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SCHOOL OF HEALTH SCIENCES

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Who are we?

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EACPHS Eugene Applebaum College of Pharmacy and Health Sciences

Joseph A. Roche BPT, Dip. Rehab. PT, Ph.D.

Recent Publications

- PubMed
- ResearchGate

< Return to listing

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Goals for this educational session and scholarly discussion

Goal 1. Give an overview of what we have learned about COVID-19 through our research

Goal 2. Summarize what COVID-19 has taught us in terms of the urgent need to reimagine healthcare

Goal 3. Introduce our HUMAN OCCUPATION & MOVEMENT BASED HEALTH OUTCOMES MODEL ™

Why are we here?

Received: 20 April 2020 | Accepted: 22 April 2020
DOI: 10.1096/fj.202000967

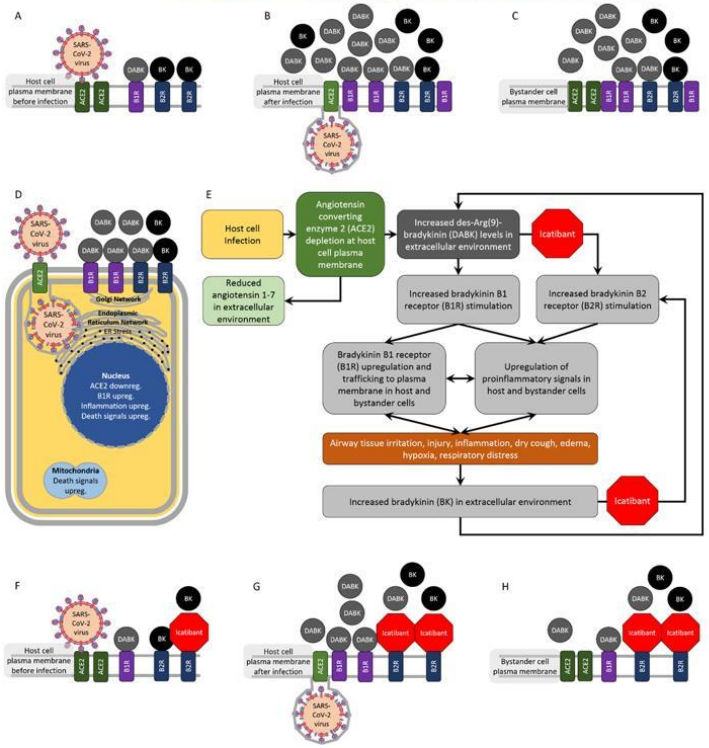
HYPOTHESES

THE FASEB JOURNAL

A hypothesized role for dysregulated bradykinin signaling in COVID-19 respiratory complications

Joseph A. Roche[1] | Renuka Roche[2]

The FASEB Journal. 2020;00:1–5. https://doi.org/10.1096/fj.202000967



Excerpt from Editorial Review

Congratulations on the acceptance of your article. Please share the good news with your institution's media relations department as we believe your hypothesis and potential role of the kinin system in COVID19 is worth promoting. Your hypothesis is very interesting and hopefully with publication in FJ interest will emerge for a clinical trial as you've indicated.

We greatly appreciate your contribution to The FASEB Journal and hope you will consider us for future papers.

Sincerely,
Charles N. Serhan, Ph.D.,D.Sc.
Associate Editor
The FASEB Journal

- Published two papers on COVID-19
- Engaged with clinicians, scientists, funding agencies and industry partners around the world
- Provide peer-review for scholarly papers and grant proposals on COVID-19
- Being invited to serve as a peer-reviewer is validation of being considered an expert in the content area

What qualifies us to lead this session?

Ray Roche

Clinical training and work experience as an **occupational therapist (OT)** with **specialization in Acute Care**

PhD training in Rehabilitation Science and Pediatric Neurology with intense didactic and research focus on biomedical science

Teach Neuroscience, OT across the lifespan

Research includes pharmacotherapy for genetic muscle diseases, and now COVID-19

Joseph Roche

Clinical training and work experience as a **physical therapist (PT)** with diverse clinical experiences including Acute Care

PhD training in Rehabilitation Science and Physiology with intense didactic and research focus on biomedical science

