THE CIRCADIAN ADVANTAGE:
Mitochondria, Light, and Bioenergetics

Josh Rosenthal, M.D.
Integrative Sleep and Regenerative Medicine

Quantum Life Wellness

Let's Cover...

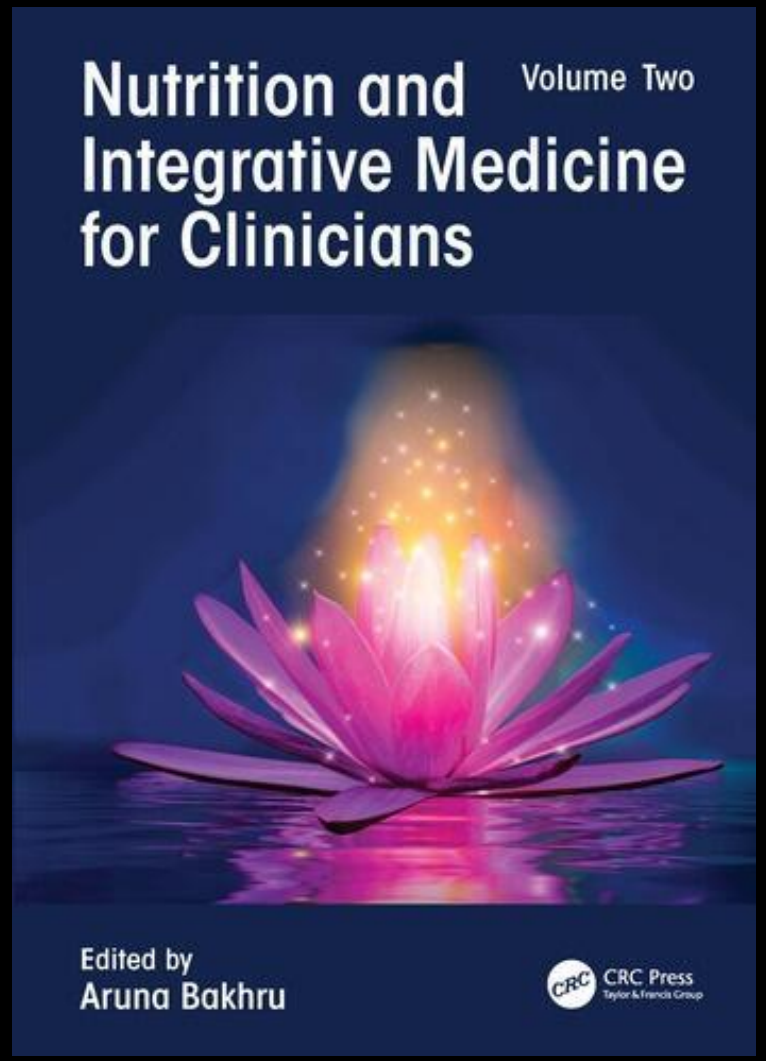
- Epigenetics
- Circadian Biology
- The Hidden Toxin Ruining The Eye
- **The Biophysics of Transforming Your Health**
- **Making Syntonics Even Better?**

Josh Rosenthal, M.D.

- Holistic Sleep Specialist
- Regenerative Medicine Practitioner
- Circadian Epigeneticist
- Author

- Mitochondrial & Circadian Therapies
  - MitoCircadian ™ Approach
  - Optimize Bioenergetics
    → Health, Hormones, and Happiness Follow
  - Offer Treatment in NY, FL, PA

Timing IS Everything



20 Circadian and Mitochondrial Effects of Light

Joshua Rosenthal

CONTENTS

https://www.routledge.com/Nutrition-and-Integrative-Medicine-for-Clinicians-Volume-Two/Bakhru/p/book/9781032110127

My Journey Towards The Light

- 5 years of circadian disruption (Residency) led me to 220 lbs.
- After graduating, I decided to “lose weight”.
- 50lbs later + patients who couldn’t sleep without OSA

  ➔ Questions ➔ Answers

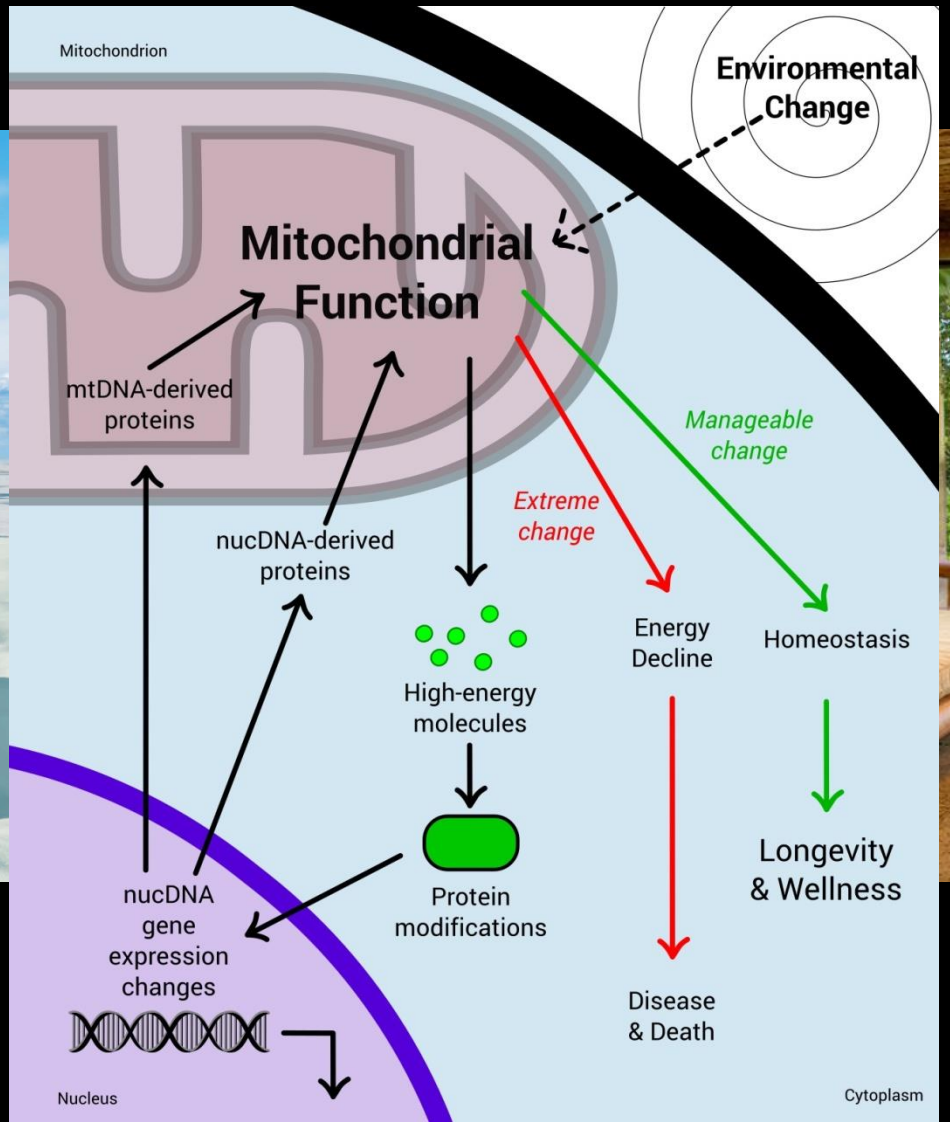
What Happens When Your Clock Is Right?

Optimal Performance = Input + Timing

Energy

Information

Epigenetics

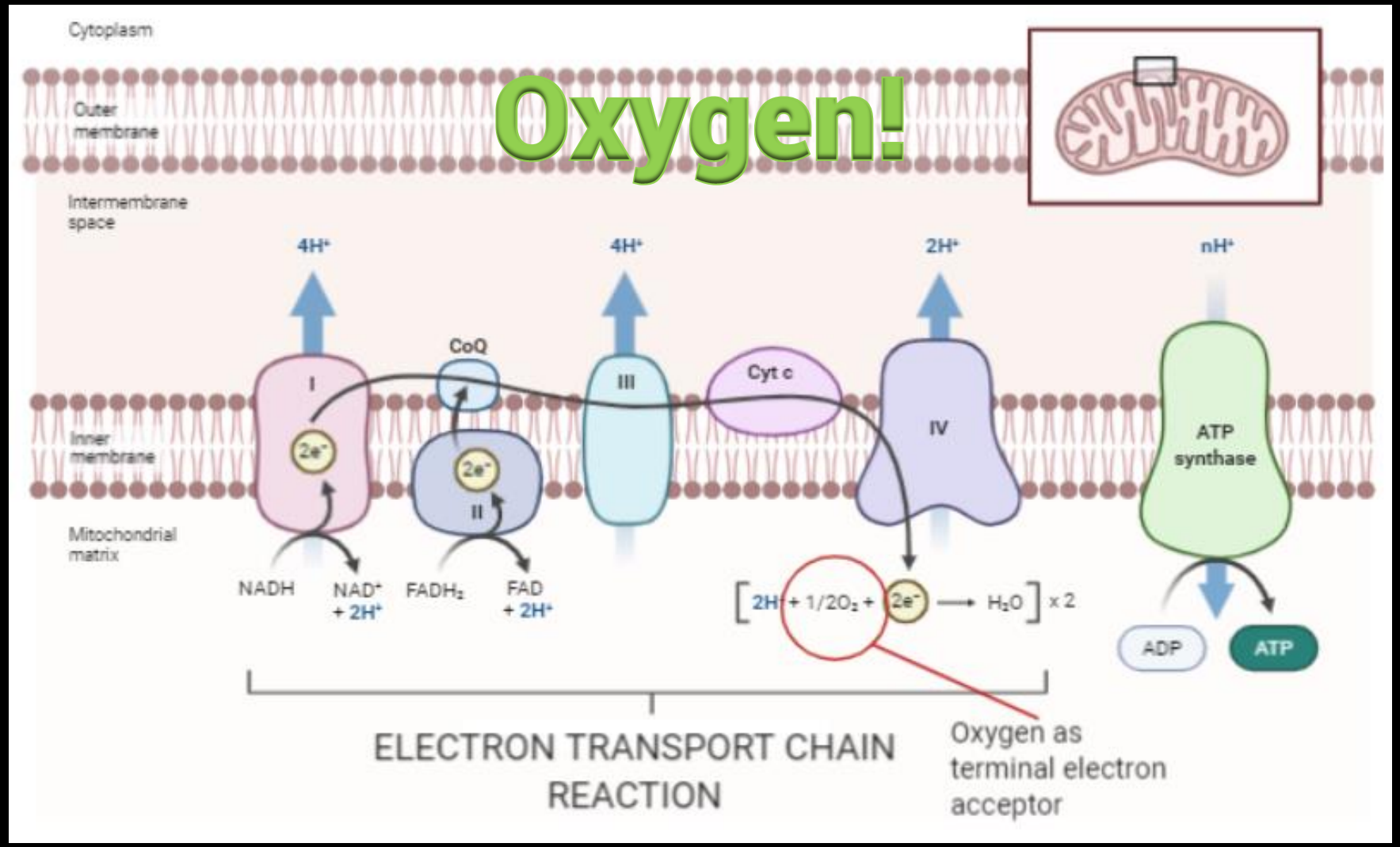


Mitochondria = Quantum Machine

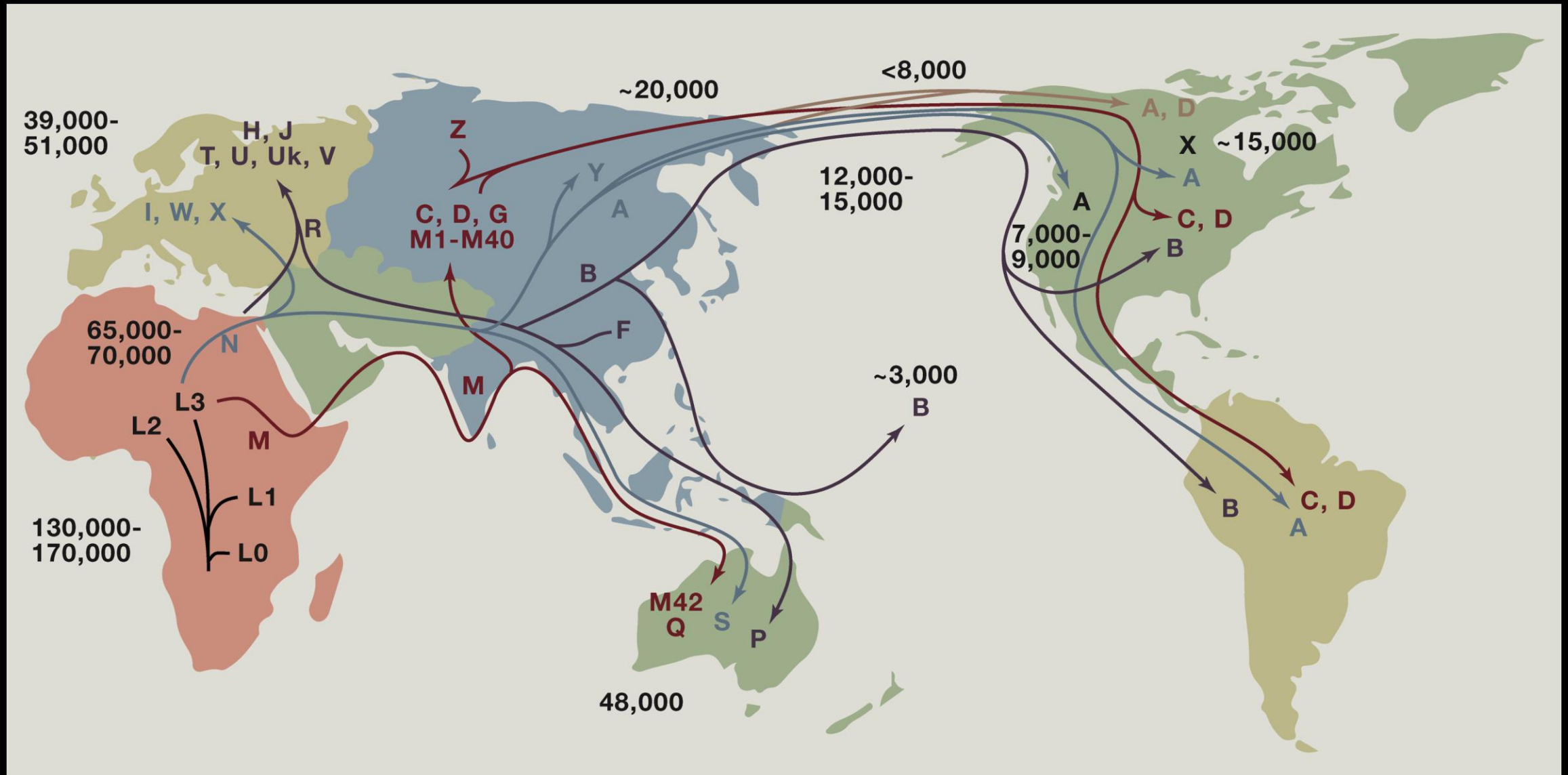
Electron Chain Transport

- Input:
  - Electrons
  - *NOT* Carbs, Protein, Fat
- Output:
  - ATP
  - **Light**
  - **Electromagnetism**

Why We Breathe



Environmentally Optimized Haplotypes



Mitochondria translate the environment

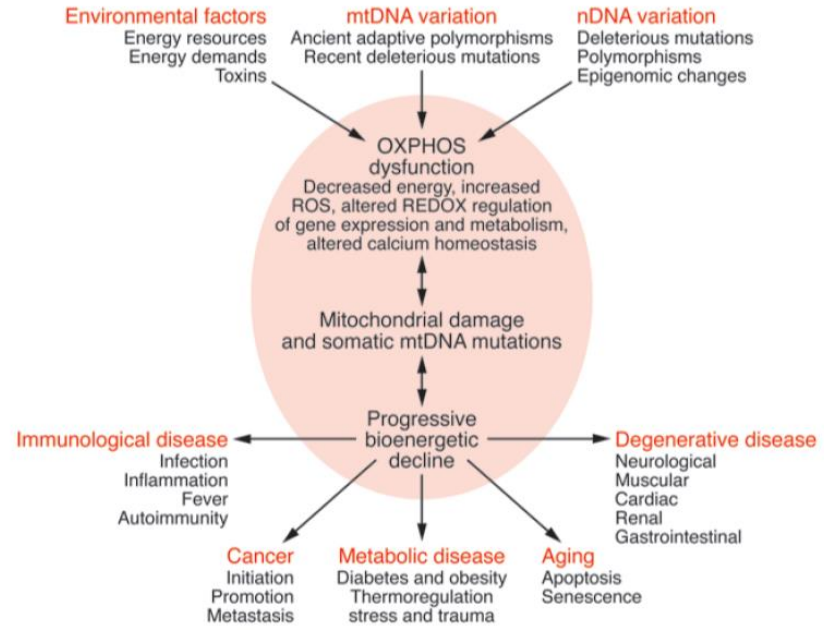
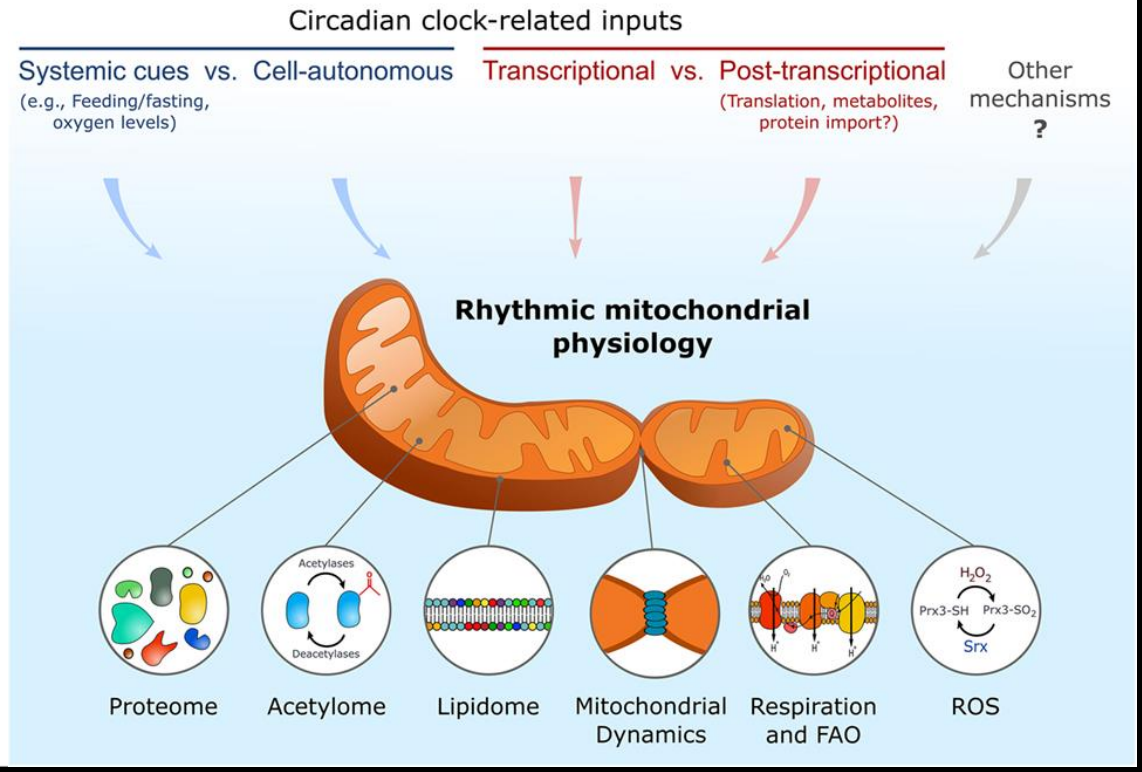


Figure 1
Bioenergetic paradigm for metabolic and degenerative diseases, cancer, and aging. Mitochondrial OXPHOS can be perturbed by nDNA genetic alterations and/or epigenomic regulation, by mtDNA ancient adaptive of recent deleterious mutations, or by variation in the availability of calories

J Clin Invest. 2013;123(4):1405–1412. :10.1172/JCI61398
A mitochondrial bioenergetic etiology of disease
Douglas C. Wallace

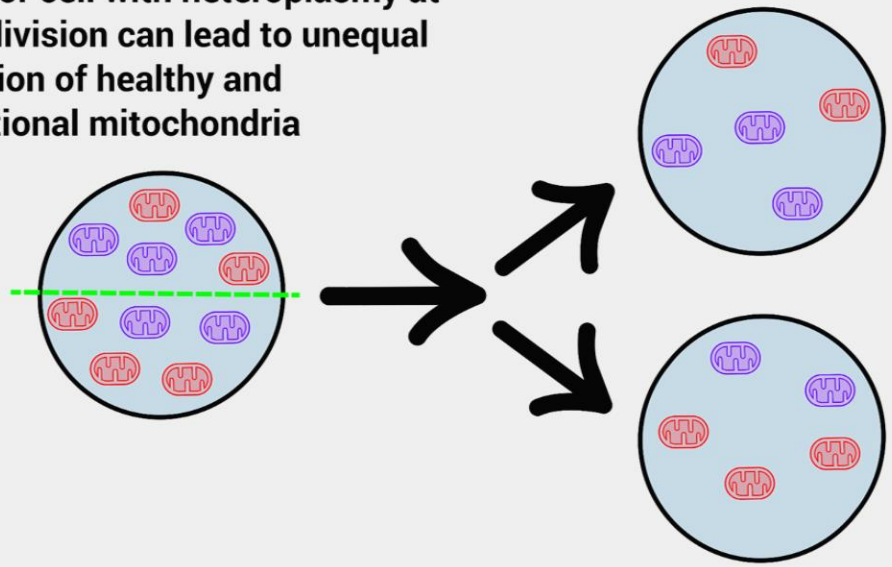


Front. Endocrinol., 19 December 2016 | https://doi.org/10.3389/fendo.2016.00162
The Circadian Nature of Mitochondrial Biology;
Gal Manella and Gad Asher

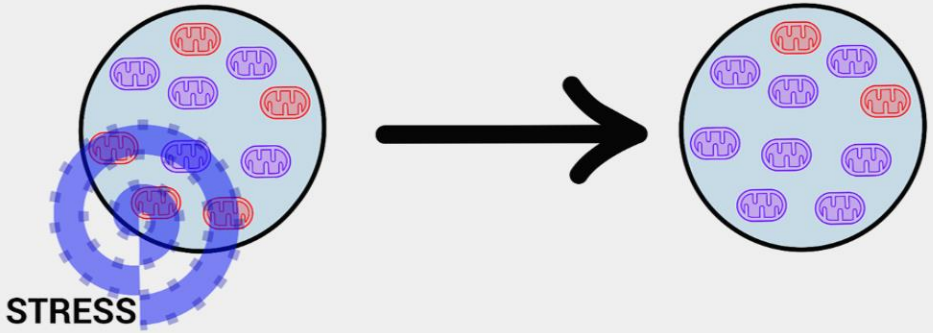
Normal Mitochondria

Dysfunctional or Mutant Mitochondria

Progenitor cell with heteroplasmy at time of division can lead to unequal distribution of healthy and dysfunctional mitochondria

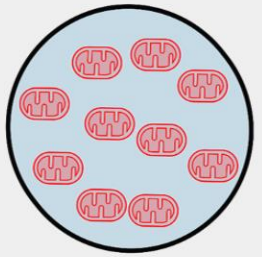


Cell can be damaged by continued oxidative stress leading to mitochondrial dysfunction.

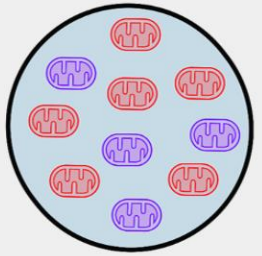


When the level of mutant mitochondria pass a certain threshold, the cell will express dysfunction

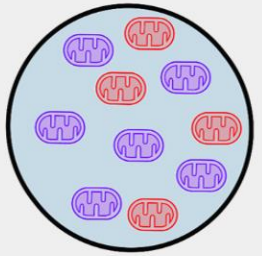
100% Normal



40% Mutant Normal

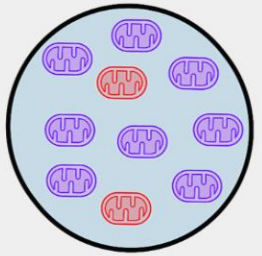


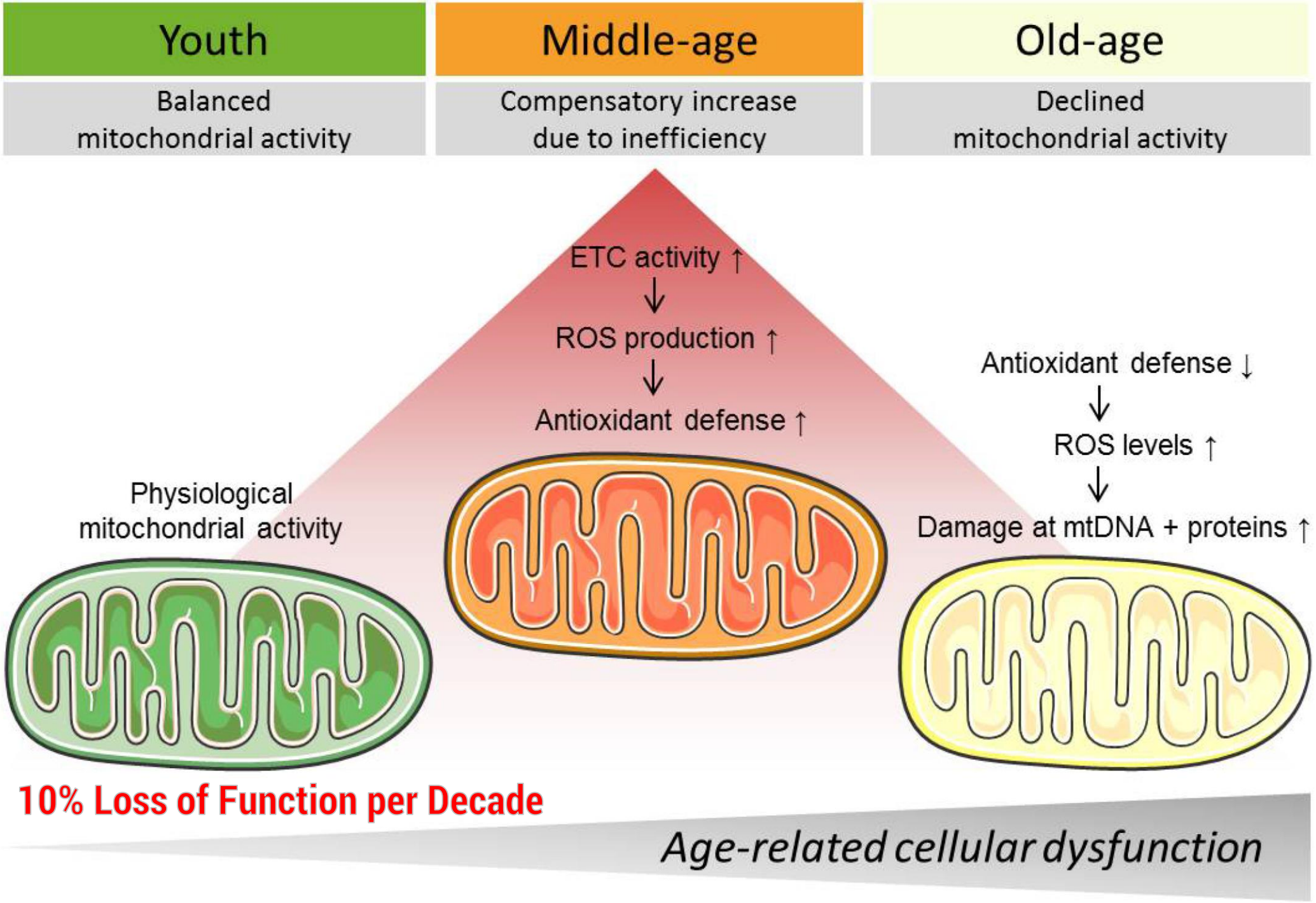
60% Mutant Normal



Threshold 70% Mutant

80% Mutant Disease




Youth
Middle-age
Old-age
Balanced mitochondrial activity
Compensatory increase due to inefficiency
Declined mitochondrial activity
ETC activity ↑
↓
ROS production ↑
↓
Antioxidant defense ↑
Antioxidant defense ↓
↓
ROS levels ↑
↓
Damage at mtDNA + proteins ↑
Physiological mitochondrial activity
10% Loss of Function per Decade
Age-related cellular dysfunction

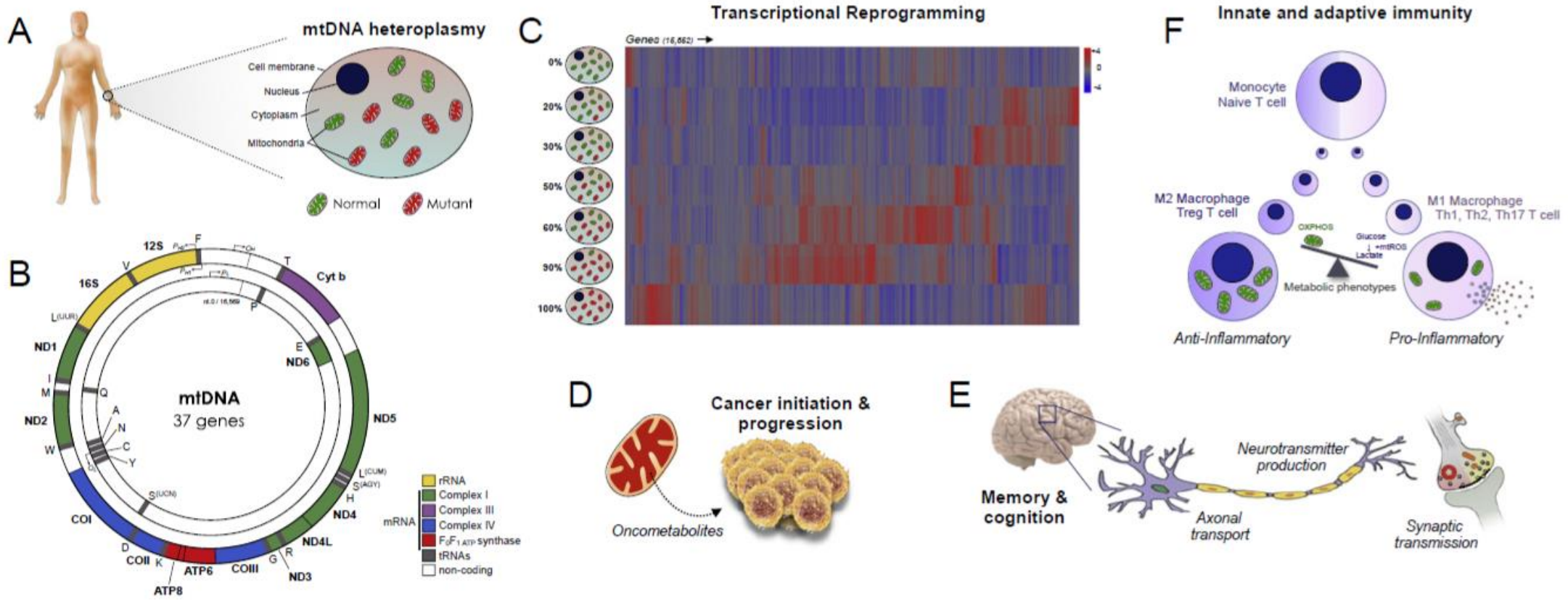
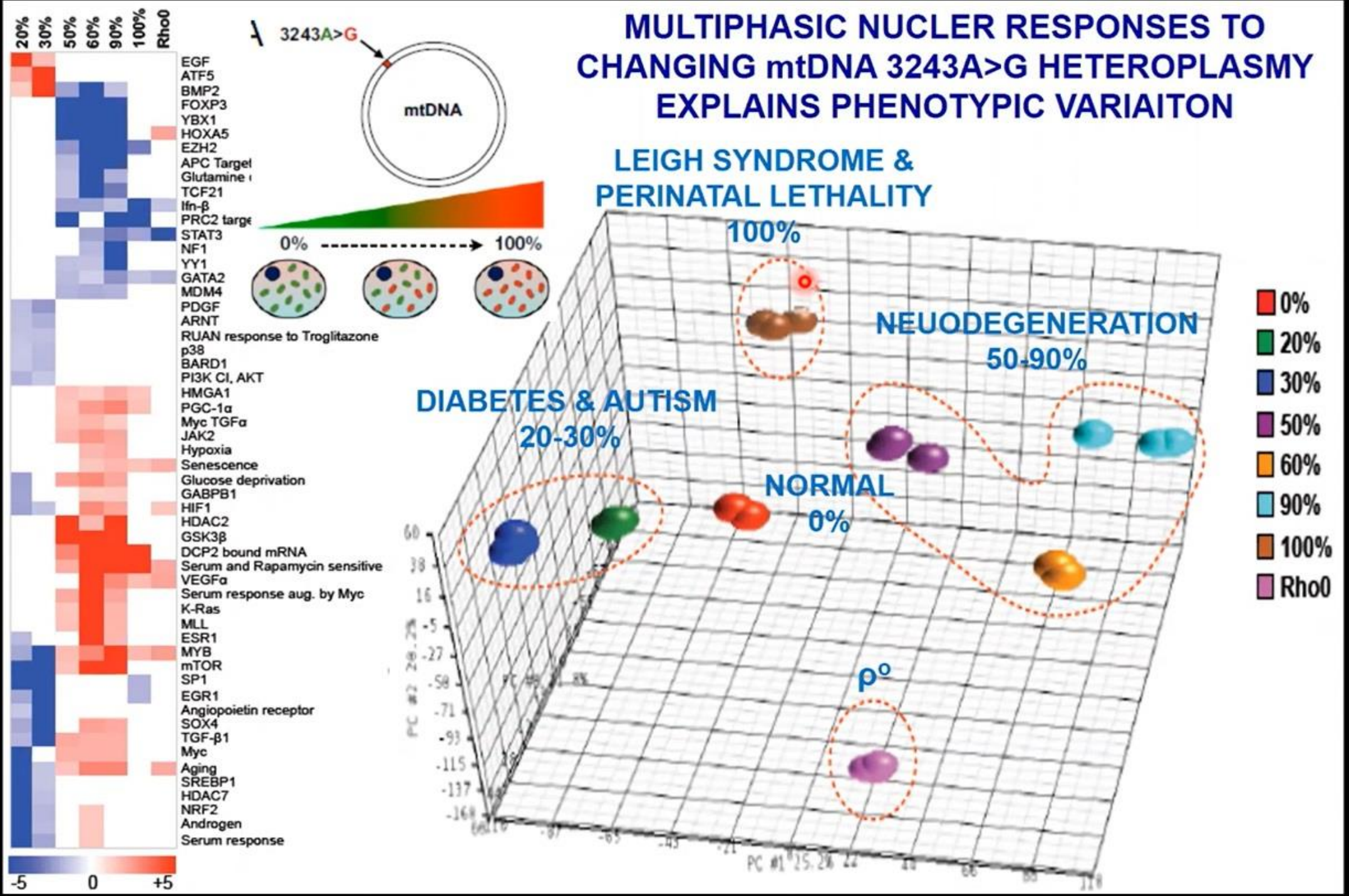


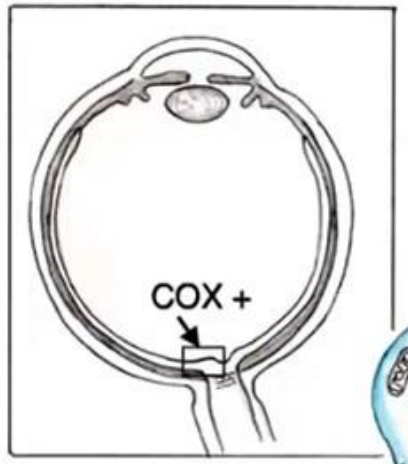
Fig. 2. Multifaceted mitochondrial pathogenesis. (**A**) Somatic tissues contain 100–1000's of mitochondrial DNA (mtDNA) molecules each, such that a mixture of normal and mutated copies can coexist in a state of heteroplasmy. (**B**) The mitochondrial genome, containing 37 genes essential to respiratory chain assembly and function. (**C**) mtDNA heteroplasmy for the most common pathogenic MELAS-causing m.3243A>G mutation of the $tRNA^{Leu(UUR)}$ gene causes genome-wide transcriptional reprogramming; data adapted from (Picard et al., 2014b). (**D**) Mitochondrial signals promoting cancer initiation and progression. (**E**) Abnormal mitochondrial function and positioning alters multiple components of the nervous system. (**F**) Metabolic programming of immune cell differentiation and proliferation into anti- and pro-inflammatory phenotypes, driven by the balance of oxidative phosphorylation (OXPHOS) vs. glycolysis and mitochondrial reactive oxygen species (mtROS).

