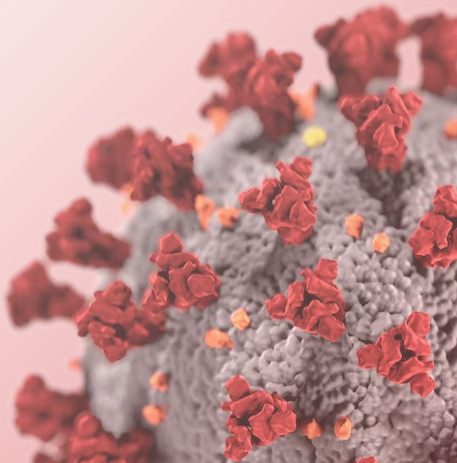
FLCCC ALLIANCE
EDUCATIONAL CONFERENCE 2022

UNDERSTANDING & TREATING
SPIKE PROTEIN-INDUCED DISEASES

October 14-16, 2022 • Orlando, Florida

Management of Spike Protein Pathogenesis via Autophagy

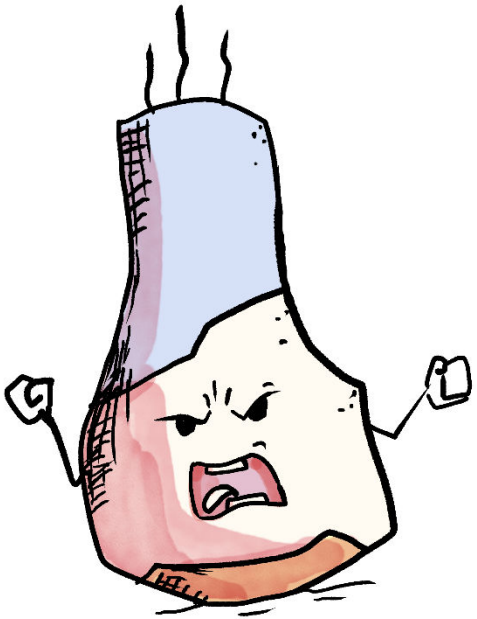
Intermittent Fasting, Spermidine, and Resveratrol



Presented By:

Mobeen Syed MD.

Spike Proteins Persistence



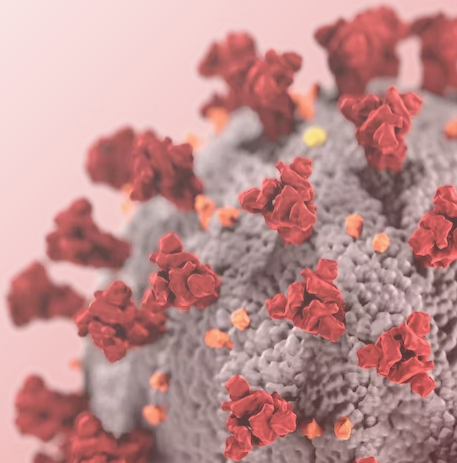
FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

FLCCC ALLIANCE
EDUCATIONAL CONFERENCE 2022

UNDERSTANDING & TREATING
SPIKE PROTEIN-INDUCED DISEASES

October 14-16, 2022 • Orlando, Florida

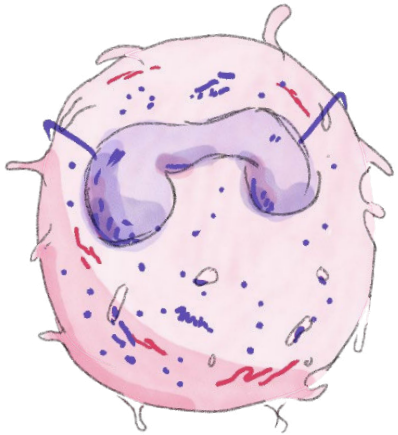
Spikopathy
Spikopathogenesis

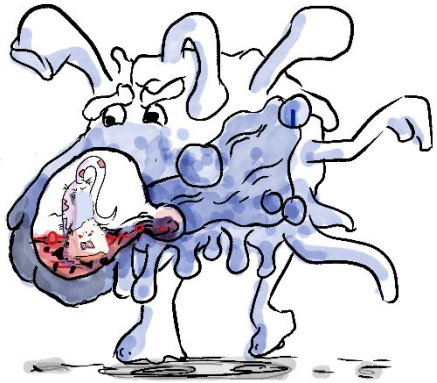


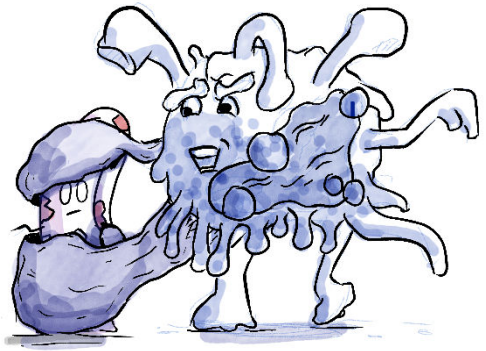
Spike Proteins Persistence

Persistence in monocytes

https://www.frontiersin.org/articles/10.3389/fimmu.2021.746021/full



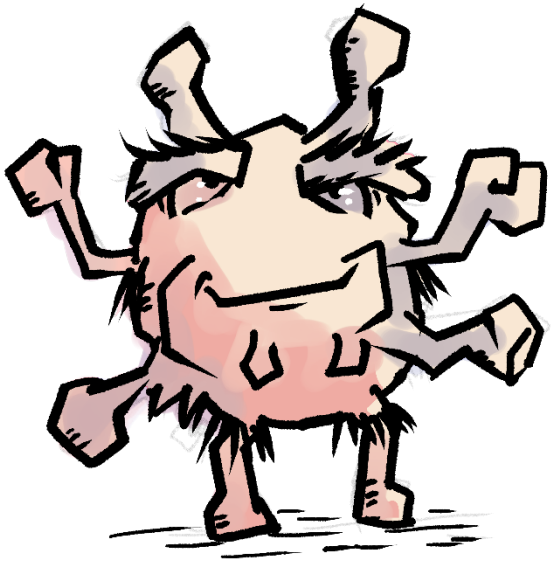




FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

Spike Proteins Persistence

Persistence due to the viral reservoirs

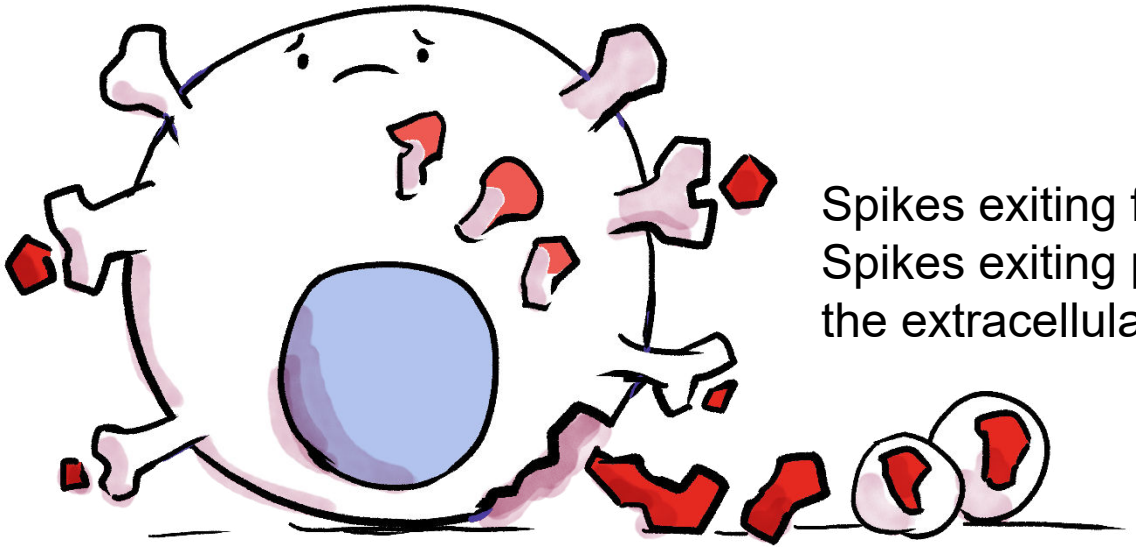


FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

Spike Proteins Persistence

Persistence due to the continuous production from the vaccine mRNA

https://www.mdpi.com/2227-9059/10/7/1538/pdf



Spikes exiting from broken cell
Spikes exiting packaged within the extracellular vesicles (EVs)

https://www.jimmunol.org/content/207/10/2405

https://www.nature.com/articles/s41586-021-03738-2

FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

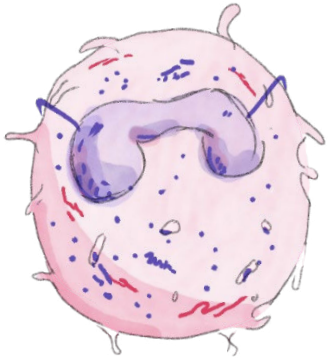
Immune Response Abnormalities

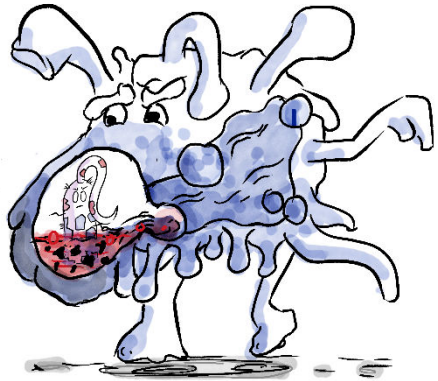
Chronically activated monocytes. https://www.frontiersin.org/articles/10.3389/fimmu.2021.746021/full

