Buck Institute for Research on Aging

Daria Timonina

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Live better longer.

My journey

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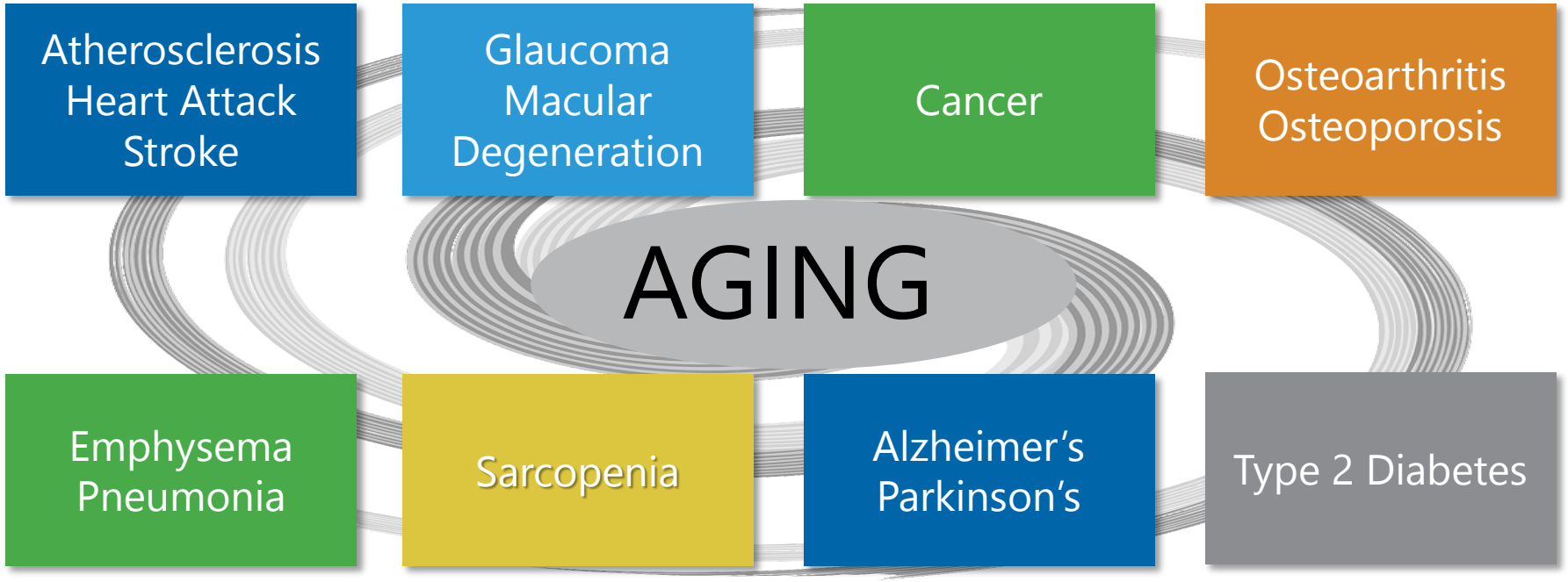
Aging is the #1 risk factor for chronic disease



We believe these diseases should not be an inevitable part of growing old.

Our mission is to end the threat of age-related disease for this and future generations.

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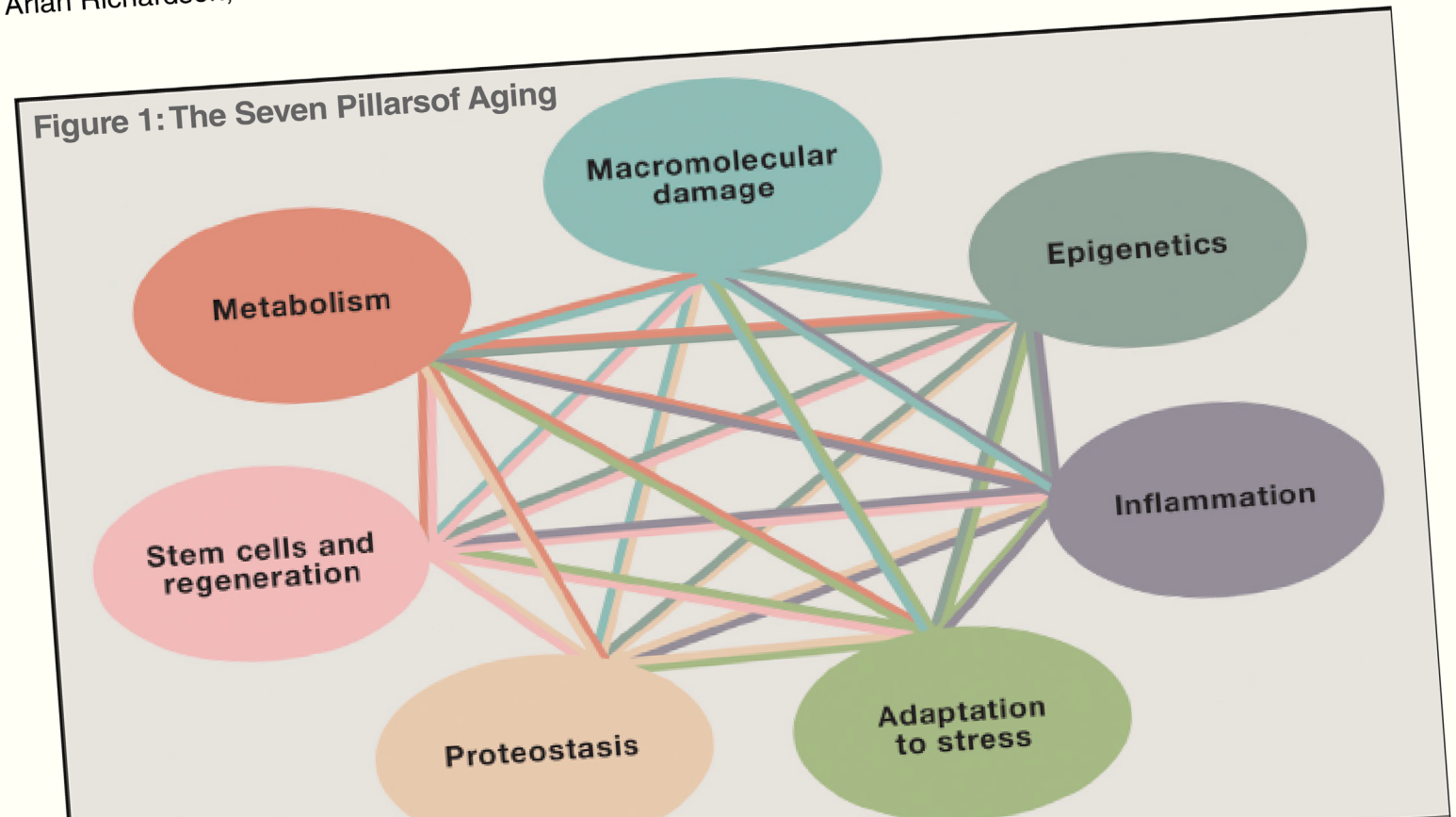
Cell 159, November 6, 2014

