

**Tuesday, September 8 @
3:00 pm PT / 6:00 pm ET**



A SAFE, ACCESSIBLE TREATMENT FOR ME/CFS? THE MITOCHONDRIAL STABILIZER IVO-21 STUDY



**Solve ME/CFS
CATALYST AWARD
HONOREE**



Dr. Jay H. Chung
National Institutes of Health



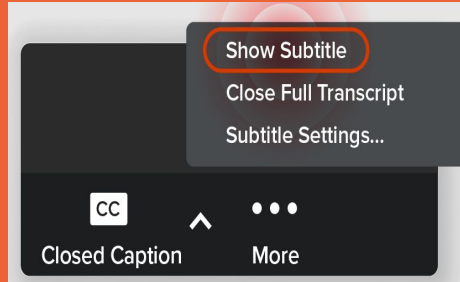
Jessica Maya, PhD
VP of Scientific Programs
Solve M.E.

About Our Webinars

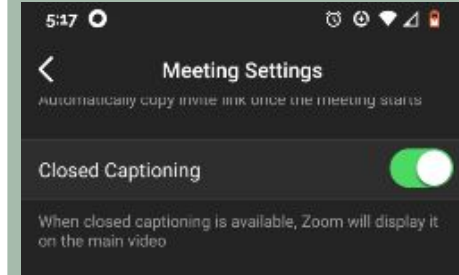
Q & A:



Captions:



Captions:



- If time permits, a Q&A session will follow the presentation
- Enter your questions in the box at the bottom of the screen (not in the chat) and **upvote your favorite questions**
- Closed captioning is available on the Zoom control settings as shown above

About Our Webinars



SolveME

@SolveME



Subscribed



- Webinars are recorded and will be available on our YouTube channel:
<http://youtube.com/SolveME>
- **Solve M.E. does not provide medical or legal advice**
 - We are not endorsing the presenter or the content of the presentation
 - Consult your doctor — do not use experimental or non-FDA approved treatments without medical supervision
 - These webinars are for informational and educational purposes only



Solve M.E.

www.SolveME.org

**Tuesday, September 8 @
3:00 pm PT / 6:00 pm ET**



A SAFE, ACCESSIBLE TREATMENT FOR ME/CFS? THE MITOCHONDRIAL STABILIZER IVO-21 STUDY



**Solve ME/CFS
CATALYST AWARD
HONOREE**



Dr. Jay H. Chung
National Institutes of Health



Jessica Maya, PhD
VP of Scientific Programs
Solve M.E.

Dr. Jay H. Chung **National Institutes of Health (NIH)**

Dr. Jay H. Chung earned his bachelor's degrees in electrical engineering and computer science and biology from M.I.T. before receiving an M.D. and Ph.D. in genetics from Harvard Medical School, where he was awarded the James Tolbert Shipley Prize for Excellence in Research. After an internship and residency in internal medicine at the Brigham and Women's Hospital, he became an endocrinology fellow at the National Institute of Diabetes and Digestive and Kidney Diseases at the NIH, where he trained with Gary Felsenfeld. He is currently a tenured senior investigator and chief of the Laboratory of Obesity and Aging Research in NHLBI. Dr. Chung has received numerous awards for his research, including the NHLBI Director's Awards and Orloff Scientific Awards.



Dr. Chung's Deck

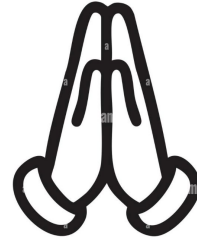
A Safe, Accessible Treatment for ME/CFS? The Mitochondrial Stabilizer IVO-21 Study

Presentation for Solve ME/CFS
(September 8, 2026)

Jay H. Chung MD, PhD
Laboratory of Obesity and Aging Research
NHLBI, NIH



Thank you, SOLVE ME/CFS



Diseases

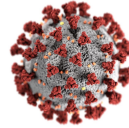
- 1. Acute: heart attack, stroke...**
- 2. Chronic: diabetes, cancer, hypertension...**

Illnesses

- 3. Acute: food poisoning, flu...**
- 4. Chronic: Normal tests, imaging studies..**

ME/CFS (myalgic encephalomyelitis/chronic fatigue syndrome)

Long COVID

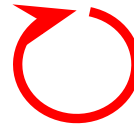


infection

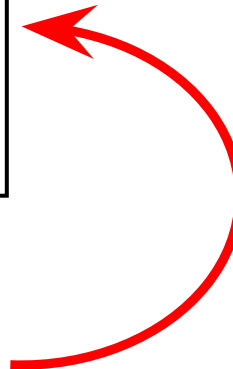


Illness

1. Pain
2. Post-exertional malaise (crash)
3. Fatigue
4. Brain fog
5. Insomnia
6. Dizziness/POTS



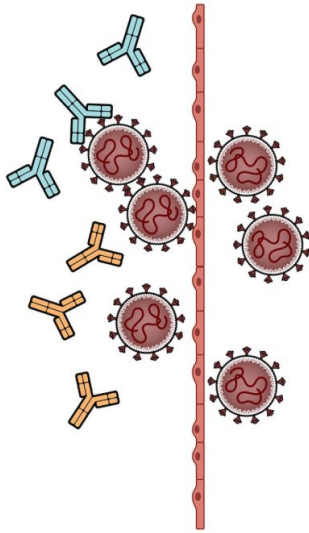
recover



relapse

Infection-immune theories of ME/CFS and long COVID

A sustained or renewed sensing of immune stimuli



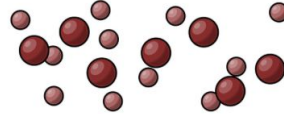
1 Viral reservoir

Persistence of ongoing viral replication at sites difficult to clear

Viral RNA



Nucleocapsid and other viral proteins



Spike protein

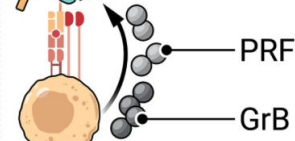


2 Viral fragments

Viral RNA and proteins, such as spike protein, can serve as a source of persistent antigen

Increased killing of healthy cells

Autoantibodies target self-antigens

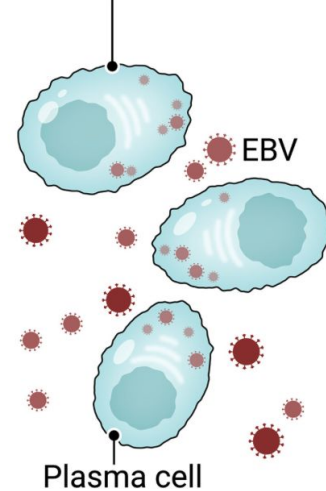


Autoreactive CD8⁺ T cell (effector)

3 Autoreactivity

Recognition of autoantigens where the immune system mistakenly attack self; this can also lead to autoimmune diseases

EBV reactivation



4 Transcriptional activation or reactivation of latent viruses

Perceived as a new or ongoing threat

Anti-virals are not effective ME/CFS or long COVID

Clinical Therapeutics/Volume 41, Number 5, 2019

Commentary

Pharmaceutical Interventions in Chronic Fatigue Syndrome: A Literature-based Commentary

Spencer Richman, B.Sc.^{1,2}; Matthew C. Morris, Ph.D.^{1,2};
Gordon Broderick, Ph.D.^{1,2,3,5}; Travis J.A. Craddock, Ph.D.^{3,4,6};
Nancy G. Klimas, M.D.^{3,6}; and Mary Ann Fletcher, Ph.D.^{3,6}

¹Gosnell School of Life Sciences, Rochester Institute of Technology, Rochester, NY, USA;
²Center for Clinical Systems Biology, Rochester General Hospital, Rochester, NY, USA;
³Institute for Neuro Immune Medicine, Nova Southeastern University, Fort Lauderdale, FL, USA; ⁴Departments of Psychology and Neuroscience, Computer Science, Nova Southeastern University, Fort Lauderdale, FL, USA; ⁵Department of Biomedical Engineering, Rochester Institute of Technology, Rochester, NY, USA; and ⁶Department of Clinical Immunology, Nova Southeastern University, Fort Lauderdale, FL, USA



