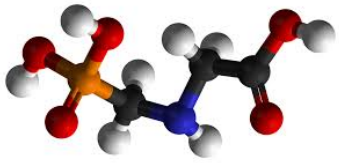
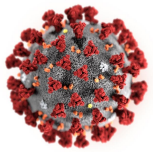


COVID-19, Glyphosate, Deuterium and SARS-CoV-2 Vaccines

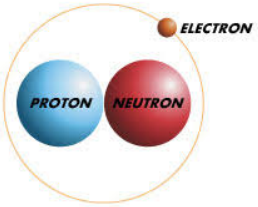


Stephanie Seneff

MIT CSAIL

The 2nd Budapest COVID Medical Conference

August 18, 2021



1

"We have never seen this before, however, the vision is so horrible and so awful and terrifying that I myself I don't even want to know what happens next."

-- Professor Sucharit Bhakdi, retired microbiologist

2

Outline

- Part 1: Defective Immune Cell Mitochondria & COVID-19
  - Importance of NAD(P)(H) Redox System to Mitochondrial Health
  - SARS-CoV-2 Infection in the Lungs Restores Mitochondrial Health
  - Rebooting the Mitochondria
- Part 2: The COVID-19 Vaccines
  - Overview
  - Exosomes, MicroRNAs and Heart Disease
  - Exosomes, MicroRNAs and Prion Diseases
  - Other Consequences of Vaccine-induced MicroRNAs
  - Spike Antibodies and Autoimmune Disease
  - Reverse Transcription of Spike RNA into DNA

3

Part 1: Defective Immune Cell Mitochondria & COVID-19

4

The Big Picture

- Deuterium is a natural isotope of hydrogen augmented with a neutron
- Mitochondria depend on low deuterium in their water to function well
- The supply of deuterium-depleted water (DDW) to mitochondria depends critically on nicotinamide adenine dinucleotide (NAD) as a proton carrier
- Glyphosate disrupts the supply of DDW to mitochondria via NAD
- Defective mitochondria in immune cells causes immune deficiency
- SARS-CoV-2 infection in the lungs launches a cascade response to restore mitochondrial health to the immune cells, with the help of the virus
  - Once the macrophages are reinvigorated, they can clear the virus
  - If the immune system is too sick to fix, the person dies

5

Importance of NAD(P)(H) Redox System to Mitochondrial Health

6

The Big Picture

- NAD (Nicotinamide Adenine Dinucleotide) is an essential cofactor in oxidation/reduction reactions

  It exists in four forms: with and without hydrogens and with and without phosphate

  NAD+ (no H, no P)
  NADH (with H, no P)
  NADP+ (no H, with P)
  NADPH (with H, with P)

  The enzymes that supply NAD+ and NADP+ with H are specially designed to avoid deuterium

- Mitochondria are organelles inside cells that supply energy in the form of ATP
- Mitochondria depend critically on a proton-ATPase pump to make ATP
  - Protons derived from NADH and NADPH are pumped into the intermembrane space
- Deuterium "gums up" the pump (like sugar in the gas tank)
- Glyphosate interferes with the supply of NADH and NADPH to the organism

7

Glyphosate Impairs NAD(P)(H) Pathways*

- Glyphosate is the active ingredient in the pervasive herbicide Roundup
  - It kills weeds by suppressing EPSP synthase in the shikimate biological pathway
- Tryptophan is a major product of this blocked pathway
  - Tryptophan is produced by gut microbes depending on EPSP synthase
  - *NAD(P)(H) is derived from tryptophan*
- Glyphosate induces ROS in mitochondria and depletes glutathione (antioxidant)
  - Also increases ratio of GSSG/GSH
- Glyphosate inhibits glucose 6 phosphate dehydrogenase (G6PD), which restores NADPH from NADP+
- Glyphosate inhibits succinate dehydrogenase, an essential enzyme in both the citric acid cycle and oxidative phosphorylation

*S Seneff, Toxic Legacy, Chelsea Green Publishers, July 2021.

8

"COVID-19: NAD+ deficiency may predispose the aged, obese and type2 diabetics to mortality through its effect on SIRT1 activity"*

- NAD+ is a cofactor heavily involved in proton-coupled electron transfer (PCET)
- Sirtuins are an ancient family of 7 NAD+-dependent signaling proteins that regulate metabolism
- Intracellular NAD+ levels are depleted in association with diabetes and obesity, risk factors for bad outcome in COVID-19
  - Diabetes and obesity rates have been rising dramatically in the United States in step with the rise in glyphosate usage on core crops**
- Depletion of SIRT1 causes uncontrolled increases in inflammatory markers TNF-α, IL-6 and IL-1β
  - Increased risk to cytokine storm due to inability to activate SIRT1

*R Miller et al. Medical Hypotheses 2020; 144: 110044
**N Swanson et al. Journal of Organic Systems, 9(2), 2014

9

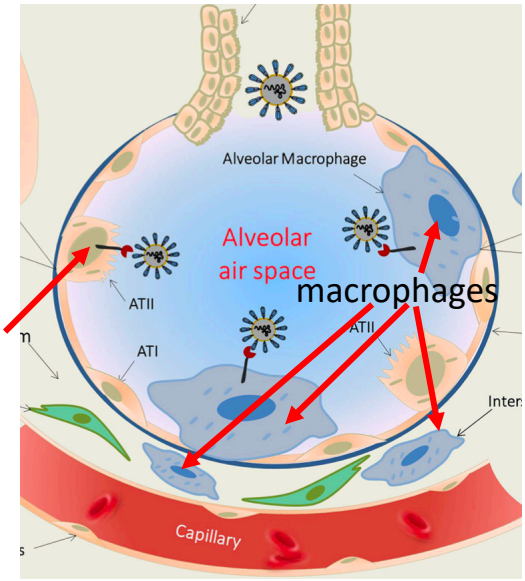
SARS-CoV-2 Infection in the Lungs Restores Mitochondrial Health

10

Initial COVID-19 Events

- SARS CoV-2 viruses enter through the bronchioles and infect epithelial cells lining the lung's alveoli
- Residential macrophages fail to clear the virus because they are defective
- Viruses proliferate wildly
- Macrophages send out alarm signals which draw in more macrophages
- Capillary wall becomes leaky to support invasion
- Blood pressure drops; fluid begins to fill the alveolar space
- Person feels as if they are drowning

Infected Epithelial cell



*Frank L van de Veerdonk et al. eLife 2020; 9: e5755.