Geroscience: Linking Aging to Chronic Disease

Brian K. Kennedy, Shelley L. Berger, Anne Brunet, **Judith Campisi**, Ana Maria Cuervo, Elissa S. Epel, Claudio Franceschi, **Gordon Lithgow**, Richard L. Morimoto, Jeffrey Pessin, Thomas A. Rando, Arlan Richardson, Eric E. Schadt, Tony Wyss-Coray, and Felipe Sierra



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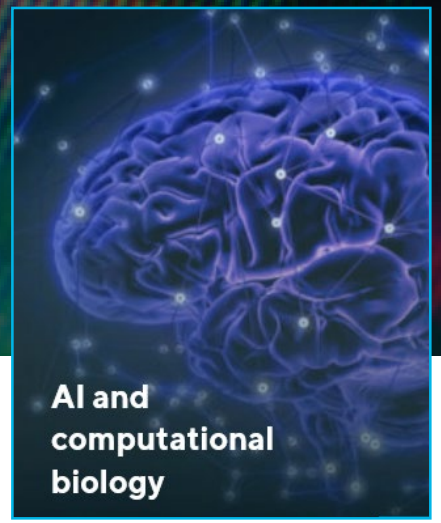
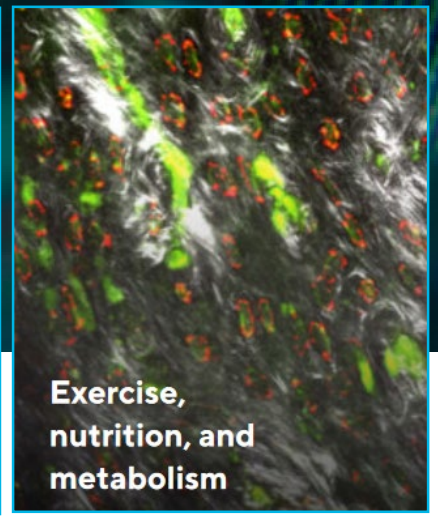
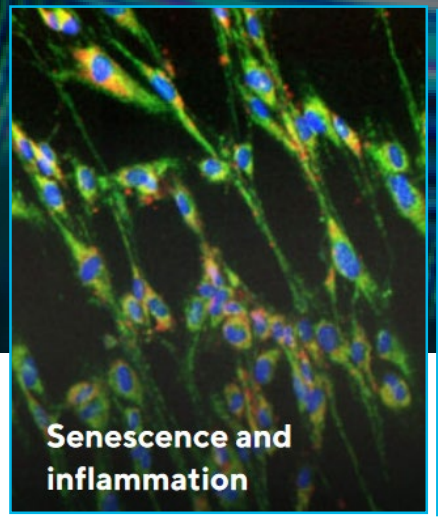
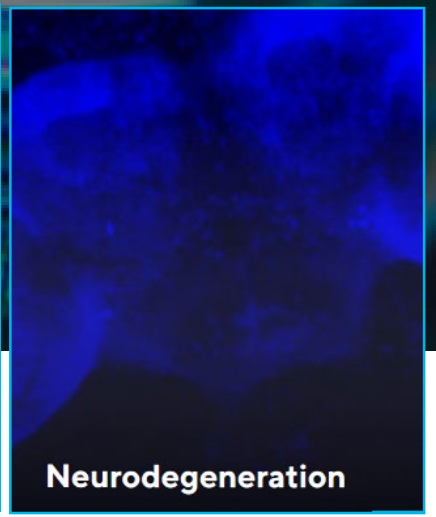
Buck's Focus Areas

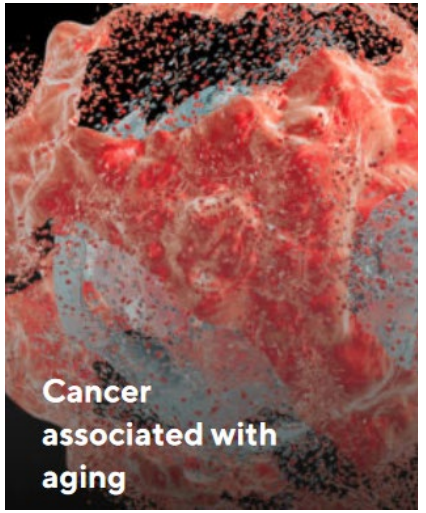
Tackling aging through multiple avenues of inquiry