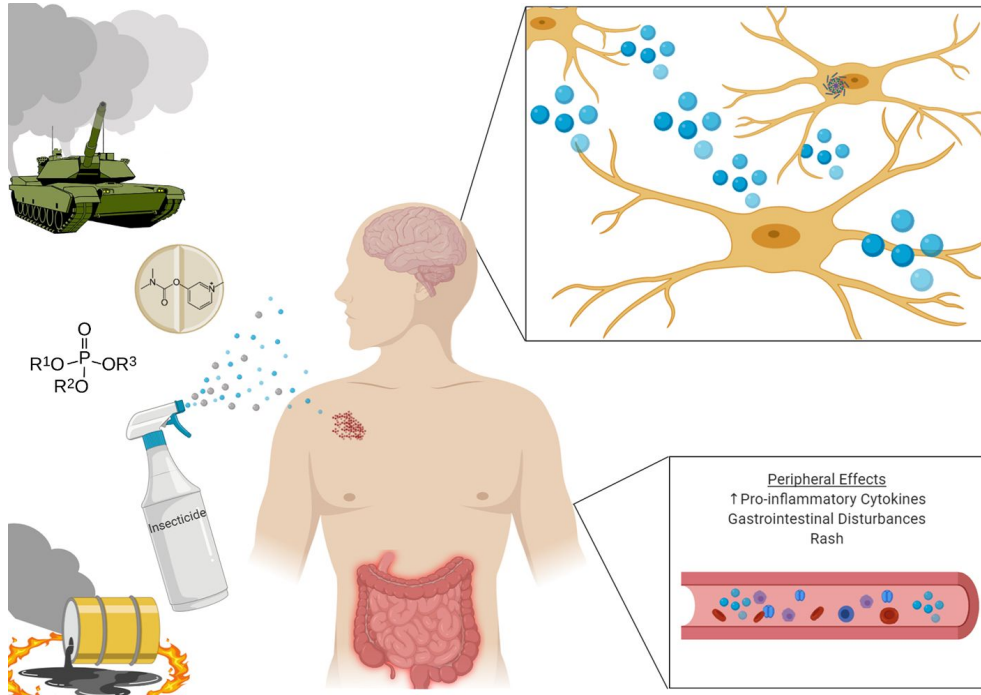
Nirmatrelvir-ritonavir targeting viral persistence in post-COVID-19 condition (long COVID) in the USA (RECOVER-VITAL): a randomised, double-blind, placebo-controlled, phase 2 trial

Lindsey R Baden, Nirav S Shah, Sean T H Liu, Jonathan Cohen, James May, Andre Kumar, Grace A McComsey, Peter Chen, Michelle Floris-Moore, Nora G Singer, Inti Fernandez, Alex J Slandzicki, Zanthia Wiley, Alexandra Kadl, David A Kaminsky, Harvey Hsu, Tiffany A Walker, Aluko A Hope, Luis Ostrosky-Zeichner, Jason D Goldman, Michael J Peluso, Thomas F Patterson, Sairam Parthasarathy, Janet M Mullington, Paul Bolin Jr, Sarah E Jolley, Jerry A Krishnan, Mario Castro, Sally L Hodder, Priscilla Pemu, Helen Y Chu, Michael G Risbano, Maya R Jerath, Eleftherios Mylonakis, Ryan T Hurt, Radica Alicic, Nabila S Azad, Marc A Sala, Michelle S Harkins, Jeffrey Parsonnet, Neil Stafford, Philip Robinson, Sabiha Hussain, Xian Qiao, Sophie Two Hawk, Michael Lillestol, Nathan Erdmann, Kelly A Gebo, Praveen Sudhindra, Joseph Sassine, Gailen D Marshall, Tulika Chatterjee, Caryn G Morse, Eyal Kedar, William W Stringer, Jennifer A Frontera, Michael Jordan, Caitlin Blaskewicz, Jorge L Santana, Rachel A Foot, Cherry Wongtrakool, Matthew William McCarthy, Alem Mehari, Arch Amon, Alison K Cohen, Nita Jain, Christine Maughan, Doug Lindsay, Rachel Olson, Samuel Broderick, Pearl Rowe, Sean M O'Brien, David R Walt, Bruce D Levy, Leonard A Jason, Phillip A Low, Cyndya A Shibao, Barry Make, Lucinda Bateman, Susan Redline, David Knopman, Adrian F Hernandez, Tracy L Nolen, Craig Reist, Lisa Berdan, Richard Whitley, Kanecia O Zimmerman; for the RECOVER-VITAL Clinical Trial Group*



Is Gulf War Syndrome ME/CFS?

(250,000 out of 750,000 soldiers, primarily army)



1. What is Gulf War Illness

Chronic multi-symptom illness may include symptoms such as

- Pain
- Cognitive difficulties and headaches
- Fatigue
- Gastrointestinal distress
- Sleep issues
- Respiratory problems
- Joint and muscle pain
- Skin problems

Treatment has focused on treating the symptoms and not the underlying causes, which are still poorly understood.

Exposure in 1990: It is unlikely that there is a toxin reservoir after >35 years

'Havana syndrome' and the mystery of the microwaves

8 September 2021

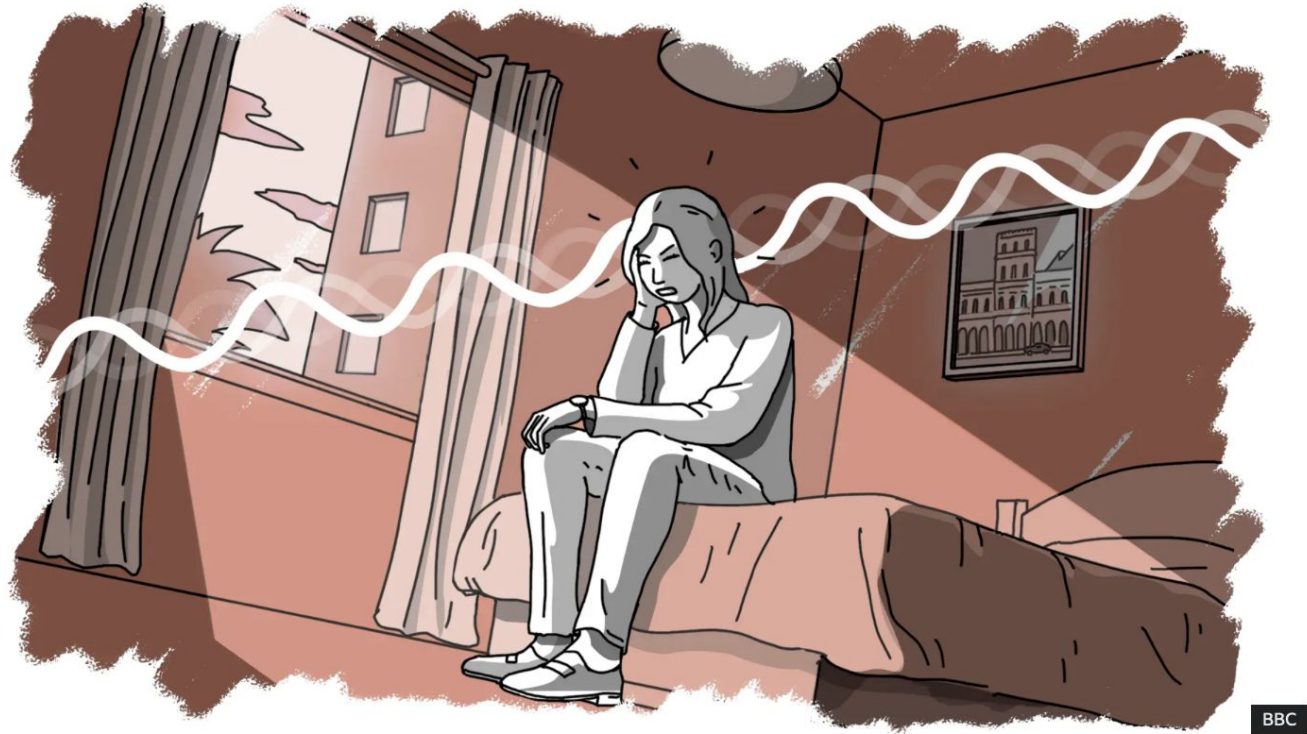
Share

Save

 Add as preferred on Google

Gordon Corera

Security correspondent, BBC News



BBC

There are diverse triggers unrelated to infection (20%): surgery, psychological trauma, ICU..

ME/CFS likely extends beyond a purely post-infectious phenomenon.

ME/CFS may reflect an underlying vulnerability to cellular stress in susceptible individuals.

Our goal is to define the biological basis of this vulnerability and leverage that understanding to develop effective therapies.

Many Treatments Have Been Tried—But None Has Yet Solved ME/CFS or Long COVID

Treatments that have been tested:



Immune therapies

Rituximab • IVIG • anti-inflammatory drugs



Blood flow & autonomic therapies

Pyridostigmine • beta blockers • fluids and salt



Energy & mitochondrial approaches

CoQ10 • metabolic therapies • supplements



Antiviral therapies

Paxlovid and other antiviral approaches



Symptom-directed treatments

Low-dose naltrexone • antihistamines • rehabilitation • pacing

Metabolic therapies that have been tried

Approach	Basic rationale
CoQ10	Support mitochondrial electron transport
NAD ⁺ precursors	Increase NAD ⁺ availability for mitochondrial metabolism
Ribose	Provide substrate for nucleotide/ATP synthesis
Acetyl-L-carnitine	Facilitate fatty-acid transport into mitochondria
D-ribose + CoQ10	Support ATP production
Metformin Low dose rapamycin	Alter cellular metabolism and inflammatory signaling
Mitochondrial supplements	Attempt to improve oxidative phosphorylation
Dietary/metabolic interventions	Alter fuel utilization

different perspective on chronic illnesses

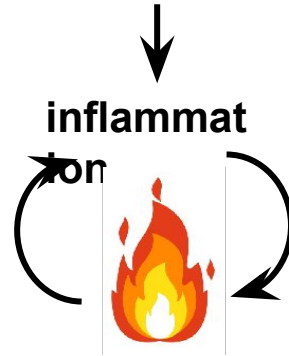
Key question: Regardless of how the “fire” was initially started, what keeps the fire going?

