiling, Proteomic/ Metabolomic Clocks, Glycosylation patterns of IgG

**Telomere Length Testing / Omega-3 Index**

**Figure. Absolute and Relative Mean Changes in Telomere Length Over 5 Years by Quartile of Omega-3 Fatty Acid Level, Adjusted for Age and Baseline Telomere Length**



Error bars indicate 95% confidence intervals. T/S indicates telomere-to-single-copy gene ratio.  $P < .001$  for linear trend for both absolute and relative change. See [Table 1](#) for definitions of quartiles.



Original Article

# Red blood cell polyunsaturated fatty acids and mortality in the Women's Health Initiative Memory Study

William S. Harris PhD<sup>a,b</sup>, Karen L. Margolis MD, MPH<sup>e</sup>, Theodore M. Brasky PhD<sup>g</sup>

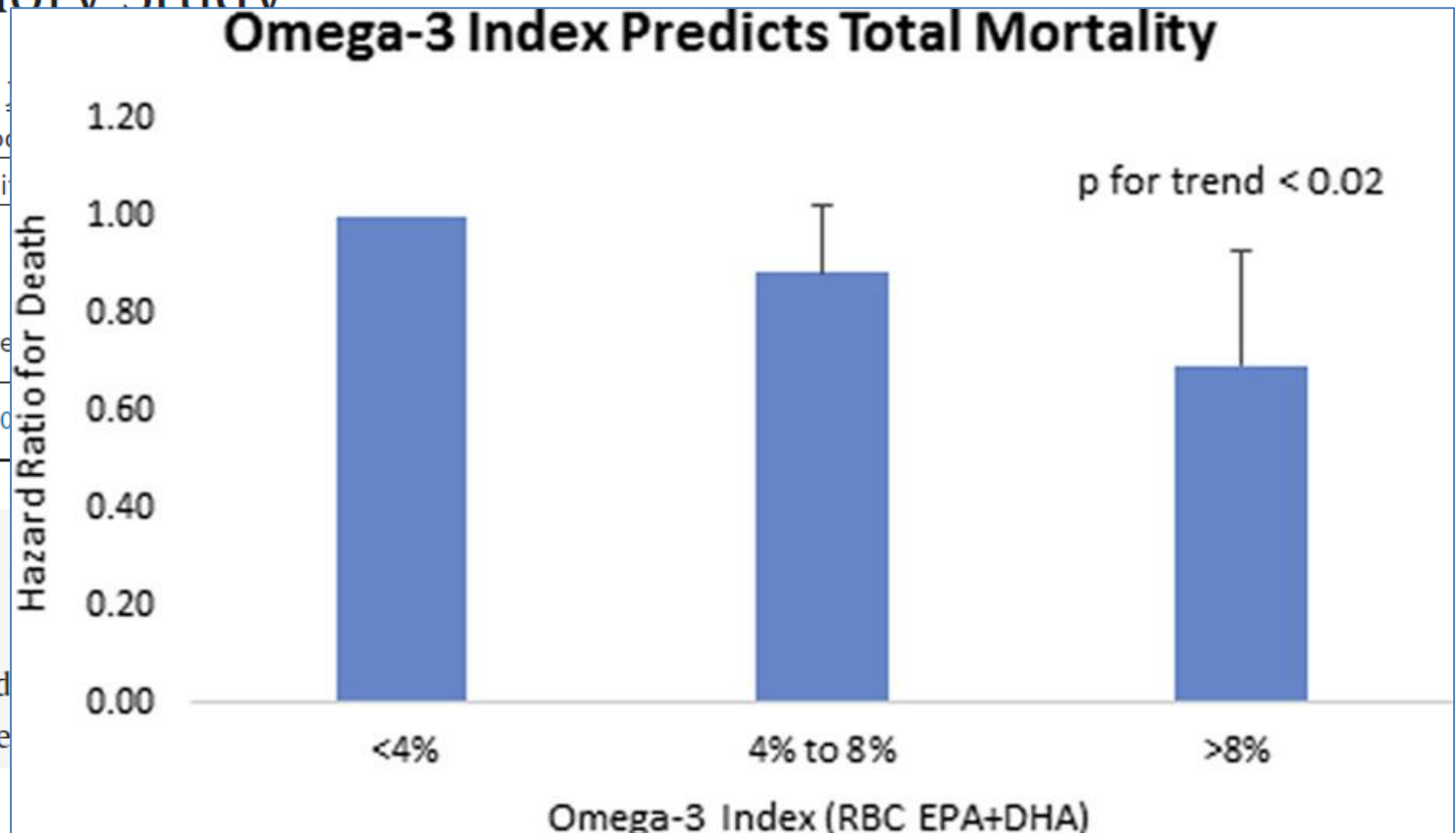
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<https://doi.org/10.1016/j.jacl.2016.12.0>

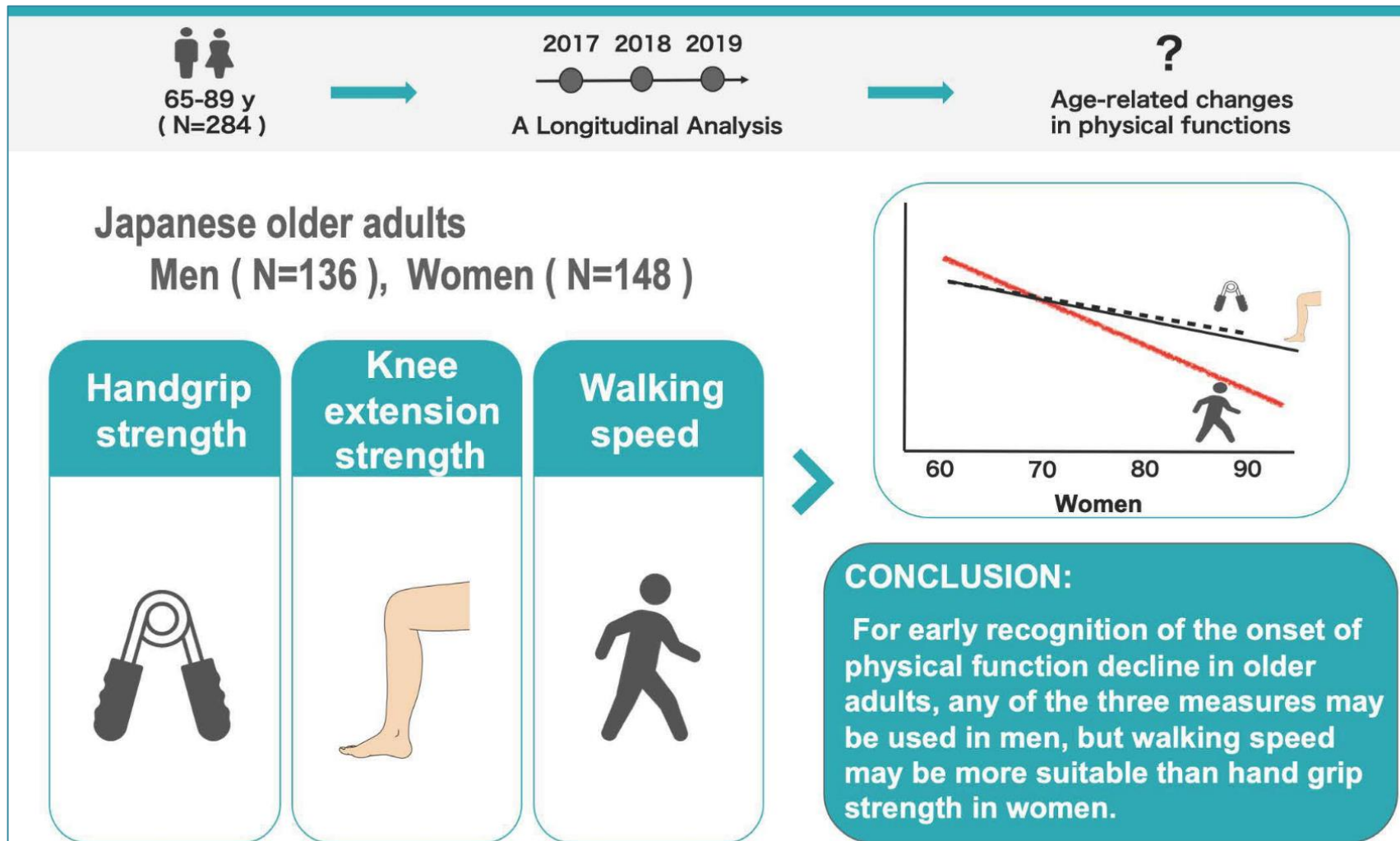
## Highlights

- Relations between red blood cell polyunsaturated fatty acids and mortality studied in 6501 women



# Physical / Functional Biomarkers

1. **Grip Strength** Measured using a handgrip dynamometer.
2. **Walking Speed (Gait Speed)**
3. **Standing Balance and Timed Up and Go (TUG)**
4. **Chair Rise Test (Sit-to-Stand Test)**
5. **Flexibility and Range of Motion**