11

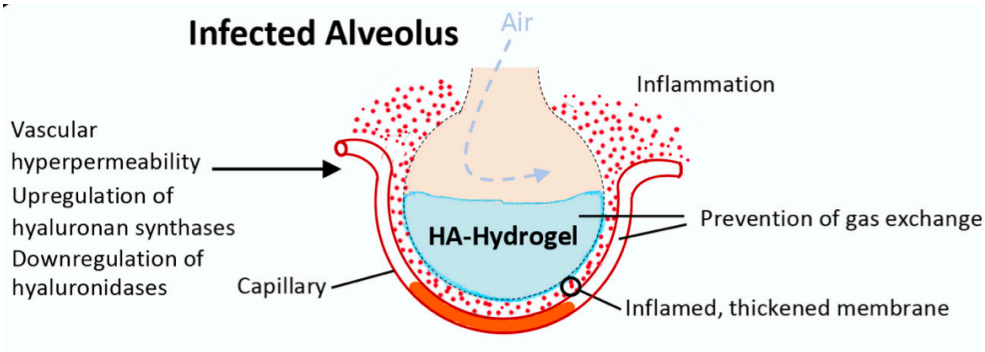
Is a Bradykinin Storm Brewing in COVID-19?*

- Hypertension is a risk factor for COVID-19, but *hypotension* develops instead during the disease process
  - ACE2 receptor is upregulated by 199-fold in the lungs in severe COVID-19 patients, and ACE is downregulated (8-fold)
  - ACE degrades (clears) bradykinin
  - Bradykinin receptors are upregulated by nearly 3000-fold!
  - Bradykinin induces vasodilation and hypotension
- Inflammatory cytokines induce capillary leakage and inhibit alveolar fluid reabsorption leading to alveolar flooding**

*https://www.the-scientist.com/news-opinion/is-a-bradykinin-storm-brewing-in-covid-19—67876
Michael R Garvin et al. eLife 2020; 9: e59177.
**Andrew M Luks and Erik R Swenson. Ann Am Thorac Soc 2020 Apr 24 [Epub ahead of print]

12

Bradykinin-induced hyperpermeability of the lung capillaries causes formation of hyaluronic-acid hydrogel that inhibits gas exchange*



*Michael R Garvin et al. eLife 2020; 9: e59177.

13

SARS CoV-2 causes massive over-production of hyaluronic acid in the lungs*

- "Hyaluronic acid can trap roughly 1000 times its weight in water and when bound to water the resulting hydrogel obtains a stiff viscous quality similar to 'Jello' "
- Multiple enzymes that synthesize hyaluronic acid are massively upregulated in COVID-19 lungs: HAS1 (9113 fold), HAS2 (493 fold), and HAS3 (32 fold)
- Excess hyaluronic acid is associated with pulmonary thrombosis, ground glass opacities, and acute respiratory distress syndrome
- "Hyaluronic acid in the bronchoalveolar space of the lungs could form a *viscous hydrogel* that would negatively impact gas exchange"

*Michael R Garvin et al. eLife 2020; 9: e59177.

14

How the Virus Facilitates Repair of the Deuterium Problem - Hypothesis

- Hydrogel traps deuterium leaving DDW in the fluid water in the lungs
- SARS-CoV-2 virus contains lipids such as linoleic acid in its membrane (stolen from host cell)
- Inflammatory response due to weak innate immunity causes release of lipoxygenase
  - Lipoxygenase extracts protons from lipids in viral membrane and converts oxygen into deuterium depleted water (DDW)
- Produces leukotrienes which induce further reaction
  - Arterioles constrict access to capillary
  - Venules open up leaks
- *Macrophages "drink the sweet nectar" – and supply their mitochondria with much-needed deuterium depleted water ??*
  - This empowers them to clear the virus

Lipoxygenase has a fantastic ability to select hydrogen over deuterium in its product (water)*

*Pengfei Li et al. J Phys Chem Lett 2018; 9(22): 6444-6449.

15

Viruses are stabilized by excess deuterium!

- The nucleocapsid protein in SARS-CoV-2 starts to unfold at 35 degrees Centigrade (95 degrees Fahrenheit) and is completely denatured at 55 degrees Centigrade (131 degrees Fahrenheit)*
  - A fever is a natural defense against the virus
- Viruses take up deuterium and trap it in their protein coat and in their internal single strand of RNA**
  - Deuterium stabilizes the viral protein and RNA and protects from temperature denaturation
  - *The virus removes deuterium from the body fluids*
- When the deuterium level in the body fluids is high, the virus becomes more stable

*Milan Surjit and Sunil K Lal. Infection, Genetics and Evolution 8 (2008) 397-405.

**Jiangsen MAO et al., Chinese Science Bulletin 2004 Vol. 49 No. 3 253-257.

16

Rebooting the Mitochondria

17

"Mitochondrial Transfer via *Tunneling Nanotubes* is an Important Mechanism by which Mesenchymal Stem Cells Enhance Macrophage Phagocytosis in the *In Vitro* and *In Vivo* Models of ARDS"*

"In conclusion, MSC [mesenchymal stem cells] *transfer their mitochondria to macrophages* both *in vitro* and *in vivo*. Mitochondrial donation results in enhancement of macrophage phagocytosis potentially through improvement in bioenergetics and presents a novel mechanism of the antimicrobial effect of MSC."

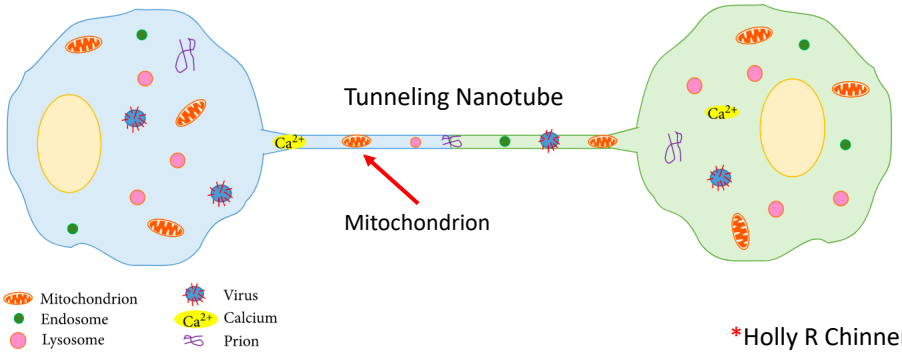
ARDS = Acute Respiratory Distress Syndrome

*Megan V Jackson et al. Stem Cells 2016;34:2210–2223

18

Do the mitochondria and lysosomes get repaired in transit?

"Tunneling nanotubes (TNTs) transport cellular organelles such as mitochondria, endosomes, and lysosomes, as well as other cargoes such as viruses, prions, and Ca^{2+} signals."*



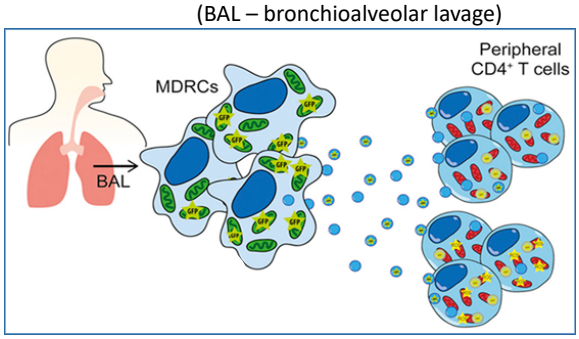
*Holly R Chinnery and Kate E Keller. BioMed Research International 2020; 2020: Article ID 7246785.

19

"Exosomal transfer of mitochondria from airway myeloid-derived regulatory cells to T cells"*

- Myeloid-derived regulatory cells (MDRCs) are cells that emerge from the bone marrow and infiltrate inflammatory sites, e.g., in asthma
- MDRCs in the airways transfer mitochondria to T cells via *exosomes*
  - These mitochondria have been shown to be functional in the recipient cell

(BAL – bronchioalveolar lavage)



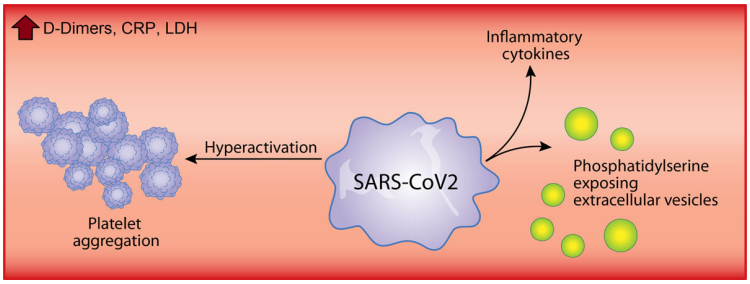
- Hypothesis: Immune cells (e.g., T cells, macrophages, dendritic cells, …) can sweep up DDW and mitochondria via macropinocytosis
- *Intercellular communication is essential for resolving inflammation*

*Kenneth P. Hough et al. Redox Biol 2018; 18: 54-64.