Positive feedback loop (vicious cycle)



Inflammation: fuel to the fire

Stressor
(e.g. infection, physical or psychological trauma...)



Frontiers in **Neurology**

HYPOTHESIS AND THEORY
published: 25 May 2022
doi: 10.3389/fneur.2022.877772



Molecular Mechanisms of Neuroinflammation in ME/CFS and Long COVID to Sustain Disease and Promote Relapses

Warren Tate^{1,2*}, Max Walker¹, Eiren Sweetman^{1,3}, Amber Helliwell¹, Katie Peppercorn^{1,2}, Christina Edgar¹, Anna Blair⁴ and Aniruddha Chatterjee⁵

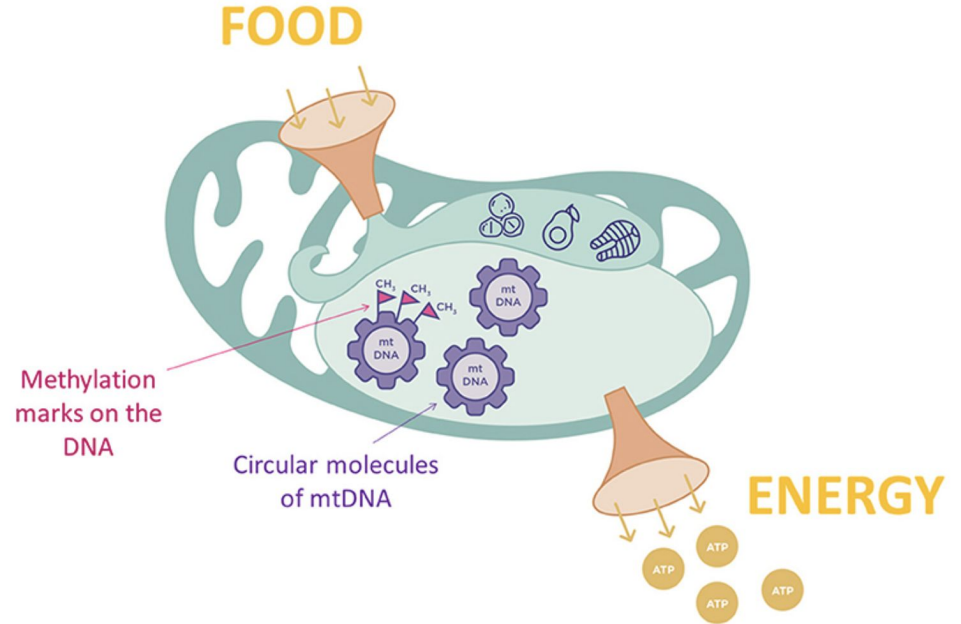
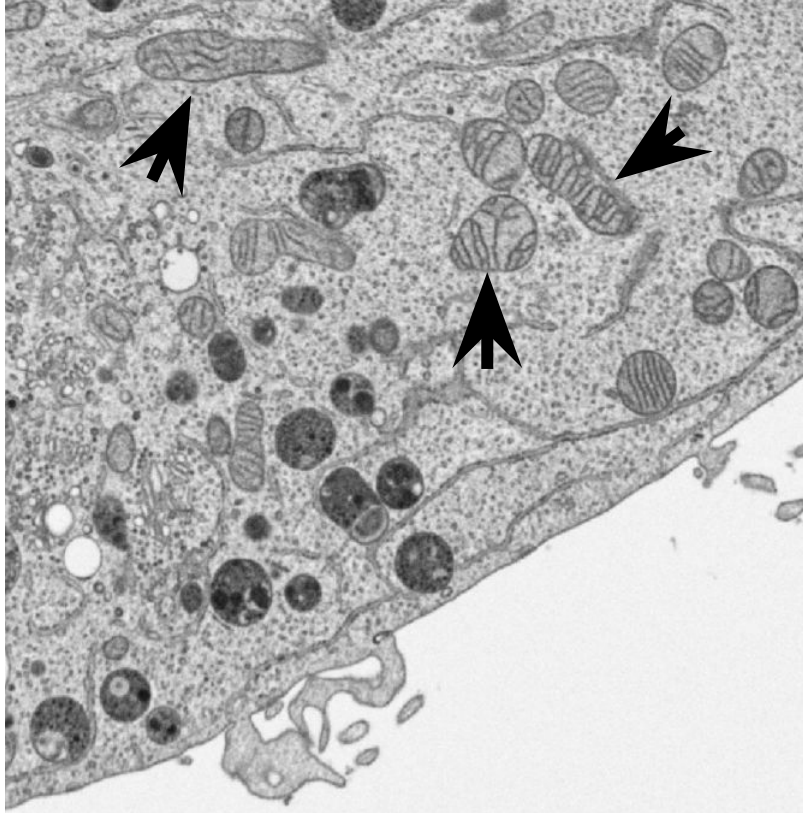
**Will not be detectable in a blood test-
Too diluted by the time it gets to your arm**



197
9

Could there be an enemy within?

Mitochondria convert food into energy

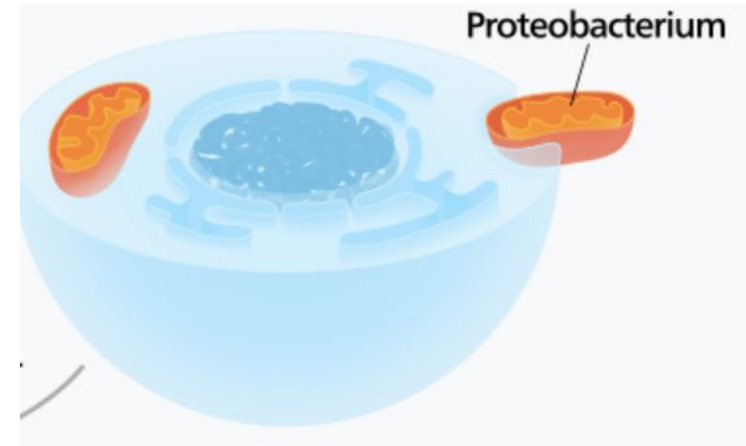
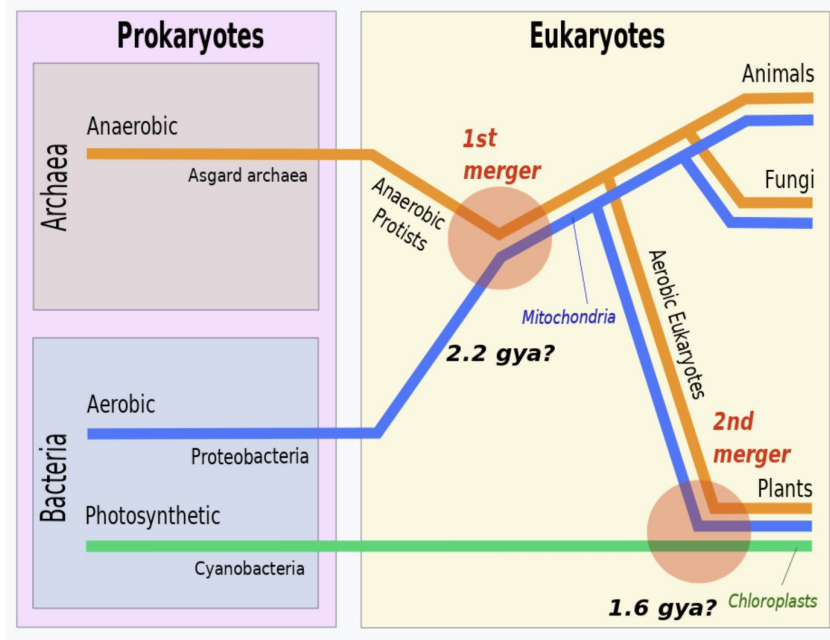


Dysfunctional mitochondria = broken metabolic engine



That mitochondrial dysfunction causes fatigue is obvious, but how does it cause inflammation?