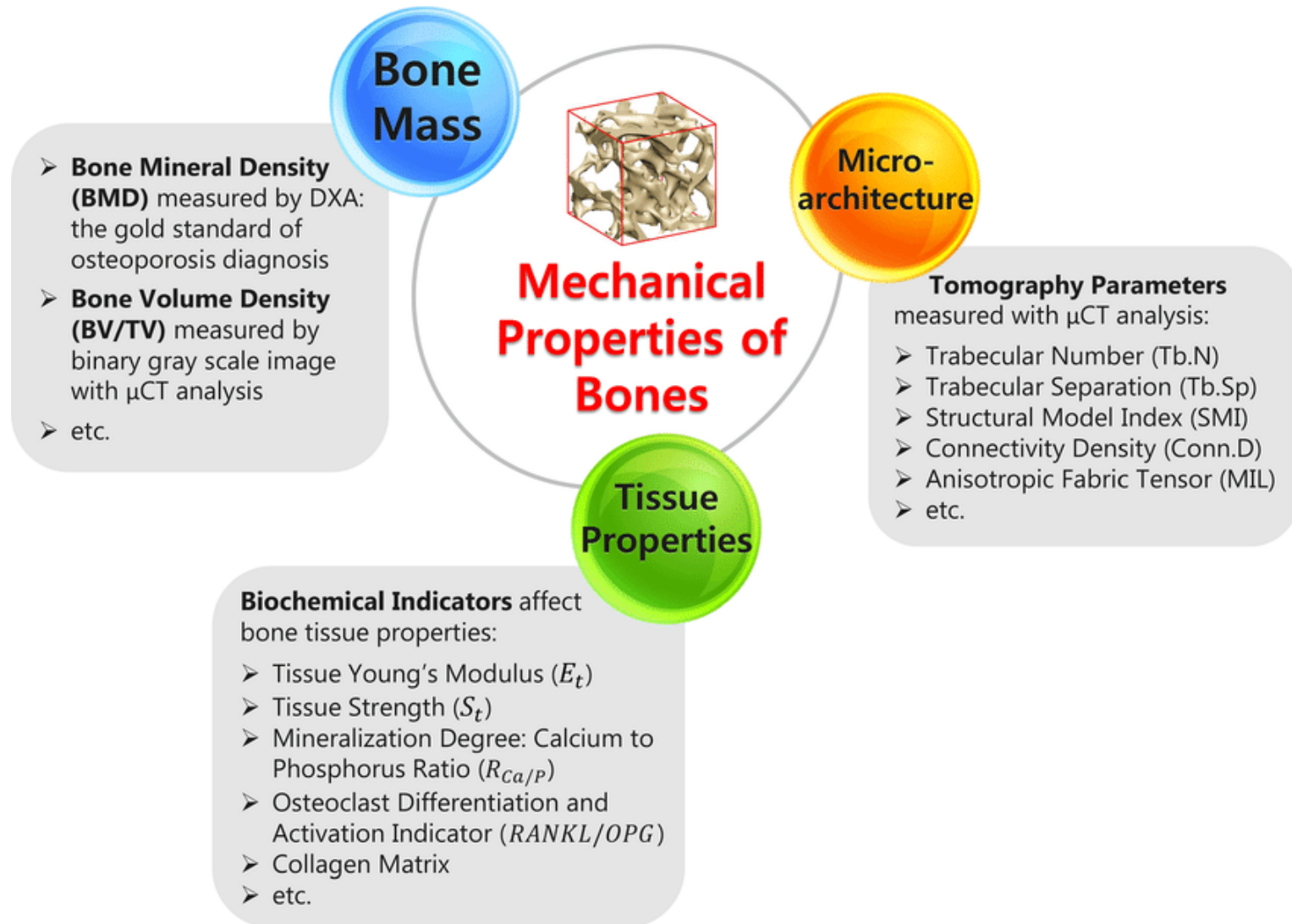


6. VO2 Max

7. Blood Pressure Response to Exercise

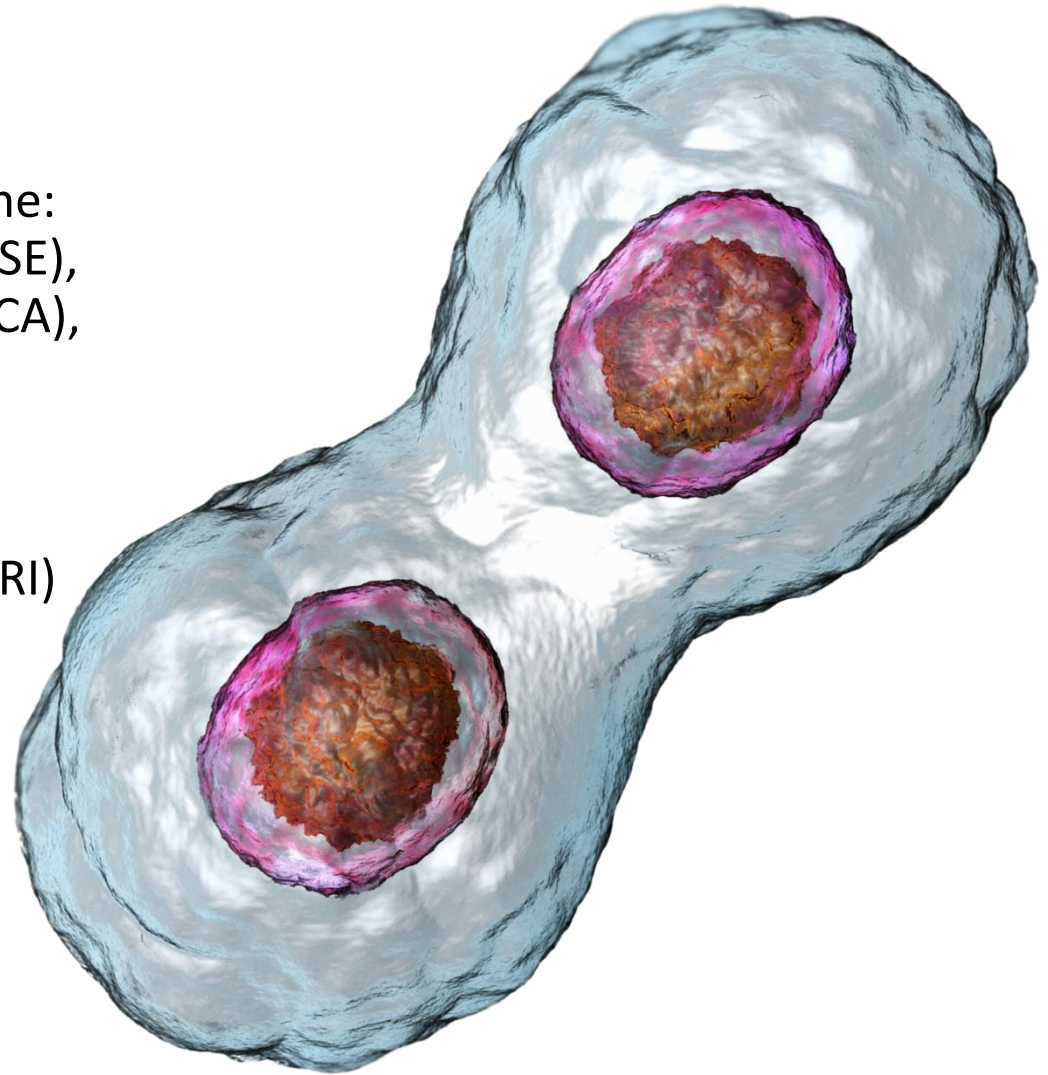
8. Body Mass Index (BMI) and Waist-to-Hip Ratio

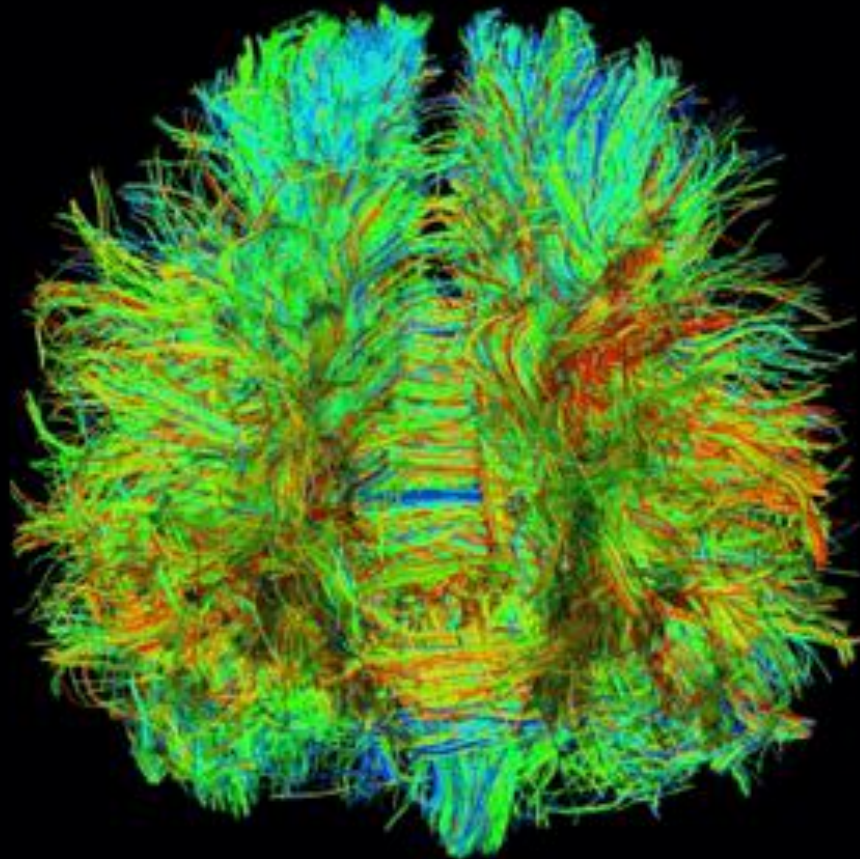
9. Muscle Mass and Body Composition inc bone density. DEXA vs peripheral quantitative computed tomography QCT (pQCT) and quantitative ultrasound (QUS)



# Cognitive Biomarkers

- 1. Cognitive Performance Tests** help identify early signs of cognitive decline: Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Trail Making Test (TMT).
- 2. Brain Volume and Structural Integrity** (MRI)
- 3. Brain Functional Connectivity** (fMRI)
- 4. Cerebral Blood Flow** (CBF)
- 5. Electroencephalography** (EEG)
- 6. Neurotrophic Factors** (BDNF)
- 7. Cognitive Reserve Indicators**
- 8. Sleep Quality and Architecture**
- 9. Cerebrospinal Fluid** (CSF)