20

A Role for Platelets!*

- Each platelet contains 7 or 8 mitochondria
- Platelet mitochondria are very susceptible to oxidative stress
- Activated platelets form blood clots that can lead to disseminated intravascular coagulation (DIC) or multiple organ failure
- *Mitochondria get released into the extracellular space from the platelets either free or embedded in exosomes*



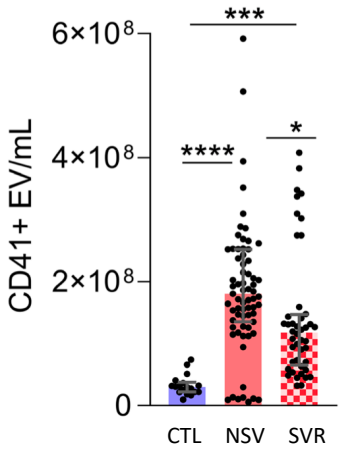
*Jumana Saleh et al. Mitochondrion 2020; 54: 1-7.

21

Megakaryocytes and Platelets in the Lungs*

- Megakaryocytes localized to the lungs are a source of new platelets
- Both megakaryocytes and platelets release extracellular vesicles in response to inflammation
- CD41 is a marker for megakaryocytes and platelets
- CD41 expression as well as extracellular vesicle release were highest in *non-severe COVID-19*

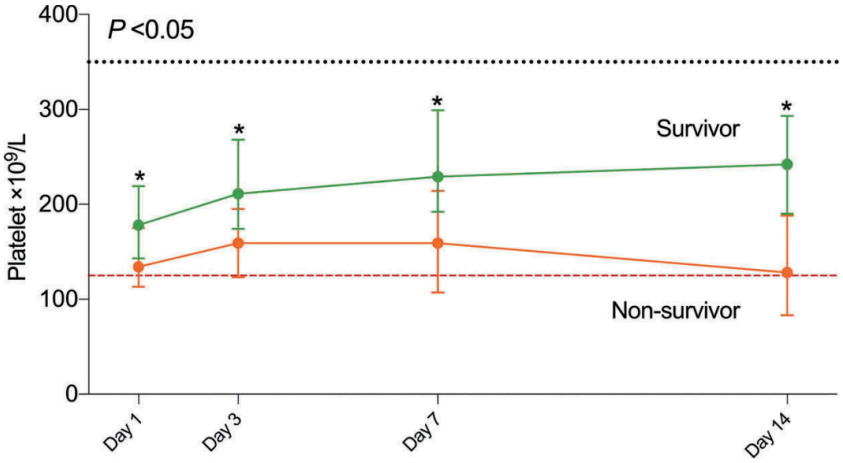
CTL – Control; NSV – non-severe; SVR = severe COVID



*Younes Zaid et al. Circulation Research 2020;127:1404–1418.

22

Platelet Counts Over Time: Survivors and Nonsurvivors of COVID-19*



*Yanli Liu et al., Platelets 2020; 31(4): 490-496.

23

Summary: Part 1

- COVID-19 affects different countries to different degrees and the primary discriminator could be glyphosate exposure
- Glyphosate disrupts the body's ability to properly manage deuterium
  - Deuterium toxicity results in impaired innate immune function
- The process that unfolds during acute COVID-19 aims to restore mitochondrial and lysosomal health to the immune cells
  - Inflammation, swelling and alveolar hydrogel reflect mechanisms that produce deuterium depleted water
  - Platelets and mesenchymal stem cells supply fresh mitochondria to macrophages via tunneling nanotubes and exosomes
  - Macrophages use macropinocytosis to acquire DDW and mitochondria
  - Eventually reboots the mitochondria to support viral clearance

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Part 2: The COVID-19 Vaccines

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The Big Picture

- The mRNA COVID-19 “vaccines” have been carefully bio-engineered to optimize for inducing high levels of antibodies to the spike protein
  - These antibodies can attack the tissues through molecular mimicry
- The injection bypasses the mucosal barriers and the vascular barriers and raises alarm bells in the immune cells
- The toxic prion-like spike proteins produced in large amounts in germinal centers in the spleen get distributed throughout the body via exosomes
- Exosomes deliver spike and microRNAs to the brain to induce protein misfolding and neurodegenerative diseases as well as brain cancer
- The price of the vaccine is a retuning of the immune system *policy* towards autoimmune disease and neurodegenerative disease

Hypothesis: Chronic inflammation is a way to create DDW in the injured organ(s)

26

Overview

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"Worse than the Disease? Reviewing Some Possible Unintended Consequences of the mRNA Vaccines Against COVID-19" *

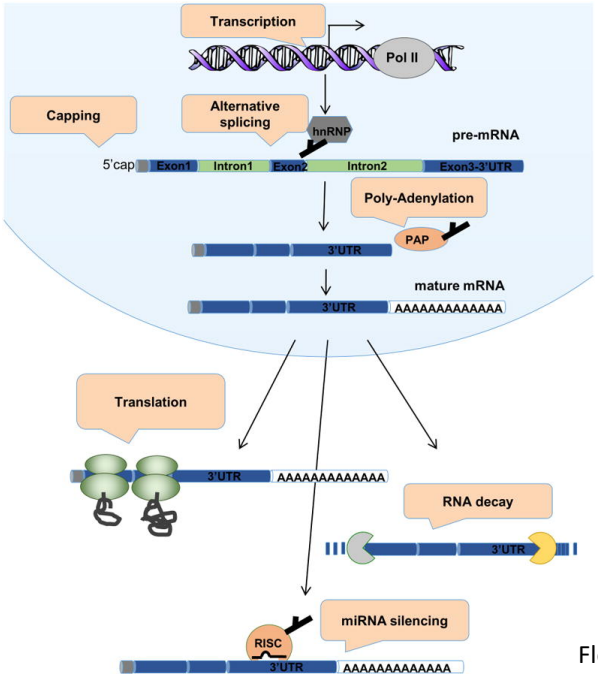
The mRNA vaccines are a poorly evaluated novel technology with many unknowns

Some potential adverse consequences:

- Pathogenic priming, multisystem inflammatory disease and autoimmunity
- Allergic reactions and anaphylaxis
- Antibody dependent enhancement
- Activation of latent viral infections
- Neurodegeneration and prion diseases
- Emergence of novel variants of SARS-CoV-2
- Potential for integration of the spike protein gene into human DNA

*S Seneff and G Nigh. IJVTPR 2021; 2(1): 38-79.