Post-doctoral training in Muscle Biology

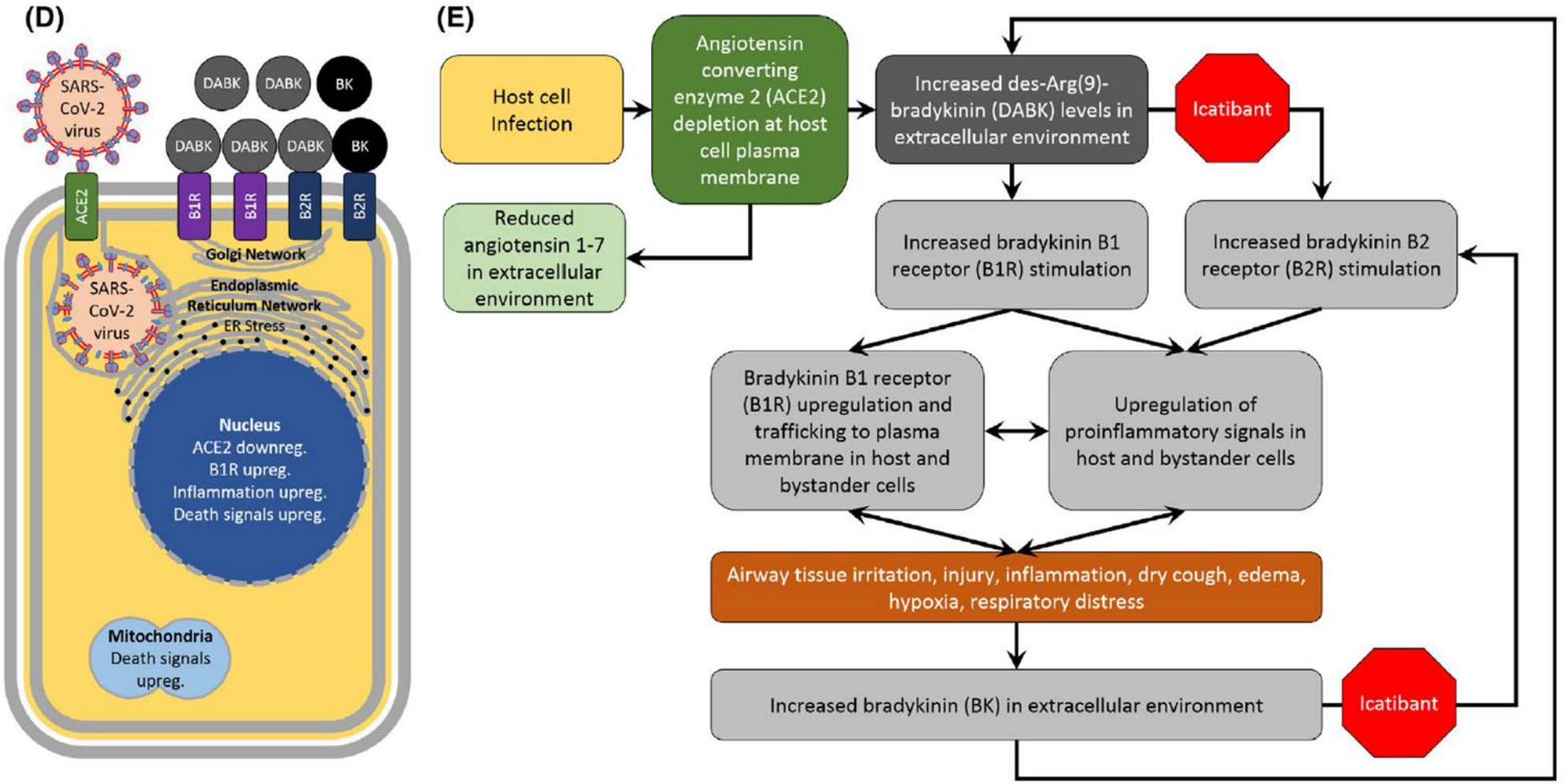
Teach Pharmacology, Biomaterials, and Muscle Biology

Research includes pharmacotherapy for genetic muscle diseases, and now COVID-19

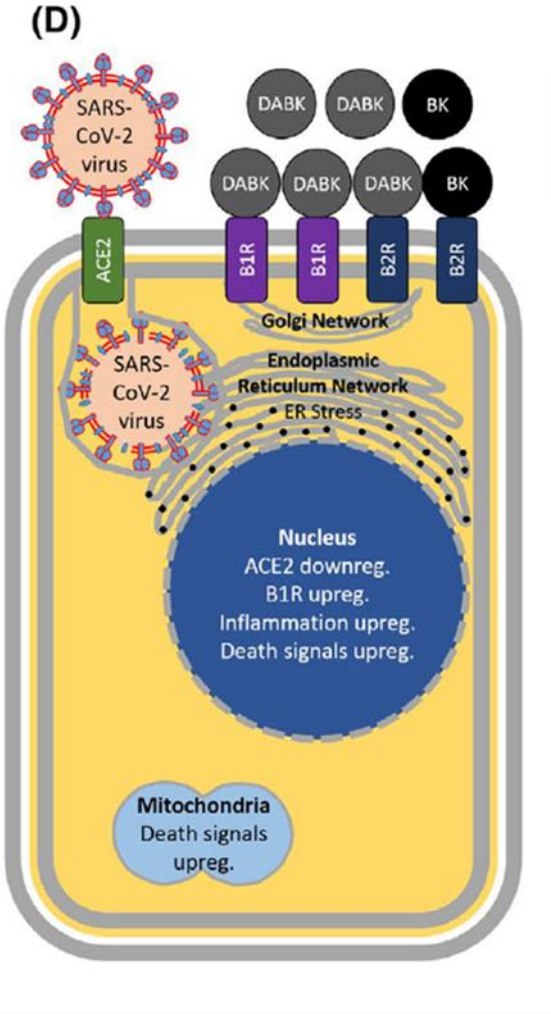
Goal 1.

An overview of what we have learned about COVID-19 through our research

Our model for dysregulated bradykinin signaling in COVID-19 complications



What’s up with the minion?



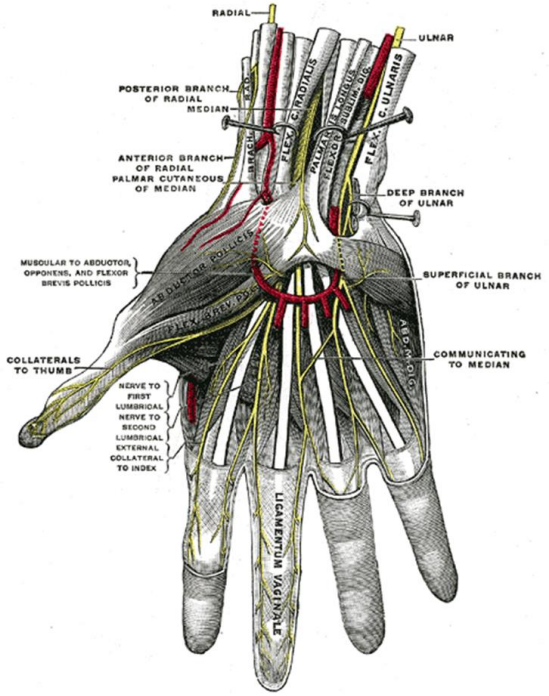
A little background

- How human cells make proteins
- How the coronavirus disease 2019 (**COVID-19**) causing virus (**SARS-CoV-2**) hijacks the protein-making machinery and other cellular functions
- Possible reasons why COVID-19 is causing such severe acute and post-acute symptoms in some individuals

How human cells make proteins

Why bother about proteins?

