COVID-19 SYNDROME & RECOVERY

Acute COVID

“LONG HAUL”

Kathleen O’Neil-Smith, MD

TREAT WELLNESS™

Prototypical Disease:

*A **Golden** Opportunity for Regenerative Medicine*

TREAT WELLNESS™

My journey
Going Full Circle!

Physiology and Nutrition B.S.
USARIEM Research
US National Rowing Team, member f/b coach
H.S & College Science, Math and Wellness
Med school
Pathology Internship @ MGH x 1 year
Internal Medicine 3 years @ BWH
Palliative Care→ Geriatrics → IM/PCP ---> AARM

TREAT WELLNESS™

COVID-19 & “Long Haul”

What can we learn? A LOT!

- C-19 pandemic still affecting communities globally
- Multiple variants continue to be found
- Chronic multi-symptom health issues emerging
- Requires a unique approach to treatment; beyond simply managing symptoms: brain fog, SOB, chronic cough, muscle/joint pain, fatigue

TREAT WELLNESS™

Healthy Immune System vs Immunopathology

- How do we optimize immune system health?
- How do we minimize immunopathology?
- Are there biomarkers can we use to assess immune health vs. immunopathology?

TREAT WELLNESS™

IMMUNOPATHOLOGY: LESSONS FROM THE PAST

- 1985: Incline Village , Nevada— bad flu season
  "The Chronic Fatigue Syndrome";Cheney and Lapp —> alteration in immune system function and state of chronic Inflammation
- Maes and Pall: "CFS" associated with functional mitochondriopathy, immune dysfunction, oxidation stress with sustained tissue-specific inflammation, —> and complex multi-organ symptoms
- 1990's: "Gulf War Syndrome"(GWS) —> fatigue, myalgia, cognitive deficits —> associated with mitochondria defects with a lasting deleterious impact on immune function
- Long-haul post COVID-19 -->similarities w/ CFS and GWS: is there a shared putative immune mechanism or IMMUNOPATHOLOGY ?

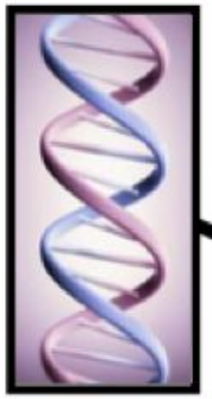
Understanding “IMMUNOPATHOLOGY”

- Immunosenescence = aging of the immune system
- COVID-19 infection damages immune cells and accelerates immunosenescence
- It is imperative that for CDPM(C), we examine the underlying and baseline status of the immune system as the immune system is involved in all disease processes.
- If immune system status is unknown, NON-SPECIFIC immune “boosting” activity may result in adverse outcomes for those with pre-existing altered immune system function

TREAT WELLNESS™

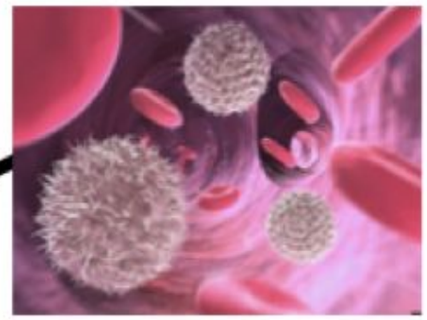
Recipe For Immune Mediated Diseases

Which Ingredients Are Necessary?

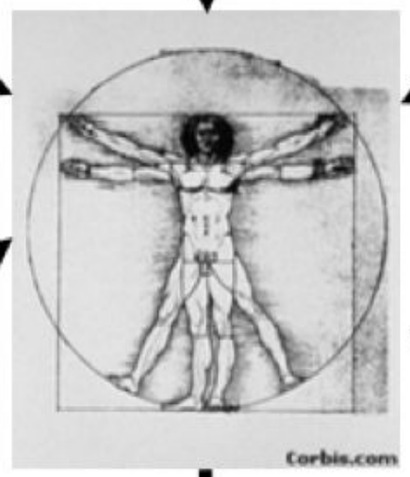


Human Genome

Increased Gut Permeability



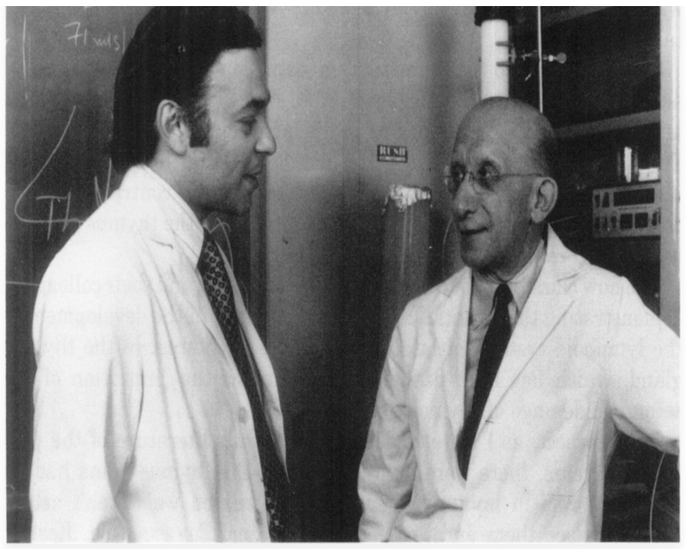
Immune Response



nvironmental Factors

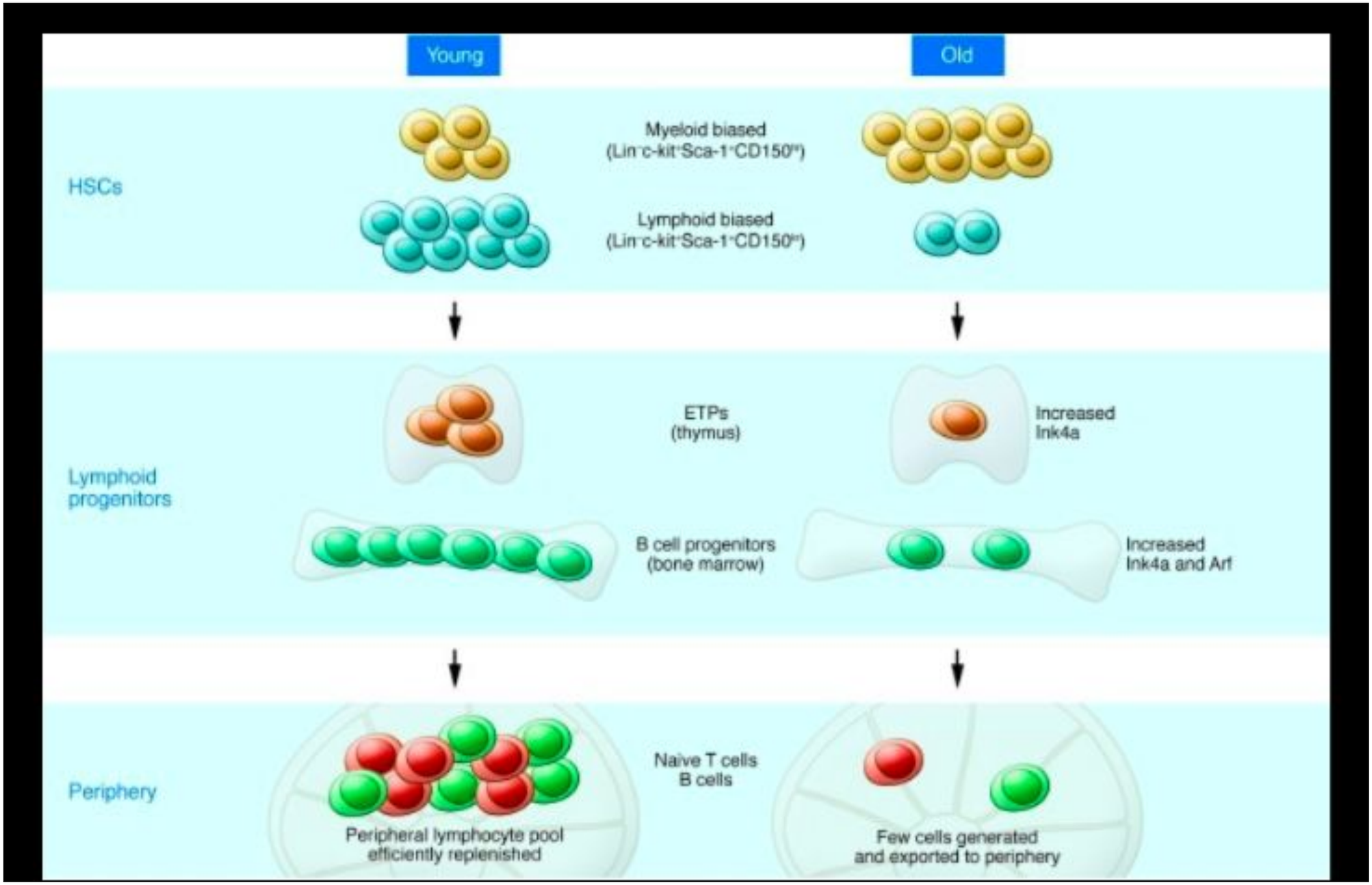
Microbiome

Reference Box



Drs. Goldstein and White
Founders of Thymosin

https://doi.org/10.1196/annals.1415.045


Young
Old
HSCs
Myeloid biased
(Lin⁻c-kit⁺Sca-1⁺CD150ʰⁱ)
Lymphoid biased
(Lin⁻c-kit⁺Sca-1⁺CD150ˡᵒ)
Lymphoid progenitors
ETPs
(thymus)
Increased Ink4a
B cell progenitors
(bone marrow)
Increased Ink4a and Arf
Periphery
Naïve T cells
B cells
Peripheral lymphocyte pool efficiently replenished
Few cells generated and exported to periphery

