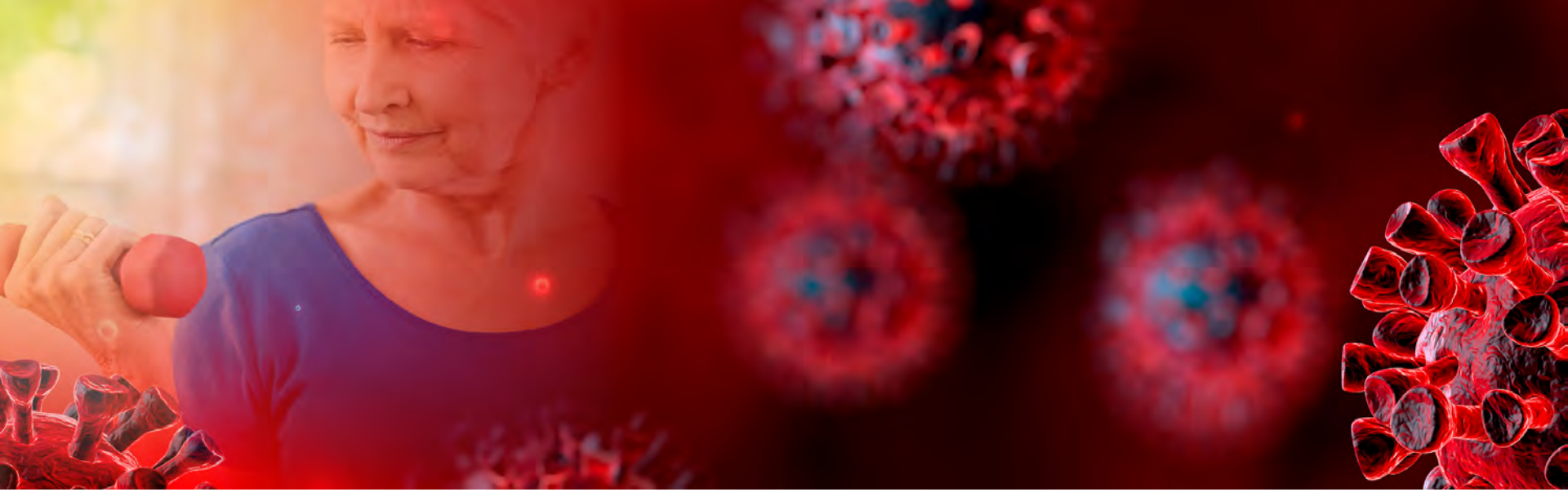

# *Maintaining Immune Health in the Face of COVID-19 and Future Viruses*

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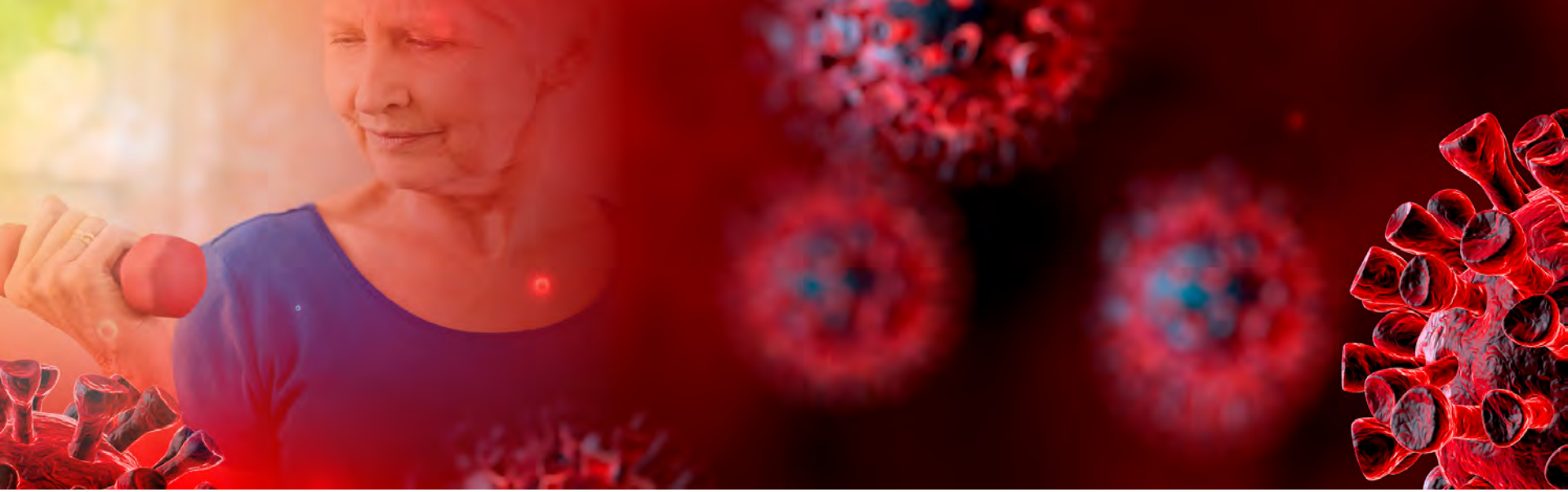