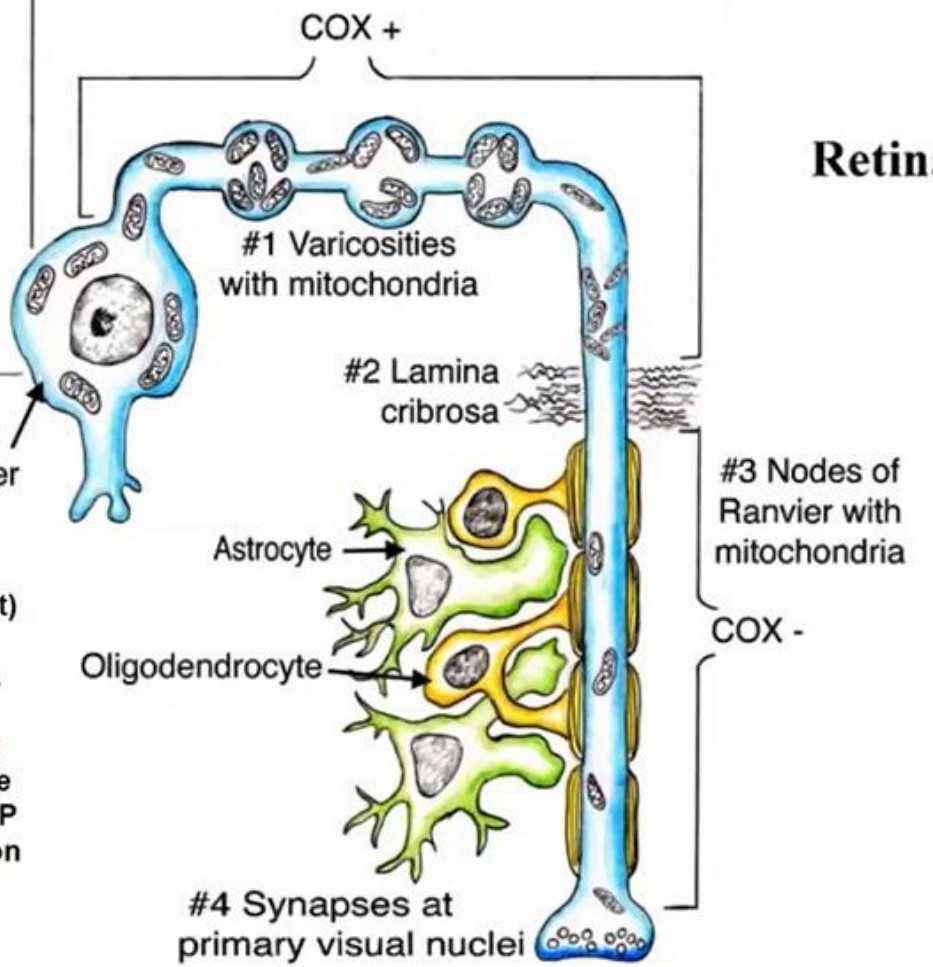
Mitochondrion Volume 30, September 2016, Pages 105-116
The rise of mitochondria in medicine Martin Picard, Douglas C.Wallace, Yan Burelle

MULTIPHASIC NUCLER RESPONSES TO CHANGING mtDNA 3243A>G HETEROPLASMY EXPLAINS PHENOTYPIC VARIAITON

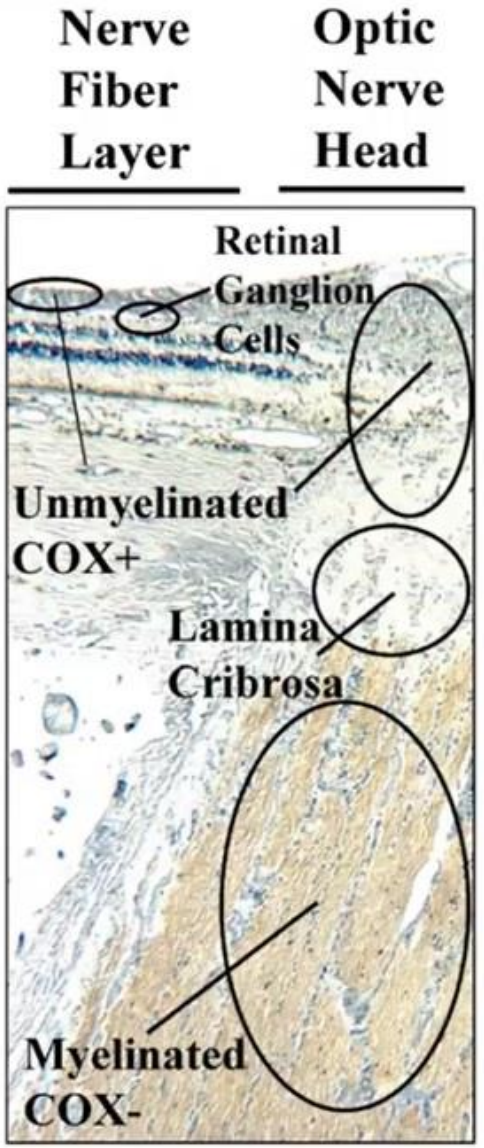


RETINAL GANGLION CELLS AND OPTIC NERVE ANATOMICAL PREDISPOSITION TO NEURO-OPHTHALMOLOGICAL DISEASE





Patients: Control (left) & LHON 11778G>A (right).
Histology: Optic Nerve stained MBP (top) & Axon with EM (bottom).



Carelli V, Ross-Cisneros FN, & Sadun AA, 2004, Mitochondrial Dysfunction as a Cause of Optic Neuropathies. Prog Retinal & Eye Research 23:53-89

The Other Energy Source – LIGHT!

- Red Light (AKA LLLT, PBM)
  - 42% of Sun
  - Free energy in Mitochondria
  - 100% Efficiency
- Ultraviolet Light
  - Melanin and Beyond

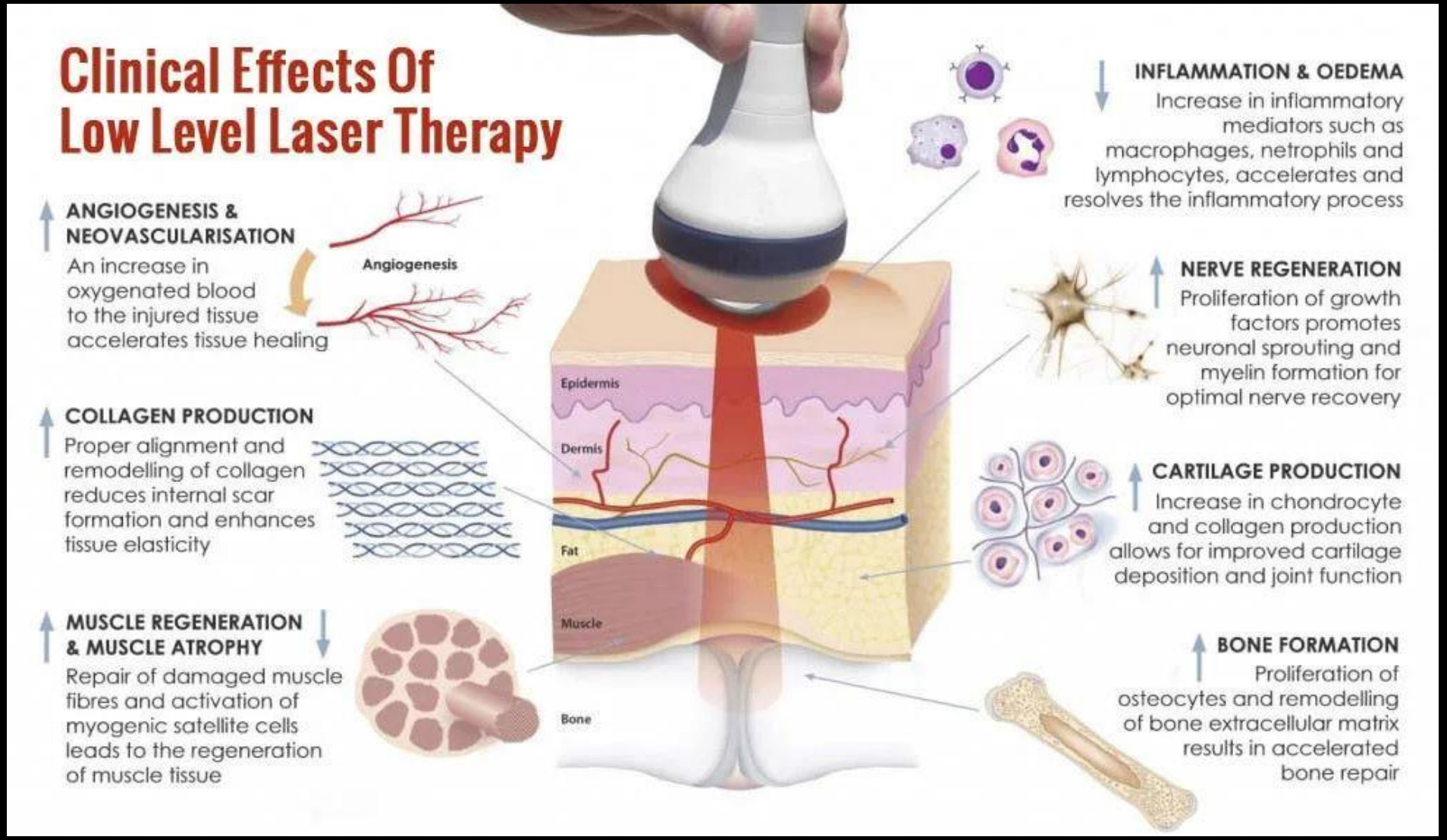
ROYGBIV… IR & UV

Photobiomodulation (PBM)

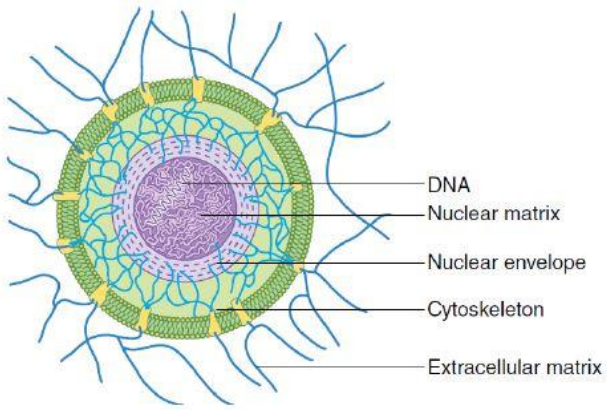
- RED/IR LIGHT IS AWESOME…NUFF SAID

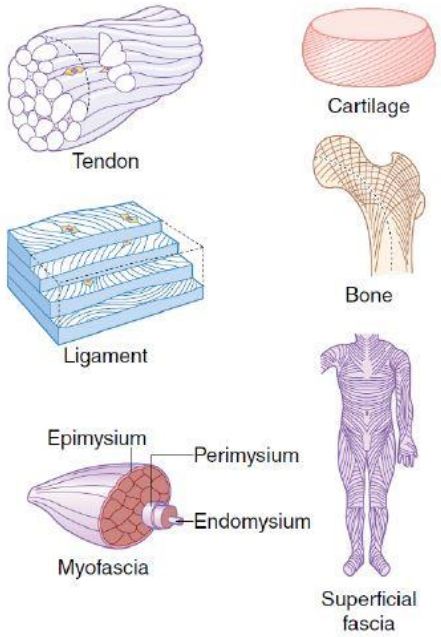
- See talk “Photobiomodulation for Aging, Parkinsons” by Anita Saltmarche BScN, MHSc

Collagen Production



The Wires



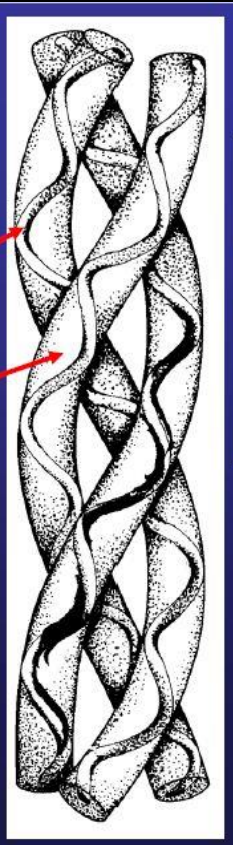


The living matrix

Collagen is a semiconductor!

Collagen protein

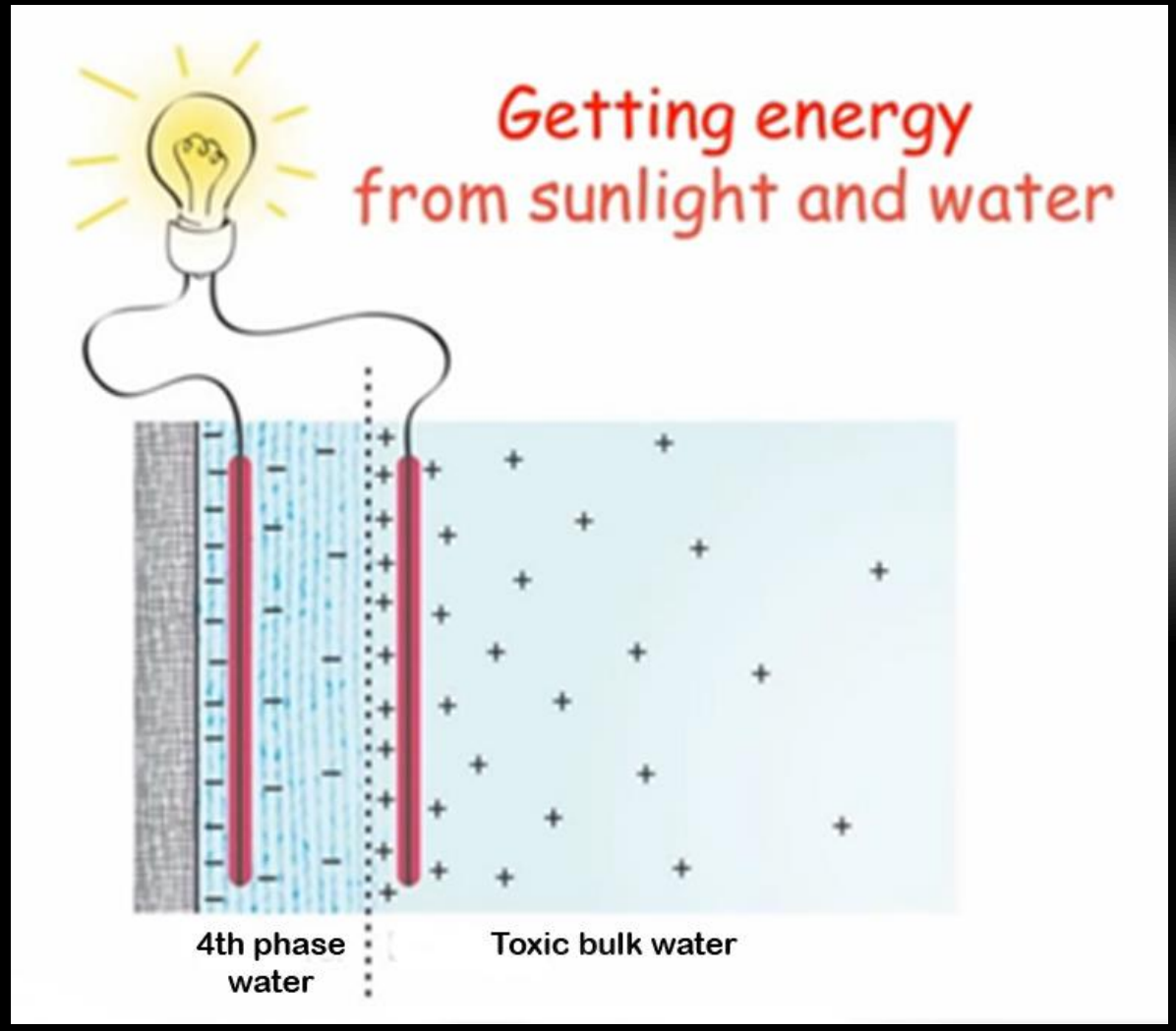
Hydration shell

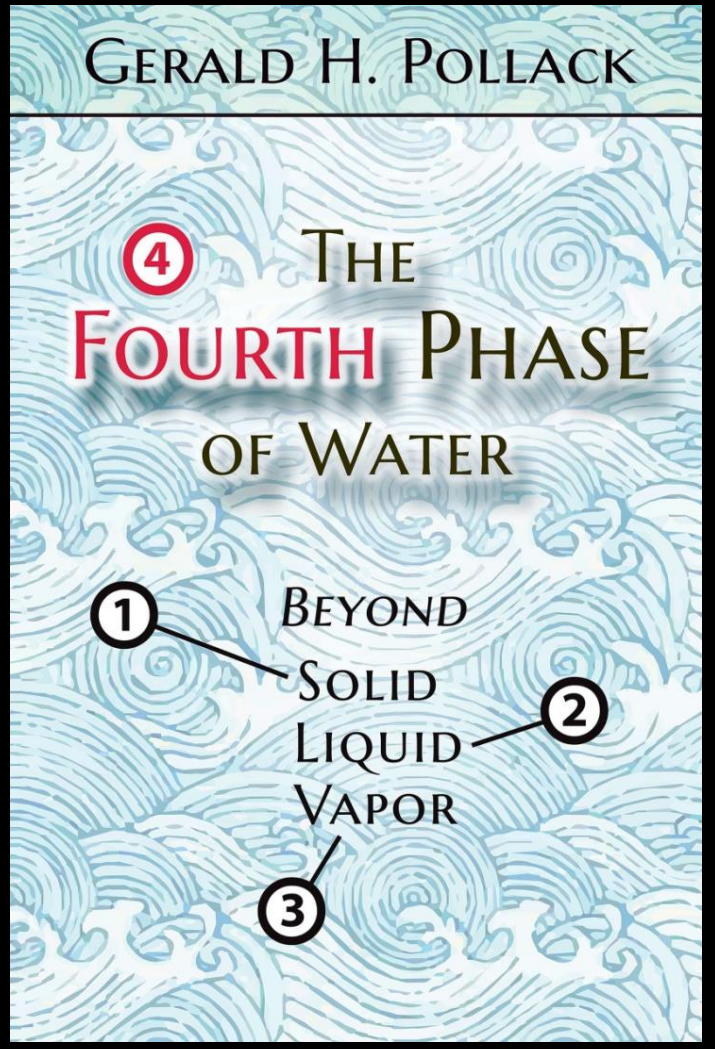


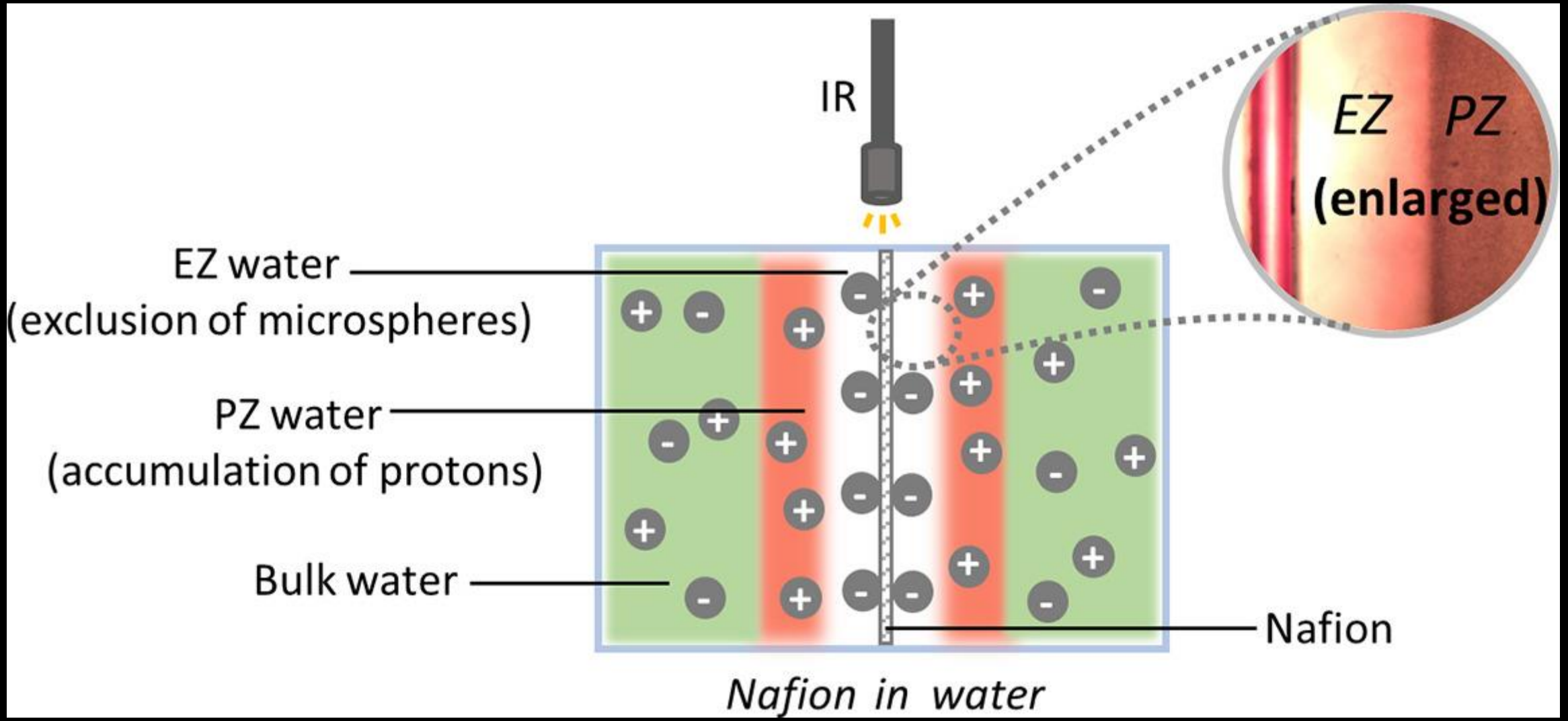
Gascoyne, Pethig and Szent-Gyorgyi, 1981. Water structure-dependent charge transport in proteins. Proc. Natl. Acad. Sci. 78:261-265.

A small increase in water content can yield a huge increase in conductivity.

WATER You Talking About?

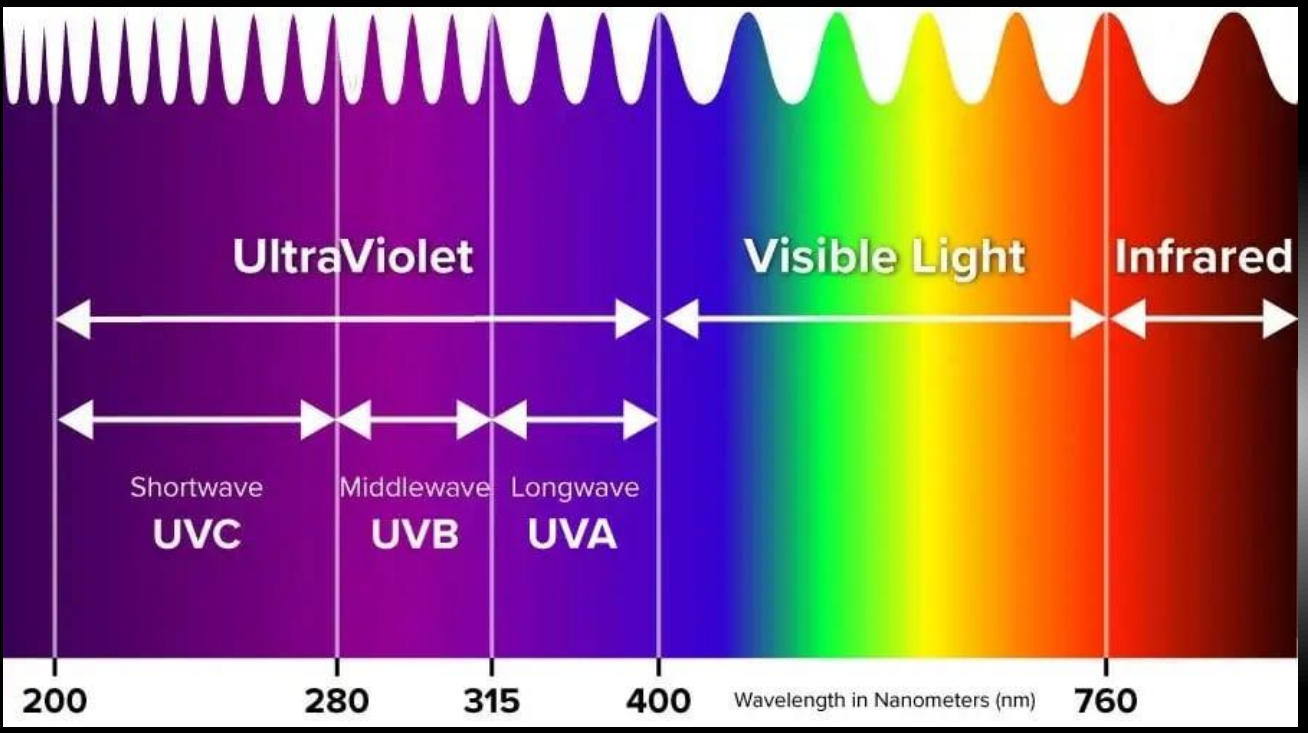


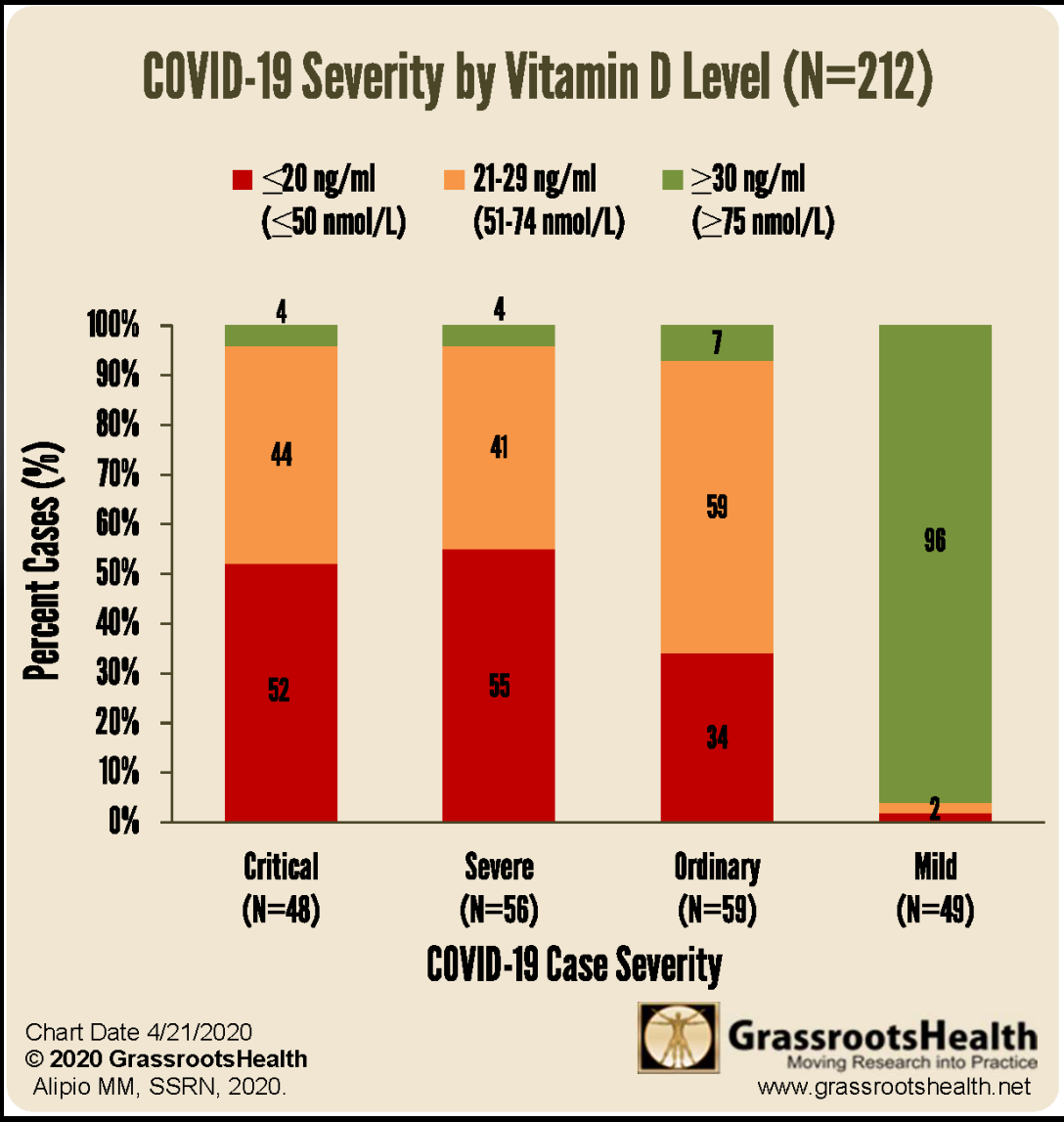




https://doi.org/10.1016/j.colcom.2021.100397

Got UV?