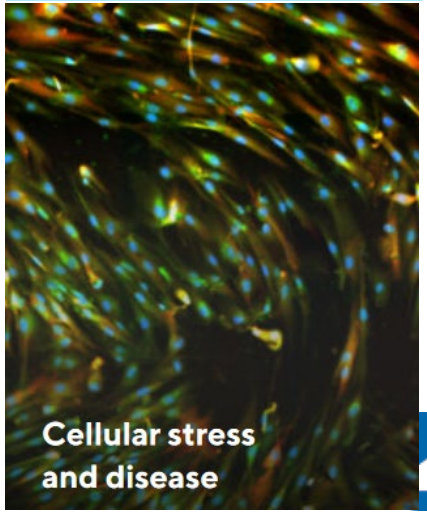












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The Buck Tackles Covid19

buckinstitute.org/covid-19

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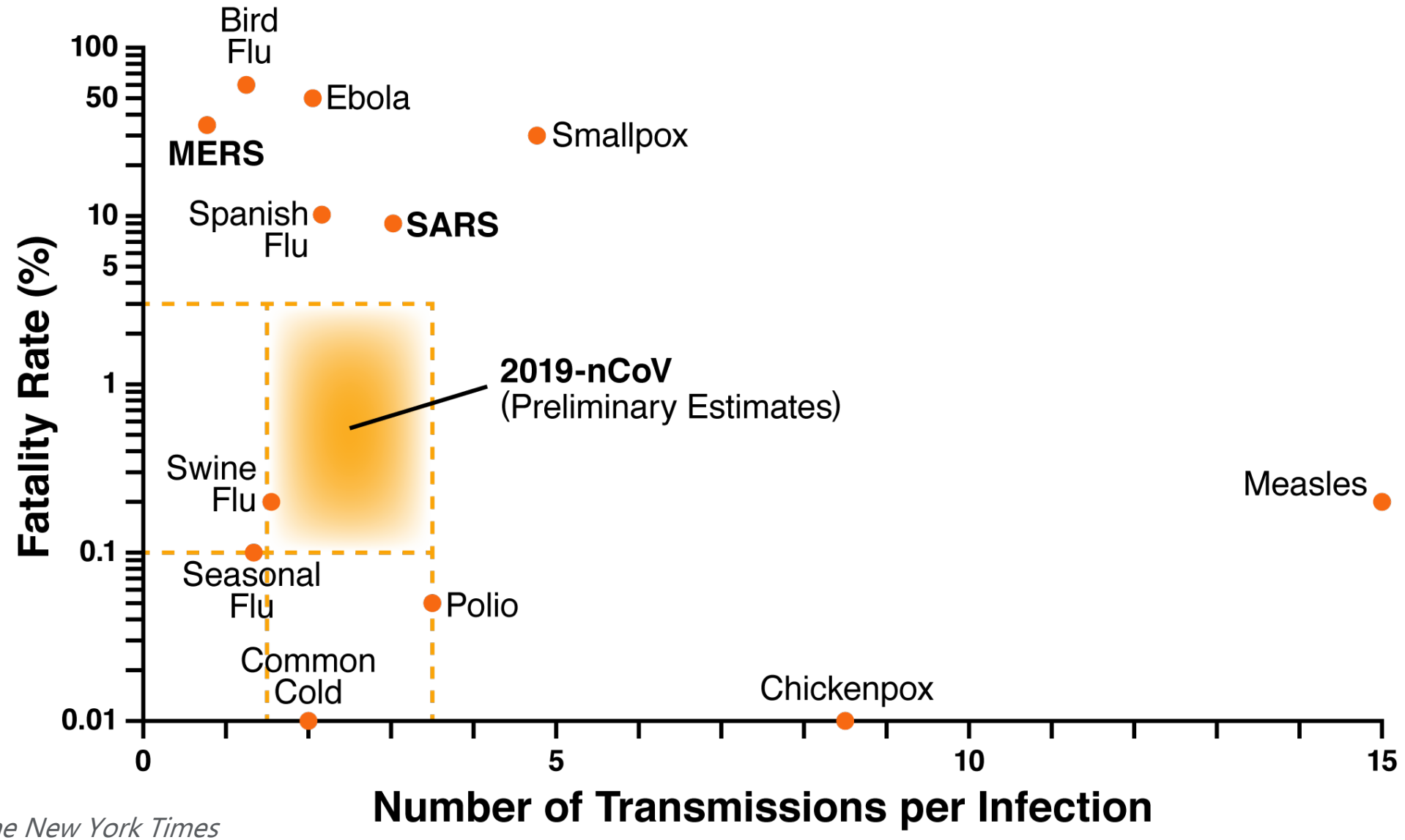
Mortality and Spread: Where SARS-CoV-2 lands



Source: *The New York Times*

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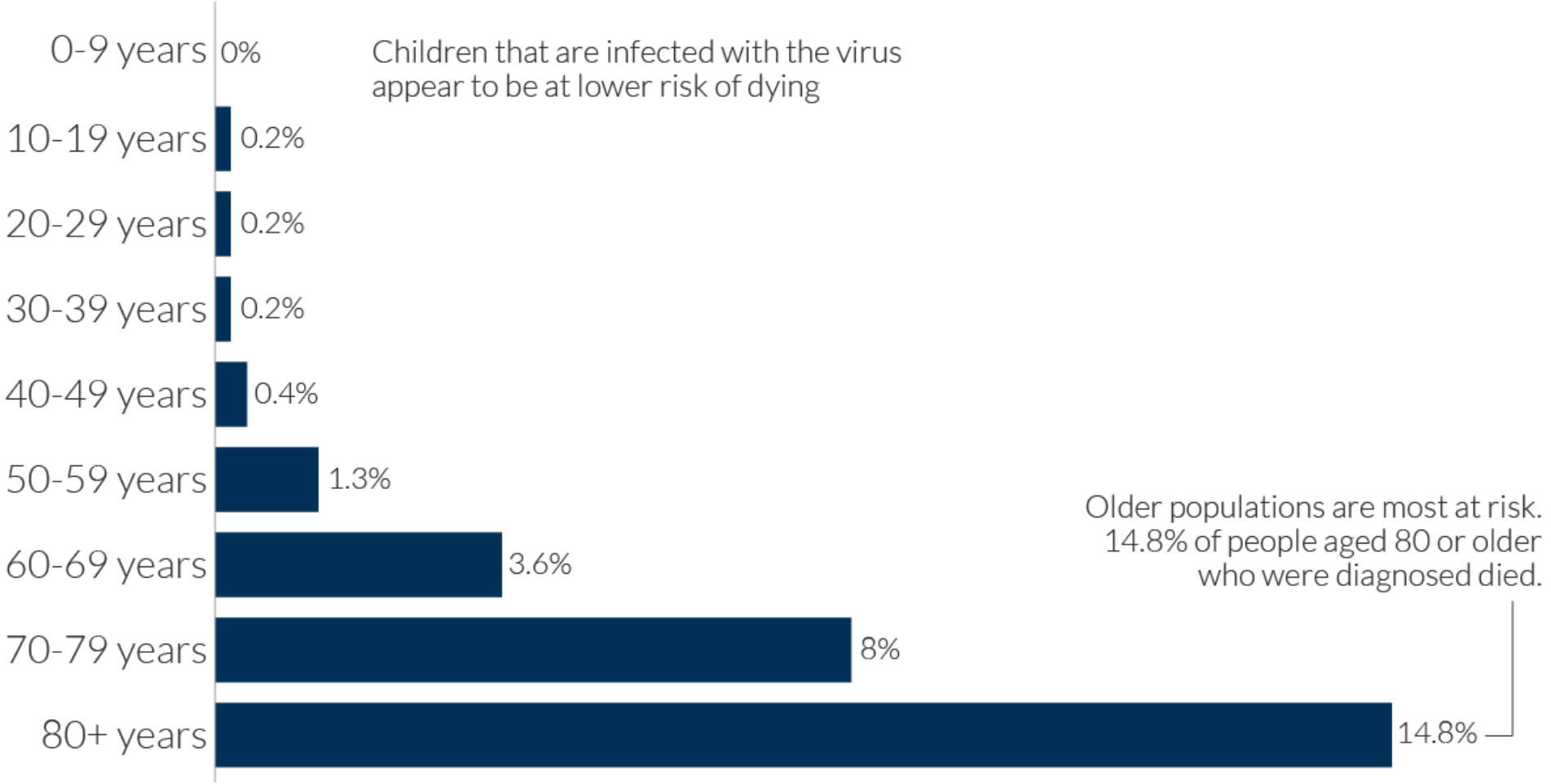
COVID-19 Mortality Increases as a Function of Age

Case fatality rate (CFR) is calculated by dividing the total number of deaths from a disease by the number of confirmed cases.
Data is based on early-stage analysis of the COVID-19 outbreak in China in the period up to February 11, 2020.



Data source: Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. *Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020.* China CDC Weekly.

Risk Factors – a study from New York

Comorbidities	
Total No.	5700
Cancer	320 (6)
Cardiovascular disease	
Hypertension	3026 (56.6)
Coronary artery disease	595 (11.1)
Congestive heart failure	371 (6.9)
Chronic respiratory disease	
Asthma	479 (9)
Chronic obstructive pulmonary disease	287 (5.4)
Obstructive sleep apnea	154 (2.9)
Immunosuppression	
HIV	43 (0.8)
History of solid organ transplant	55 (1)
Kidney disease	
Chronic[c]	268 (5)
End-stage[d]	186 (3.5)

Liver disease	
Cirrhosis	19 (0.4)
Chronic	
Hepatitis B	8 (0.1)
Hepatitis C	3 (0.1)
Metabolic disease	
Obesity (BMI ≥30)	1737 (41.7)
No.	4170
Morbid obesity (BMI ≥35)	791 (19.0)
No.	4170
Diabetes[e]	1808 (33.8)

Comorbidities[f]	
None	350 (6.1)
1	359 (6.3)
>1	4991 (88)

Source: "Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area." Safiya Richardson et al.