28



The RNA Life Cycle*

The mRNA vaccines are cleverly designed to contain mRNA that is perfectly set up to churn out spike proteins with no way to turn off the spigot

- 5' cap and long poly-A tail
- Modified nucleotides to resist breakdown (methylpseudouridine)
- Enhancement of G and C over A and T to promote rapid protein synthesis
- Incorporation of PEG for stabilization

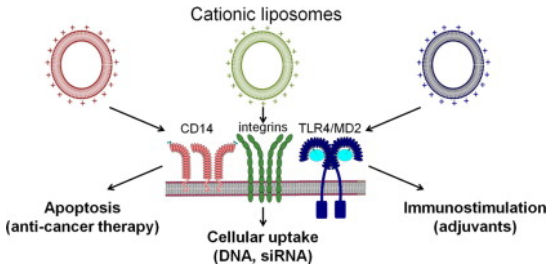
*Figure 1. Florian J. Bock et al. Mol Cell. 2015 June 18; 58(6): 959–969.

29

"The mRNA-LNP platform's lipid nanoparticle component used in preclinical vaccine studies is highly inflammatory"*

"Intradermal injection of these LNPs led to rapid and robust inflammatory responses, characterized by massive neutrophil infiltration, activation of diverse inflammatory pathways, and production of various inflammatory cytokines and chemokines."

Diagram from: Caroline Lonez et al. Advanced Drug Delivery Reviews 2012; 64(15): 1749-1758.



*Sonia Ndeupen et al. bioRxiv preprint. March 4, 2021. doi: 10.1101/2021.03.04.430128.

30

DarkHorsePodcast - Dr. Brett Weinstein, Dr. Robert Malone and Mr. Steve Kirsch*

- There was no evaluation of reproductive toxicity or genotoxicity in animals before the mRNA vaccines were authorized for humans
- A FOIA request from doctors in Canada yielded a Pfizer study written in Japanese
- The lipid nanoparticles went everywhere in the body but were found in especially high concentrations in the animals' *lymph nodes, spleen, ovaries, adrenal glands, liver and bone marrow.*

Dr. Malone is arguably the inventor of mRNA vaccine technology

https://www.youtube.com/watch?v=-_NNTVJzqtY (CENSORED)
Part 1: https://www.brighteon.com/fc163ab1-82f9-4f2b-b921-7b877923f315
Part 2: https://www.brighteon.com/00b257ec-2077-40b6-88a9-93d8d8451959

31

The Action is in the Germinal Centers*

- The germinal center (GC) is a specialized microstructure that forms in secondary lymphoid tissues (e.g., lymph nodes and spleen)
  - produce long-lived antibody-secreting plasma cells and memory B cells
  - provide protection against reinfection
- Within the GC, B cells undergo somatic mutation to achieve successful selection
  - B cell clones that bind antigen with high affinity emerge from this process
- *However, this mutation process can also be dangerous, as it can create autoreactive clones that can cause autoimmunity*

*Marisa Stebegg et al. Frontiers in Immunology 2018; 9: Article 2469.

32

"SARS-CoV-2 mRNA vaccines induce persistent human germinal centre responses"*

- Persistent germinal center (GC) reactions are critical for generating high-affinity and durable antibody responses
- "Overall, our data demonstrate a remarkable capacity of SARS-CoV-2 mRNA-based vaccines to induce robust and prolonged GC reactions."
- "The induced GC reaction recruited cross-reactive memory B cells as well as newly engaged clones that target unique epitopes within SARS-CoV-2 S protein."

*Jackson S Turner et al. Nature 2021 Jun 28 [Epub ahead of print] doi: 10.1038/s41586-021-03738-2.

33

Exosomes, MicroRNAs and Heart Disease

34

The Big Picture

- Stressed immune cells release exosomes containing *microRNAs* that signal to tissue cells and can induce an inflammatory response
  - In particular, *miR-155* plays a special role in SARS-CoV-2, facilitated by spike
- The spike protein S1 subunit detaches and becomes free to bind to ACE2 receptors which are present at high levels in the heart
  - The suppression of ACE2 by spike S1 causes upregulation of angiotensin II, which induces inflammation and cardiovascular disease
- S1 has been found in COVID-19 patients long after the virus is cleared, and is believed to play a critical role in "long COVID"
- S1 has also been found in the vasculature following vaccination
- miR-155 overexpression is linked to worse outcomes in heart attack

35

"Exosomes provide unappreciated carrier effects that assist transfers of their miRNA to targeted cells; I. They are 'The Elephant in the Room'" *

- micro-RNAs are short sequences of RNA that suppress selected proteins by binding to the promoter in their messenger RNA
  - There are thousands of different miRNAs each with specific functions
  - They survive well inside the protective coat of lipid nanoparticles (exosomes)
  - Cell-cell communication is often carried out through the exchange of exosomes
- Exosomes released by immune cells are taken up by tissue cells to influence metabolic policy in the recipient cell through the specific miRNAs contained in the exosome

*Philip W. Askenase. RNA Biology 2021 May 4; 1-16.

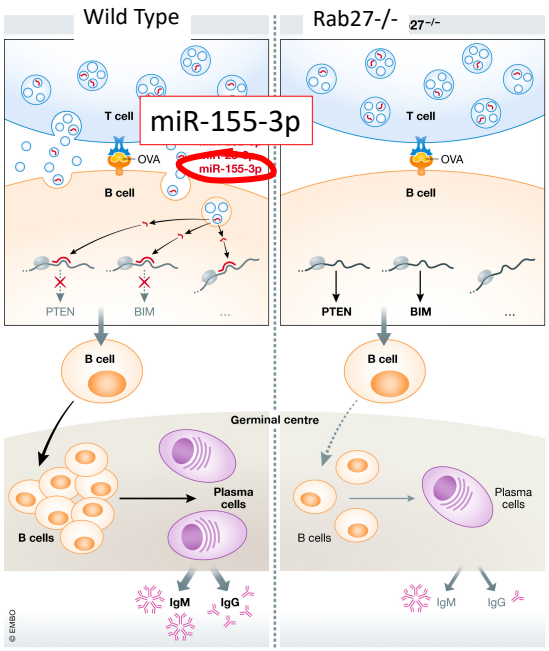
36

"Exosomes take (germinal) center stage"*

- Horizontal transfer of *microRNAs* via *exosomes* from T to B cells is necessary for germinal center formation and efficient antibody production
- *miR-155-3p* silences PTEN and BiM, supporting B cell maturation and proliferation
- *However, miR-155 is also associated with many autoimmune diseases***

*Figure 1. Jennifer Pérez-Boza and Dirk M Pegtel. EMBO Rep 2020; 21: e50190

**Salar Pashangzadeh et al. Frontiers in Immunology 2021; 12: 669382



Rab27 is essential for exosome secretion

37

A role for miRNA-155 in SARS-CoV-2*

"Small RNA profiling showed strong expression of the immunity and inflammation-associated microRNA miRNA-155 upon infection with both viruses (SARS-CoV and SARS-CoV-2)

SARS-CoV-2 elicited approximately *two-fold higher stimulation* of the interferon response compared to SARS-CoV … , and induction of cytokines such as CXCL10 or IL6."

Interferon-γ upregulates miR-155**

*Wyler Emanuel et al. bioRxiv preprint. May 5, 2020. doi: https://doi.org/10.1101/2020.05.05.079194.