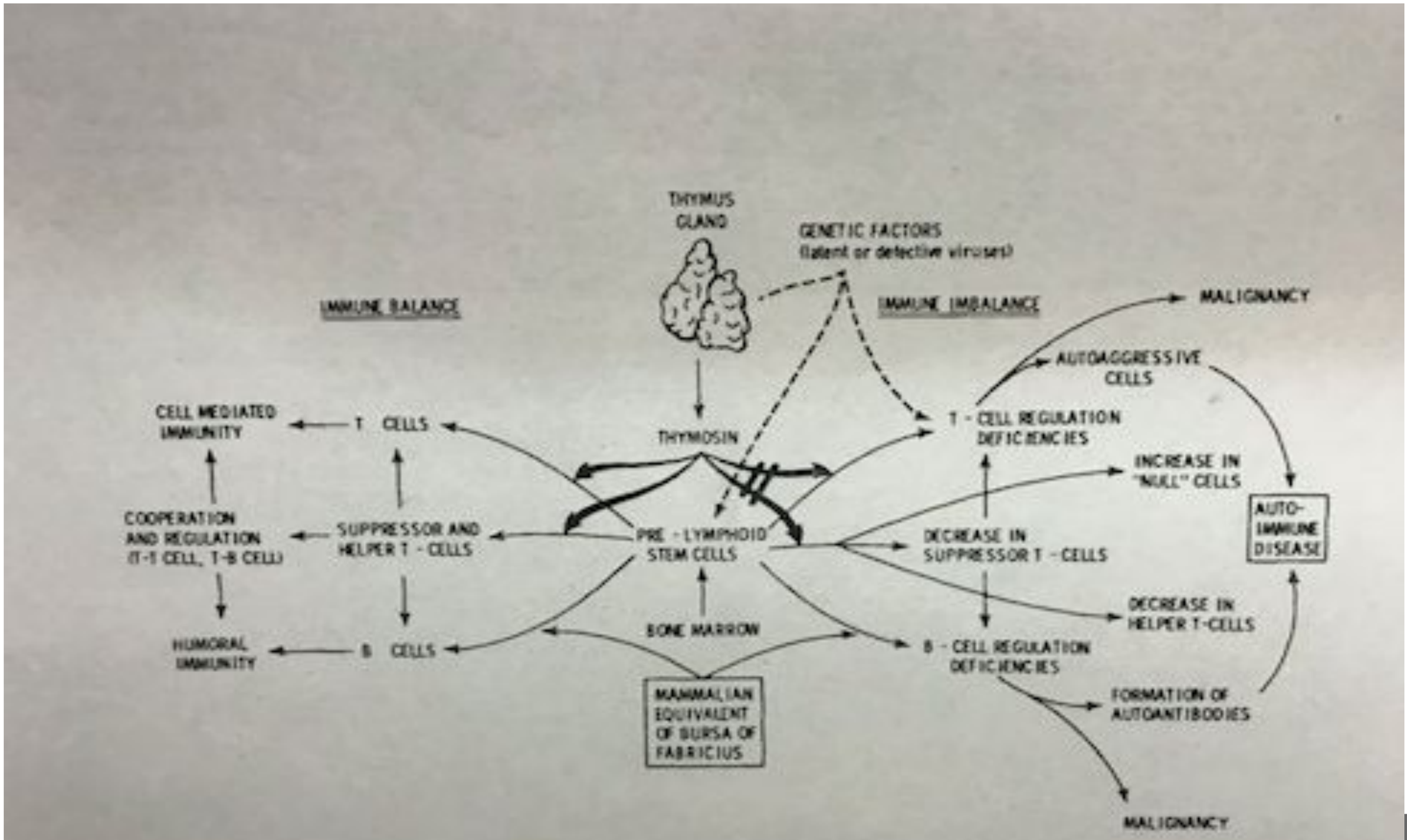


FIGURE 3. Proposed role of thymosin in the etiology of autoimmune disease.

Goldstein L. et al. / Ann N Y Acad Sci. 1976;274:390-401

TEXT

Factors impacting IMMUNOPATHOLOGY

- Optimal nutrition status is essential for a well-functioning immune system to protect one from illness (healthy microenvironment)
- Studies of C-19 patients indicate that co-morbidities and aging linked to changes in immune system function are associated with increased severity of C-19 dx, ie increased CK storm
- The type of immune system imbalance prior to exposure to C-19, AND pre-existing activities in certain immune cells are two additional factors that affect disease severity if infected with COVID-19

TREAT WELLNESS™

COVID 19 & “Long Haul”

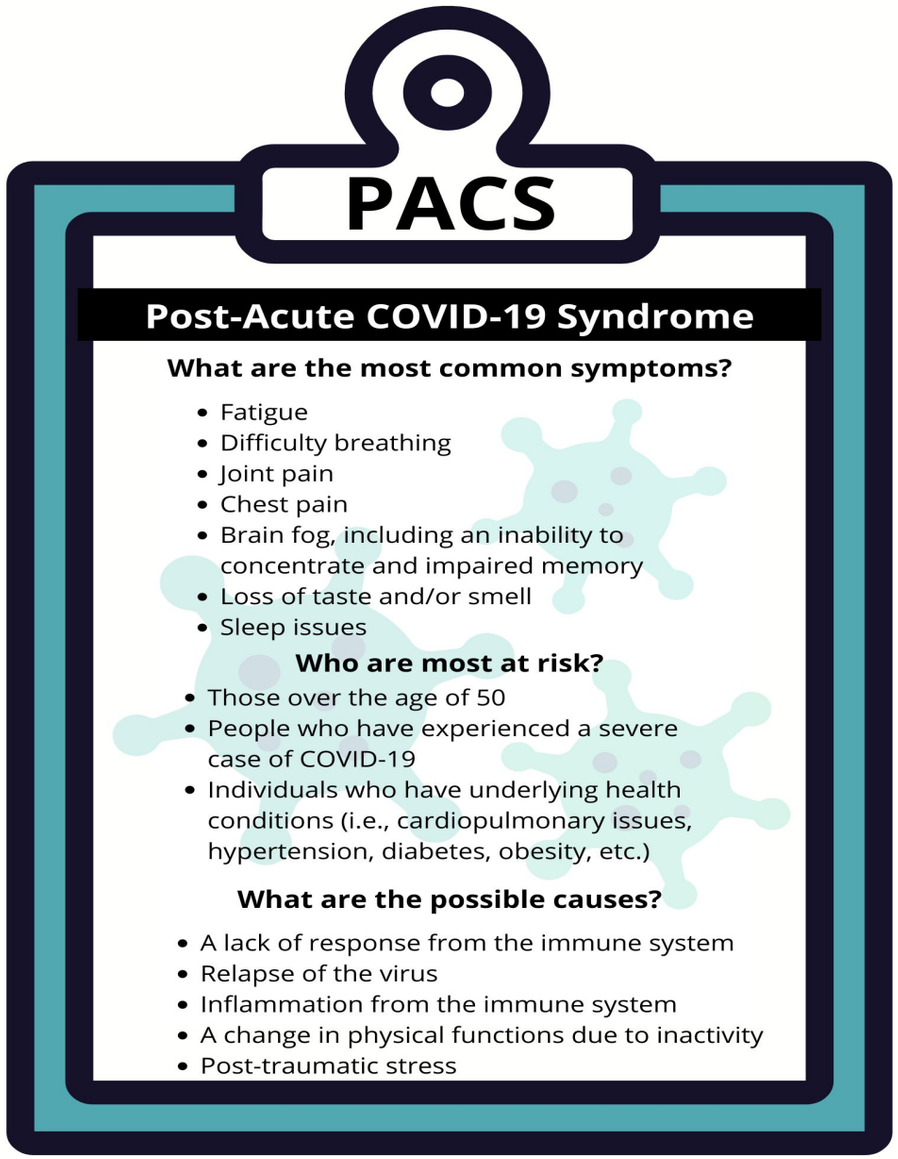
Aging→ immunosenescence

Immune system imbalance prior to exposure to C-19

Comorbidities

Pre-existing activities in immune cells

Optimal nutrition status



IMMUNOPATHOLOGY:

The influence of DIET AND LIFESTYLE (Non-heritable FACTORS) on the immune system

VARIATION IN THE HUMAN IMMUNE SYSTEM IS LARGELY DRIVEN BY NON-HERITABLE INFLUENCES: CELL 2015 JAN 15, BRODIN

TREAT WELLNESS™

VARIATION IN THE HUMAN IMMUNE SYSTEM IS LARGELY DRIVEN BY NON-HERITABLE INFLUENCES

- A large collaborative study (Karolinska, UNC, Stanford) demonstrated that there is considerable variation in immune system status and function among healthy populations
- The differences were not genetically determined
- The differences were driven by lifestyle factors: the exposome, including diet and environmental factors to which the immune system had been exposed!

TREAT WELLNESS™

CELL 2015
JAN 15, BRODIN

VARIATION IN THE HUMAN IMMUNE SYSTEM IS LARGELY DRIVEN BY NON-HERITABLE INFLUENCES

- Researchers-> 204 different immune parameters, including immune cell types, cytokine responses, serum proteins derived from the immune system
- 77% dominated by and 58% were almost completely determined by non-heritable factors
- Some of these factors became variable and accumulated at different rates with age
- This supports understanding the importance of the EXPOSOME: the cumulative influence of environmental exposures

TREAT WELLNESS™

Variation in the human immune system is largely driven by non-heritable influences

Petter Brodin [1], Vladimir Jojic [2], Tianxiang Gao [2], Sanchita Bhattacharya [3], Cesar J Lopez Angel [4], David Furman [4], Shai Shen-Orr [5], Cornelia L Dekker [6], Gary E Swan [7], Atul J Butte [8], Holden T Maecker [9], Mark M Davis [10]

Abstract

There is considerable heterogeneity in immunological parameters between individuals, but its sources are largely unknown. To assess the relative contribution of heritable versus non-heritable factors, we have performed a systems-level analysis of 210 healthy twins between 8 and 82 years of age. We measured 204 different parameters, including cell population frequencies, cytokine responses, and serum proteins, and found that 77% of these are dominated (>50% of variance) and 58% almost completely determined (>80% of variance) by non-heritable influences. In addition, some of these parameters become more variable with age, suggesting the cumulative influence of environmental exposure.

- PMID: 25594173
- PMCID: PMC4302727
- DOI: 10.1016/j.cell.2014.12.020

IMPORTANCE OF THE EXPOSOME

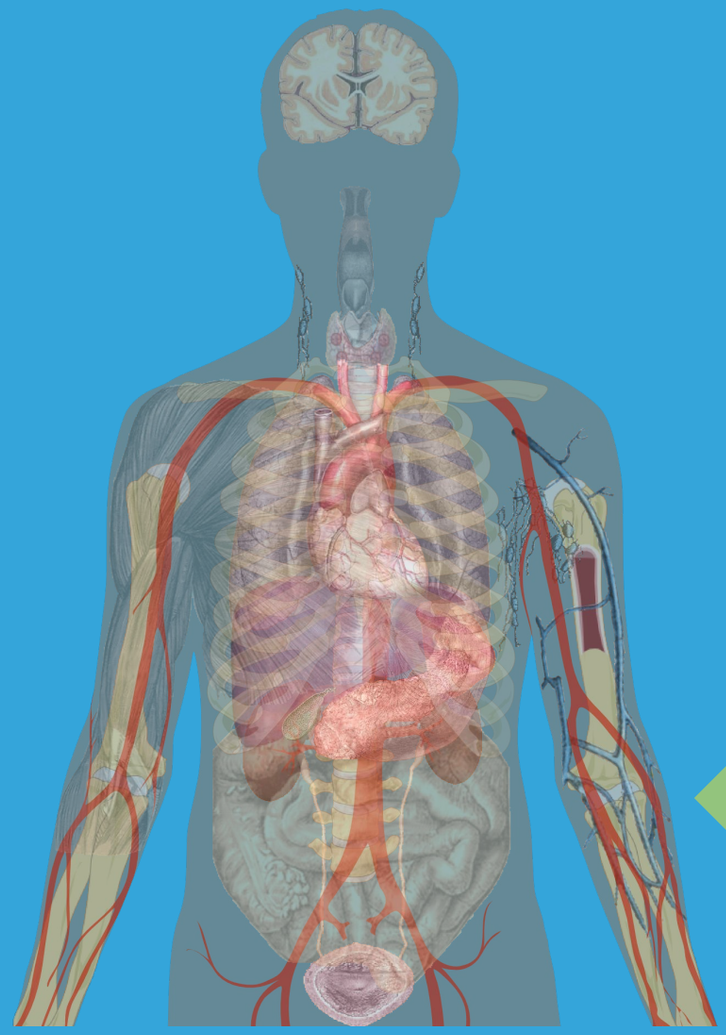
- The EXPOSOME: the cumulative influence of environmental, diet and lifestyle exposures can lead to differing "immune identities".

