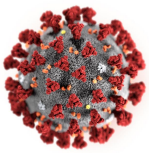

SARS-CoV-2 Vaccines: Is the Risk Worth the Benefit?

Stephanie Seneff
MIT CSAIL
WAPF Wise Traditions Conference
November 6, 2021

1

Download these slides

Powerpoint:
https://people.csail.mit.edu/seneff/2021/WAPF_2021_Part2.pptx

PDF:
https://people.csail.mit.edu/seneff/2021/WAPF_2021_Part2.pdf

My personal web page:
stephanieseneff.net

2

"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

3

Outline

- Overview of mRNA Vaccines
- Breakthrough Variants
- Antibody Dependent Enhancement
- Immune System, Exosomes, and MicroRNAs
- Exosomes, MicroRNAs and Heart Disease
- Exosomes, MicroRNAs and Prion Diseases
- Other Consequences of Vaccine-induced MicroRNAs
- Spike Antibodies and Autoimmune Disease
- Summary

4

Overview of mRNA Vaccines

5

Worldwide Statistics on Pandemic Death

Virus	World Population	Deaths	Normalized Percentage
Spanish Flu (H1N1)	**~2B**	**50M**	**2.5%**
COVID-19 (SARS-CoV-2)	**~7.9B**	**4.6M***	**0.05%**

- While *any* death is unfortunate, normalized deaths due to Covid-19 are **~50** times fewer than those due to the Spanish Flu in 1918-1920
- Flare-ups of H1N1 have continued throughout the last century
- Could SARS-CoV-2 have the same fate of lingering indefinitely, i.e. becoming endemic?

* As of September 2021

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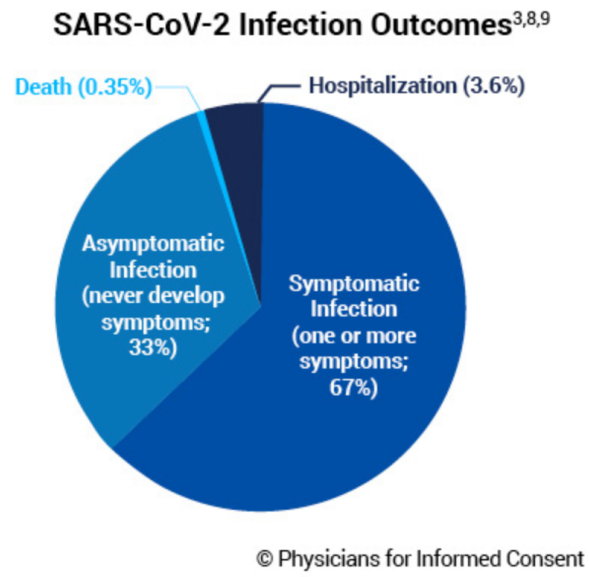

as of August 24, 2021
United States only

https://physiciansforinformedconsent.org/physicians-for-informed-consent-publishes-comprehensive-analysis-of-u-s-covid-19-infection-fatality-rate-by-age-group/

7

The New COVID-19 mRNA Vaccines

- The Pfizer and the Moderna vaccines are based on revolutionary technology that involves creating a nanoparticle containing a greatly modified form of the messenger RNA from the SARS-CoV-2 virus that codes for the spike protein
- Polyethylene glycol (PEG) is included in the vaccine to keep the RNA from breaking down too quickly

"Instead of delivering a virus or a viral protein, RNA vaccines deliver genetic information that allows the body's own cells to produce a viral protein. Synthetic mRNA that encodes a viral protein can borrow this machinery to produce many copies of the protein. These proteins stimulate the immune system to mount a response, without posing any risk of infection."*

*https://news.mit.edu/2020/rna-vaccines-explained-covid-19-1211

8

Why are the COVID-19 mRNA vaccines so troubling to so many?

- They were developed at warp speed (< 1 year), whereas unprecedented vaccine development typically takes 10-15 years, and only 2% make it through the process to final production and distribution
- As a result, multiple corners were cut in their development: technology, testing, safety evaluation, deployment, follow-through, …
- Data were kept out of reach of the scientific community, and dissenting opinions are being suppressed
- There are multiple unknowns in possible adverse outcomes that we may not recognize until years have passed and much damage has been done

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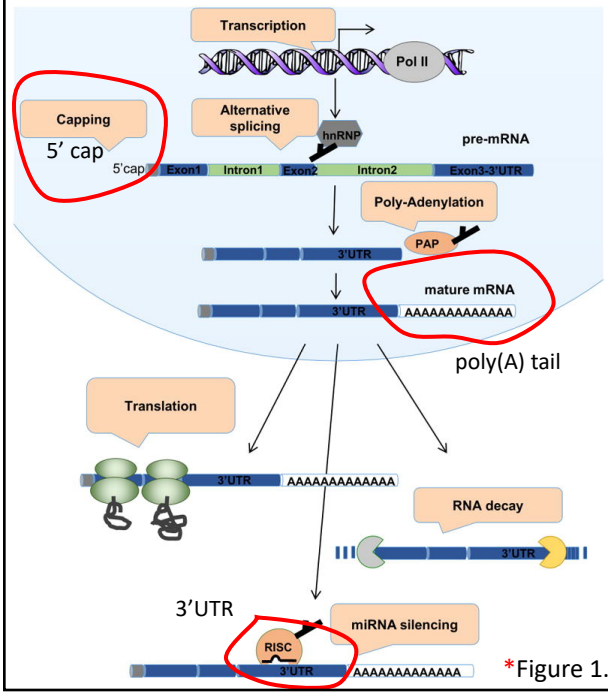

