Maintaining Immune Health in the Face of COVID-19 and Future Viruses
Webinar: Maintaining Immune Health in the Face of COVID-19 and Future Viruses

Presentation Slides: Nir Barzilai, MD
Disproportionate death in older adults with COVID-19 - Data from China, EU and US

Fight the virus, defend the host!
Not only for COVID-19 but future viruses
Anything hopeful about aging that is relevant to defending the host against COVID-19?

Aging has a biology that can be targeted! (Geroscience)

**Gero-protectors** can revert the decline in immunity and increase the resiliency to sickness in older adults

How do we defend the older adults?
Aging is the strongest risk factor for all age related diseases...

Aging drives diseases

Geroscience

Hallmarks of Aging

- Decrease in chromosome maintenance (DNA repair efficiency) (Telomere erosion)
- Epigenetic Changes
- Metabolic Dysregulation
- Immune Dysfunction
- Proteostasis failure
- Accumulation of senescence cells
- Decrease in quality and quantity of Mitochondria
- Inflammation

Bedside problems:

- Sleep
- Immunity
- Circulation
- Skin
- Thermoregulation
- Cognition
- Mobility
- Strength
- Weight
- Balance

1) Increase immunity
2) Increase the body ability to sustain serious illness!
• Healthspan & lifespan has been extended in numerous animal models.
• Relevant drugs have been used in humans. (Metformin, Rapamycin,....)

Dietary restriction extends lifespan (rats)

Rapamycin + metformin (ITP)
Webinar: Maintaining Immune Health in the Face of COVID-19 and Future Viruses

Presentation Slides: George Kuchel, MD, FRCP, AGSF
What is it about immune aging that makes older adults so vulnerable to COVID-19?

George A. Kuchel, MD, FRCP, AGSF
Travelers Chair in Geriatrics and Gerontology
Director, UConn Center on Aging, University of Connecticut
Chief, Geriatric Medicine, UConn Health

kuchel@uchc.edu
Vulnerability of Older Adults to COVID-19:
Nearly all aspects of immune response and host defense are impacted by aging

Sungnak et al. Nature Med 2020
Vulnerability of Older Adults to COVID-19: Impact of Immune Aging on Ability to Handle Familiar and Unfamiliar Pathogens

Immune Cell
Aged Immune Cell
Pathogen

Acknowledgements to G Hargis & C Bonin, UConn
Vulnerability of Older Adults: Must consider dynamic processes involving resilience mechanisms needed to maintain homeostasis in the face of a stressor (pathogen).

**SARS-CoV-2 VIRUS**

- Virus
- Mechanisms to Infect Cells or Replicate

**IMMUNE DEFENSES**

- Strong

**HEALTH & FUNCTION**

- Infection
- Recovery

**Role of Biological Aging**

- Virus virulence, quantity, length of exposure

**Strengthened Vaccines**

- Antiviral drugs

**Geroprotectors**

- Dynamic processes involving resilience mechanisms needed to maintain homeostasis in the face of a stressor (pathogen)

Artwork by Geneva Hargis, UConn
Potential Role of Another Geroprotector (Metformin) in Reducing Onset and Progression of Multiple Chronic Diseases

*TAME Trial (Targeting Aging with Metformin)*

Inclusion Criteria: Age 65-80, nondiabetic, some comorbidities allowed; n = 3,000

Double blind placebo-controlled trial

Primary Outcome: TIME TO MAJOR DISEASES (FDA)
Secondary Outcome: FUNCTIONAL AGING
Tertiary Outcomes: BIOMARKERS (NIA)

Impact of Metformin on Flu Vaccine Responses (VEME-AFAR/NIA, Jenna Bartley, PhD - UConn)

UCONN CENTER ON AGING
Potential Role of One Geroprotector (RTB101) in Reducing Respiratory Infections

Phase 2b: RTB101 reduces the incidence of respiratory tract infections caused by multiple viruses including coronavirus.

Pathogen associated with laboratory-confirmed RTIs:
- Coronavirus: RTB101 10mg QD (7 vs. 15 in Placebo)
- Metapneumovirus: RTB101 10mg QD (3 vs. 5 in Placebo)
- Rhinovirus/Enterovirus: RTB101 10mg QD (7 vs. 16 in Placebo)
- Influenza A: RTB101 10mg QD (7 vs. 9 in Placebo)
- Influenza B: RTB101 10mg QD (3 vs. 7 in Placebo)
- Parainfluenza: RTB101 10mg QD (2 vs. 2 in Placebo)
- Respiratory Syncytial Virus: RTB101 10mg QD (2 vs. 7 in Placebo)

UCONN CENTER ON AGING
Webinar: Maintaining Immune Health in the Face of COVID-19 and Future Viruses

Presentation Slides: Janet Lord, FMedSci
Taking the Fight to Coronavirus: Exercise and Nutrition

Professor Janet M Lord FMedSci
Director of the Institute of Inflammation and Ageing
Director of the MRC-Versus Arthritis Centre for Musculoskeletal Ageing Research
The Aged Body and COVID-19

Inflammaging

Human Nasal cells

Ace2 expression

Contrl IL4  IL17A  IFNγ IFNα2

Modified from Sungnak W et al (2020)

Skeletal Muscle – A key immune regulator

- Muscle releases Myokines
  - IL6, IL7, IL15, MNRTL

- Macrophages
  - ↑ IL10
  - ↑ IL-RA
  - ↓ TNF

- NK cells
  - ↑ Killing Virus infected cells
  - ↑ Cell numbers

- Fat
  - ↓ inflammatory macrophages
  - ↓ Adipokines

Graphs and data:

1. CRP (mg/l) vs. Physical Activity Status
   - Sedentary
   - Moderate
   - Trained

2. TNF (pg/ml) vs. Steps per day
   - Young
   - Old
   - Cyclists
   - Duggal NA et al (2018)
Recovery after COVID-19

- COVID-19 patients experience extreme fatigue, meaning they exercise less.
- Patients can be bed bound for several weeks, losing muscle as a result (1kg of muscle can be lost per week of bed rest).
- Regular exercise, especially resistance exercise, is important to regain muscle and help immune function.

Foster MA et al (2020) JCEM
The gut microbiome (bacteria) has a major influence on the immune system, including inflammation.

- Antibiotics often given to Covid19 patients destroy the gut bacteria.
- Eating a diet high in fruit and vegetables helps to have a healthy gut.

Vitamin D enhances immune function, and also is important for muscle health.

Zinc has been shown to reduce infections.

4 weeks on a diet low in carbohydrates (the paleo diet) has been shown to reduce inflammation (Gyorkos et al, 2019)
Summary

• Older adults account for most of the mortality due to COVID-19.

• The biology of aging drives diseases of aging, underlying the cause for this excess mortality.

• Hallmarks of aging are targets for gero-therapeutics.

• Exercise is immune modulator and a resiliency builder.

• Metformin and mTOR inhibitors maybe modulating response to viral infection in older adults.

• Interaction between environment (exercise and nutrition) and drugs can: 1) target immune decline and inflammaging and 2) increase whole body resiliency to severe illness.

• This is relevant to future pandemics, blinded to cause.