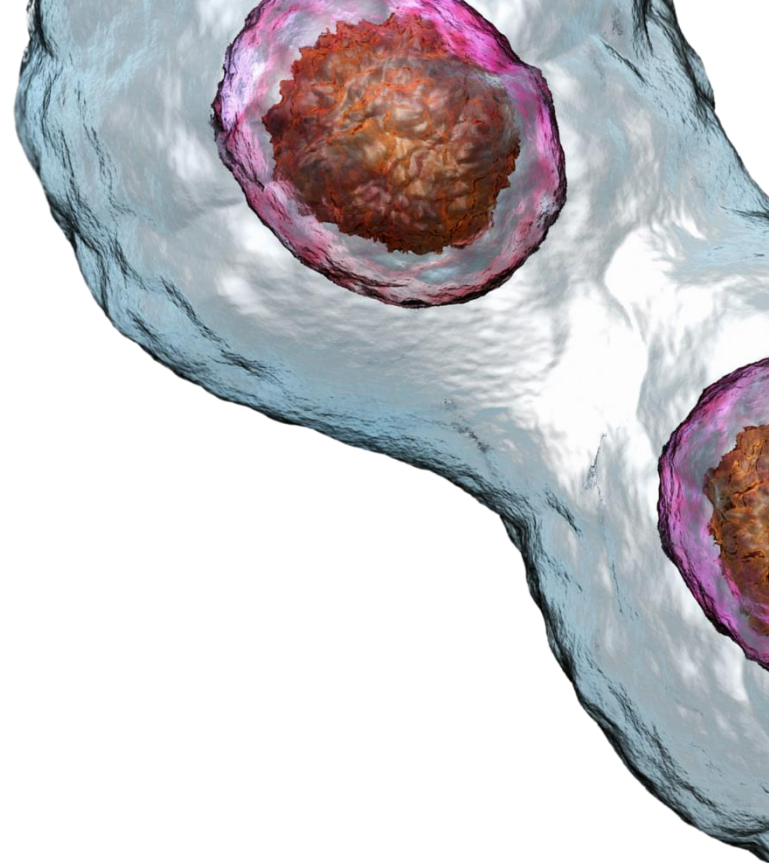




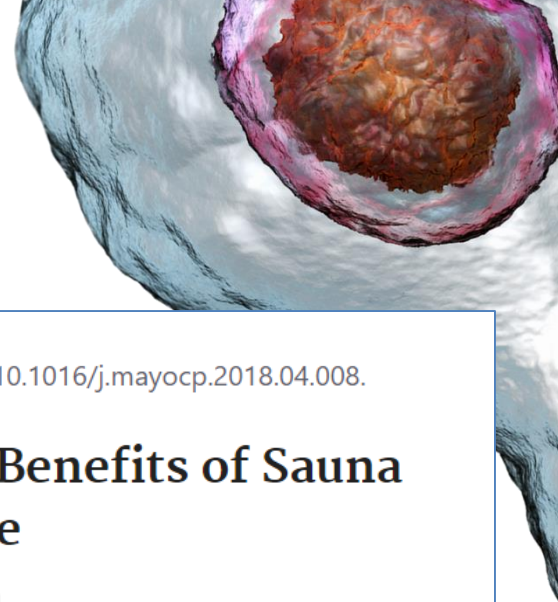
# Timeless Therapies

1. Sauna and Heat Therapy
  2. Breathwork
  3. Fasting and Caloric Restriction
  4. Meditation and Mindfulness
  5. Yoga, Tai Chi and Qigong
  6. Cold Water Immersion
- 

Dr. Olivia Lesslar BIR, MBBS



# Ancient Therapies, Modern Assays



Sauna

Heat  
Therapy

Hyperthermia  
Therapy

Review > Mayo Clin Proc. 2018 Aug;93(8):1111-1121. doi: 10.1016/j.mayocp.2018.04.008.

## Cardiovascular and Other Health Benefits of Sauna Bathing: A Review of the Evidence

Jari A Laukkanen<sup>1</sup>, Tanjaniina Laukkanen<sup>2</sup>, Setor K Kunutsor<sup>3</sup>

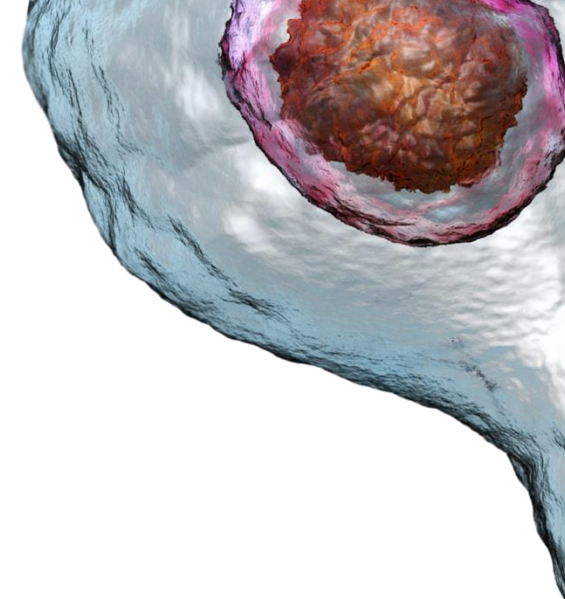
Affiliations + expand

PMID: 30077204 DOI: 10.1016/j.mayocp.2018.04.008

### Abstract

Sauna bathing, an activity that has been a tradition in Finland for thousands of years and mainly used for the purposes of pleasure and relaxation, is becoming increasingly popular in many other populations. Emerging evidence suggests that beyond its use for pleasure, sauna bathing may be linked to several health benefits, which include reduction in the risk of vascular diseases such as high blood pressure, cardiovascular disease, and neurocognitive diseases; nonvascular conditions such as pulmonary diseases; mortality; as well as amelioration of conditions such as arthritis, headache, and flu. The beneficial effects of sauna bathing on these outcomes have been linked to its effect on circulatory, cardiovascular, and immune functions. It has been postulated that regular sauna bathing may improve cardiovascular function via improved endothelium-dependent dilatation, reduced arterial stiffness, modulation of the autonomic nervous system, beneficial changes in circulating lipid profiles, and lowering of systemic blood pressure. This review summarizes the available epidemiological, experimental, and interventional evidence linking Finnish sauna bathing and its effects on cardiovascular outcomes and other disease conditions on the basis of a comprehensive search for observational studies, randomized controlled trials, and non-randomized controlled trials


# Ancient Therapies, Modern Assays



 Experimental Gerontology  
Volume 154, 15 October 2021, 111509 

Review

## Sauna use as a lifestyle practice to extend healthspan


Rhonda P. Patrick <sup>a</sup>  , Teresa L. Johnson <sup>b</sup>  

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### Highlights

- Sauna use mimics physiological and protective responses induced during exercise.
- Repeated sauna use optimizes stress responses via [hormesis](#) and heat shock proteins.
- Sauna use appears to reduce morbidity and mortality in a dose-dependent manner.

- Sauna use has been shown to:
- improve HRV, indicating enhanced parasympathetic activity.
  - lower blood pressure
  - increase NO, a vasodilator that improves blood flow and reduces blood pressure,
  - increase HSP70 and HSP90 levels, providing cellular protection and improved protein folding.
  - increase Growth Hormone and Endorphins

# Ancient Therapies, Modern Assays



## Breathwork

 **frontiers**  
in Human Neuroscience

[Front Hum Neurosci.](#) 2018; 12: 353.

Published online 2018 Sep 7. doi: [10.3389/fnhum.2018.00353](https://doi.org/10.3389/fnhum.2018.00353)

PMCID: PMC6137615

PMID: [30245619](https://pubmed.ncbi.nlm.nih.gov/30245619/)

How Breath-Control Can Change Your Life: A Systematic Review on Psycho-

**Results:** The main effects of slow breathing techniques cover autonomic and central nervous systems activities as well as the psychological status. Slow breathing techniques promote autonomic changes increasing Heart Rate Variability and Respiratory Sinus Arrhythmia paralleled by Central Nervous System (CNS) activity modifications. EEG studies show an increase in alpha and a decrease in theta power. Anatomically, the only available fMRI study highlights increased activity in cortical (e.g., prefrontal, motor, and parietal cortices) and subcortical (e.g., pons, thalamus, sub-parabrachial nucleus, periaqueductal gray, and hypothalamus) structures. Psychological/behavioral outputs related to the abovementioned changes are increased comfort, relaxation, pleasantness, vigor and alertness, and reduced symptoms of arousal, anxiety, depression, anger, and confusion.

slow breathing techniques (<10 breaths/minute) and their effects on healthy subjects.

# Morning breathing exercises prolong lifespan by improving hyperventilation in people living with respiratory cancer

Wei-Jie Wu, MB<sup>a</sup>, Shan-Huan Wang, MB<sup>a,b</sup>, Wei Ling, MD<sup>a</sup>, Li-Jun Geng, MPhil<sup>a</sup>, Xiao-Xi Zhang, PhD<sup>a</sup>, Lan Yu, MPhil<sup>a,c</sup>, Jun Chen, MPhil<sup>a,c</sup>, Jiang-Xi Luo, MD<sup>a,c</sup>, Hai-Lu Zhao, PhD<sup>a,\*</sup>

## Abstract

Disturbance of oxygen–carbon dioxide homeostasis has an impact on cancer. Little is known about the effect of breath training on cancer patients. Here we report our 10-year experience with morning breathing exercises (MBE) in peer-support programs for cancer survivors.

We performed a cohort study to investigate long-term surviving patients with lung cancer (LC) and nasopharyngeal cancer (NPC) who practiced MBE on a daily basis. End-tidal breath holding time (ETBHT) after MBE was measured to reflect improvement in alveolar O<sub>2</sub> pressure and alveolar CO<sub>2</sub> pressure capacity.

Patients (female, 57) with a diagnosis of LC (90 patients) and NPC (32 patients) were included. Seventy-six of them were MBE trainees. Average survival years were higher in MBE trainees (9.8±9.5) than nontrainees (3.3±2.8). The 5-year survival rate was 56.6% for MBE trainees and 19.6% for nontrainees (RR=5.371, 95% CI=2.271–12.636,  $P < 0.001$ ). Survival probability of the trainees further increased 17.9-fold for the 10-year survival rate. Compared with the nontrainees, the MBE trainees shows no significant differences in ETBHT (baseline,  $P=0.795$ ; 1–2 years,  $P=0.301$ ; 3–4 years,  $P=0.059$ ) at baseline and within the first 4 years. From the 5th year onwards, significant improvements were observed in ETBHT, aCO<sub>2</sub>%, PaCO<sub>2</sub>, and PaO<sub>2</sub> ( $P=0.028$ ). In total, 18 trainees (40.9%) and 20 nontrainees (74.1%) developed new metastasis (RR=0.315, 95% CI=0.108–0.919,  $P=0.031$ ).