The RNA Life Cycle*

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 added to make it look like a human protein
- Select hearty 3'UTR to resist silencing
- Modified nucleotides to resist breakdown (methylpseudouridine)
- Enhancement of G and C over A and U to promote rapid protein synthesis

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

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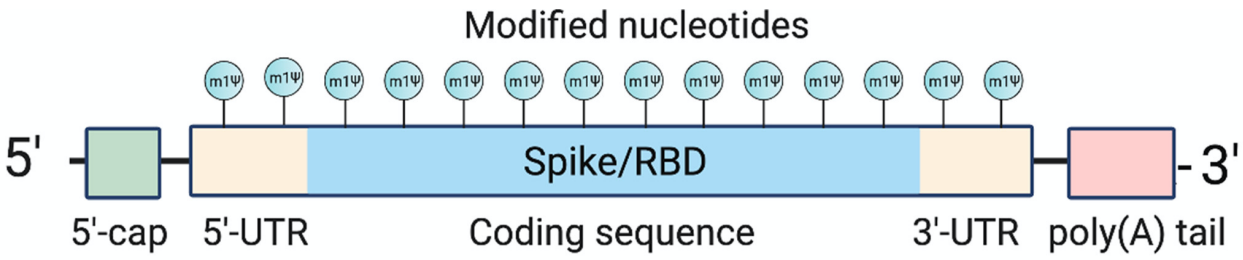


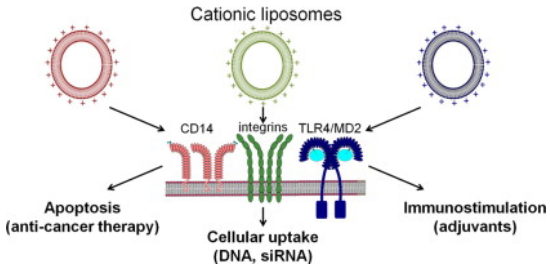
- mRNA vaccines contain the genetic code to make spike protein
- The mRNA is incorporated into a lipid particle that simulates a human LDL particle
- A synthetic cationic (positively charged) lipid is added to act as an adjuvant – very toxic to the cells
- Large quantities of polyethylene glycol (PEG) are added to further protect the mRNA from breakdown
- The RNA is carefully engineered to resist breakdown and to produce spike protein at high rate

11

"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.

12

"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.

13

Anaphylactic Shock

- According to the CDC, "anaphylaxis after COVID-19 vaccination is rare and has occurred in approximately 2 to 5 people per million vaccinated in the United States"*
- A careful study based on hospital employees in Boston who received the mRNA vaccines revealed that 2.47 people per 10,000 vaccinations experienced classic symptoms of anaphylaxis following vaccination**
  - This is 50 times the number reported in the VAERS database
  - The mRNA vaccines contain polyethylene glycol (PEG) – a likely trigger of shock
- Anaphylaxis occurs immediately after vaccination so it should be easy to identify
  - Other symptoms are probably even more under-reported in VAERS

*CDC. Selected Adverse Events Reported after COVID-19 Vaccination.
** Kimberly G. Blumenthal et al. JAMA 2021;325(15): 1562-1565
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html

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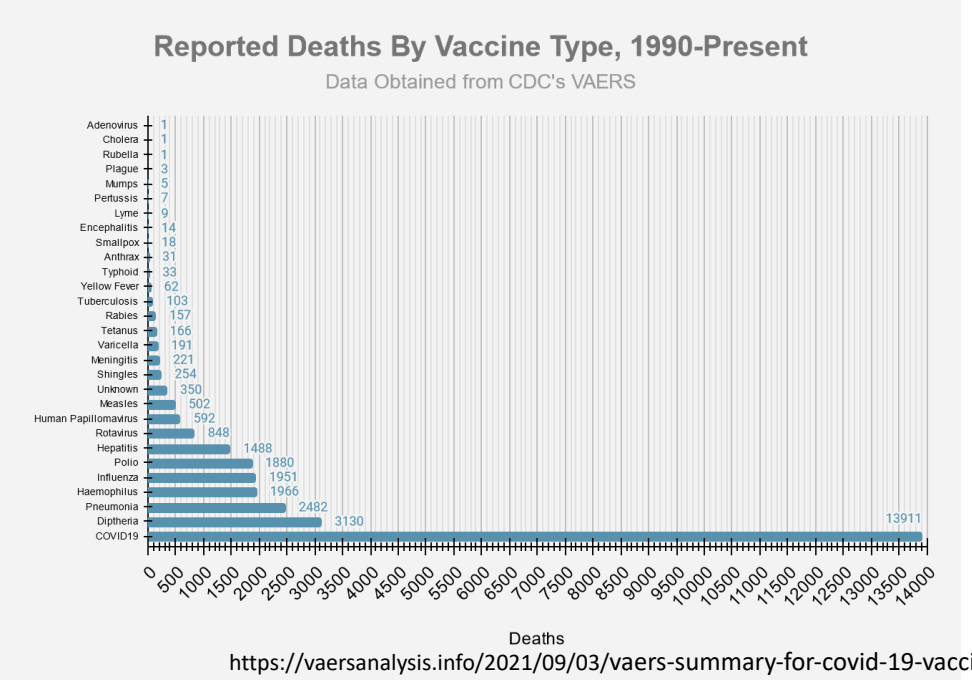


As of August 27,2021

https://vaersanalysis.info/2021/09/03/vaers-summary-for-covid-19-vaccines-through-8-27-2021/

15

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 an early developer 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

16

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.