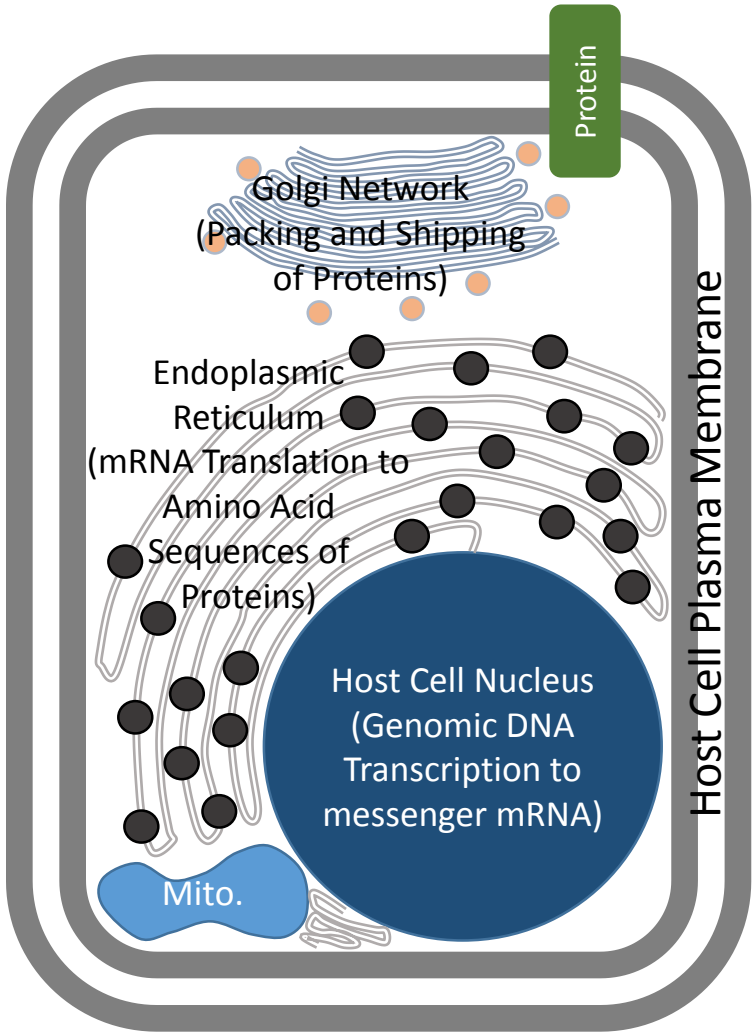
This palm’s structure is mainly carbohydrate-based



This palm’s structure is mainly protein-based

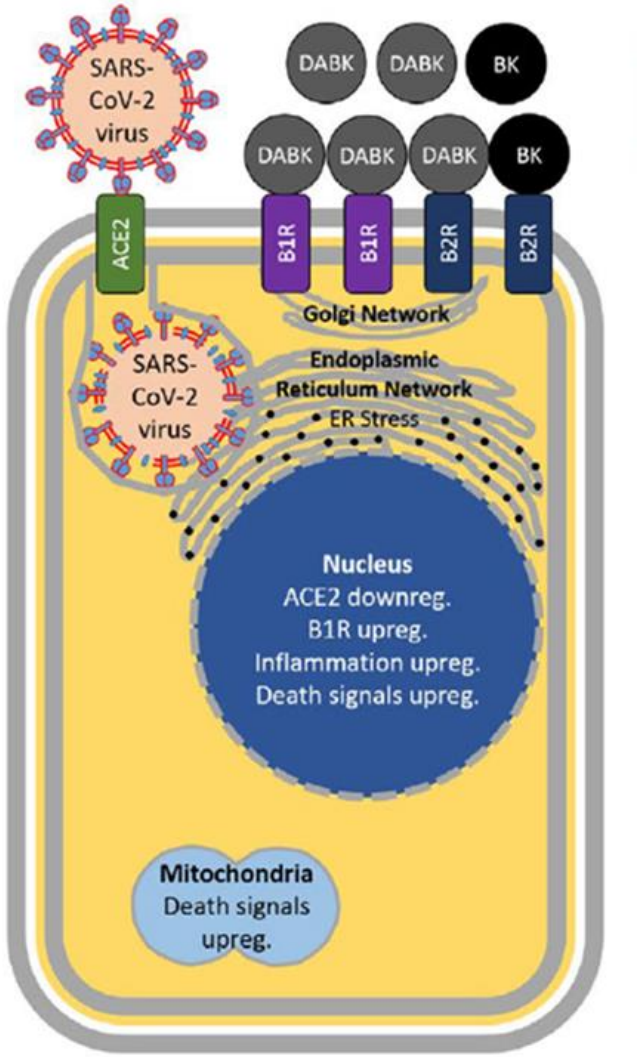
Proteins essentially make us who we are, both structurally and functionally