- The accumulation of immune cells that have had mutational injury and epigenetic changes as a result of lifestyle and environmental factors may increase the inflammatory state of the individual and thus the severity of COVID-19 disease if infected

TREAT WELLNESS™

External Environment:

- ❏ Diet
  - ❏ industrialized foods
- ❏ Lifestyle
  - ❏ excess stress
  - ❏ lack of movement
  - ❏ excess sympathetic tone
  - ❏ low parasympathetic tone
- ❏ Pollution
- ❏ Radiation
- ❏ Drugs



Exposome:

- ❏ Adjuvants
  - ❏ metals
  - ❏ immune modulators
  - ❏ endocrine disruptors
- ❏ Receptor binding proteins
- ❏ Reactive electrophiles

TREAT WELLNESS™

HOW DO WE ADDRESS IMMUNOPATHOLOGY?

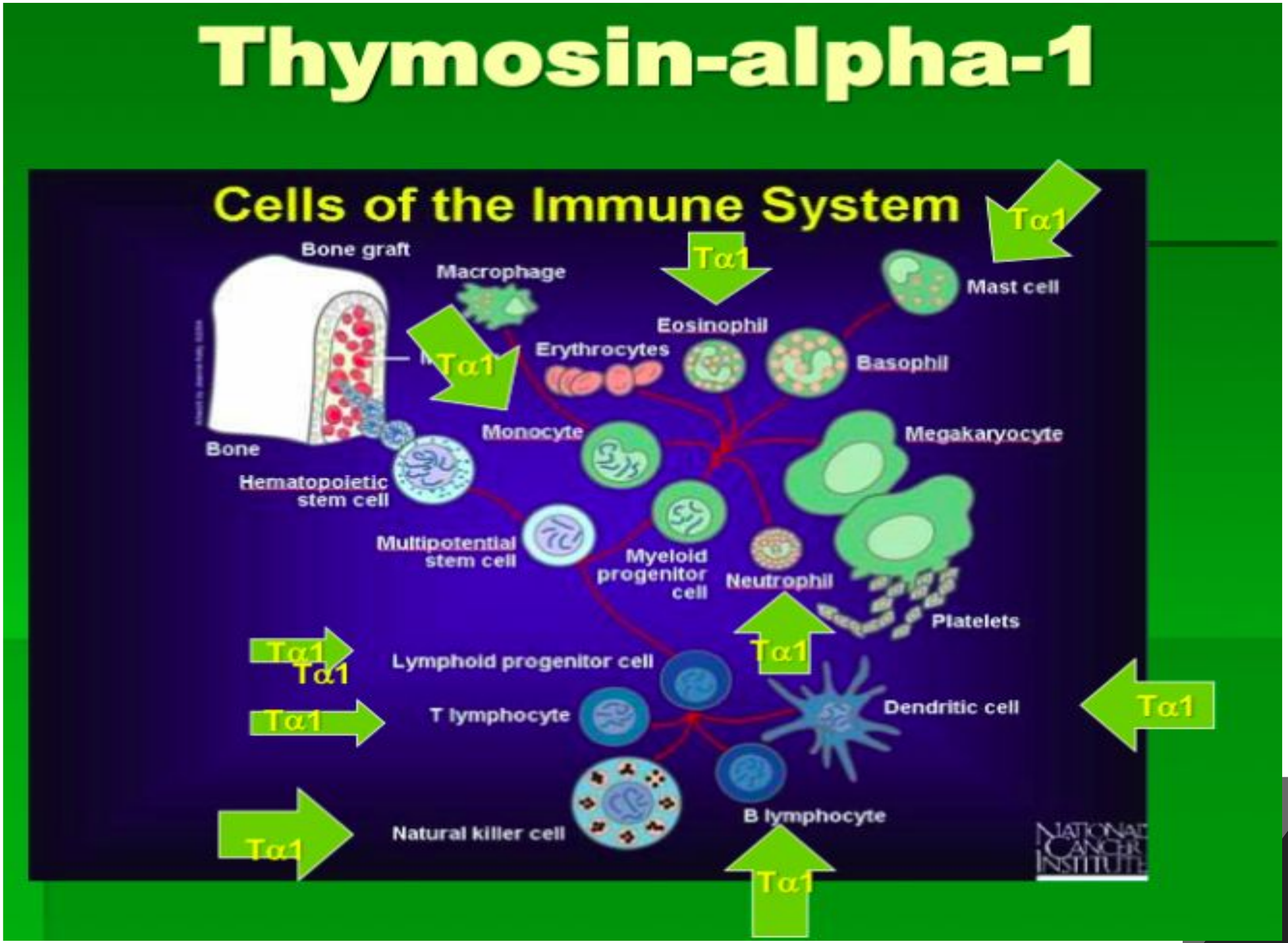
- Reduce the production rate of damaged immune cells
- Eliminate immune cells that carry messages from past exposures
- Replace immunosenescent cells with new immune cells not imprinted with prior memories

TREAT WELLNESS™

Exfoliation of facial skin

TREAT WELLNESS™

Thymosin-alpha-1



Immune Dysregulation

- Studies show that immune dysregulation and immunosenescence results in an increase in T_H 2 relative to T_H 1
- This T_H 2 / T_H 1 imbalance is assoc. w/ many common chronic illnesses, including:
  - ➢ Chronic fatigue syndrome/fibromyalgia
  - ➢ Autoimmune disease
  - ➢ Chronic infections (including CMV, Lyme, viral, parasites)
  - ➢ Oxidative Stress: GSH depletion-→TH1—TH2 shift
  - ➢ Glucose, tobacco, alcohol
  - ➢ Dysbiosis
  - ➢ Hormones (estrogens stimulate TH2; progesterone and testosterone TH1)
  - ➢ Depression
  - ➢ Zinc and other mineral deficiencies

TEXT

CHRONIC DISEASE PREVENTION AND MANAGEMENT CLINICS

- Address the exposome, including diet and lifestyle factors
- GOAL of CDPMC's:

  → Recognize that prior immune system health is an important factor that we need to measure
- → Address the 'health of the microenvironment', aka the ECM
- → Practice Immune Rejuvenation !

TREAT WELLNESS™

BMJ NUTRITION PREVENTION & HEALTH: MAY 2020; PHILIP CALDER, PHD," NUTRITION, IMMUNITY AND COVID-19"

- Daily dietary nutrients that support immune system function:
- Vitamin A, C, D, E, Zinc, Omega 3, Probiotics
- If previous immune injury 2/2 infection (eg.,EBV,CMV) or adjuvant exposure with sustained chronic immune dysfunction, and a residual memory of past exposures, ……
- Are these dietary nutrients sufficient to meet the needs of a patient who now experiences *additional immune injury* as a consequence of COVID-19 infection?

TREAT WELLNESS™

TEXT

COVID-19 INFECTION (mod-sev)
does not happen in isolation!

- Injury with COVID to a previously injured immune system worsens the imbalanced immune system state……resulting in
- Over-activation of the NLRP3 inflammasome
- Heightened activation of inflammatory CK's
- Creation of "bystander" damage to hematopoietic stem cells as..mutational and epigenetic changes to the progenitor immune cells

TREAT WELLNESS™

Why do people have varying infection when exposed to COVID-19 (COV-2)?

- No infection (90%)
- Mild Infection (9%)
- Severe Infection (1%)

Variation in immune response is due to age, chronic disease, exposome.....

TREAT WELLNESS™

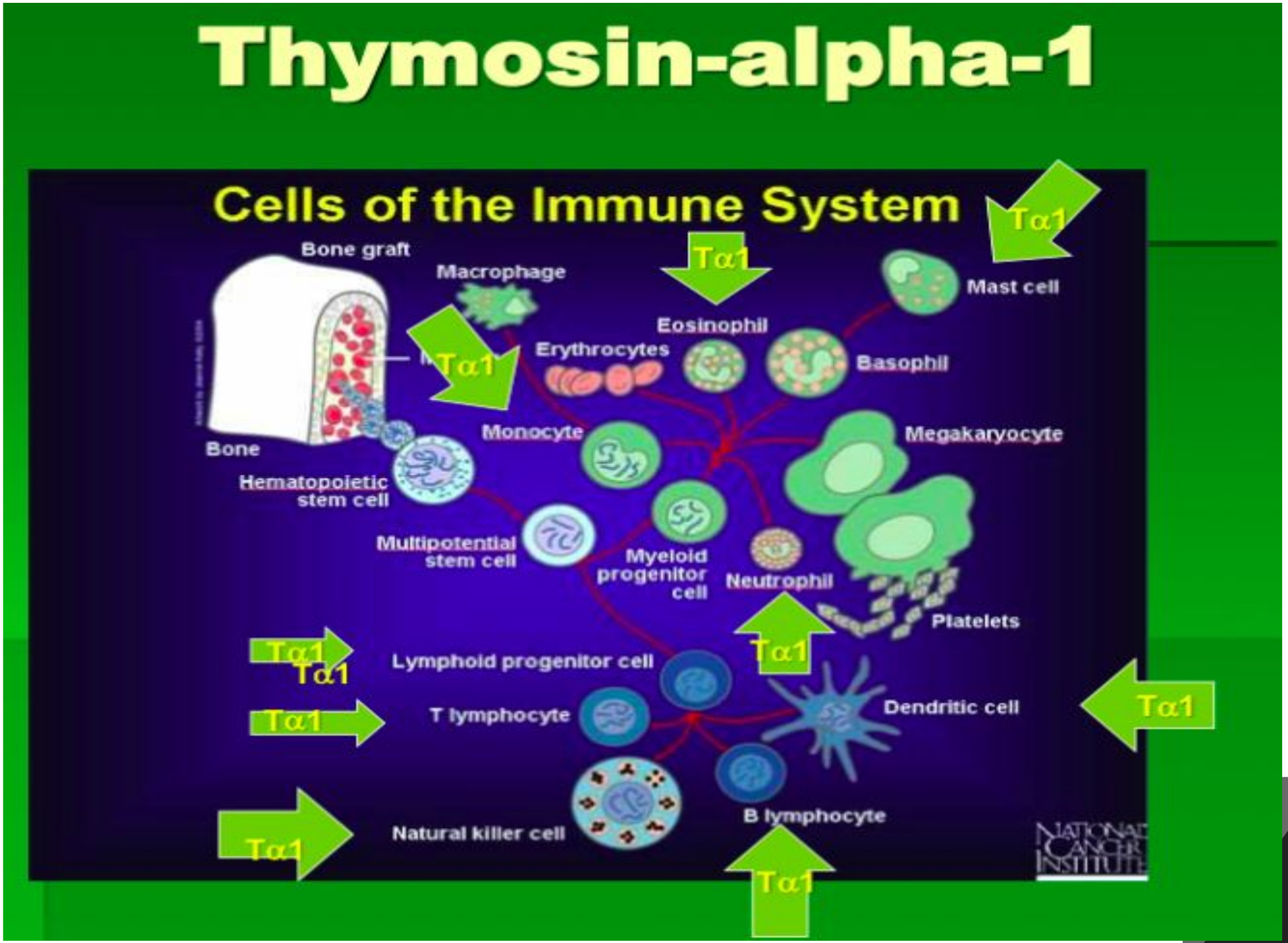
	No Infection	**Mild Infection**	**Severe Infection**
Exposome	Mild	Moderate	Severe
Mucosal Immunity, Increase Permeability	Strong	Good	Compromised
Antibody Production	Good/Rapid	Good/Delayed	Compromised
Immune System NK cells, etc...	Strong	Moderate	Compromised