17

"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."
- This leads to a very strong induction of memory B cells that produce antibodies specific to the spike protein

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

18

"A longitudinal study of SARS-CoV-2-infected patients reveals a high correlation between neutralizing antibodies and COVID-19 severity"*

- A study of 140 SARS-CoV-2 infected patients revealed that those with the most severe disease were the ones who developed the strongest antibody response to the spike protein
- The antibodies fade rapidly following viral clearance
- My conclusion: a strong innate immune system can fight off the virus without ever having the need to produce antibodies
  - Antibodies are invoked only after innate immune system failure

*Vincent Legros et al., Cellular & Molecular Immunology 2021; 18: 318-327.

19

Breakthrough Variants

20

The Big Picture

- Antibodies to the virus in an immune-compromised person can lead to rapid evolution of new antibody-resistant strains
  - There are parallels between getting antibody therapy from recovered COVID patients and getting antibodies that were induced by a vaccine
- The rapid emergence of the Delta strain may have been facilitated by the massive vaccination campaign
- Preliminary evidence suggests that vaccinated people and unvaccinated people are equally susceptible to infection with Delta
- Israel (vaccinated very early) is facing a fourth wave (Delta variant) as vaccine effectiveness wanes

21

"SARS-CoV-2 evolution during treatment of chronic infection"*

- Cancer patient being treated for recurrent lymphoma with a drug that depletes antibody-producing B cells caught COVID-19
  - Persistent viral RNA shedding and risk of transmission in the hospital
  - Patient died 101 days after diagnosis, after being given two rounds of plasma from recovered patients, *which contained antibodies against the virus*
  - Following antibody exposure, SARS-CoV-2 had acquired several mutations that might have allowed it to elude the antibodies.
- This is a good model for what happens when you vaccinate an immune-compromised person

*SA Kemp et al., Nature 2021; 592: 277-282.

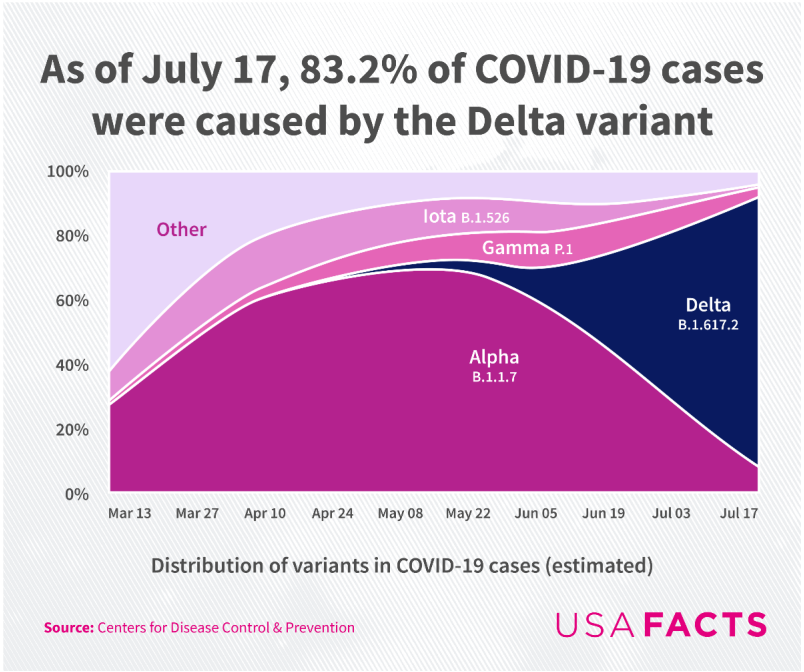
22

"SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma"*

- "Sera from the Moderna and Pfizer-BioNTech vaccinees show *significantly reduced neutralization* of 501Y.V2"
- "A substantial proportion of *non-neutralizing* antibodies remain active against 501Y.V2."
- "These data highlight the prospect of reinfection with antigenically distinct variants and *foreshadows reduced efficacy* of spike-based vaccines."
- "These data highlight the urgent requirement for rapidly adaptable vaccine design platforms and the need to identify less-mutable viral targets for incorporation into future immunogens."

*Constantinos Kurt Wibmer et al. Nature Medicine 2021; 27: 622-625.

23



As of September 20, the number had risen to over 99%

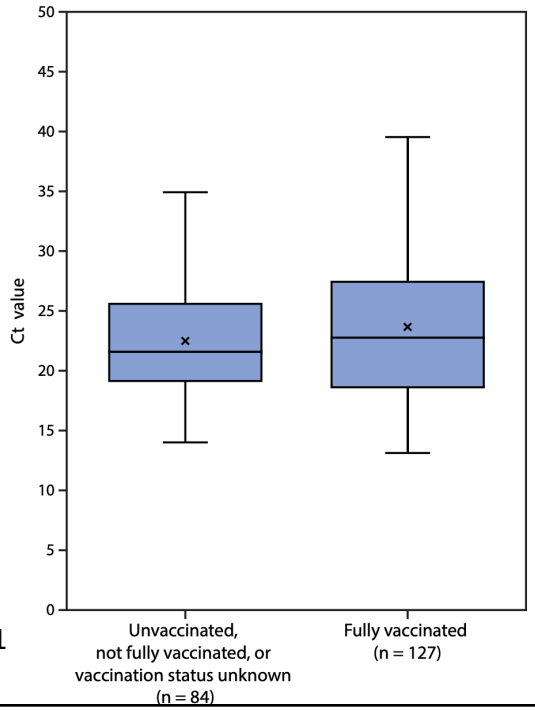
24

Vaccines Provide Poor Protection from Delta Strain in Cape Cod*

- 74% of cases were fully vaccinated
- 80% of fully vaccinated had symptoms

Plot shows PCR threshold values for specimens from vaccinated vs unvaccinated patients in Barnstable County, Massachusetts.