How proteins are made



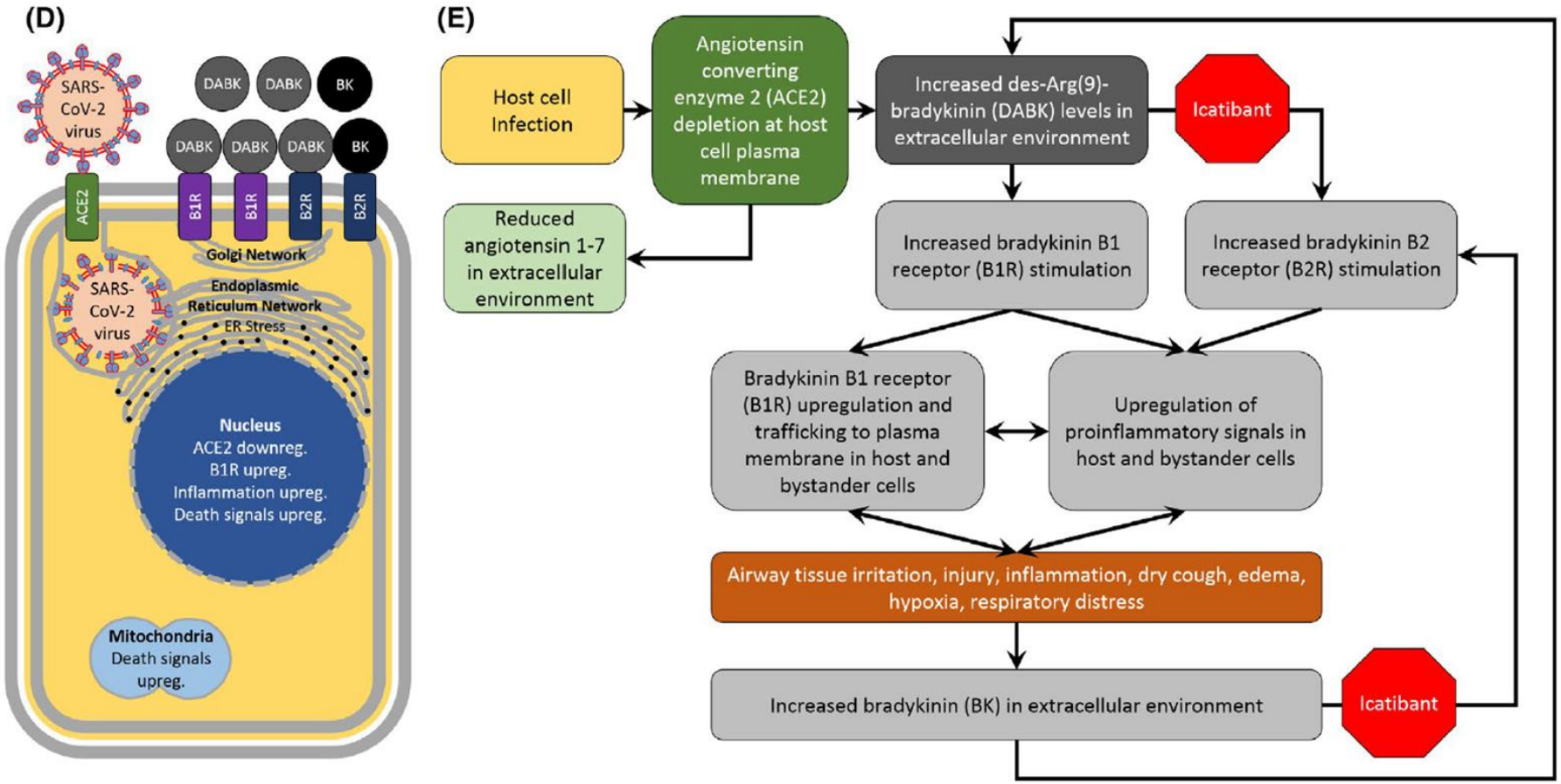
- The genetic code to make proteins is stored in genomic DNA
- Through **TRANSCRIPTION,** genomic DNA information helps make messenger RNA (mRNA)
- mRNA exits the nucleus and binds to protein producing factories called ribosomes (the little grey spheres in the pic) in the endoplasmic reticulum
- Through **TRANSLATION**, ribosomes use mRNA code to arrange amino acids (protein building blocks) in very precise sequences. These sequences of amino acids are further modified to become proteins
- Some proteins are secreted out of the cell into the blood or extracellular space, and others are shipped to various parts of the cell

How the COVID-19 virus (SARS-CoV-2) uses our cells to promote itself



- SARS-CoV-2 is a positive-sense single-stranded RNA virus
- **The virus can be read by host cell ribosomes just like the host cell's own mRNA**
- The virus uses the host cell's protein producing machinery to make viral proteins
- Some of the viral proteins assemble viral replication complexes, which make more viral genomes
- The virus uses the host cell's protein packing and shipping machinery to ship more copies of virus out of the cell so that other cells can be infected (this is relevant to social distancing and other precautions to limit community spread)

Our model for dysregulated bradykinin signaling in COVID-19 complications



What our hypothesis paper has achieved

- **Helped identify an FDA-approved drug (ICATIBANT) that has the potential to reduce disease severity by targeting dysregulated bradykinin signaling**
- Suggested that experimental drugs could be tested in clinical trials or under the compassionate use clause
- **Explained symptoms like dry cough, loss of taste and smell, increased thirst, and presence of blood clots**
- Explained why some patients might have more severe disease than others based on genetics and medical history
- Generated interest among clinicians and scientists

What we would like our COVID-19 research to achieve

- Generate data to test the hypothesis that blocking dysregulated bradykinin signaling decreases COVID-19 respiratory and other complications

QUIZ 1. Q1.

What is the proper name for the virus that causes COVID-19?

A. COVID-19 HIV
B. SARS-CoV-2
C. HCoV
D. Wuhan bat virus

Correct answers at the end of slide deck. Indicated with bold and underlined fonts.

QUIZ 1. Q2.

Which of the following statements is TRUE regarding SARS-CoV-2?