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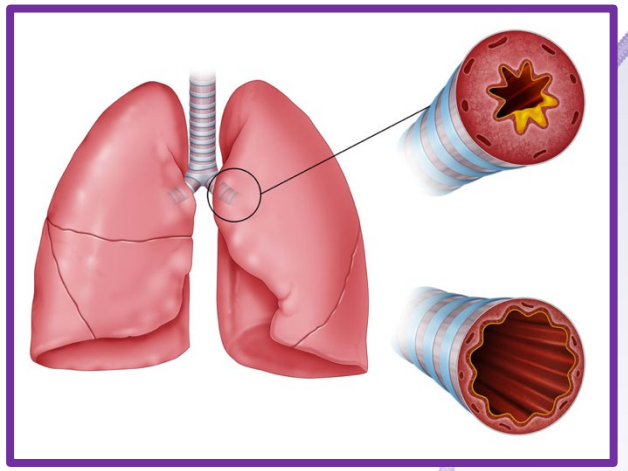
COVID-19 enters body through airways (infection)

Virus binds to receptor on cell surface (ACE2) to enter the cell



Body's immune system is activated to try and fight virus, resulting in severe lung inflammation, difficulty breathing and fluid accumulation

David Furman / Dan Winer / Eric Verdin
dampening the inflammatory response in the lung

Virus hijacks cell machinery to produce and assemble multiple copies of virus (replication)

Nevan Krogan
hijacked proteins as drug targets

Newly synthesized viral particles leave cell to infect other cells (propagation)

Start of a collaboration with QBI-UCSF

Nevan Krogan lab at UCSF
Adjunct Faculty, Buck

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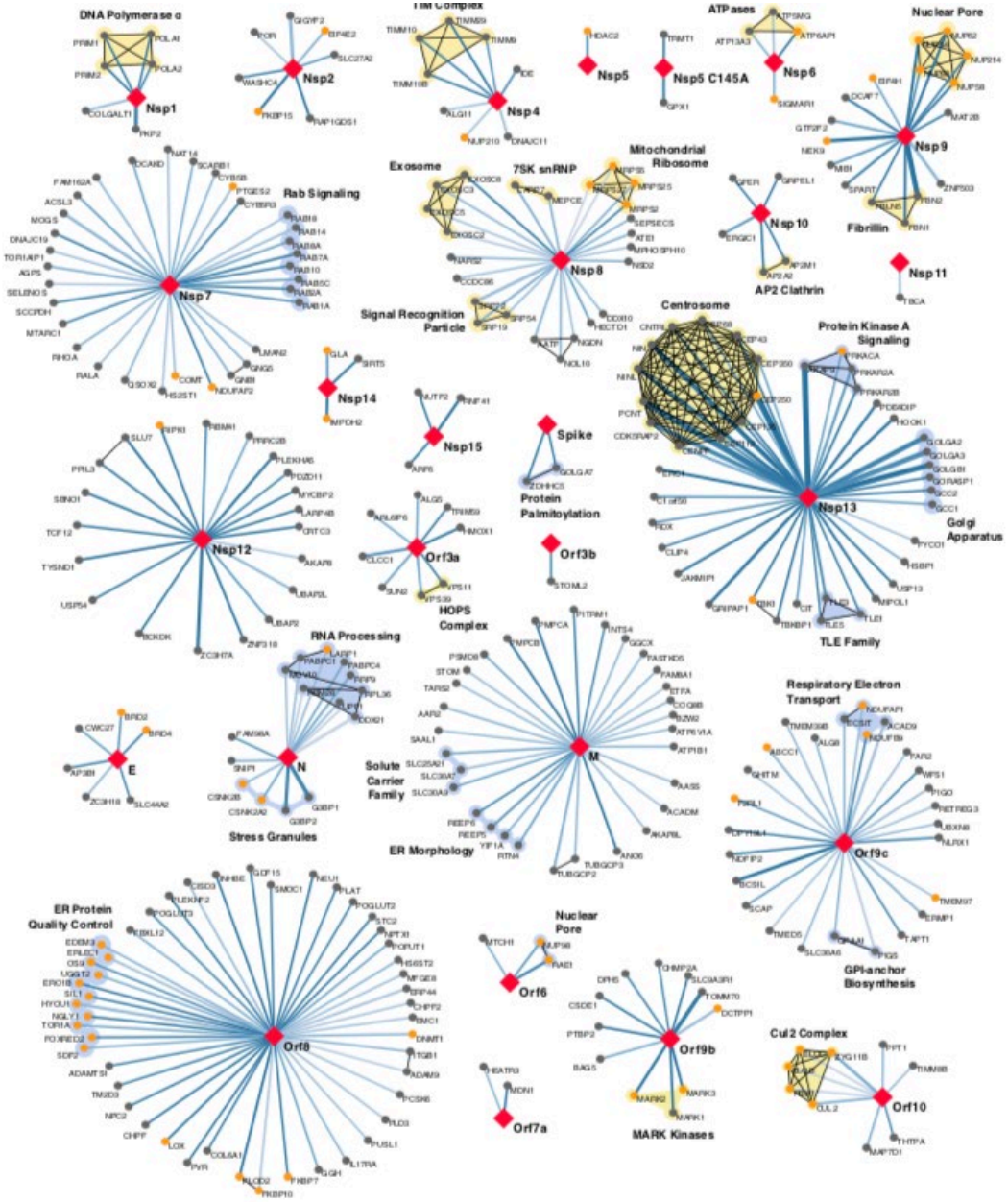
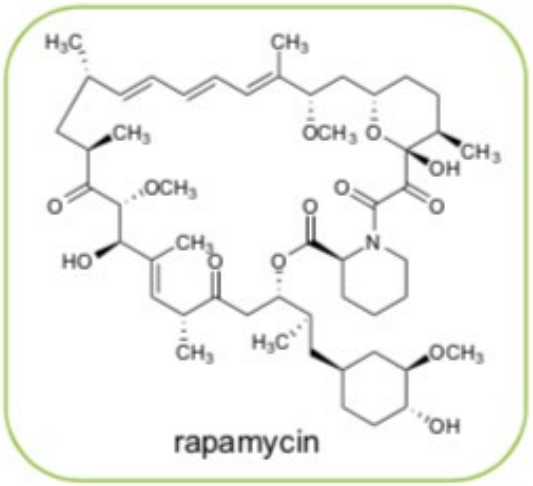
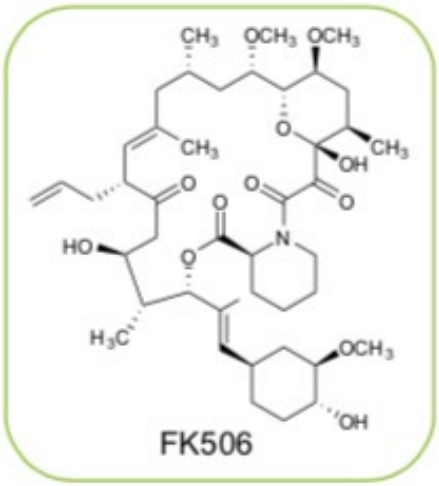
UCSF