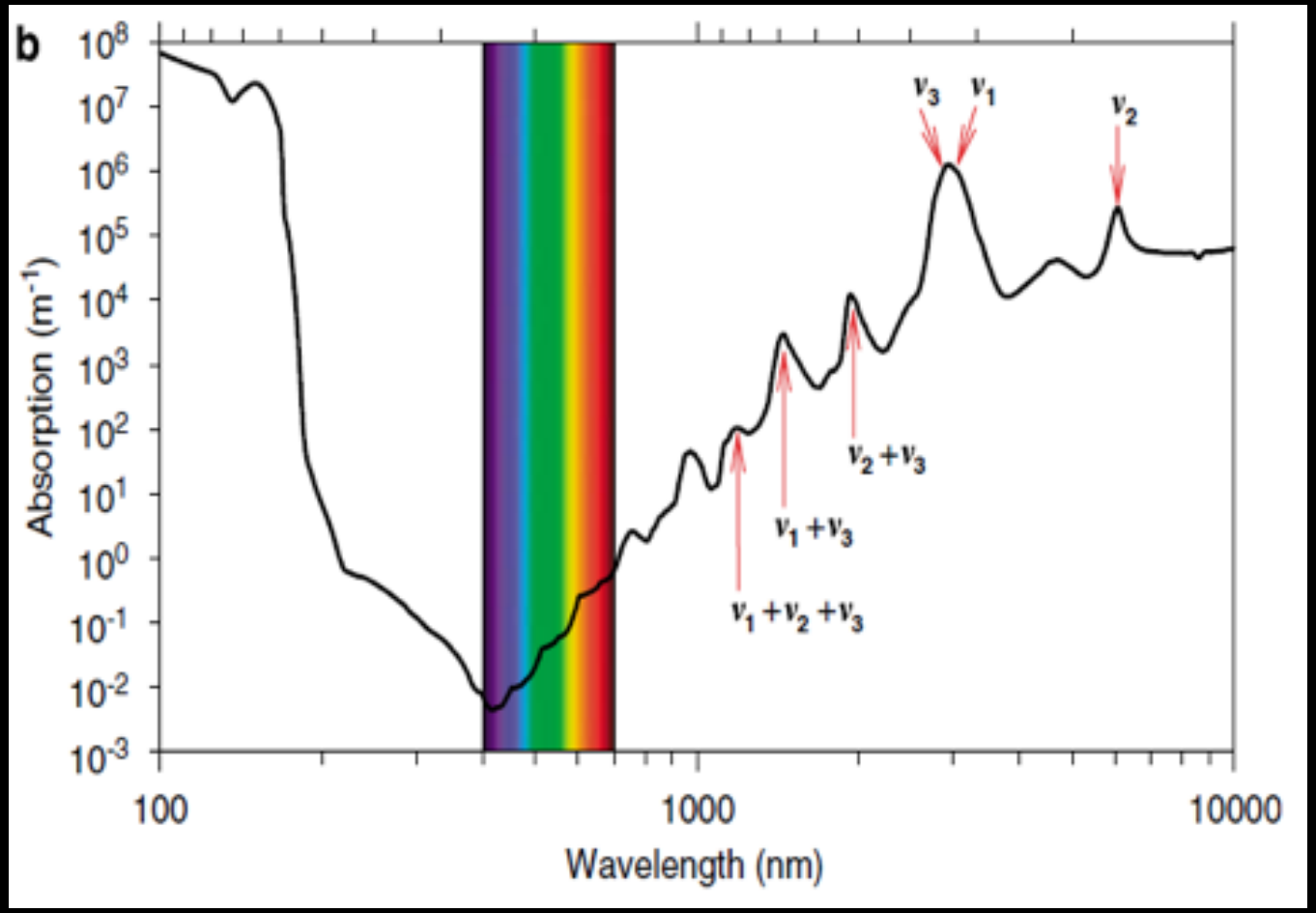

UltraViolet
Visible Light
Infrared
Shortwave
UVC
Middlewave
UVB
Longwave
UVA
200
280
315
400
Wavelength in Nanometers (nm)
760


COVID-19 Severity by Vitamin D Level (N=212)
≤20 ng/ml (≤50 nmol/L)
21-29 ng/ml (51-74 nmol/L)
≥30 ng/ml (≥75 nmol/L)
Percent Cases (%)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
4
44
52
4
41
55
7
59
34
96
2
Critical (N=48)
Severe (N=56)
Ordinary (N=59)
Mild (N=49)
COVID-19 Case Severity
Chart Date 4/21/2020
© 2020 GrassrootsHealth
Alipio MM, SSRN, 2020.
GrassrootsHealth
Moving Research into Practice
www.grassrootshealth.net

Benefits of Vit D

- Boosts the Immune System
- Protects against Cancer
- Induces Autophagy
- Prevents Cognitive Decline
- Promotes Bone Health
- Improves Anxiety and Depression
- Helps with Weight Loss
- Decreases Cardiovascular Disease and Diabetes

UV + Water



Water, The Cradle of Life via its Coherent Quantum Frequencies
https://waterjournal.org/current-volume/geesink/

UVA and Photorepair

- Fritz Albert Popp found that 380nm light is wavelength cells use to repair themselves
- Found carcinogen, benzo[a]pyrene, absorbed 380nm and scrambled this frequency, while benign chemicals did not

[CANCER RESEARCH 60, 2458–2463, May 1, 2000]

Photorepair Prevents Ultraviolet-induced Apoptosis in Human Cells Expressing the Marsupial Photolyase Gene[1]

Vanessa Chiganças, Eliane Namie Miyaji, Alysson Renato Muotri, Jacqueline de Fátima Jacysyn, Gustavo Pessini Amarante-Mendes, Akira Yasui, and Carlos Frederico Martins Menck[2]

Departamento de Microbiologia, Instituto de Ciências Biomédicas, Universidade de São Paulo, São Paulo 05508-900, SP, Brazil [V. C., A. R. M., C. F. M. M.]; Centro de Biotecnologia, Instituto Butantan, São Paulo 05503-900, SP, Brazil [E. N. M.]; Departamento de Imunologia, Instituto de Ciências Biomédicas, Universidade de São Paulo, São Paulo 05508-900, SP, Brazil [J. d. F. J., G. P. A-M.]; and Department of Molecular Genetics, Institute of Development, Aging and Cancer, Tohoku University, Sendai 980-8575, Japan [A. Y.]

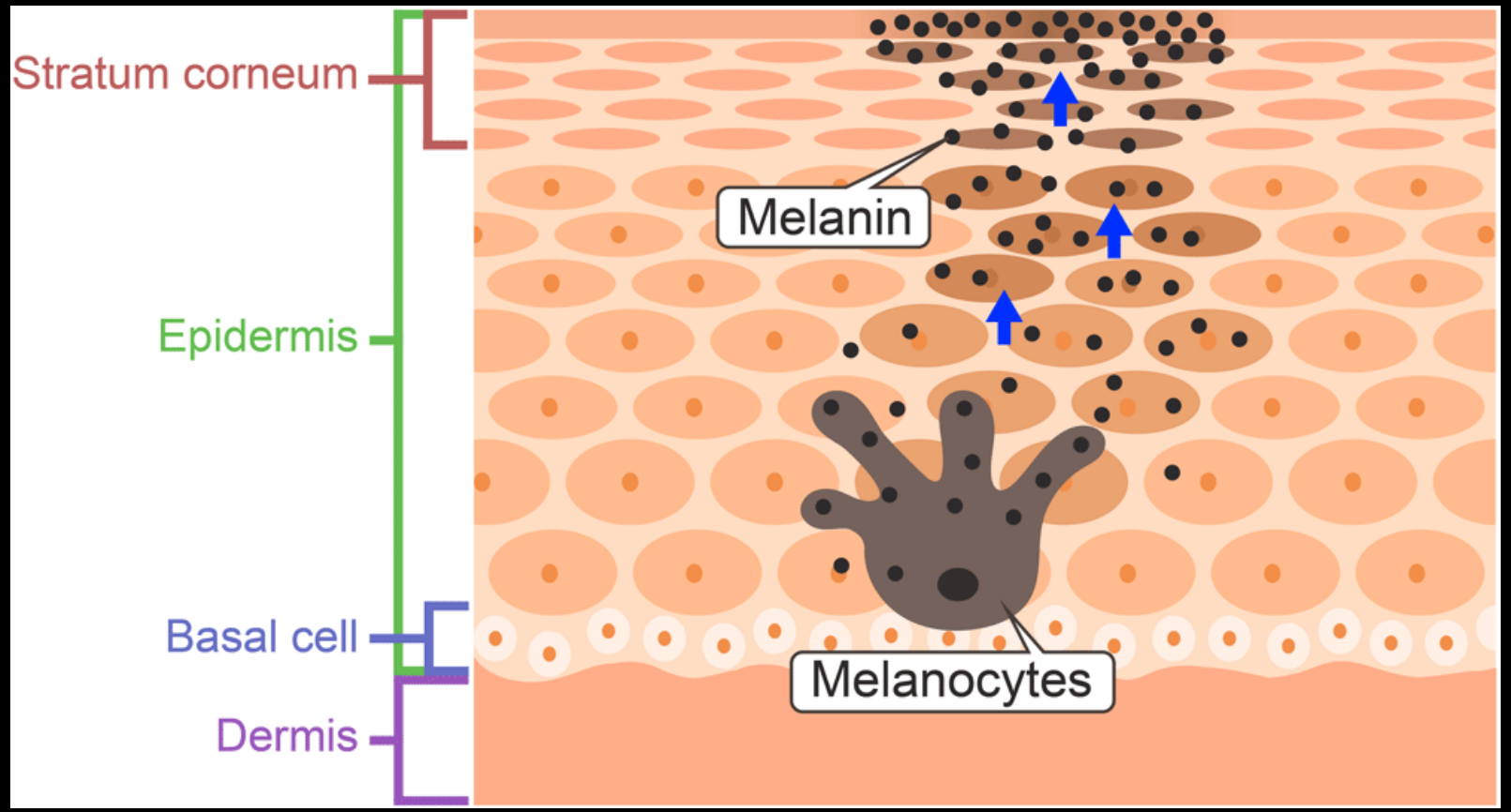
ABSTRACT

Photolyase absorbs blue light and employs the energy to remove UV-induced DNA damage, cyclobutane pyrimidine dimers, or pyrimidine pyrimidone (6–4) lesions. These enzymes have been found in many living organisms ranging from bacteria to aplacental mammals, but their photoreactivation effect, such as survival increase of UV-irradiated cells by light-illumination, has not been identified in placental mammals, including humans. Therefore,

be the appearance of CPDs[3] because the elimination of these lesions by photoreactivation in marsupial (11, 12) and fish (13) cells interferes with the induction of apoptosis. Photoreactivation is a known mechanism of DNA repair performed by photolyases, which remove specifically UV-induced lesions, such as CPD or (6–4) PP. These enzymes contain chromophores capable of capturing photons of blue light and a mechanism for converting this electronic excitation in CPD and (6–4) PP

Melanin

- Hair, eye, skin
- Also BRAIN
- Absorbs ALL EMF frequencies
  - Visible, UV light
  - X Rays
  - Gamma Rays



SPECIAL QUANTUM PROPERTIES

NEWS

Scientists Are Making Batteries Out Of Melanin "The voltage we got out was high..."

BY JASON WILLIAMS ON AUGUST 17, 2019

Imagine, a group of scientists figuring out how to make a battery out of your melanin, essentially what makes you 'black'. What does this mean for you?

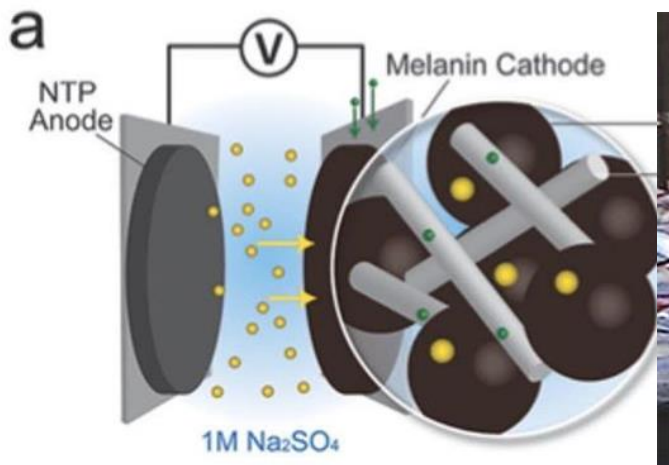
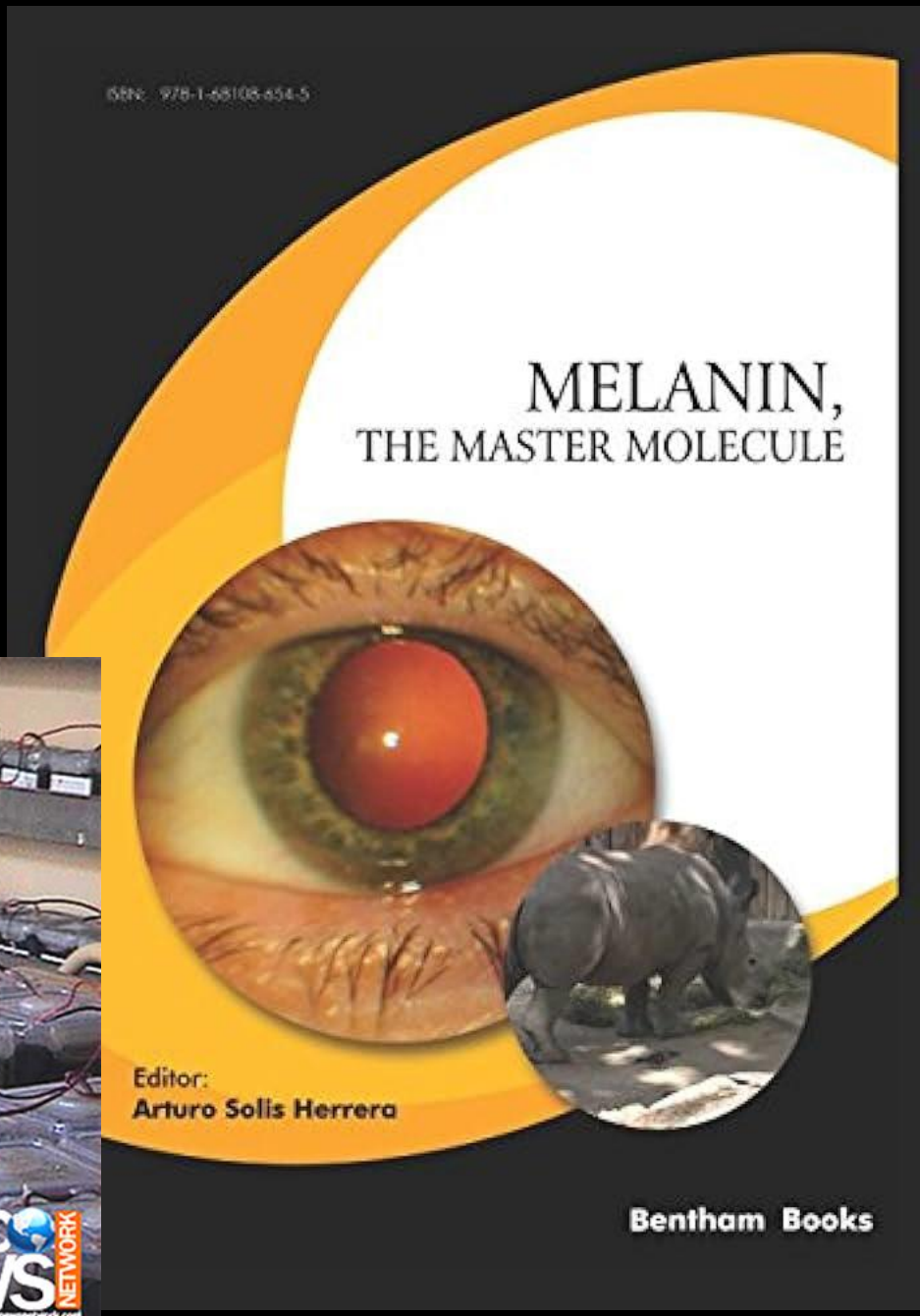


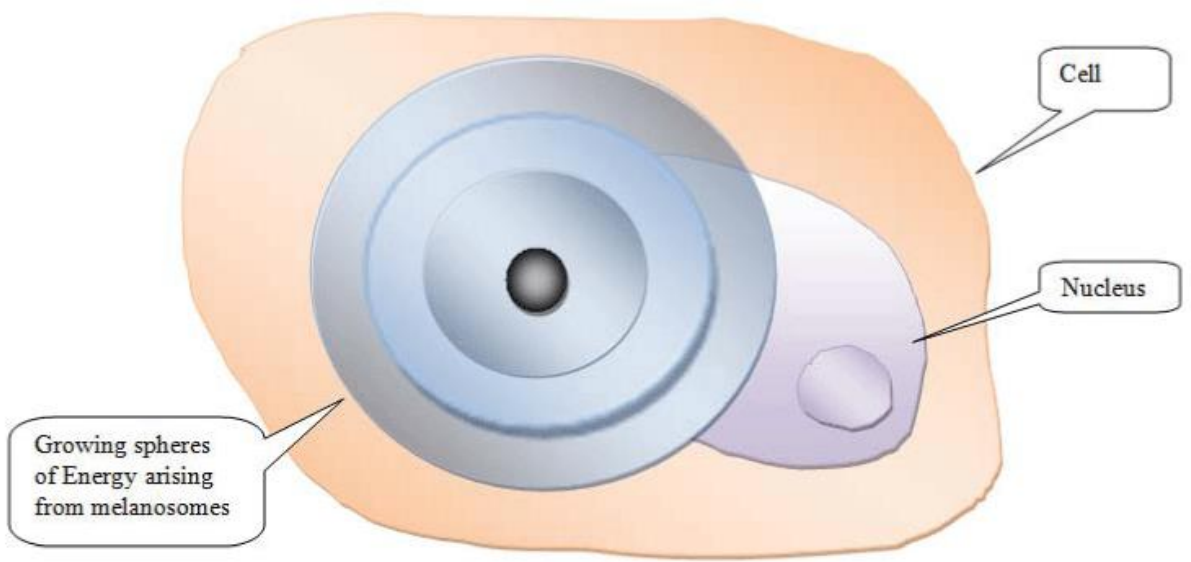
Photo Credit: Carnegie Mellon U



Human Photosynthesis

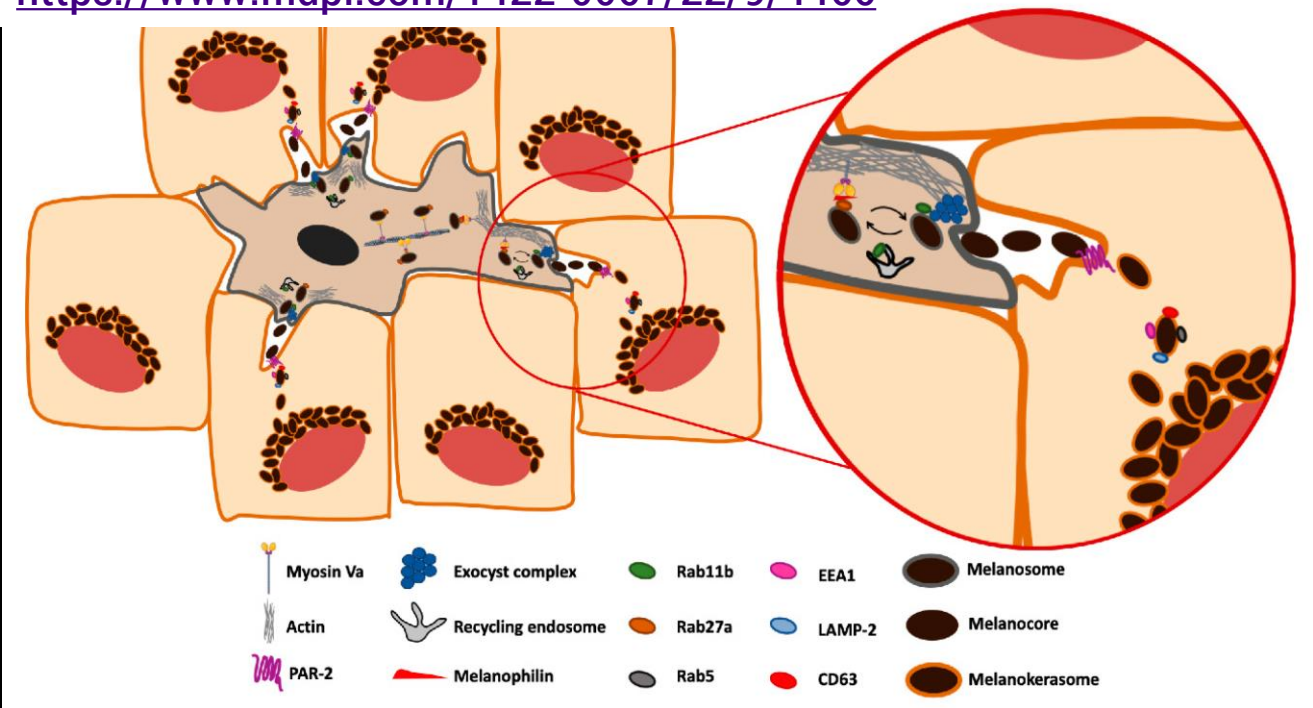
$2H_2O\ (liq) \rightarrow 2H_2(gas) + O_2(gas)$

$2H_2(gas) + O_2(gas) \rightarrow 2H_2O\ (liq) + 4e^-$



http://dx.doi.org/10.4172/1948-593X.1000079

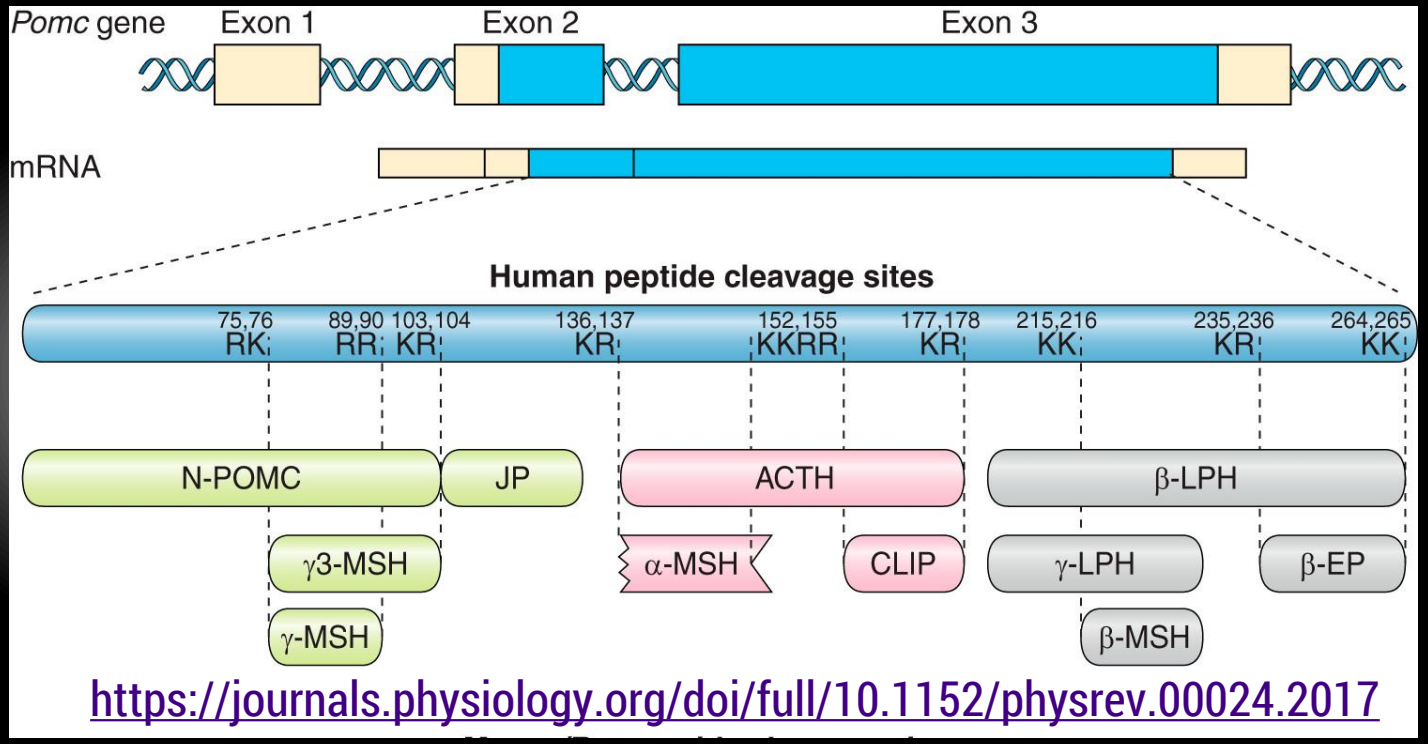
https://www.mdpi.com/1422-0067/22/9/4466



Melanin & The Eye

Pro-opiomelanocortin (POMC)

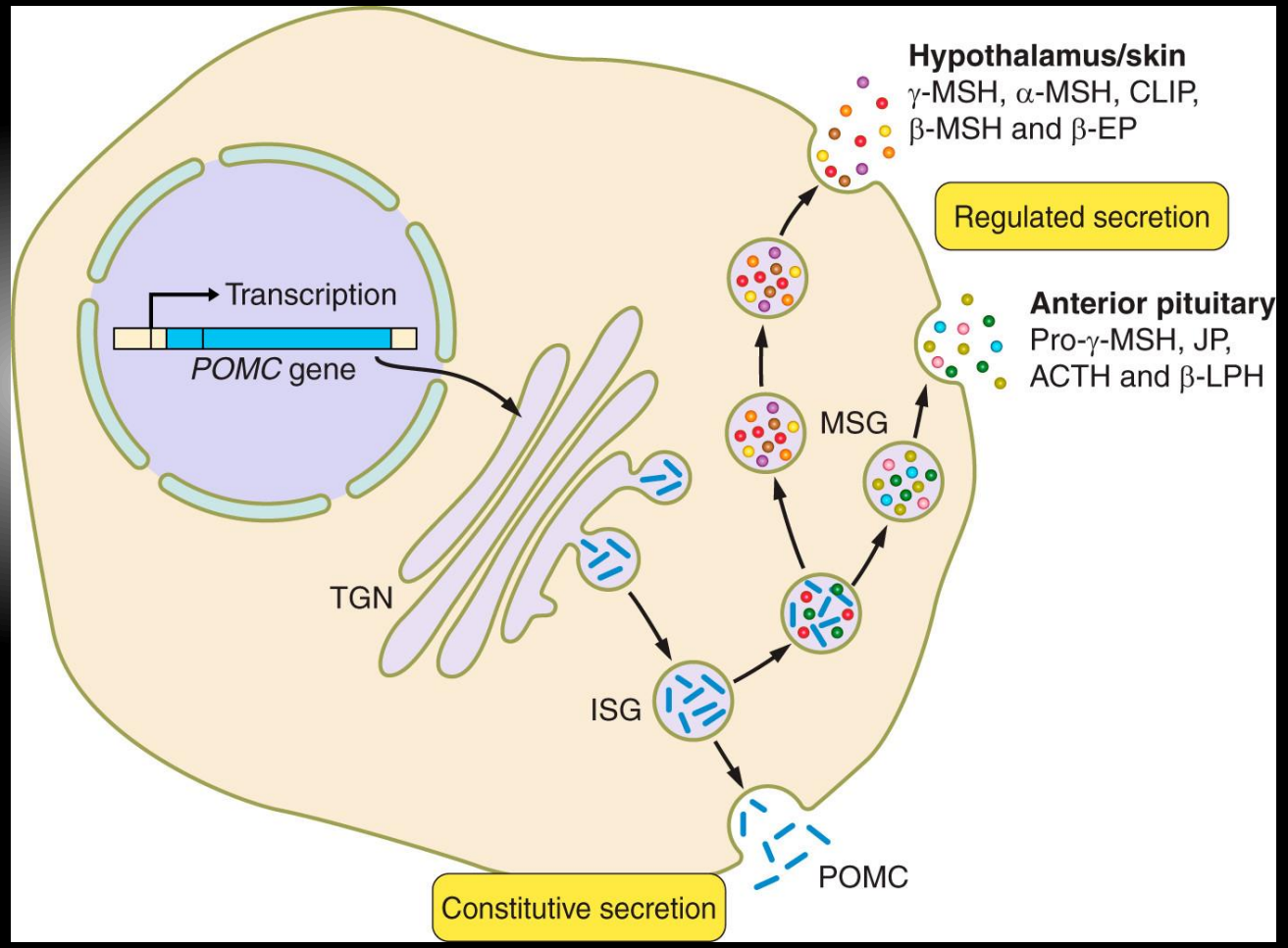
- Prohormone polypeptide
- Gives rise to:
  - α MSH
  - β MSH
  - γ MSH
  - ACTH
  - CLIP
  - β Endorphin



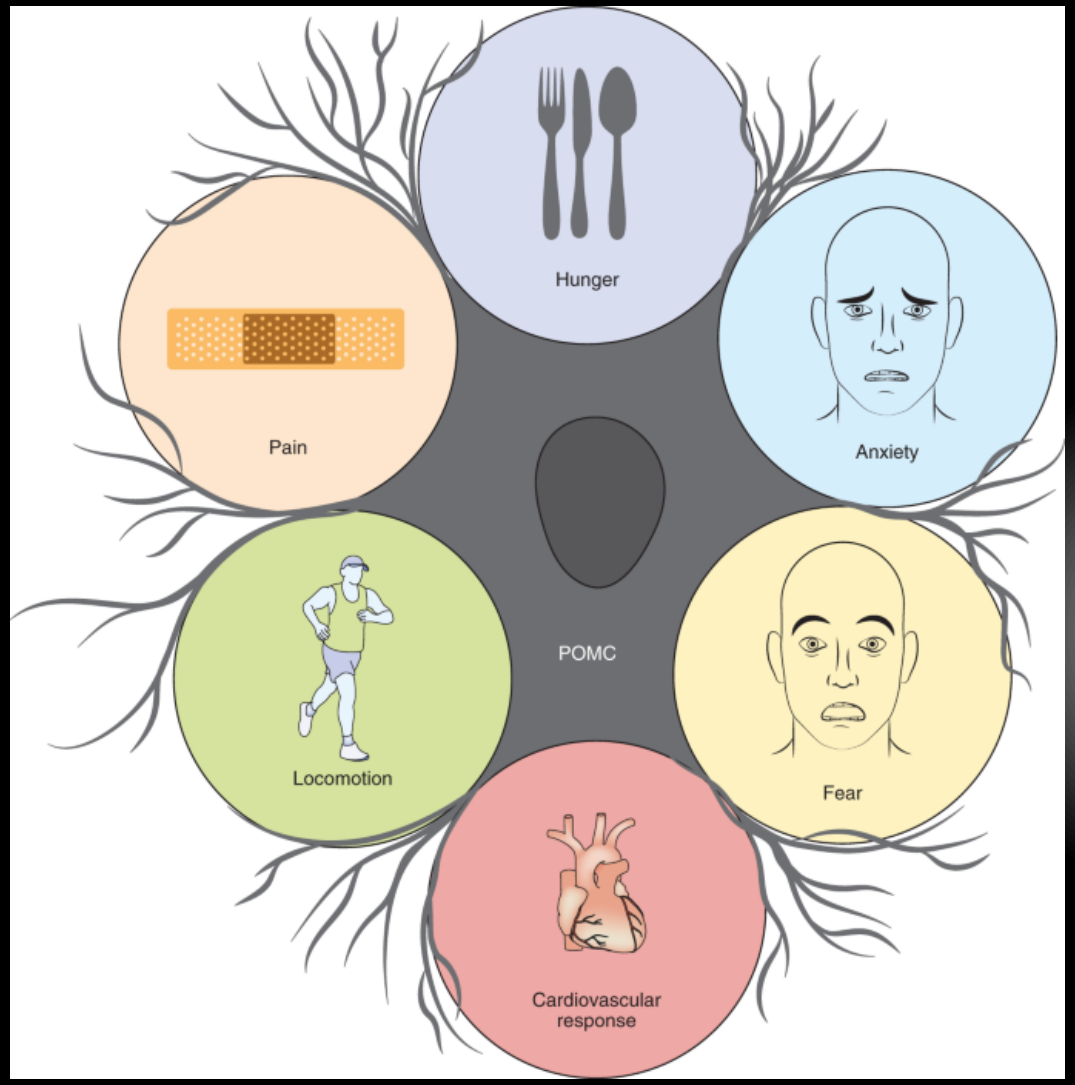
- MSH binding sites through CNS. Diverse functions including:
  - Learning & Memory, Fever Supression, Nerve Regeneration
  - Inflammatory & Immune Responses, Sexual Behavior

Pro-opiomelanocortin (POMC)

- MSH → MCR's
  - Energy Balance & Beyond
- β Endorphin → Morphine
  "Addicted to Sun"
- ACTH → HPA Axis
  - Cortisol & Androgens
- CLIP → Insulin & SWS



https://journals.physiology.org/doi/full/10.1152/physrev.00024.2017



POMC neuronal heterogeneity in energy balance and beyond: an integrated view

https://www.nature.com/articles/s42255-021-00345-3

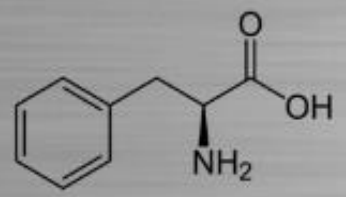
MCR	Ligand	Modified from[d]	Biological effects	Tested mod
MC1R	α-MSH = ACTH > β-MSH > γ-MSH[a]	Endogenous ligands	Induces skin pigmentation, anti-inflammatory	Rodents
	BMS-470539[a]	Novel small molecule	Anti-inflammatory	LPS-induced PAF-induced inflammation
	AP1189[a]	Novel small molecule	Anti-inflammatory	Zymosan-inc K/BxN serum
	Agouti[b]	Endogenous ligand	Inhibits eumelanin production	Lethal yellow alleles (A^y an
MC2R	ACTH[a]	Endogenous ligand	Induces steroidogenesis, anti-inflammatory	Rodents
MC3R	γ-MSH ≥ ACTH = β-MSH = α-MSH[a]	Endogenous ligands	Energy homeostasis, cardiovascular function	Rodents
	MTII[a]	α-MSH	Inhibits neutrophil migration and cytokine generation	Crystal-induc
	D-Trp^8-γMSH[a]	γ-MSH	Anti-inflammatory, stimulates food intake	Crystal-induc ischemia-rep inflammatory
	AP214[a]	α-MSH	Anti-inflammatory	Zymosan-inc inflammatory
	AP1189[c]	Novel small molecule	Anti-inflammatory, promotes resolution of acute inflammation	Zymosan-inc K/BxN serum
	SHU-9119[b]	α-MSH	Inhibits D-Trp^8-γMSH-induced anti-inflammatory effects	Crystal-induc
	AVM-127[b]	γ-MSH	inhibits α-MSH-induced pro-erection	Male rats
MC4R	α-MSH = ACTH > β-MSH > γ-MSH[a]	Endogenous ligands	Energy homeostasis, erectile function, cardiovascular function	Rodents
	THIQ[a]	Novel small molecule	Anti-inflammatory, inhibits food intake, promotes penile erection	LPS-induced male rat ex c
	Ro27-3225[a]	α-MSH	Inhibits 4 h food intake	Rats
	PT-141[a]	MTII	Induces transient erections	Male Spragu men
	AgRP[b]	Endogenous ligands	Increases food intake, decreases mean arterial pressure and heart rate	Lethal yellow alleles(A^{vy}), diabetic (db/
	ML00253764[b]	Novel small molecule	Reduces tumor-induced weight loss	CT26 colore tumor and L tumors
	Ro27-4680[b]	α-MSH	Increases acute food intake	Rats
MC5R	α-MSH > ACTH > β-MSH > γ-MSH[a]	Endogenous ligands	Exocrine function, anti-inflammatory	Rodents
	PG-901[a]	SHU-9119	Anti-hypertrophic, reduces cellular glucose uptake	STZ-diabetic rats