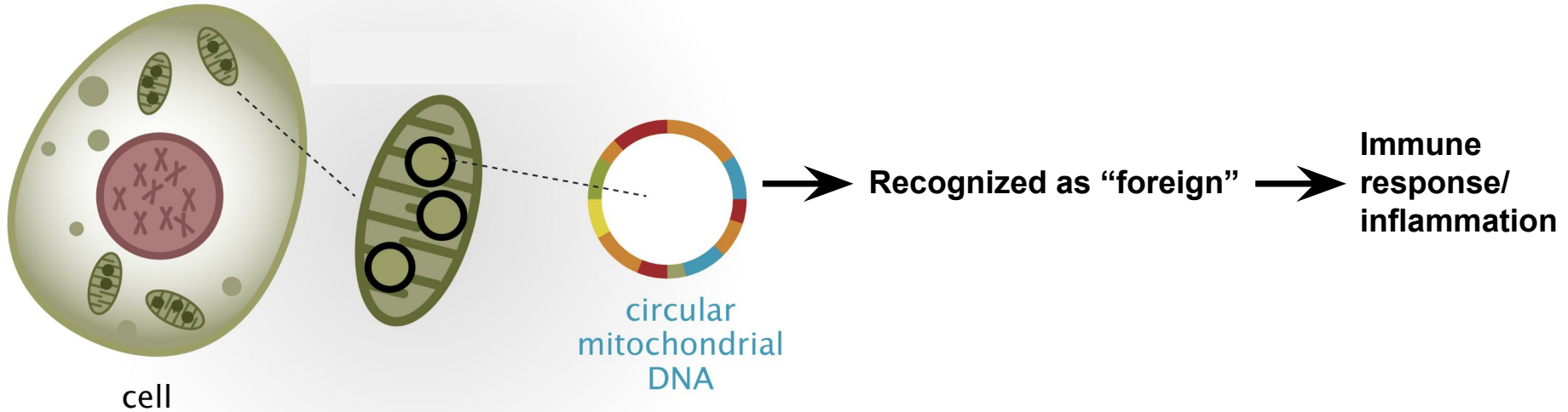
Mitochondrion is derived from proteobacteria (endosymbiosis)



Rickettsia
prowazekii

Mitochondrial DNA (mtDNA) is different from our chromosomal DNA and our immune system recognizes it as foreign if it is released from mitochondria

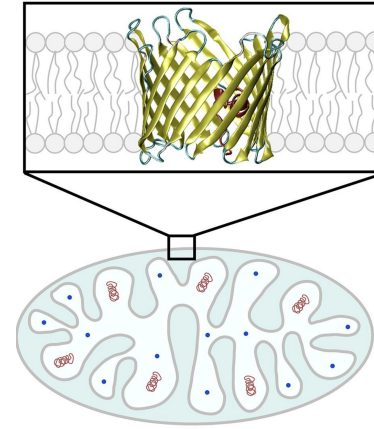
Mitochondria has bacteria-like DNA



(c) CMG, UZ Brussels, Belgium

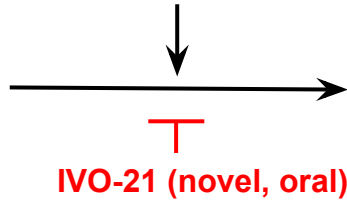
Mitochondrial membrane protein VDAC links stress to inflammation

VDAC (voltage-dependent anion channel)

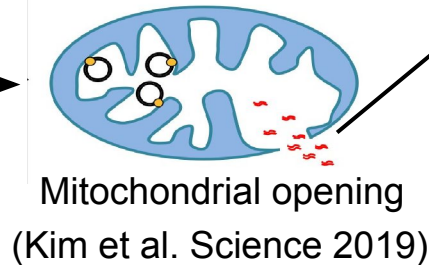


Stress

oxidative stress
infection
trauma



**VDAC
becomes sticky**

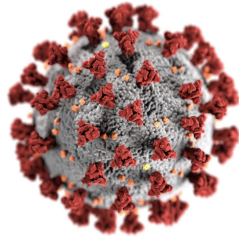


mtDNA release
mtRNA release

Anti-viral response
Anti-bacterial response

IL-1, IL-6
Pain
Brain fog
Fatigue...

IVO-21 inhibits COVID-19 spike protein-induced ROS and mtDNA release



Covid 19

Received: 7 February 2023 | Revised: 18 March 2023 | Accepted: 10 April 2023

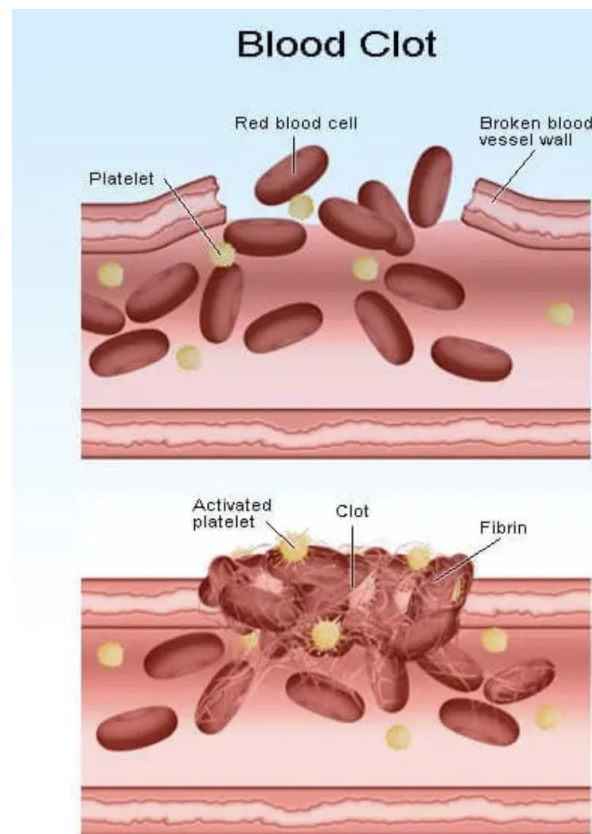
<https://doi.org/10.1016/j.jtha.2023.04.039>

REVIEW ARTICLE

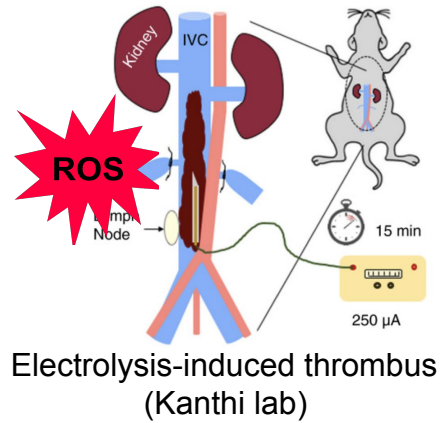
Thromboinflammation in long COVID—the elusive key to postinfection sequelae?

Leo Nicolai^{1,2} | Rainer Kaiser^{1,2} | Konstantin Stark^{1,2}

jth



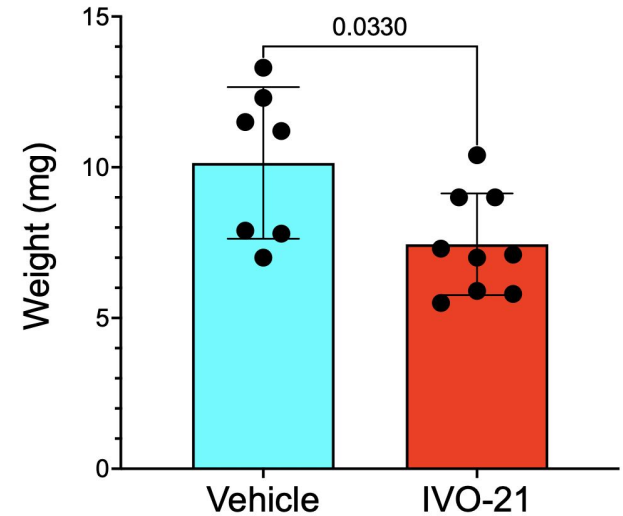
IVO-21 protects against thromboinflammation in mice without bleeding risk