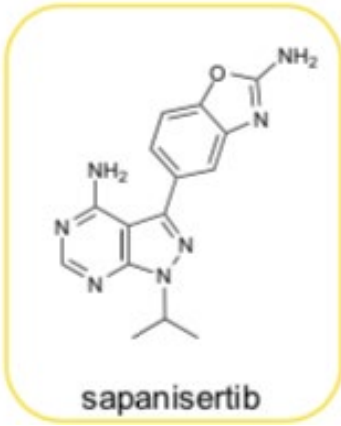
GLADSTONE INSTITUTES

SARS-CoV-2 interactome and potential drug targets









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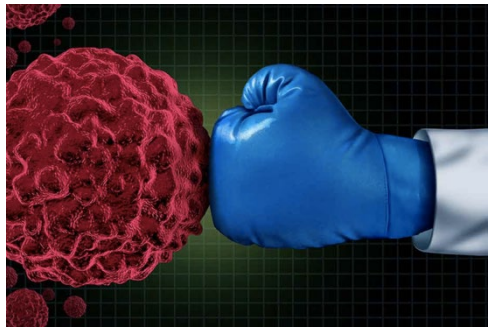
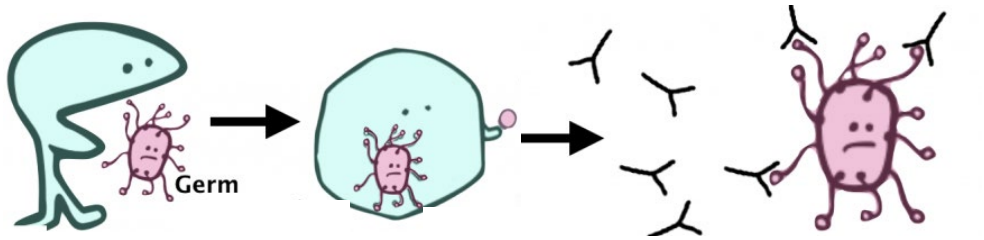
Animal models of SARS-CoV suggest that disease severity in aged animals is caused by an exacerbated innate immune response.

Innate Immune Response



Adaptive Immune Response



Questions we're exploring:

Is there an imbalance between the innate / adaptive immune response in aged patients?

Does chronic inflammation 'prime' the immune system for a strong innate response?

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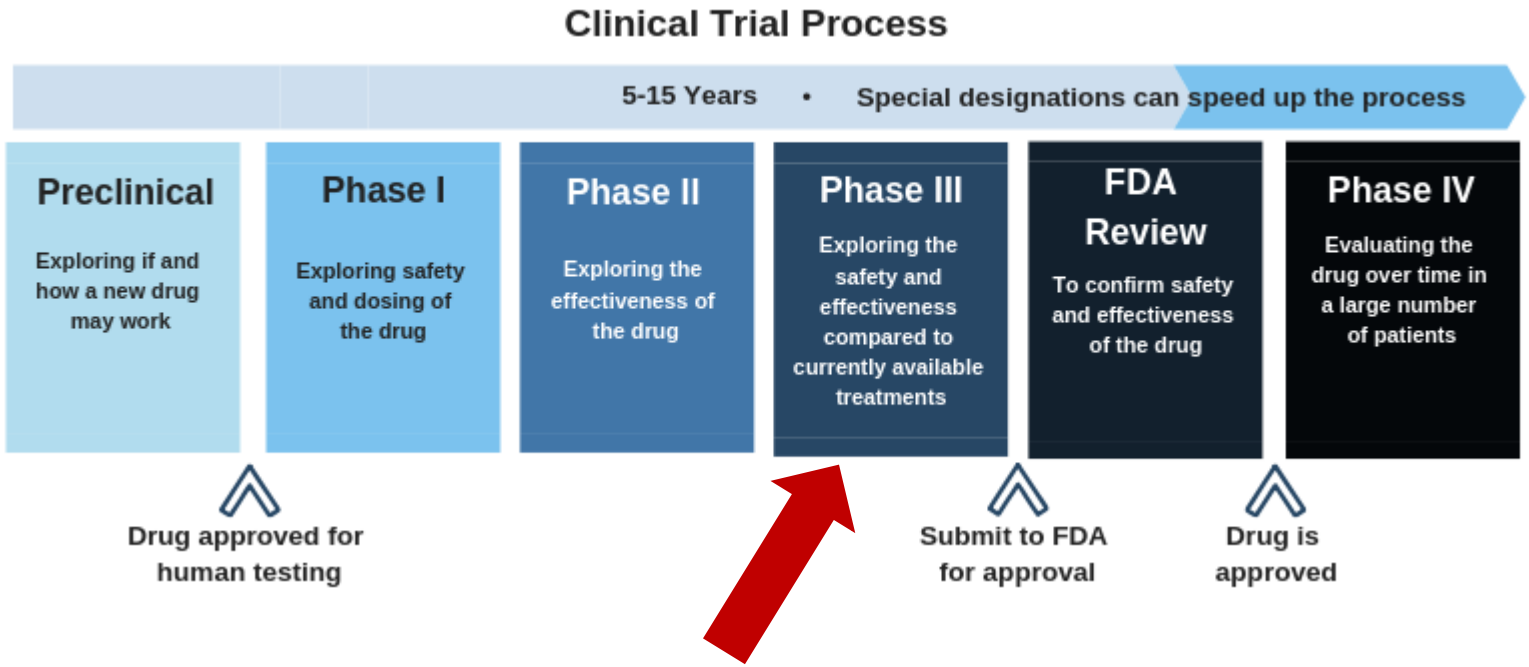
Current Therapeutics