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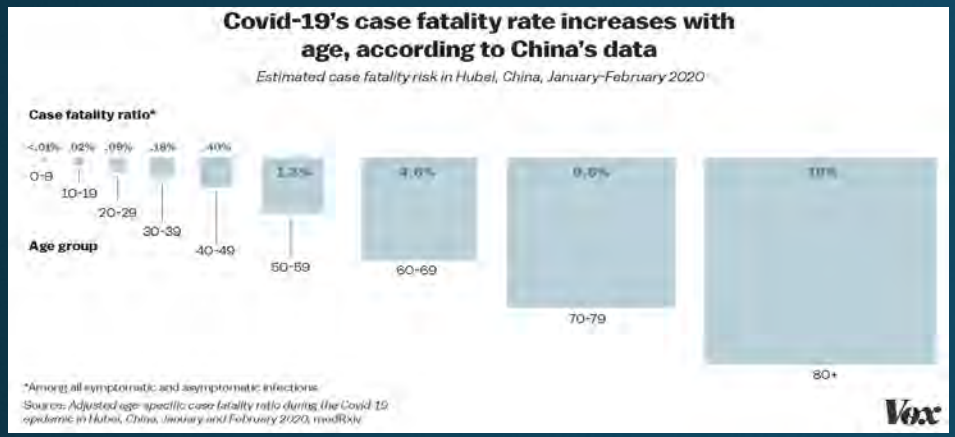
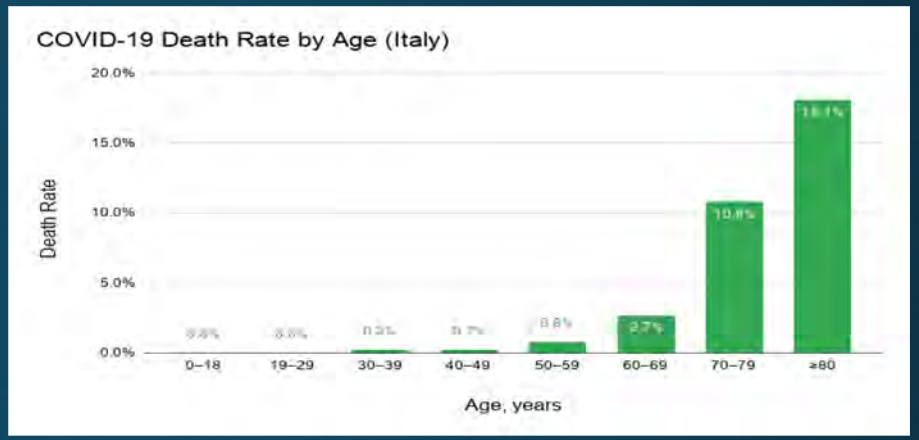
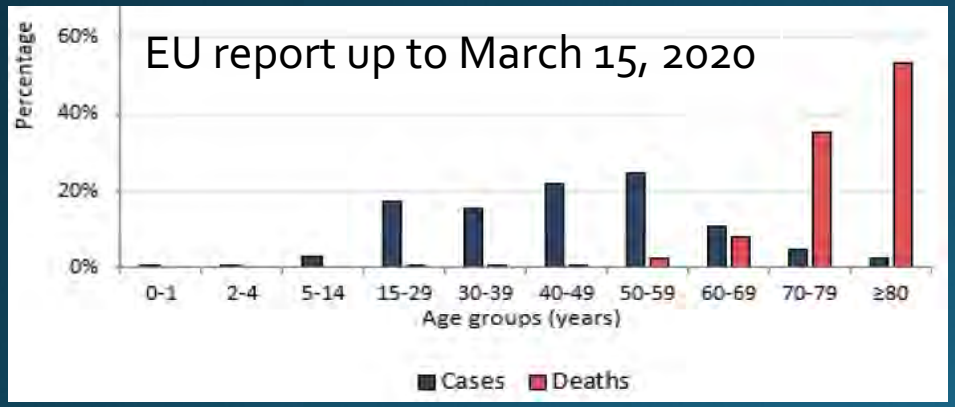
# *Webinar: Maintaining Immune Health in the Face of COVID-19 and Future Viruses*

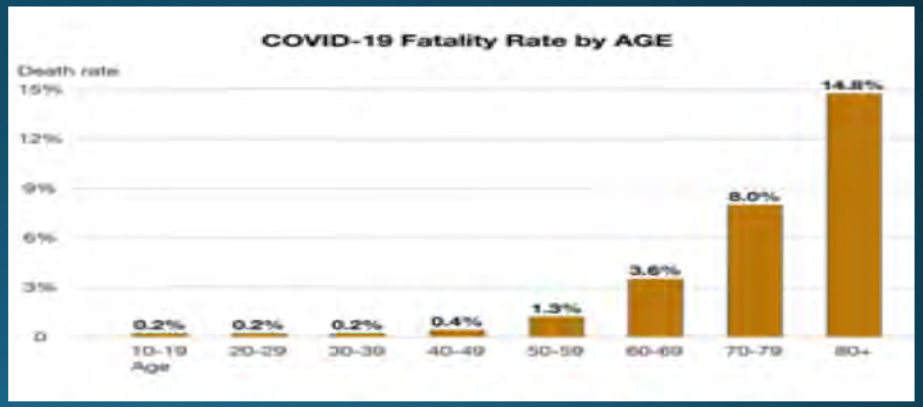
Presentation Slides: Nir Barzilai, MD

# 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?

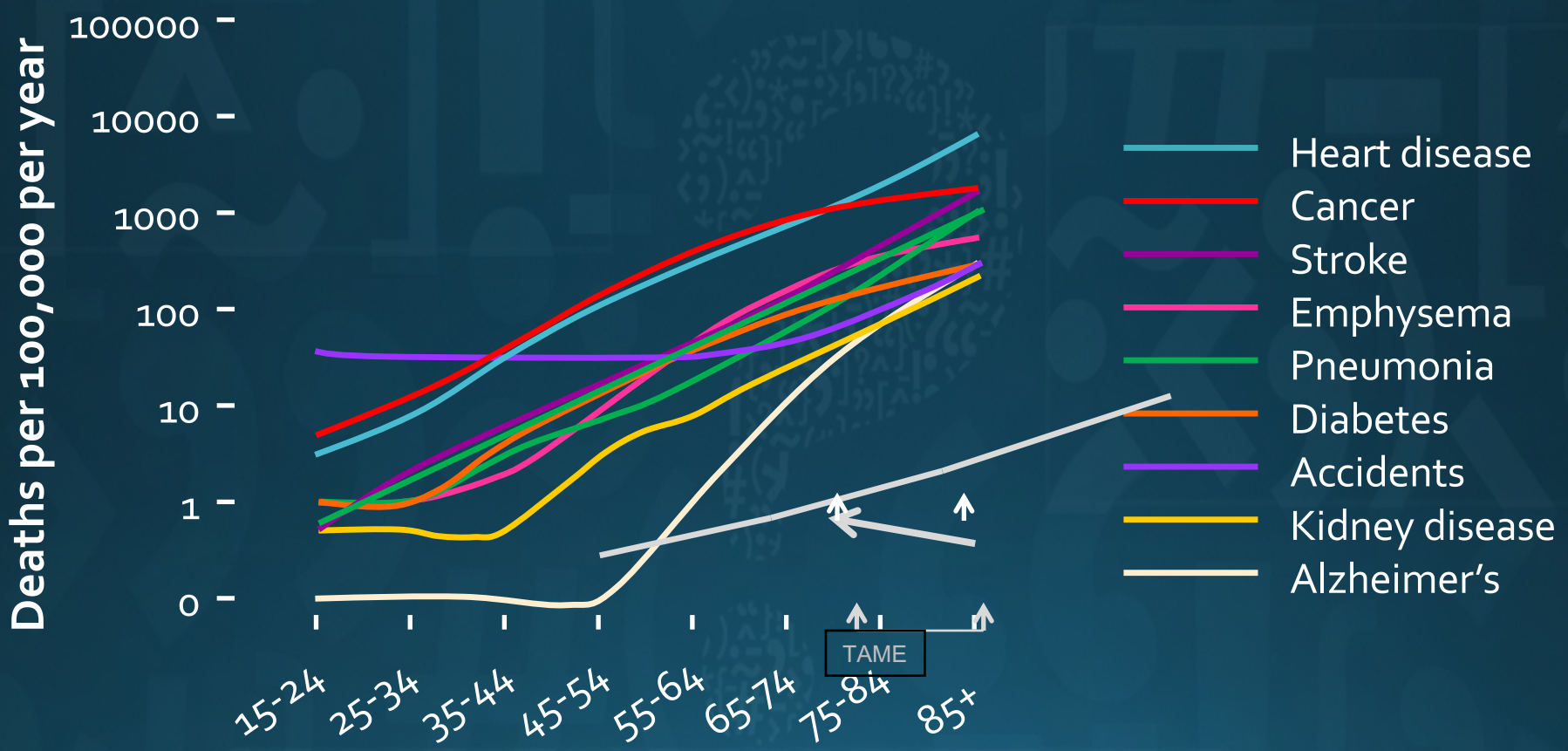
Aging has a biology that
can be targeted!
(Geroscience)