MBE might benefit for the long-term survival in patients with LC and NPC due to improvement in hyperventilation.

**Abbreviations:** ETBHT = end-tidal breath holding time, LC = lung cancer, MBE = morning breathing exercises, NPC = nasopharyngeal carcinoma.

**Keywords:** hyperventilation, lung cancer, morning breathing exercises, nasopharyngeal cancer






## Yoga Breathing, Meditation, and Longevity

Richard P. Brown, Patricia L. Gerbarg

First published: 28 August 2009 | <https://doi.org/10.1111/j.1749-6632.2009.04394.x> | Citations: 154

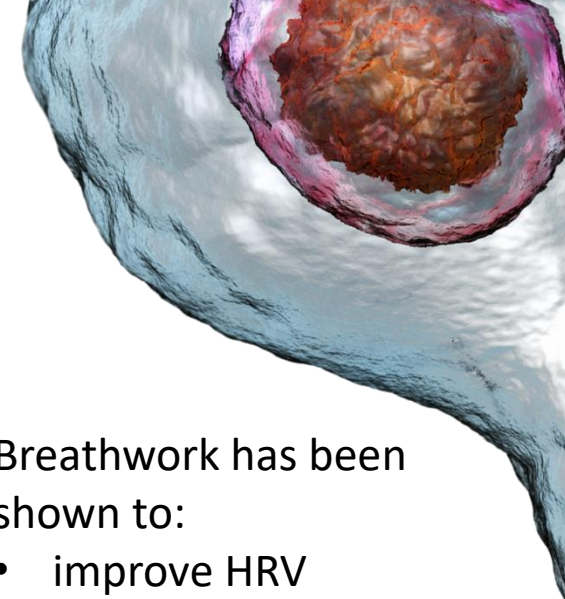
✉ Address for correspondence: Patricia L. Gerbarg, M.D., 86 Sherry Lane, Kingston, NY 12401. Voice: 845-331-8881; fax: 845-331-3562. [PGerbarg@aol.com](mailto:PGerbarg@aol.com)

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### Abstract

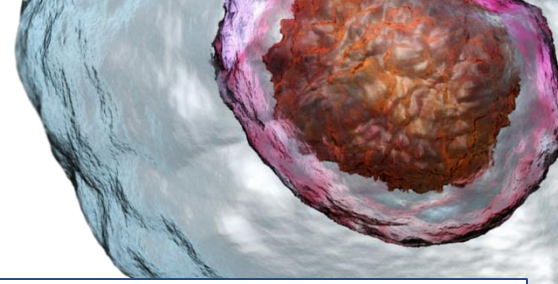
Yoga breathing is an important part of health and spiritual practices in Indo-Tibetan traditions. Considered fundamental for the development of physical well-being, meditation, awareness, and enlightenment, it is both a form of meditation in itself and a preparation for deep meditation. Yoga breathing (pranayama) can rapidly bring the mind to the present moment and reduce stress. In this paper, we review data indicating how breath work can affect longevity mechanisms in some ways that overlap with meditation and in other ways that are different from, but that synergistically enhance, the effects of meditation. We also provide clinical evidence for the use of yoga breathing in the treatment of depression, anxiety, post-traumatic stress disorder, and for victims of mass disasters. By inducing stress resilience, breath work enables us to rapidly and compassionately relieve many forms of suffering.



Breathwork has been shown to:

- improve HRV
- improve oxygen delivery and metabolic function
- increase alpha and theta waves (on EEG), which are associated with relaxation, meditation, and altered states of consciousness
- normalise saliva cortisol levels
- reduce pro-inflammatory cytokines like TNF- $\alpha$  and increase anti-inflammatory cytokines like IL-10.

# Ancient Therapies, Modern Assays



Fasting

Restricted Eating  
Windows

Intermittent  
fasting

Extended Fasts

Wet vs Dry

Review > *Microb Physiol.* 2024;34(1):142-152. doi: 10.1159/000540068. Epub 2024 Jul 2.

## Health Benefits of Intermittent Fasting

B Lakshmi Reddy <sup>1</sup>, Vamsee S Reddy <sup>1</sup>, Milton H Saier Jr <sup>1</sup>

Affiliations + expand

PMID: 38955141 PMCID: PMC11262566 (available on 2025-07-02) DOI: 10.1159/000540068

### Abstract

We propose that intermittent fasting (time-restricted eating), in agreement with the conclusions of other biologists, as revealed in recent publications, promotes the achievement of numerous health benefits including the extension of human and animal lifespans. Background: There is evidence, obtained both with animal model systems and with humans, that intermittent fasting has health benefits. These benefits include extended longevity, weight loss, and counteracting various disease conditions. Such procedures positively influence the benefits of human tissue-specific microbiomes and minimize the consequences of organellar apoptosis. Key Messages: In this review, we attempt to summarize the predominant evidence, published in the scientific literature, relevant to the conclusions that in general, and in many specific instances, intermittent fasting has long-term benefits to animals, including humans, with respect to overall and specific organismal health and longevity.

**Keywords:** Cancer; Circadian rhythm; Health; Intermittent fasting; Metabolism.

© 2024 The Author(s). Published by S. Karger AG, Basel.

# Safety, health improvement and well-being during a 4 to 21-day fasting period in an observational study including 1422 subjects

the end of the fasting period complemented the pre-post analysis using mixed-effects linear models. Significant reductions in weight, abdominal circumference and blood pressure were observed in the whole group (each  $p < 0.001$ ). A beneficial modulating effect of fasting on blood lipids, glucoregulation and further general health-related blood parameters was shown. In all groups, fasting led to a decrease in blood glucose levels to low norm range and to an increase in ketone bodies levels (each  $p < 0.001$ ), documenting the metabolic switch. An increase in physical and emotional well-being (each  $p < 0.001$ ) and an absence of hunger feeling in 93.2% of the subjects supported the feasibility of prolonged fasting. Among the 404 subjects with pre-existing health-complaints, 341 (84.4%) reported an improvement. Adverse effects were reported in less than 1% of the participants. The results from 1422 subjects showed for the first time that Buchinger periodic

**Citation:** Wilhelmi de Toledo F, Grundler F, Bergouignan A, Drinda S, Michalsen A (2019) Safety, health improvement and well-being during a 4 to 21-day fasting period in an observational study including 1422 subjects. *PLoS ONE* 14(1): e0209353. <https://doi.org/10.1371/journal.pone.0209353>

**Editor:** Massimiliano Ruscica, Università degli Studi di Milano, ITALY

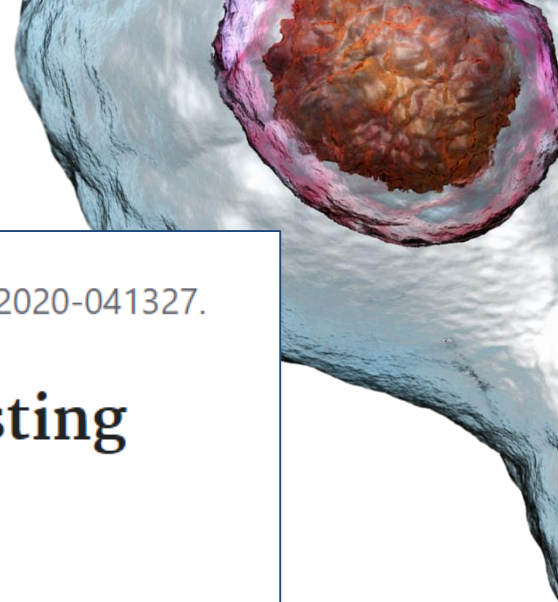
**Received:** June 18, 2018

**Accepted:** December 3, 2018

## Abstract

Only few studies document longer periods of fasting in large cohorts including non-obese participants. The aim of this study was to document prospectively the safety and any changes in basic health and well-being indicators during Buchinger periodic fasting within a specialised clinic. In a one-year observational study 1422 subjects participated in a fasting program consisting of fasting periods of between 4 and 21 days. Subjects were grouped in fasting period lengths of 5, 10, 15 and  $20 \pm 2$  days. The participants fasted according to the Buchinger guidelines with a daily caloric intake of 200–250 kcal accompanied by a moderate-intensity lifestyle program. Clinical parameters as well as adverse effects and well-being

# Ancient Therapies, Modern Assays



Review

> [Annu Rev Nutr. 2021 Oct 11:41:333-361. doi: 10.1146/annurev-nutr-052020-041327.](#)

## Cardiometabolic Benefits of Intermittent Fasting

Krista A Varady <sup>1</sup>, Sofia Cienfuegos <sup>1</sup>, Mark Ezpeleta <sup>1</sup>, Kelsey Gabel <sup>1</sup>

Affiliations + expand

PMID: 34633860 DOI: [10.1146/annurev-nutr-052020-041327](#)

### Abstract

This review aims to summarize the effects of intermittent fasting on markers of cardiometabolic health in humans. All forms of fasting reviewed here—alternate-day fasting (ADF), the 5:2 diet, and time-restricted eating (TRE)—produced mild to moderate weight loss (1-8% from baseline) and consistent reductions in energy intake (10-30% from baseline). **These regimens may benefit cardiometabolic health by decreasing blood pressure, insulin resistance, and oxidative stress.** Low-density lipoprotein cholesterol and triglyceride levels are also lowered, but findings are variable. Other health benefits, such as improved appetite regulation and favorable changes in the diversity of the gut microbiome, have also been demonstrated, but evidence for these effects is limited. Intermittent fasting is generally safe and does not result in energy level disturbances or increased disordered eating behaviors. In summary, intermittent fasting is a safe diet therapy that can produce clinically significant weight loss (>5%) and improve several markers of metabolic health in individuals with obesity.