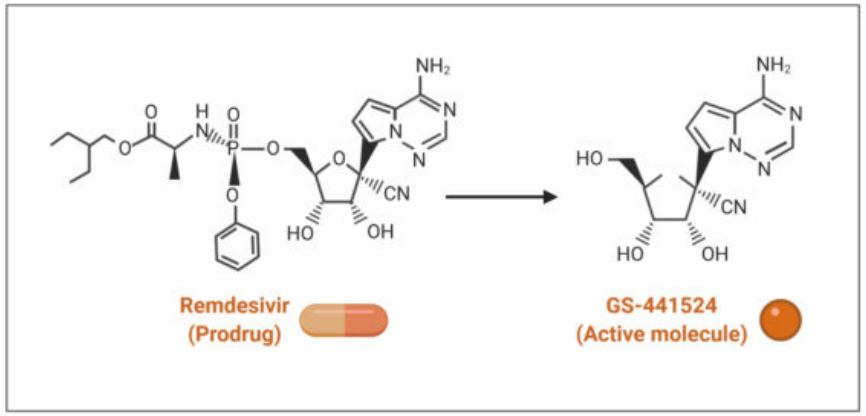
First and Foremost: Remdesivir

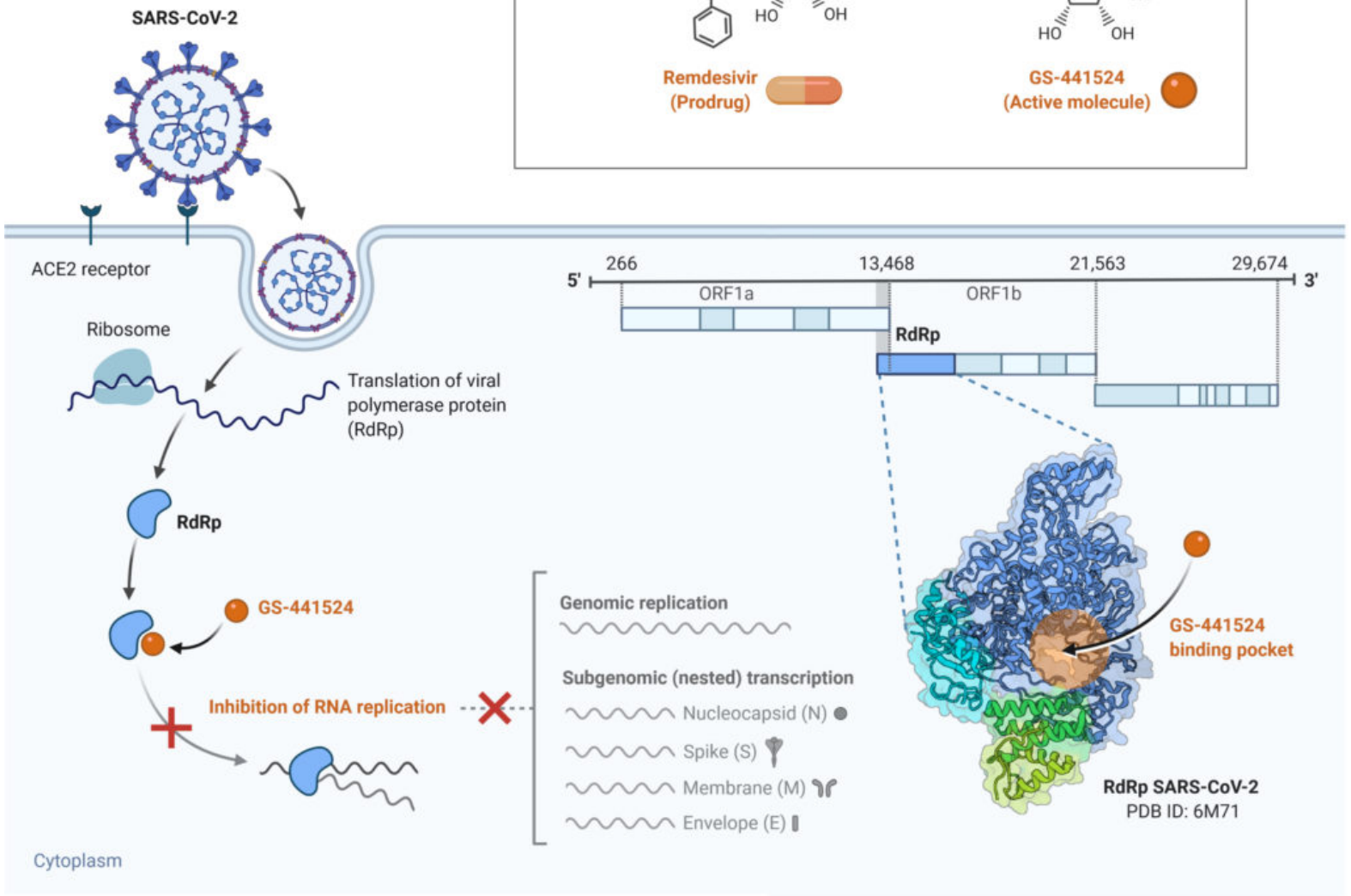
- Brought to trial in 2015 for Ebola
- Broad antiviral



Remdesivir

Potential repurposed drug candidate for COVID-19





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Hydroxychloroquine

- Primarily used as an anti-malarial, rheumatoid arthritis treatment, and treatment for lupus
- Anti-inflammatory used in auto-immune diseases

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.journals.elsevier.com/journal-of-critical-care

A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19

Andrea Cortegiani [a,*], Giulia Ingoglia [a], Mariachiara Ippolito [a], Antonino Giarratano [a], Sharon Einav [b]

[a] Department of Surgical, Oncological and Oral Science (Di.Chir.On.S.), Section of Anaesthesia, Analgesia, Intensive Care and Emergency, Policlinico Paolo Giaccone, University of Palermo, Italy
[b] Intensive Care Unit of the Shaare Zedek Medical Medical Centre, Hebrew University Faculty of Medicine, Jerusalem, Israel

NIH clinical trial of hydroxychloroquine, a potential therapy for COVID-19, begins

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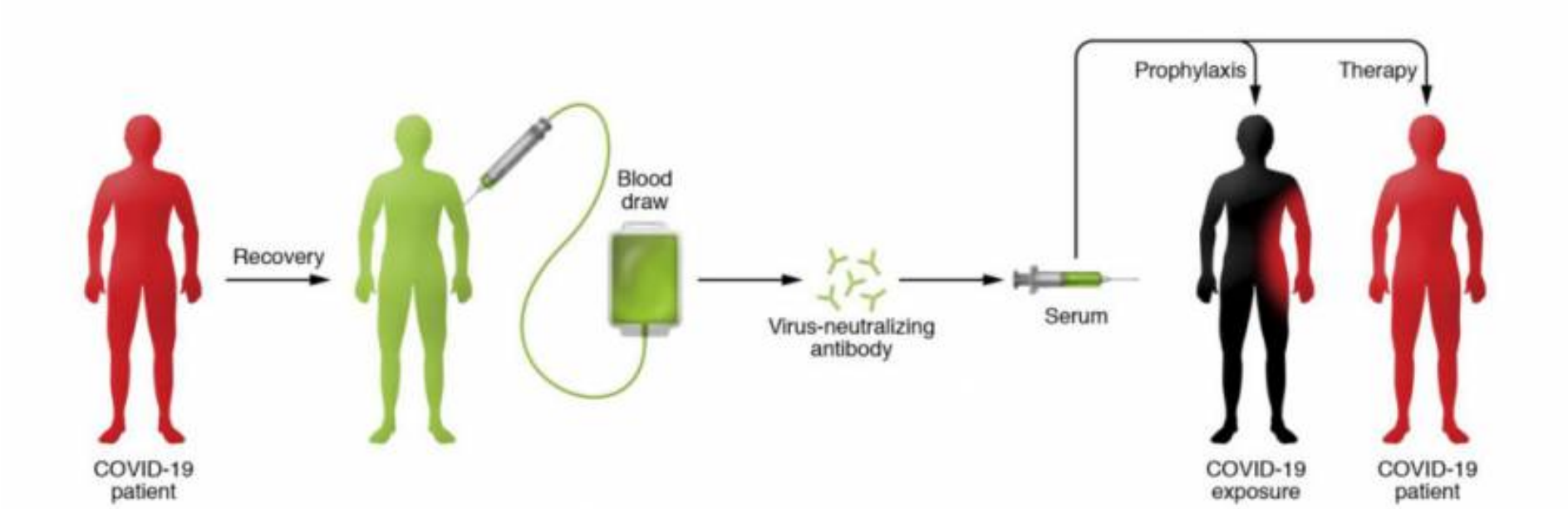
Plasma Therapy