July, 2021



*Morbidity and Mortality Weekly Report , July 30, 2021
Centers for Disease Control

25

"An Effective COVID-19 Vaccine Needs to Engage T Cells"*

- All the COVID vaccines currently on the market are specific to the spike protein
  - Natural infection induces antibodies to many other viral proteins
- T cells exposed to *internal* viral proteins can become *memory T cells* that respond very quickly to a new infection
  - They are much more long lasting than memory B cells (up to 17 years!)
- These memory T cells can induce a rapid antibody response *in B cells* to a mutated form of the spike protein
- Memory B cells can lose their effectiveness because their antibodies are specific to an obsolete version of the spike protein
- Conclusion: natural infection induces far better protection than the vaccines

*Karsten Sauer and Tim Harris. Frontiers in Immunology 2020; 11: 581807.

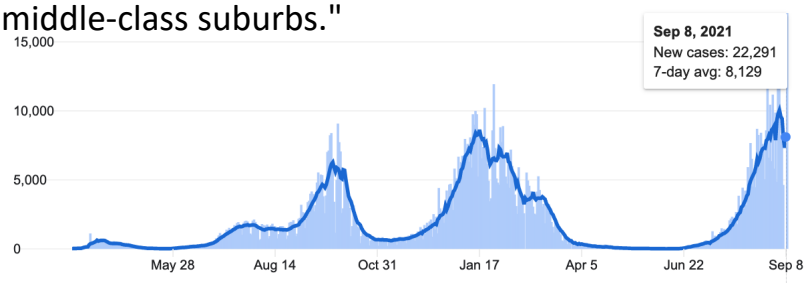
26

The New York Times August 18,2020

Israel, Once the Model for Beating Covid, Faces New Surge of Infections

One of the most vaccinated societies, Israel now has one of the highest infection rates in the world, raising questions about the vaccine's efficacy.

"Unlike previous epicenters of infection in Israel's crowded, less-vaccinated ultra-Orthodox communities, this scourge primarily took hold in well-vaccinated, middle-class suburbs."



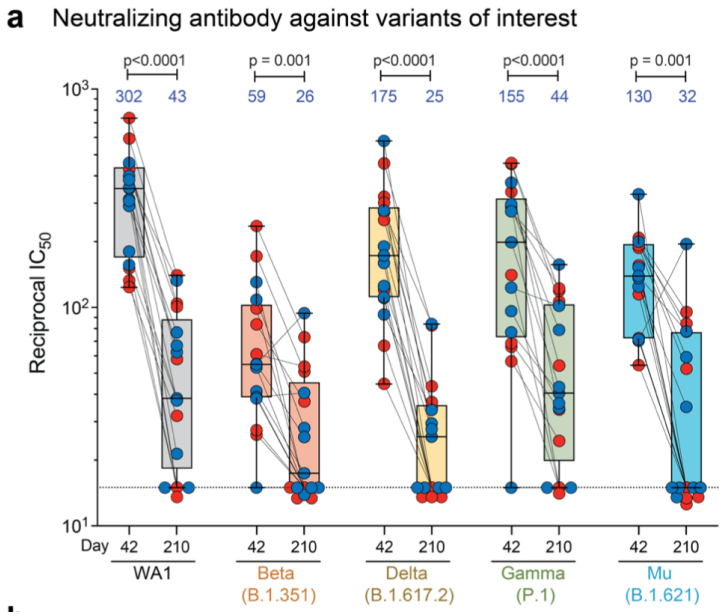
27

Outbreak in Israeli Hospital, July 2021*

- 24% of the patients (23 people) were infected
  - An additional 19 people (staff and family members) were also infected
- 39 out of 42 cases were fully vaccinated.
  - Median time of 25 weeks after vaccination
- Index patient was fully vaccinated
- Several transmissions occurred among people wearing face masks
- 14/23 patients became severely sick or died (five deaths)
- The two unvaccinated patients had mild disease
- Warning about waning immunity

*Pnina Shitrit et al. Euro Surveill 2021; 26(39): 2100822.