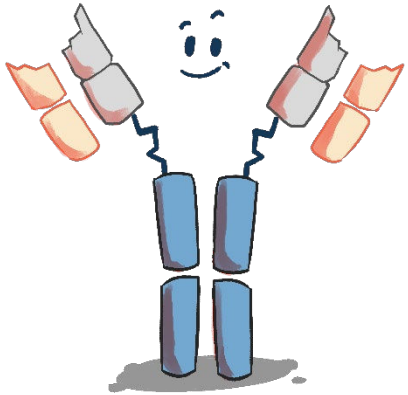
Macrophage activation syndrome. https://pubmed.ncbi.nlm.nih.gov/35084316/

Anti-idiotypic antibodies (anti-ACE2 antibodies.)

https://www.nejm.org/doi/10.1056/NEJMcibr2113694



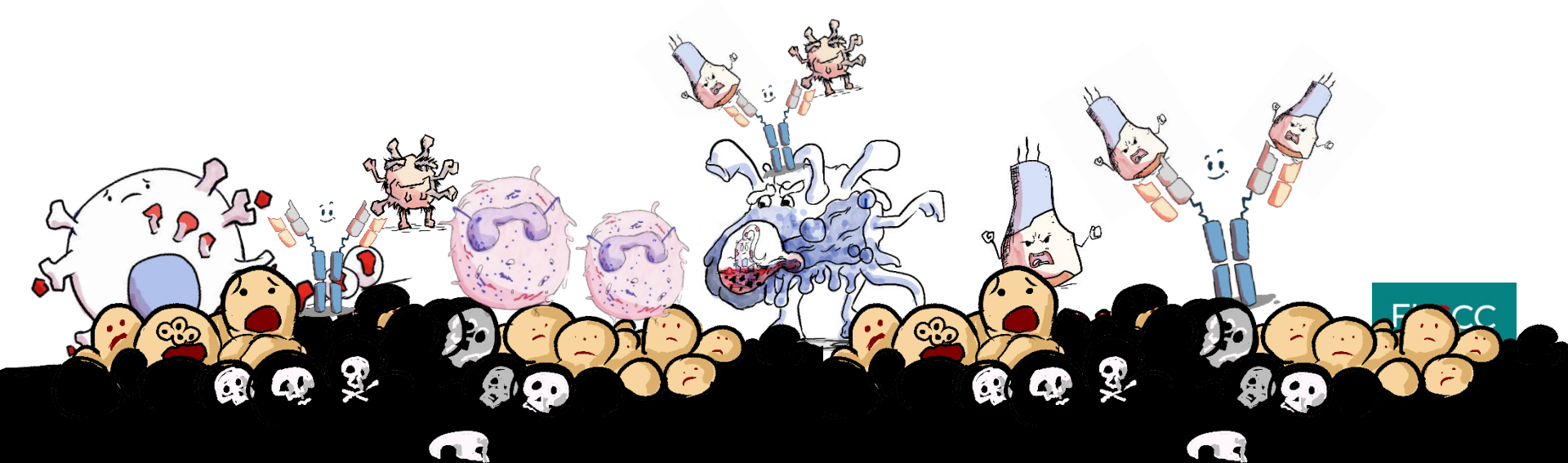




FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

Spikopathy

Immune dysregulation, inflammation, and tissue damage due to the presence of spike protein.



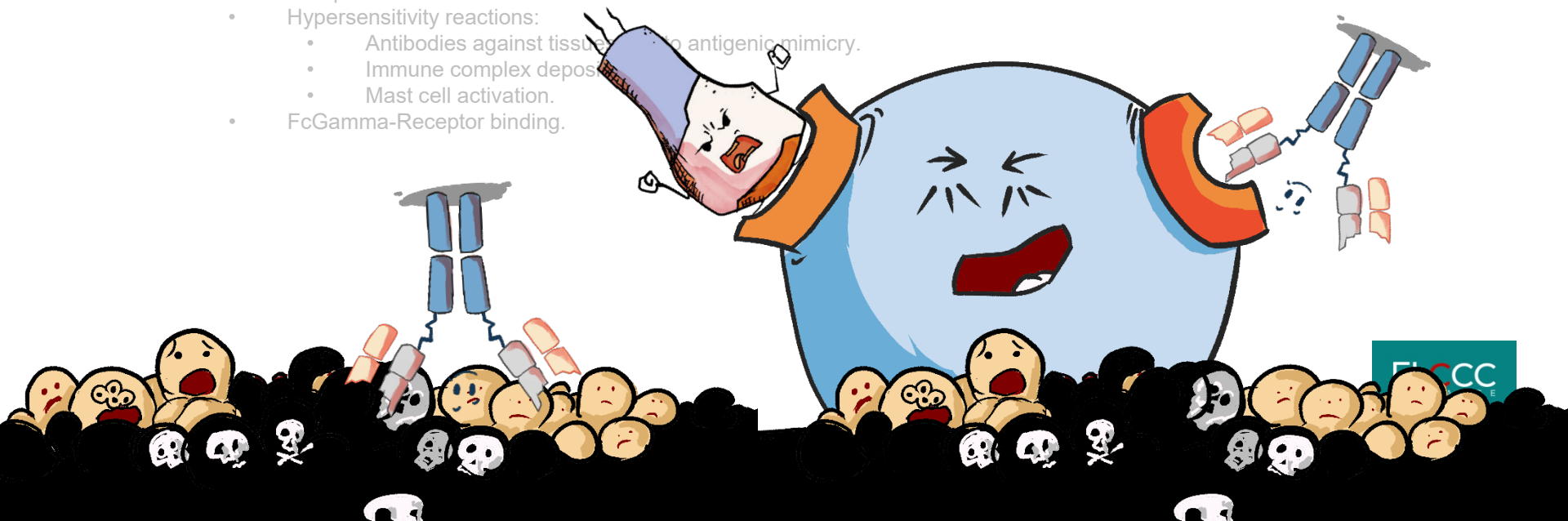
Spikopathogenesis

- Direct action of the spike proteins on the ACE2 receptors.
  - Inflammatory and anti-inflammatory system imbalance.
  - Nitric oxide production irregularity.
  - Etc.
- Anti-idiotype antibodies
  - ACE2 binding.
  - Activation of the biological processes due to the antibodies.
    - Complement activation.
    - Hypersensitivity reactions:
      - Antibodies against tissue [illegible] to antigenic mimicry.
      - Immune complex depos[illegible]
      - Mast cell activation.
    - FcGamma-Receptor binding.