A. It is a positive-sense RNA virus that acts like host cell mRNA
B. It is a negative-sense RNA virus that acts like host amino acids
C. It is retrovirus that integrates into the host cell genome
D. It can replicate even without the help of host cells

Correct answers at the end of slide deck. Indicated with bold and underlined fonts.

Goal 2.

What COVID-19 has taught us in terms of the urgent need to reimagine healthcare

Evidence-based healthcare must be attentive to basic, preclinical, and clinical evidence at a global level, even as new data emerge

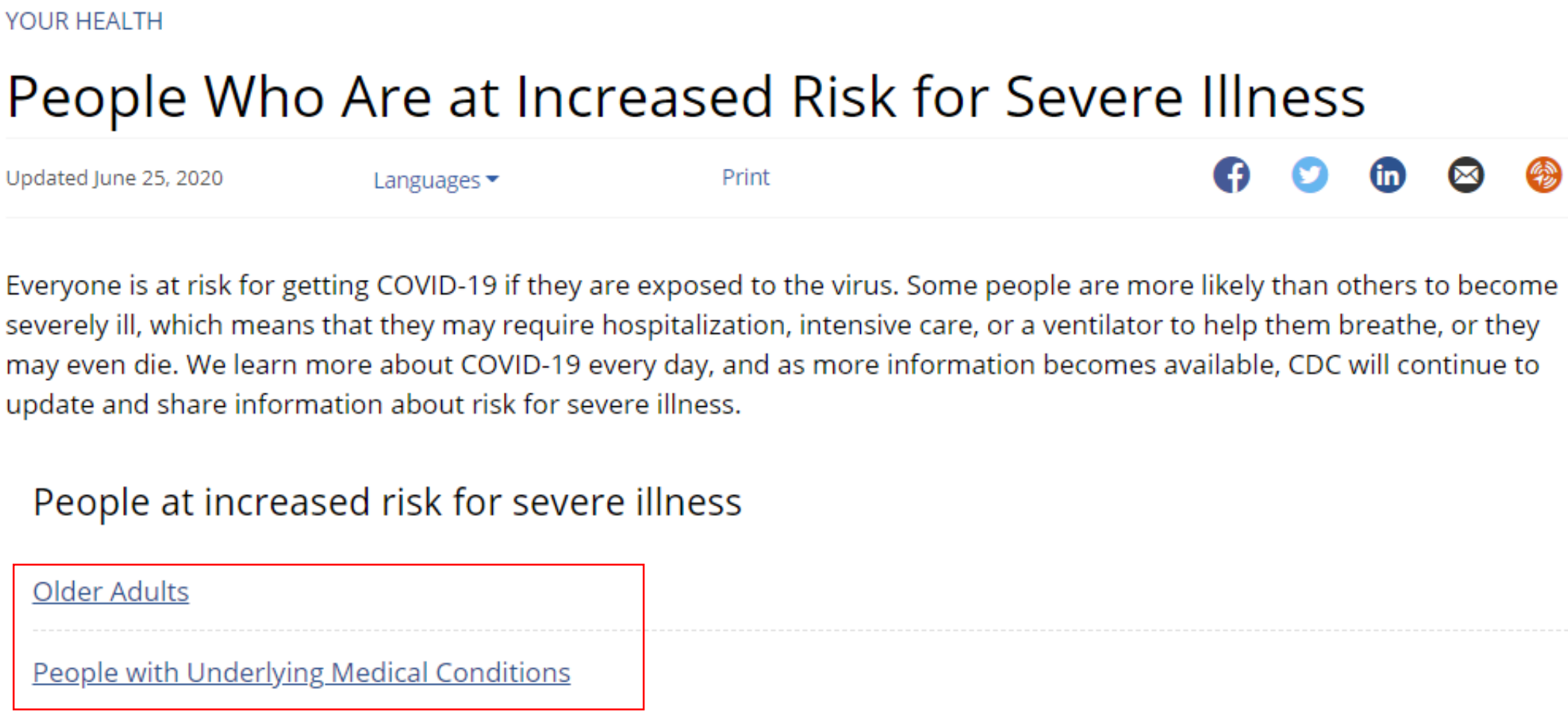
What we have learned from the COVID-19 literature

- Cited 60 articles in our FASEBJ hypothesis paper
- Cited evidence on COVID-19, which was published and listed on PUBMED since January-February 2020
- Cited evidence on original SARS virus that caused local outbreaks in Asia back in 2003
- **Publications on COVID-19 from Asia and Europe provided warnings regarding the danger of COVID-19 and the need to prepare**
- There was published evidence, which could have helped develop a proactive healthcare plan to handle COVID-19

Reference supporting the availability of emerging evidence on COVID-19 as early as January 2020.

Timely research papers about COVID-19 in China. DOI: https://doi.org/10.1016/S0140-6736(20)30375-5

COVID-19 and pre-existing health conditions



YOUR HEALTH

People Who Are at Increased Risk for Severe Illness

Updated June 25, 2020 Languages Print

Everyone is at risk for getting COVID-19 if they are exposed to the virus. Some people are more likely than others to become severely ill, which means that they may require hospitalization, intensive care, or a ventilator to help them breathe, or they may even die. We learn more about COVID-19 every day, and as more information becomes available, CDC will continue to update and share information about risk for severe illness.

People at increased risk for severe illness

Older Adults

People with Underlying Medical Conditions

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-increased-risk.html

Insulin resistance is an underlying condition, which one in three persons has in the U.S.