**Yu-An Hsu et al. Chin J Physiol 2016; 59(6): 315-322.

38

"Persistence of SARS CoV-2 S1 Protein in CD16+ Monocytes in Post-Acute Sequelae of COVID-19 (PASC) Up to 15 Months Post-Infection"*

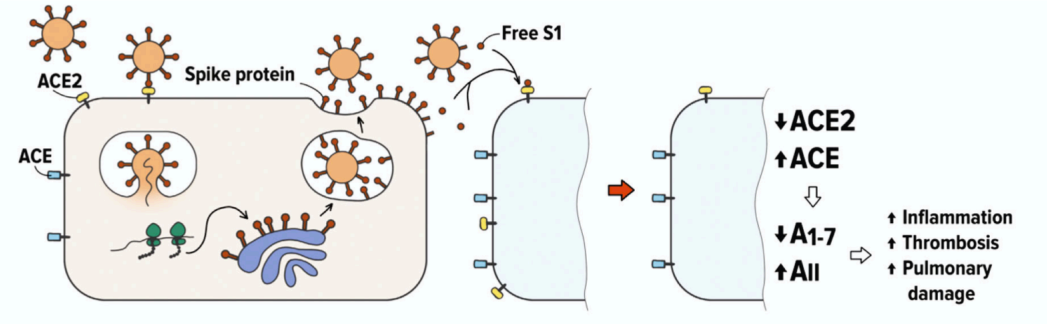
- Enzymatic cleavage of the spike protein by furin proteases causes the S1 segment to be released and circulate freely in the vasculature
- S1 survives in the monocytes long after infection has cleared
- Could be the cause of "long COVID."

*Bruce K. Patterson et al. bioRxiv July 9, 2021. doi: 10.1101/2021.06.25.449905.

39

"Free SARS-CoV-2 Spike Protein S1 Particles May Play a Role in the Pathogenesis of COVID-19 Infection"*

- S1 molecules carry intact RBD domains, and their binding to ACE2 may induce ACE2 downregulation and deleterious downstream effects



*Andrey V. Letarov et al. Biochemistry (Moscow) 2020 Dec 30: 1–5.

40

"Free SARS-CoV-2 Spike Protein S1 Particles May Play a Role in the Pathogenesis of COVID-19 Infection"*

- S1 [illegible] ay in[illegible]

Eleven out of 13 health care workers had detectable levels of spike protein and/or S1 in their blood plasma as early as 1 day and up to 28 days following the first mRNA vaccine, with a peak level on average after five days.**

**Ogata et al. Clinical Infectious Diseases 2021; ciab465. [Epub ahead of print] doi: 10.1093/cid/ciab465.

*Andrey V. Letarov et al. Biochemistry (Moscow) 2020 Dec 30: 1–5.

41

Myocarditis and Pericarditis Cases in VAERS, through June 25, 2021*

- 16-and-over vaccination began December 14, 2020
- 12-15-year-old vaccination began May 10, 2021

Myo/Pericarditis Cases – COVID-19 Vaccines VS. All Flu Vaccines

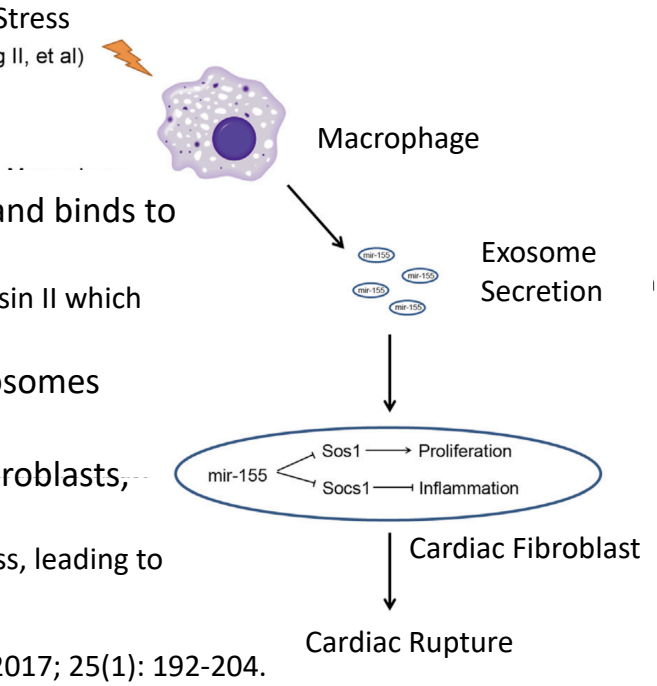
AGE RANGE	FLU REPORTS IN 20 YEARS	COVID19 REPORTS IN 6 MOS.*
6-18	16	467
19-29	61	538
30-39	28	257

*https://www.openvaers.com/covid-data

42

How Spike Protein can Cause Cardiac Issues*

- Spike protein S1 unit causes stress and binds to ACE2 receptors, disabling them
  - This causes accumulation of Angiotensin II which activates macrophages
- Macrophages secrete abundant exosomes containing miR-155
- These exosomes are taken up by fibroblasts, suppressing their proliferation
  - This interferes with the healing process, leading to cardiac rupture



*Chunxiao Wang et al. Molecular Therapy 2017; 25(1): 192-204.

43

miR-155 overexpression linked to worse outcomes in heart attack*

- Measured three miRNA levels in autopsy samples of 50 patients with MI

"innate immunity resulting in an intense inflammatory reaction plays an important role in the pathogenesis of the VR after MI in humans."

VR = ventricular rupture

MI = myocardial infarction

MI1: heart attack within first 24 hours of clinical symptoms
MI2: heart attack 2-7 days after onset of clinical symptoms

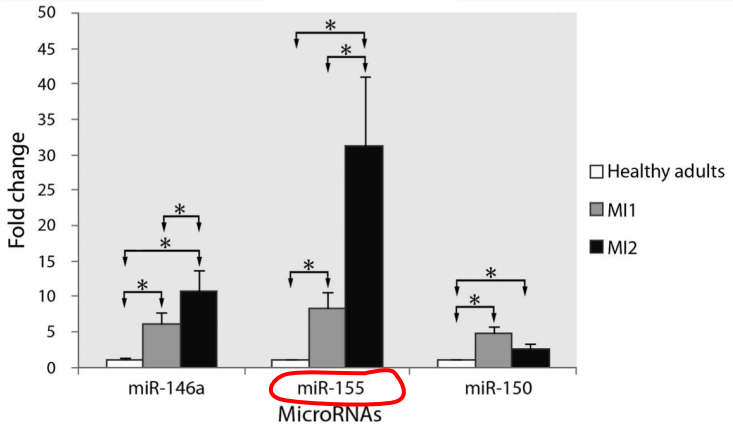


*Figure 1. Nina Zidar et al. Disease Markers 2011; 31: 259-265.

44

Exosomes, microRNAs and Prion Diseases

45

Exosomes and Parkinson's Disease*

- Parkinson's disease often begins in the gut as an immune reaction to prion-like proteins produced by pathogens
- The spike protein is a prion-like protein
  - It contains five glycine zippers (GxxxG) – a characteristic signature of prions
- Stressed immune cells in the digestive tract and spleen upregulate α-synuclein and release it packaged up in exosomes, along with foreign misfolded proteins
- The exosomes travel along the vagus nerve to the brain stem nuclei
- Damage to the substantia nigra causes Parkinson's disease
- The whole process can take years or decades before symptoms appear

*S Seneff and G Nigh. IJVTPR 2021; 2(1): 38-79.

46

Trends Neurosci. 2020 Dec; 43(12): 931–933.
Published online 2020 Oct 21. doi: 10.1016/j.tins.2020.10.009

Is COVID-19 a Perfect Storm for Parkinson's Disease?