https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.121.318902

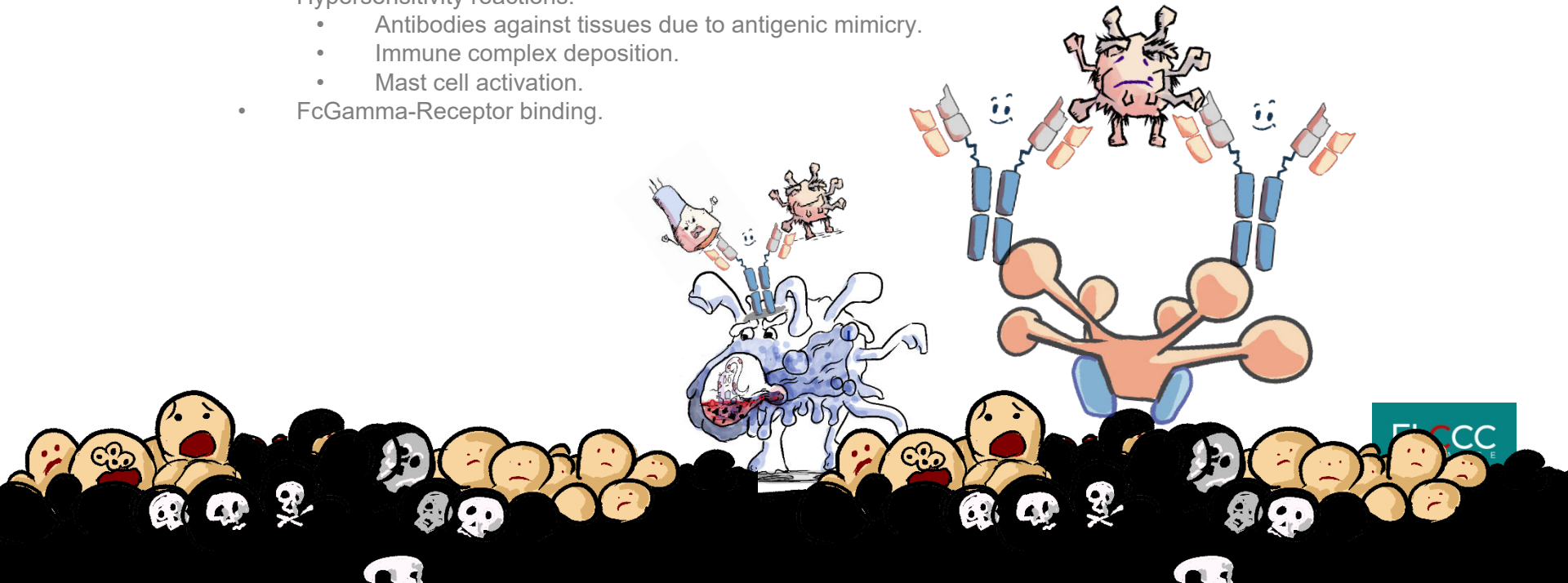
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8487226/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8820157/



Spikopathogenesis

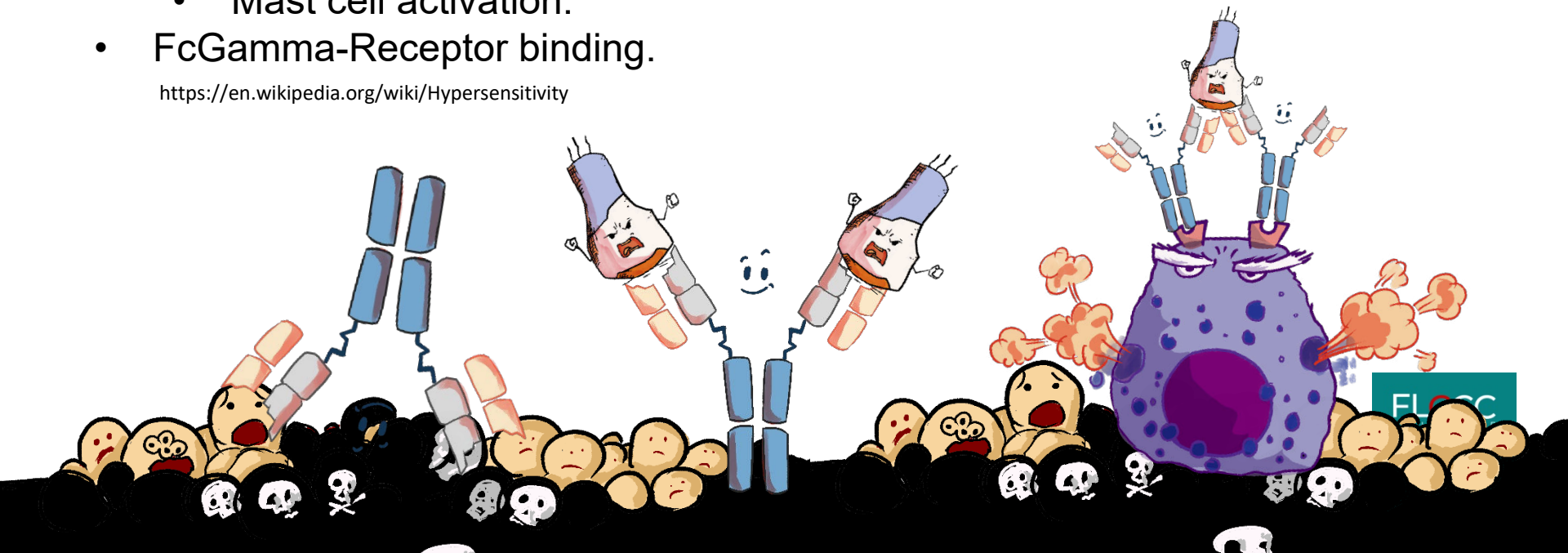
- Anti-idiotype antibodies
  - ACE2 binding.
  - Activation of the biological processes due to the antibodies.
    - Complement activation.
    - Hypersensitivity reactions:
      - Antibodies against tissues due to antigenic mimicry.
      - Immune complex deposition.
      - Mast cell activation.
    - FcGamma-Receptor binding.



Spikopathogenesis

- Hypersensitivity reactions:
  - Antibodies against tissues due to antigenic mimicry.
  - Immune complex deposition.
  - Mast cell activation.
- FcGamma-Receptor binding.

https://en.wikipedia.org/wiki/Hypersensitivity

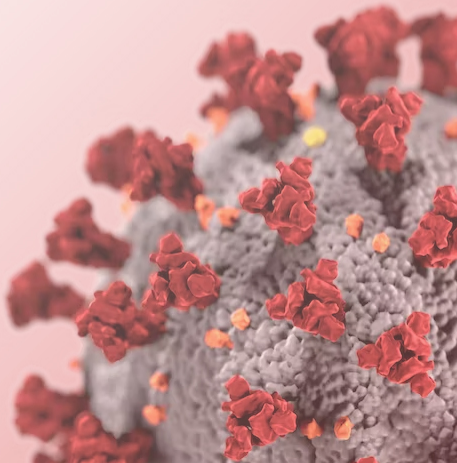


FLCCC ALLIANCE
EDUCATIONAL CONFERENCE 2022

UNDERSTANDING & TREATING
SPIKE PROTEIN-INDUCED DISEASES

October 14-16, 2022 • Orlando, Florida

Management Approach

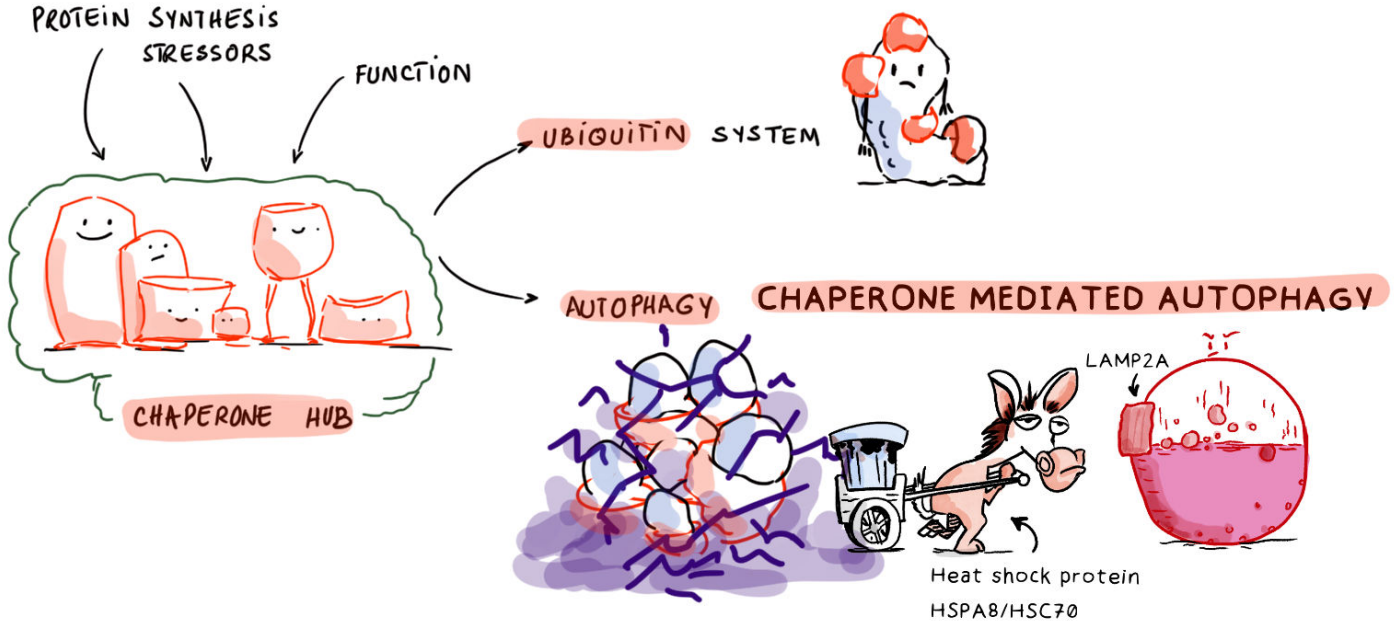


Management Approach

- Calm down the immune system.
- Trash removal:
  - Remove the spikes loaded in the cells.
  - Remove new production of the spikes by removing mRNA.
- Recycle old but active immune cells:
  - Cells stuck in a suppressed apoptotic state.
  - Cells that are continuously active but are senescent.
  - Cells that are dysregulated.
  - Memory cells producing anti-ACEII and other antibodies.
- Enable new cell generation.
  - Reset the immune response.
  - Reduce the production of inflammatory mediators.
  - Reduce inflammation and tissue damage.
  - Repair and restore tissues.