vehicle



IVO-21

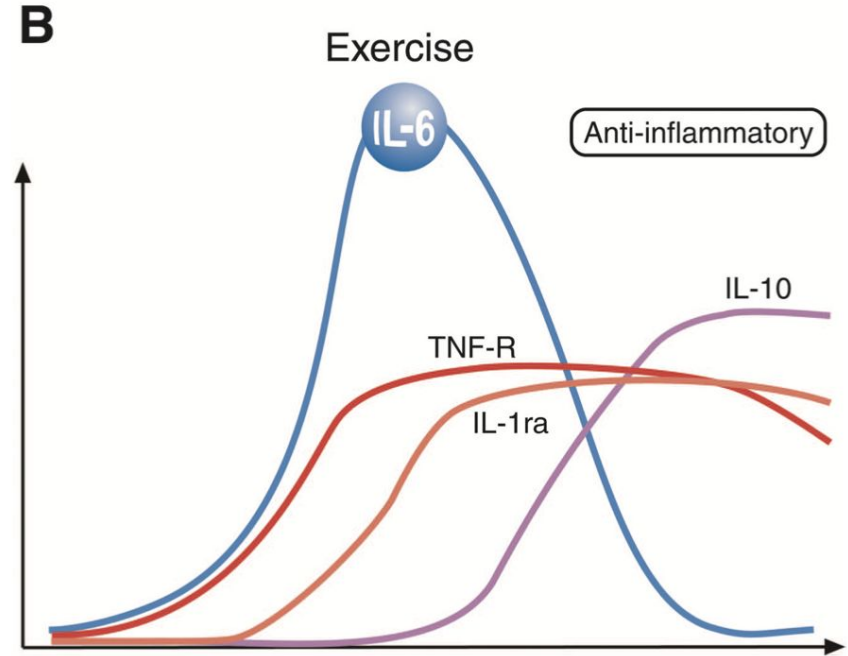
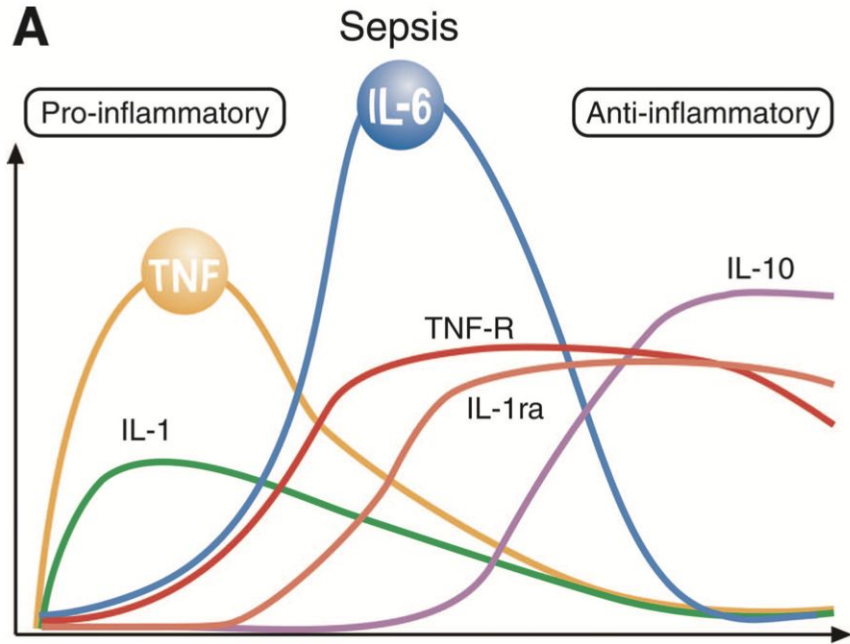


Does the inflammation cycle explain post-exertional malaise (crash)?



Physical or mental exertion

Inflammatory cytokine IL-6 is elevated in Long Covid in the resting state (could IL-6 explain post-exertional malaise?)

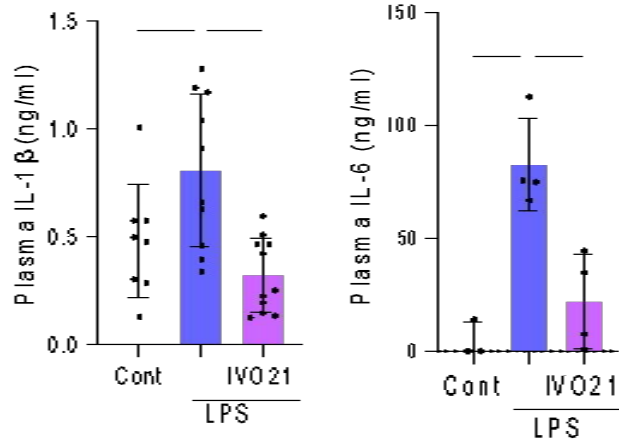


IL-6 is elevated after both sepsis and exercise

IVO-21 mitigates the inflammation cycle

Human cells

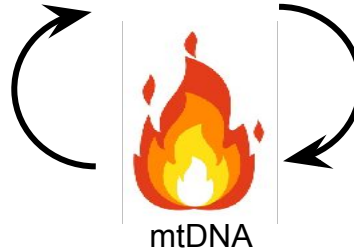
mice



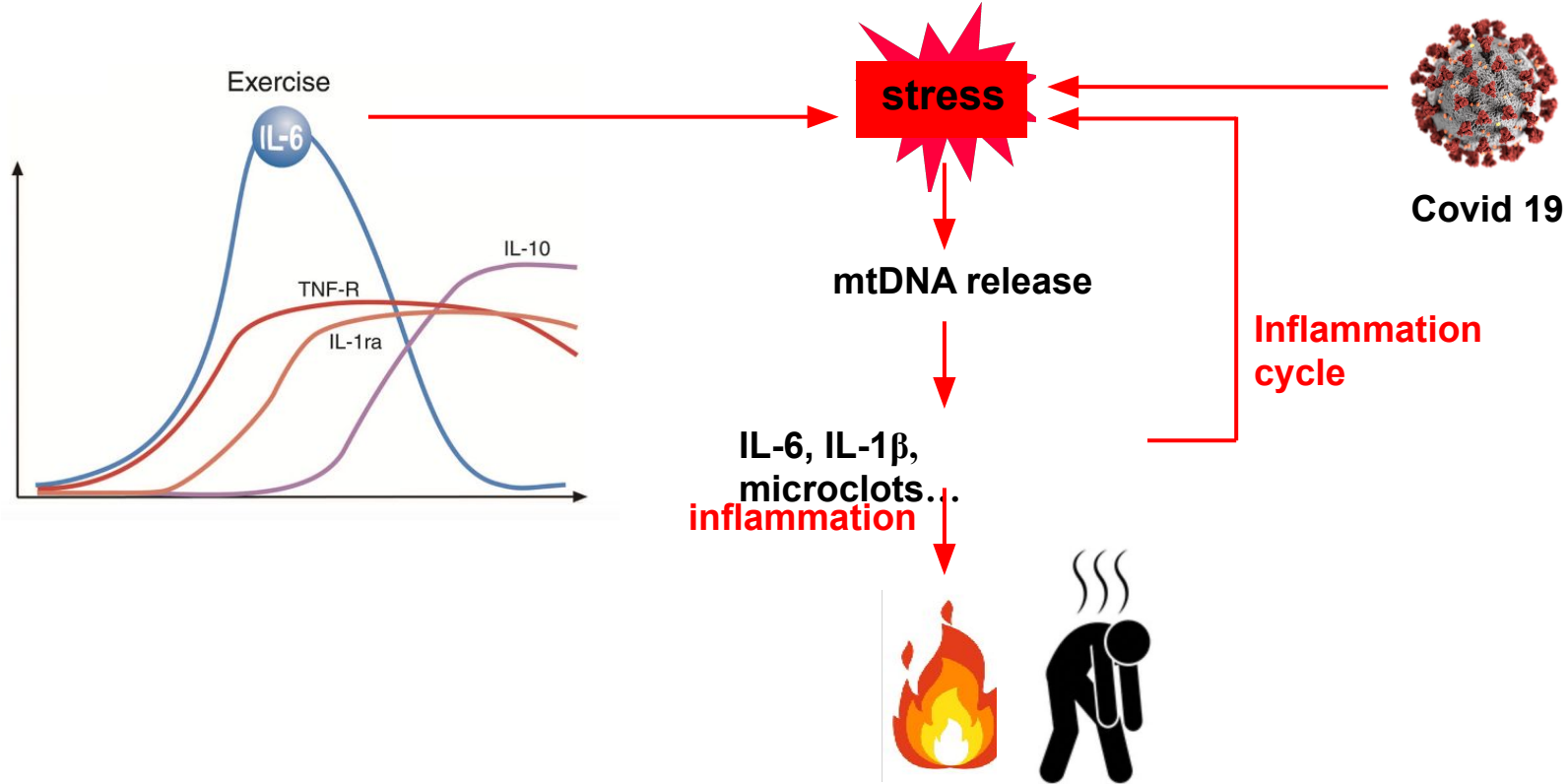
LPS=bacterial cell wall lipid

mtDNA:

inflammation/cell damage



Post-exertional IL-6 drives malaise in a vicious cycle?