Patrik Brundin,[1,*] Avindra Nath,[2] and J. David Beckham[3]

- Loss of smell is a common early symptom of Parkinson's and of COVID-19
- Virus can gain access to brain along nerve fibers
  - Olfactory nerve
  - Vagus nerve
- Neuroinvasion of SARS-COV-2 could upregulate α-synuclein
  - High levels of α-synuclein leads to misfolding and toxicity
- Dopaminogenic neurons in substantia nigra express high levels of the ACE2 receptor

47

Trends Neurosci. 2020 Dec; 43(12): 931–933.
Published online 2020 Oct 21. doi: 10.1016/j.tins.2020.10.009

Is COVID-19 a Perfect Storm for Parkinson's Disease?

Patrik Brundin,[1,*] Avindra Nath,[2] and J. David Beckham[3]

Three independent case reports have described the development of Parkinson's disease following COVID-19.*

- Vagus nerve
- Neuroinvasion of SARS-COV-2 could upregulate α-synuclein
  - High levels of α-synuclein leads to misfolding and toxicity
- Dopaminogenic neurons in substantia nigra express high levels of the ACE2 receptor

* Ernesto Estrada *Viruses* 2021; *13:* 897.

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SARS-CoV-2 Spike Activates Human Microglia in the Brain via Exosomes Loaded with miRNAs*

- "SARS-CoV-2 spike transfected cells release a significant amount of exosomes loaded with microRNAs such as *miR-148a and miR-590"*
- "MicroRNAs gets internalized by human microglia in the brain"
- "These results uncover a bystander pathway of SARS-CoV-2 mediated CNS damage through hyperactivation of human microglia"

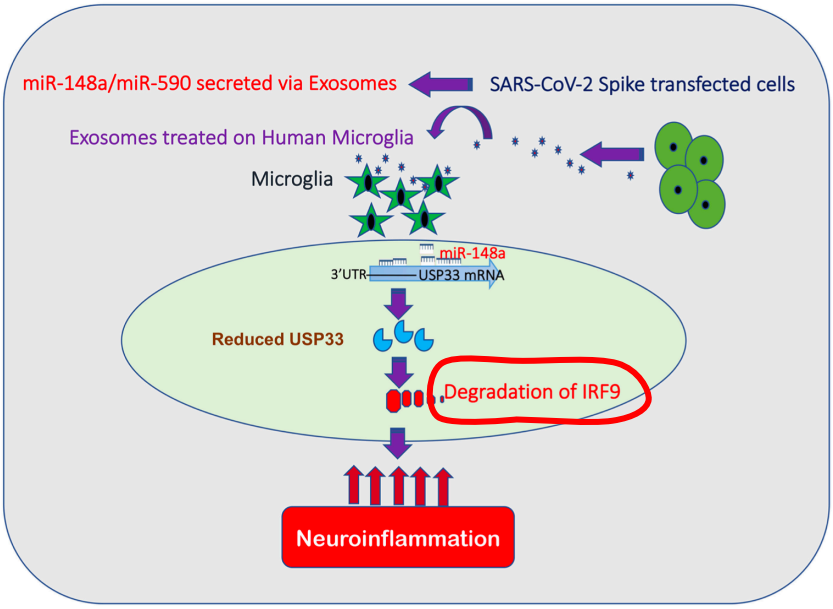
*Ritu Mishra and Akhil C. Banerjea. Frontiers in Immunology April 14, 2021 [Epub ahead of print] Doi: 10.3389/fimmu.2021.656700.

49

Spike Protein Induces Brain Inflammation*

- MicroRNAs released from infected cells into exosomes
- Exosomes taken up by microglia in the brain
- Causes suppression of IRF9 → neuroinflammation

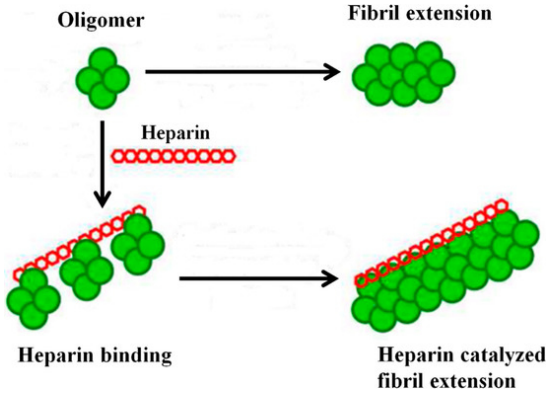
*Figure 7.
R Mishra and AC Banerjea. Frontiers in Immunology Apr 14, 2021 [Epub ahead of print]



50

"SARS-CoV-2 spike protein interactions with amyloidogenic proteins: Potential clues to neurodegeneration"*

- The receptor binding domain (RBD) of the spike protein binds to heparin and to heparin-binding proteins
- Heparin binding accelerates aggregation of amyloid proteins
  - Amyloid-β, α-synuclein, tau, prion and TDP-43
- This could lead to neurodegeneration in the brain



*D Idrees and V Kumar. Biochemical and Biophysical Research Communications 2021; 554: 94e98.

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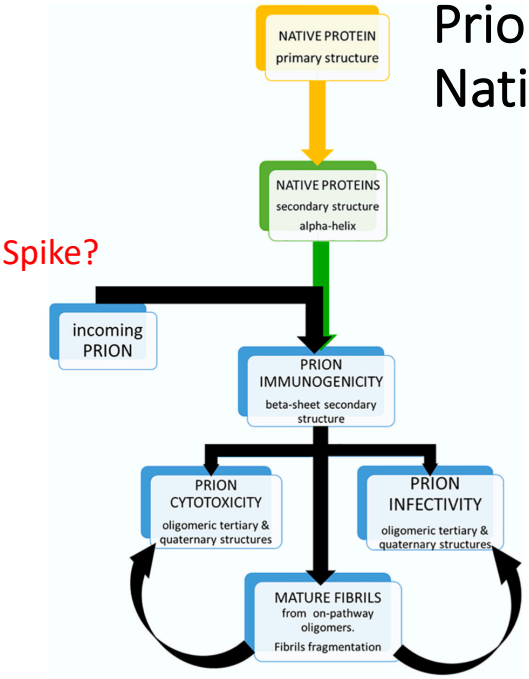


Prion Corruption of Natively Folded Proteins*

- Foreign prion proteins (e.g., spike) act like crystals to induce misfolding of susceptible human proteins (e.g., α-synuclein, amyloid- β, etc.)
- Proteins change from α-helix to β-sheet configuration
- This leads to formation of oligomers and fibrils → neurodegenerative disease (Parkinson's, Alzheimer's, ALS, CKD, ..)

*Dana Butnaru and Joab Chapman. Autoimmun Rev 2019; 18(3): 231-240.

52

"COVID-19 Vaccine Associated Parkinson's Disease, A Prion Disease Signal in the UK Yellow Card Adverse Event Database."*

"All the COVID-19 vaccines on the market contain spike protein or its nucleic acid sequence creating a possible catastrophic epidemic of prion disease in the future."

"This analysis should serve as an urgent warning to those mindlessly following advice of politicians and public health officials regarding COVID immunization."

*J Bart Classen. J Med - Clin Res & Rev. 2021; 5(7): 1-6.