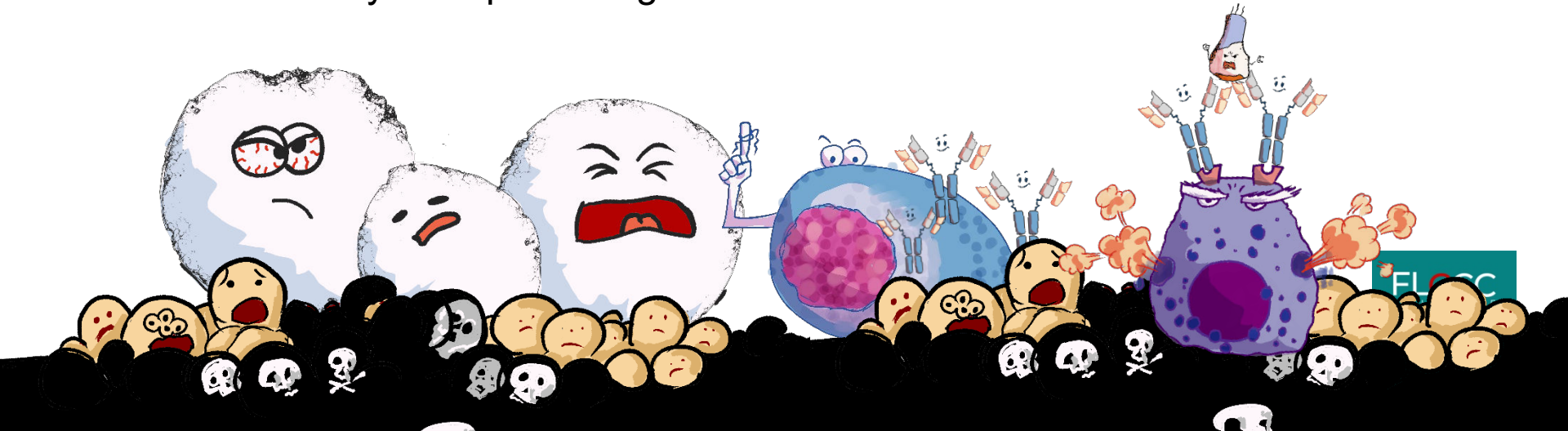
Management Approach

- Calm down the immune system.
- Trash removal:
  - Remove the spikes loaded in the cells.
  - Remove new production of the spikes by removing mRNA.



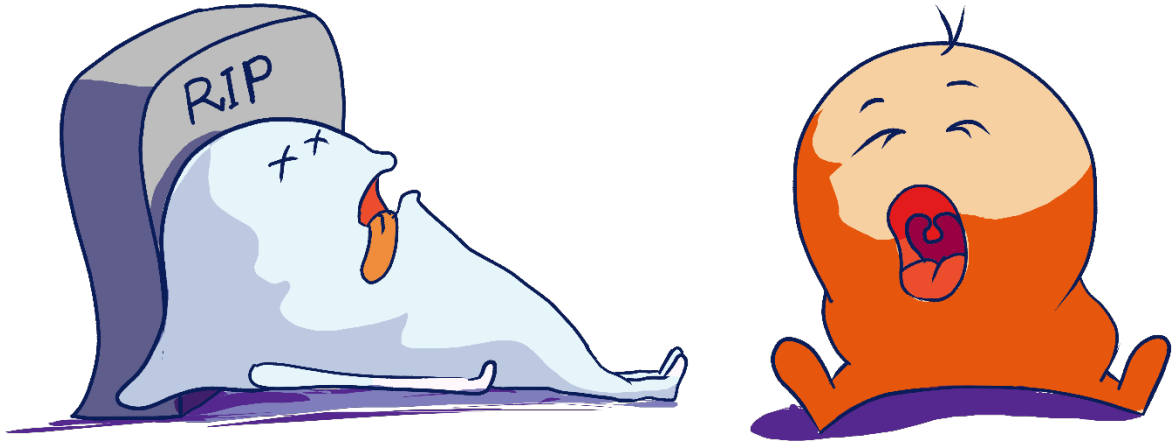
Management Approach

- Calm down the immune system.
- Recycle old but active immune cells:
  - Cells stuck in a suppressed apoptotic state.
  - Cells that are continuously active but are senescent.
  - Cells that are dysregulated.
  - Memory cells producing anti-ACEII and other antibodies.



Management Approach

- Calm down the immune system.
- Enable new cell generation.
  - Reset the immune response.
  - Reduce the production of inflammatory mediators.
  - Reduce inflammation and tissue damage.
  - Repair and restore tissues.



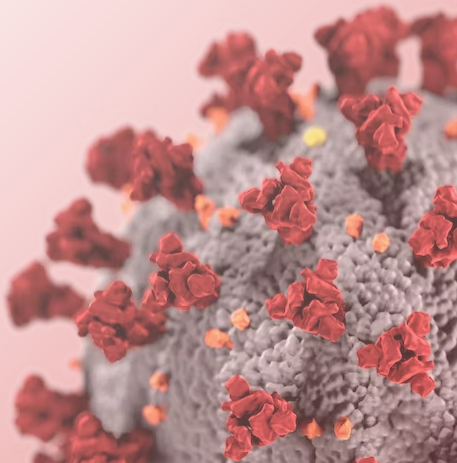
FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

FLCCC ALLIANCE
EDUCATIONAL CONFERENCE 2022

UNDERSTANDING & TREATING
SPIKE PROTEIN-INDUCED DISEASES

October 14-16, 2022 • Orlando, Florida

Autophagy

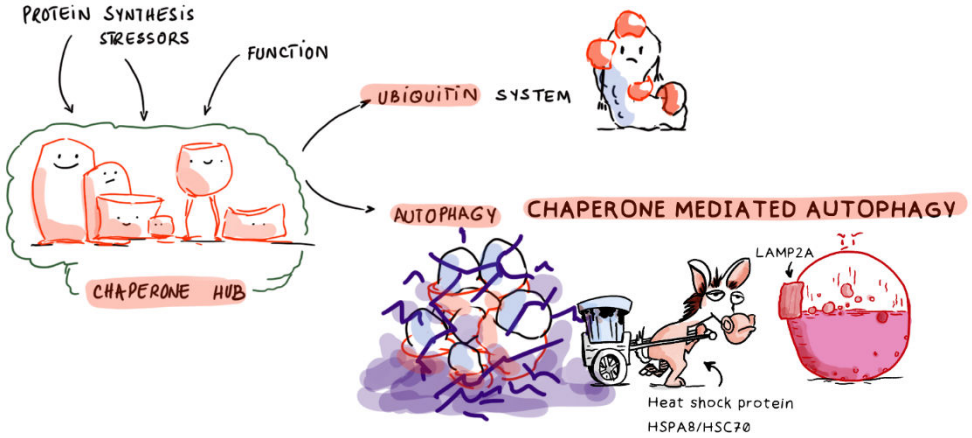


Enter Autophagy

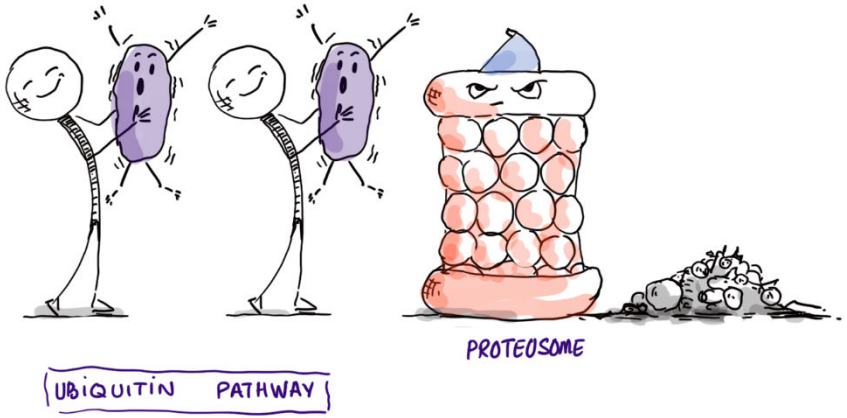
- Self eating
- Protein recycling pathways:
  - Lytic
    - Macro and micro autophagy
    - Chaperone mediated autophagy
  - Ubiquitin
    - Caspases
    - Endosomal recycling

References in the appendix: Heat-shock proteins references.