Effectiveness of convalescent plasma therapy in severe COVID-19 patients

Kai Duan[a,b,1], Bende Liu[c,1], Cesheng Li[d,1], Huajun Zhang[e,1], Ting Yu[f,1], Jieming Qu[g,h,i,1], Min Zhou[g,h,i,1], Li Chen[j,1], Shengli Meng[b], Yong Hu[d], Cheng Peng[e], Mingchao Yuan[k], Jinyan Huang[l], Zejun Wang[b], Jianhong Yu[d], Xiaoxiao Gao[e], Dan Wang[k], Xiaoqi Yu[m], Li Li[b], Jiayou Zhang[b], Xiao Wu[d], Bei Li[e], Yanping Xu[g,h,i], Wei Chen[b],

Experimental, but showed promise in other viruses like swine flu, SARS, and MERS

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Vaccine Potential—Later than we think!

Human patients late this year; regulatory filing in later half of 2021

Intend to begin human testing soon of mRNA vaccine

"Lead vaccine candidate" to go into Phase I clinical trial by September

And SEVERAL others…

Other things happening in the therapeutics-sphere…

Azithromycin, antibiotic, and Xeljanz, a treatment for pneumonia

Phase III trial of Actemra, which is effective against pneumonia caused by the virus

Phase IV trial of lopinavir/ritonavir originally created for HIV

Coronavirus Treatment Acceleration Program (CTAP)—Allows drug and vaccine developers to rapidly correspond with FDA

Repurposing Pharmaceuticals for Aging

Project by Daria Timonina

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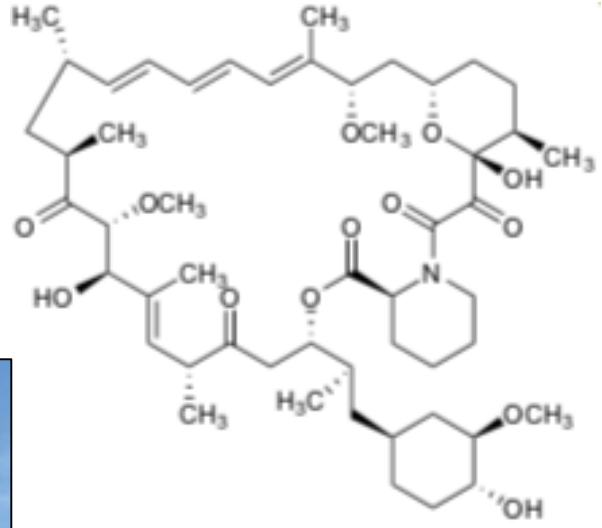
Rapamycin



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Found to extend lifespan in model organisms

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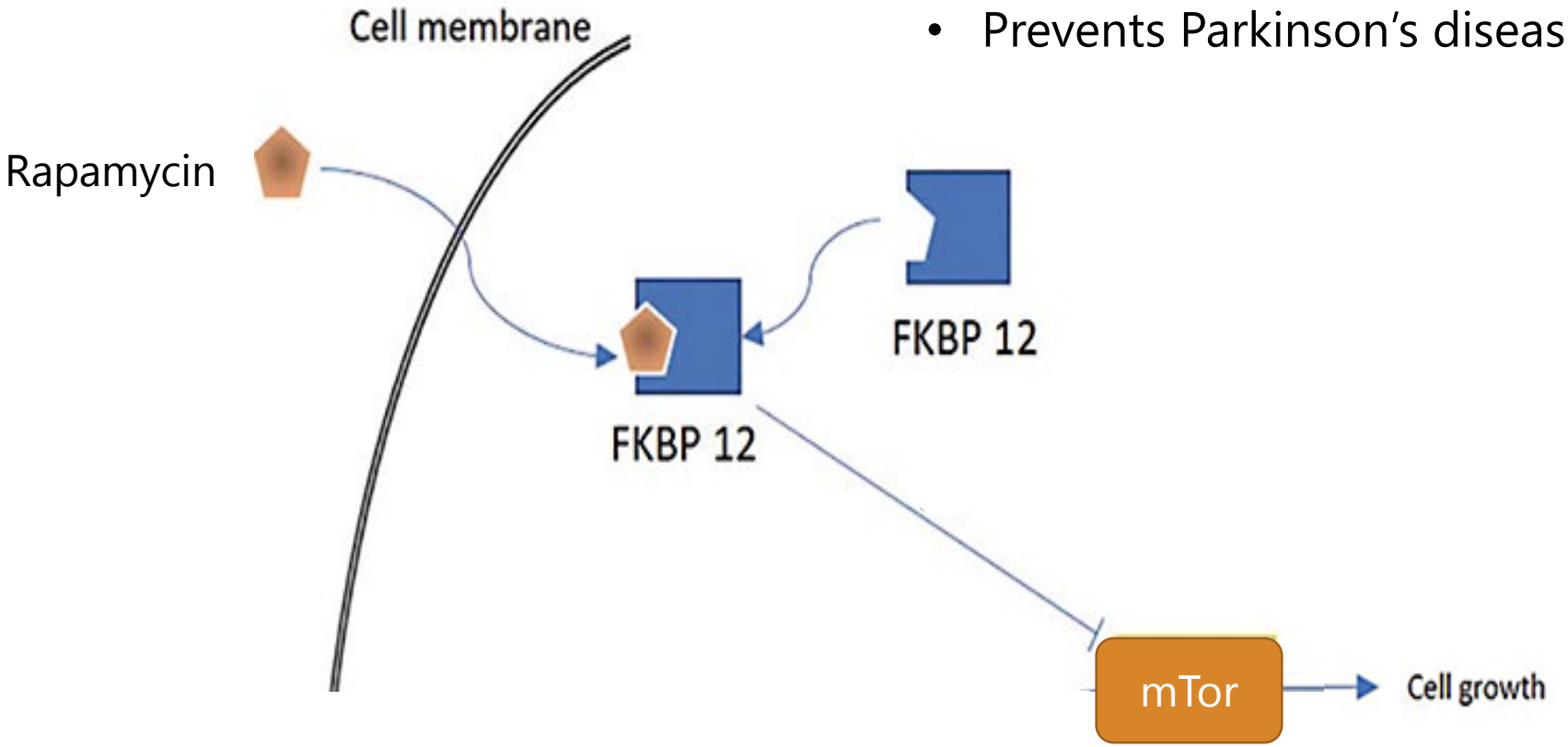
How does it work?