POST VIRAL INFECTION MUTATIONAL INJURY

- Resembles "CHIP" -
  clonal hematopoiesis of indeterminate potential.
- During COVID-19 infection, *alteration of genes in the CHIP-driver sequence in hematopoietic stem cells*, may create a *long-term inflammatory phenotype* associated with *mitochondrial and immune system dysfunction*
- These gene alterations impact the complex symptom profile in the long haul C-19 patients

TREAT WELLNESS™

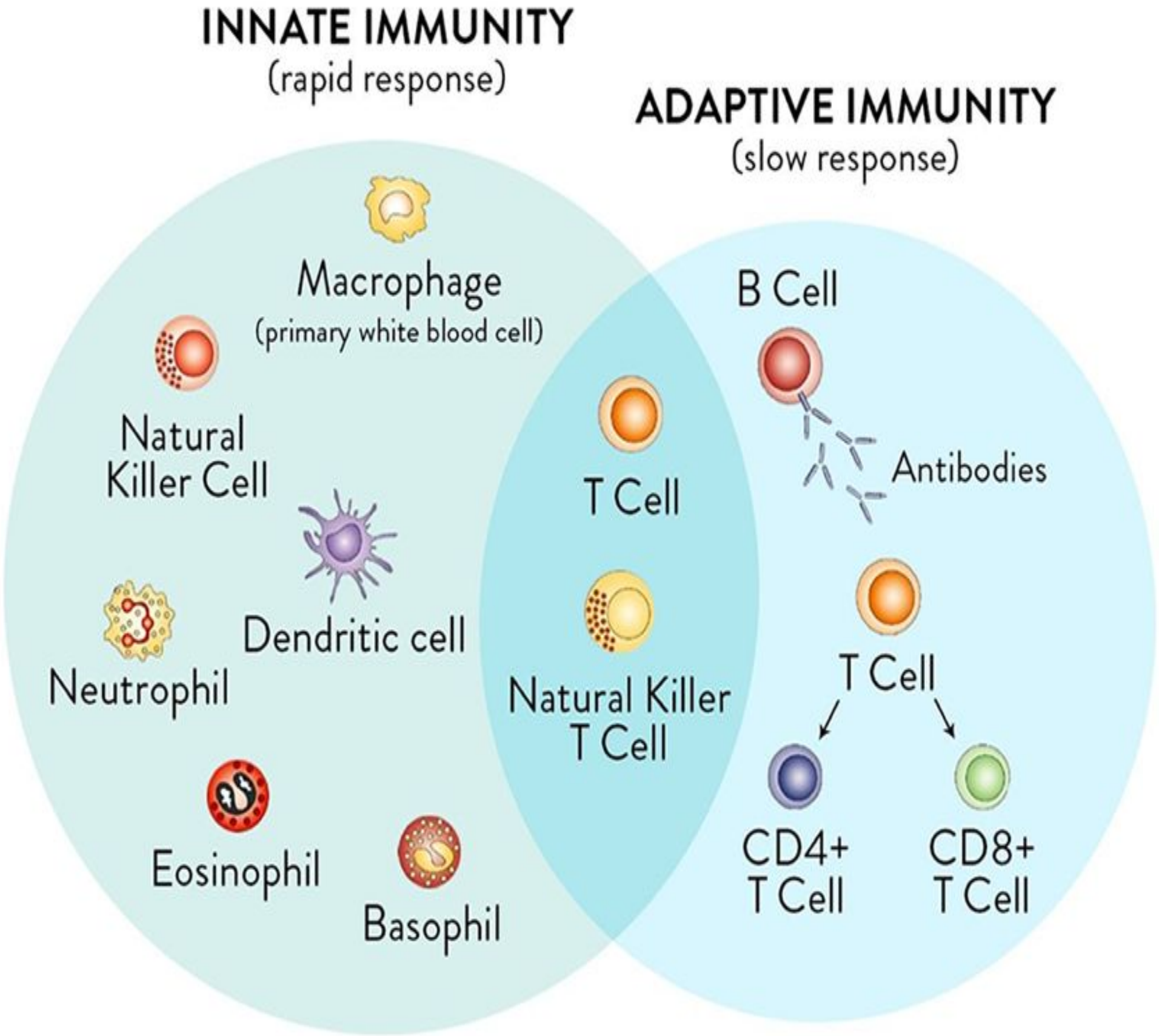
Thymosin-alpha-1



PREVENTION OF ANY CHRONIC DISEASE

- Identify immune "identity"of your patient at baseline; immunopathology, previously injured immune system?
- Rejuvenate the immune system through selective activation of autophagy and mitophagy in immune cells
- Understand how various lifestyle, dietary factors and the exposome can influence the autophagy process, positively and negatively

TREAT WELLNESS™



TREAT WELLNESS™

GOAL: ADDRESS IMMUNOPATHOLOGY?

- Reduce the production rate of damaged immune cells, including damage to hematopoietic stem cells, the progenitor cells that produce new immune cells and improve immune function
- Eliminate immune cells that carry messages from past exposures
- Replace immunosenescent cells with new more resilient immune cells not imprinted with prior memories

TREAT WELLNESS™

TEXT

COVID -19:TREATMENT CONSIDERATIONS

- Prevention — ideally is personalized lifestyle medicine with immune system rejuvenation
- Post-exposure Prophylaxis
- Acute COVID-19 Treatment options
- Long Haul C-19: long term management to optimize immune health and to restore aberrant immune system function—- Immune Support vs Immune-Rejuvenation

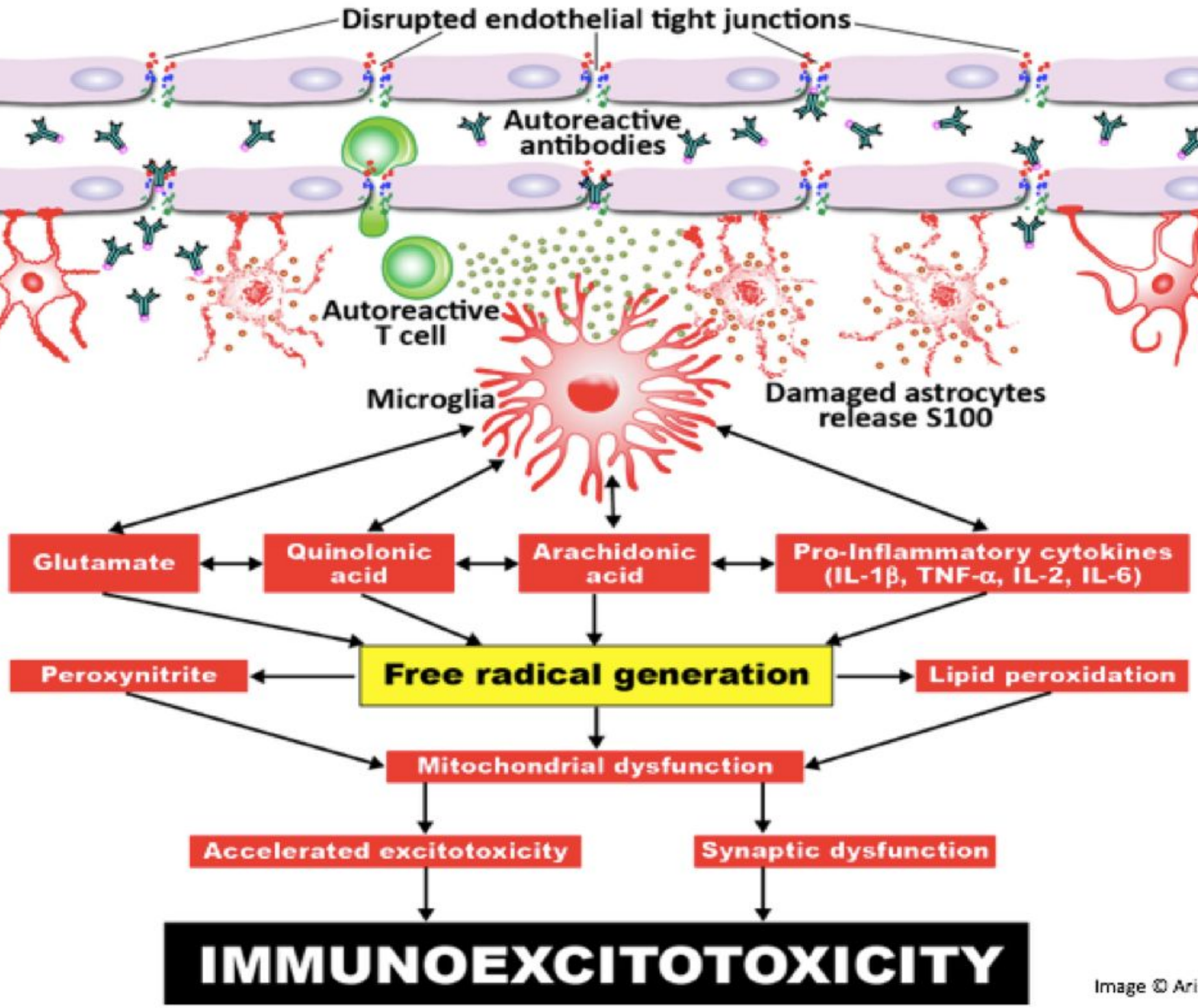
TREAT WELLNESS™

TEXT

A SAMPLING OF BIOMARKERS ASSESSING IMMUNE SYSTEM FUNCTION

- CBC with diff : Monocyte, basophils, eosinophils, immature granulocytes, etc...
- Assess the TH1. Vs TH2 balance
- NK cell function, CD4, CD8….
- IgA, IgM, IgG, IgE, secretory and plasma levels
- IGF-1, EndoPat test and sudomotor testing, etc
- Cytokine biomarkers: IL-6, Complement, TNF-alpha
- Complete stool analysis: PCR, Culture of Microbiota