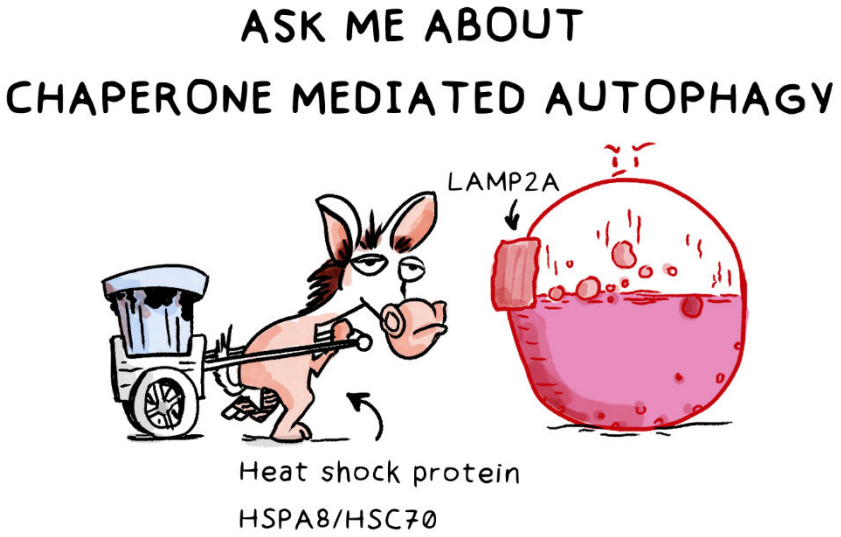
Enter Autophagy



Enter Autophagy



Enter Autophagy

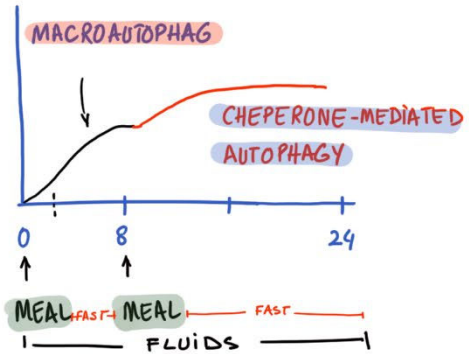


FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

Enter Autophagy

References in the appendix: Autophagy References

ANA MARIA CUERVO, MD., PH.D.



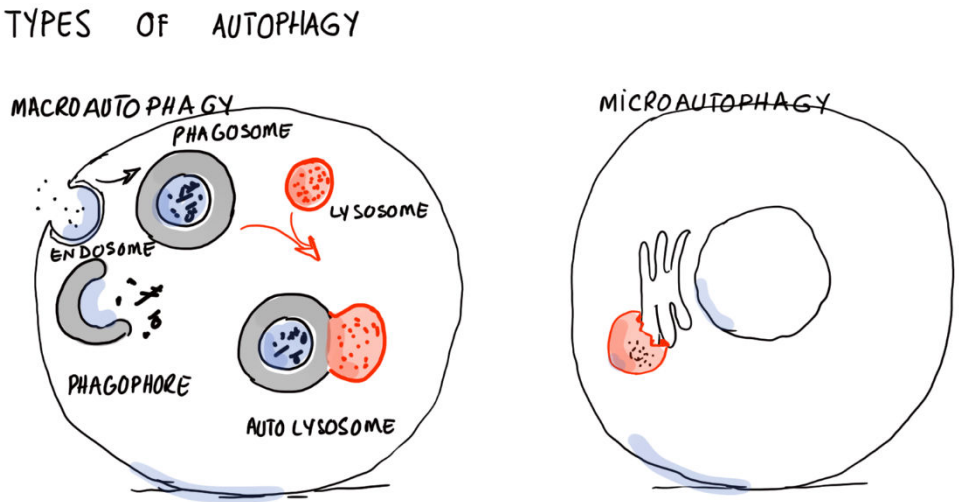
PROF. DEPT OF DEVELOPMENT AND MOLECULAR BIOLOGY

PROF. DEPT OF MEDICINE

ALBERT EINSTEIN COLLEGE OF MEDICINE

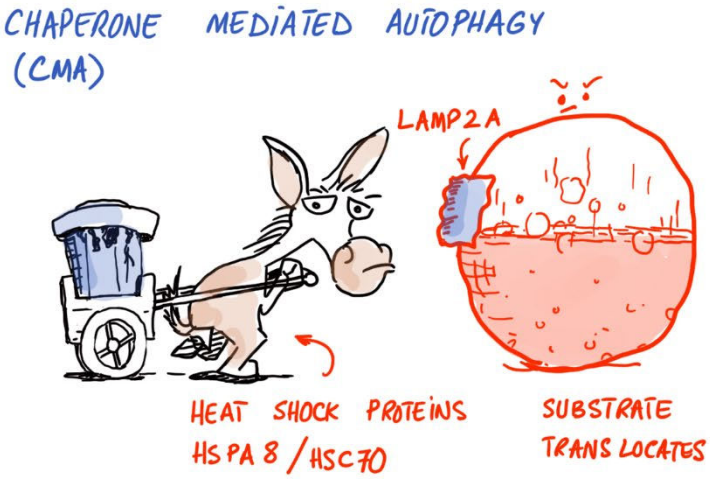
FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

Enter Autophagy



FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

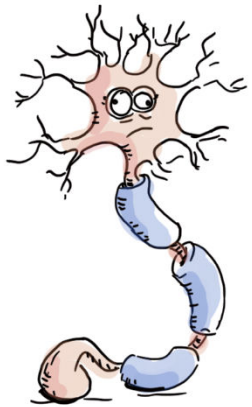
Enter Autophagy



Enter Autophagy

CONSIDER SLEEPING WITHIN 16 HOURS FAST PART.

NEURONS PERFORM AUTOPHAGY WHILE WE SLEEP IN LOW ACTIVITY STATE



Induce Autophagy

- Activate heat-shock proteins (HSPs)
  - Stress on the cells:
    - Exercise
      - Cytoskeletal changes.
      - Acidic environment.
    - Intermittent fasting
    - Thermal (far infrared/sauna)
    - Near infrared
- Use molecules:
  - Spermidine
  - Resveratrol
  - Coffee
  - More

FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

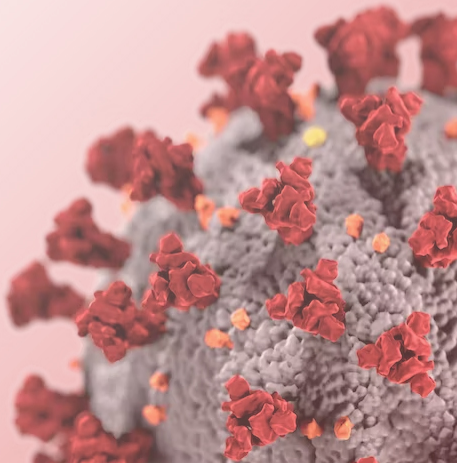
FLCCC ALLIANCE
EDUCATIONAL CONFERENCE 2022

UNDERSTANDING & TREATING
SPIKE PROTEIN-INDUCED DISEASES

October 14-16, 2022 • Orlando, Florida

Near Infrared

References in the appendix: Near Infrared References



Near Infrared Therapy

Photobiomodulation

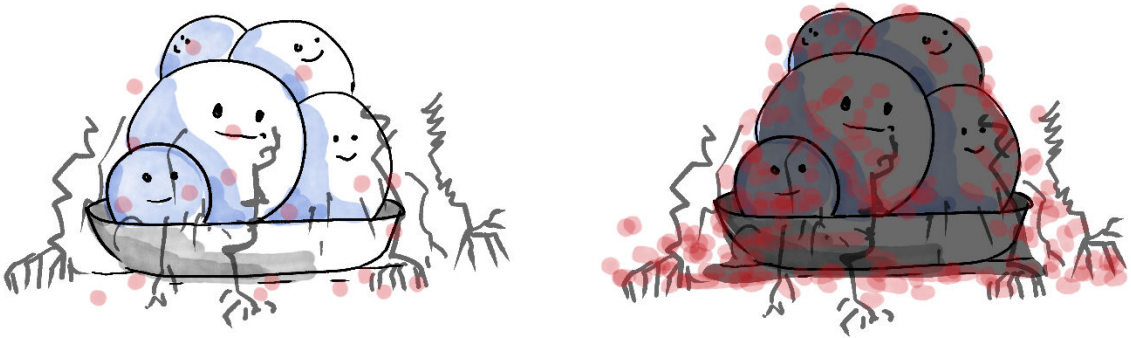
Short periods of illumination with infrared/near infrared light given repititively over several days.