53

Other Consequences of Vaccine-induced MicroRNAs

54

"The microRNA miR-148a functions as a critical regulator of B cell tolerance and autoimmunity"*

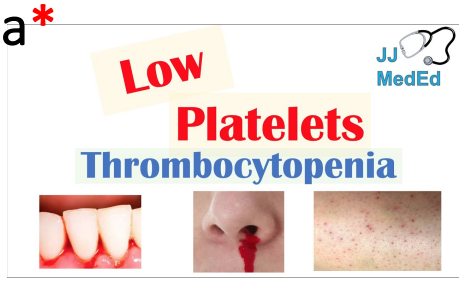
- Immunotolerance ensures that the immune cells can react to foreign antigens but do not attack self tissues
- *Overexpression of miR-148a disrupts B cell tolerance*
- Autoreactive B cells are linked to lupus, rheumatoid arthritis, diabetes and multiple sclerosis
- Patients with lupus show increased expression of miR-148a
- miR-148a suppresses expression of the autoimmune suppressor Gadd45α, the tumor suppressor PTEN and the pro-apoptotic protein Bim

  →increased risk *systemically* to autoimmune disease and cancer

*Alicia Gonzalez-Martin et al. Nature Immunology 2016; 17(4): 433-440.

55

Thrombocytopenia & miR-148a*



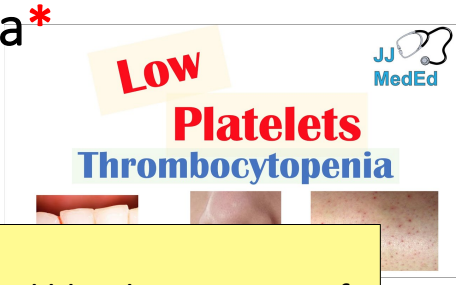
- One third of the body's platelets are housed in the spleen
- Platelets have an Fc receptor for the constant fragment of immunoglobulin G in antigen-antibody complexes
  - Receptor activation leads to platelet activation, aggregation and thrombosis
- TULA-2 (T-cell ubiquitin ligand-2) suppresses platelet activation
  - It inhibits the platelet Fc receptor and protects from thrombocytopenia
- miR-148a targets TULA-2 mRNA and downregulates TULA-2 protein expression

CONCLUSION: miR-148a overexpression can lead to heparin-induced thrombocytopenia (in the absence of heparin)

*Yuhang Zhou et al. Blood 2015; 126(26): 2871–2881.

56

Thrombocytopenia & miR-148a*



- One third of the body's platelets are housed in the spleen
- Plate
  - fragr
  - Re
- TULA
  - It
- miR-

Higher expression of *miR-155* in peripheral blood monocytes of immune thrombocytopenia patients also correlated positively with the reduction in platelet count.*

*BH Qian et al. Acta Haematol 2015; 133(3): 257-63.

pression

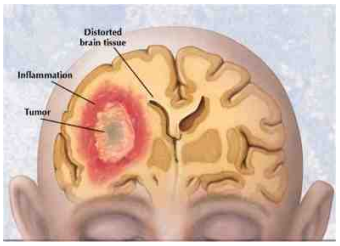
CONCLUSION: miR-148a overexpression can lead to heparin-induced thrombocytopenia (in the absence of heparin)

*Yuhang Zhou et al. Blood 2015; 126(26): 2871–2881.

57

Glioblastoma and Other Cancers

- Glioblastoma is the most aggressive form of brain cancer
- *microRNA-148a* is linked to bad outcomes*
  - High levels were a risk indicator for shortened life span in glioblastoma patients
  - Increased cell growth, survival, migration, and invasion



- *MicroRNA-590-3p* enhances the radioresistance in glioblastoma cells**
  - miR-590-3p expression was higher in high grade than in low grade gliomas
  - miRNA-590 overexpression is also linked to breast cancer, cervical cancer, clear cell renal carcinoma and hepatocellular carcinoma

*Jungeun Kim et al. Cancer Res. 2014 March 1; 74(5): 1541–1553.
**Long Chen et al. Experimental and Therapeutic Medicine 2017; 14: 1818-1824.

58

"New-Onset Neurologic Symptoms and Related Neuro-Oncologic Lesions Discovered After COVID-19 Vaccination: Two Neurosurgical Cases and Review of Post-Vaccine Inflammatory Responses"*

Two cases: Metastatic malignant melanoma and glioblastoma

"We hypothesize that the inflammatory response to the COVID vaccine may have played a role in increasing clinical symptoms in these patients, potentially in relation to the COVID-19 spike protein."

"it is known that spike proteins can initiate inflammatory cascades and cross the blood-brain barrier (BBB) in COVID-19 infections."

Could it be that miR-148a and miR-590 were delivered to the brain in spike-protein-containing exosomes?

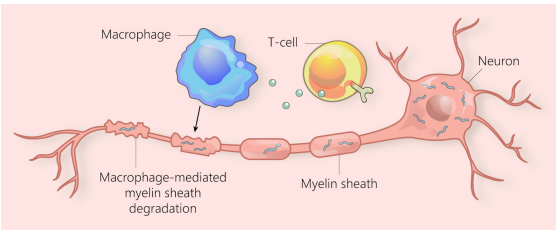
*EH Einstein et al. Cureus 2021; 13(6): e15664.

59

"miR-155 as an Important Regulator of Multiple Sclerosis Pathogenesis. A Review"*

- "miR-155 is among those miRNAs that are *most strongly implicated in autoimmune diseases*"
  - polarizes myeloid cells (granulocytes, monocytes, macrophages, and dendritic cells) towards a pro-inflammatory form
  - is strongly overexpressed in B-cell-activated lymphomas
  - causes pro-inflammatory polarization of microglia in the brain to M1-like phenotype, and neurotoxicity
- miR-155 was up-regulated 12-fold in active white matter lesions in association with multiple sclerosis compared with healthy controls

*Karina Maciak et al. International Journal of Molecular Sciences 2021; 22: 4332.

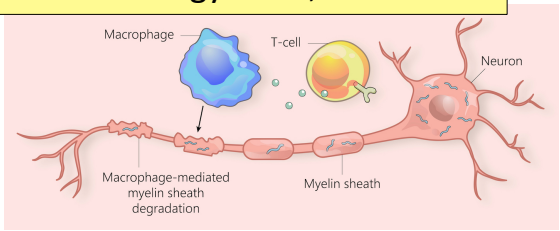


60

"miR-155 as an Important Regulator of Multiple Sclerosis Pathogenesis. A Review"*

- "miR-155 is among those miRNAs that are *most strongly implicated in autoimmune diseases*"
  - Other diseases linked to miR-155 over-expression include systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, primary immune thrombocytopenia, inflammatory bowel disease, Graves' ophthalmopathy, myasthenia gravis and idiopathic inflammatory myopathies .*
  - *Salar Pashangzadeh et al. Frontiers in Immunology 2021; 12: 669382
- mi
  matter lesions in association with multiple sclerosis compared with healthy controls

*Karina Maciak et al. International Journal of Molecular Sciences 2021; 22: 4332.