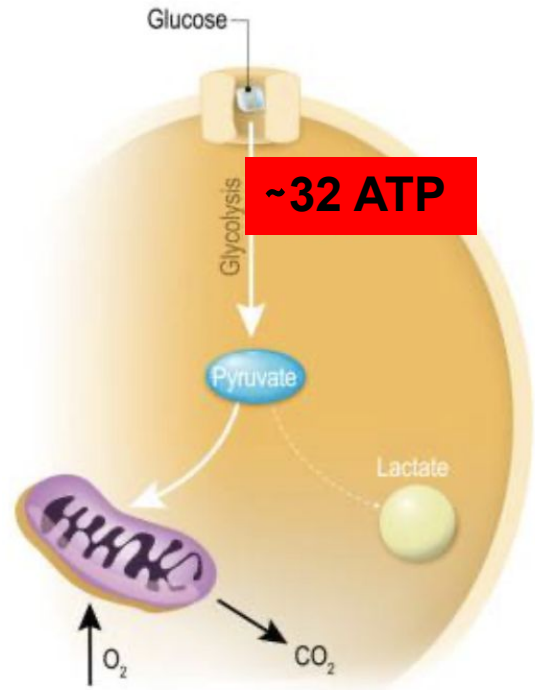
Different ways of making energy: marathon runner vs sprinter



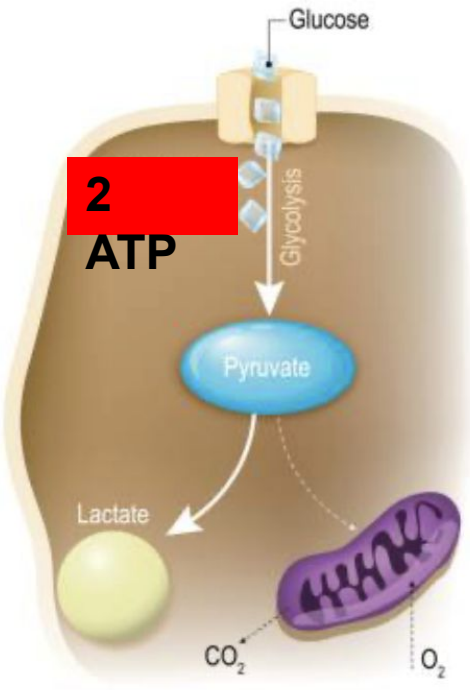
Slow-twitch fiber
(mitochondria)

Fast-twitch fiber
(glycolysis)

Mitochondria
(oxidative phosphorylation)



Glycolysis
(no mitochondria)

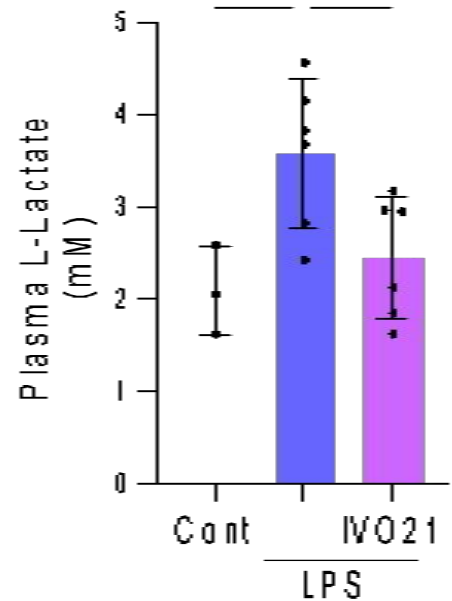


Lactic acid is inflammatory

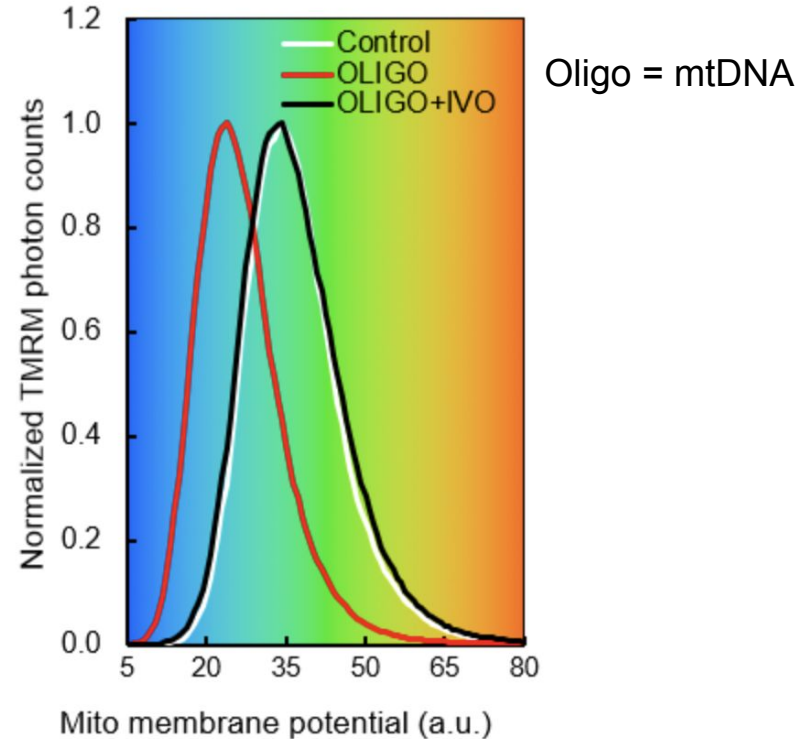
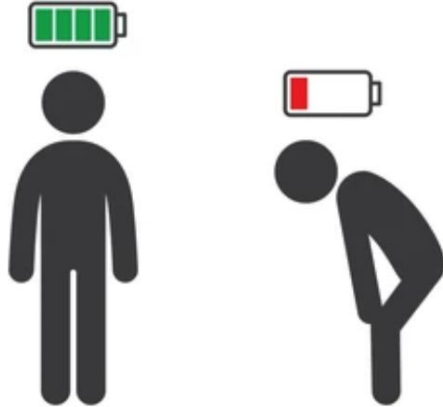
Lactic Acid Fermentation Is Required for NLRP3 Inflammasome Activation

Hsin-Chung Lin^{1,2}, Yu-Jen Chen^{3,4,5}, Yau-Huei Wei⁶, Hsin-An Lin⁷, Chien-Chou Chen⁷, Tze-Fan Liu⁸, Yi-Lin Hsieh⁹, Kuo-Yang Huang⁹, Kuan-Hung Lin¹⁰, Hsueh-Hsiao Wang⁸ and Lih-Chyang Chen^{8*}

¹ Graduate Institute of Medical Sciences, National Defense Medical Center, Taipei, Taiwan, ² Division of Clinical Pathology, Department of Pathology, Tri-Service General Hospital, Taipei, Taiwan, ³ Department of Radiation Oncology, MacKay Memorial Hospital, New Taipei City, Taiwan, ⁴ Department of Medical Research, MacKay Memorial Hospital, New Taipei City, Taiwan, ⁵ Department of Nursing, MacKay Junior College of Medicine, Nursing, and Management, Taipei, Taiwan, ⁶ Center for Mitochondrial Medicine and Free Radical Research, Changhua Christian Hospital, Changhua, Taiwan, ⁷ Department of Medicine, Tri-Service General Hospital SongShan Branch, Taipei, Taiwan, ⁸ Department of Medicine, MacKay Medical College, New Taipei City, Taiwan, ⁹ Graduate Institute of Pathology and Parasitology, National Defense Medical Center, Taipei, Taiwan, ¹⁰ Institute of Biomedical Sciences, MacKay Medical College, New Taipei City, Taiwan



IVO-21 restores mitochondrial “charge”



IVO-21 increases lysosomal activity

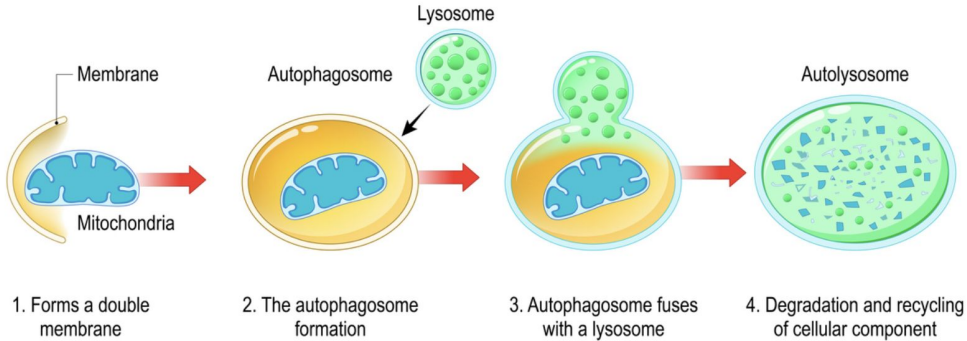
rapamycin



mTOR



autophagy

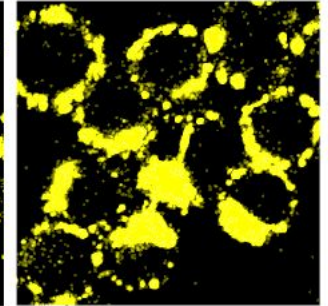
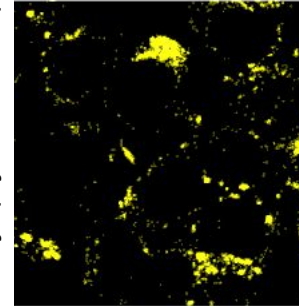
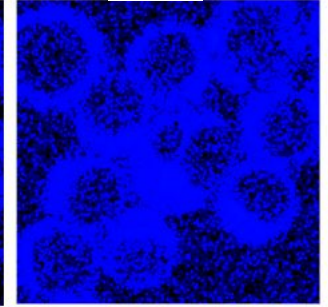
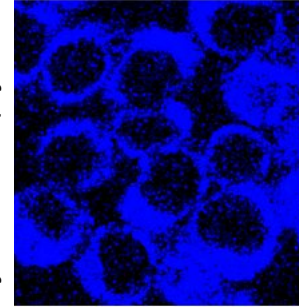