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…

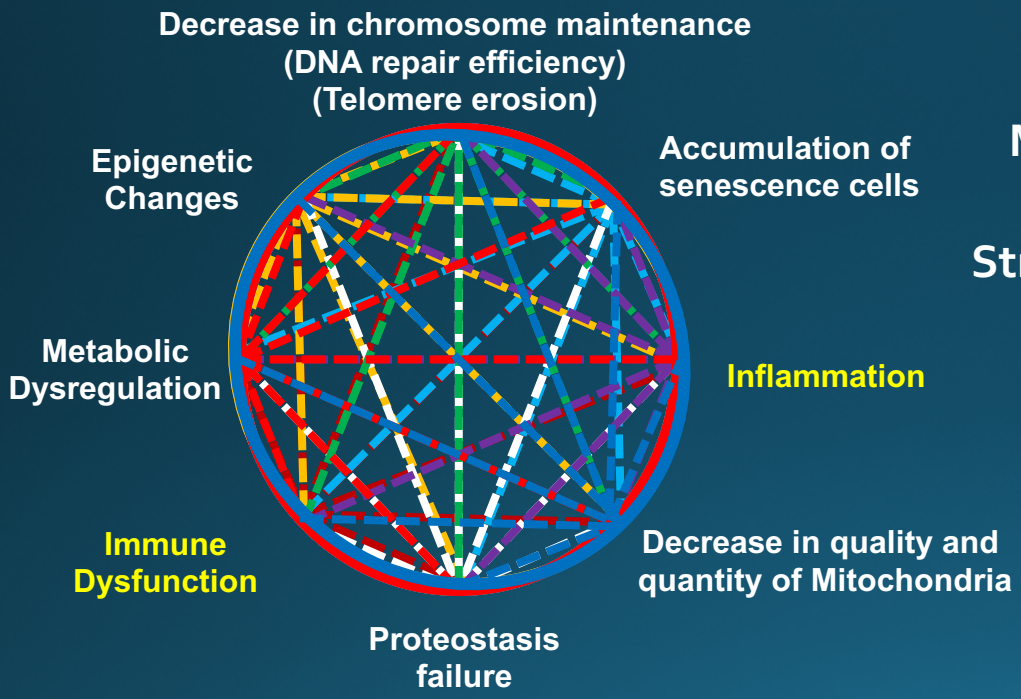
## Aging drives diseases



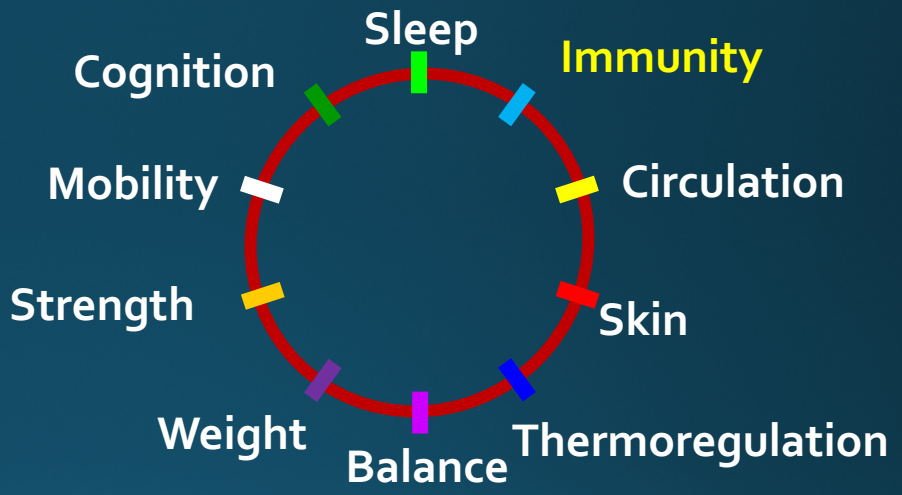

Source: The Milbank Quarterly, Vol. 80, No. 1, 2002 from 1997 U.S. Vital Statistics

