WEBINAR: COVID-19: Can the Science of Aging move us Forward?
March 24, 2020
Vulnerability of Older Adults to COVID-19: Importance of frailty, biological aging and geroscience-guided therapies

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Vulnerability of Older Adults to COVID-19: Importance of frailty, biological aging and geroscience-guided therapies

According to CDC highest Risk Populations for COVID-19 deaths include:
• Older adults
• All individuals (but especially older adults) with chronic diseases
• These may include heart and lung disease, diabetes and others
• Older men are at greater risk than older women
• What does this all mean?

Is date of birth (chronological aging) the best measure? Frailty, chronic diseases, physiology, social factors and biology add essential clinical information

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Acknowledgements to J McElhaney
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Experience from influenza (flu) vaccination:
• All older adults should be vaccinated
• Older adults represent over 90% of all flu-related deaths in most years
• Vaccine is 80% effective in preventing flu-related hospitalization in non-frail older adults, yet it is less effective in those who are frail (Andrew MK et al. J of Infectious Diseases 2017)
• Declines in antibody and cell-mediated responses seen with aging (Nikolich-Zugich, Nature Imm 2018)
• These are augmented by frailty, chronic diseases, physiological aging (McElhaney et al, Front Imm 2016)

Potential lessons for COVID-19 and future pandemics involving novel pathogens:
• Inevitable delays in vaccine and drug development impact mostly the most vulnerable
• A geroscience-guided approach designed to target biological drivers shared by aging and common chronic conditions could improve clinical outcomes against varied novel pathogens long before pathogen-specific vaccines and drugs become available (J. Mannick)
• COVID-19 vaccine will most likely be less effective in older adults with chronic conditions
Vulnerability of Older Adults to COVID-19:
Impact of Immune Aging on Ability to Handle Familiar and Unfamiliar Pathogens

Infection Response Magnitude

Young

Old

Immune Cell
Aged Immune Cell
Pathogen

Younger Adult

Older Adult

Nikolich-Zugich, Nature Imm 2018

Acknowledgements to G Hargis & C Bonin

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

Acknowledgements to A Masters & S Keilich
Vulnerability of Older Adults to COVID-19: 
Older men have more innate cell activity (inflammation) 
but less adaptive cell activity (T and B cell function) compared to older women 

Marquez ...Kuchel, Banchereau, Ucar *Nature Communications* Feb 6;11(1):751, 2020
Vulnerability of Older Adults to COVID-19: Metformin and Emergence of Geroscience-Guided Therapies

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Kulkarni et al Cell Metabolism (In Press)
Vulnerability of Older Adults to COVID-19:
*TAME Trial (Targeting Aging with Metformin)*

- Metformin extends health span and life span in animals
- It is a first-line, generic drug to treat diabetes
- >60 year experience and outstanding safety record

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Vulnerability of Older Adults to COVID-19:  
*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:**  \(\text{TAME Trial (Targeting Aging with Metformin)}\)

**Secondary Outcome:**  \(\text{FUNCTIONAL AGING}\)

**Tertiary Outcomes:**  \(\text{BIOMARKERS (NIA)}\)

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

Gordon *et al.* A SARS-CoV-2-Human Protein-Protein Interaction Map Reveals Drug Targets and Potential Drug-Repurposing.

- Not yet peer-reviewed but posted on bioRxiv (3/22)  
  [https://www.biorxiv.org/content/10.1101/2020.03.22.002386v1](https://www.biorxiv.org/content/10.1101/2020.03.22.002386v1)
- AP-MS identification of 66 “druggable” human proteins or host factors targeted by 69 existing FDA-approved drugs, drugs in clinical trials and/or preclinical compounds. These include metformin and rapamycin.
- CAUTION!!...Mechanism?; Effects in cell infection assays?; Dose?; *In vivo* effects in animal models?; Human studies?