28

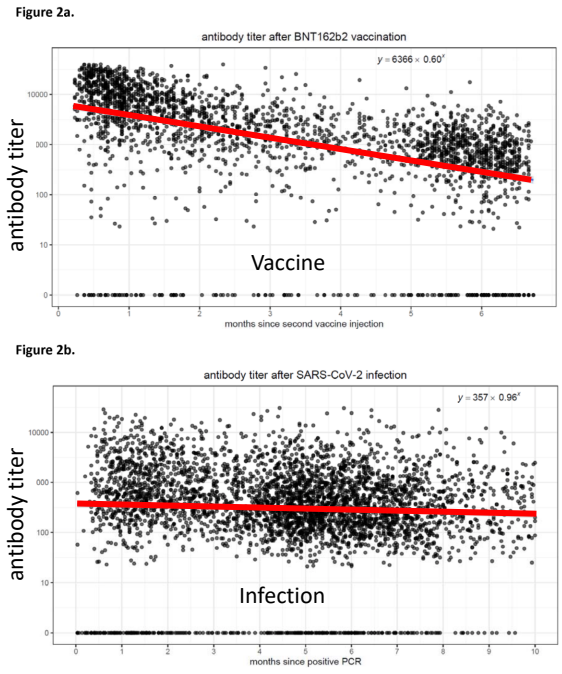


Neutralizing antibodies fall dramatically in six months*

Red: males; Blue: females

*Mehul S. Suthar et al. bioRxiv preprint Sept. 20, 2021. Doi: 10.1101/2021.09.30.462488.

29



"Large-scale study of antibody titer decay following BNT162b2 mRNA vaccine or SARS-CoV-2 infection"*

Initial levels of antibody are much higher in vaccinated patients (Pfizer mRNA vaccine), but they decrease faster.

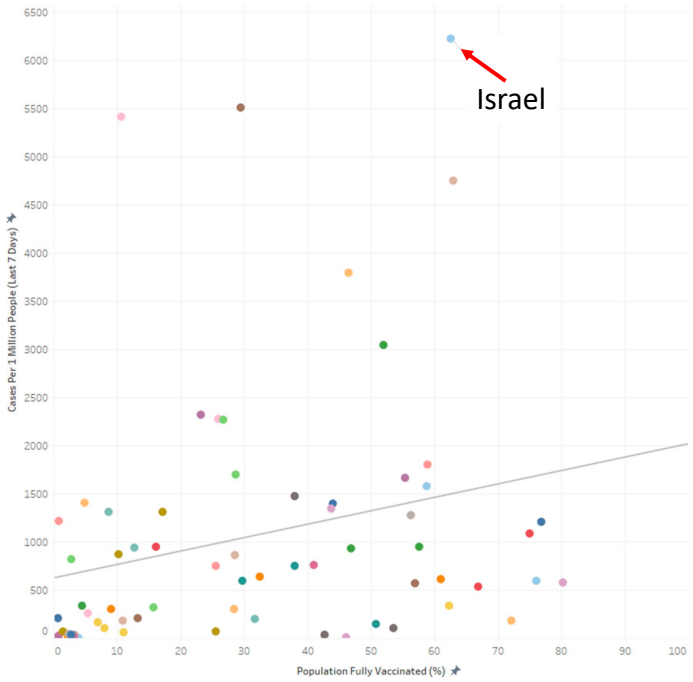
*Ariel Israel et al. medRxiv preprint Aug. 22, 2021. doi: 10.1101/2021.08.19.21262111.

30

Positive trend between vaccination rate and infection rate*

Number of cases during one week before September 3. 2021

*S. V. Subramanian et al. European Journal of Epidemiology Sept 30, 2021 [Epub ahead of print]



31

Antibody-Dependent Enhancement (ADE)

32

Antibody-Dependent Enhancement (ADE)*

The vaccine has the potential to backfire:

- Antibody enhances uptake into macrophages via *Fcγ receptors* leading to increased viral infection and replication
- Antibody increases release of cytokines causing enhanced risk of excessive inflammation and cytokine storm

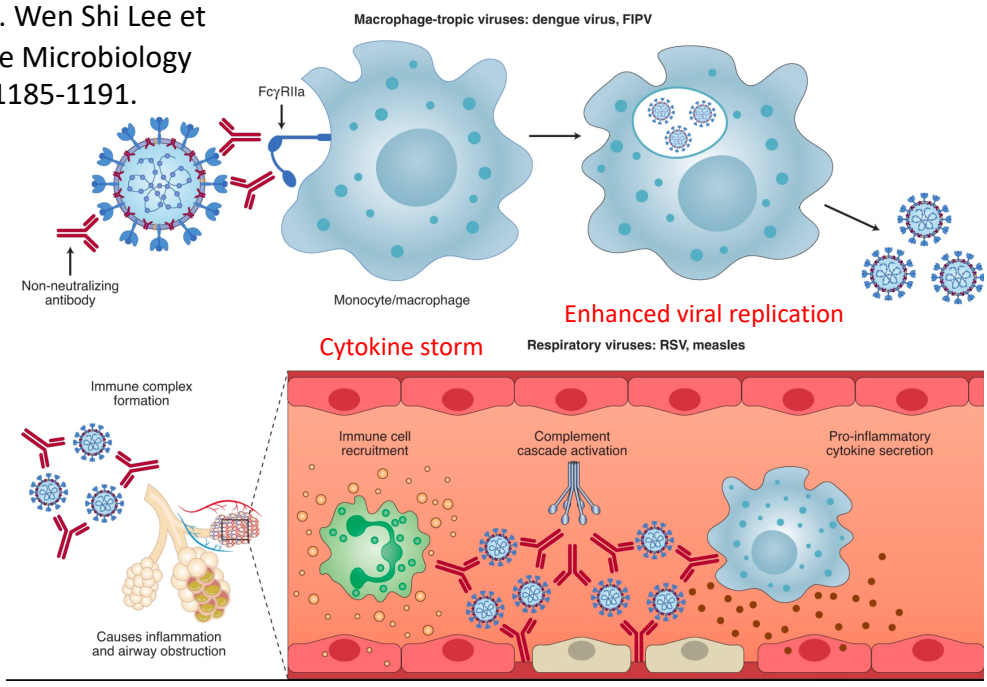
"ADE has been observed in SARS, MERS and other human respiratory virus infections including RSV and measles, which suggests a real risk of ADE for SARS-CoV-2 vaccines and antibody-based interventions."*