# Geroscience

## Hallmarks of Aging



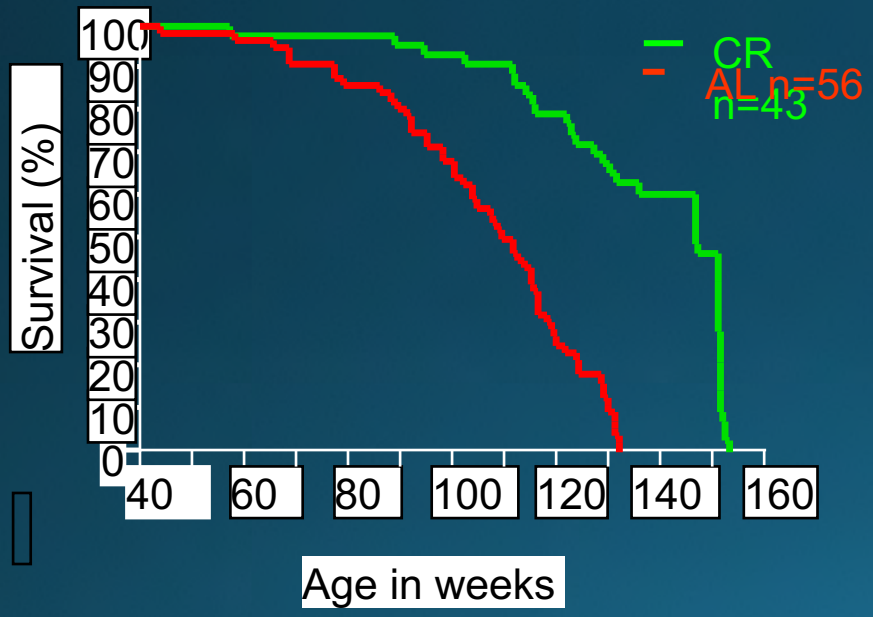

## Bedside problems:



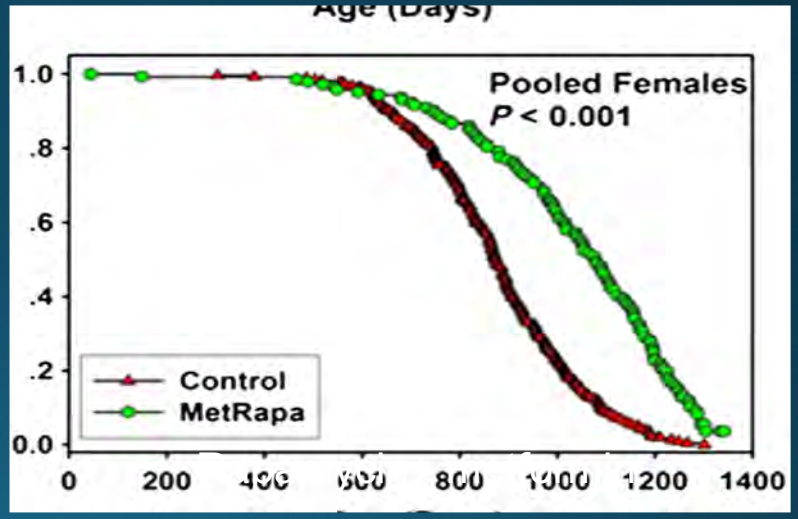

1) Increase immunity
2) Increase the body ability to sustain serious illness!

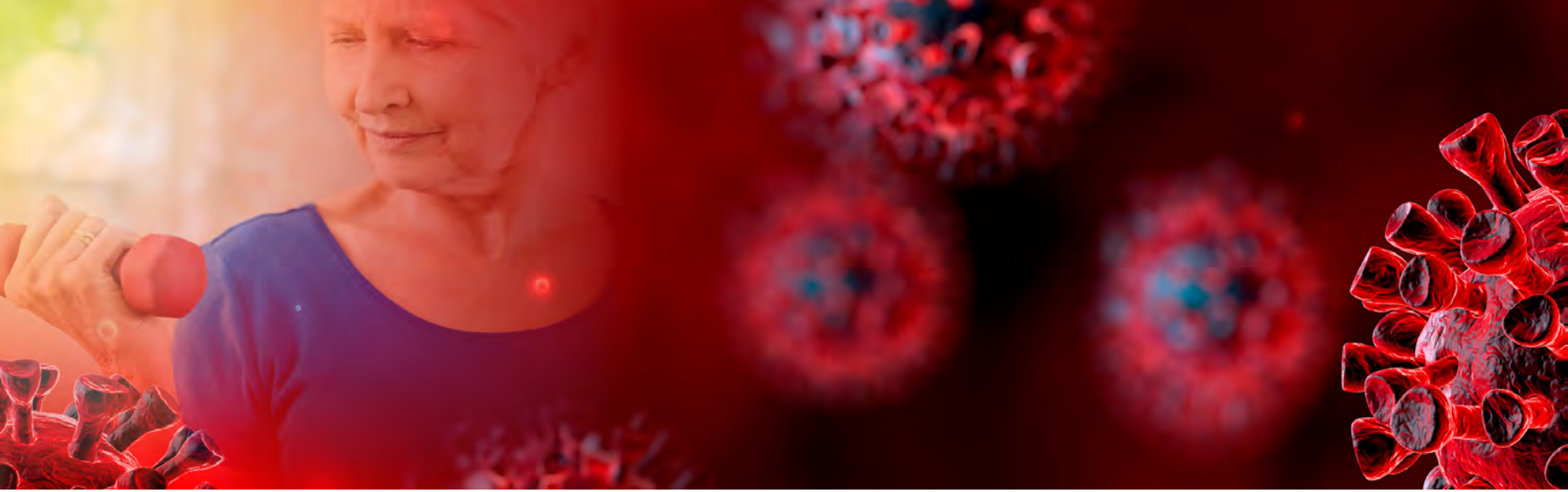
- **Healthspan & lifespan has been extended in numerous animal models.**
- **Relevant drugs have been used in humans.**
  **(Metformin, Rapamycin,….)**

**Dietary restriction extends lifespan (rats)**




**Rapamycin + metformin (ITP)**





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# *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



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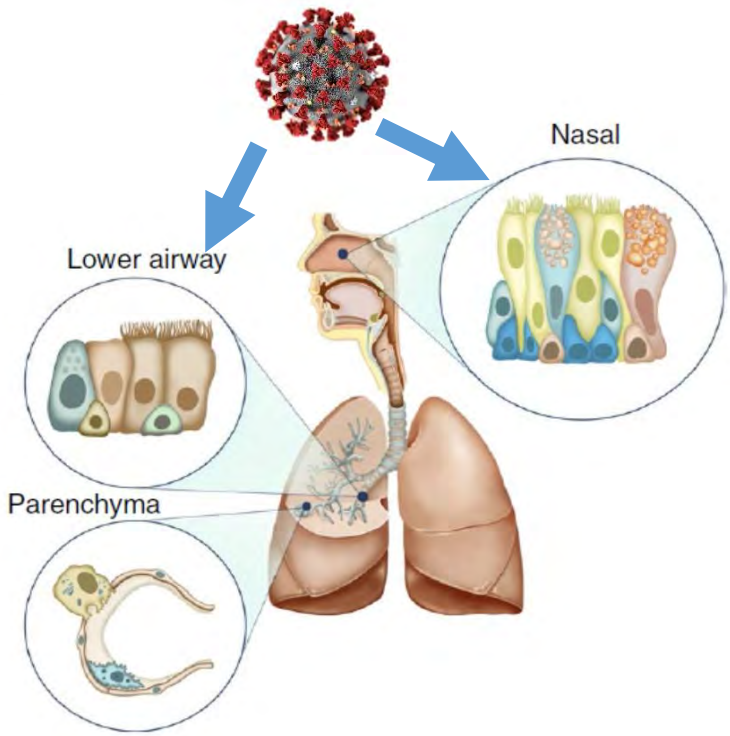
# Vulnerability of Older Adults to COVID-19:

*Nearly all aspects of immune response and host defense are impacted by aging*




List of epithelial cells

| Nasal | Lower airway | Parenchyma |
|---|---|---|
| Goblet 1 | Basal 1 | Alveolar type I |
| Goblet 2 | Basal 2 | Alveolar type II |
| Ciliated 2 | Ciliated 1 | |
| | Club | |

Sungnak *et al.* Nature Med 2020

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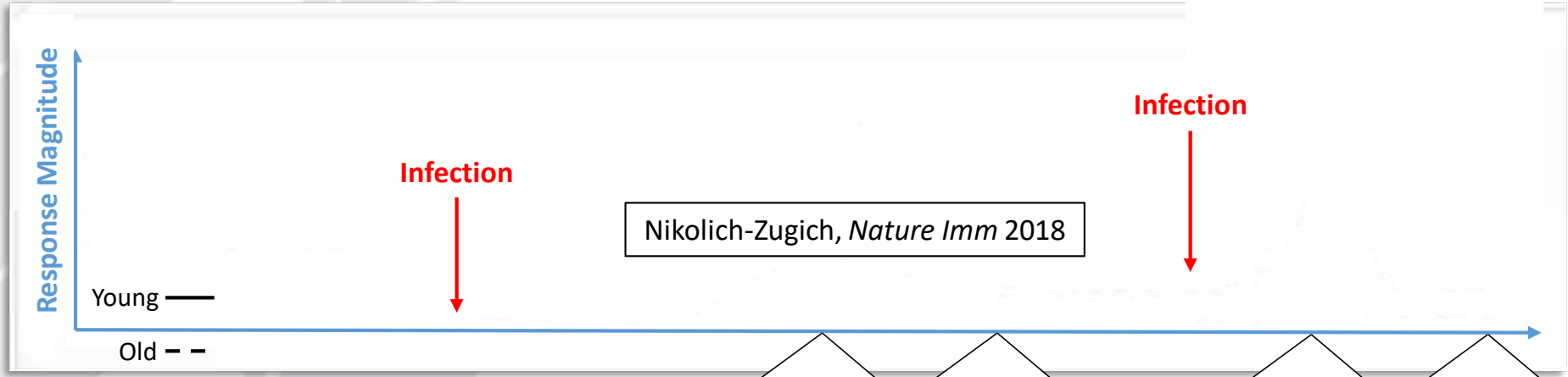
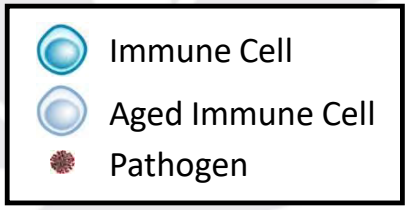
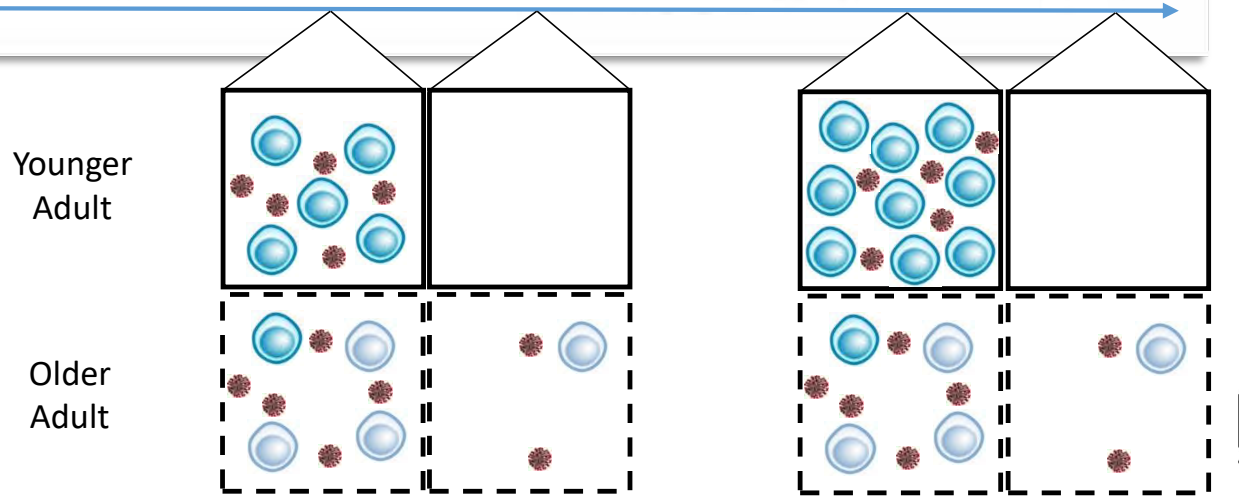
# Vulnerability of Older Adults to COVID-19:

## *Impact of Immune Aging on Ability to Handle Familiar and Unfamiliar Pathogens*




Acknowledgements to G Hargis & C Bonin, UConn

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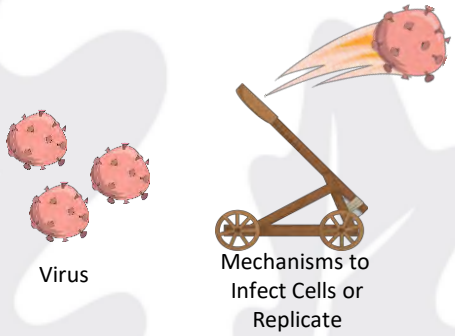
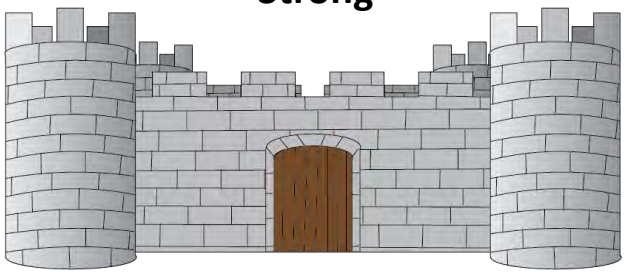
**Vulnerability of Older Adults:** Must consider dynamic processes involving resilience mechanisms needed to maintain homeostasis in the face of a stressor (pathogen)