Total 328 million

New CDC report: More than 100 million Americans have diabetes or prediabetes

Diabetes growth rate steady, adding to health care burden

Press Release

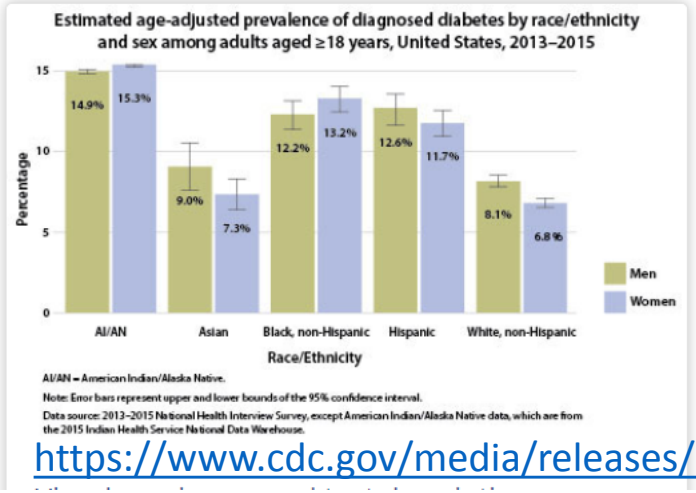
For Immediate Release: Weekday, July 18, 2017

Contact: Media Relations

(404) 639-3286

More than 100 million U.S. adults are now living with diabetes or prediabetes, according to a new report released today by the Centers for Disease Control and Prevention (CDC). The report finds that as of 2015, 30.3 million Americans – 9.4 percent of the U.S. population –have diabetes. Another 84.1 million have prediabetes, a condition that if not treated often leads to type 2 diabetes within five years.

The report confirms that the rate of new diabetes diagnoses remains steady. However, the disease continues to represent a growing health problem: Diabetes was the seventh leading cause of death in the U.S. in 2015. The report also includes county-level data for the first time,



https://www.cdc.gov/media/releases/2017/p0718-diabetes-report.html

A clarification on COVID-19 and underlying health conditions

- One in every three persons in the U.S. is insulin resistant or is developing insulin resistance
- One in three persons is at risk for developing COVID-19 complications due to insulin resistance
- **Prevention of acquired illnesses, such as insulin resistance and its cardiovascular complications, would likely have reduced the impact of COVID-19 on the U.S. population**
- Emphasizes the need for preventative health and wellness policies and programs

No semblance of a unified response system

- This was striking.
- Quality of care seemed to depend upon geography and where a patient receives care.
- Positive outcomes seemed to depend on the which medical system and state/ place where the patient was located.
- There seemed to be a loose network of self-organizing local hospital systems but not a regional or national response framework.

QUIZ 2. Q1.

According to the CDC, what percentage of the U.S. population is diabetic or pre-diabetic?

A. 100%
B. About 50%
C. About 30%
D. About 0.1%

Correct answers at the end of slide deck. Indicated with bold and underlined fonts.

QUIZ 2. Q2.

Since when have there been PUBMED-listed articles on COVID-19?

A. January 2003
B. January 1919
C. January 2019
D. January 2020

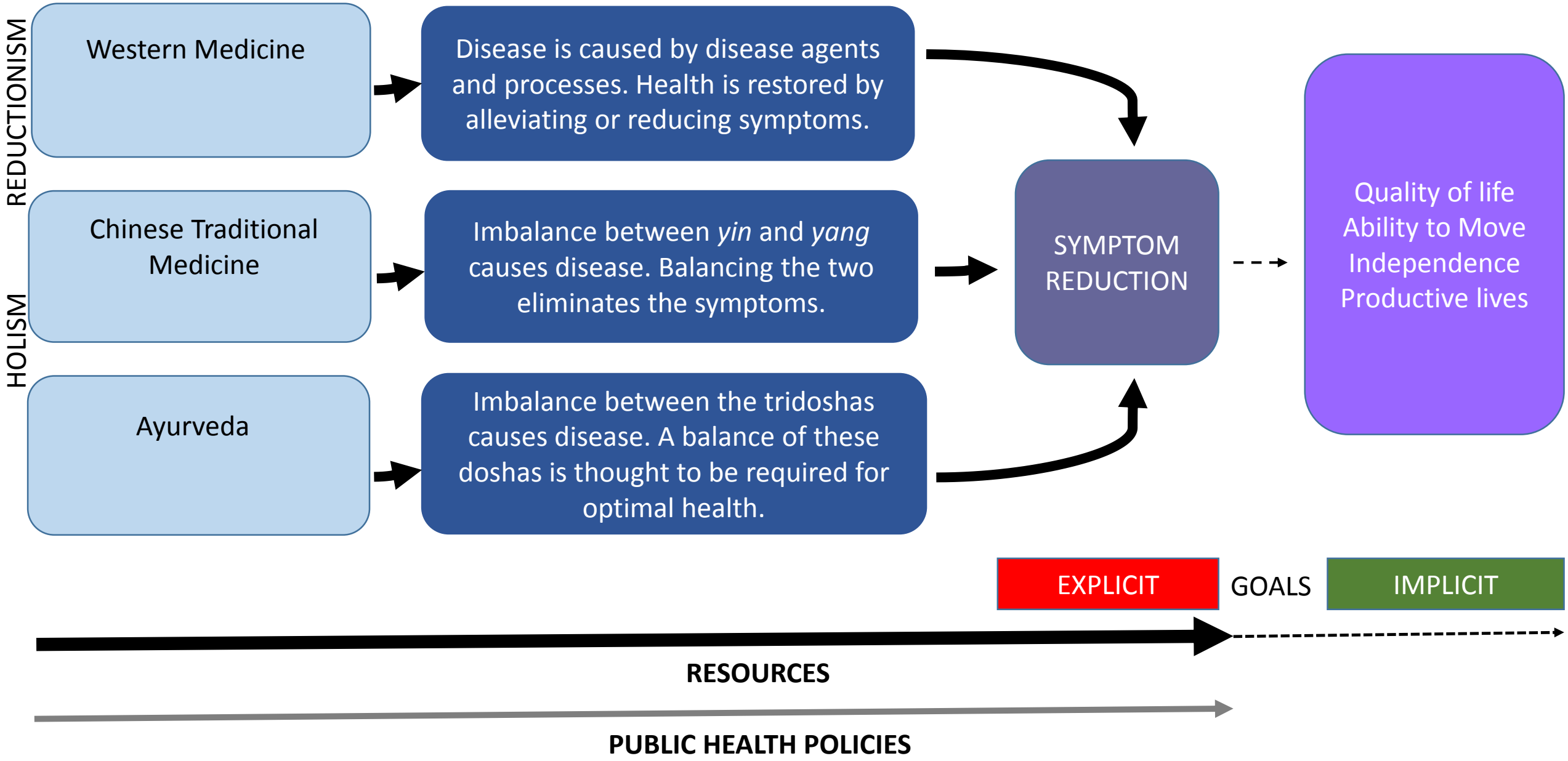
Correct answers at the end of slide deck. Indicated with bold and underlined fonts.