[a]indicates agonis

https://doi.org/10.3389/fendo.2019.00683

and is derived fro

AROMATIC AMINOACIDS AND PHOTOADAPTATION

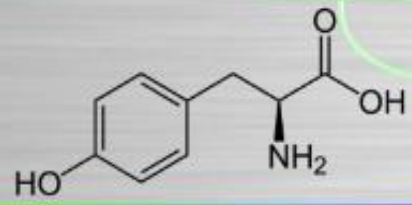


Phenylalanine

Tyrosine

Photosynthesis

Signal transduction proteins



Precursor

T3, T4

Flavonoids

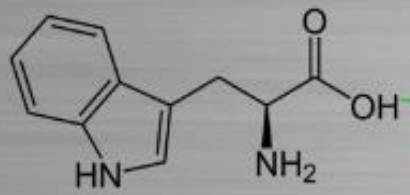
DOPA

Melanin

Dopamine

Adrenalin

Noradrenalin



Tryptophan

Neurotransmitter

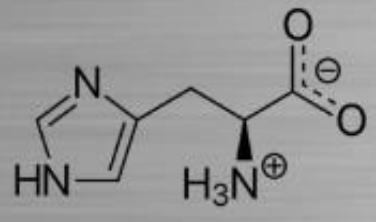
Neurohormone

Serotonin

Melatonin

Tryptamine

Psychedelic drugs



Histidine

Stabilizes oxy-hemoglobin

Histamine

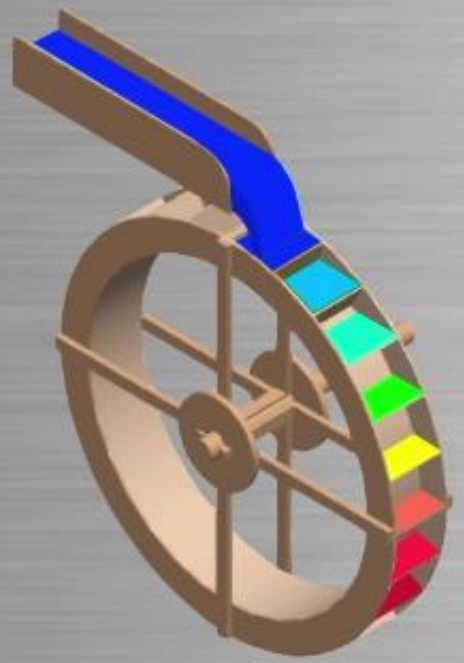
Erythema

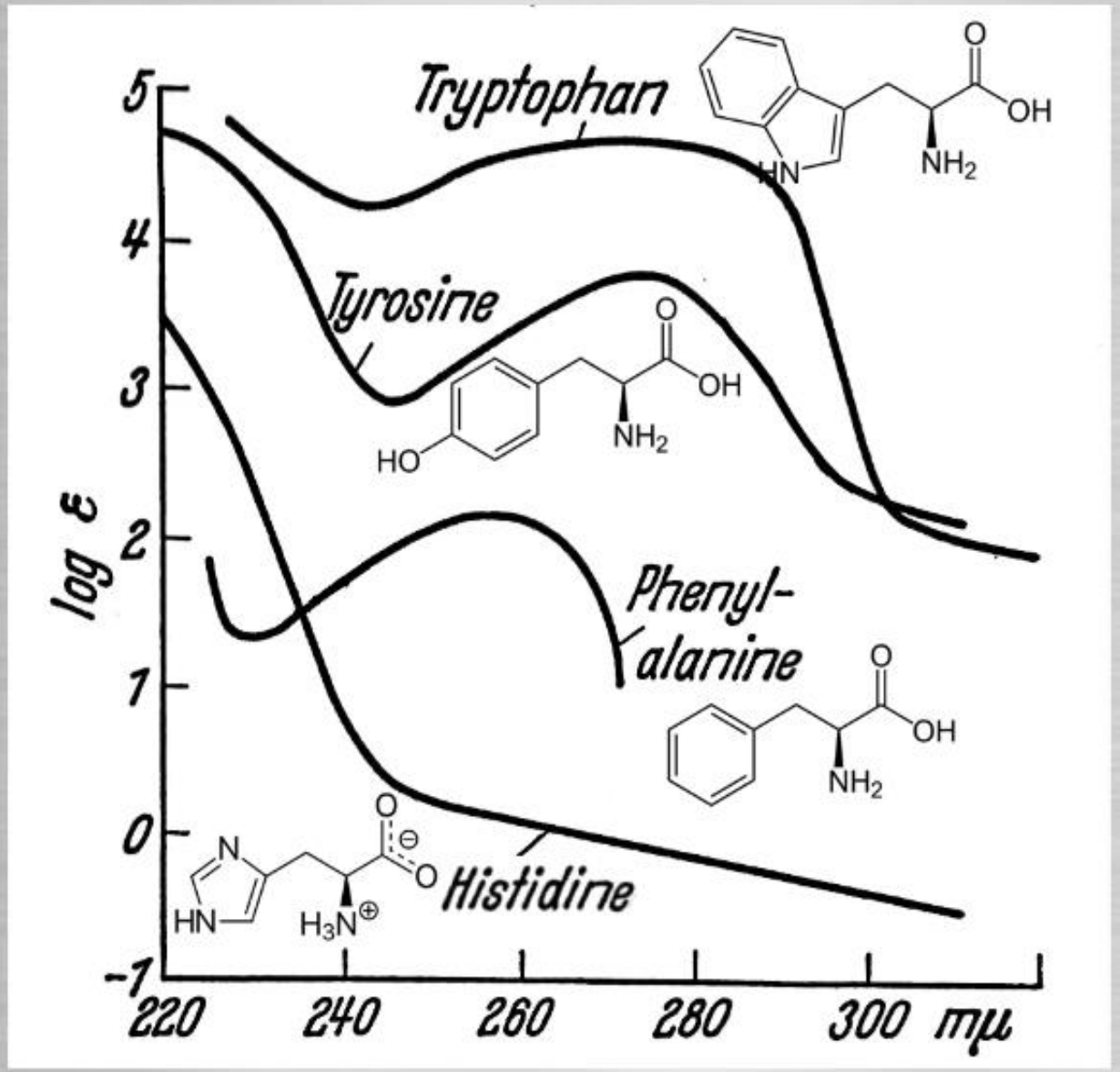
Urocanic acid

UV-Filter

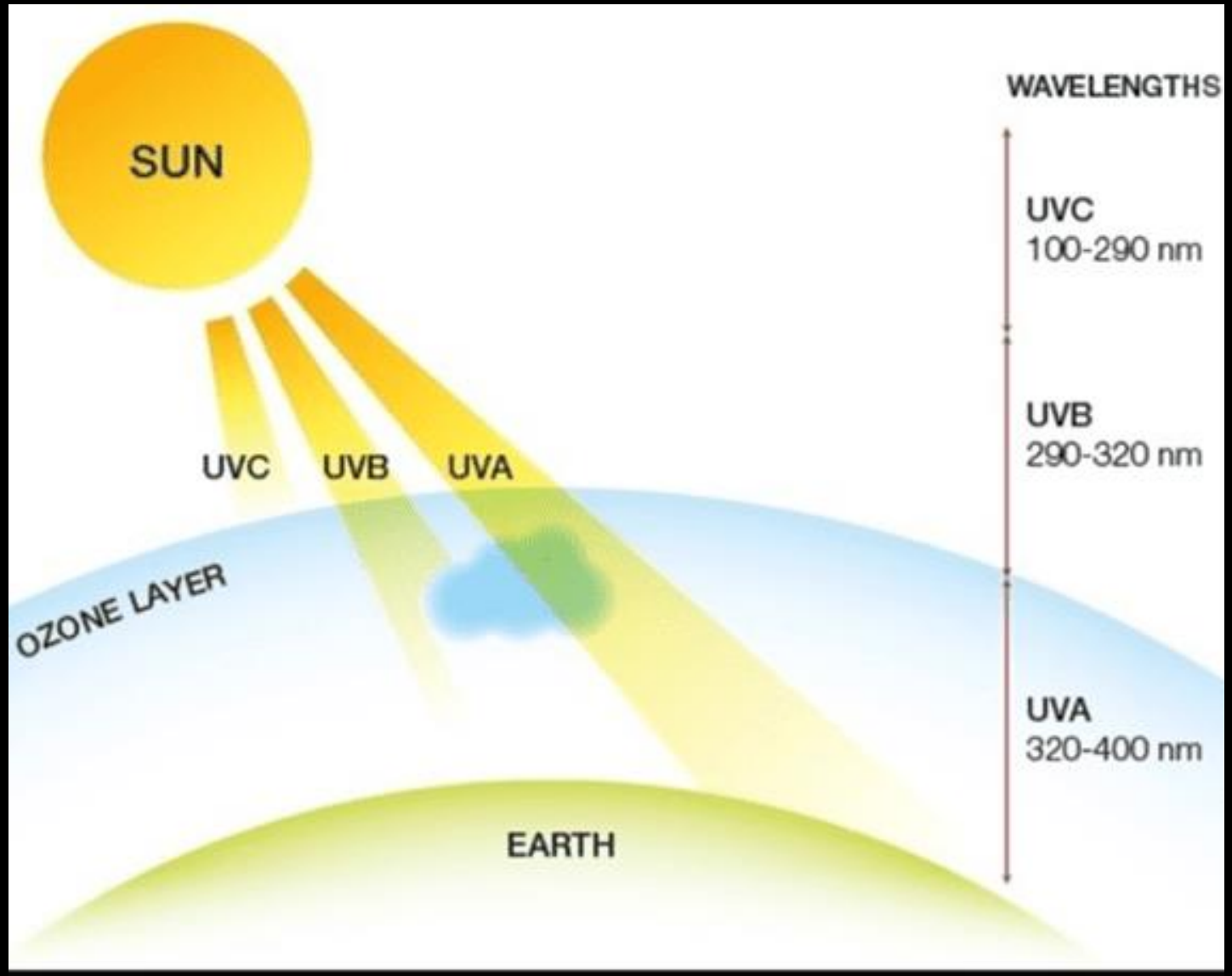
AROMATIC AMINOACIDS ABSORB UV LIGHT

UV



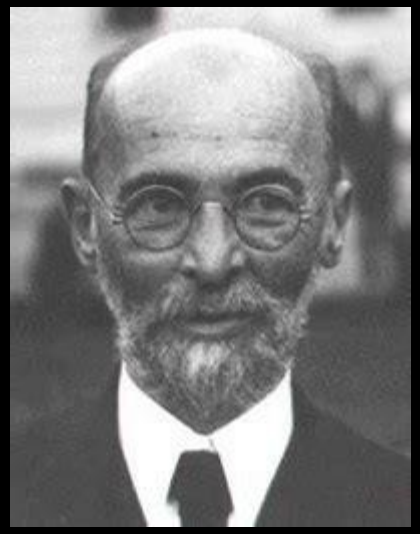


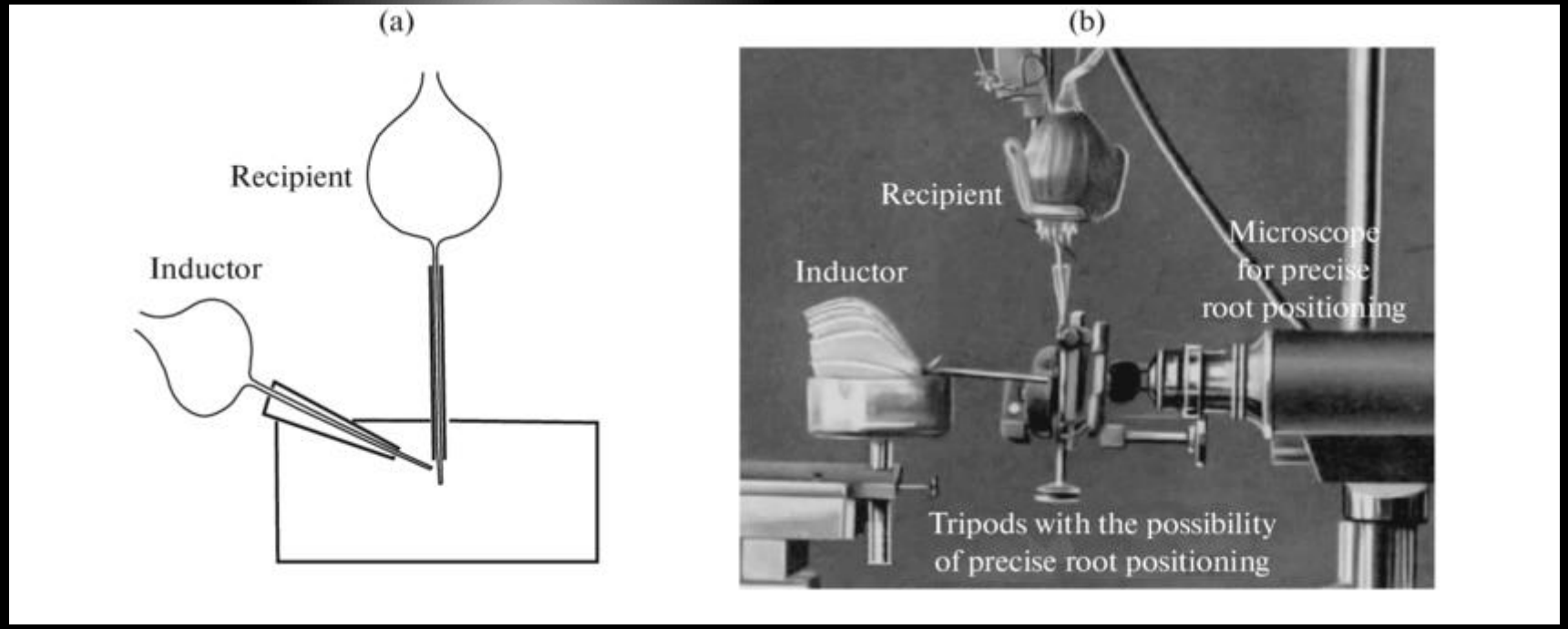
Where's The UVC?



Alexander Gurwisch (1874-1954)

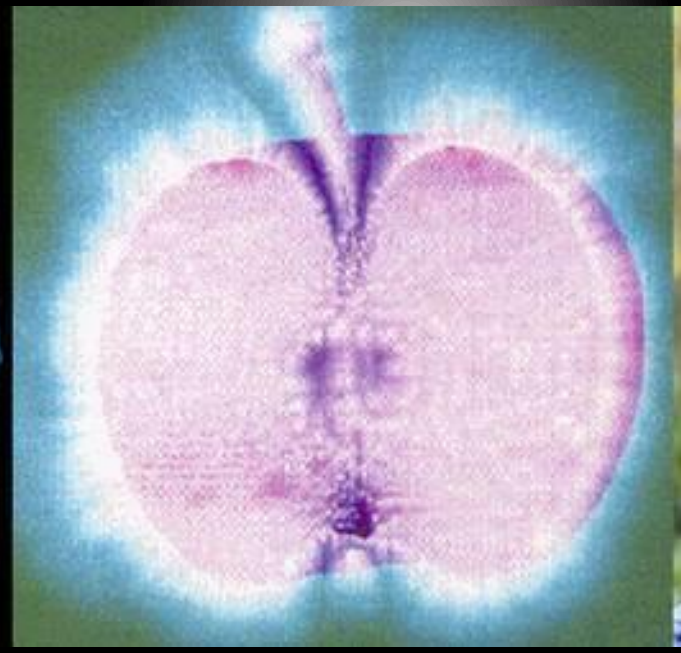
- “Mitogenic Radiations” from onion root were the discovery of living biophotons



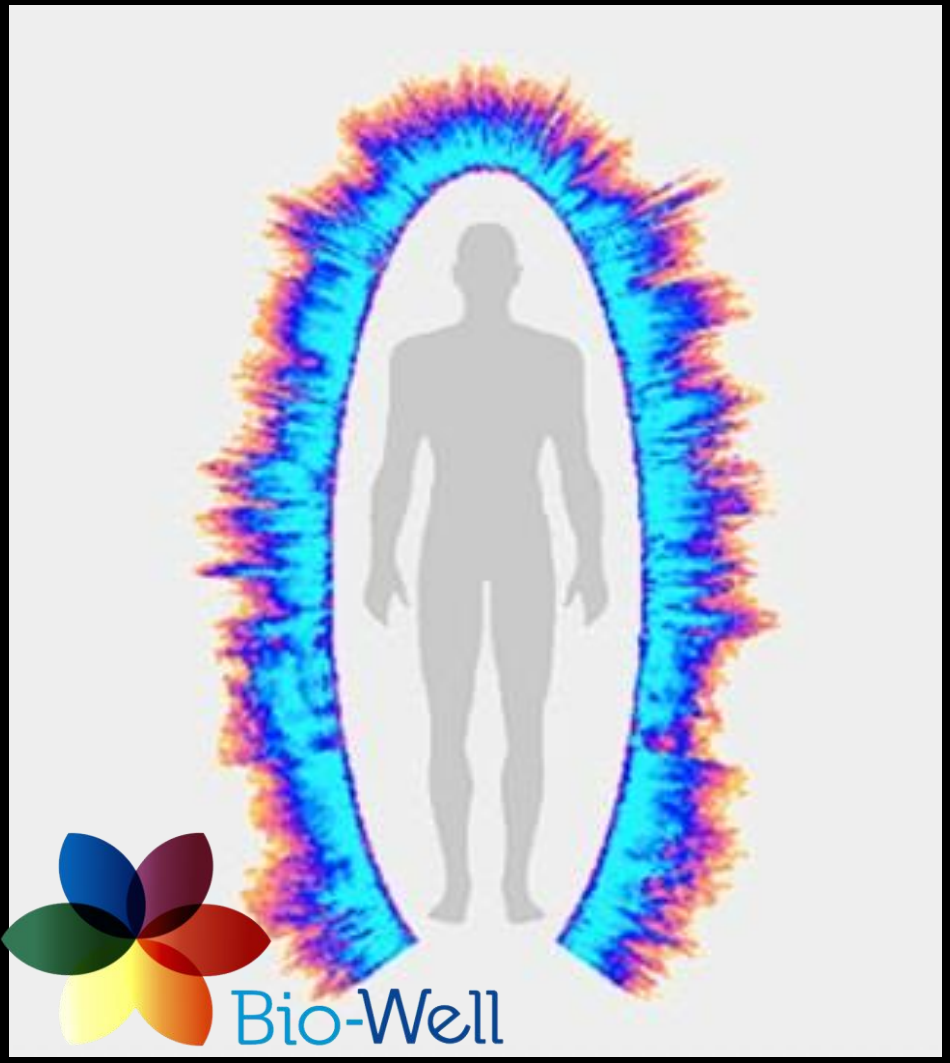


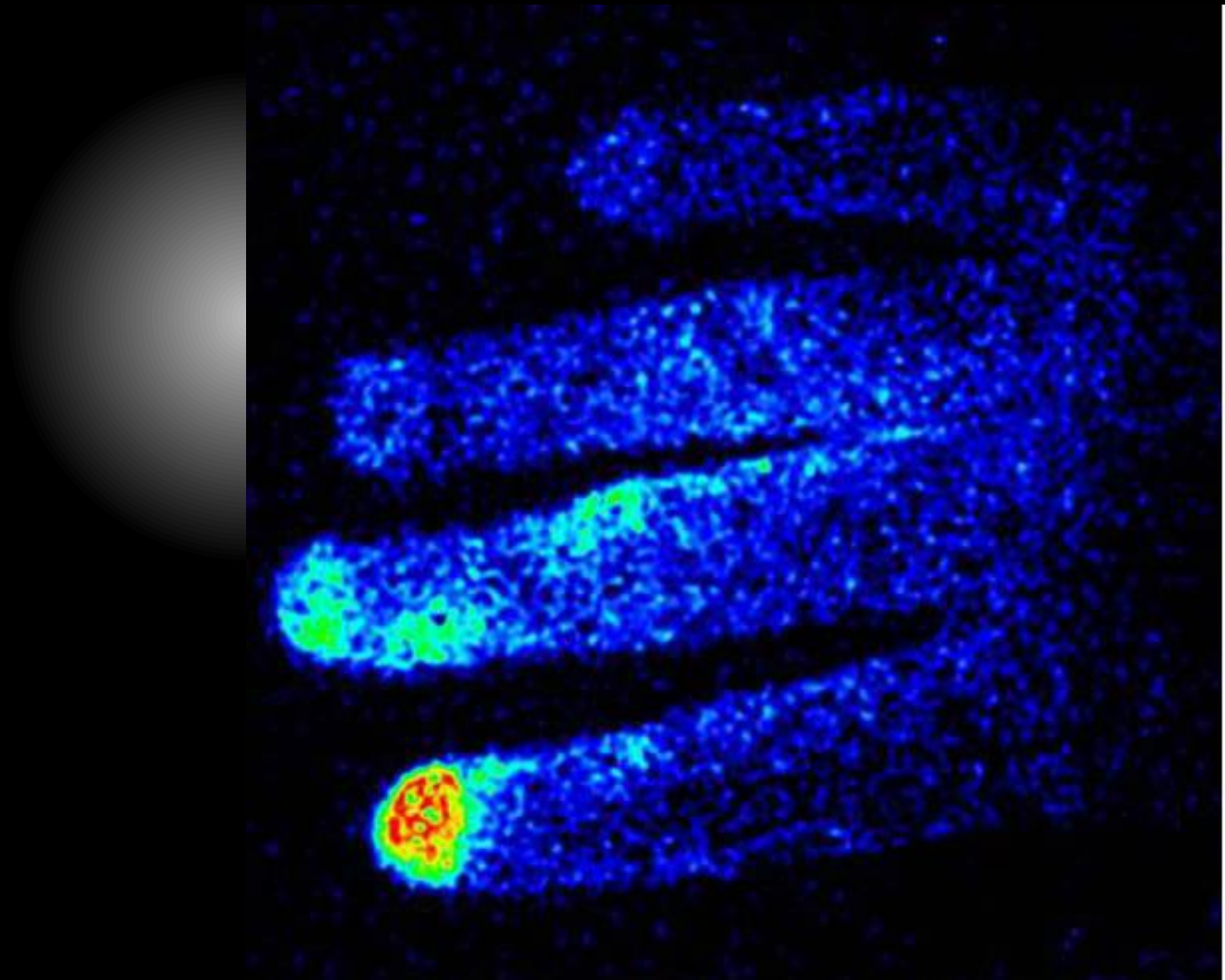
Fritz-Albert Popp (1938-2018)

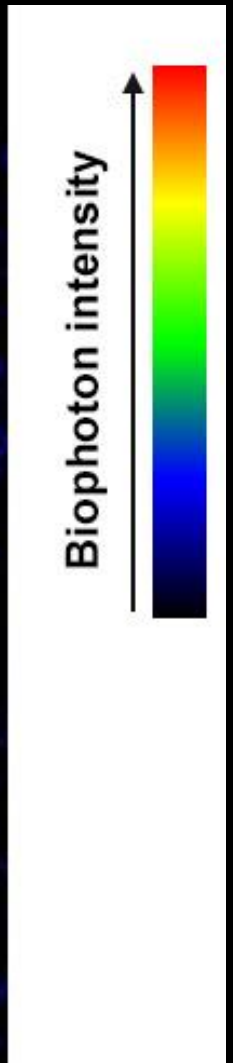
- Photomultiplier To Detect Ultraweak Photon Emissions