# Ancient Therapies, Modern Assays

## Fasting

Intermittent Fasting, Time-Restricted Eating, Extended Fasting – Wet, Dry.  
Associated with benefits such as improved metabolic health, enhanced autophagy, and extended lifespan.

### **Metabolic Markers**

- Glucose, Insulin, and HOMA-IR: insulin sensitivity and glucose metabolism.
- Ketone Bodies ( $\beta$ -Hydroxybutyrate): enhanced metabolic flexibility.

### **Autophagy and Cellular Health**

- LC3 and Beclin-1 Levels: These proteins are markers of autophagy

### **Hormonal Changes**

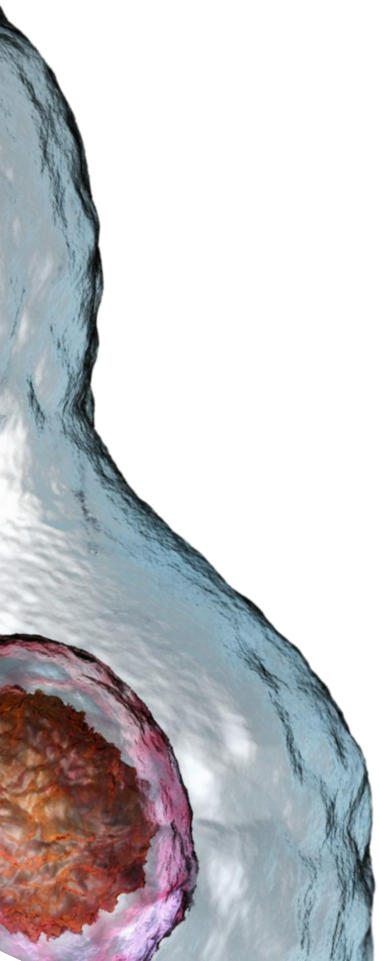
- Growth Hormone and IGF-1: Reduced insulin-like growth factor 1 (IGF-1) is associated with reduced cancer risk and improved longevity.

### **Inflammatory Markers**

- CRP, IL-6, and TNF- $\alpha$

### **Microbiome Analysis**

- Gut Microbiome Diversity and Composition



# Skeletal muscle mitochondrial uncoupling, adaptive thermogenesis and energy expenditure

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Ko Willems van Dijk<sup>a</sup> and Patrick Schrauwen<sup>b</sup>

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**Current Opinion in Clinical Nutrition and Metabolic Care** 2011, 14:243–249

## Purpose of review

The prevalence of obesity is still increasing, despite obesity treatment strategies that aim at reducing energy intake. In addition to this, exercise programmes designed to increase energy expenditure have only a low efficiency and have generated mixed results. Therefore, strategies based on increasing energy expenditure via nonexercise means are currently under investigation. One novel strategy is the modulation of adaptive thermogenesis.

## Recent findings

Among others, adaptive thermogenesis can be modulated by changing dietary composition, treatment with hormone mimetics as well as by cold exposure. In humans, a large part of the adaptive thermogenic response is, in addition to a putative role of brown adipose tissue, determined by the skeletal muscle mass via the process of mitochondrial uncoupling. Here, we describe the molecular processes involved in mitochondrial uncoupling, state-of-the-art techniques to measure mitochondrial uncoupling *in vitro* and *in vivo*, as well as the current strategies to mitochondrial uncoupling.

## Summary

Data generated in rodents and humans implicate that increasing adaptive thermogenesis by increasing skeletal muscle mitochondrial uncoupling indeed elevates total energy expenditure and thus may provide a promising target for the treatment of obesity.

## Keywords

adaptive thermogenesis, capsinoids, energy balance, uncoupling



# Cold Exposure Benefits

## BAT

Cold exposure activates brown adipose tissue which contain uncoupling protein 1 (UCP1), which allows them to generate heat instead of ATP. Non-shivering thermogenesis increases mitochondrial activity and promotes mitochondrial biogenesis

## Metabolic Flexibility

By slightly uncoupling the electron transport chain, UCP1 reduces the buildup of ROS. Mild uncoupling promotes metabolic flexibility.

## Antioxidant Enzymes

Cold exposure enhances the expression of antioxidant enzymes, such as superoxide dismutase (SOD) and glutathione peroxidase

## Mitochondrial QC

Activation of mitochondrial quality control mechanisms, including mitophagy (the selective degradation of damaged mitochondria)

## Lipid Metabolism

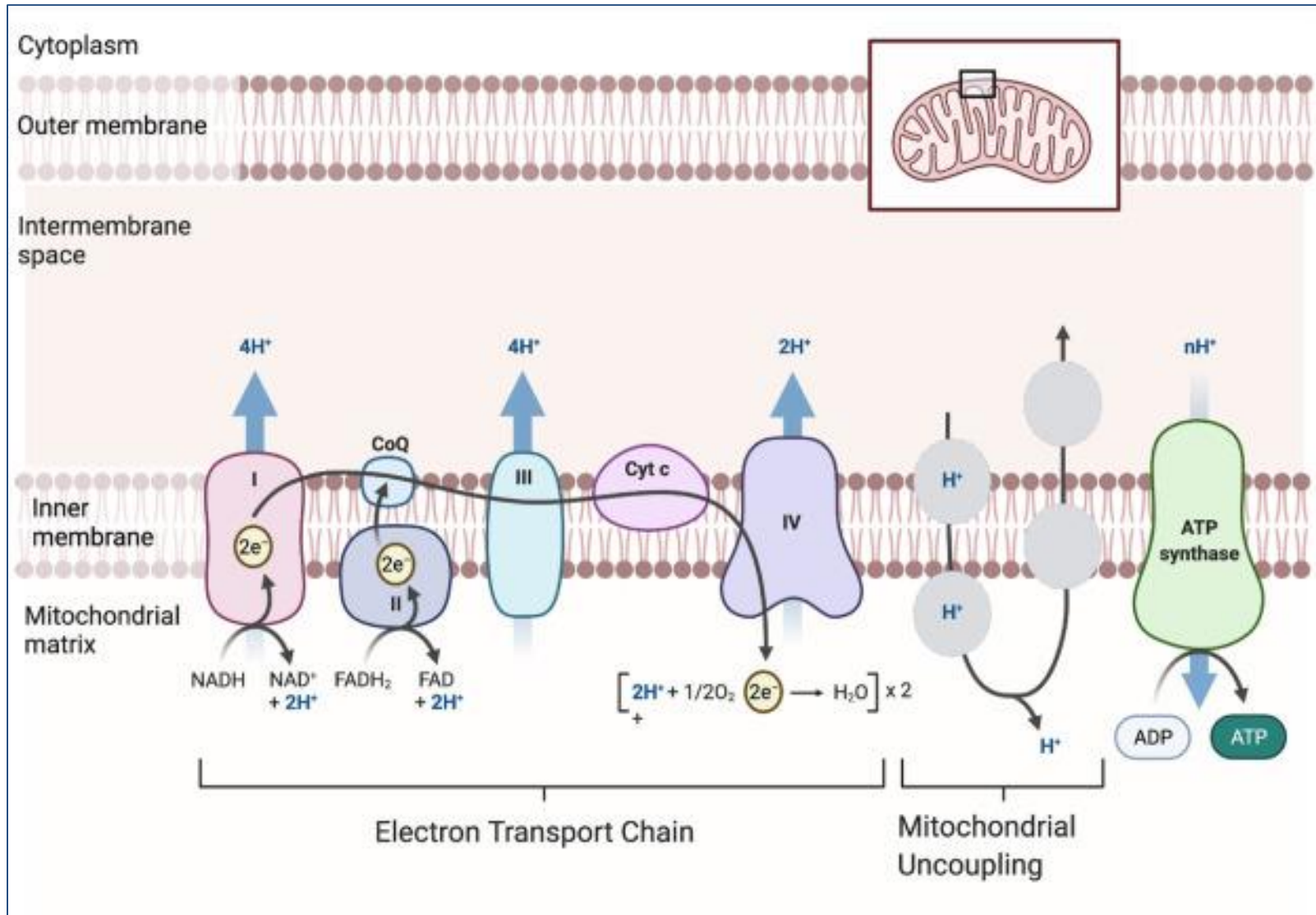
Upregulation of Enzymes such as CPT1 (carnitine palmitoyltransferase 1) involved in Lipid Metabolism.

## PGC-1 $\alpha$

Cold exposure upregulates PGC-1 $\alpha$ , a master regulator of mitochondrial biogenesis and oxidative metabolism. NRF1 and NRF2 transcription factors are activated by cold exposure and work with PGC-1 $\alpha$  to promote the synthesis of mitochondrial DNA, proteins, and respiratory enzymes.