Goal 3.

HUMAN OCCUPATION & MOVEMENT BASED HEALTH OUTCOMES MODEL ™

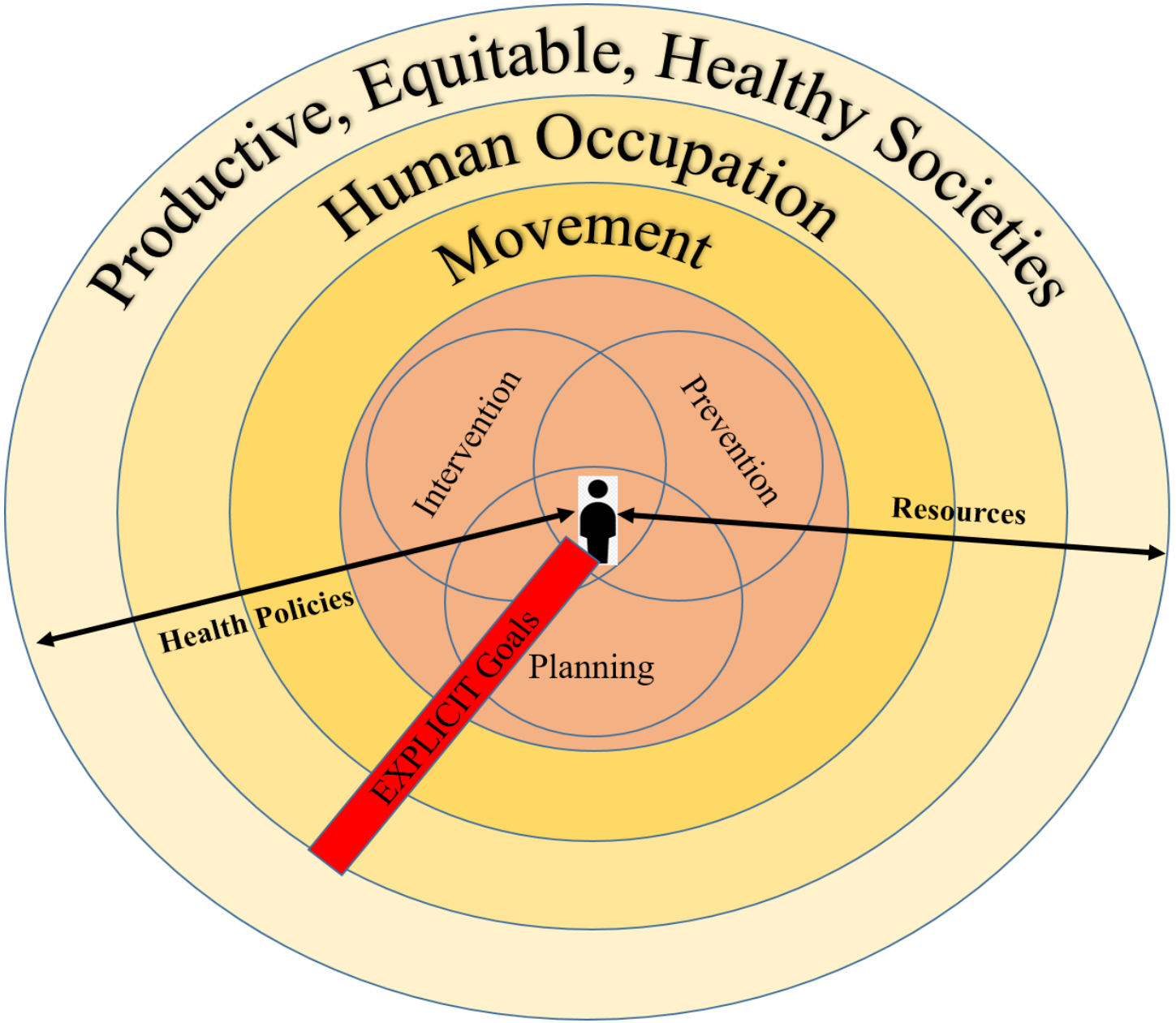
Healthcare Buzzwords

CURRENT HEALTHCARE OUTCOMES MODEL

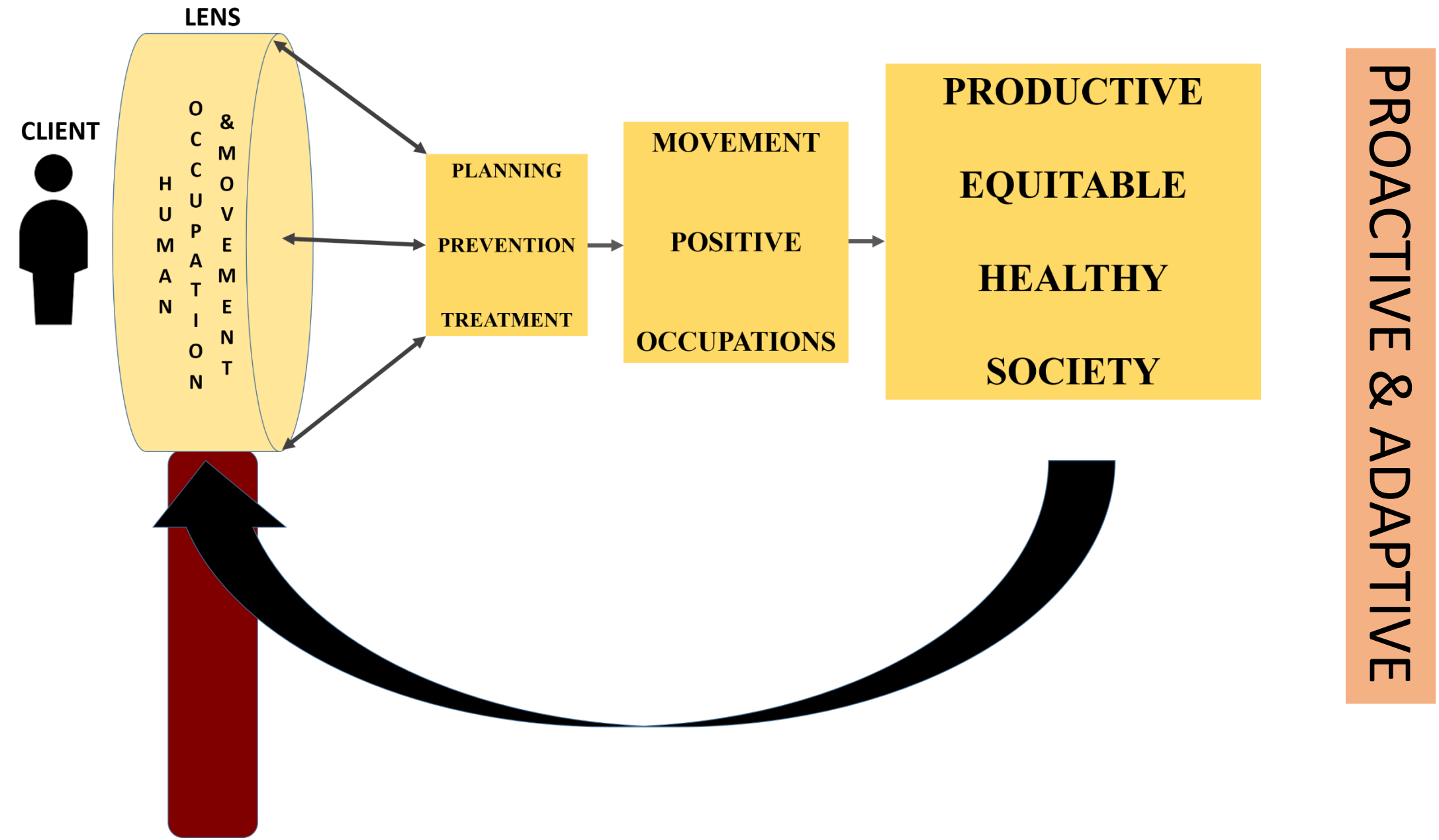


HUMAN OCCUPATION & MOVEMENT BASED HEALTH OUTCOMES MODEL™

HEALTHCARE REIMAGINED



HUMAN OCCUPATION & MOVEMENT BASED HEALTH OUTCOMES MODEL™



Case Study

- Patient with post-COVID-19 sequelae
- Hospital delivery worker
- 30 yr-old male
- Severe low back pain
- Moderate fatigue, muscle cramps and weakness, breathing difficulty
- Mild “mental fog”

PRIORITIES

Existing models: ?

HUMAN OCCUPATION & MOVEMENT BASED HEALTH OUTCOMES MODEL: ?

QUIZ 3. Q1.

What is the main focus of current healthcare systems?

A. Symptom reduction
B. Human Occupation and Movement
C. Preventative care
D. Human movement experience

Correct answers at the end of slide deck. Indicated with bold and underlined fonts.

QUIZ 3. Q2.

Which of the following healthcare systems would you prefer?

A. Symptom reduction based model
B. Human occupation and movement outcomes based model

This is a thought question for which there is no correct answer per se.

The speakers hope to have convinced the learner that, healthcare systems need to be revamped in order to better prepare for health crises like COVID-19.

In a reimagined healthcare system, the speakers propose that, human occupation and movement (i.e. functional outcomes) must be the explicit goal of healthcare, with symptom reduction being a means to that end.

Summary

- COVID-19 is caused by a virus that has an RNA genome, which uses host cells to make viral proteins and viral copies
- The bradykinin signaling pathway is likely the cause for severe inflammation in COVID-19 and there are approved drugs that might block this
- COVID-19 has taught us important lessons based on which healthcare must be reimagined and optimized
- One possible model to optimize healthcare is to use HUMAN OCCUPATION & MOVEMENT BASED HEALTH OUTCOMES ™ to drive healthcare rather than just address symptoms

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Thank you for your commitment
to lifelong learning

KNOWLEDGE IS POWER

Your scope of practice
should not limit
your scope of knowledge

- *Drs. Joseph and Ray Roche*

Answers to Quiz Questions related to Learning Objectives

QUIZ 1. Q1.

What is the proper name for the virus that causes COVID-19?

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B. <u>SARS-CoV-2</u>
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