## SARS-CoV-2 VIRUS

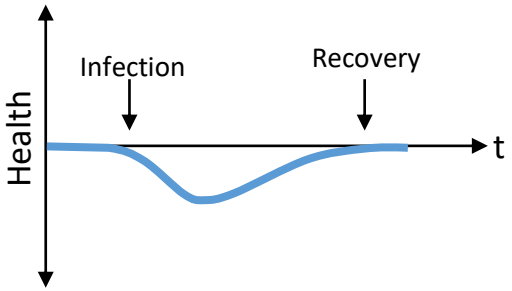



## IMMUNE DEFENSES

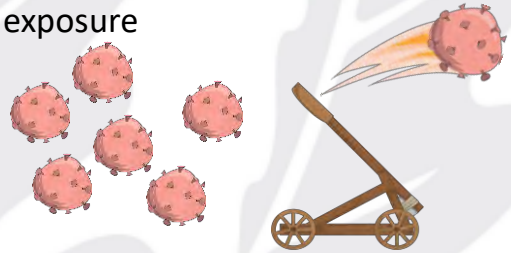
**Strong**



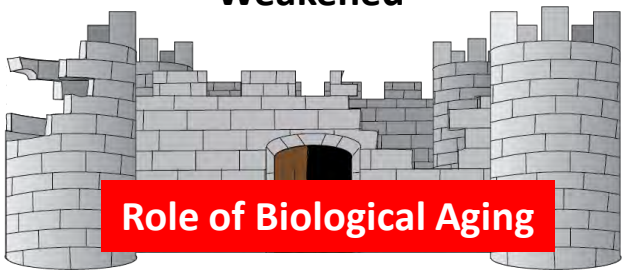
## HEALTH & FUNCTION

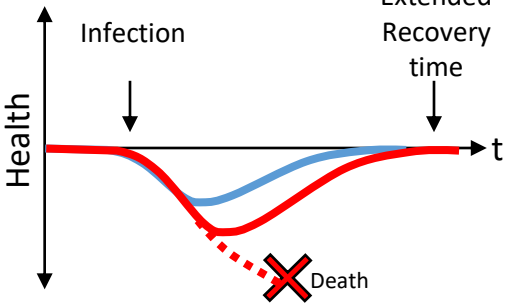



Virus virulence, quantity, length of exposure



**Weakened**

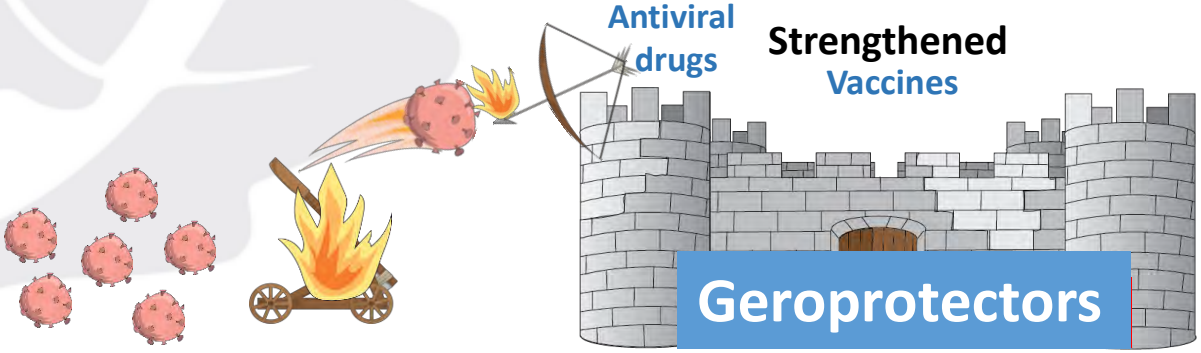


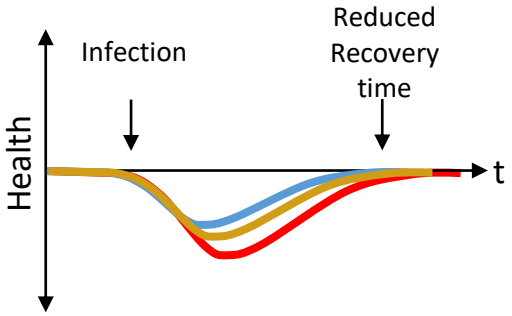




Antiviral drugs

**Strengthened**

Vaccines




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)**

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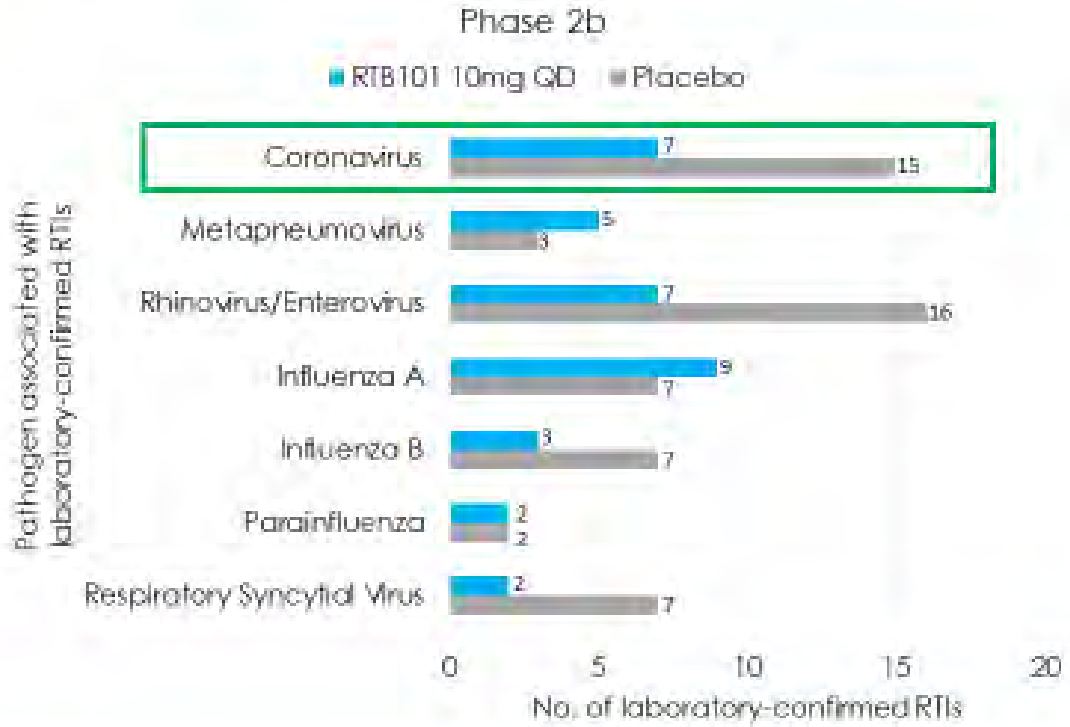