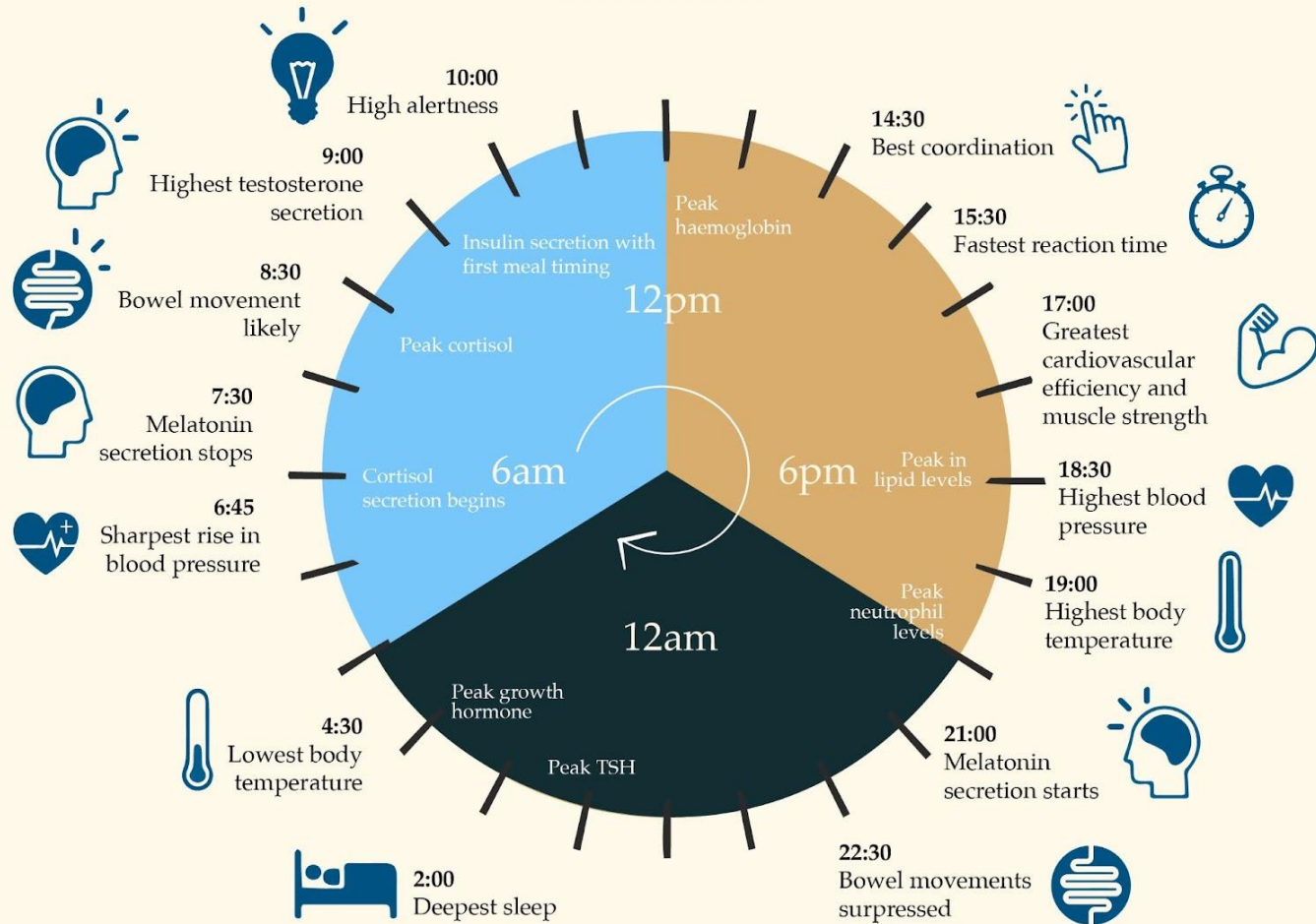
# Ancient Therapies, Modern Understanding

## The Mitochondria





Noon



Midnight

@DrOliviaLesslar

# Circadian Rhythm

Review > [J Biol Rhythms](#). 2001 Aug;16(4):348-64. doi: 10.1177/074873001129002060.

## Photoperiodism in humans and other primates: evidence and implications

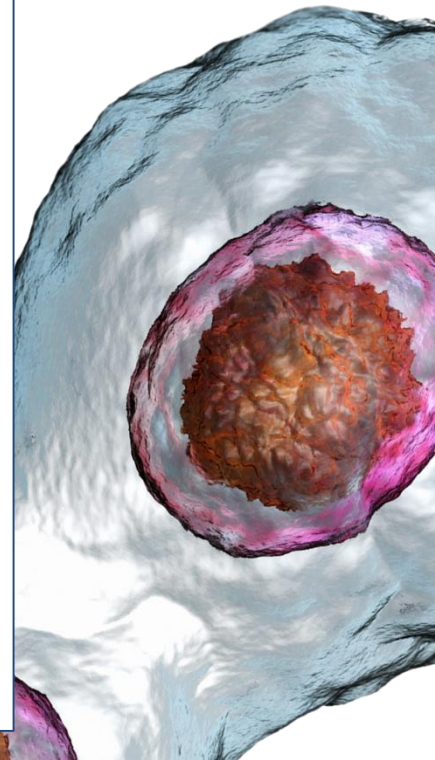
T A Wehr <sup>1</sup>

Affiliations + expand

PMID: 11506380 DOI: [10.1177/074873001129002060](#)

### Abstract

Most of the anatomical and molecular substrates of the system that encodes changes in photoperiod in the duration of melatonin secretion, and the receptor molecules that read this signal, have been shown to be conserved in monkeys and humans, and the functions of this system appear to be intact from the level of the retina to the level of the melatonin-duration signal of change of season. While photoperiodic seasonal breeding has been shown to occur in monkeys, it remains unclear whether photoperiod and mediation of photoperiod's effects by melatonin influence human reproduction. Epidemiological evidence suggests that inhibition of fertility by heat in men in summer contributes to seasonal variation in human reproduction at lower latitudes and that stimulation of fertility by lengthening of the photoperiod in spring contributes to the variation at higher latitudes. Parallels between the seasonality of human reproduction and seasonal affective disorder suggest that they may be governed by common biological processes. **Historical and experimental evidence indicates that human responses to seasonal changes in the natural photoperiod may have been more robust prior to the Industrial Revolution and that subsequently they have been increasingly suppressed by alterations of the physical environment.**



# Biophotons



## Ultraviolet Region (200-400 nm)

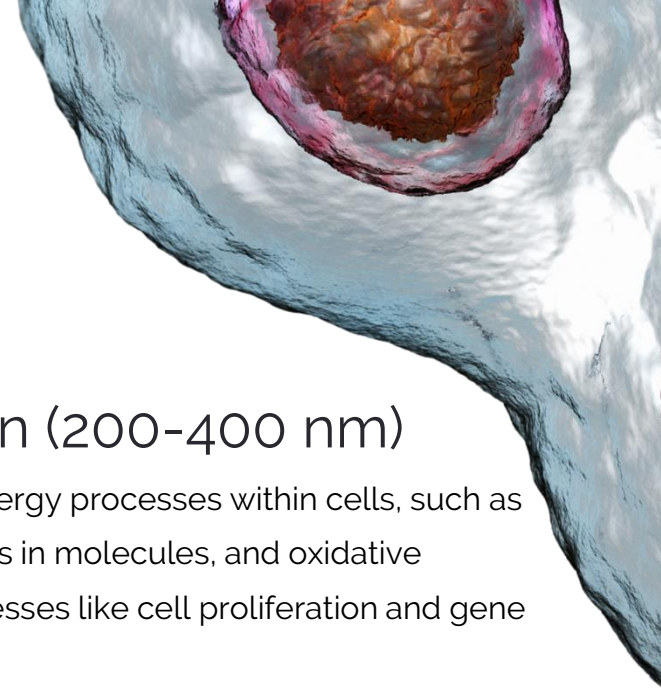
Often associated with high-energy processes within cells, such as DNA repair, electron transitions in molecules, and oxidative reactions. May influence processes like cell proliferation and gene expression.

## Visible Light Region (400-700 nm)

The majority of biophoton emissions fall within the visible spectrum, particularly in the blue, green, and red light ranges. Visible biophotons are typically associated with metabolic activities, including mitochondrial function, free radical production, and cellular respiration.

## Near-Infrared Region (700-1,000 nm)

NIR biophotons are emitted during less energetic cellular processes, such as the relaxation of excited states in chromophores, and are often linked to deep tissue signaling and thermal regulation.