TREAT WELLNESS™

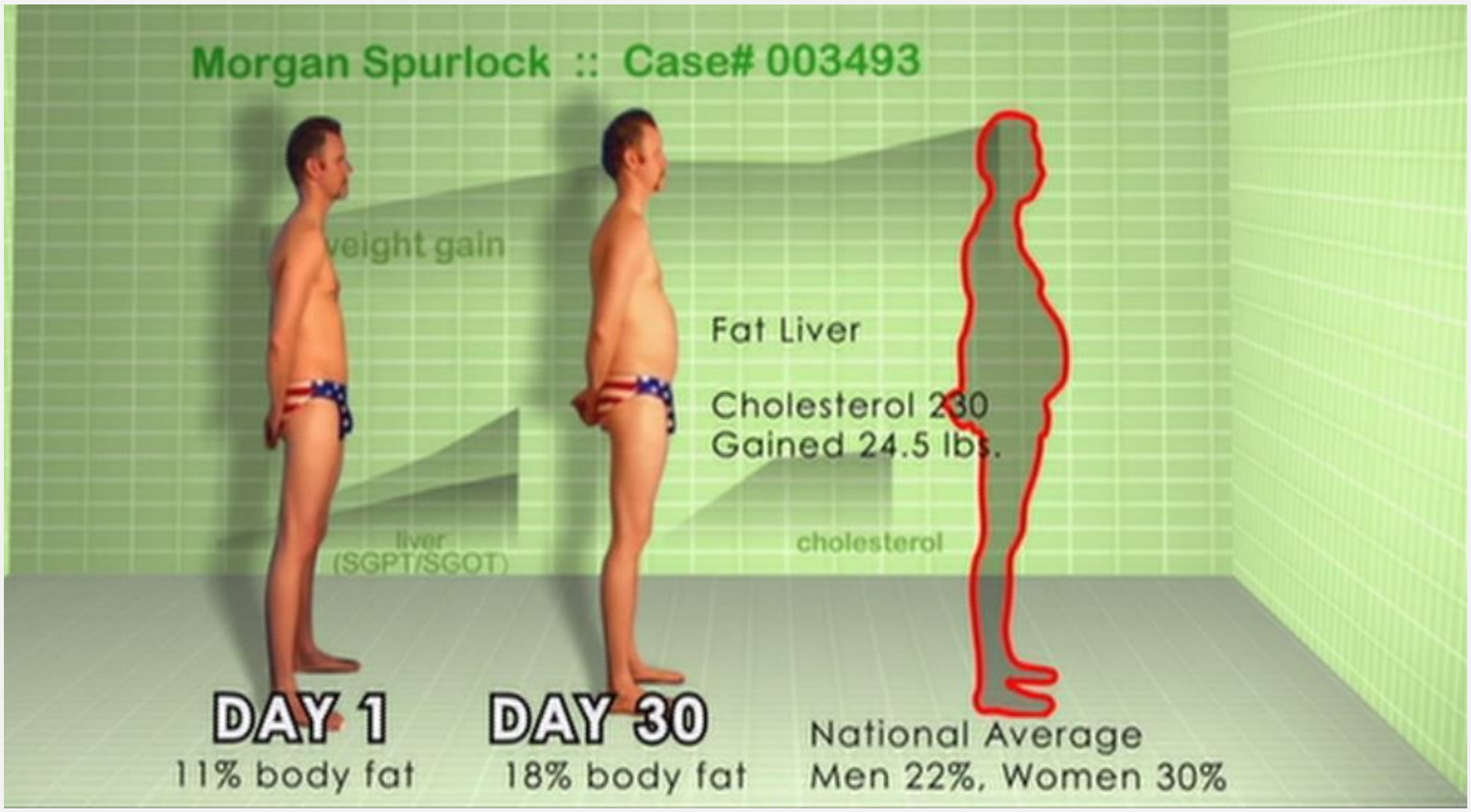


Encarnacion Montecino-Rodriguez, Beata Berent-Maoz, and Kenneth Dorshkind

Approaches to inhibit or reverse aging should be widely available and applicable to a large cohort. In addition to pharmacologic interventions, caloric restriction (CR) may also meet these criteria. CR has been reported to have multiple beneficial effects on the immune system of both rodents and non-human primates that include a delay in the accumulation of senescent T cells (112) and a stimulation of thymopoiesis (113). This latter effect is at first puzzling, because CR reportedly reduces IGF-1 secretion (114), and low levels of IGF-1 have, as discussed above, been associated with thymic involution. However, CR may also increase GH levels (114), which could be thymopoietic, or may work through IGF-1–independent pathways. For example, CR has been reported to block the age-related elevation of the thymic proadipogenic master regulator, PPARγ (113)

10.1172/JCI64096

Supersize Me!



Source: Google Images

Correcting age-related deficiencies in lymphocyte progenitors or mature T and B cells may result in significant restoration of immune function in the elderly. However, these cells would still reside in an aged microenvironment that could eventually dampen their potential to mature or function. Consistent with this view, Haynes and colleagues (111) found that CD4+ T cells generated from old HSCs were functional in young but not old hosts, implying that the aged thymic or peripheral microenvironments critically influence the degree to which immune system rejuvenation can occur. In view of this point, optimal interventions may need to address the effects of aging on multiple cellular targets.

10.1172/JCI64096

Regenology

https://www.advancednutrients.com/articles/harvesting-big-buds/

LIFESTYLE FACTORS FOR PREVENTION & IMMUNE SYSTEM AUTOPHAGY

- The USUAL suspects: REDUCE refined starch, sugar INCREASE PUFA's-->Omega 3 fatty acids, polyphenols and flavonoids
- Application of Calorie Restriction→ fasting physiology
- Promote a healthy microbiota composition with prebiotics and probiotics
- Promote a personalized healthy microenvironment to "nourish"cells

TREAT WELLNESS™

Immunomodulatory Therapies

- Goal: to Increase TH1 and decrease TH2… restore homeostasis
- Boosting NK cell and lowering inflammatory cytokines
  - Peptides (Thymosin alpha-1/Thymosin B4)
  - IVIG
  - Allergy elimination: IgE, IgA, IgG (gluten, nuts,etc)
  - Antivirals (Disease progression in EBV/HIV is directly correlated to the TH1/TH2 balance)
  - Transfer factors
  - Mushroom extracts
  - High dose B12
  - GcMAF/Neupogen
  - Probiotics
  - Silver
  - Antioxidants/Glutathione (low glutathione decreases TH1 and increases TH2)
  - Chelation (heavy metals stimulate TH2 and lower TH1)

Immune Support vs Immune Rejuvenation

Test→ please don't guess

Basic labs --quest, labcorp, empire, boston heart etc

Specialty labs: Stool testing(GIFx GI MAP, IgE,G,A food testing (Cyrex etc), Nutreval, Spectracell, ION test, Methylation Panel, Precision Point (MCAS- Intestinal Barrier Assessment , Sanesco (Adrenal testing), and others

TREAT WELLNESS™

IMMUNE SUPPORT

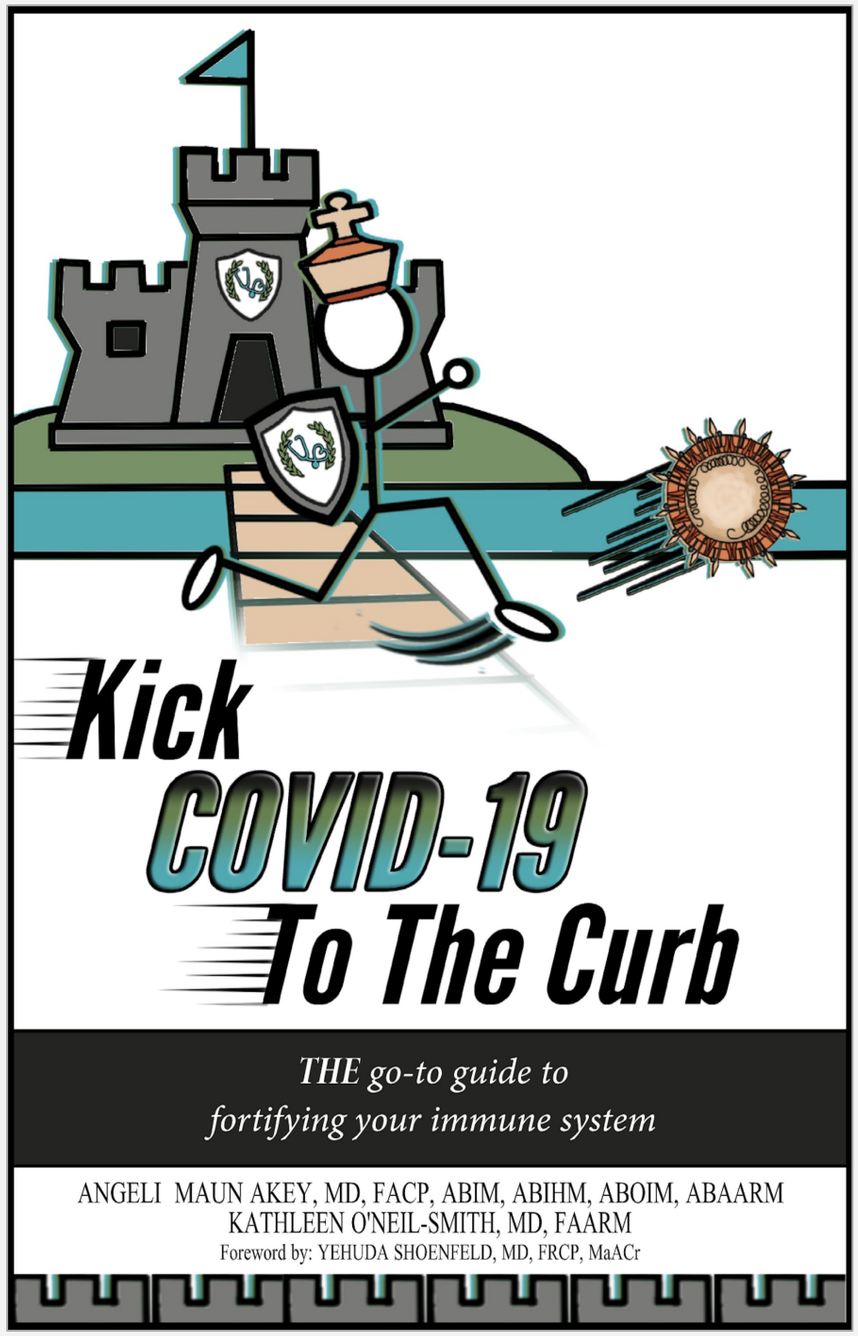
- Generalized boosting of existing compromised immune system
- Could amplify pre-existing immune issues
- Does not address a broken or dysfunctional immune system
- Addresses immune function as a stand alone system
- A quick fix vs focus on long-term immune health
- Focus on protecting patient vs exposome: dangers of the world

TREAT WELLNESS™

IMMUNO-REJUVENATION

- Reprograms immune system for balance & resilience
- Improve immune function from the molecular to the global ecosystem
- Addresses and reverses damaged and aging immune systems
- An integrative approach to addressing the causes of immune dysfunction via holistic healing over time
- Integrates the role of immunity across multi-systems: metabolic, cognitive , behavioral etc
- Embraces the interconnected nature of the immunity of the you, the we and the planet

TREAT WELLNESS™



Ebook is available for <u>$9.99</u> on Amazon Kindle, Google Play, and Barnes and Noble!

&

<u>$14.95</u> on Audible

TREAT WELLNESS™

FOREWARD

The COVID (Corona) Virus:
WHAT WE HAVE TO KNOW!