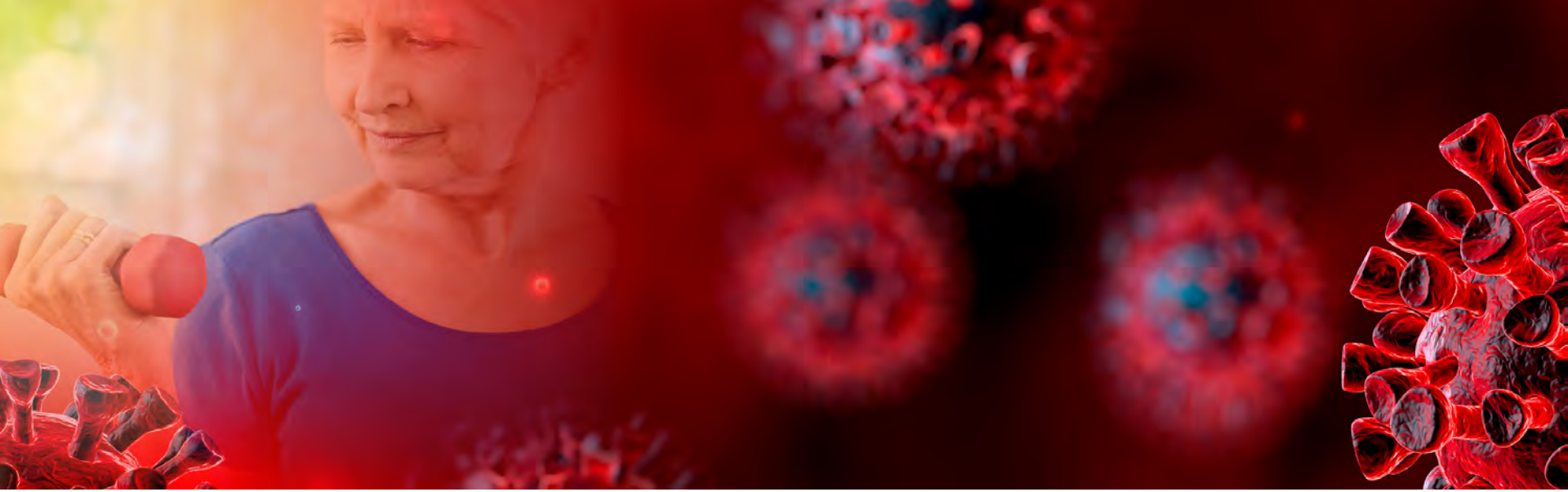
# Potential Role of One Geroprotector (RTB101) in Reducing Respiratory Infections

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





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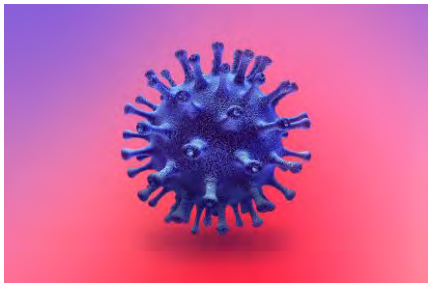
# *Webinar: Maintaining Immune Health in the Face of COVID-19 and Future Viruses*

Presentation Slides: Janet Lord, FMedSci

UNIVERSITY OF BIRMINGHAM

INSTITUTE OF INFLAMMATION AND AGEING

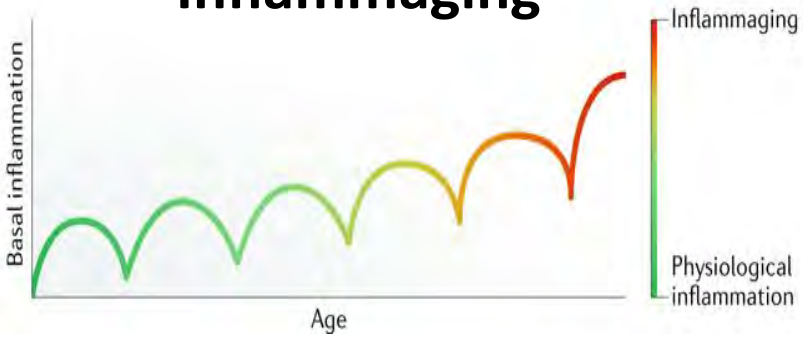


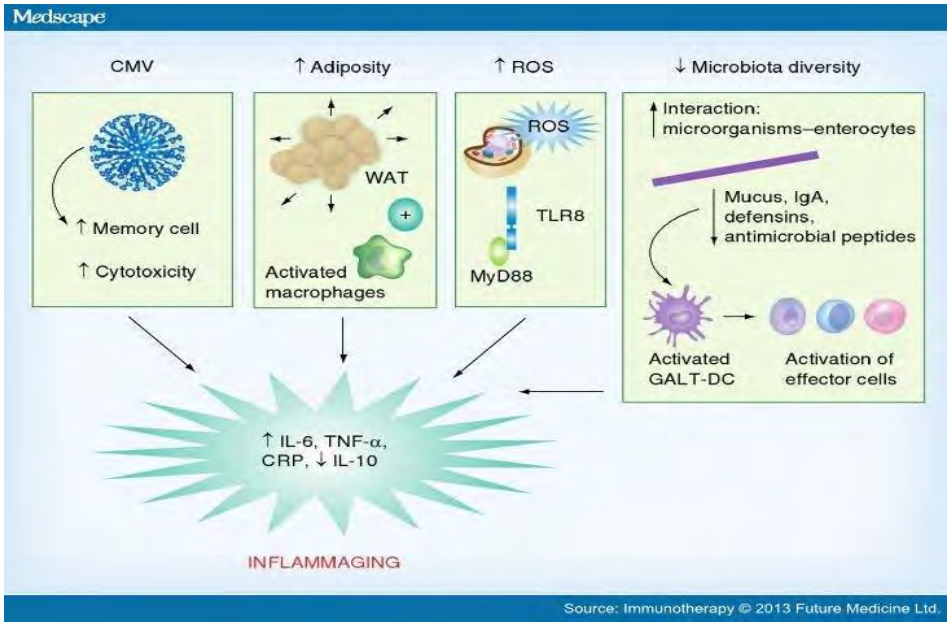
# Taking the Fight to Coronavirus: Exercise and Nutrition