Mitochondria perform oxidative bursts. regenerative and/or anti-inflammatory.

FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

Near Infrared Therapy

50% decline in inflammatory response in treated cells.
720 nm light 2 W/m2 - 6 W/m2 were equallty effecitve.



HEK-Blue hTLR4 (human cell culture that express TLR4.)
LPS exposure with or without infrared lights.

FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

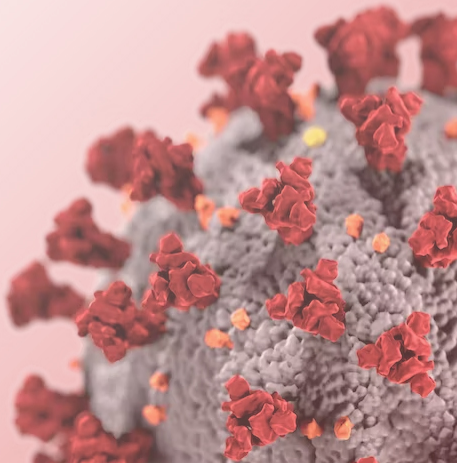
FLCCC ALLIANCE
EDUCATIONAL CONFERENCE 2022

UNDERSTANDING & TREATING
SPIKE PROTEIN-INDUCED DISEASES

October 14-16, 2022 • Orlando, Florida

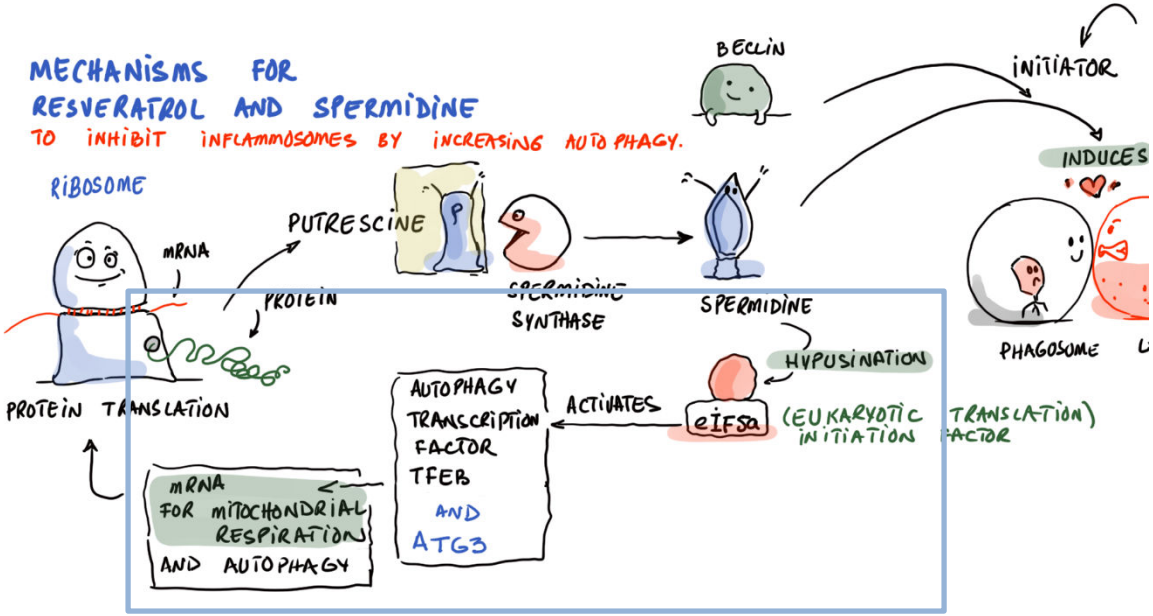
Spermidine

References in the appendix: Autophagy References



Spermidine

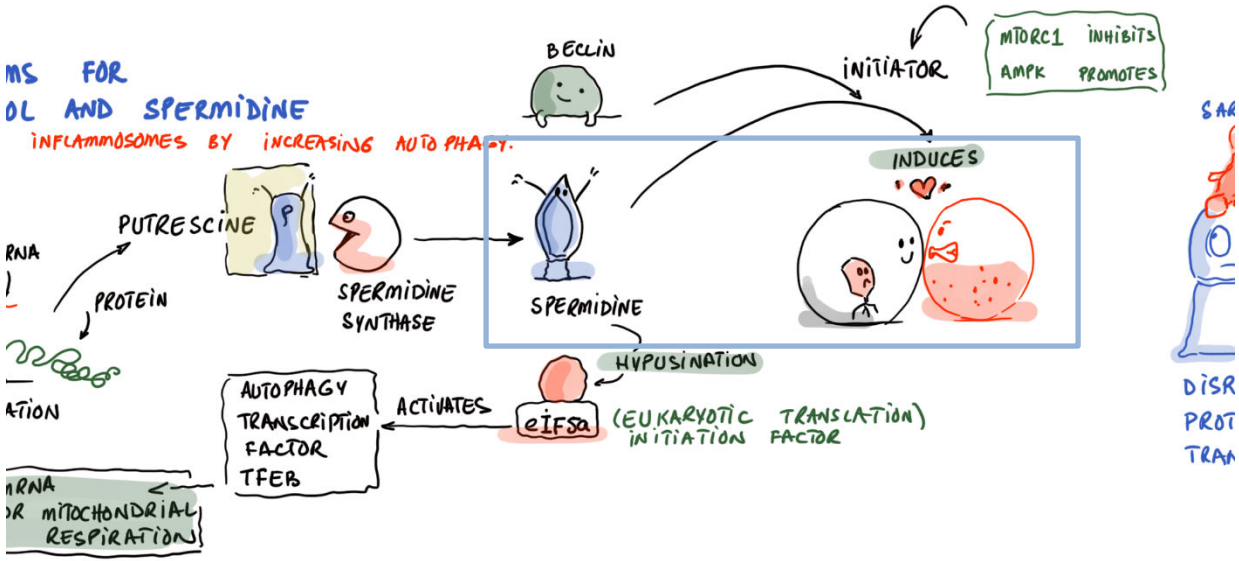
- Spermidine helps induce eIF5a. Which in turn induces genes to start autophagy (ATG3 and TFEB) and improve mitochondrial respiration. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8386697/ and https://www.nature.com/articles/s41467-021-24007-w)



FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

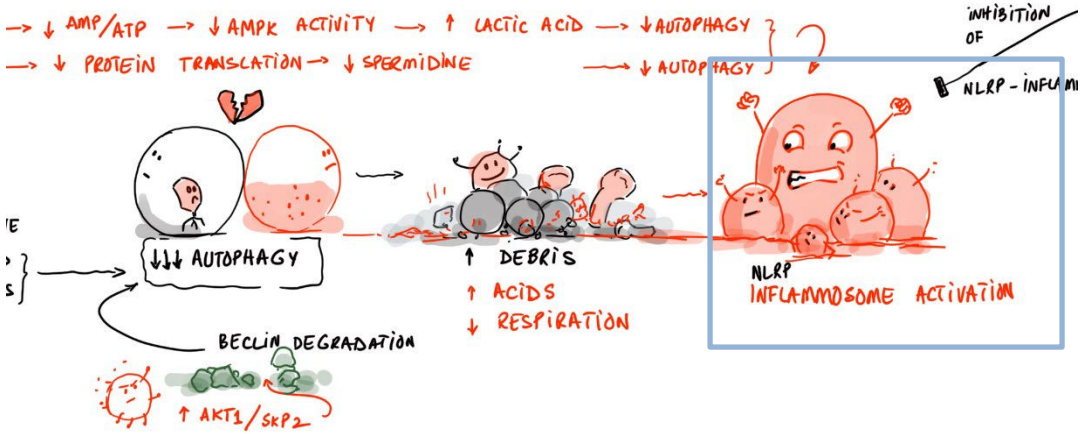
Spermidine

- Spermidine directly induce phagosome lysosome fusion. (https://www.nature.com/articles/cdd2014215)