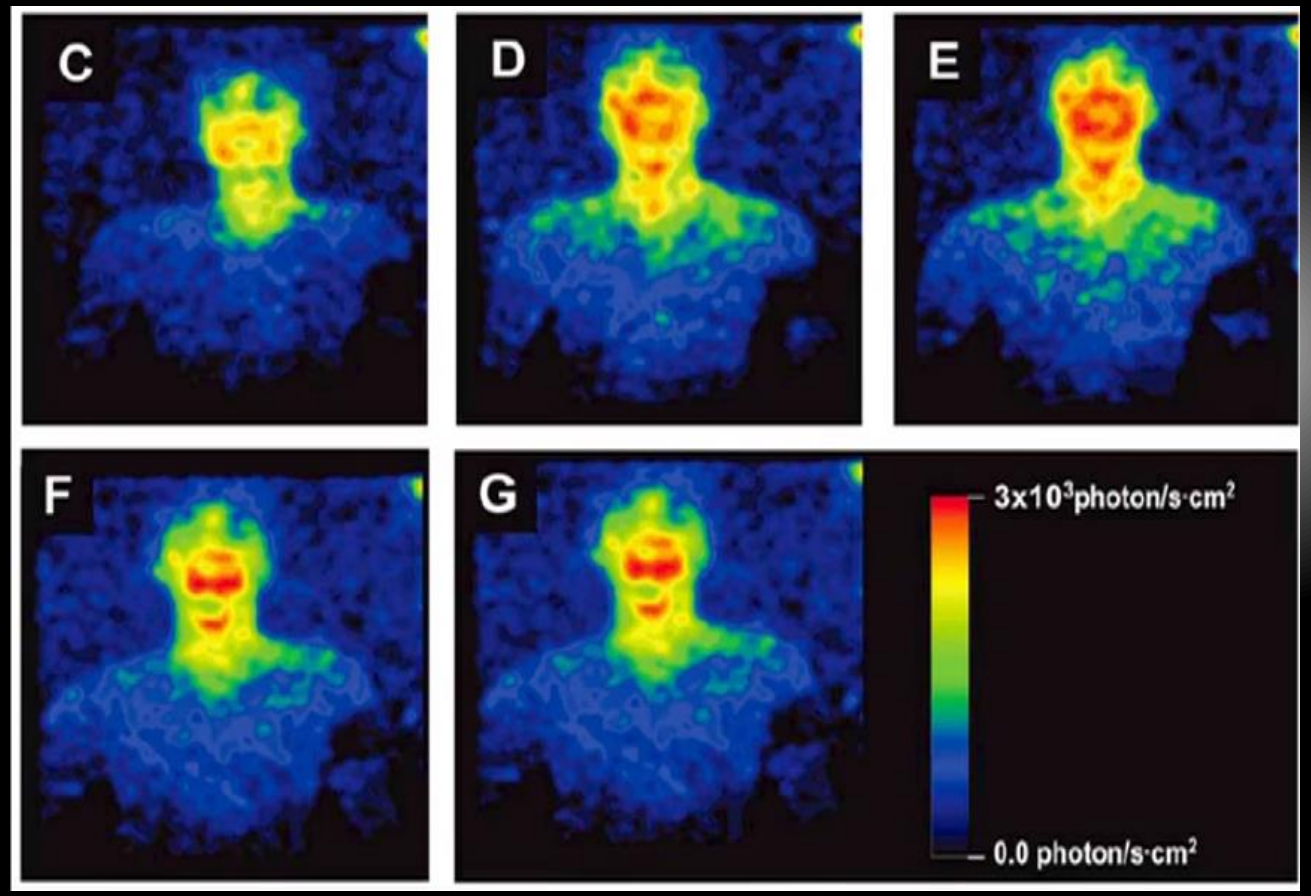


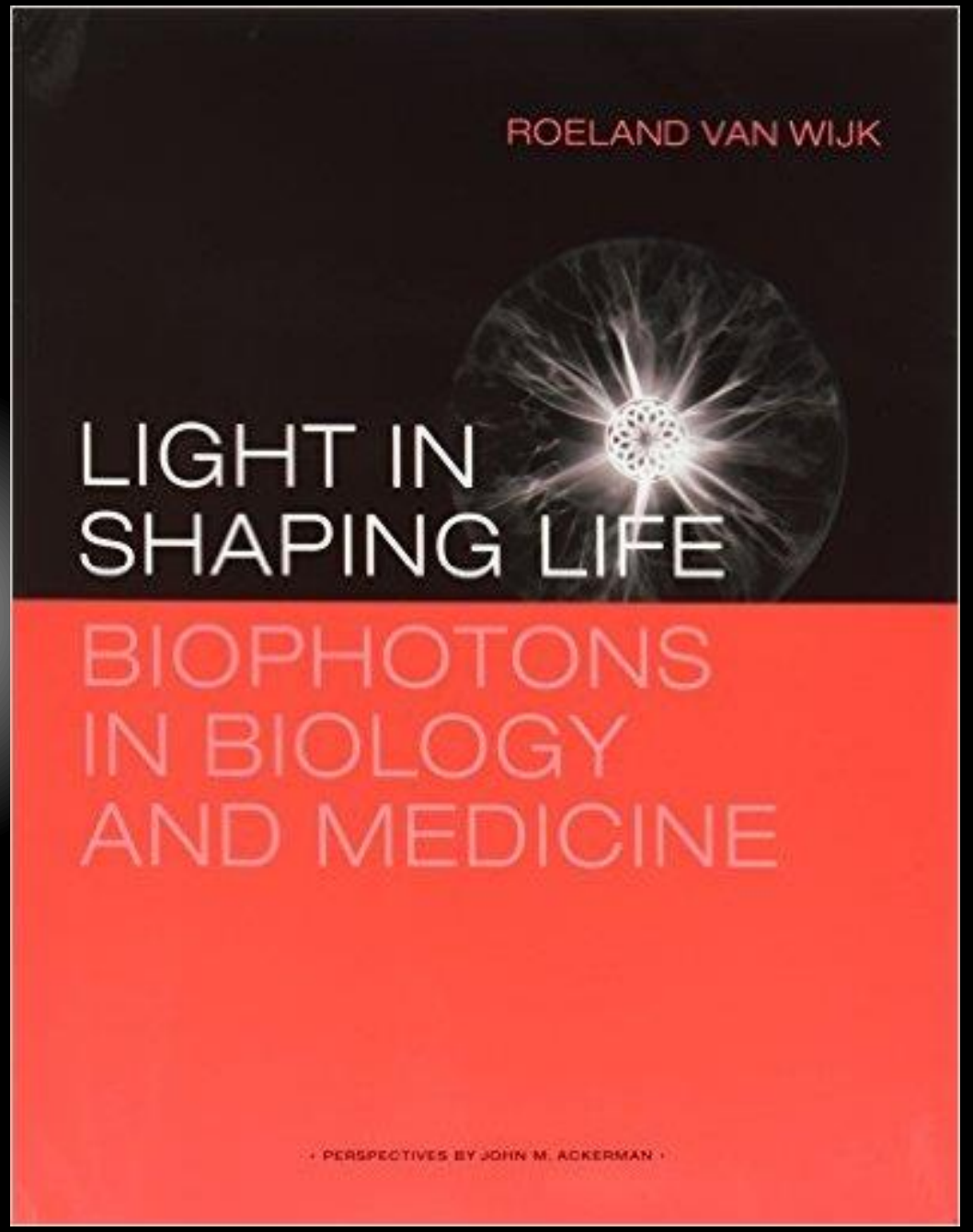
Hue-mans



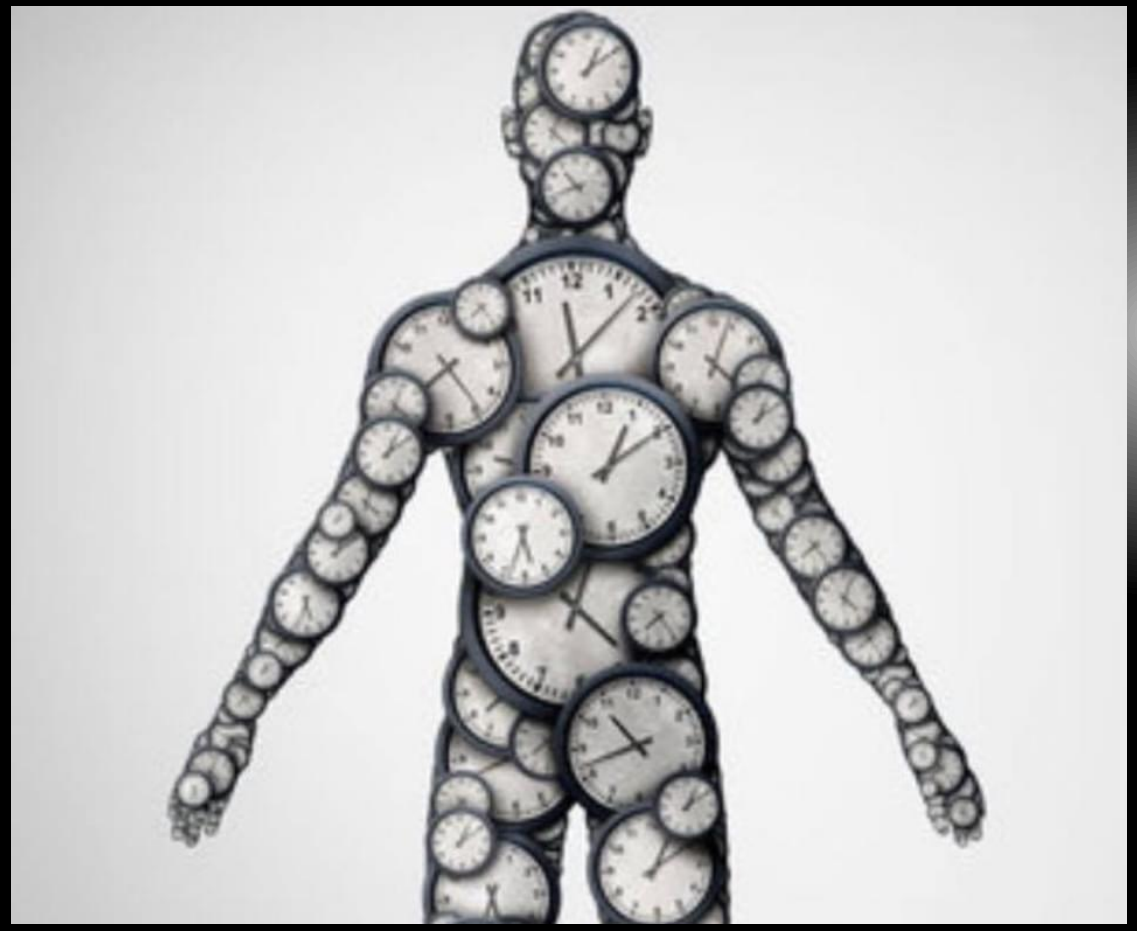


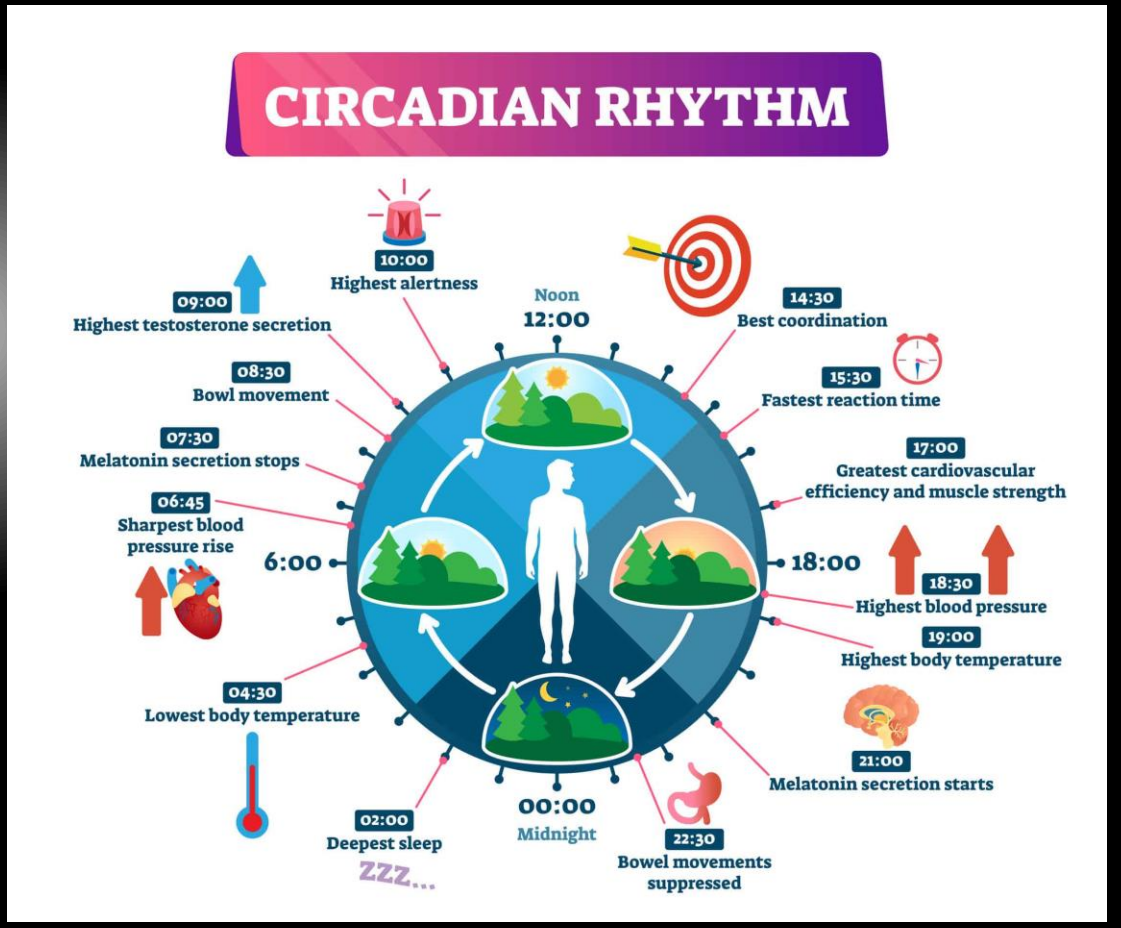



C
D
E
F
G
3x10³photon/s·cm²
0.0 photon/s·cm²


ROELAND VAN WIJK
LIGHT IN SHAPING LIFE
BIOPHOTONS IN BIOLOGY AND MEDICINE
PERSPECTIVES BY JOHN M. ACKERMAN

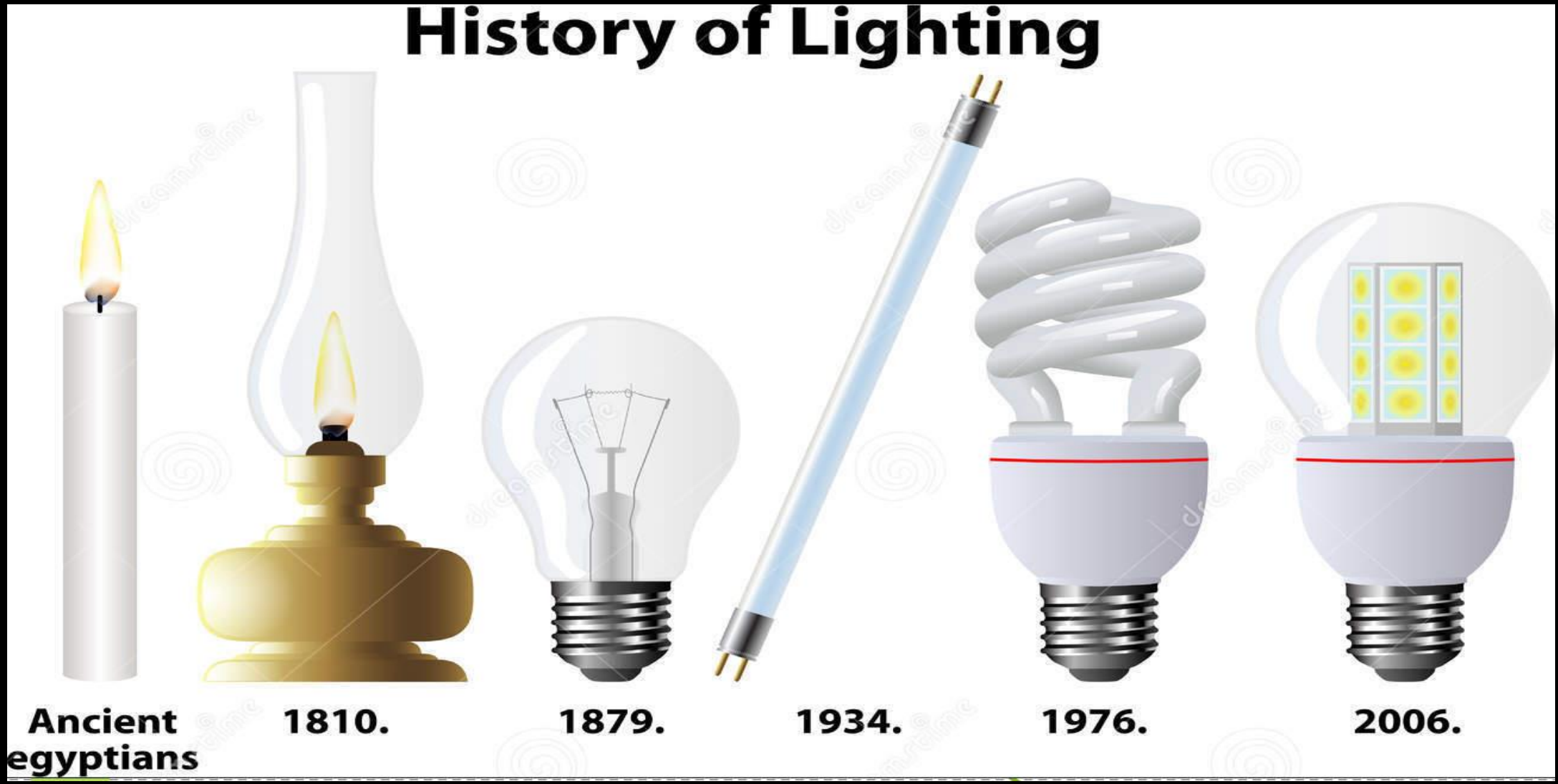
Timing Is Everything



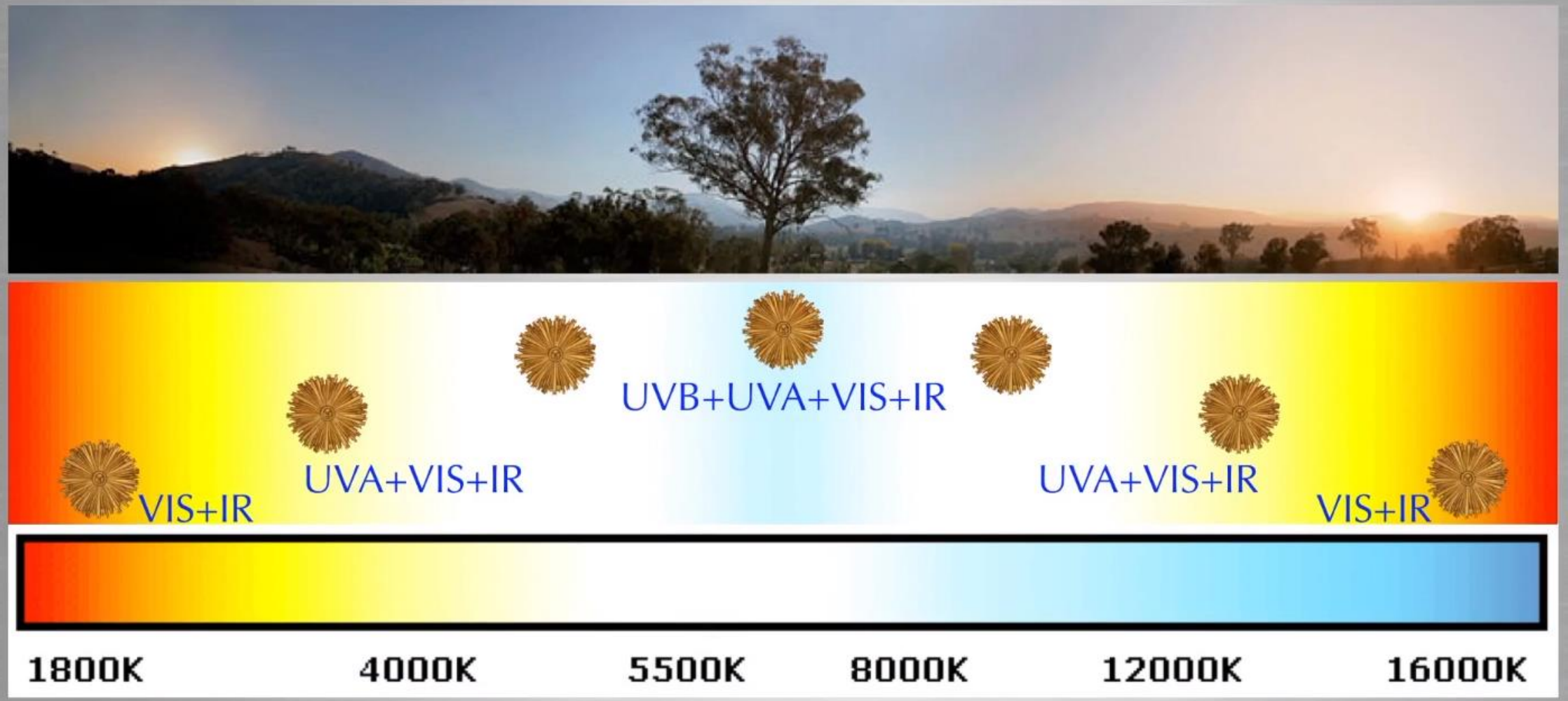


Evolution of Clothing = Circadian Dysruption

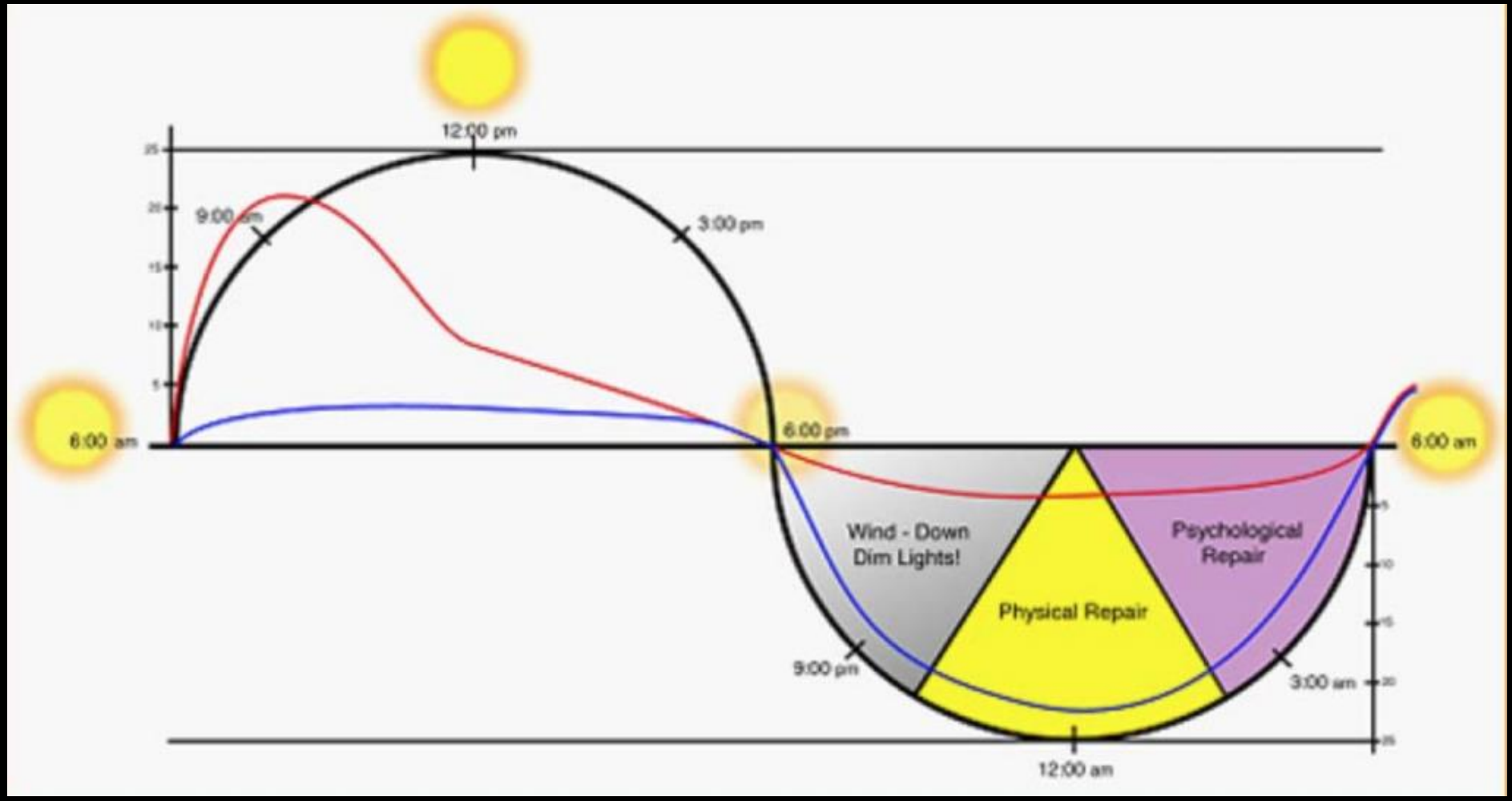
Evolution of Light = Circadian Dysruption



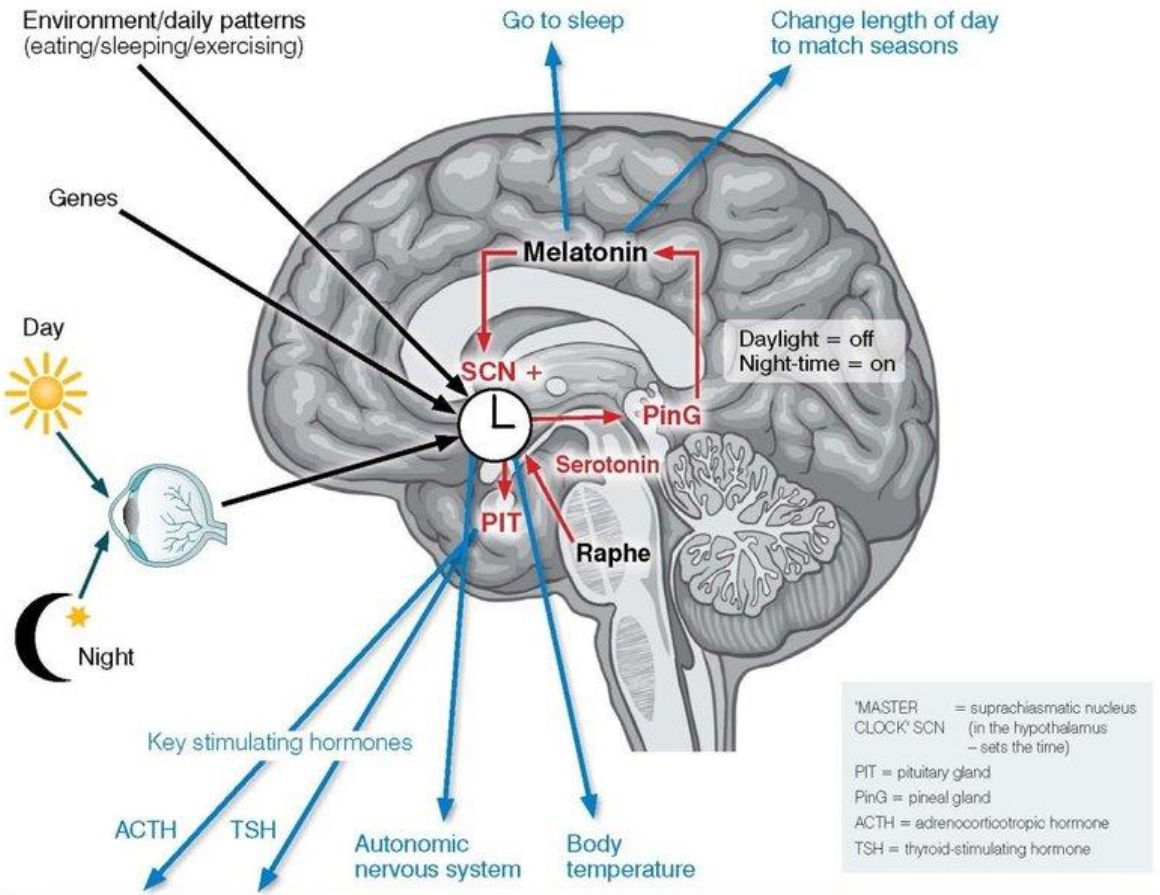
COLORS OF DAYLIGHT



Time to Make the Donuts



Setting the 24-hour circadian rhythm



'MASTER CLOCK' SCN = suprachiasmatic nucleus (in the hypothalamus – sets the time)

PIT = pituitary gland

PinG = pineal gland

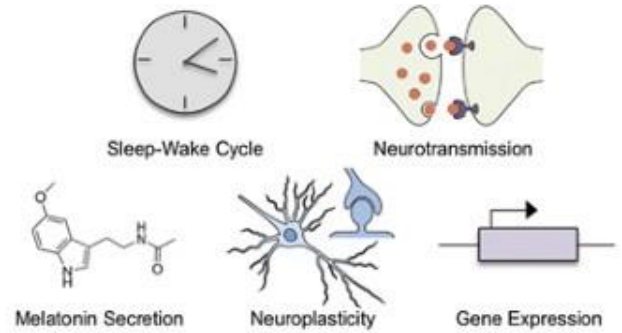
ACTH = adrenocorticotropic hormone

TSH = thyroid-stimulating hormone

ORGAN LEVEL

Adrenal gland	Thyroid gland	Heart	Pancreas	Liver	Fat	Muscle	Gut
cortisol	thyroid hormone		insulin	glycogen	lipid metabolism		

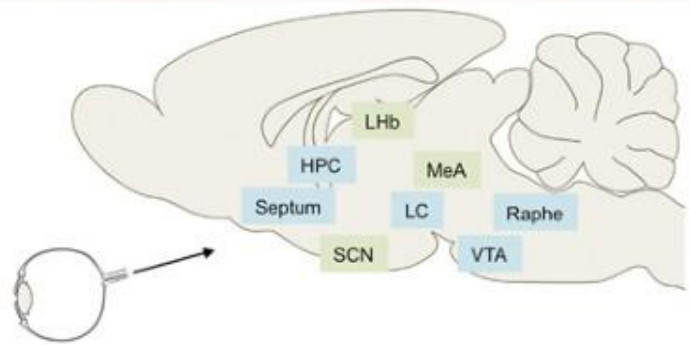
Food and activity

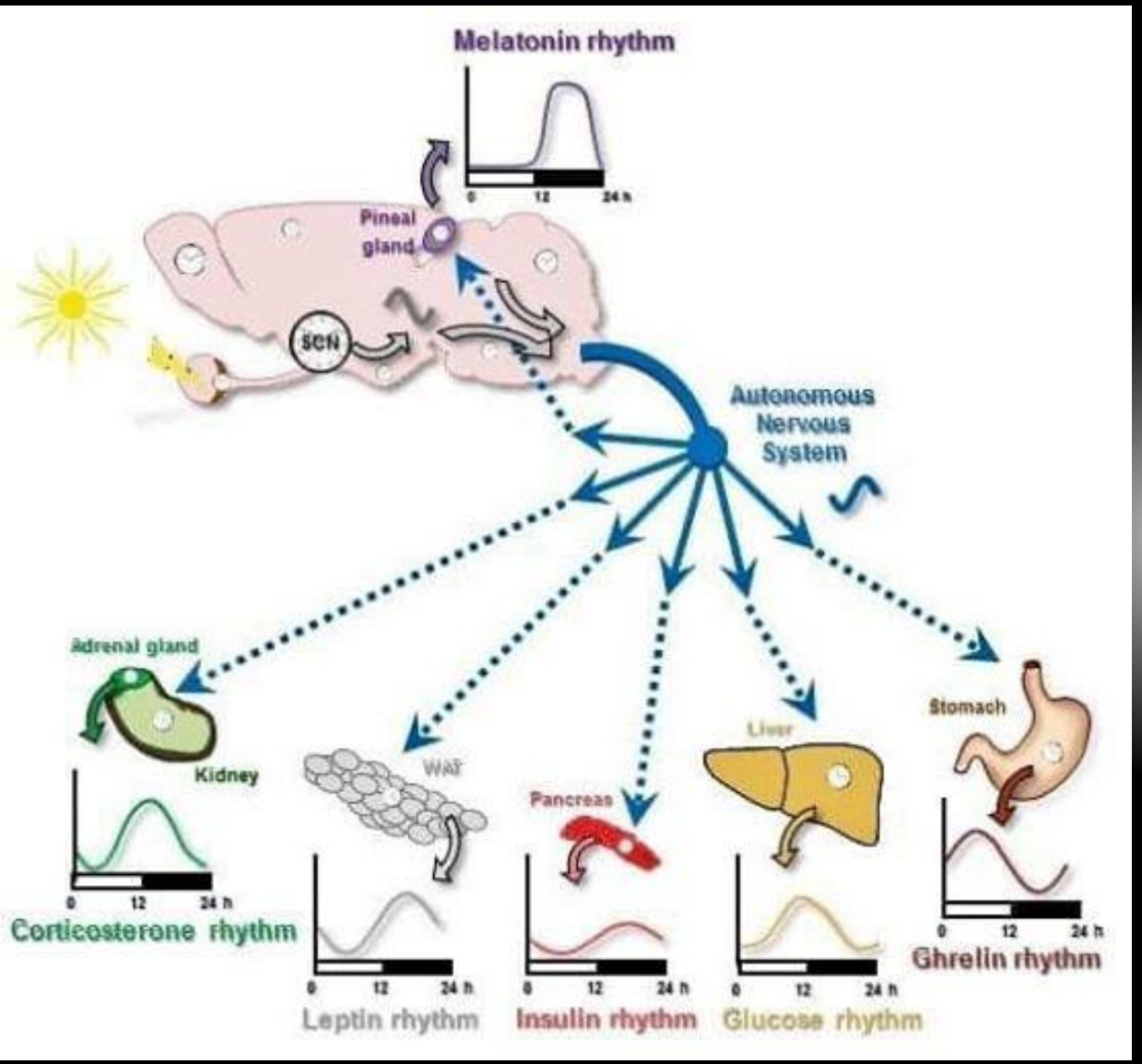


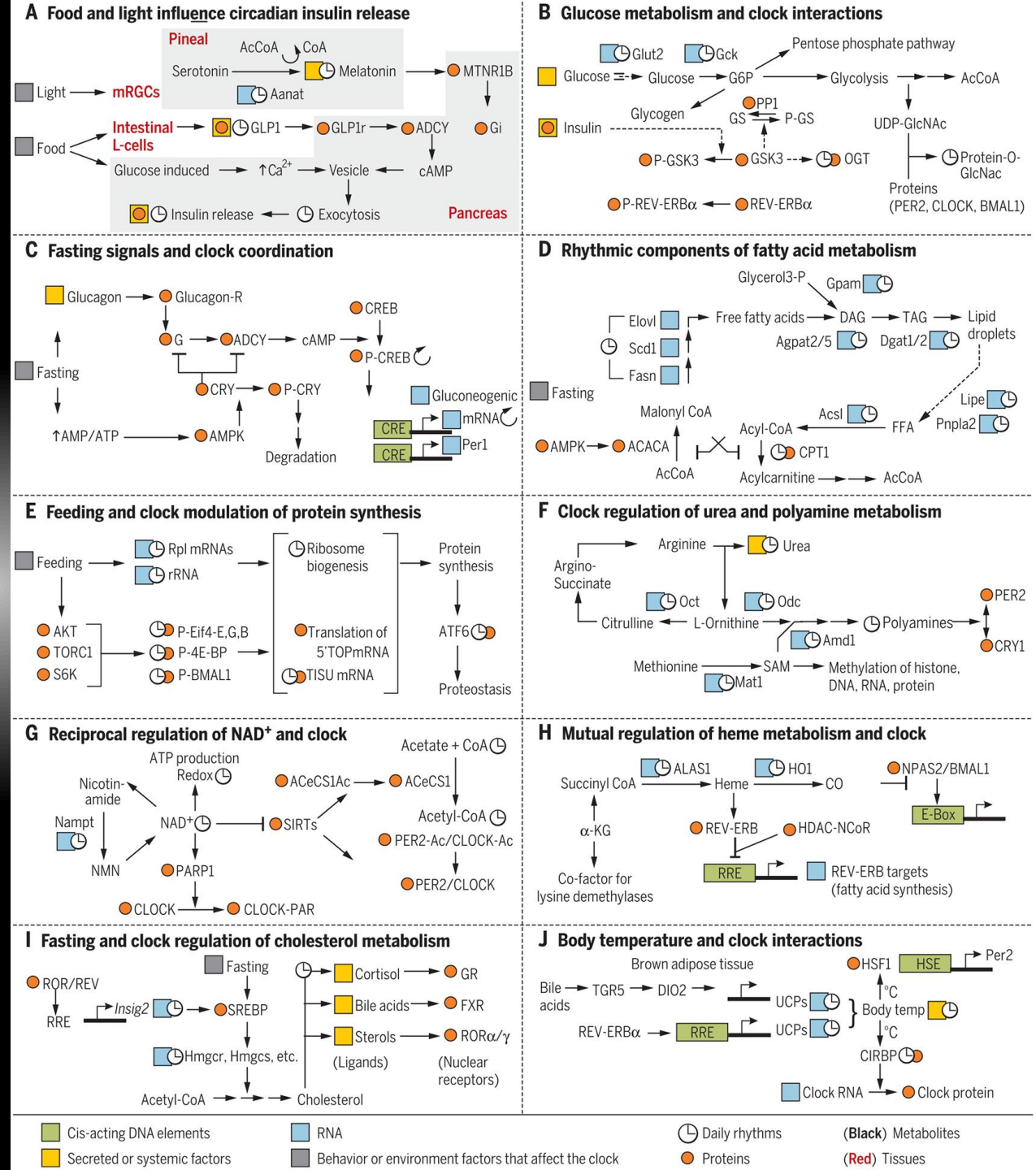
Light at Night

- Indirect disruption of homeostatic processes involved in mood
- Direct ipRGC stimulation of brain regions involved in mood

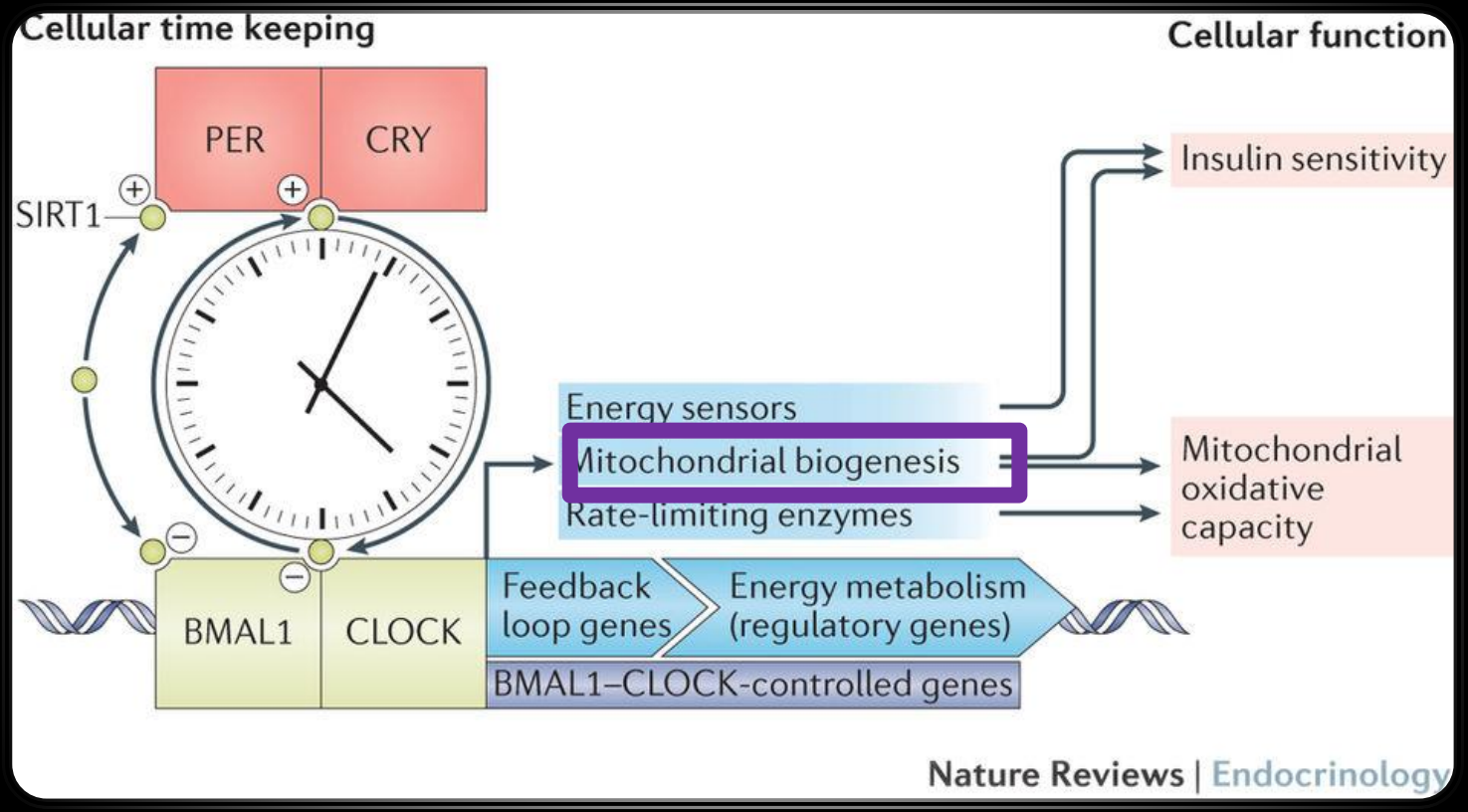
→ **Depressed Mood**
And deficits in learning & memory, cognition, stress response




Melatonin rhythm
0 12 24 h
Pineal gland
SCN
Autonomous Nervous System
Adrenal gland
Kidney
WAT
Pancreas
Liver
Stomach
0 12 24 h
Corticosterone rhythm
Leptin rhythm
Insulin rhythm
Glucose rhythm
Ghrelin rhythm


A Food and light influence circadian insulin release
Pineal
AcCoA
CoA
Serotonin
Melatonin
Aanat
MTNR1B
Light
mRGCs
Intestinal L-cells
GLP1
GLP1r
ADCY
Gi
Food
Glucose induced
↑Ca2+
Vesicle
cAMP
Insulin release
Exocytosis
Pancreas
B Glucose metabolism and clock interactions
Glut2
Gck
Pentose phosphate pathway
Glucose
Glucose
G6P
Glycolysis
AcCoA
Glycogen
PP1
GS
P-GS
Insulin
UDP-GlcNAc
P-GSK3
GSK3
OGT
Protein-O-GlcNac
Proteins (PER2, CLOCK, BMAL1)
P-REV-ERBα
REV-ERBα
C Fasting signals and clock coordination
Glucagon
Glucagon-R
CREB
G
ADCY
cAMP
P-CREB
Fasting
CRY
P-CRY
Gluconeogenic
↑AMP/ATP
AMPK
mRNA
CRE
Per1
Degradation
D Rhythmic components of fatty acid metabolism
Glycerol3-P
Gpam
Elovl
Free fatty acids
DAG
TAG
Lipid droplets
Scd1
Agpat2/5
Dgat1/2
Fasn
Fasting
Malonyl CoA
Acsl
Lipe
Acyl-CoA
FFA
Pnpla2
AMPK
ACACA
CPT1
AcCoA
Acylcarnitine
AcCoA
E Feeding and clock modulation of protein synthesis
Feeding
Rpl mRNAs
rRNA
Ribosome biogenesis
Protein synthesis
AKT
TORC1
S6K
P-Eif4-E,G,B
P-4E-BP
P-BMAL1
Translation of 5'TOPmRNA
TISU mRNA
ATF6
Proteostasis
F Clock regulation of urea and polyamine metabolism
Arginine
Urea
Argino-Succinate
Oct
Odc
PER2
Citrulline
L-Ornithine
Polyamines
CRY1
Amd1
Methionine
SAM
Methylation of histone, DNA, RNA, protein
Mat1
G Reciprocal regulation of NAD+ and clock
Acetate + CoA
ATP production
Redox
Nicotin-amide
ACeCS1Ac
ACeCS1
Nampt
NAD+
SIRTs
Acetyl-CoA
PER2-Ac/CLOCK-Ac
NMN
PARP1
PER2/CLOCK
CLOCK
CLOCK-PAR
H Mutual regulation of heme metabolism and clock
ALAS1
HO1
NPAS2/BMAL1
Succinyl CoA
Heme
CO
E-Box
α-KG
REV-ERB
HDAC-NCoR
RRE
Co-factor for lysine demethylases
REV-ERB targets (fatty acid synthesis)
I Fasting and clock regulation of cholesterol metabolism
Fasting
Cortisol
GR
ROR/REV
Bile acids
FXR
RRE
Insig2
SREBP
Sterols
RORα/γ
Hmgcr, Hmgcs, etc.
(Ligands)
(Nuclear receptors)
Acetyl-CoA
Cholesterol
J Body temperature and clock interactions
Brown adipose tissue
HSF1
HSE
Per2
Bile acids
TGR5
DIO2
UCPs
°C
Body temp
REV-ERBα
RRE
UCPs
°C
CIRBP
Clock RNA
Clock protein
Cis-acting DNA elements
Secreted or systemic factors
RNA
Behavior or environment factors that affect the clock
Daily rhythms
Proteins
(Black) Metabolites
(Red) Tissues

Clocks control metabolism



What Does this really mean?