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

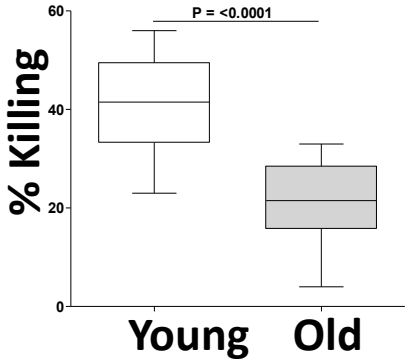
## Inflammaging




## Human Nasal cells


Modified from Sungnak W et al (2020)




Hazeldine J et al (2012)

UNIVERSITY OF BIRMINGHAM | INSTITUTE OF INFLAMMATION AND AGEING

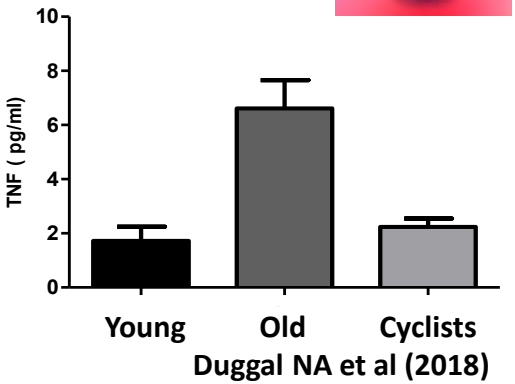
# Skeletal Muscle – A key immune regulator

**Muscle releases Myokines**

**IL6, IL7, IL15, MNRTL**

## Macrophages

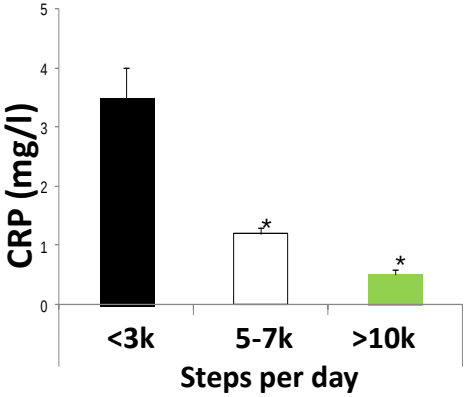
↑IL10
↑IL-RA
↓TNF



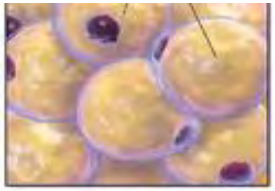

Duggal NA et al (2018)

## NK cells

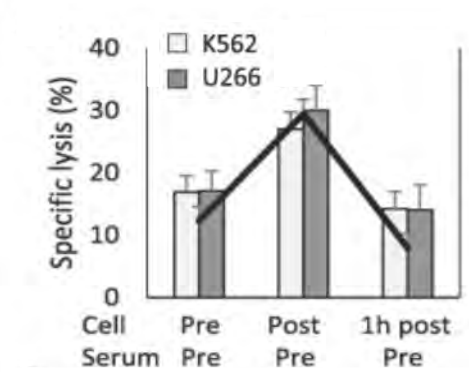
↑ Killing Virus infected cells
↑ Cell numbers




## Fat

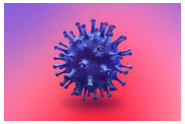


↓ inflammatory macrophages
↓Adipokines

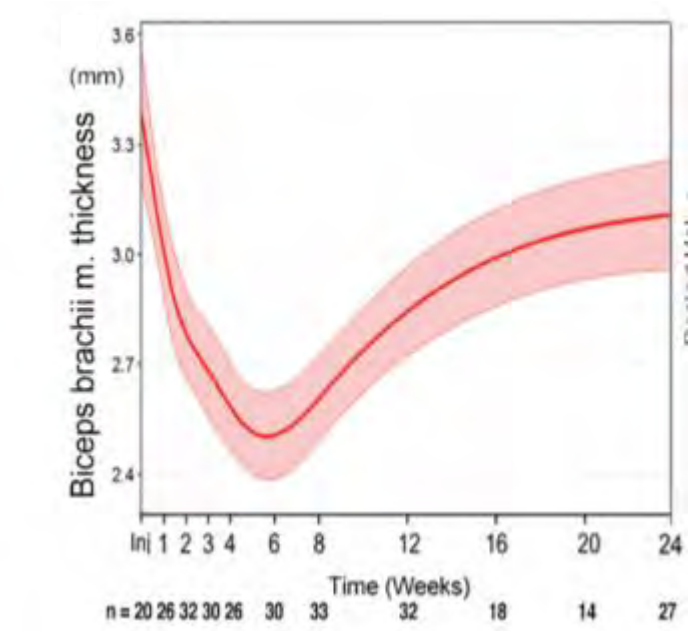



Gupta P et al (2018)

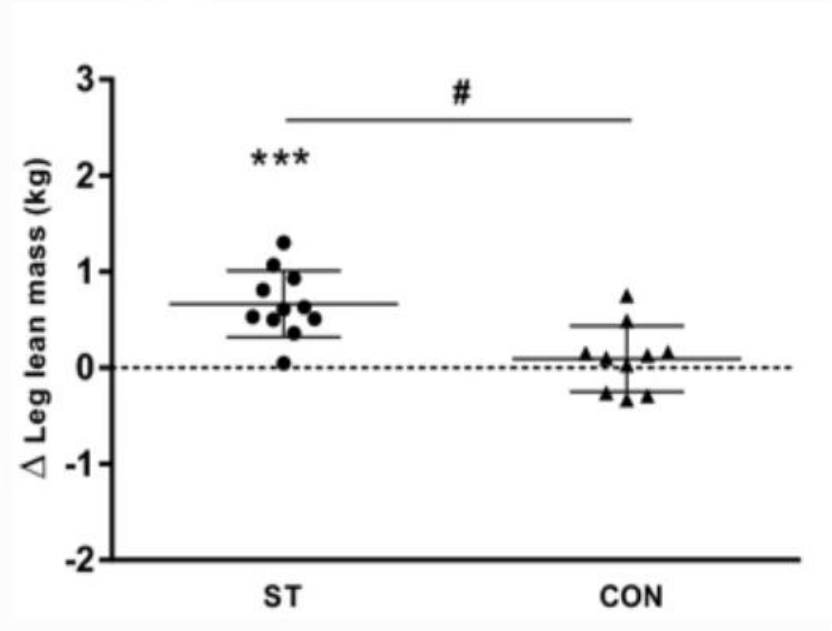
# Recovery after COVID-19



- 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.

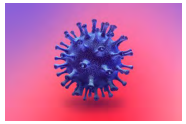



Foster MA et al (2020) JCEM




Aas SN et al (2020) Aging Clin Exp Res

# Nutrition and Immunity



- 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.