## Imaging of Ultraweak Spontaneous Photon Emission from Human Body Displaying Diurnal Rhythm

Masaki Kobayashi , Daisuke Kikuchi, Hitoshi Okamura 

Published: July 16, 2009 • <https://doi.org/10.1371/journal.pone.0006256>

Article

Authors

Metrics

Comments

Media Coverage



### Abstract

Introduction

Results and Discussion

Materials and Methods

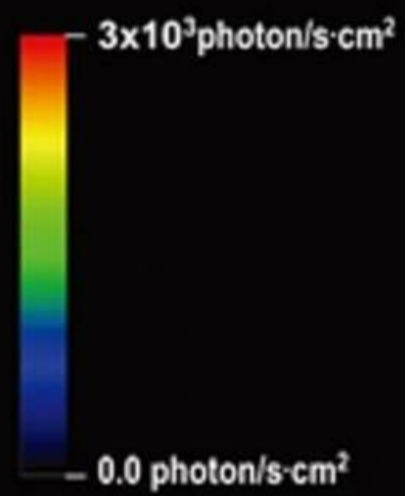
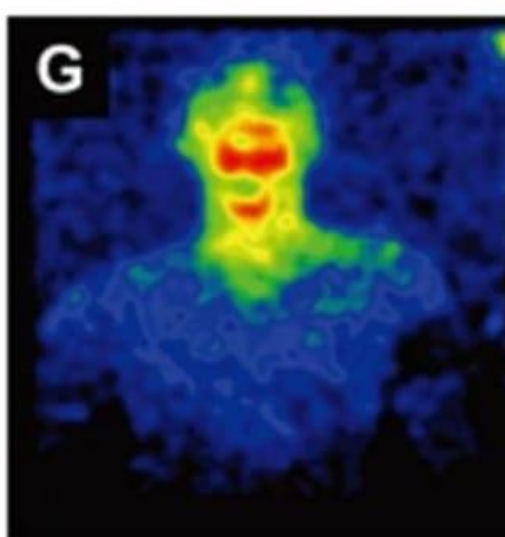
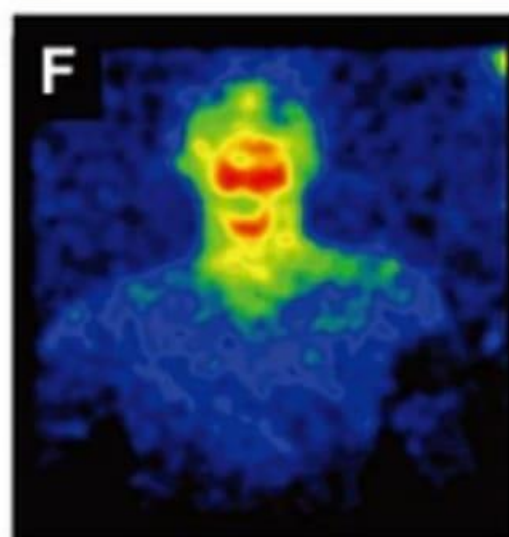
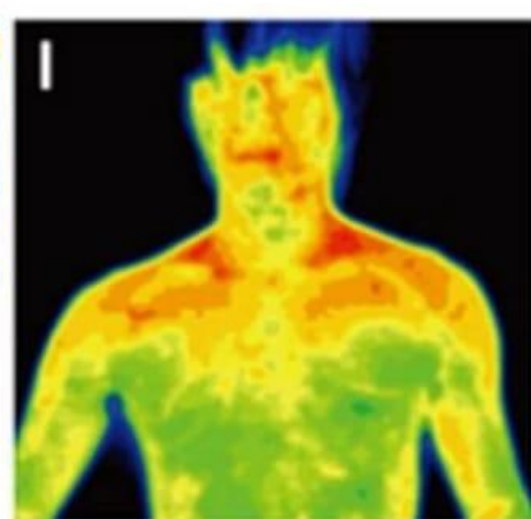
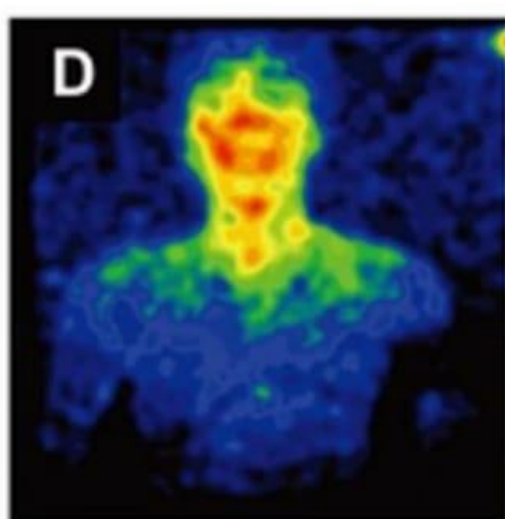
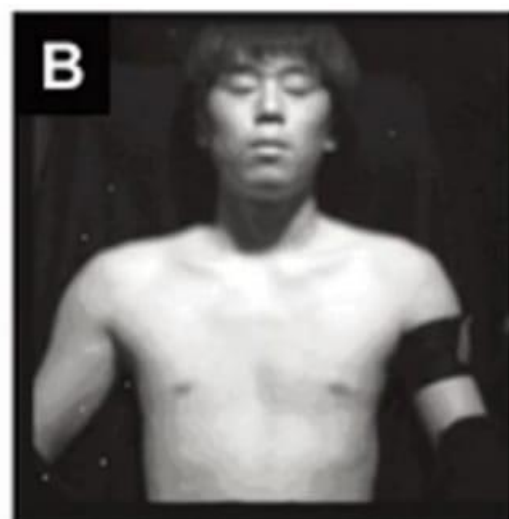
Supporting Information

Acknowledgments

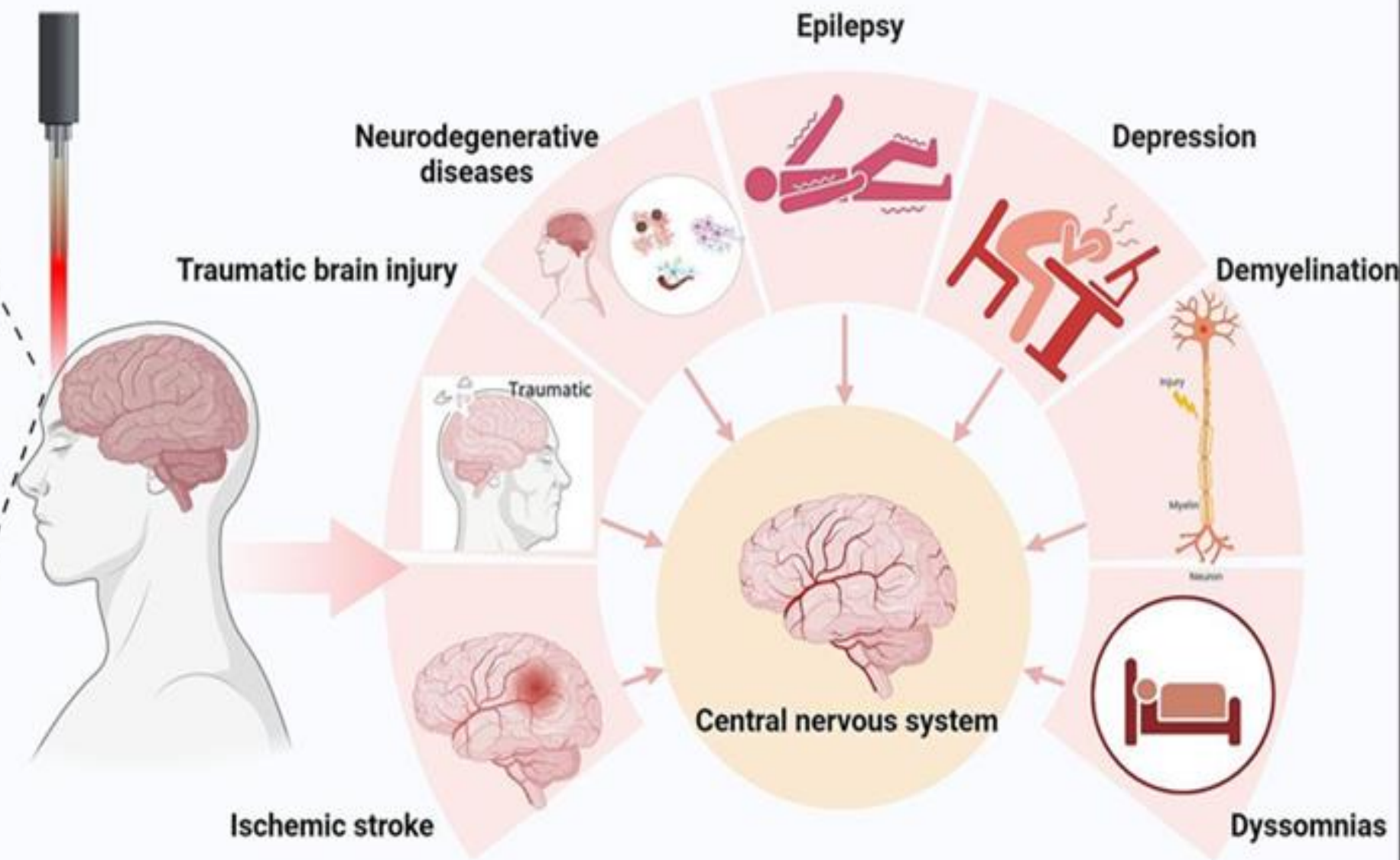
Author Contributions

### Abstract

The human body literally glimmers. The intensity of the light emitted by the body is 1000 times lower than the sensitivity of our naked eyes. Ultraweak photon emission is known as the energy released as light through the changes in energy metabolism. We successfully imaged the diurnal change of this ultraweak photon emission with an improved highly sensitive imaging system using cryogenic charge-coupled device (CCD) camera. We found that the human body directly and rhythmically emits light. The diurnal changes in photon emission might be linked to changes in energy metabolism.



# Recent advances in light energy biotherapeutic strategies with photobiomodulation on central nervous system disorders



**Photobiomodulation exerts beneficial effects in central nervous system disorders**

# PsychoNeuroImmunology PNI



## Neuroendocrine System

Stress and emotions influence hormone levels which affect immune function and metabolism.



## Immune System

Psychological states can suppress or dysregulate the immune system, affecting health outcomes.



## Psychology and Emotional States

Psychological and emotional states drive physiological processes that contribute to or protect against illness.



## Behavioral Responses

Behavioral factors can either mitigate or exacerbate the effects of stress on the body, influencing health and disease progression.

By understanding how the body and mind work together to perceive, respond to, and manage threats, we can develop more effective strategies for health.

# Blue Zones Lessons



## S.O.L.U.T.I.O.N.S.

Choose meals that are Seasonal, Organic, Local, Unprocessed, Traditional, Intuitively-eaten, rich in Omega-3s, Nutrient-dense, and Sustainable; adapting to life phases.



## DOWN SHIFT

Manage stress with routines, relaxation, or cultural practices to reduce inflammation and support health.



## 80% RULE

Eat until 80% full; savor meals to support digestion and prevent overeating.



## WINE AT 5

Moderate alcohol consumption, especially wine with meals, may support cardiovascular health and social bonding.



## RIGHT TRIBE

Surround yourself with supportive, like-minded people who encourage healthy behaviors.



## LOVED ONES FIRST

Prioritize family, fostering close, multigenerational relationships that provide emotional support.



## PURPOSE

Find purpose through work, hobbies, or community, providing meaning and enhancing well-being.



## MOVE NATURALLY

Engage in daily physical activities like walking, gardening, or manual tasks, integrating movement into life without structured exercise.