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Spike Antibodies and Autoimmune Disease

62

"Substantial Differences in SARS-CoV-2 Antibody Responses Elicited by Natural Infection and mRNA Vaccination"*

- After the second dose of the vaccine, antibody titers were *up to 10 times higher* than those of patients who had recovered from natural COVID-19 infection.
- This does not mean that the vaccinated people are better protected than those who recovered from the disease
- High antibody titers opens you up for autoimmune disease, especially when miR-148a is overexpressed

*Rafael Assis et al. bioRxiv preprint. May 19, 2021. doi: https://doi.org/10.1101/2021.04.15.440089

63

"Potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases"*

Cross reaction between spike protein antibody and tissue proteins

Protein/organelle	Diseases
• transglutaminase	Celiac disease
• extractable nuclear antigens	Scleroderma, lupus
• myelin basic protein	Multiple sclerosis, autism
• mitochondria	Lupus, primary billiary cirrhosis, hepatitis, myocarditis
• nuclear antigen	Sjogren's syndrome, mixed connective tissue disease, lupus
• myosin	Myocarditis, dilated cardiomyopathy, Chagas' heart disease, Kawasaki disease, rheumatic fever
• thyroid peroxidase	Hashimoto's thyroid disease
• S100B	Brain metastases from lung disease, epilepsy, multiple sclerosis, and Parkinson's disease

*Aristo Vojdani and Datis Kharrazian, Clinical Immunology 217 (2020) 108480.

64

"High frequency of cerebrospinal fluid autoantibodies in COVID-19 patients with neurological symptoms"*

Conclusions:

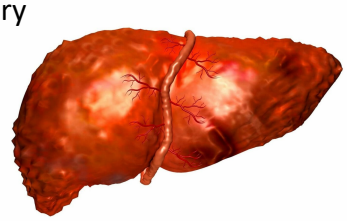
"The high frequency of autoantibodies targeting the brain in the absence of other explanations suggests a causal association with clinical symptoms, in particular with hyperexcitability (myoclonus, seizures). Several underlying autoantigens and their *potential molecular mimicry with SARS-CoV-2* still await identification. However, the presence of autoantibodies may already now explain some aspects of multi-organ disease in COVID-19 and can guide immunotherapy in selected cases."

*Christiana Franke et al. Brain, Behavior, and Immunity 93 (2021) 415-419.

65

Autoimmune Hepatitis Following COVID-19 Vaccine: Two Case Studies

- 35-year-old woman developed autoimmune hepatitis one week post-COVID-19 vaccination (Pfizer) associated with *antinuclear* antibodies*
- 71-year-old woman noticed jaundice four days post-vaccination with Moderna vaccine**
  - Total IgG was markedly raised at 21.77g/L
  - Massive eosinophil infiltration typical of drug-induced liver injury
  - Liver enzymes elevated
- Liver injury has been linked to COVID-19 as well***



*Fernando Bril et al. Journal of Hepatology 2021; 75: 221-255
**Cathy McShane et al. Journal of Hepatology July 7, 2021 (Epub ahead of print] DOI: 10.1016/j.jhep.2021.06.044
***Jose D Debes et al. Dig Liver Dis. 2020; 52(9): 953-955.

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Annexin A2!

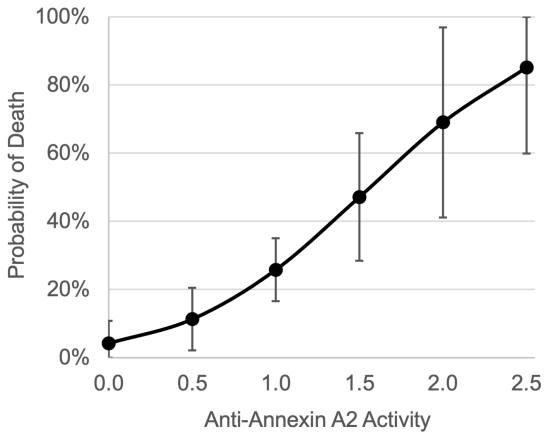
- Cytokines upregulate Annexin A2 in COVID-19 (and presumably following vaccination)
- Annexin A2 is a membrane scaffolding protein that facilitates reactions involving thioredoxin to protect from hydrogen peroxide damage
  - A single molecule of annexin A2 can inactivate several H_2O_2 molecules**
- Antibodies to spike S2 bind to Annexin A2, suppressing its action***

**Patrícia A. Madureira and David M. Waisman. Int J Mol Sci 2013; 14: 3568-3594.
***Yi-Ting Fang et al. Molecular Immunology 2010; 47: 1000-1009.

67

Annexin A2 autoantibodies predict death following COVID-19*

- Annexin A2 is critical for fibrinolysis, lung elasticity, cell membrane repair, and integrity of the pulmonary vasculature
- Anti-Annexin A2 IgG antibodies were measured by ELISA in 86 hospitalized COVID-19 patients



*Marisol Zuniga et al. Eur Respir J 2021; in press. Doi: 10.1183/13993003.00918-2021.

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Reverse Transcription of Spike RNA into DNA

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Search Bloomberg Sign

Business

deutraMed(TM) Inc. Announced Progress With mRNA Vaccine Cold Chain Stabilization Technology

November 17, 2020, 2:01 AM GMT-10

"The advance being announced today provides evidence of our progress to *stabilize mRNA*. Stabilized mRNA provides foundational support for preserving bio-molecules used in medicine. I am proud of our leading deuterium experts in our Scientific Advisory Board who identified *multiple deuterium technology pathways* and recommended Biomolecule Stabilization as a top priority in 2019. Clearly the impact of COVID-19 on the world has heightened the urgency of our technology and our scientists are starting to create results."

-- Dr. Joseph P. Porwoll, Chairman of deutraMed

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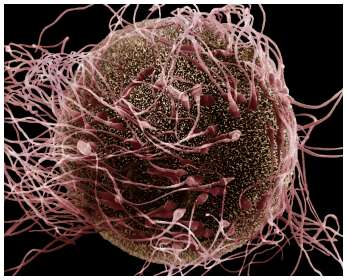
Sperm can insert DNA (from RNA) into the fertilized embryo and transfer it to offspring*

- "We recently discovered a reverse transcriptase (RT) activity [*e.g., LINE-1*] in mouse spermatozoa that can reverse-transcribe *exogenous RNA molecules* into cDNA copies"
- "Spliced EGFP cDNA is transferred from spermatozoa to early embryos at fertilization and propagated to fetuses and born animals" *and passed on to their offspring!*
  - Sperm release DNA-containing plasmids that are taken up by the fertilized egg
- Sperm-mediated "reverse" gene transfer happens "when these cells are incubated with *exogenous RNA molecules*"



*Carmine Pittoggi et al., Molecular Reproduction and Development 2006; 73: 1239-1246.

71

"Polθ reverse transcribes RNA and promotes RNA-templated DNA repair"*

- Polymerase **θ** (Pol**θ**) is highly expressed in human cancer cells
  - Promotes RNA-templated DNA repair
  - Promotes resistance to genotoxic therapies
  - Undergoes a significant structural transformation to accommodate a DNA/RNA template
  - Behaves just like retroviral reverse transcriptases
  - Accommodates a full RNA-DNA hybrid within its active site
- Efficient reverse transcriptase activity of Pol**θ** (equal to that of the HIV retrovirus) appears to be unique among human polymerases

*Gurushankar Chandramouly et al. Science Advances 2021; 7: eabf1771.

72

Summary: Part II

- The novel vaccine technology for COVID-19 prevention is untested and will potentially cause devastating neurodegenerative, autoimmune, oncological and vascular diseases in the vaccinated population
  - A primary mechanism may be through the release of massive numbers of exosomes containing spike protein and specific microRNAs
- Antibodies to the spike protein also bind to many human proteins associated with diverse autoimmune diseases through molecular mimicry
- There is real potential for the mRNA to be converted to DNA and sustained in plasmids in germ cells or cancer cells long-term
  - Continued production of spike protein would likely enhance symptoms of autoimmune and protein-misfolding diseases
  - There is even the possibility of transfer to future generations and integration into the human genome

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