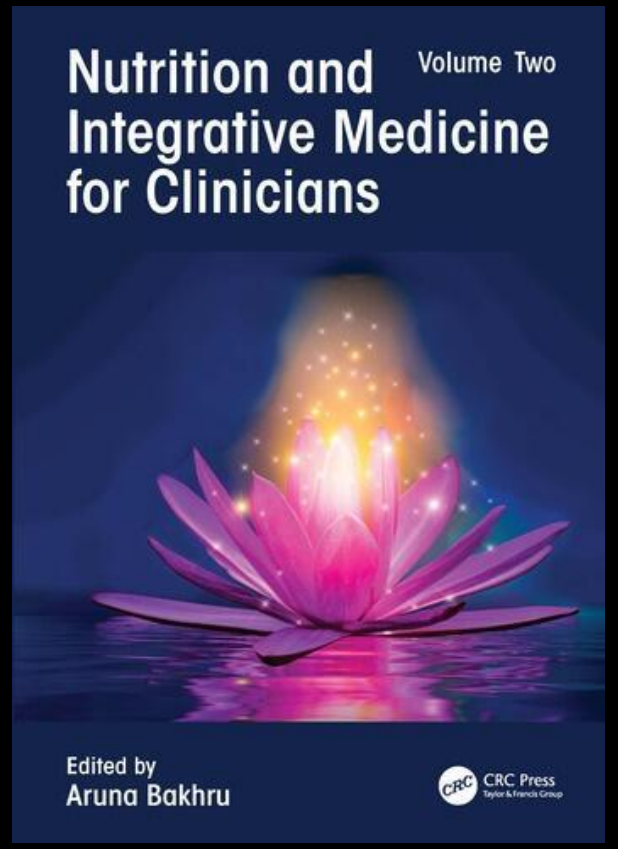
- Every human gene has clock genes in front of it
- 100,000 biochemical reactions per second in the cell
  - How would nature control this?

- Epigenetics is the KEY
- ENVIRONMENTAL SIGNALS RULE
  - Best signals from environment are electromagnetic!!!

Artificial "Blue" Light at Night

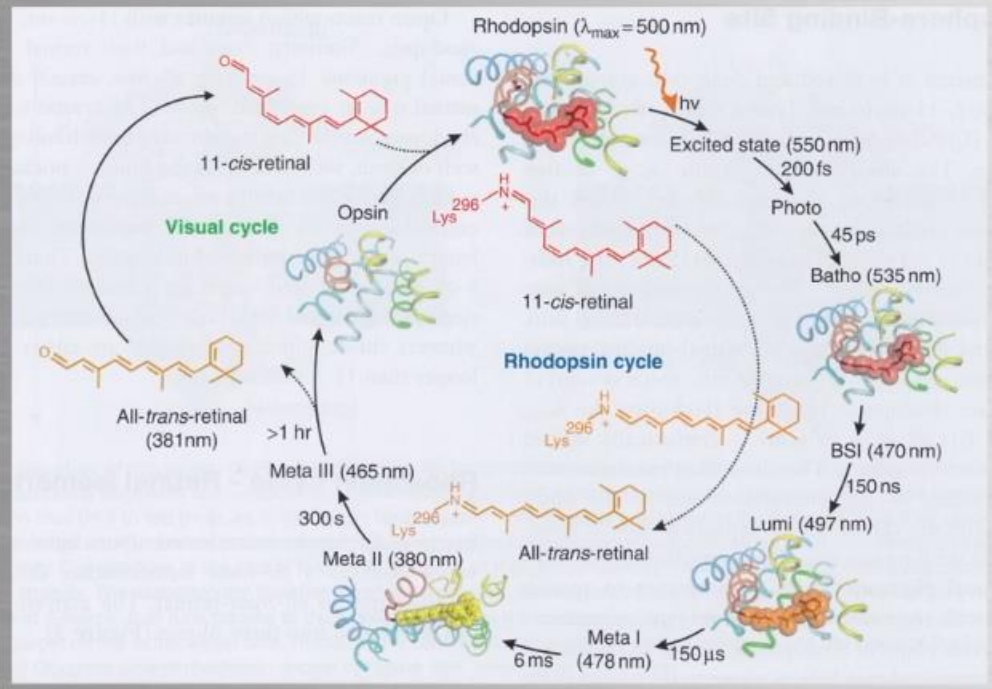
- Mostly BLUE Frequencies In Current Devices And Bulbs
- Associated w/ Depression, Anxiety, Cancers…
- Greatest Suppressor Of Melatonin
- Free Radical Stress On Cells.
- Photo-oxidizes DHA & Other Lipids
- Creates Toxic Vit A Intermediates

THE ULTIMATE MITOCHONDRIAL TOXIN



TWO TYPES OF BLUE LIGHT HAZARD (BLH)

NOELL: Class I BLH
Rhodopsin mediated



HAM: Class II BLH
Lipofuscin mediated

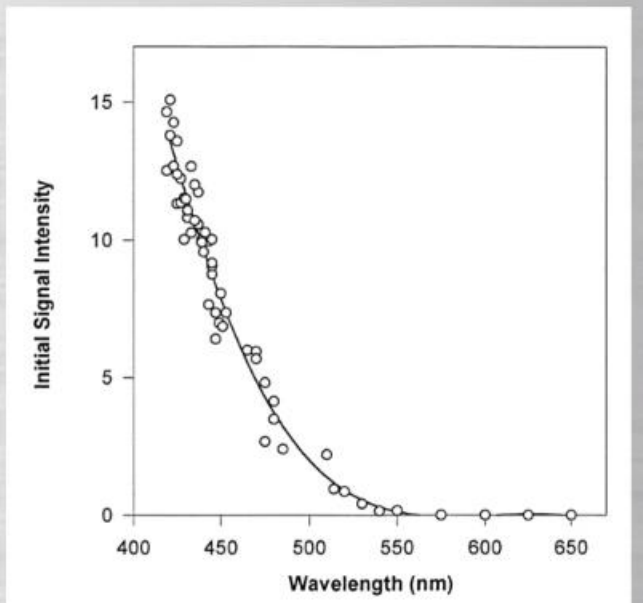
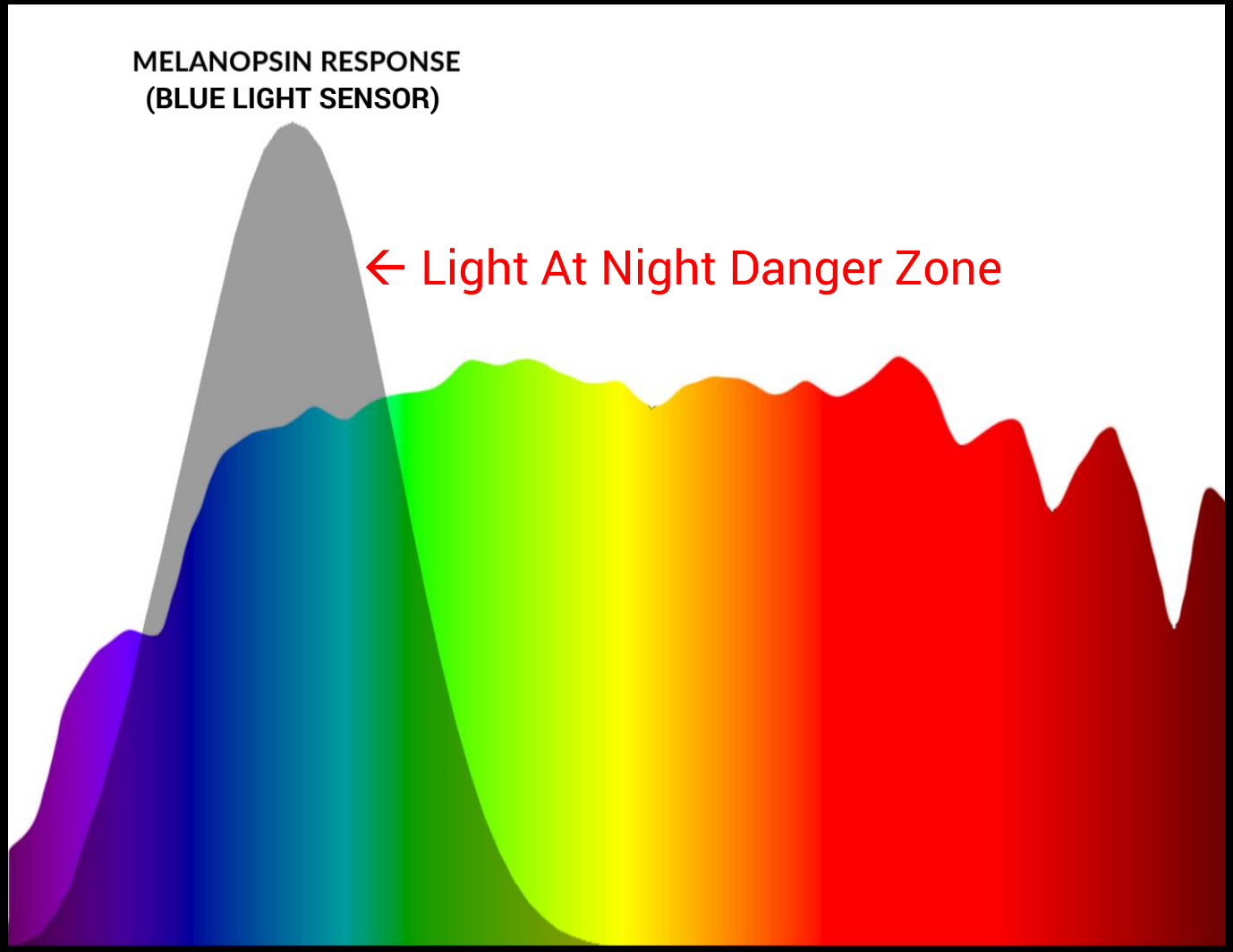


Fig. 3. Action spectrum of singlet oxygen generation by a photoexcited lipofuscin extract in benzene.

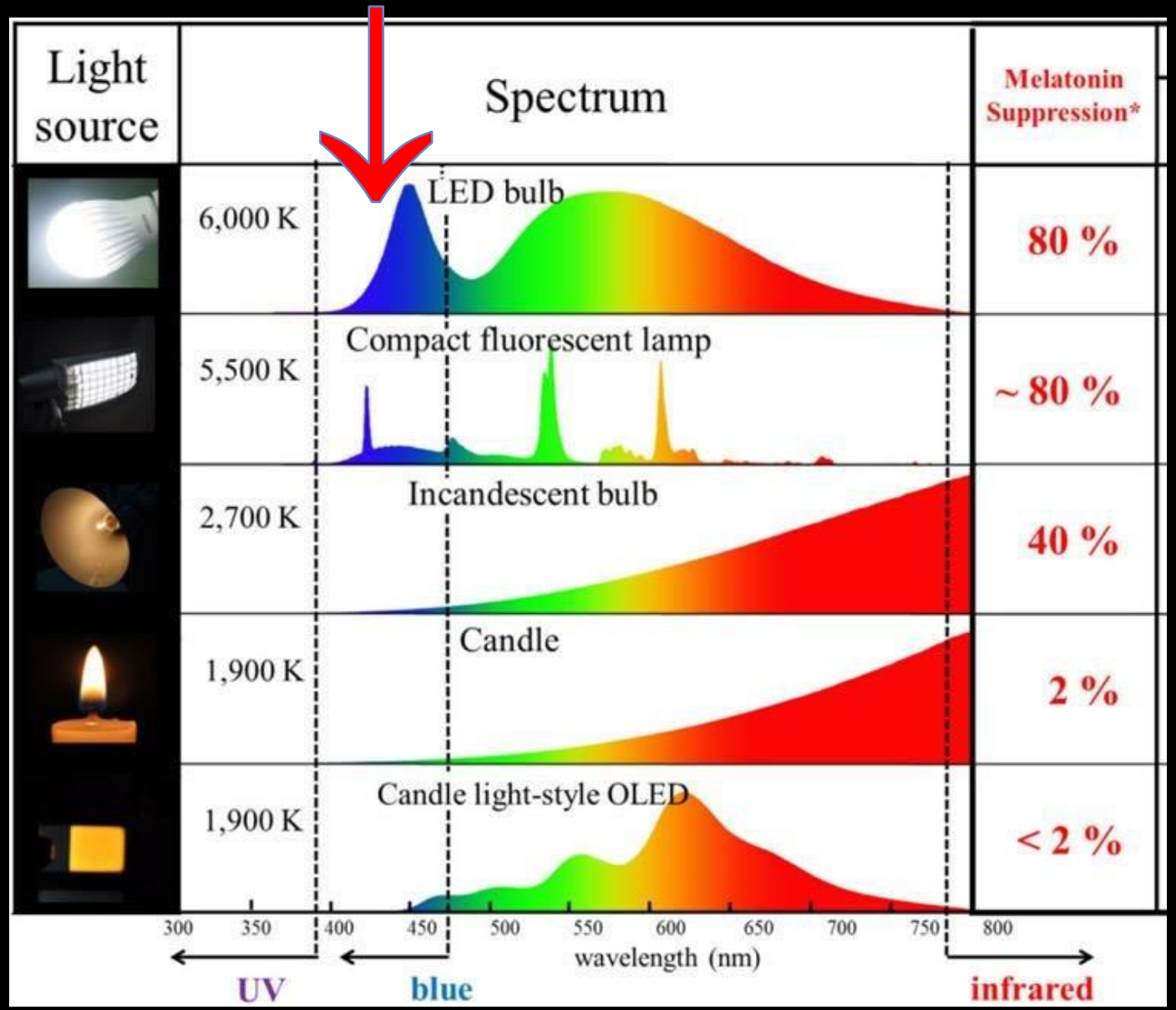
BLUE LIGHT HAZARD CORRECTION FACTORS

nm	B(λ)
400	0.100
405	0.200
410	0.400
415	0.800
420	0.900
425	0.950
430	0.980
435	1.000
440	1.000
445	0.970
450	0.940
455	0.900
460	0.800
465	0.700
470	0.620
475	0.550
480	0.450
485	0.400

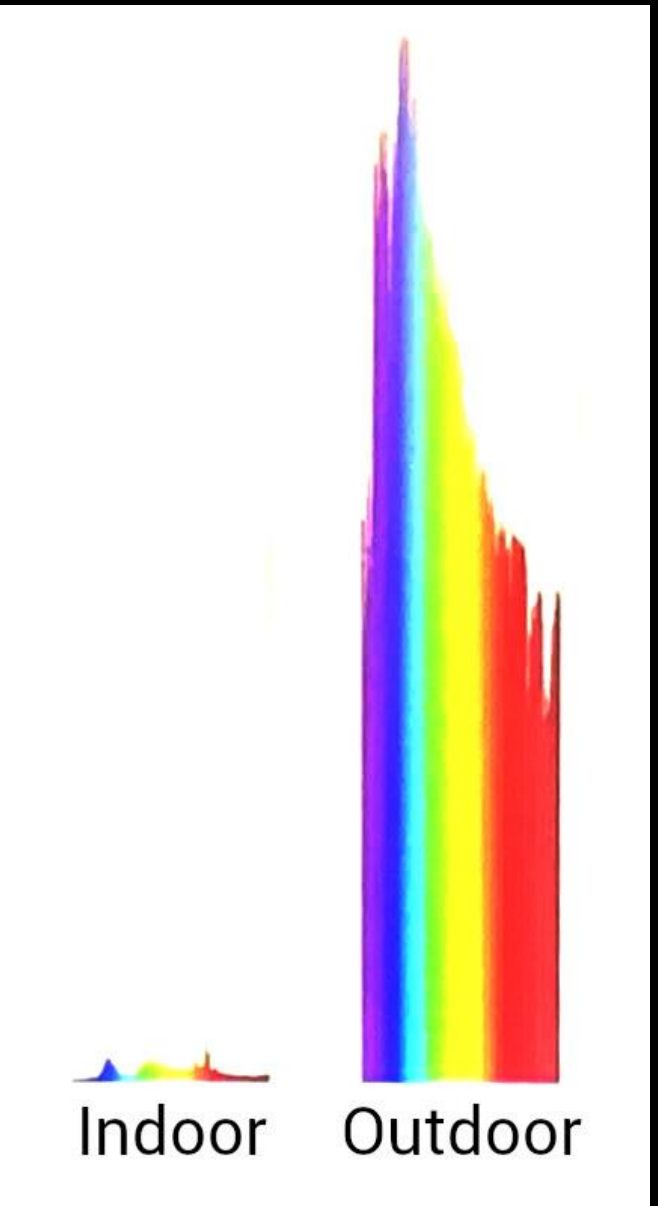
A.L.A.N.'s Target

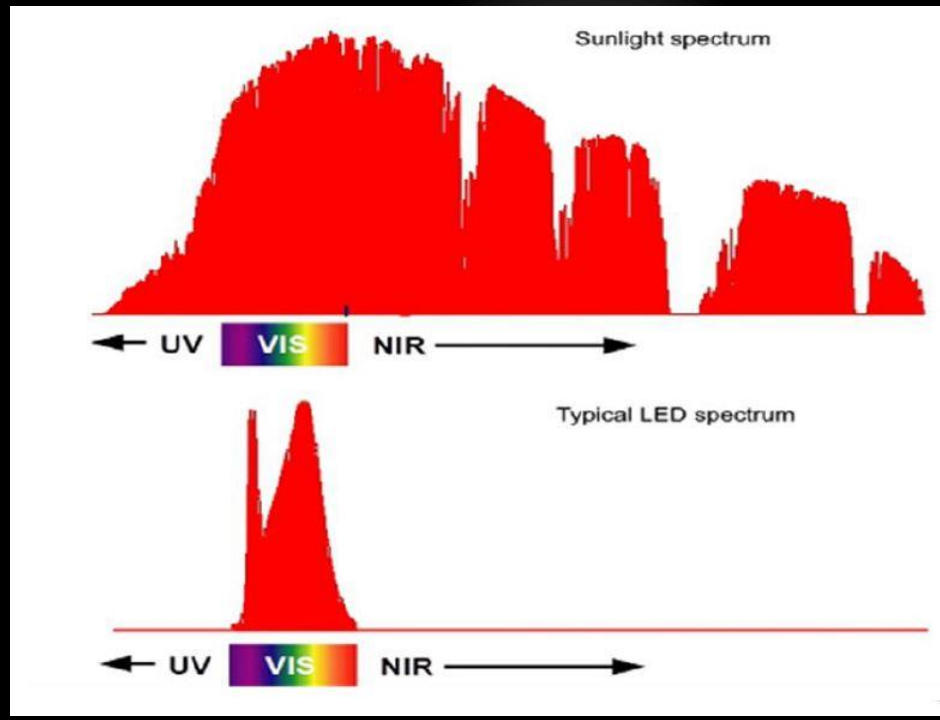


The Hidden Blue Toxin



Light is Light, Right?





Sun's radiant energy 100nm-3,000+nm

PC White LED 380nm-700nm

Journal of Photochemistry and Photobiology B: Biology

Volume 238, January 2023, 112617

Blue light pollution causes retinal damage and degeneration by inducing ferroptosis

Xuan Li [a], Sen Zhu [b c], Fujian Qi [b]

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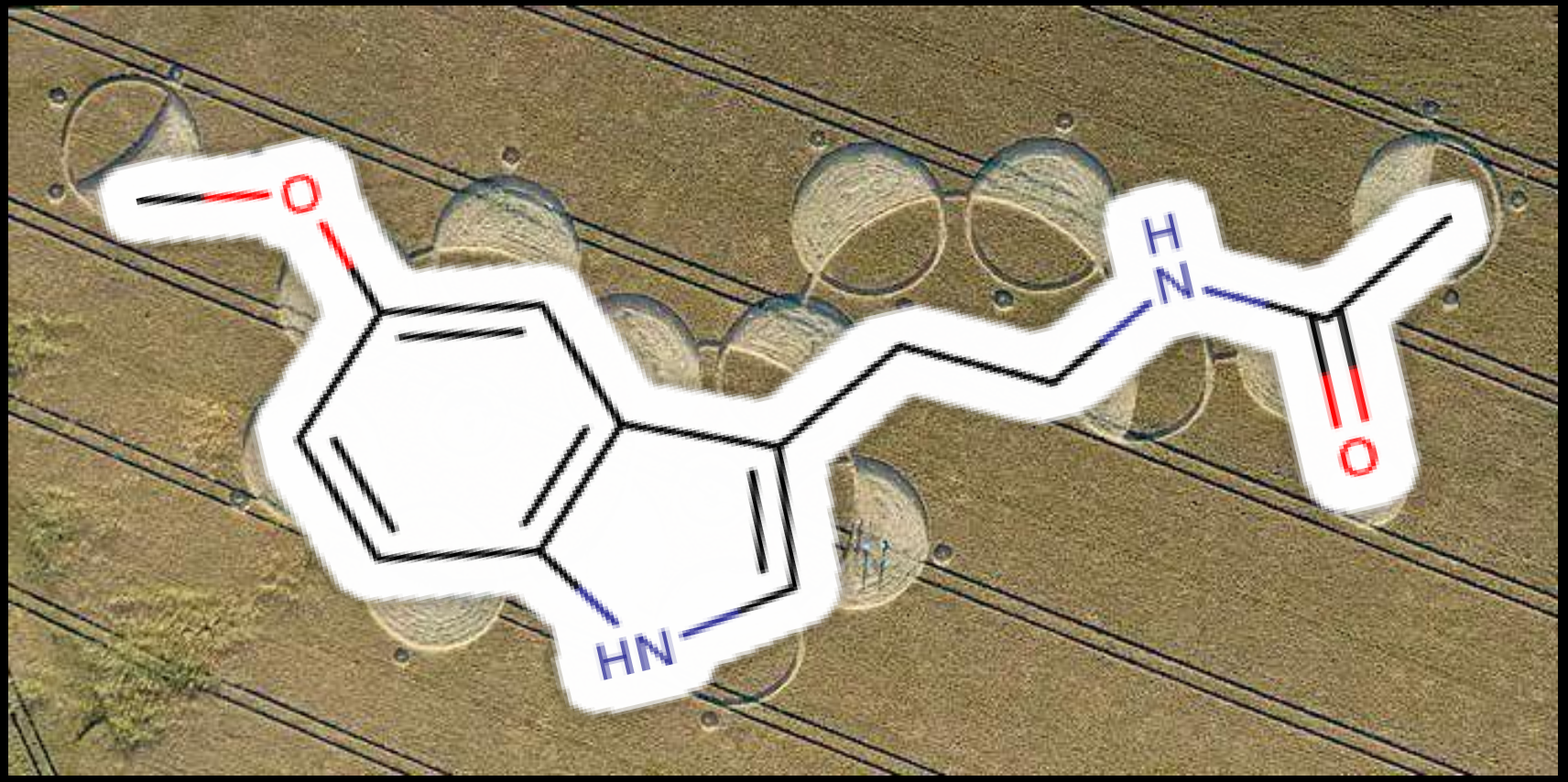
https://doi.org/10.1016/j.jphotobiol.2022.112617

Highlights

- Blue light triggers Fe^{2+} burst and lipid peroxidation in retinal cells.
- Blue light disrupts the GSH-GPX4 antioxidant system.
- Blue light disrupts the FSP1-CoQ_{10}-NADH antioxidant system.
- Blue light induces the ferroptosis in retinal cells.

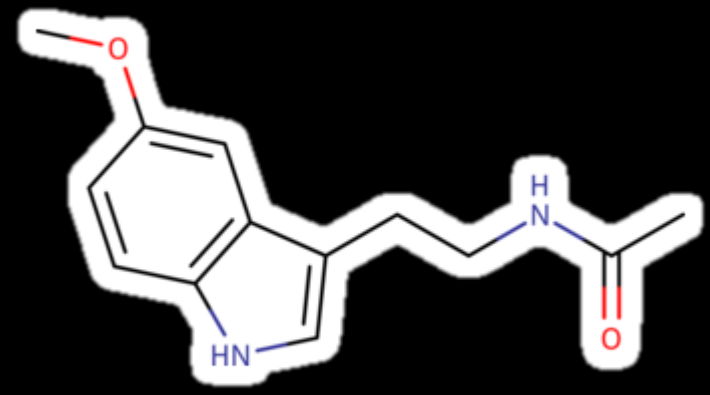
Melatonin's Importance



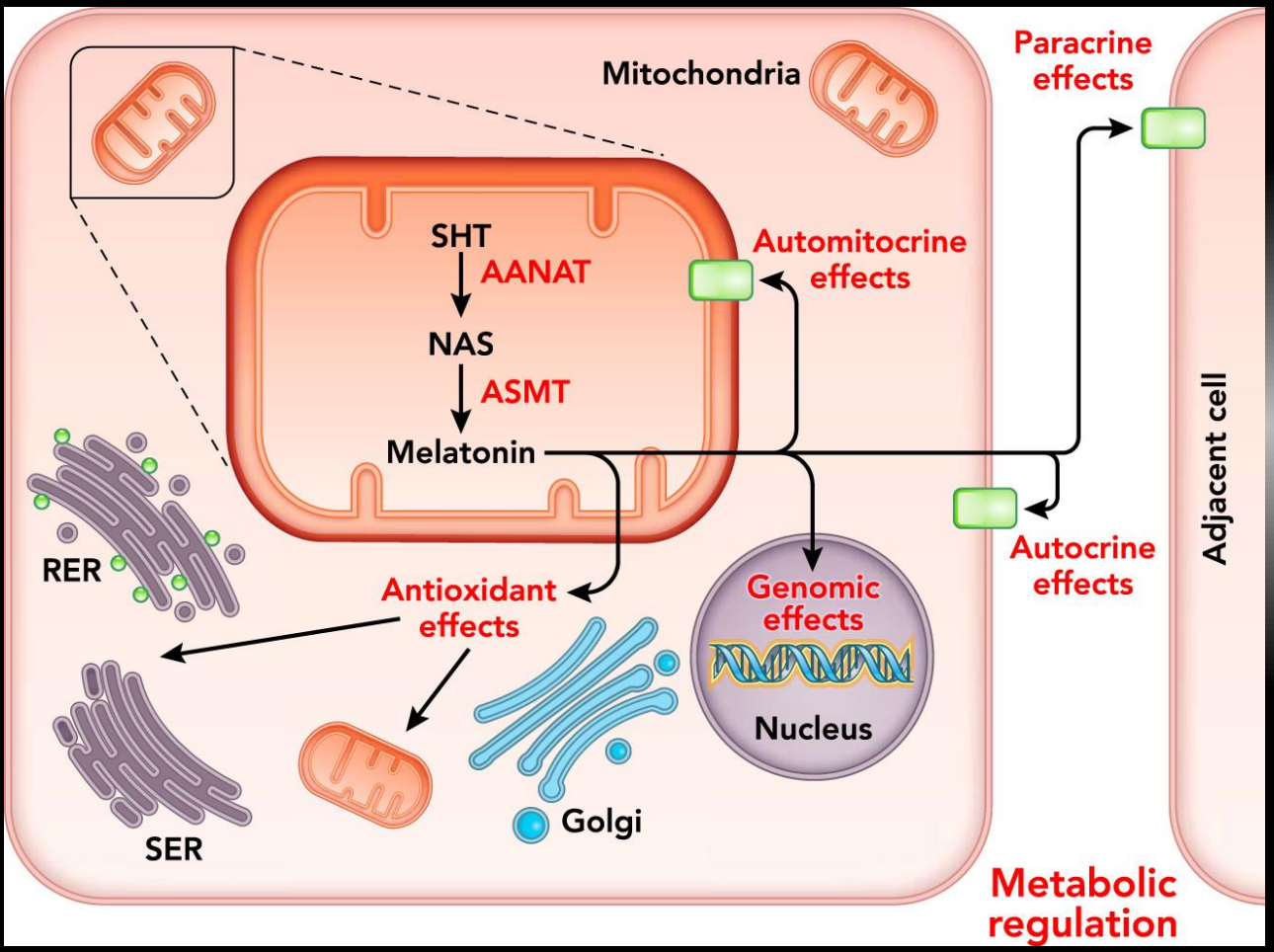
Crop circle at Roundway – 2011. Appeared 12 hours after Norway Massacre

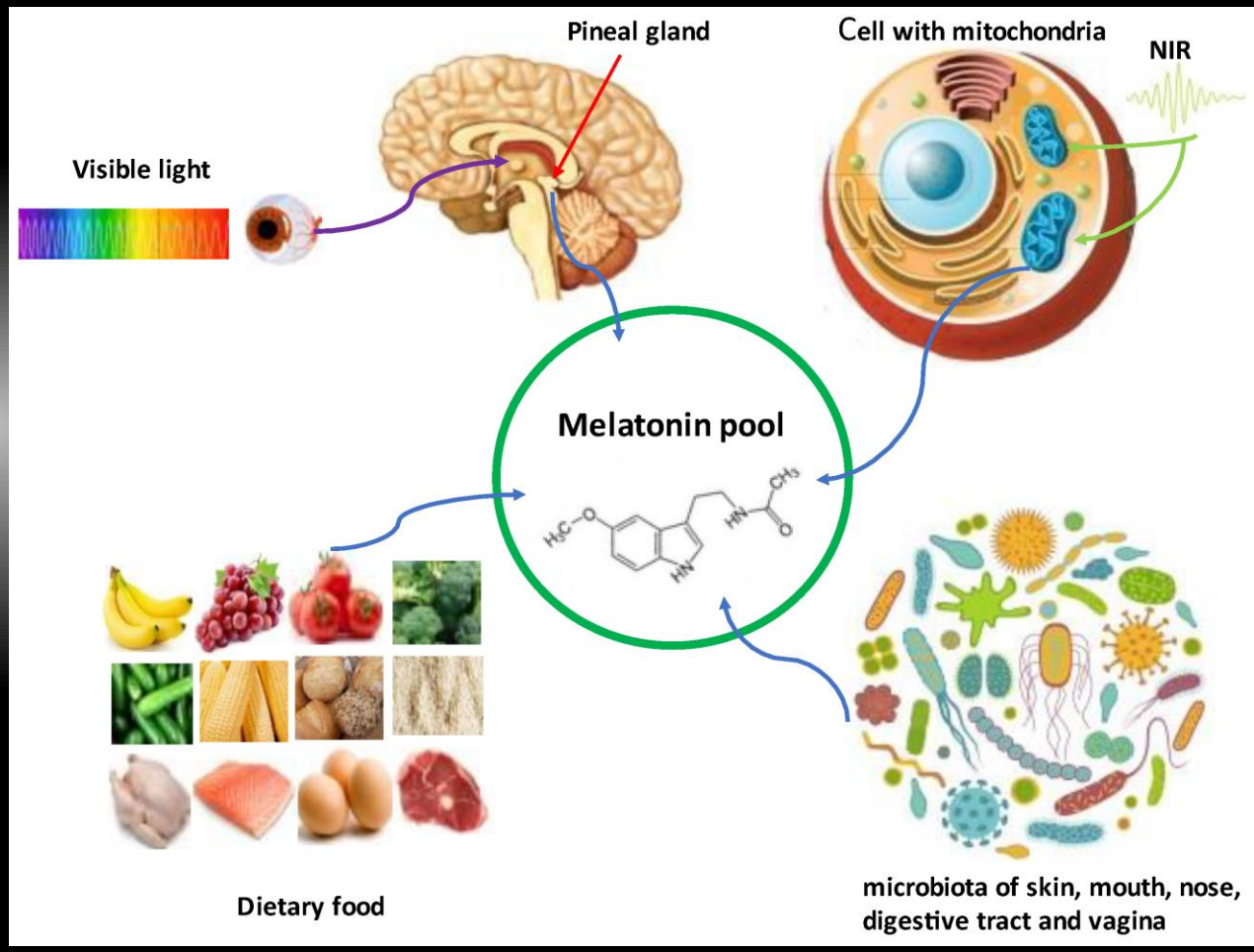
Melatonin

- Known As Hormone Of Sleep
- Very Powerful Antioxidant Of The Body
- Affects Cortisol Levels
- Lowers Estrogen
- Known To Be Anti-cancer
- Controls Regenerative Processes
- Suppressed Most By ARTIFICAL LIGHT AT NIGHT