"Thus, the absence of ADE evidence in COVID-19 vaccine data so far does not absolve investigators from disclosing the risk of enhanced disease to vaccine trial participants, and it remains a realistic, non-theoretical risk to the subjects."**

*Wen Shi Lee et al., Nature Microbiology 2020; 5: 1185-1191.
**T Cardozo and R Veazey, Int J Clin Pract 2021; 75(3): e13795.

33

*Figure 1. Wen Shi Lee et al., Nature Microbiology 2020; 5: 1185-1191.



34

"Informed consent disclosure to vaccine trial subjects of risk of COVID-19 vaccines worsening clinical disease"*

Conclusion*:*

"The **specific and significant COVID-19 risk of ADE** should have been and should be prominently and independently disclosed to research subjects currently in vaccine trials, as well as those being recruited for the trials and future patients after vaccine approval, in order to meet the medical ethics standard of patient comprehension for informed consent."

*Timothy Cardozo and Ronald Veazey. Int J Clin Pract. 2021; 75: e13795.

35

Delta Variant[a,a] Increases Risk of ADE*

"However, in the case of the Delta variant, *neutralizing* antibodies have a decreased affinity for the spike protein, whereas *facilitating* antibodies display a strikingly increased affinity."

"The emergence of SARS-CoV-2 variants may tip the scales in favor of infection enhancement."

*Nouara Yahi et al. Journal of Infection August 9, 2021 [Epub ahead of print] https://doi.org/10.1016/j.jinf.2021.08.010

36

"The SARS-CoV-2 Delta variant is poised to acquire complete resistance to wild-type spike vaccines"*

- The Delta variant completely escaped from anti-N-terminal domain (NTD) *neutralizing antibodies*
- Delta variant responsiveness to anti-NTD *infectivity-enhancing* antibodies is increasing
- The Delta variant will continue to acquire further mutations
- "When four common mutations were introduced into the receptor binding domain (RBD) of the Delta variant (Delta 4+), some Pfizer BioNTech-immune sera lost neutralizing activity and enhanced the infectivity"

Δ

*Yafei Liu et al. biRxiv preprint. Aug 23, 2021. DOI: 10.1101/2021.08.22.457114

37

Immune System, Exosomes and MicroRNAs

38

Immune System 101

- The innate immune system is actually very powerful if it is healthy
- If the innate system can't clear the virus, the adaptive system gets involved
- The adaptive system releases antibodies to help tag and trap the viruses, and inflammatory cytokines which induce release of reactive oxygen species

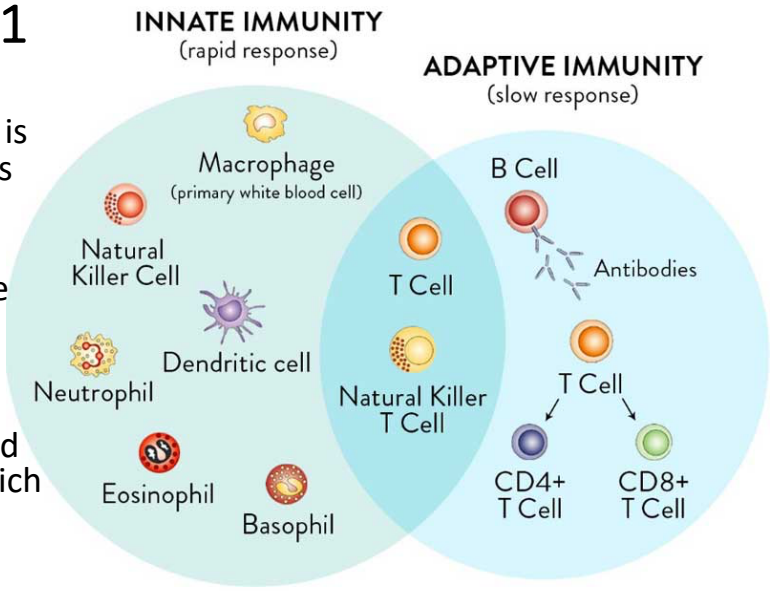
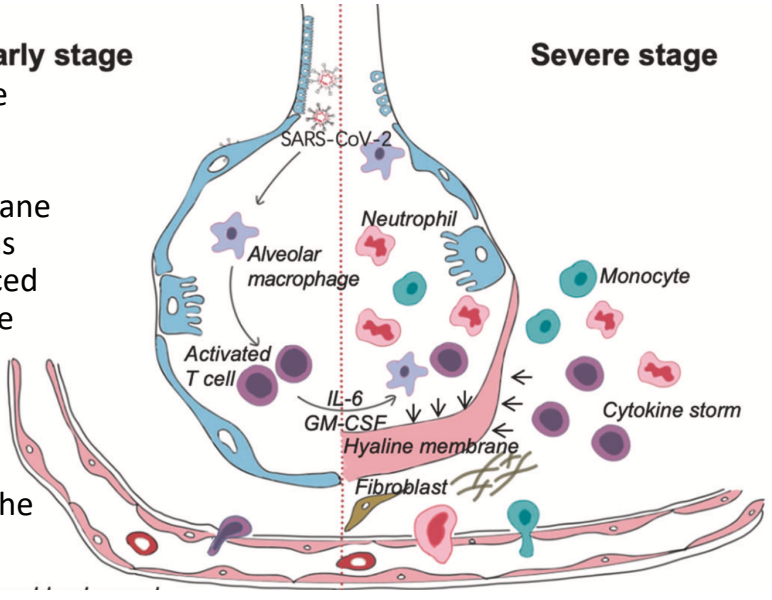