Lysosomal removal of damaged mitochondria

lysosome (LysoTracker)
acidity (LysoSensor)

vehicle

IVO



WASF3 disrupts mitochondrial respiration and may mediate exercise intolerance in myalgic encephalomyelitis/chronic fatigue syndrome

Ping-yuan Wang^{a,1}, Jin Ma^{a,1}, Young-Chae Kim ^a, Annie Y. Son^a, Abu Mohammad Syed ^a, Chengyu Liu ^b, Mateus P. Mori ^a, Rebecca D. Huffstutler^a, JoEllyn L. Stolinski^c, S. Lalith Talagala^c, Ju-Gyeong Kang^a, Brian T. Walitt^d, Avindra Nath ^d, and Paul M. Hwang ^{a,2}

Edited by Se-Jin Lee, University of Connecticut School of Medicine, Farmington, CT; received February 17, 2023; accepted June 27, 2023

August 14, 2023 | 120 (34) e2302738120 | <https://doi.org/10.1073/pnas.2302738120>

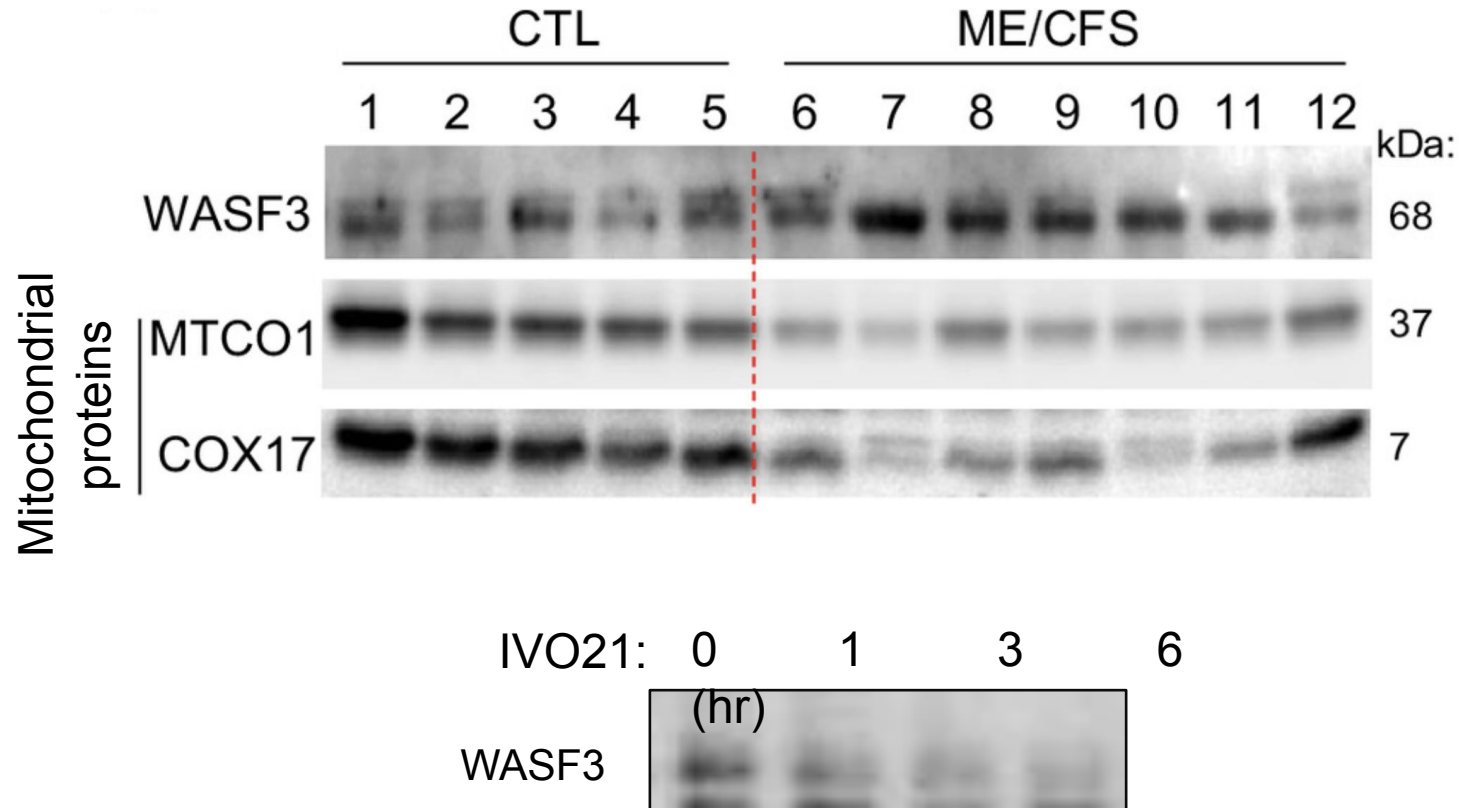
[Helpline](#)[Donate](#)

[About](#)  [Information](#)  [Research](#)  [Health & Social Care](#)  [Get Involved](#)  [Contact Us](#)  [Shop](#)  

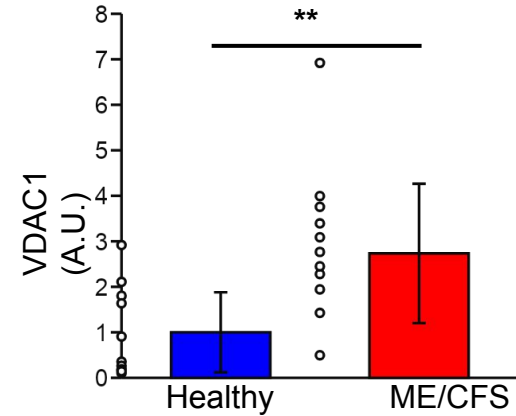
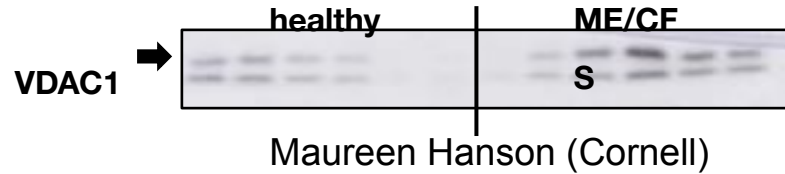
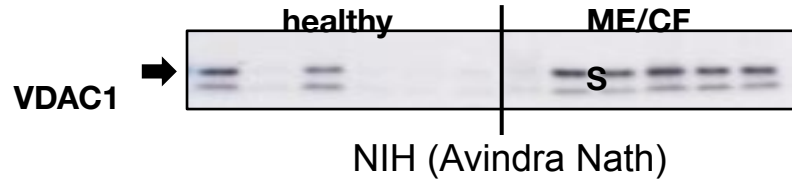
**Protein found that
disrupts energy levels
in ME/CFS**