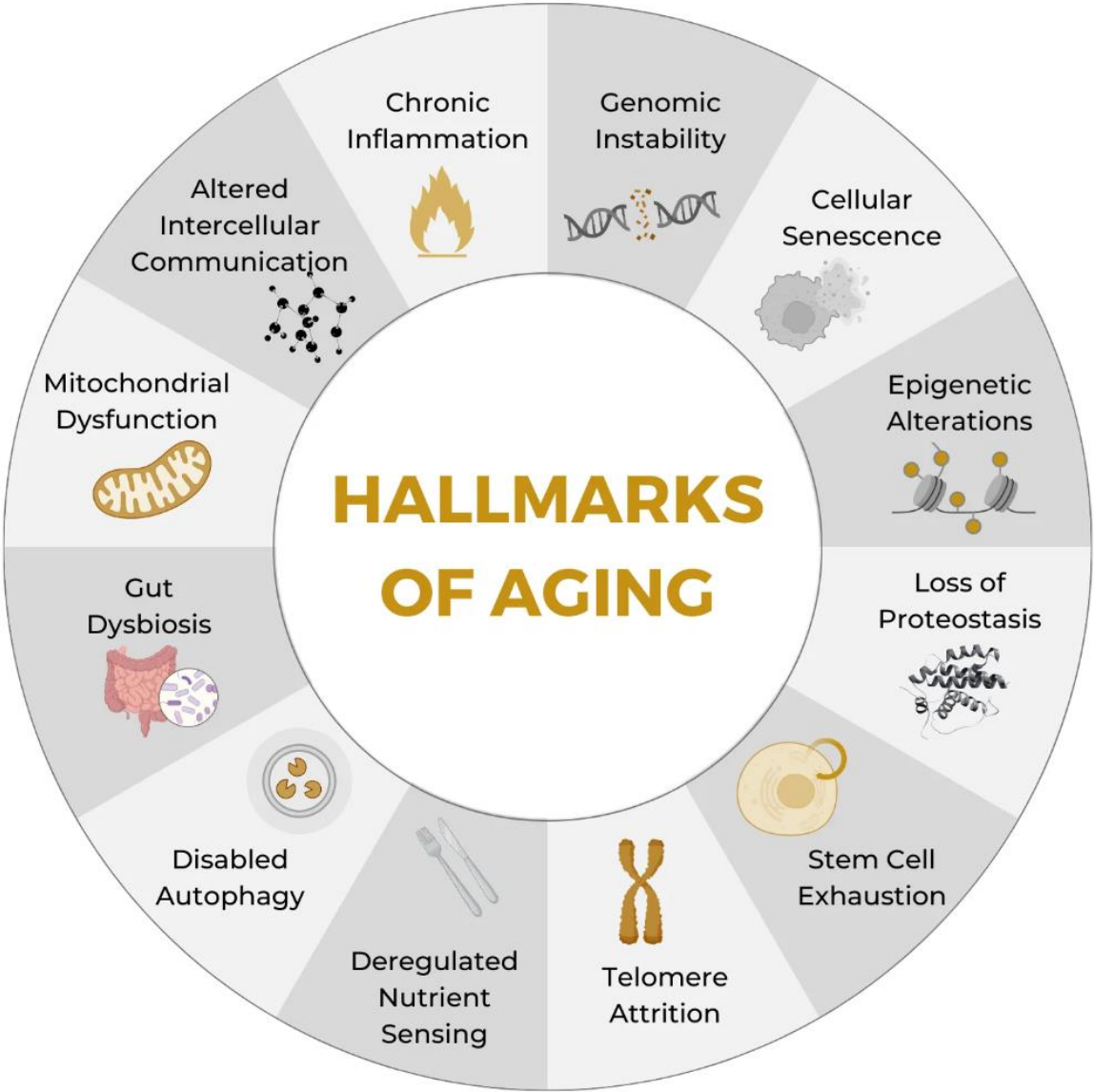
## BELONG

Seek connection and transcendence through faith, nature, or shared communities, fulfilling the desire to be part of something greater.

9 simple, life-changing principles inspired by the Blue Zones Project®



# PNI and Longevity



# PNI and Longevity

## **Genomic Instability**

Mechanisms activated by psychological, emotional, and physical stress, drive mutagenesis particularly in maladapted cells, enhancing adaptation in challenging and rapidly changing environments. *"Stress-Induced Mutagenesis, Gambler Cells, and Stealth Targeting Antibiotic-Induced Evolution"*

doi: 10.1128/mbio.01074-22

## **Telomere Attrition**

Various chronic stress situations have been associated with shorter telomere length, including caregiving for sick children with chronic conditions or elderly dementia patients, major depression, childhood adversity, and exposure to intimate partner violence. *"Perceived stress and telomere length: A systematic review, meta-analysis, and methodologic considerations for advancing the field."*

doi: 10.1016/j.bbi.2016.02.002

## **Loss of Proteostasis**

Chronic stress can disrupt proteostasis, which is the the maintenance of a balanced and functional proteome, by impairing the function of molecular chaperones and the ubiquitin-proteasome system.

*"Proteostasis and resilience: on the interphase between individual's and intracellular stress"* doi: 10.1016/j.tem.2022.02.003

# PNI and Longevity

## **Stem Cell Exhaustion**

Chronic stress negatively impacts stem cell function and regenerative capacity. *"Psychological Considerations in Hematopoietic Stem Cell Transplantation"* doi: 10.1016/j.psym.2019.02.004

## **Altered Intercellular Communication**

Stress hormones can disrupt cell signaling and communication, leading to systemic inflammation and impaired tissue function. For instance, chronic stress can increase pro-inflammatory cytokines, contributing to a pro-aging environment. *"The geroscience agenda: Toxic stress, hormetic stress, and the rate of aging"* doi: 10.1016/j.arr.2020.101167

## **Dysbiosis**

The gut-brain axis, influenced by stress, can lead to dysbiosis, an imbalance in the gut microbiome. This imbalance is linked to various age-related diseases, including metabolic disorders and neurodegeneration. *"Stress, depression, diet, and the gut microbiota: human–bacteria interactions at the core of psychoneuroimmunology and nutrition"* doi: 10.1016/j.cobeha.2019.01.011

# PNI and Longevity

## **Cellular Senescence**

Stress can accelerate cellular senescence by increasing the production of reactive oxygen species (ROS) and inflammatory cytokines. *"Psychoneuroimmunology and aging"*  
doi: 10.1159/000022021

## **Chronic Inflammation**

Psychological stress contributes to persistent low-grade inflammation. As described in Inflammatory Bias Theory. *"The Interplay Between Stress, Inflammation, and Emotional Attention: Relevance for Depression"* doi: 10.3389/fnins.2019.00384

## **Epigenetic Alterations**

Emotional distress can lead to epigenetic changes, such as DNA methylation and histonemodification, which affect gene expression. For example, early-life stress can cause lasting epigenetic changes that predispose individuals to age-related diseases. *"Genetic and Epigenetic Consequence of Early-Life Social Stress on Depression: Role of Serotonin-Associated Genes."*  
doi: 10.3389/fgene.2020.601868

# PNI and Longevity

## **Compromised autophagy**

Compromised autophagy negatively affects longevity by impairing the body's ability to maintain cellular homeostasis, remove damaged components, and protect against age-related diseases.

*"Autophagy as a Cellular Stress Response Mechanism in the Nervous System"*

doi: 10.1016/j.jmb.2020.01.017

## **Deregulated Nutrient Sensing**

Nutrient sensing pathways, such as insulin/IGF-1 signaling and mTOR, are influenced by psychological stress. Chronic stress can lead to insulin resistance and dysregulated glucose metabolism. *"Molecular mechanisms linking stress and insulin resistance"*

doi: 10.17179/excli2021-4382

## **Mitochondrial Dysfunction**

Mitochondria are sensitive to stress hormones, and chronic stress can impair mitochondrial function, leading to reduced energy production and increased oxidative stress. *"Severe life stress, mitochondrial dysfunction, and depressive behavior: A pathophysiological and therapeutic perspective"*

doi: 10.1016/j.mito.2020.11.010

# Thank you!

<https://liber8.health/our-science/>



wellness@lifespanmedicine.com.au

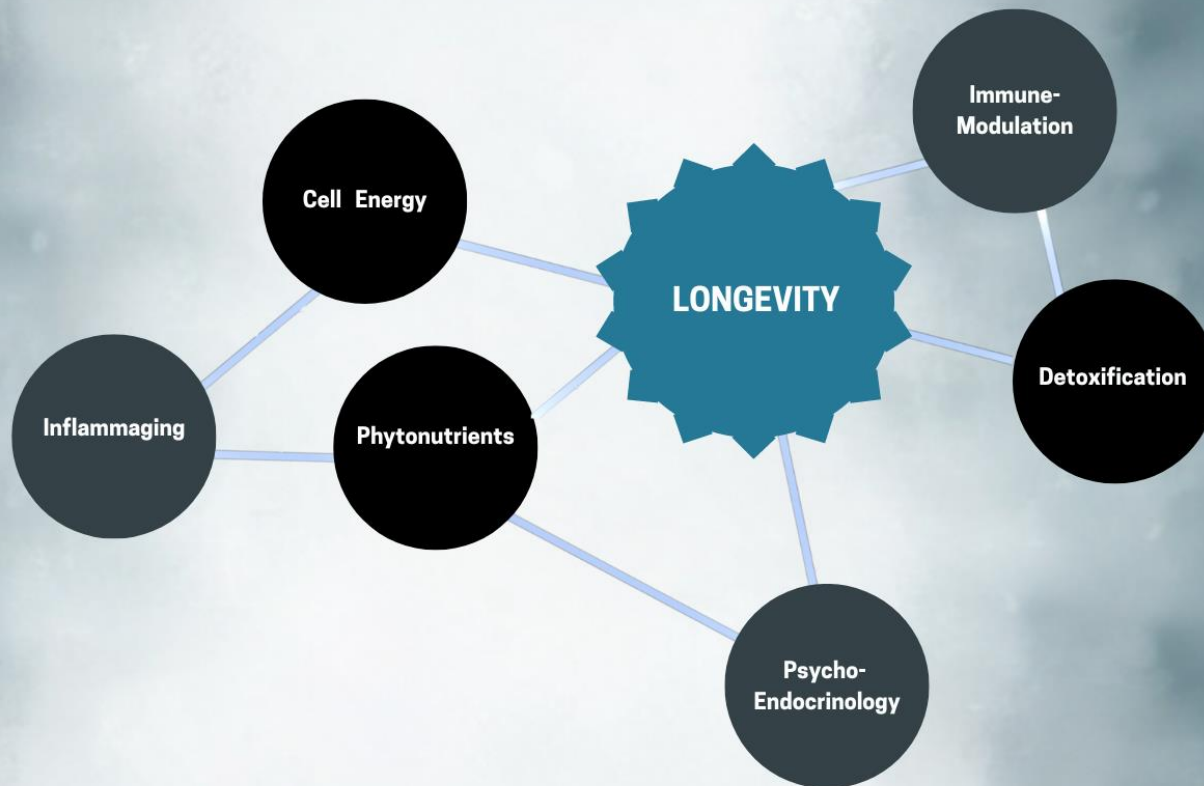


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