This new pandemic is characterized by an avalanche of clinical and scientific publications, a PHENOMENON OF NO PRECEDENCE. This book, written by Dr. Angeli Maun Akey and Dr. Kathleen O'Neil-Smith, is a successful effort to encompass all the knowledge accumulated thus far in a simple way. They should be blessed for their efforts. It entails details about this peculiar virus, its infectivity, sensitivities, and pathogenicity.

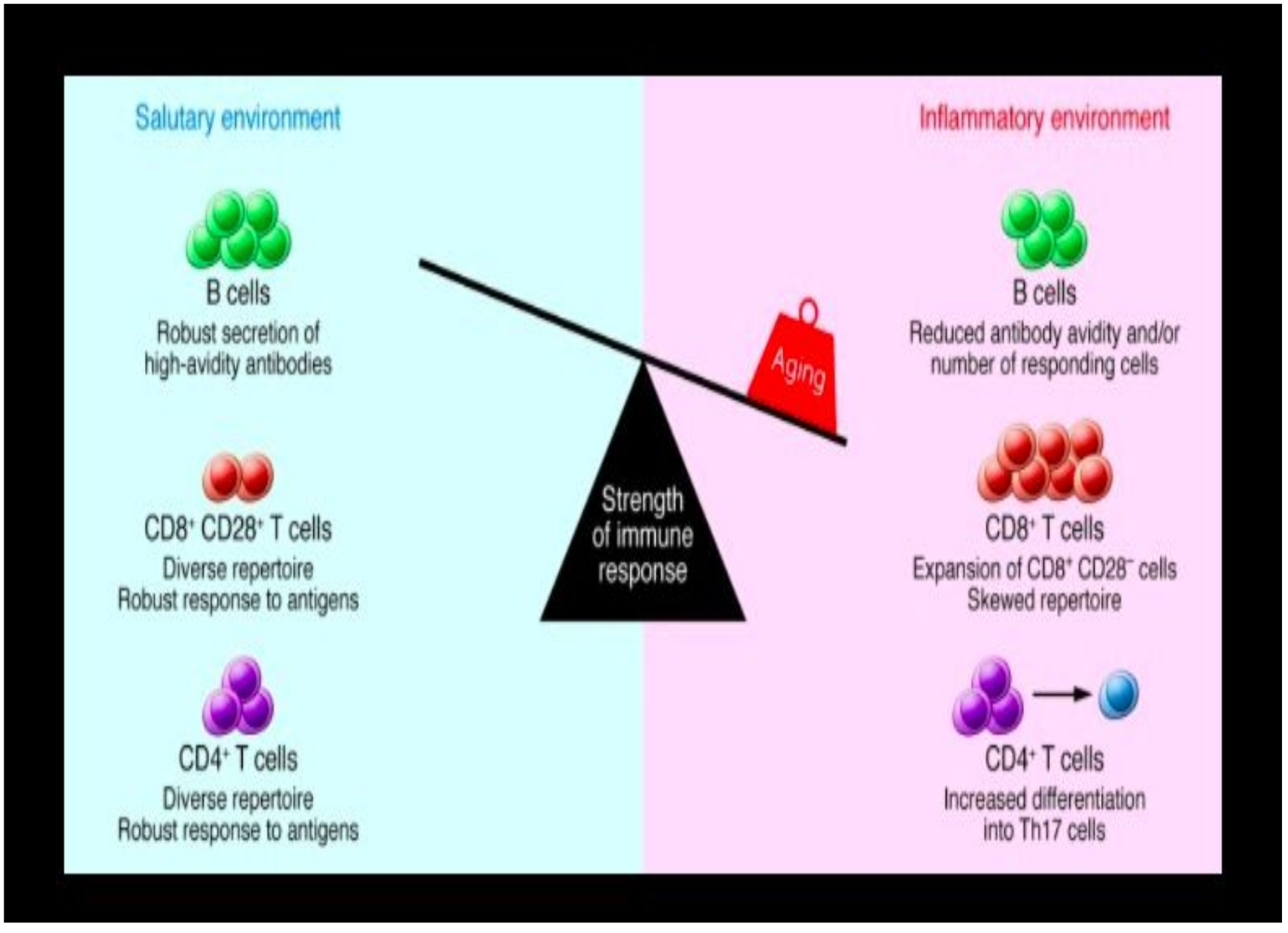
TREAT WELLNESS™

Supplement	Why?	Dosage	*Hyperlink to references
Tier I (Basic)			
Vitamin C (ascorbic acid)	Different studies showed that ascorbic acid (vitamin C) positively affects the development and maturation of T-lymphocytes, in particular NK (natural killer) cells involved in the immune response to viral agents. It also decreases oxidative stress and balances communication between the white blood cells and modulates the cytokine network favorably typical of the body's inflammatory responses. Modulates meaning 'not too much, not too little' inflammation to destroy the virus.	500 mg to 4000 mg daily based on GI tolerance	https://doi.org/10.1016/j.explore.2020.03.007 http://orthomolecular.org/resources/omns/v16n21.shtml https://doi.org/10.3390/nu9040339
Zinc	Studies show "Zinc may prevent coronavirus entry into cells and appears to reduce coronavirus virulence." It is found to inhibit RNA polymerase activity; Zinc + Zinc ionophores have been shown to block SARS-CoV2 multiplication.	15 mg to 30 mg daily, acutely sick up to 100 mg per day for short term use	https://doi.org/10.1016/j.explore.2020.03.007 https://jvi.asm.org/content/91/8/e01564-16 https://doi.org/10.3389/fnut.2014.00014
Omega-3 Fatty Acid	Omega-3 fatty acids have anti-inflammatory properties and promote immune function in cell types such as macrophages and neutrophils.	4000 mg per day but consult your healthcare professional, as can thin blood	https://doi.org/10.3390/ijms20205028
Vitamin D3	Shown in studies to neutralize respiratory viruses in the lung. There is additional evidence that Vitamin D3 decreases inflammasome activation and reduces cytokine IL-1b secretion.	5000 IUs a day Discuss with your physician	https://doi.org/10.4158/EP09101.ORR https://doi.org/10.1136/bmj.i6583 https://doi.org/10.1016/j.explore.2020.03.007 https://www.medrxiv.org/content/10.1101/2020.04.08.20058578v4

Source: Kick COVID-19 to the Curb

Tier III (Advanced)			
Quercetin	Quercetin reduces inflammasome signaling — a complex that activates inflammatory response and cell death. Also found to have Zinc-ionophore activity and may be useful when combined with Zinc (see Zinc above).	Found in onions and apples 250 to 500 mg **BID**	https://link.springer.com/article/10.1007%2Fs10753-017-0542-4 https://pubmed.ncbi.nlm.nih.gov/15668926/ https://www.evms.edu/media/evms_public/departments/internal_medicine/EVMS_Critical_Care_COVID-19_Protocol.pdf
EGCG	EGCG has antiviral activity for a range of viruses by preventing the attachment, entry, and membrane fusion. It is also found to have Zinc-ionophore activity and may be useful when combined with Zinc (see Zinc above).	Derived from green tea	https://doi.org/10.1016/j.explore.2020.03.007 https://pubs.acs.org/doi/pdf/10.1021/jf5014633
Astragalus	This reduces the expressions of cytokines and may restore immune homeostasis by regulating the functions of immune cells. It also is involved in increasing the activity of antioxidant enzymes and reducing lipid peroxidation.	Consult your healthcare professional (Integrative medicine doctors or Traditional Chinese Medicine doctors)	https://doi.org/10.1080/08923973.2019.1637890 https://www.mdpi.com/1420-3049/17/3/3155
Melatonin	Reduces oxidative lung injury and inflammatory cell recruitment during some viral infections, including respiratory syncytial and arboviruses; this supports the immune system. This makes adequate sleep especially important as this is the period of time melatonin is primarily secreted.	0.3 mg to 20 mg	https://www.sciencedirect.com/science/article/pii/S1550830720301130?via%3Dihub https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3850896/

Source: Kick COVID-19 to the Curb


Salutary environment
B cells
Robust secretion of high-avidity antibodies
CD8+ CD28+ T cells
Diverse repertoire
Robust response to antigens
CD4+ T cells
Diverse repertoire
Robust response to antigens
Aging
Strength of immune response
Inflammatory environment
B cells
Reduced antibody avidity and/or number of responding cells
CD8+ T cells
Expansion of CD8+ CD28− cells
Skewed repertoire
CD4+ T cells
Increased differentiation into Th17 cells

ACUTE COVID-19 TREATMENT

- Ivermectin 12 mg SL qd x 3-5 days
- Methylene Blue (MB) 10mg po qd
- MB oral rinse with PDT qid
- TA1 30 units sq qd
- Famotidine 40-80mg bid -tid (decrease if Renal dx)
- To consider: Enoxaparin 60mg qd, Dexamethasone 6 mg qd, Doxycycline 100mg bid vs Azithromycin 250 mg bid

TREAT WELLNESS™

ACUTE COVID-19 TREATMENT

- Supplements:
- Vit C 2500-5000 mg bid, Quercetin 600 tid -1000 mg bid
- Zn 100 mg qd, D3 10,000-50,000 iu qd
- Melatonin 12 mg @HS, ASA 81-325 mg qd (unless CI)
- Omega 3 + DGLA
- Probiotic w/ Lactobacillus and Bifidobacter species

TREAT WELLNESS™

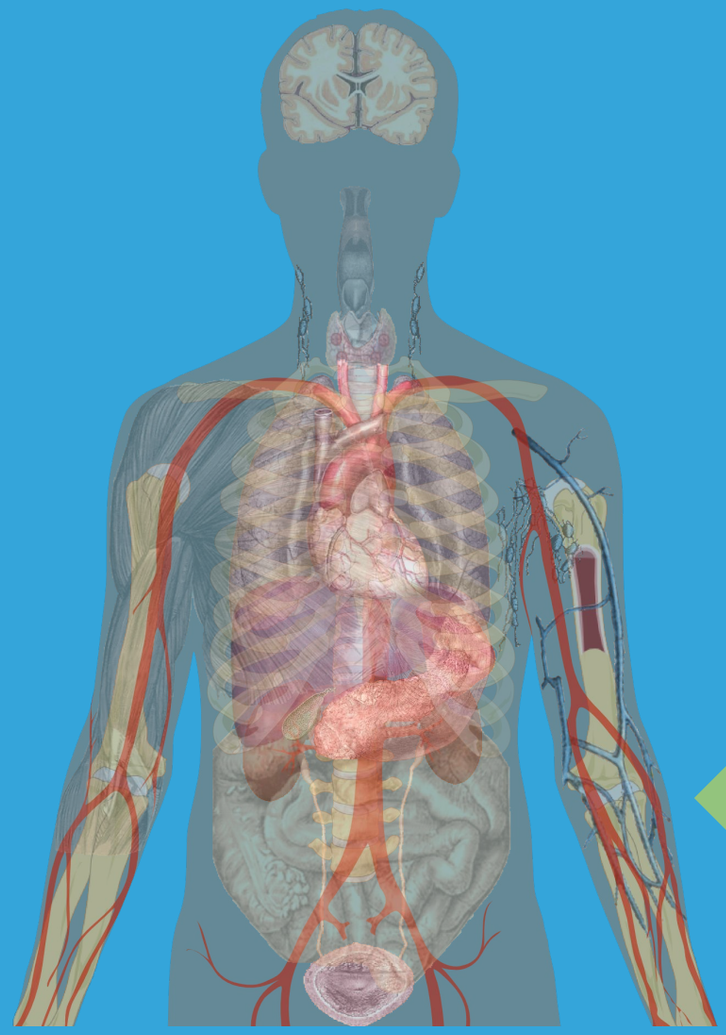
PREVENTION, POST-EXPOSURE PROPHYLAXIS & TREATMENT