Spermidine

- SARS-COV-2 (spike) reduce spermidine synthase activity. Leading to less autophagy and more inflammasome activation resulting in fiery deaths of the cells and severe inflammation. (https://www.nature.com/articles/s41467-021-24007-w)



FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

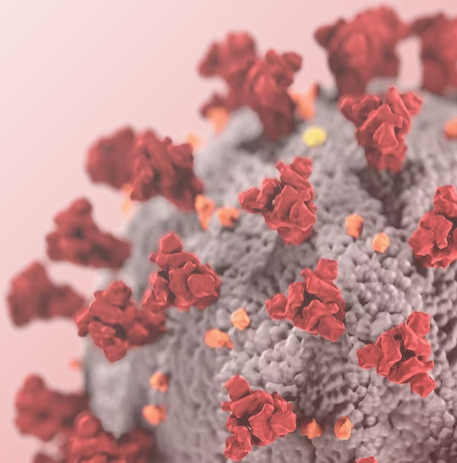
FLCCC ALLIANCE
EDUCATIONAL CONFERENCE 2022

UNDERSTANDING & TREATING
SPIKE PROTEIN-INDUCED DISEASES

October 14-16, 2022 • Orlando, Florida

Resveratrol

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8778251/



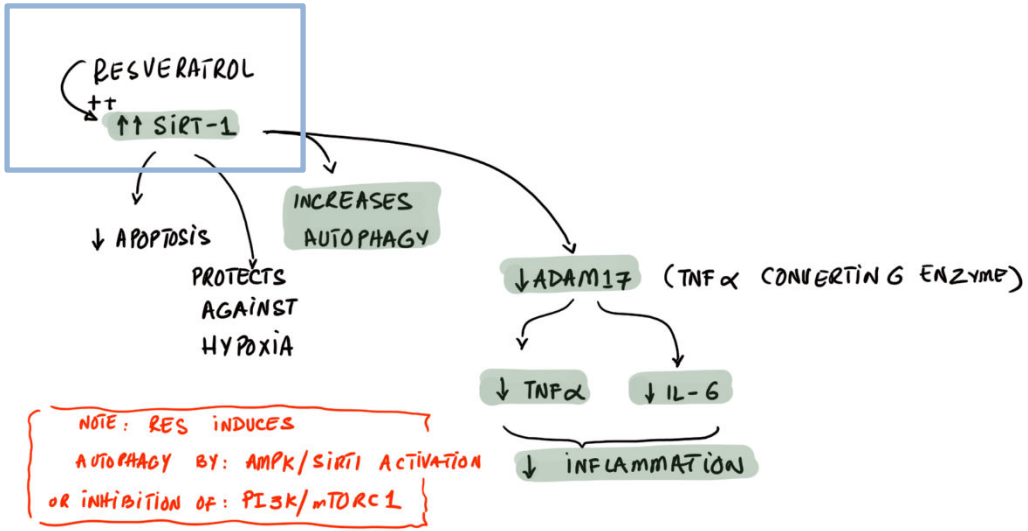
Resveratrol

- Resveratrol reduces apoptosis, increases autophagy, and reduces inflammation. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8778251/)

Resveratrol (RSV) (3,4,5-trans-trihydroxy-stilbene), a phenolic compound found in red fruits and berries, in particular in grapes pulp, skin, seeds, and stems [7], exhibits a wide range of highly active biological effects to counteract the onset of many diseases or to manage their symptoms [8]. One of the possible mechanisms by which resveratrol plays its role in maintaining health is the suppression of inflammatory reactions by acting on immune cells [9]. RSV has antioxidant, anticarcinogenic, anti-inflammatory, neuroprotective, cardioprotective, and anti-aging properties [10,11]. This natural flavonoid can mitigate toxicities related to chemo-radiation therapy in normal tissues [12] and enhance migration of cells toward injured areas, which is important from therapeutic standpoints

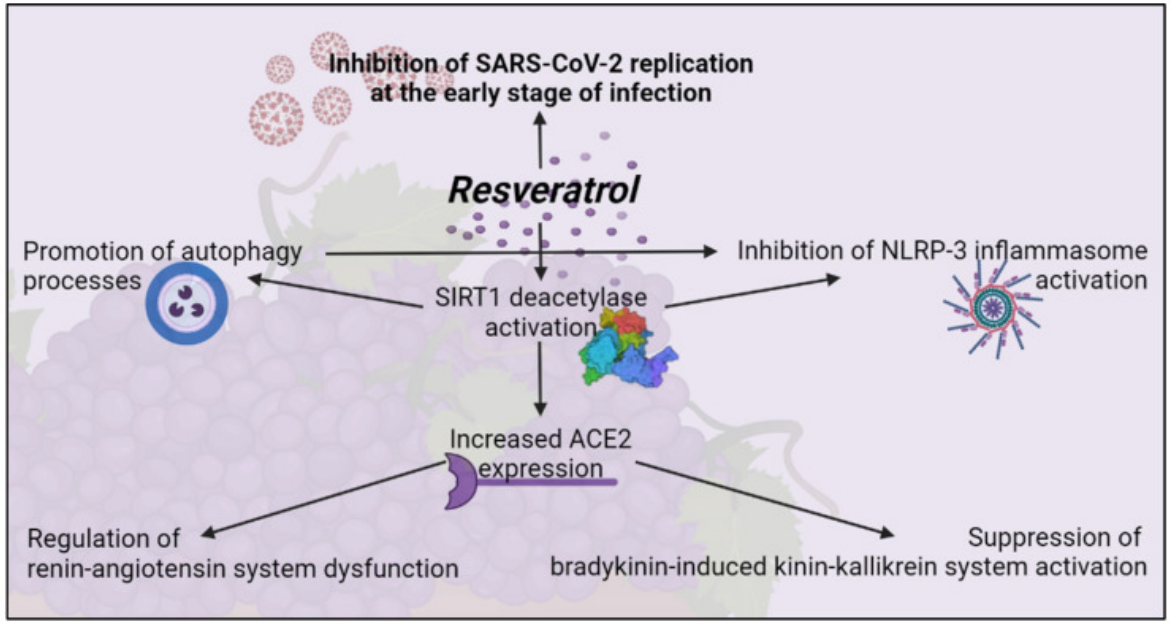
Resveratrol

- Resveratrol reduces apoptosis, increases autophagy, and reduces inflammation. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8778251/)



Resveratrol

- Resveratrol reduces apoptosis, increases autophagy, and reduces inflammation. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8778251/)



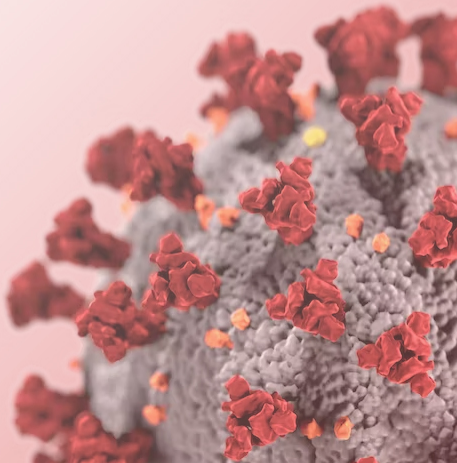
FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

Paper in AHA Journal:
SARS-CoV-2 Spike Protein Impairs Endothelial Function via Downregulation of ACE 2
https://www.ahajournals.org/doi/full/10.1161/CIRCRESAHA.121.318902

Excerpt from the paper: Although the use of a noninfectious pseudovirus is a limitation to this study, our data reveals that S protein alone can damage endothelium, manifested by impaired mitochondrial function and eNOS activity but increased glycolysis. It appears that S protein in ECs increases redox stress which may lead to AMPK deactivation, MDM2 upregulation, and ultimately ACE2 destabilization.4 Although these findings need to be confirmed with the SARS-CoV-2 virus in the future study, it seems paradoxical that ACE2 reduction by S protein would decrease the virus infectivity, thereby protecting endothelium. However, a dysregulated renin-angiotensin system due to ACE2 reduction may exacerbate endothelial dysfunction, leading to endotheliitis. Collectively, our results suggest that the S protein-exerted EC damage overrides the decreased virus infectivity. This conclusion suggests that vaccination-generated antibody and/or exogenous antibody against S protein not only protects the host from SARS-CoV-2 infectivity but also inhibits S protein-imposed endothelial injury.