Figure from https://articles.mercola.com/sites/articles/archive/2020/10/14/herd-immunity-coronavirus.aspx

39

COVID Lungs: Alveoli: Review from Part 1

- Hyaline membrane grows large
- Gelled water fills the alveoli
- "Ground Glass" opacities
- Reminiscent of hyaline membrane disease in premature newborns
- Oxygen supply is sharply reduced
- Mitochondria (systemically) are disabled
- Lungs become site where macrophage health is restored through replenishment of deuterium-depleted water in the mitochondria



40

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

- Exosomes are a type of extracellular vesicle with diverse content that are released from stressed cells
- 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 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.

41

Mitochondria, Lysosomes and Aging*

"Disruption of the mitochondrial–lysosomal axis coupled with abnormal EV [extracellular vesicle] secretion may play a role in the pathogenesis of aging and several disease conditions."

- Damaged mitochondria are normally cleared through an endosome-to-lysosome pathway
- When lysosomes are impaired, damaged mitochondria are excreted from the cell inside exosomes (extracellular vesicles)
- Excessive extracellular vesicles in the blood are a marker of aging

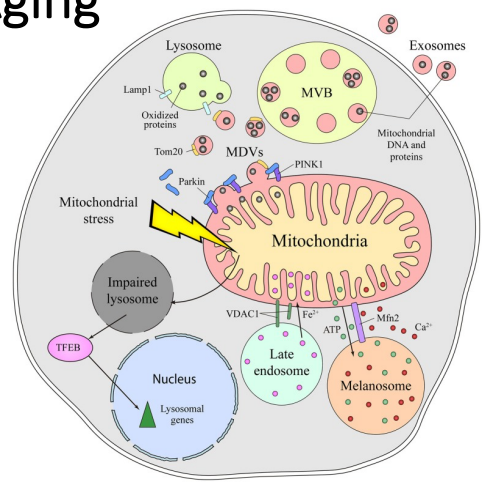
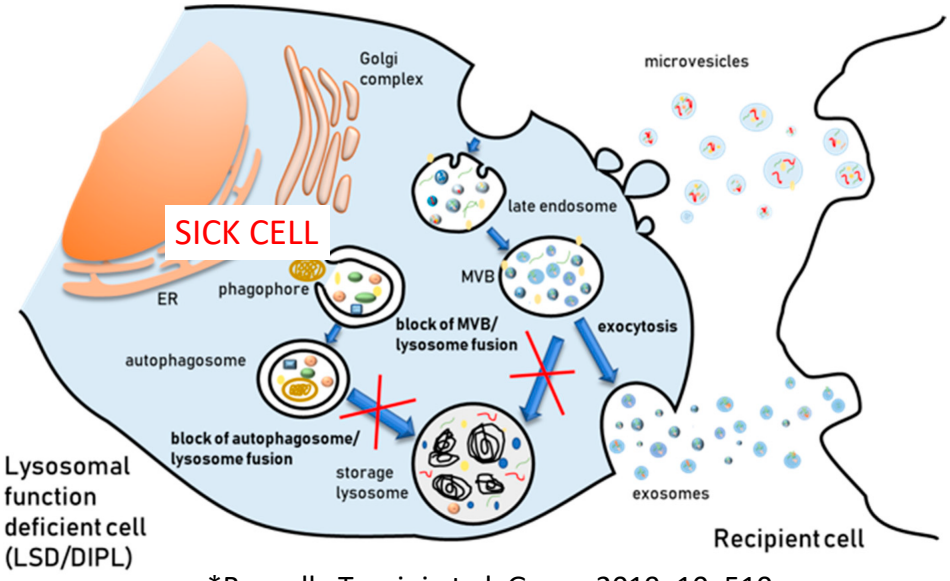


Figure 2 in GonzaloSoto-Heredero et al. Frontiers in Cell and Developmental Biology 2017; 5: 95.

*Anna Picca et al. Int J Mol Sci 2019; 20: 805.