- For any Immuno-Rejuvenation Program ……..
- 1.) Remove exposures
- 2.) Replace nutrients, etc
- 3.)Re-inoculate microbiota
- 4.)Rejuvenate the Immune System and Function

TREAT WELLNESS™

External Environment:

- ❏ Diet
  - ❏ industrialized foods
- ❏ Lifestyle
  - ❏ excess stress
  - ❏ lack of movement
  - ❏ excess sympathetic tone
  - ❏ low parasympathetic tone
- ❏ Pollution
- ❏ Radiation
- ❏ Drugs



Exposome:

- ❏ Adjuvants
  - ❏ metals
  - ❏ immune modulators
  - ❏ endocrine disruptors
- ❏ Receptor binding proteins
- ❏ Reactive electrophiles

TEXT

PREVENTION & POST-EXPOSURE PROPHYLAXIS

- Vit C 500 mg bid, Vit D3 3000 iu qd,
- Quercetin 250 bid, Zn 75 mg qd,
- Melatonin SR 0.3-2.0 mg @ HS, Famotidine 40 mg qd,
- Consider Methylene Blue mouthwash qHS w/PDT

TREAT WELLNESS™

LONG HAUL COVID-19 TREATMENT CONSIDERATIONS

- Reduce chronic inflammation at its source
- Support selective immune cell autophagy/mitophagy
- Improve immune cell mitochondrial activity
- Address the sustained tissue-specific inflammation
- Remodel the immune epigenome
- Reset immune function

TREAT WELLNESS™

THYMOSIN ALPHA 1

- 28 aa; homologous aa sequence in bovine, porcine, ovine & humans
- Modulates immune system function
- Pleiotropic mechanisms of action on immune cells; has increase number of intracellular cell signaling pathways associated with adaptogenic immune system stimulation
- Endogenous serum levels via immunoassay: 0.1-1.0 ng/ml

TREAT WELLNESS™

Thymosins: 1960's

- "The physiological processes that these peptides affect include stimulation or suppression of immune responses, regulation of actin dynamics and cell motility, neuroplasticity, repair and remodeling of vessels of the heart and other injured tissues, angiogenesis, and stem cell differentiation. "

TREAT WELLNESS™

THYMOSIN ALPHA 1

- Used in immunosuppression secondary to …
- Age
- Infection
- Cancer
- End Stage Renal Disease
- Other

TREAT WELLNESS™

THYMOSIN ALPHA 1

- Pre-clinical Studies with TA1 in immunosuppressed animals, in animal models of cancer, in animal models for improved vaccine response

- Clinical studies with TA1 —- primary Rx for acute infection, severe sepsis (ARDS), chronic infections (HBV, HCV, HIV), severe acute pancreatitis , COPD with infection, cancer (increase effectiveness of CTX, decrease adverse effects of RX), as vaccine adjuvant

- Cancers studied: HCC, NSCLCa, Melanoma,

TREAT WELLNESS™

THYMOSIN ALPHA 1

- Zadaxin. First licensed in Italy (1993) as vaccine enhancer
- Greater than 20 million doses used clinically in greater than 500,000 individuals
- Excellent safety profile

TREAT WELLNESS™

THYMOSIN ALPHA 1: TLR AGONIST (TLR-9, TLR-2)

- TLR's family of proteins found in myeloid lines and plasmacytoid dendritic cells
- Mediates innate immunity
- Enhances adaptive immune response to viruses, fungi, bacteria and cancer
- Stimulates humoral immunity to increase vaccine effectiveness

TREAT WELLNESS™

THYMOSIN ALPHA 1

- Wide ranging effects include:
- Increase macrophages—> increase phagocytosis of pathogens
- Increase NK cells to fight infection
- Increase differentiation and expansion of stem cells in IC mice
- Increases p38 MAPK pathways
- Increases IC Glutathione

TREAT WELLNESS™

THYMOSIN ALPHA 1: EFFECTS ON T CELLS

- Increase T helper cells
- Increase CD 4 cells
- Increase cytotoxic CD 8 cells
- Increase NK cells
- Increase shift toward TH1 subclass with increased expression of TH1 cytokines— IL 2, IL 7, IL 12, IFN gamma, IL 15

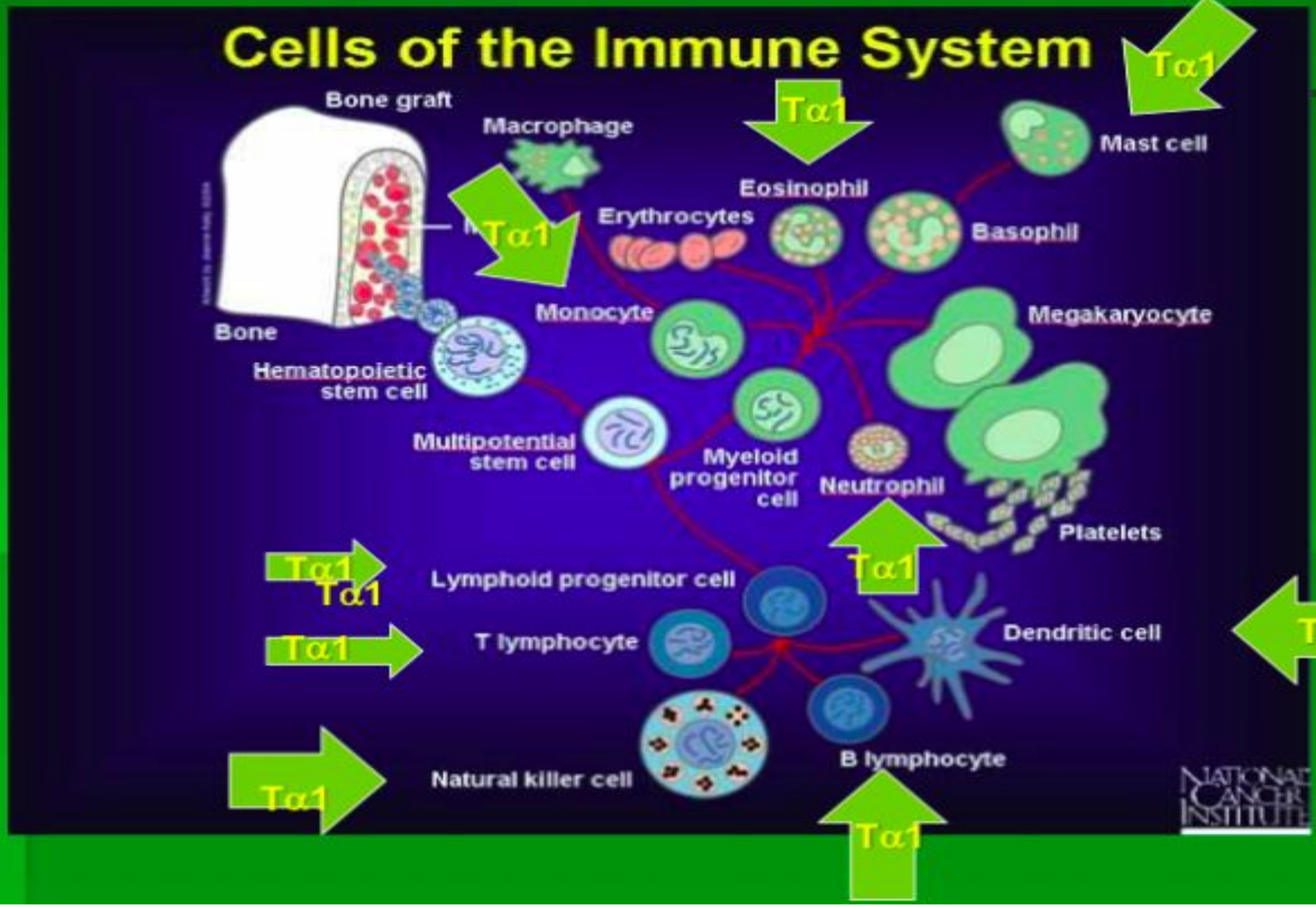
TREAT WELLNESS™

THYMOSIN ALPHA 1

- Activates dendritic cells and macrophages to increase APC's to stimulate B cell differentiation for antibody production
- Increase IDO (indoleamine 2,3 dioxygenase in DC's, which increases FOX P3—> increases IL 10 production, Treg cells, decreasing pro inflammatory cytokines

TREAT WELLNESS™

Thymosin-alpha-1



TA1 is “ADAPTOGENIC”
and MODULATES
INNATE and ADAPTIVE immune systems ”