Mitochondria Makes Melatonin

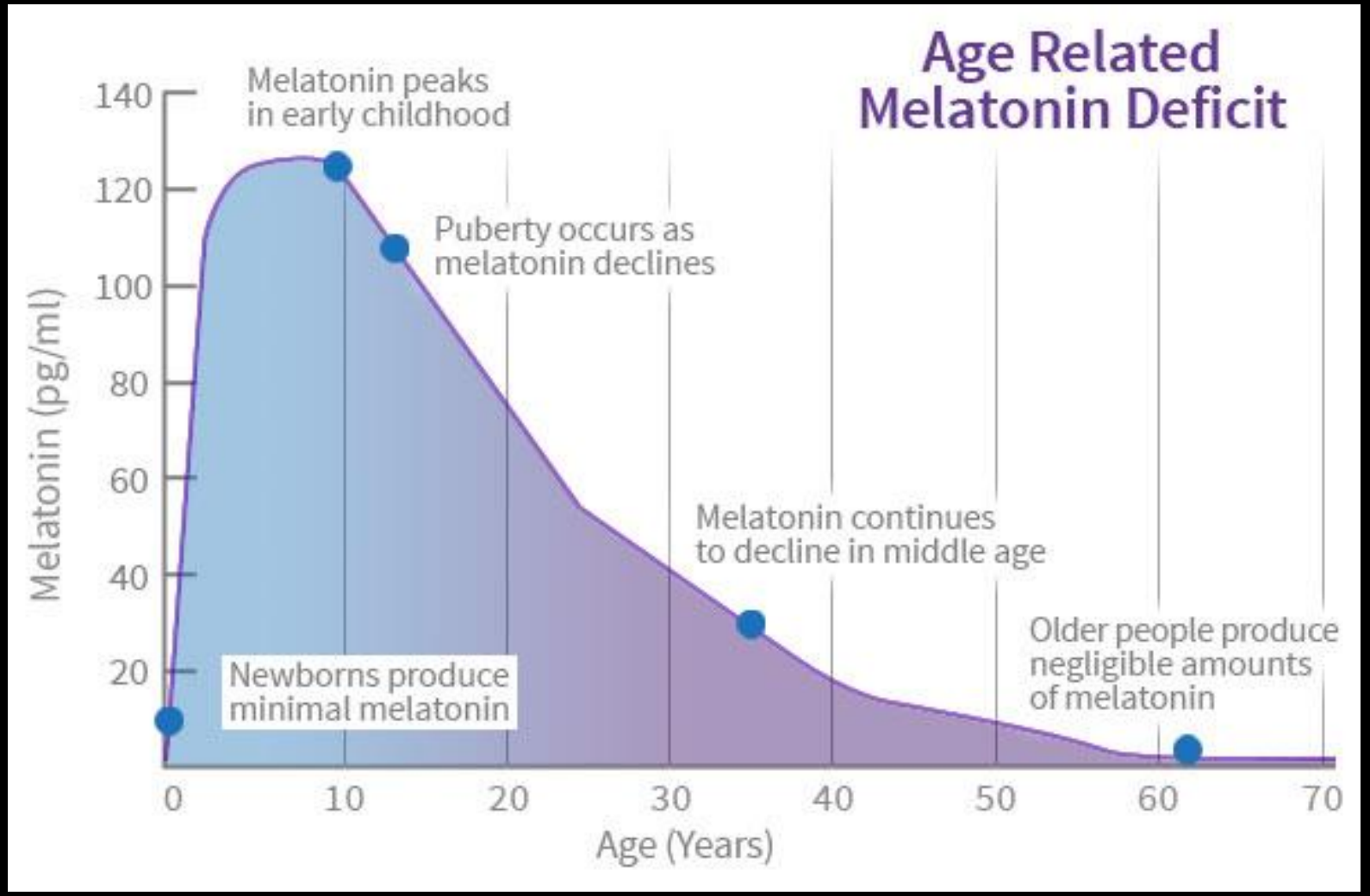




https://doi.org/10.1152/physiol.00034.2019

https://www.mdpi.com/2079-7737/12/1/89

Human Aging


Age Related
Melatonin Deficit
Melatonin peaks
in early childhood
Puberty occurs as
melatonin declines
Melatonin continues
to decline in middle age
Older people produce
negligible amounts
of melatonin
Newborns produce
minimal melatonin
Melatonin (pg/ml)
140
120
100
80
60
40
20
0
10
20
30
40
50
60
70
Age (Years)

Melanopsin is in eye, fat, and skin

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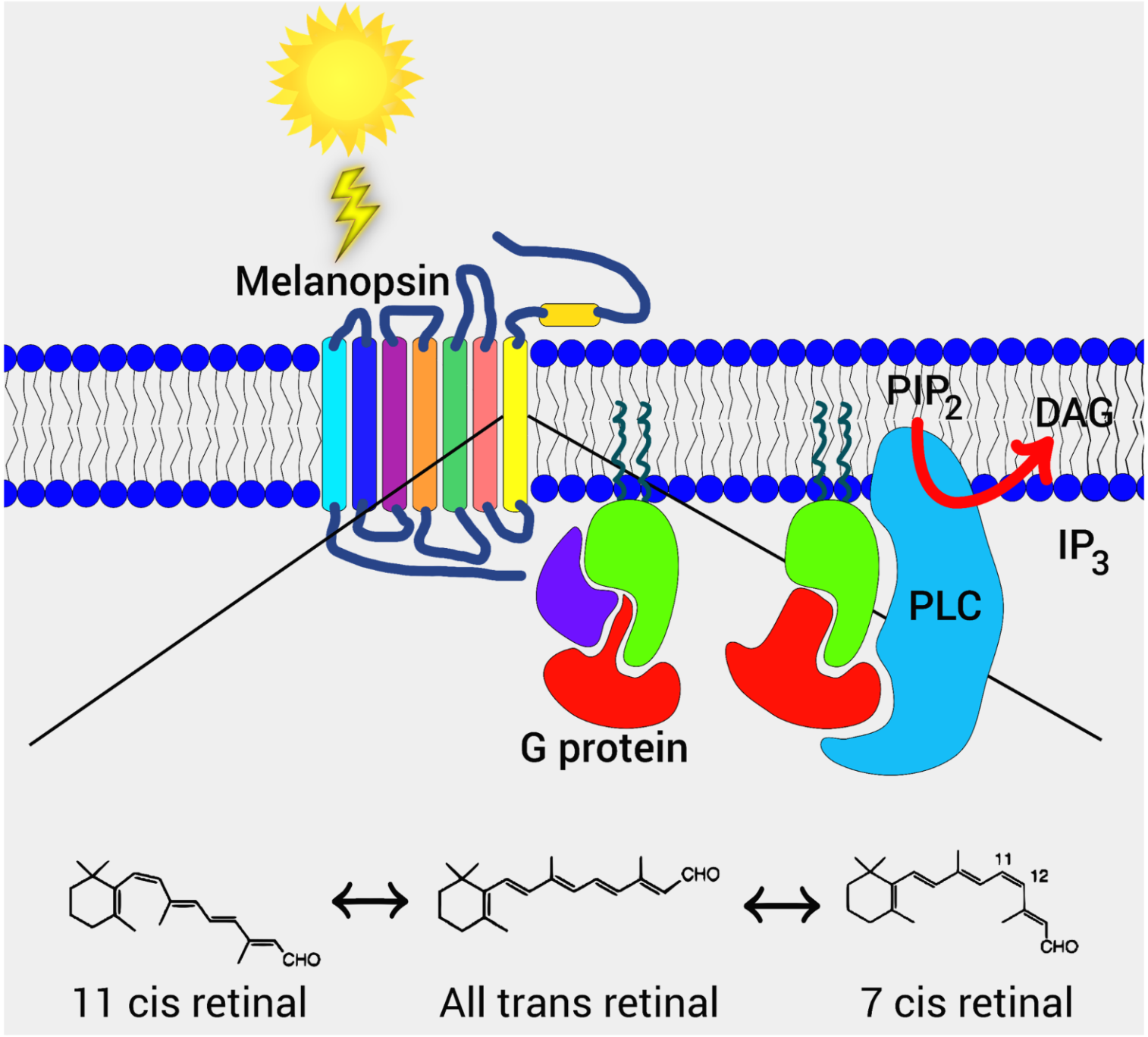
Subcutaneous white adipocytes express a light sensitive signaling pathway mediated via a melanopsin/TRPC channel axis

Katarina Ondrusova[1], Mohammad Fatehi[1], Amy Barr[1], Zofia Czarnecka[1], Wentong Long[1], Kunimasa Suzuki[1], Scott Campbell[1], Koenraad Philippaert[1], Matthew Hubert[1], Edward Tredget[2], Peter Kwan[2], Nicolas Touret[3], Martin Wabitsch[4], Kevin Y. Lee[5] & Peter E. Light[1]

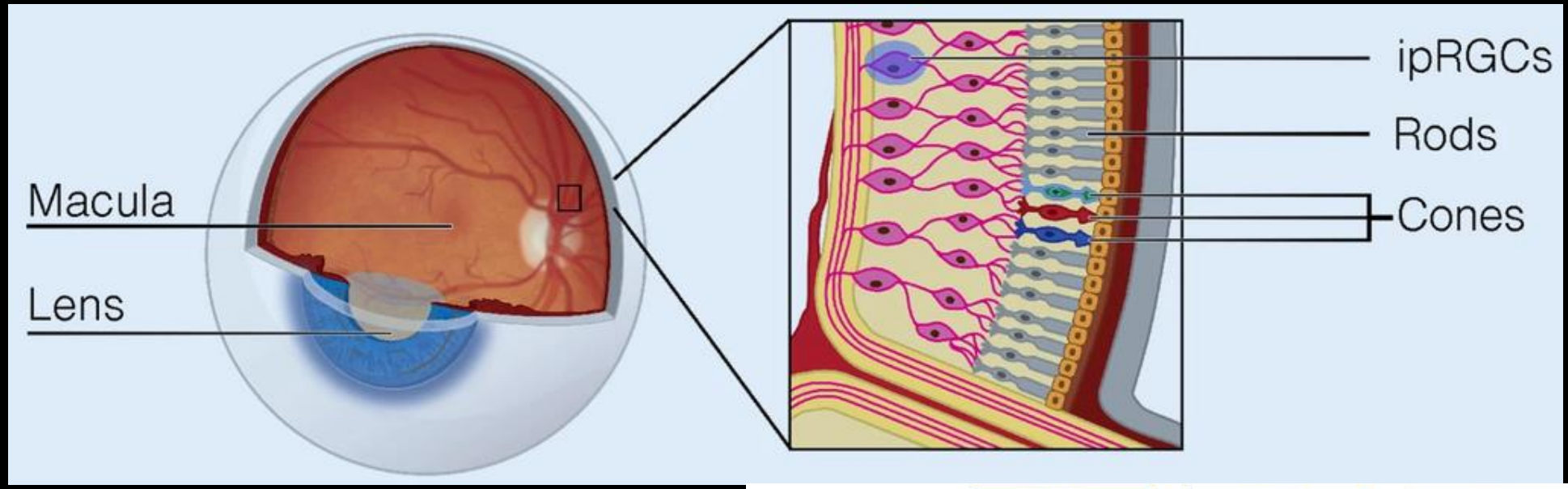
Subcutaneous white adipose tissue (scWAT) is the major fat depot in humans and is a central player in regulating whole body metabolism. Skin exposure to UV wavelengths from sunlight is required for Vitamin D synthesis and pigmentation, although it is plausible that longer visible wavelengths that penetrate the skin may regulate scWAT function. In this regard, we discovered a novel blue light-sensitive current in human scWAT that is mediated by melanopsin coupled to transient receptor potential canonical cation channels. This pathway is activated at physiological intensities of light that penetrate the skin on a sunny day. Daily exposure of differentiated adipocytes to blue light resulted in decreased lipid droplet size, increased basal lipolytic rate and alterations in adiponectin and leptin secretion. Our results suggest that scWAT function may be directly under the influence of ambient sunlight exposure and may have important implications for our current understanding of adipocyte biology. (150 words)

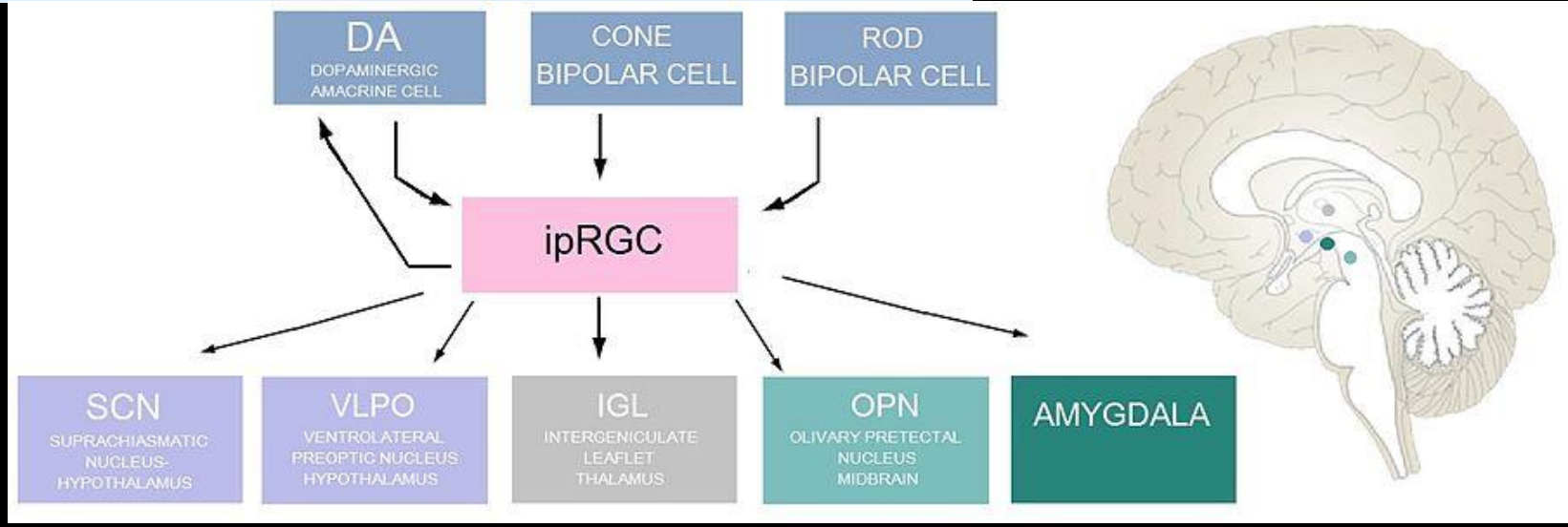

Melanopsin
PIP2
DAG
IP3
PLC
G protein
CHO
CHO
11
12
CHO
11 cis retinal
All trans retinal
7 cis retinal

Melanopsin

- Light sensing photopigment, but not for vision
  - Blue light photo-receptor (435-465 nm target) in our eyes responsible for relaying sunlight to the SCN to entrain the central pacemaker via the central retinal pathways
  - Not in rods or cones, but in ganglion cells
- Melanopsin is loosely bound to Vitamin A
  - MANMADE blue light exposure of the skin causes circadian disruption
  - Vitamin A yoked and works together with Vitamin D
  - When Vitamin A drops in the plasma from skin irradiation with the blue light it DIRECTLY limits how much Vitamin D3 can be made in the skin.

ipRGC


Macula
Lens
ipRGCs
Rods
Cones

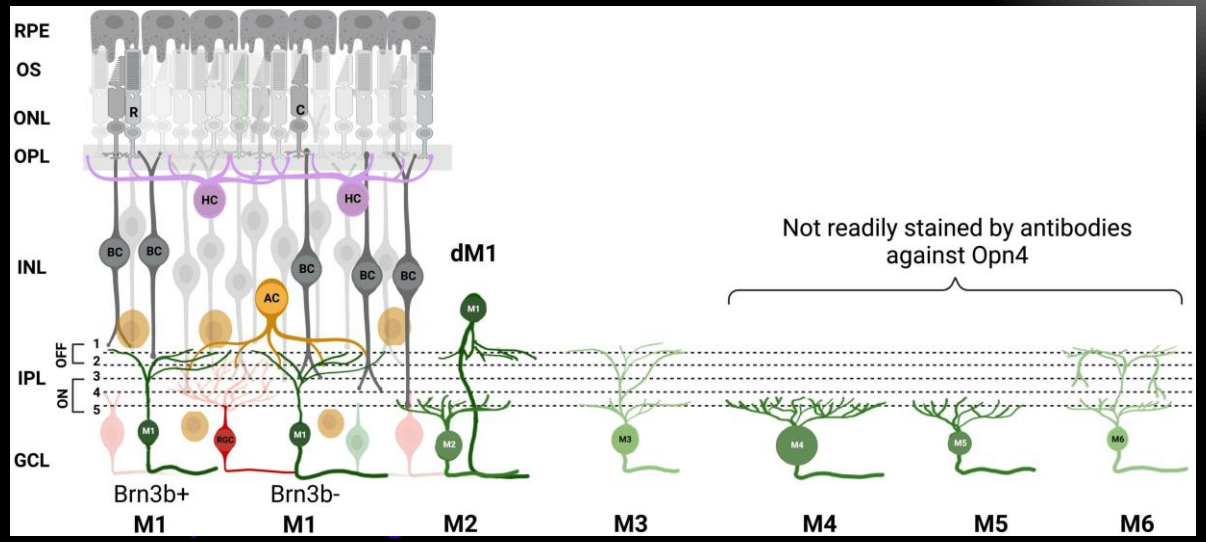

DA
DOPAMINERGIC AMACRINE CELL
CONE BIPOLAR CELL
ROD BIPOLAR CELL
ipRGC
SCN
SUPRACHIASMATIC NUCLEUS-HYPOTHALAMUS
VLPO
VENTROLATERAL PREOPTIC NUCLEUS HYPOTHALAMUS
IGL
INTERGENICULATE LEAFLET THALAMUS
OPN
OLIVARY PRETECTAL NUCLEUS MIDBRAIN
AMYGDALA

Article | Open access | Published: 17 March 2023

A melanopsin ganglion cell subtype forms a dorsal retinal mosaic projecting to the supraoptic nucleus

Michael H. Berry, Michael Moldavan, Tavita Garrett, Marc Meadows, Olga Cravetchi, Elizabeth White, Joseph Leffler, Henrique von Gersdorff, Kevin M. Wright, Charles N. Allen & Benjamin Sivyer

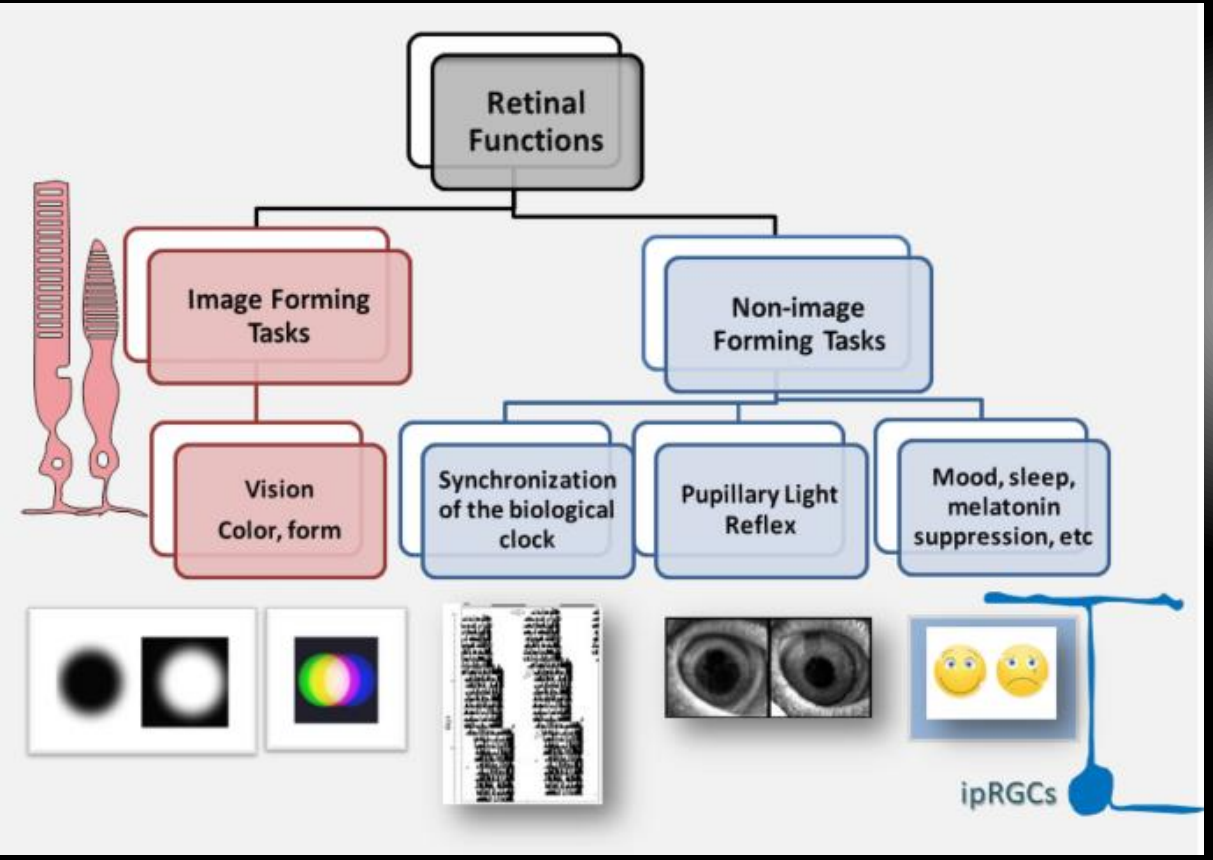
Nature Communications **14**, Article number: 1492 (2023) | Cite this article



Introduction

In addition to the rod and cone photoreceptors that are used for image-forming vision, the mammalian retina contains intrinsically photosensitive retinal ganglion cells (ipRGCs) that primarily drive non-image-forming behaviors[1,2]. ipRGCs express their own photopigment, melanopsin[3], and project to a diverse array of central brain regions[4,5,6], influencing many homeostatic functions, including circadian entrainment, pupil constriction, body temperature, sleep, and mood[7,8,9,10,11]. There are six main types of ipRGCs (M1–M6), which are categorized according to their dendritic morphology, melanopsin expression, gene expression, and central projection locations[6,12]. The most studied of these, the M1 ipRGCs, have dendrites that primarily occupy sublamina-a of the inner plexiform layer (IPL). They form the primary projections to the suprachiasmatic nucleus (SCN), which is the master circadian clock[4,7,13,14,15], and the shell of the olivary pretectal nucleus (OPN), which serves as the primary site of light-dependent pupillary constriction[8,16,17]. They also project to a number of lateral hypothalamic brain regions, such as the supraoptic nucleus (SON), ventral lateral preoptic area (VLPO), and medial amygdaloid nucleus, though the functional role of these projections remains unclear[4,6,15].

Non Visual Photoreceptors



Opsins in the human eye, brain, and skin [edit]

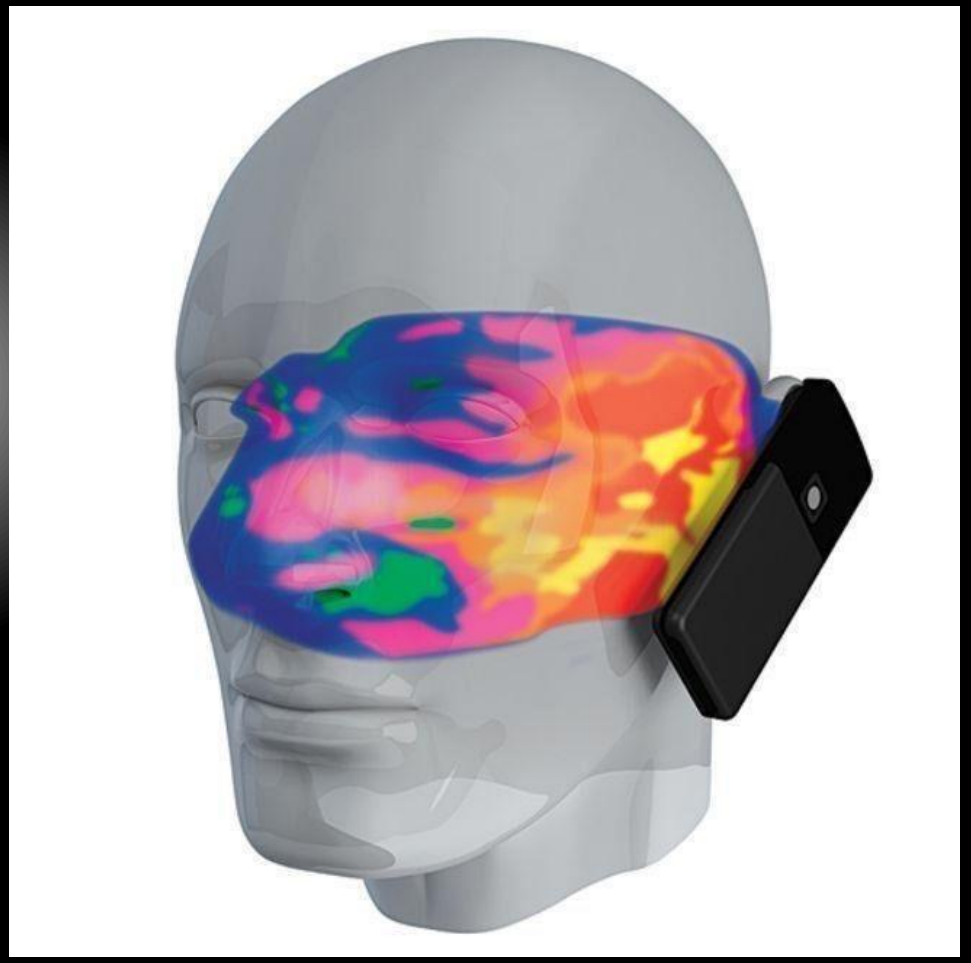
Abbr.	Name	λ_{max}	Color	Eye	Brain	Skin	Chromosomal location[44]
OPN1LW	L-cone (red-cone) opsin	557 nm	Yellow	Cone	—	—	Xq28[44]
OPN1MW	M-cone (green-cone) opsin	527 nm	Green	Cone	—	—	Xq28[44]
OPN1SW	S-cone (blue-cone) opsin	420 nm	Violet	Cone	—	Melanocytes, keratinocytes[51]	7q32.1[44]
OPN2 (RHO)	Rhodopsin	505 nm	Blue–green	Rod	—	Melanocytes, keratinocytes[51]	3q22.1[44]
OPN3	Encephalopsin, panopsin	S-M	Blue–green	Rod, cone, OPL, IPL, GCL[52]	Cerebral cortex, cerebellum, striatum, thalamus, hypothalamus[53][54]	Melanocytes, keratinocytes[51]	1q43[44]
OPN4	Melanopsin	480 nm[55]	Sky blue	ipRGC[55]	—	—	10q23.2[44]
OPN5	Neuropsin	380 nm[56]	Ultraviolet[56]	Neural retina, RPE[57]	Anterior hypothalamus[58]	Melanocytes, keratinocytes[51]	6p12.3[44]
RRH	Peropsin			RPE cells - microvilli	—	—	4q25[44]
RGR	Retinal G protein coupled receptor			RPE cells	—	—	10q23.1[44]

RPE, retinal pigment epithelium; ipRGC, intrinsically photosensitive retinal ganglion cells; OPL, outer plexiform layer; IPL, inner plexiform layer; GCL, ganglion cell layer

https://link.springer.com/article/10.1007/s10571-020-00997-x

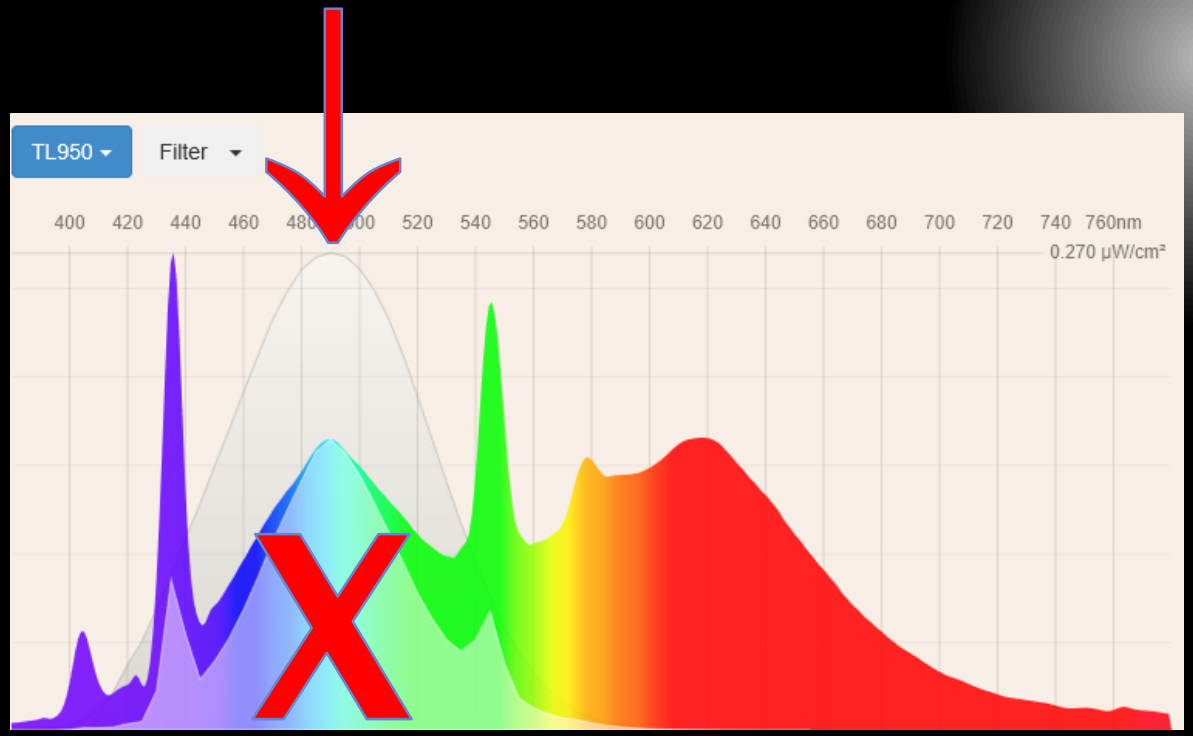
What ARE your signals?

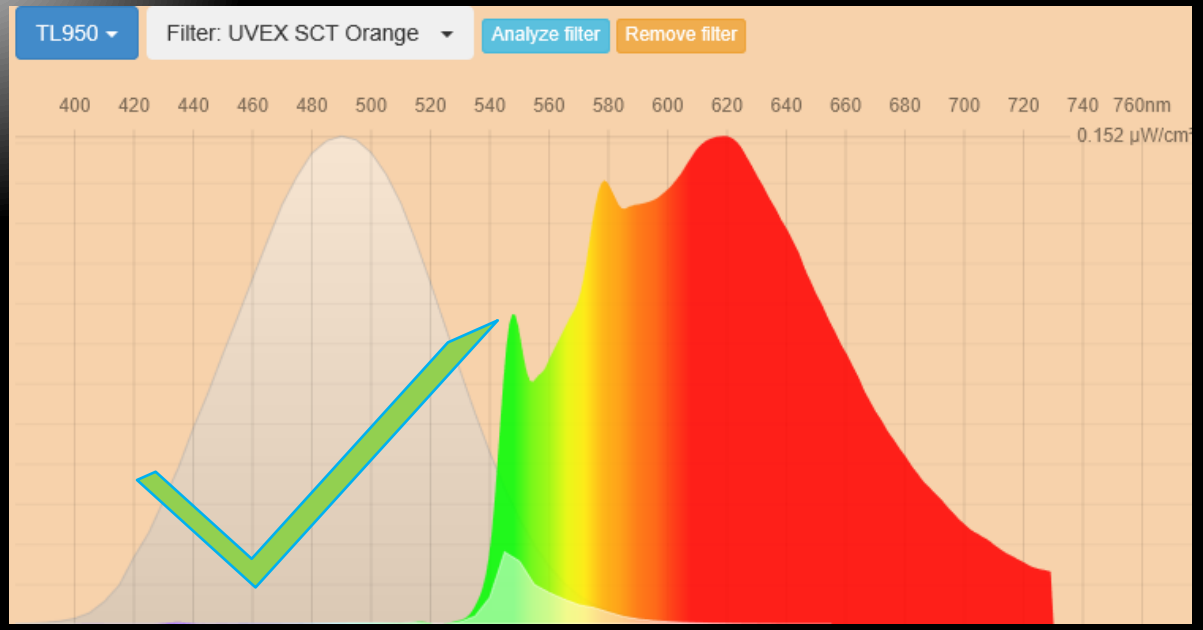
Toxins You CAN'T Touch



Artificial EMF Protection

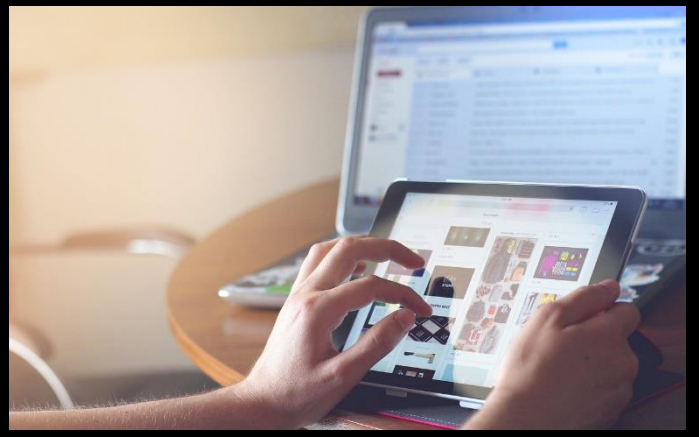
Blue Blockers Are A MUST!





The ONLY Modular BlueBlockers

Outside

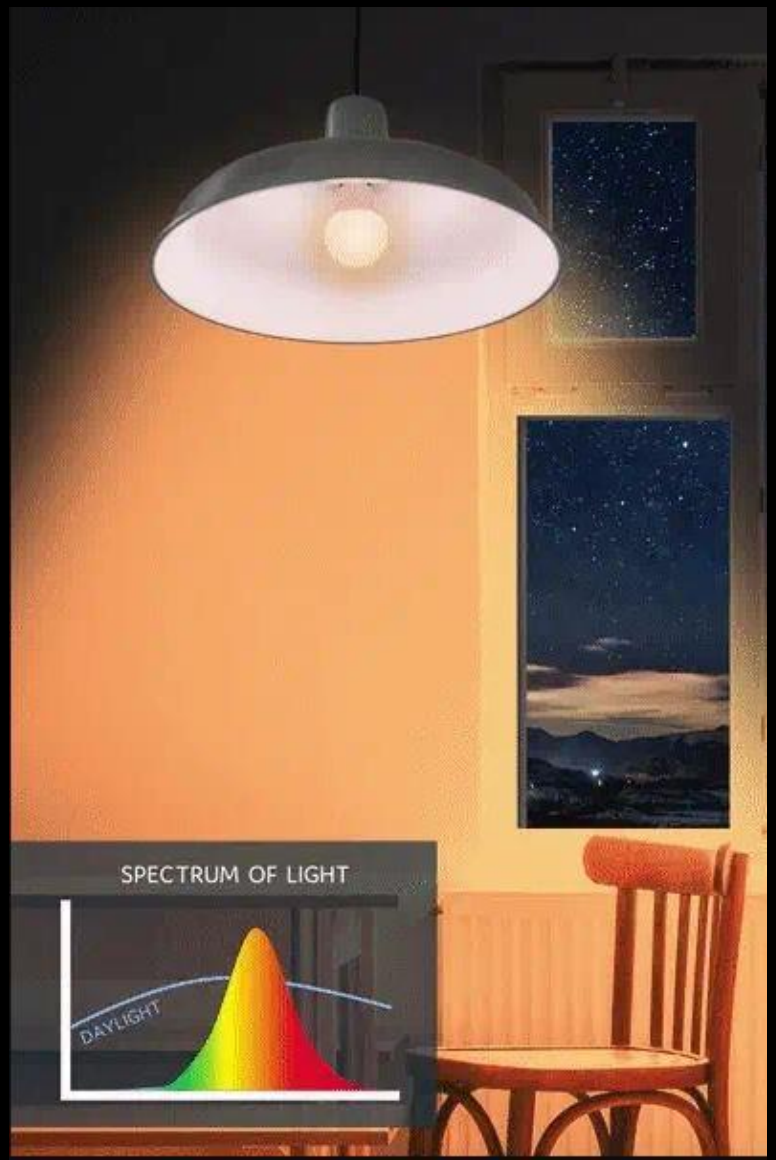


Inside

VIVARAYS

Night-time

Flip the Switch



Sleep = Nightly Regeneration

Nightly Regeneration

Review > Ageing Res Rev. 2018 Aug;45:33-52. doi: 10.1016/j.arr.2018.04.003. Epub 2018 Apr 6.