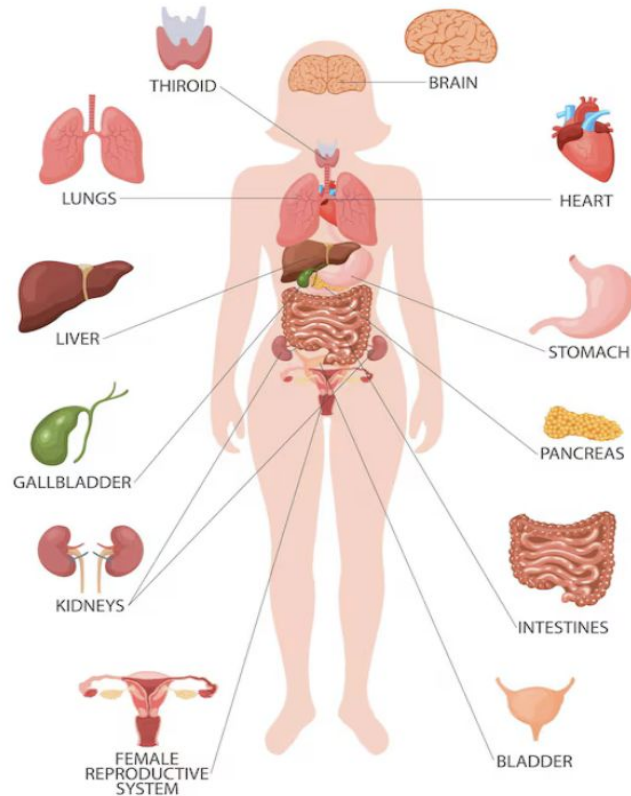
IVO-21 suppresses WASF3



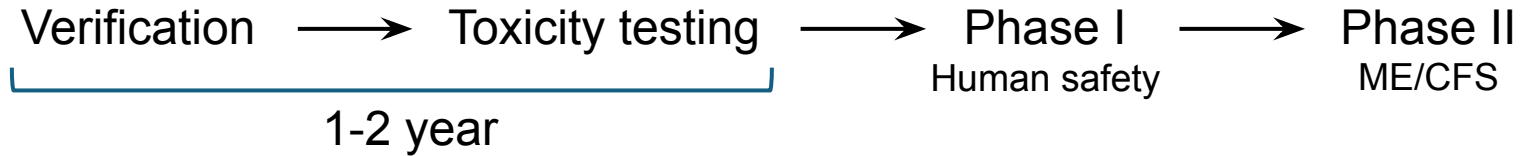
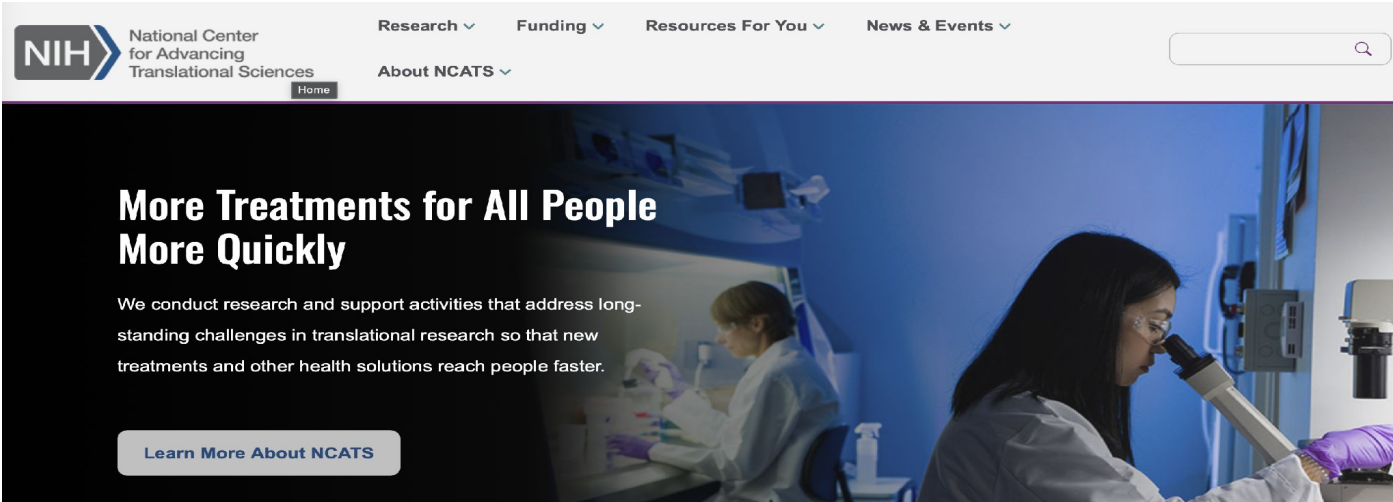
VDAC1 is elevated in ME/CFS



Clinical manifestations may depend on the organ in which the inflammatory cycle is established

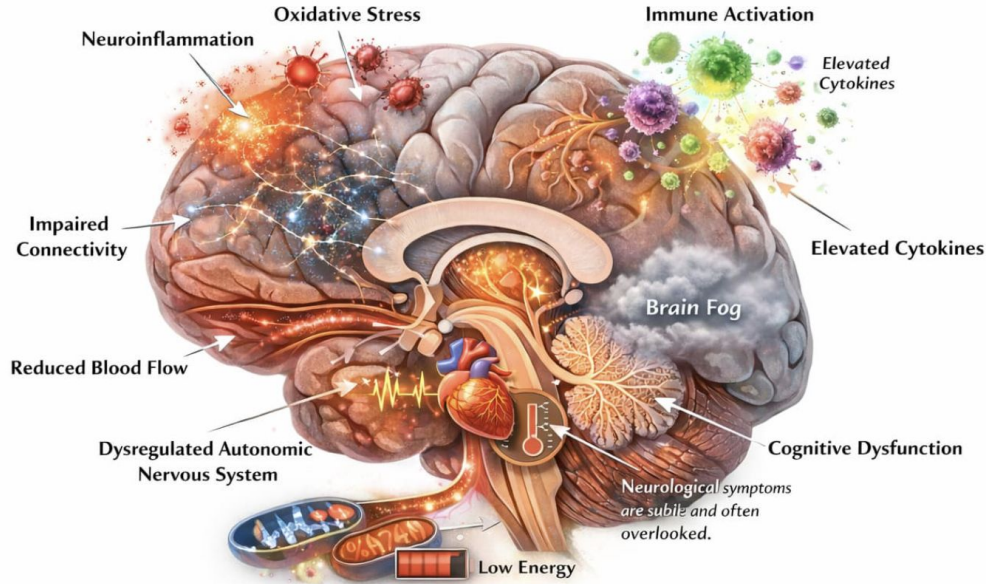


IVO-21 may not be effective if there is a hidden microbial reservoir



Why do we need animal models?

Chronic Fatigue Syndrome (ME/CFS)



Cannot recreate the complex long-term cell-cell interaction in a petri dish.

ACKNOWLEDGEMENT

Chung lab
(NHLBI)
Mina Thon
Sungjun Park

Devikala
Gurusamy
Jinsung Park
Mungyu Song
Shutong Yang
Antoine Smith

Maureen Hanson
(Cornell)
Avi Nath (NINDS, NIH)

Jay R. Knutson
(NHLBI)
Rozhin Penjweini
Nikhil Mattu
Yogendra Kanthi
(NHLBI)
Francesca Elmer
Sumith Panicker
Rolf Swenson (NHLBI)
Chandrasekaran Mushti

Yaron Rotman
(NIDDK)
Mariana Kaplan
(NIAMS)
Luz Blanco

Samer Gawrieh (Indiana U)
Naga P. Chalasani
Sunmi Lee (MD Anderson)
Lorant Szekvolgyi (U of Debreden)
Zsolt Karanyi

Tatiana Rostovtseva
(NICHD)
Mya Wolfe
Megha Rajendran
Sergey M. Bezrukov

Kyung J. Kwon-Chung
(NIAID)
Dong-Hoon Yang

Fatima Z. Alshboola (Texas A&M)
Ahmed B. Alarabib
Fadi T. Khasawneh

Cores (NIH)
Chengyu Liu
Oladele A. Oluwayiose,
Amirhossein Shamsaddini
Neelam Redekar
Abdel G. Elkahoun
Ronald J. Holewinski
Benjamin
Schwartz
Nathan Brandes

Eric Boilard (U Laval)
Martin Pelletier (U Laval)
Lynn Martin
Yann Breton
Tania Lévesque

FUNDING ACKNOWLEDGEMENTS

NIH

Amar Foundation

Solve ME/CFS



Q & A

Register for Our Sept. 22 Webinar



Tuesday, September 22 @
3-4 pm PT / 6-7 pm ET



YOUR STORY, YOUR SYMPTOMS, YOUR DATA: DISCOVER unhide®

Visualizing Your Health Trends with Validated Survey Scoring



Dr. Sally Daganzo
Private Practice



Dr. Deborah Duricka
Co-Principal Investigator
Brain Inflammation
Collaborative



Dr. Megan Fitzgerald
Scientific Director
Brain Inflammation
Collaborative



Christy Jagdfeld
CEO
Brain Inflammation
Collaborative



Christina Moon
Clinical Research Assoc.
Brain Inflammation
Collaborative



Dr. Sadie Whittaker
CSO
Solve M.E.

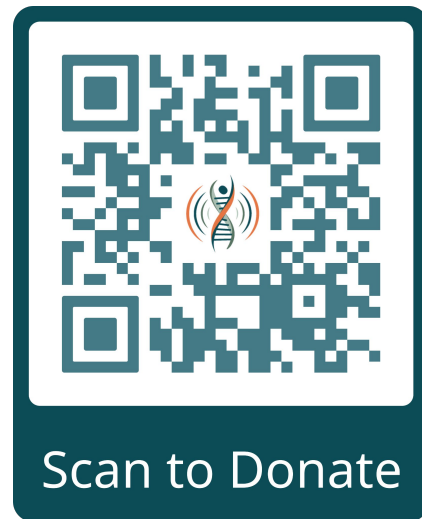
HELP US TURN RESEARCH INTO REALITY

Our research, advocacy and educational programs are only possible with donor support.

Solve M.E. leverages donor contributions into bigger gains in cures and treatment for ME/CFS, Long Covid, and associated chronic conditions.

Please consider supporting our work with a gift today. Go to SolveME.org/donate or use this QR code.

Together, we can turn research into reality.



Join our online community!



Twitter
@PlzSolveCFS



Facebook
Solve
ME/CFS
Initiative



Instagram
@solve_cfs



YouTube
SolveCFS



LinkedIn
Solve
ME/CFS
Initiative

Be at the Center of the Solution

Get updates on upcoming webinars: <http://solvecfs.org/events>

Get the latest Solve news: <http://solvecfs.org/newsletters>

Drive research and fund progress: <https://solvecfs.org/donate>