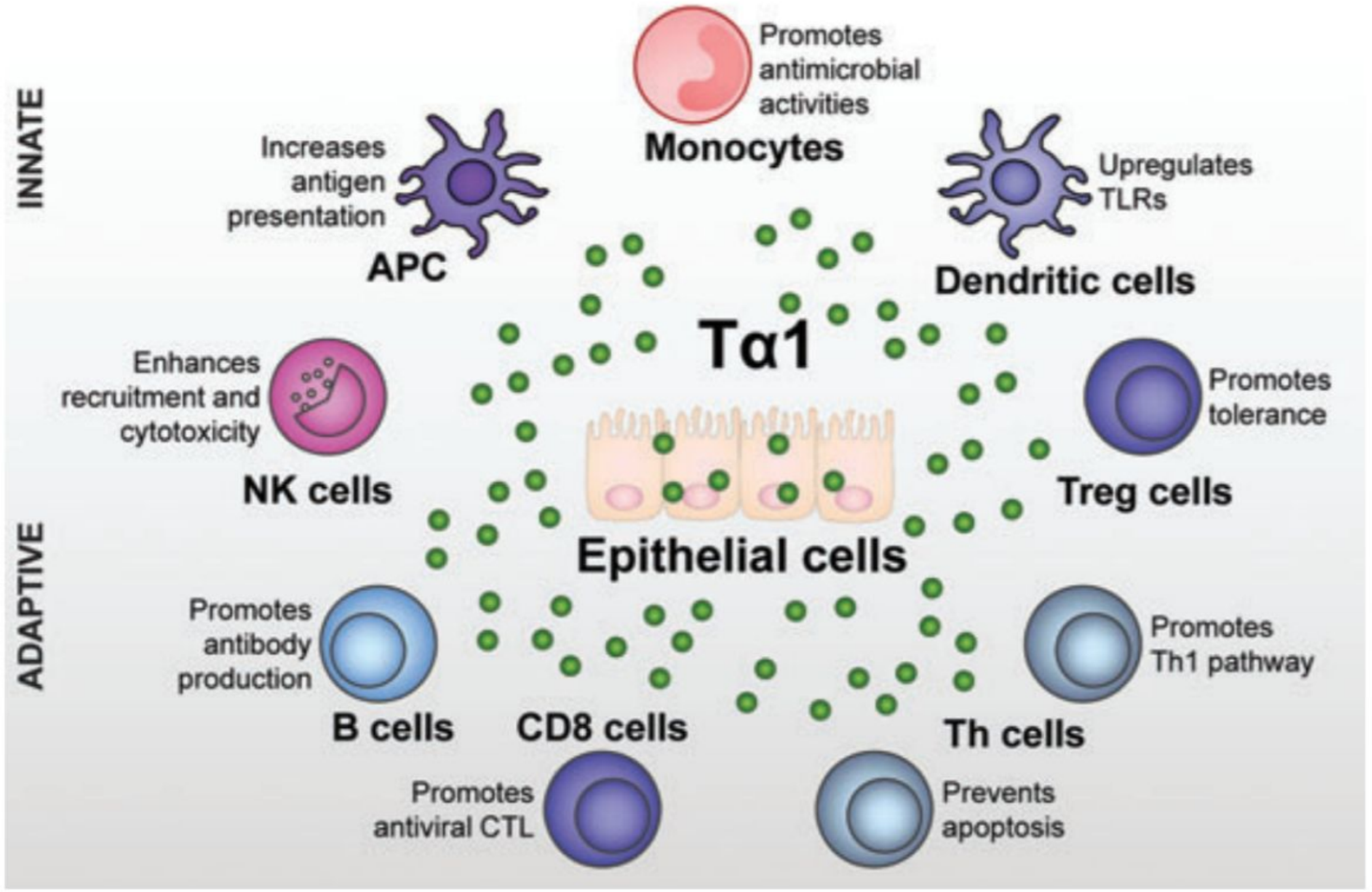


Figure 1. Pleiotropic immune activation by Tα. The drug actions of Tα1 on cells of the innate and adaptive immune system. This is a pictorial representation of all literature-supported actions of Tα1 on immune cells. APC, antigen presenting cells; CTL, cytotoxic T lymphocytes; NK cells, natural killer cells; Th cells, T helper cells; T_{reg} cells, regulatory T cells; TLRs, Toll-like receptors.

Ann. N.Y. Acad. Sci. 1269 (2012) 1–6 © 2012 New York Academy of Sciences.

Thymosin Alpha 1

Approved in over 35 countries; no documented adverse effects; used sq

- Vaccine adjunct
- Treatment of HIV, HBV and HCV
- Very low incidence of adverse effects
- FDA approved under Orphan Drug Program in US

TREAT WELLNESS™

Thymosin Alpha 1
Dose and Side effects

Thymosin A1: 3000 mcg/ml -> 300-1000 mcg sq qd

Very safe and well-tolerated

TREAT WELLNESS™

Summary: Peptide Therapy

- A new therapeutic paradigm
- Understood since the 1960's
- Peptides are gene switches and bioregulators

CASE STUDIES

CASE #1: first seen Jan 13, 2021
15 yof w/ PMS,
insomnia (4 hrs /noc),
headaches,
anxiety with “panic attacks”,
depression with exhaustion and
parents would like to rule out hypothyroidism

15 yo f with multiple symptoms

Labs:

General (Empire), Lab corp (NK cell absolute/%),
Nutreval (mitochondria function),
Cyrex (@ mother's request),
Adrenal testing with urinary NT

15 yof with multiple symptoms

POA at 1st Follow up visit: 2/10/21 (4 wks later)

Omega 3/6
PRP spray + chewables
Tri-salts
B5/B6
ATP 360 (trial of her dad's)
Snacks in pocket for hypoglycemia

IgG
D3

15 yo f with multiple symptoms

At 2nd follow-up, 3 weeks later 3/3/21

Pt feeling “much better”-- a bit more sleep, less nausea, less panic attacks, energy a bit better→ still fatigue→ family considering changing schools

Review NT and Adrenal tests: Adrenal insufficiency

Rx: GABA support in AM/PM and Serotonin support every other day; 1 week later adding Adaptogens (adrenal cortex, adaptogens and vitamin cofactors)

Follow up in 3 weeks Pending

CASE #2 14 yof with insomnia, hives, forehead acne

Telehealth Feb 1, 2021
Labs drawn Feb 3, 2021
1st review 2/22/2021 2nd
review 3/9/2021

Labs:

Empire,
Advanced Intestinal Barrier Assessment (DAO, Histamine)
Methylation Panel

CASE #2 14 yof with insomnia, hives, forehead acne

First Follow up: 2/22/21

Histamine containing & releasing foods - internet -- avocados, spinach, vinegar, aged cheese, tomato soup etc
DeHist
Omega 3 + 6
B12
Intranasal Glutathione
Vit C

CASE #2 14 yof with insomnia, hives, forehead acne

Second follow up: 3/9/21: No hives except anoche with BBQ Sauce: Review Cyrex, Methylation Panel

Gluten/Dairy free, no sauces, (actually doing Keto at present)

Plan: keto-GREEN, inositol, eggs (choline), Zinc, Iron, Potassium, B vitamin support (B2, B3, B6 , B9, B12)

Follow up in 4 weeks, sooner PRN

Case #3: 19 yo m college athlete with fatigue

CC: unable to finish his workouts and poor recovery index

Labs: Empire
Stool testing
Nutreval

Thank YOU!

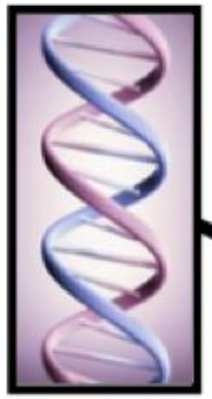
Kathleen O'Neil-Smith, MD, ABAARM

Treat Wellness, LLC
MA

treat-wellness-llc.com

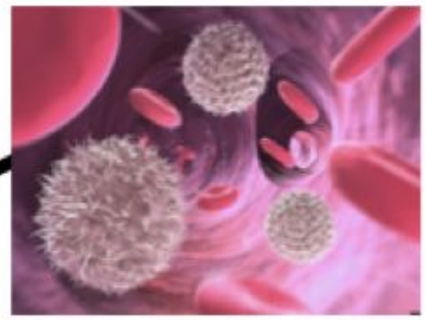
Recipe For Immune Mediated Diseases

Which Ingredients Are Necessary?

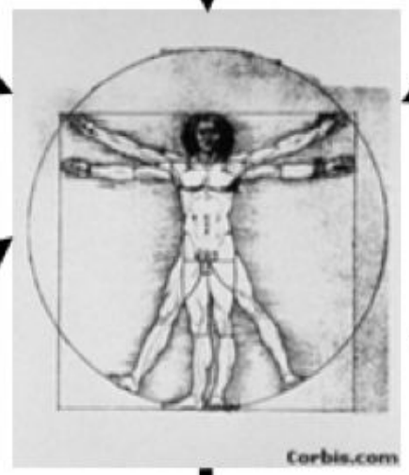


Human Genome

Increased Gut Permeability



Immune Response



Environmental Factors

Microbiome

Reference Box

Regenology

https://www.advancednutrients.com/articles/harvesting-big-buds/

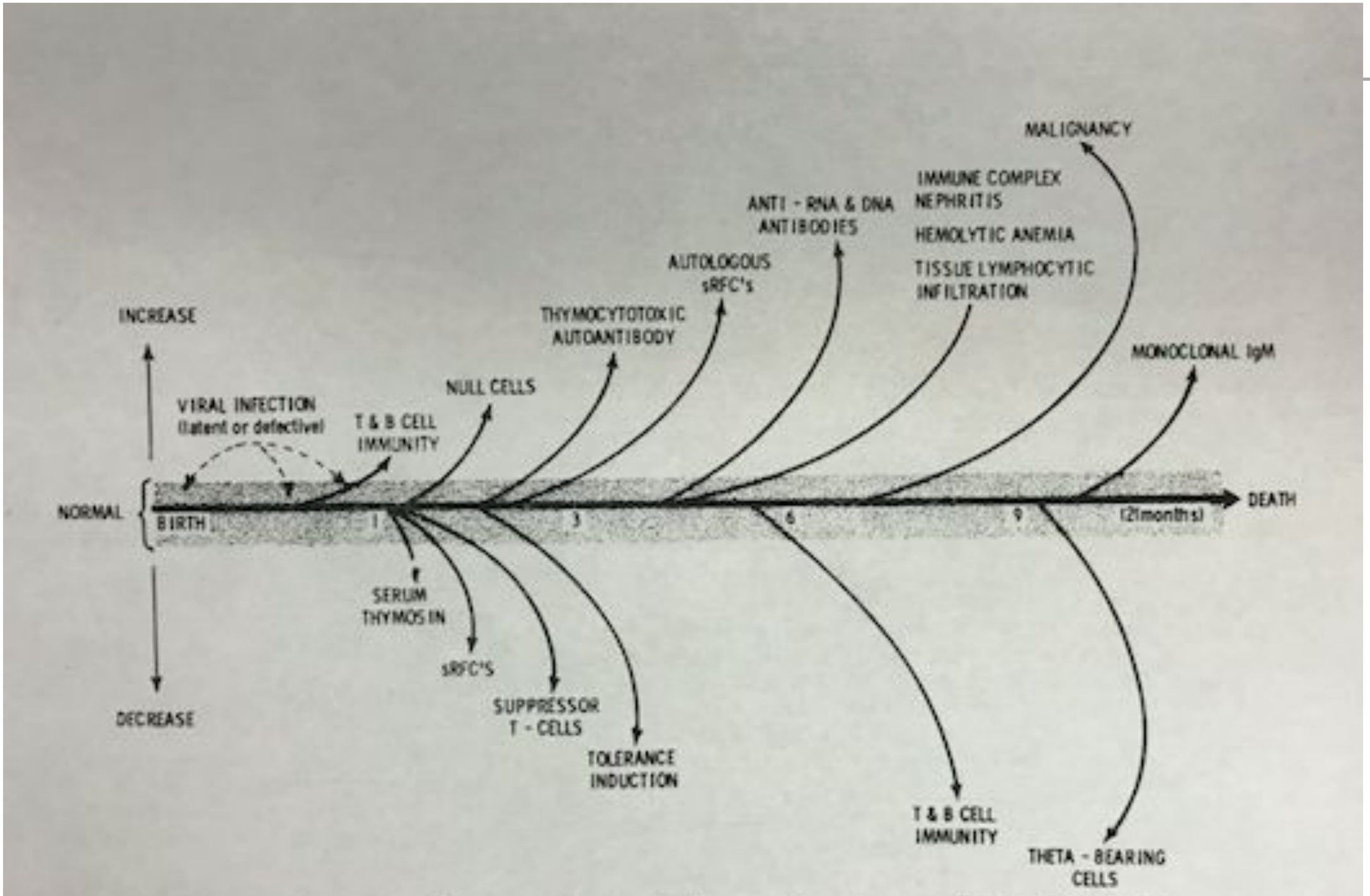


FIGURE 1. Immunological events during the development of autoimmune disease in NZB mice.

Goldstein L. et al./ Ann N Y Acad Sci. 1976;274:390-401

PACS: Post Acute COVID Syndrome