- Boosts regenerative potential of tissues
- Given in late-life, reverses age-related heart disease in mice
- Prevents Parkinson's disease in mouse models



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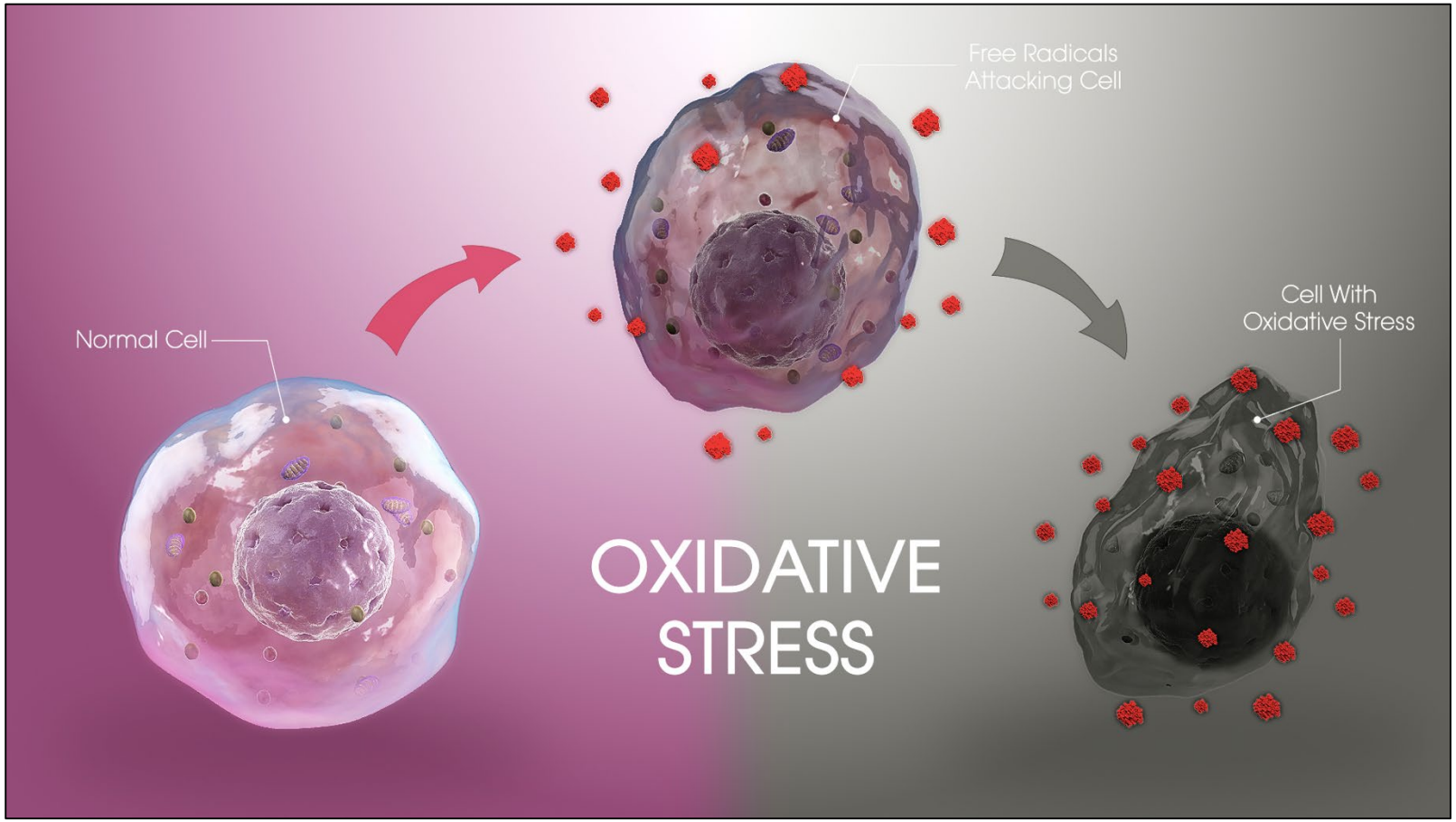
Another Role: Oxidative Stress



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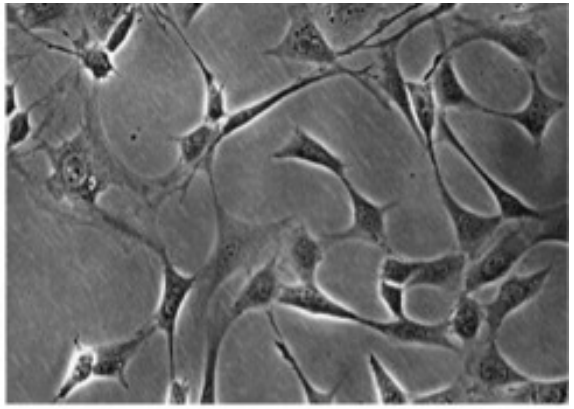
How I study this

Add Rapamycin

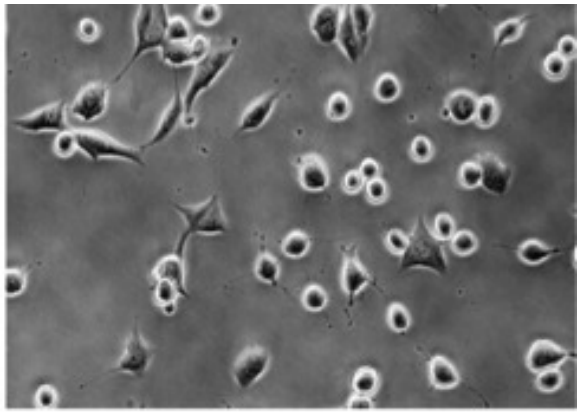
Add oxidative stress

See what is driving the effect

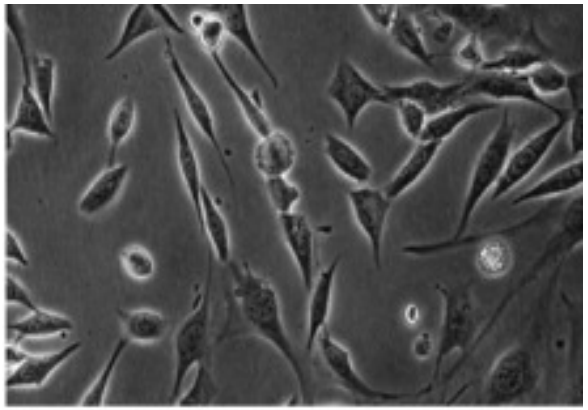
No treatment



Oxidative Stress



Rapamycin + Oxidative Stress



Reference: Rapamycin treatment increases hippocampal cell viability in an mTOR-independent manner during exposure to hypoxia mimetic, cobalt chloride. Andy Li et al

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Why it matters

Resources for Older Adults

buckinstitute.org/covid-19

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Make sure you have adequate medication

Obtain the essentials

Get digitally connected

Keep moving as much as possible

Get adequate sleep and manage stress

Reach out

DETAILS: buckinstitute.org/covid-19

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Support our Research

Get involved!
Donate online to the
Buck COVID-19 Research Fund

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www.buckinstitute.org

Your support is more vital than ever.

For more information on how you can help contact
Brian Van Weele @ bvanweele@buckinstitute.org

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