The multiple functions of melatonin in regenerative medicine

Maryam Majidinia [1], Russel J Reiter [2], Seyed Kazem Shakouri [3], Iraj Mohebbi [4], Mojgan Rastegar [5], Mojtaba Kaviani [6], Saber Ghazizadeh Darband [7], Rana Jahanban-Esfahlan [8], Seyed Mohammad Nabavi [9], Bahman Yousefi [10]

Affiliations + expand

PMID: 29630951 DOI: 10.1016/j.arr.2018.04.003

Abstract

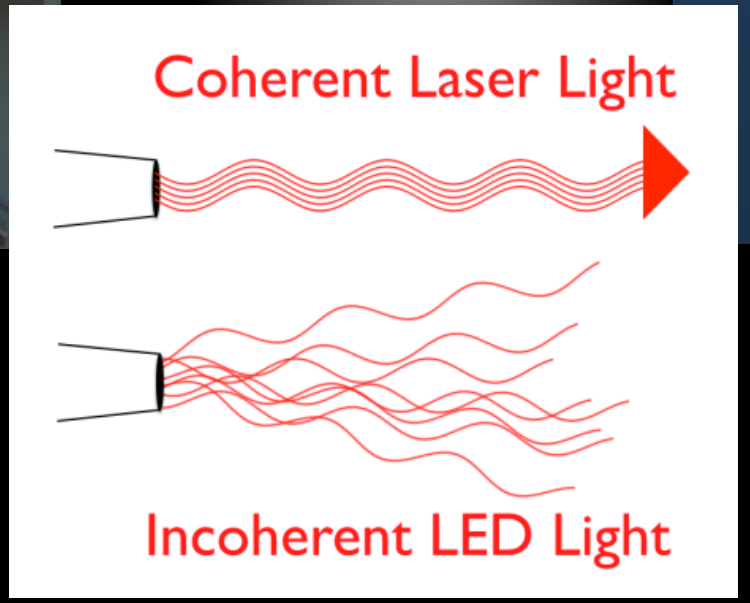
Melatonin research has been experiencing hyper growth in the last two decades; this relates to its numerous physiological functions including anti-inflammation, oncostasis, circadian and endocrine rhythm regulation, and its potent antioxidant activity. Recently, a large number of studies have focused on the role of melatonin in the regeneration of cells or tissues after their partial loss. In this review, we discuss the recent findings on the molecular involvement of melatonin in the regeneration of various tissues including the nervous system, liver, bone, kidney, bladder, skin, and muscle, among others.

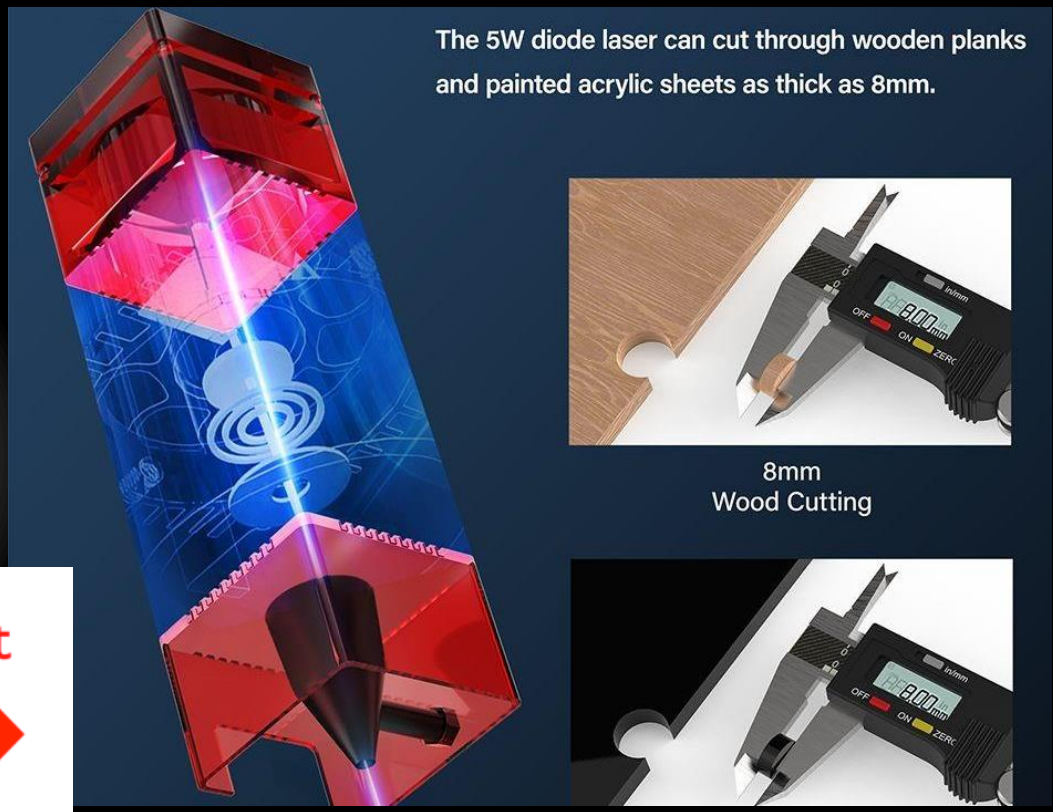
Keywords: Bone regeneration; Circadian rhythm; Kidney regeneration; Liver regeneration; Muscle regeneration; Neuroregeneration; Stem cell; Tissue engineering.

Biophysics of Regeneration

5W Light

Energy

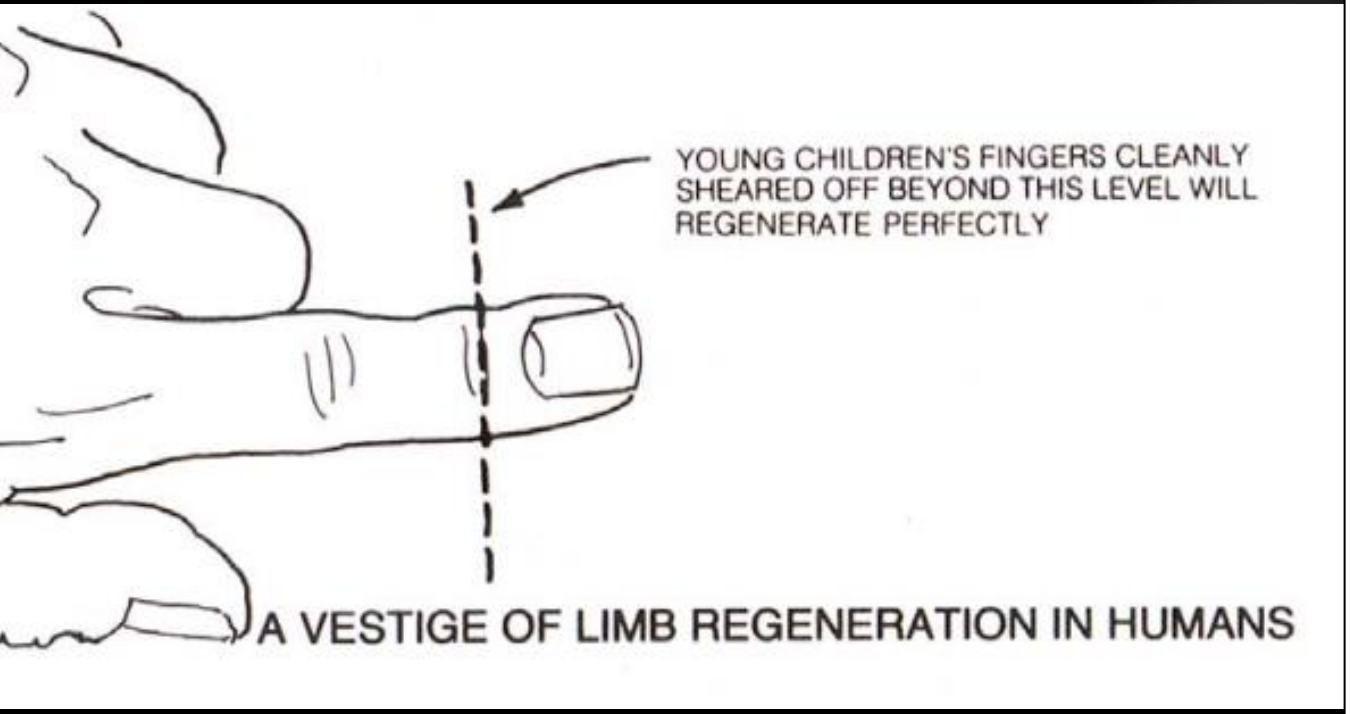




5W Laser

Information

Biophysics of Regeneration



ELSEVIER

Journal of Pediatric Surgery
Volume 9, Issue 6, December 1974, Pages 853-858

Trapped fingers and amputated finger tips in children

Cynthia M. Illingworth [1]

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https://doi.org/10.1016/S0022-3468(74)80220-4

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Summary

We have developed a simple, relatively painless and very effective method of treating trapped fingers in small children.

When a finger tip of a small child has been amputated, there is a remarkable capacity for the tip to regenerate if given a chance and if the injury is treated by a nonintervention technique.

Regenerative Pathways

- Apoptosis:
  Programmed Cell Death
  - Abnormal phenotypes cleared, errors in development corrected
  - **Melatonin**
  - Red **PBM** ↓
  - Blue Light ↑
  - **Circadian** gene *Clock*

- Autophagy:
  Process To Remove Dysfunctional Components
  - Closely linked to cell growth, development and diseases
  - **Melatonin**
  - **PBM** (Pulsed?)
  - Vitamin D
  - **Circadian** rhythm regulates autophagy and is regulated by autophagy

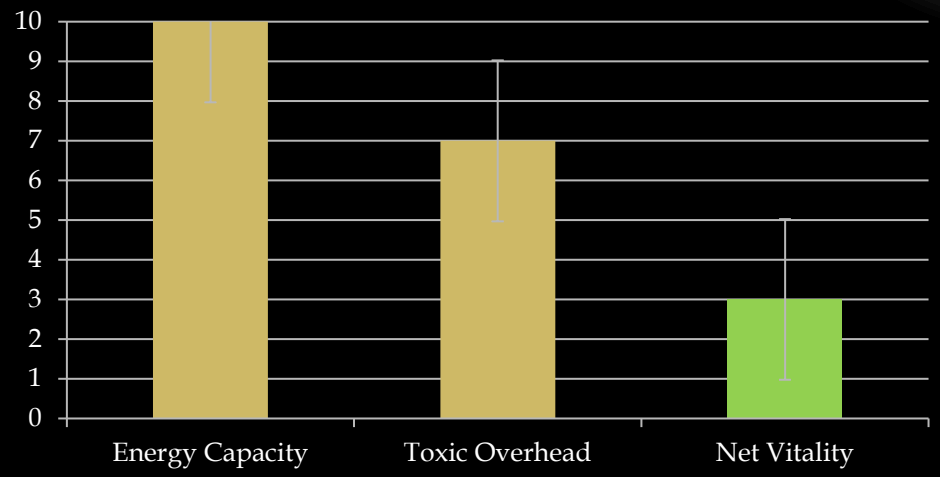
Energy Accounting for Health

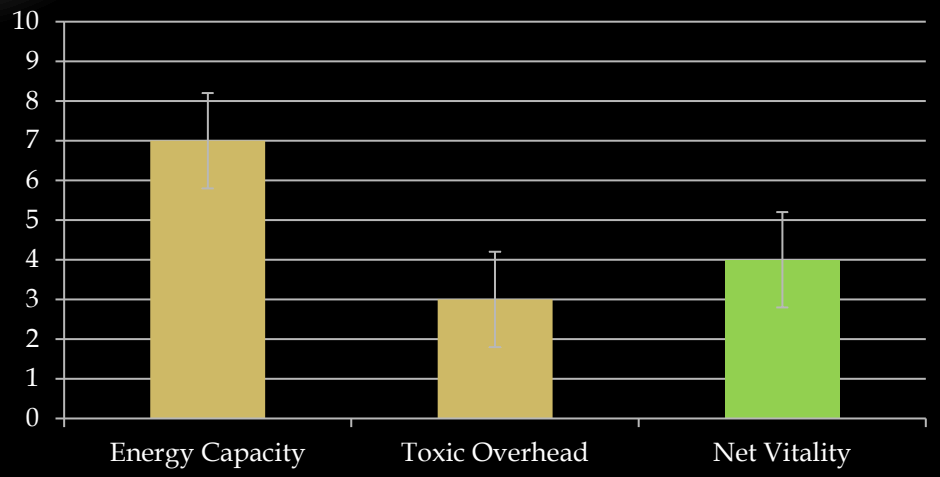
Energy Capacity – Toxicity = Net Vitality

Preference?

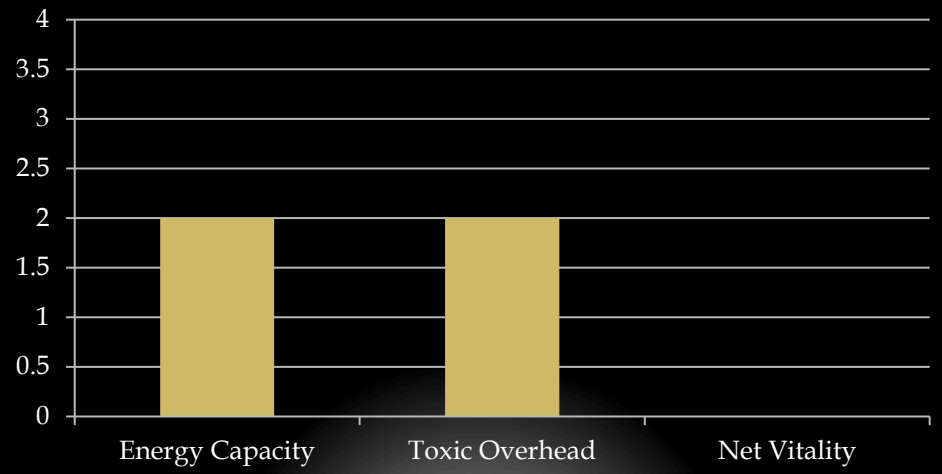
34yo

35 yo



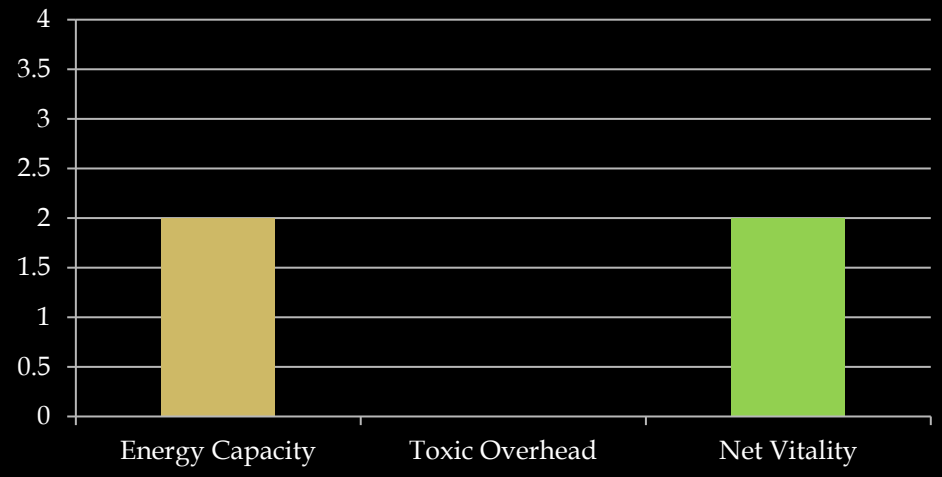


Chronic Infection

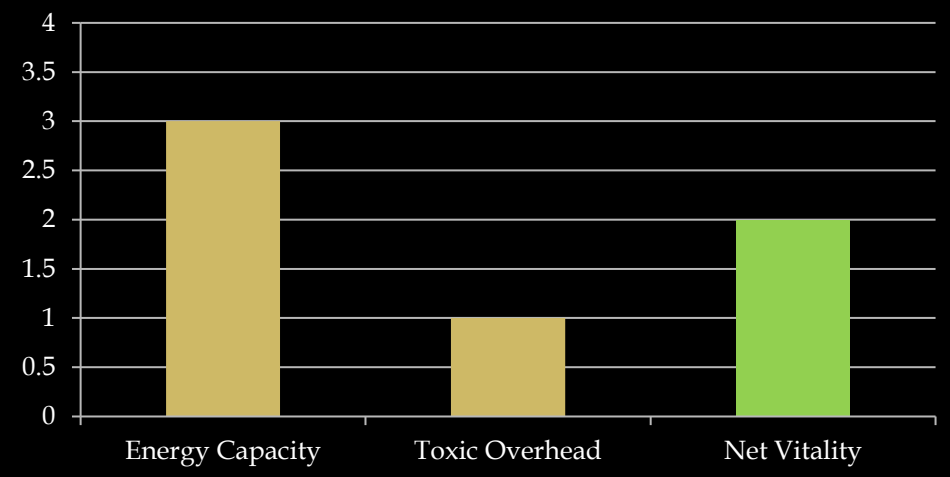


Preference?

Functional Medicine



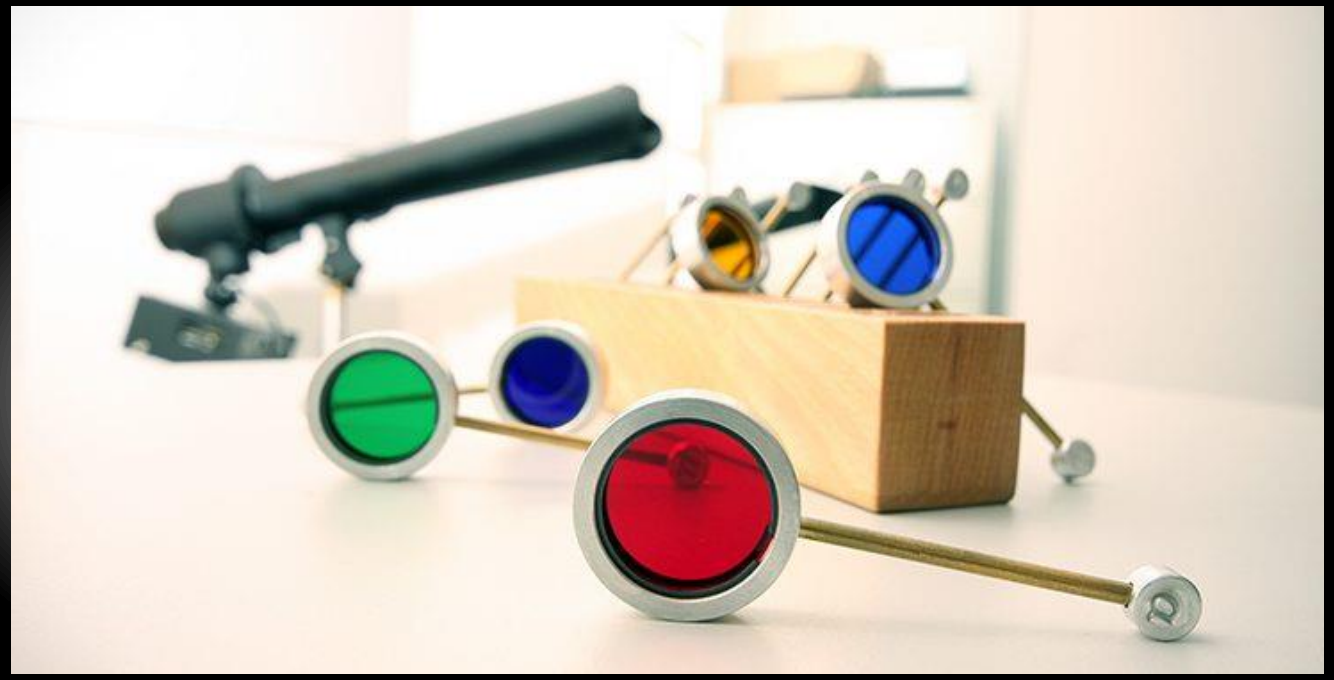
MitoCircadian™ Approach

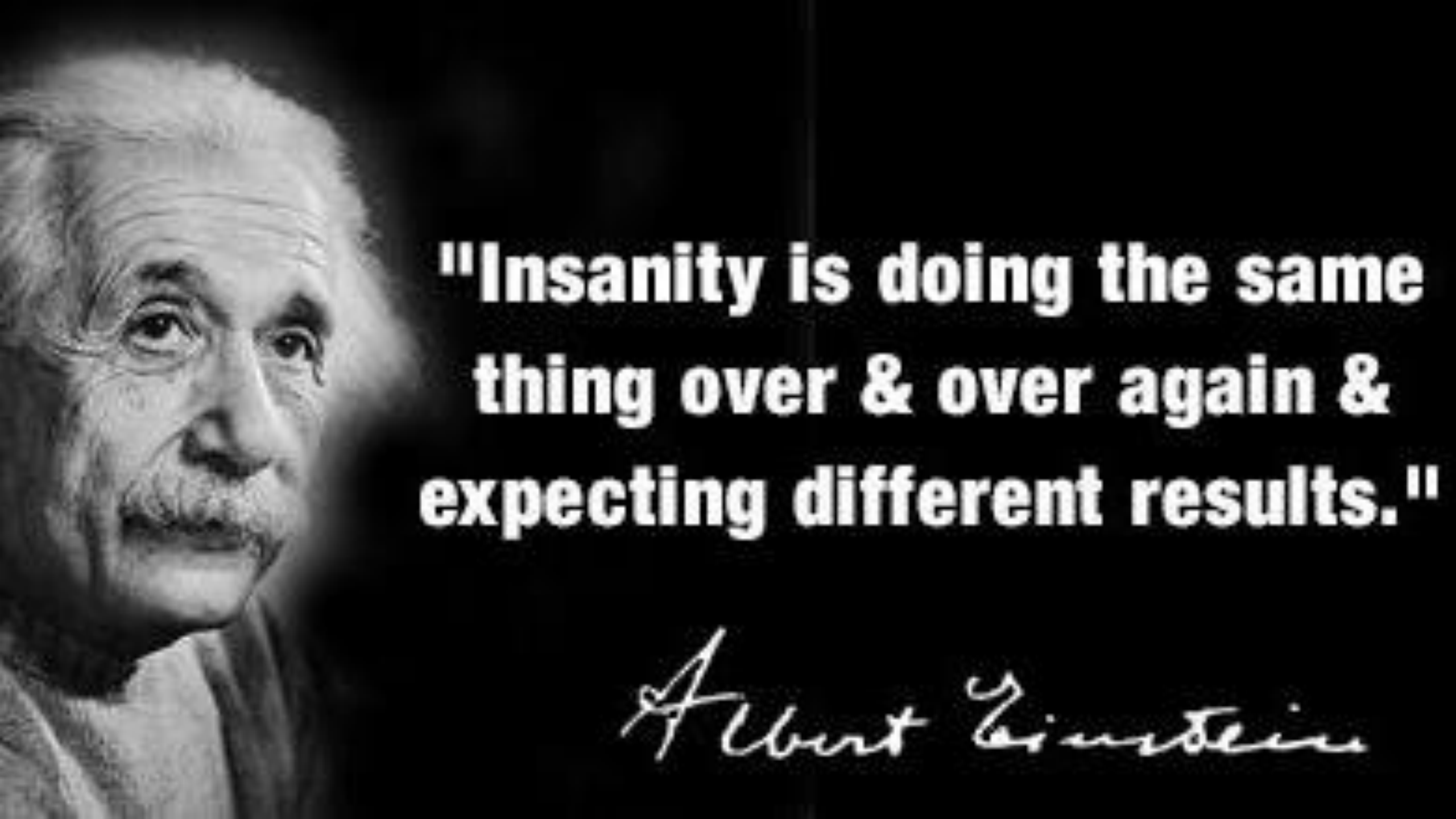


What Happens When Your Clock Is Right?

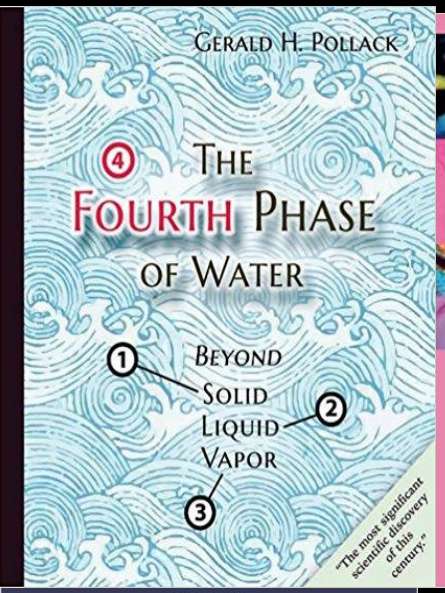
Can Syntonics Be Better?

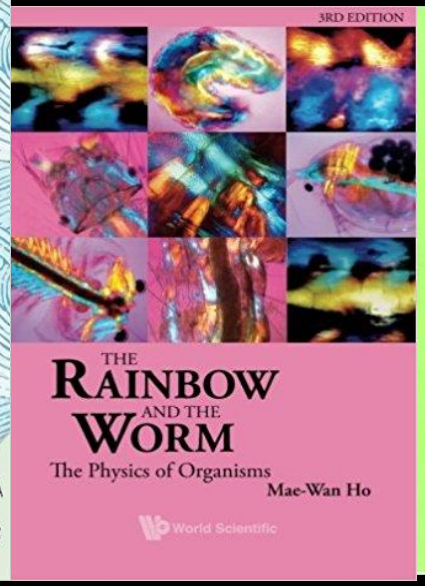
- Time of Syntonizing
  - Daytime Only
  - Nighttime Exclusions?
- Light Sources?
- Adjunctive Therapies:
  - Circadian Alignment
  - Photobiomodulation
  - Heliotherapy
  - Advance Regenerative Therapies To Repair Mitochondria

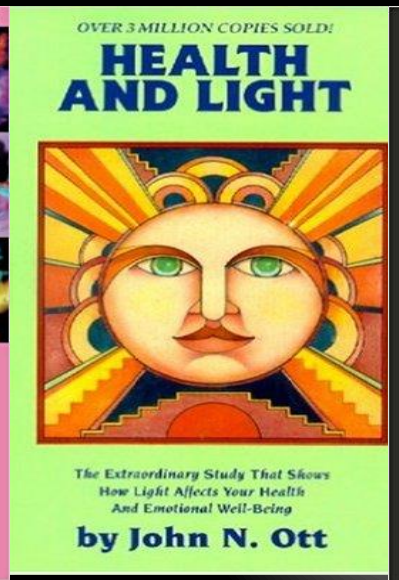


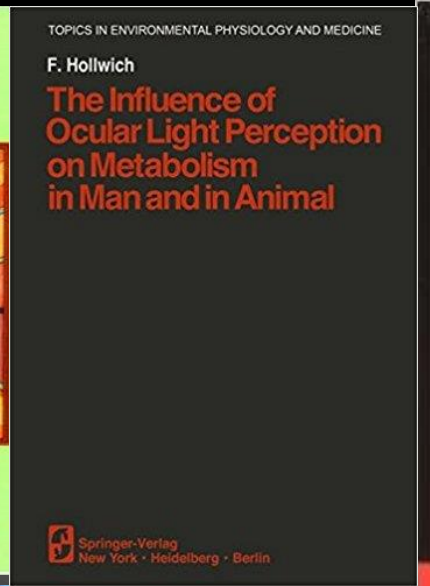

"Insanity is doing the same thing over & over again & expecting different results."
Albert Einstein

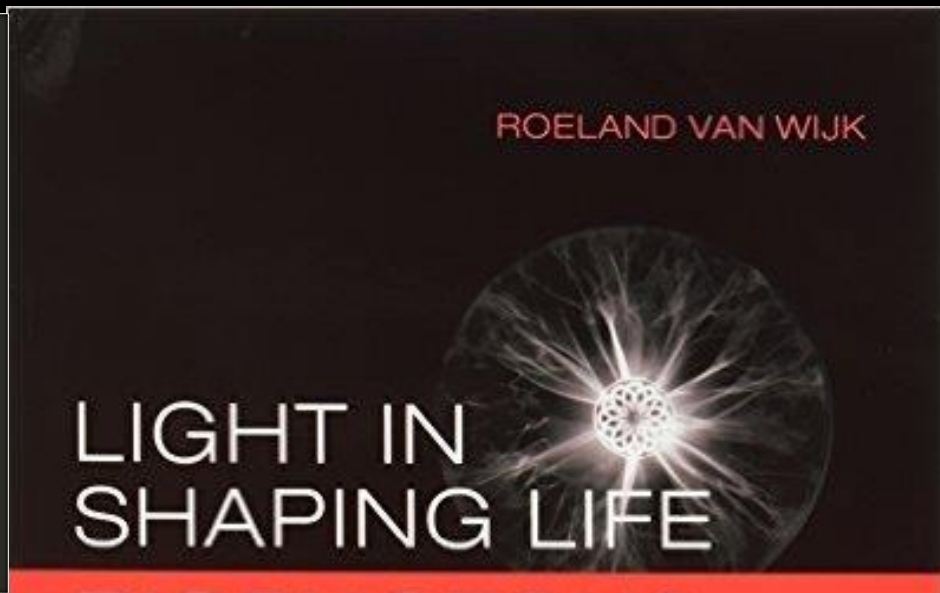
The science for this isn't new, we've got to connect the dots!

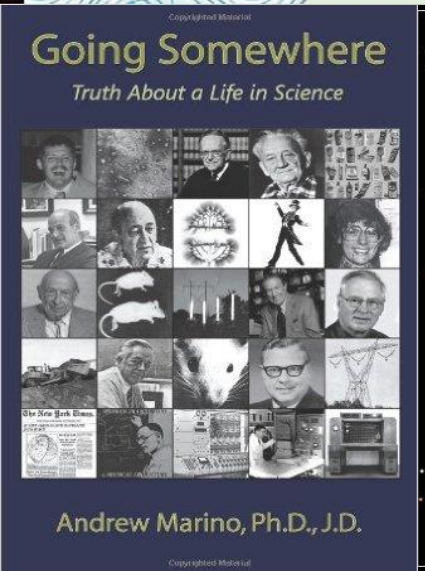


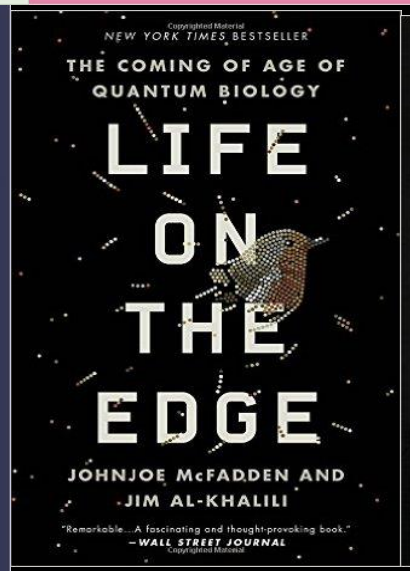


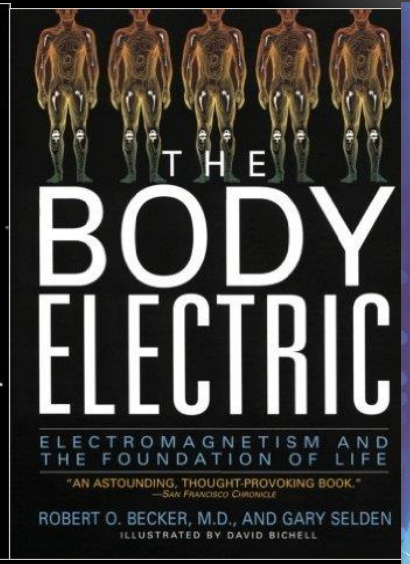


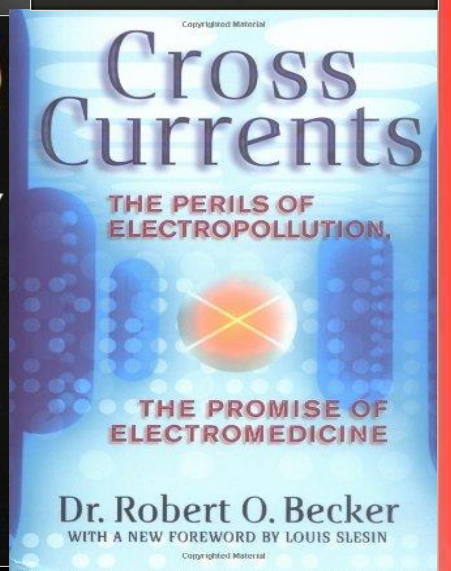












Quantum Life Wellness

Josh Rosenthal, M.D.

- qlwellness@protonmail.com
  - *Contact me if you work in NY, FL, or PA to discuss collaboration opportunities*

- Transformative Regenerative & Wellness Procedures & Programs
- MitoCircadian ™ Approach

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TLDR ☺

1 Slide Summary

Questions?

Josh Rosenthal, M.D.
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