FLCCC
ALLIANCE
EDUCATIONAL
CONFERENCE
2022

THANK YOU



Resveratrol

Paper in AHA Journal:
SARS-CoV-2 Spike Protein Impairs Endothelial Function via Downregulation of ACE 2
https://www.ahajournals.org/doi/full/10.1161/CIRCRESAHA.121.318902

Excerpt from the paper: Although the use of a noninfectious pseudovirus is a limitation to this study, our data reveals that S protein alone can damage endothelium, manifested by impaired mitochondrial function and eNOS activity but increased glycolysis. It appears that S protein in ECs increases redox stress which may lead to AMPK deactivation, MDM2 upregulation, and ultimately ACE2 destabilization.4 Although these findings need to be confirmed with the SARS-CoV-2 virus in the future study, it seems paradoxical that ACE2 reduction by S protein would decrease the virus infectivity, thereby protecting endothelium. However, a dysregulated renin-angiotensin system due to ACE2 reduction may exacerbate endothelial dysfunction, leading to endotheliitis. Collectively, our results suggest that the S protein-exerted EC damage overrides the decreased virus infectivity. This conclusion suggests that vaccination-generated antibody and/or exogenous antibody against S protein not only protects the host from SARS-CoV-2 infectivity but also inhibits S protein-imposed endothelial injury.

Nitric Oxide References

Nitric Oxide: The Missing Factor in COVID-19 Severity?

https://www.mdpi.com/2076-3271/10/1/3/htm

FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

Heat-shock Protein References

Frontiers | Heat-Shock Proteins in Neuroinflammation
https://www.frontiersin.org/articles/10.3389/fphar.2019.00920/full

How to Activate Heat Shock Proteins in a Sauna - Sauna Marketplace
https://saunamarketplace.com/how-to-activate-heat-shock-proteins-sauna/

Heat shock proteins and heat therapy for type 2 diabetes: pros and cons - PubMed
https://pubmed.ncbi.nlm.nih.gov/26049635/

Heat shock proteins and heat therapy for type 2 diabetes: pr... : Current Opinion in Clinical Nutrition & Metabolic Care
https://journals.lww.com/co-clinicalnutrition/Abstract/2015/07000/Heat_shock_proteins_and_heat_therapy_for_type_2.10.aspx

Heat shock proteins and immune system - PubMed
https://pubmed.ncbi.nlm.nih.gov/19276179/

Clinical Effects of Regular Dry Sauna Bathing: A Systematic Review - PMC
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5941775/

Heat shock proteins regulate activation-induced proteasomal degradation of the mature phosphorylated form of protein kinase C - PubMed
https://pubmed.ncbi.nlm.nih.gov/23900841/

Heat Shock Proteins - ScienceDirect
https://www.sciencedirect.com/science/article/pii/B9780123749840006859

Molecular chaperones in protein folding and proteostasis | Nature
https://www.nature.com/articles/nature10317

Pathways of chaperone-mediated protein folding in the cytosol | Nature Reviews Molecular Cell Biology
https://www.nature.com/articles/nrm1492#access-options

Chaperonin - Wikipedia
https://en.wikipedia.org/wiki/Chaperonin

Autophagy References

Yoshinori Ohsumi - Wikipedia
https://en.wikipedia.org/wiki/Yoshinori_Ohsumi
HOW LONG Does It Takes To Activate AUTOPHAGY? | Dr Ana Maria Cuervo Interview Clips - YouTube
https://www.youtube.com/watch?v=D6QcE3wVQ14
Short-term fasting induces profound neuronal autophagy - PMC
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3106288/
Autophagy: Definition, Process, Fasting & Signs
https://my.clevelandclinic.org/health/articles/24058-autophagy
6 Signs And Symptoms of Autophagy
https://www.healthline.com/nutrition/signs-of-autophagy#5.-Weight-loss
How Long do You Have to Fast for Autophagy? – spermidineLIFE® US
https://spermidinelife.us/blogs/news/how-long-do-you-have-to-fast-for-autophagy#:~:text=Studies%20have%20shown%20that%20autophagy,humans%20but%20can%20be%20possible.
How Long Do You Need to Fast for Autophagy?
https://www.medicinenet.com/how_long_do_you_need_to_fast_for_autophagy/article.htm
Ana Maria Cuervo, M.D., Ph.D. | Faculty Directory | Albert Einstein College of Medicine
https://www.einsteinmed.edu/faculty/8784/ana-maria-cuervo/
Cuervo AM - Search Results - PubMed
https://pubmed.ncbi.nlm.nih.gov/?term=Cuervo%20AM
The coming of age of chaperone-mediated autophagy - PubMed
https://pubmed.ncbi.nlm.nih.gov/29626215/
Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition) - PMC
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4835977/
How to control self-digestion: transcriptional, post-transcriptional, and post-translational regulation of autophagy - PMC
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4441840/
Chaperone-mediated autophagy sustains haematopoietic stem-cell function - PubMed
https://pubmed.ncbi.nlm.nih.gov/33442062/
Molecular definitions of autophagy and related processes - PMC
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5494474/
The different autophagy degradation pathways and neurodegeneration - PubMed
https://pubmed.ncbi.nlm.nih.gov/35134347/
How Long Do You Need to Fast for Autophagy?
https://www.medicinenet.com/how_long_do_you_need_to_fast_for_autophagy/article.htm#:~:text=Autophagy%20is%20believed%20to%20begin,around%2048%20hours%20of%20fasting.
Intermittent Fasting and Obesity-Related Health Outcomes: An Umbrella Review of Meta-analyses of Randomized Clinical Trials | Cardiology | JAMA Network Open | JAMA Network
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2787246?resultClick=1
ADULT NEUROGENESIS IN HUMANS: A Review of Basic Concepts, History, Current Research, and Clinical Implications - PMC
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6659986/#:~:text=Neurogenesis%20is%20the%20formation%20of,the%20hippocampus%20(Figure%201).
The 2016 Nobel Prize in Physiology or Medicine - Press release
https://www.nobelprize.org/prizes/medicine/2016/press-release/

FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022

Near Infrared References

Infrared light therapy relieves TLR-4 dependent hyper-inflammation of the type induced by COVID-19 - PMC
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8451450/
Not scientific but interesting article about heat-shock proteins and infrared.
Infrared Sauna Use And Heat Shock Proteins
https://saunas.org/infrared-sauna-use-and-heat-shock-proteins/
Some more references
Near-infrared spectroscopy - Wikipedia
https://en.wikipedia.org/wiki/Near-infrared_spectroscopy
Near Infrared (NIR) Light Therapy of Eye Diseases: A Review - PMC
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7738953/#:~:text=NIR%20and%20LEDs%20light%20can,modify%20biological%20functions%20of%20cells.
Sep 15, 2022 at 10:13 PM
Red Light Therapy vs. Infrared Sauna
https://youtu.be/vwgLlYcYZ_4
Red/near-infrared irradiation therapy for treatment of central nervous system injuries and disorders - PubMed
https://pubmed.ncbi.nlm.nih.gov/23492552/
The Benefits of Near-Infrared Light Therapy
https://platinumtherapylights.com/blogs/news/near-infrared-light-therapy
Near-Infrared Light and Skin: Why Intensity Matters - Abstract - Challenges in Sun Protection - Karger Publishers
https://www.karger.com/Article/Abstract/517645
The effect of red-to-near-infrared (R/NIR) irradiation on inflammatory processes - PubMed
https://pubmed.ncbi.nlm.nih.gov/31170016/#:~:text=Introduction%3A%20Near%2Dinfrared%20(NIR,blood%20flow%20and%20tissue%20oxygenation.
Near-infrared light reduces glia activation and modulates neuroinflammation in the brains of diet-induced obese mice | Scientific Reports
https://www.nature.com/articles/s41598-022-14812-8
Near-infrared light reduces β-amyloid-stimulated microglial toxicity and enhances survival of neurons: mechanisms of light therapy for Alzheimer's disease | Alzheimer's Research & Therapy | Full Text
https://alzres.biomedcentral.com/articles/10.1186/s13195-022-01022-7
Infrared light therapy relieves TLR-4 dependent hyper-inflammation of the type induced by COVID-19 - PMC
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8451450/
What Is Near-Infrared Light? - StoneLock
https://stonelock.com/what-is-near-infrared-light/#:~:text=Infrared%20Light%20(IR)%20is%20the,past%20what%20we%20can%20see.
Toll-like receptor 4 - Wikipedia
https://en.wikipedia.org/wiki/Toll-like_receptor_4
NF-κB - Wikipedia
https://en.wikipedia.org/wiki/NF-%CE%BAB
Lipopolysaccharide
https://en.wikipedia.org/wiki/Lipopolysaccharide

FLCCC ALLIANCE EDUCATIONAL CONFERENCE 2022