42

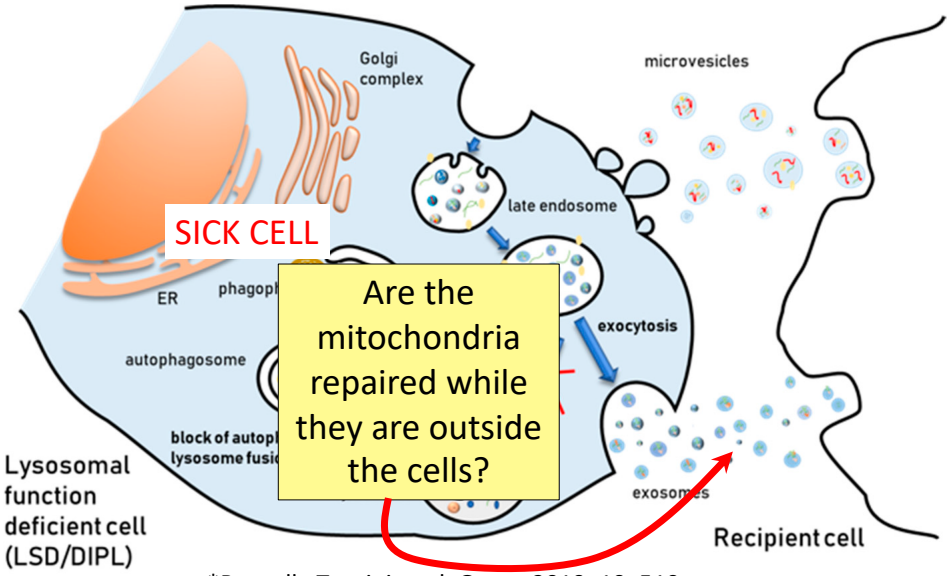
A cell that can't clear its garbage dumps its garbage



*Brunella Tancini et al. Genes 2019; 10: 510.

43

A cell that can't clear its garbage dumps its garbage



*Brunella Tancini et al. Genes 2019; 10: 510.

44

Hypothesis

- The reaction that takes place in the lungs following an infection with SARS-CoV-2 facilitates recovery of mitochondrial function in innate system immune cells that eventually enables them to clear the virus
- The vaccine introduces the genetic code to force muscle cells in the arm to make massive amounts of spike protein, without the rest of the virus particle
  - Bypasses both mucosal barrier (lungs) and vascular barrier (blood vessels)
- Vaccine essentially introduces a dangerous toxin into the body without supporting the launch of an appropriate immune response that would heal the mitochondria

45

Exosomes, MicroRNAs and Heart Disease

46

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 (myocarditis) 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-haul COVID"
- S1 has also been found in the vasculature following vaccination
- miR-155 overexpression is linked to worse outcomes in heart attack

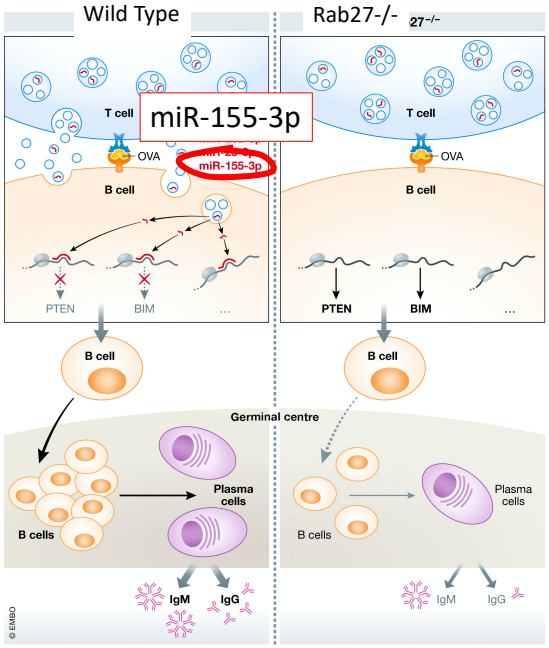
47

"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

48

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."

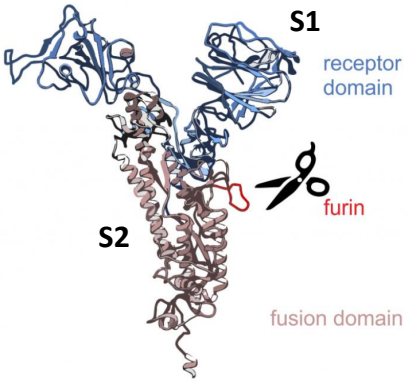
Interferon-γ upregulates miR-155**

*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.

49

SARS-CoV-2 S1 of spike persists up to 15 months post-infection in immune cells expressing an Fcγ receptor*

- Enzymatic cleavage of the spike protein by furin proteases causes the S1 segment to be released and circulate freely in the vasculature
  - S1 is the part that binds to ACE2 receptors
- S1 survives in the immune cells long after infection has cleared
- Could be the cause of *"long-haul COVID."*

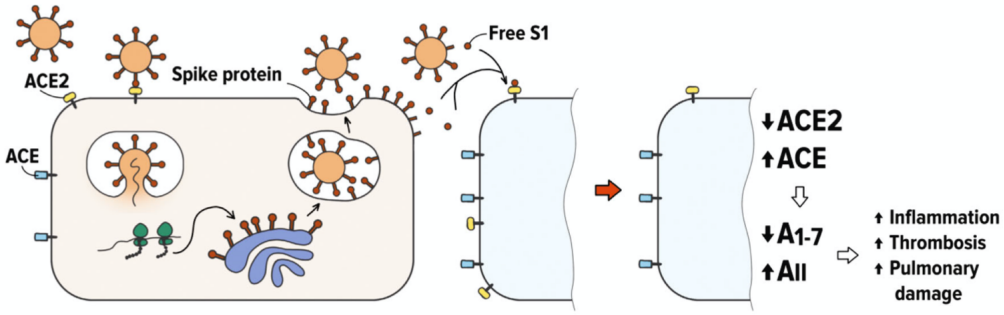


*Bruce K. Patterson et al. bioRxiv July 9, 2021. doi: 10.1101/2021.06.25.449905.

50

"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.

51

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

- S1 ay in

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.

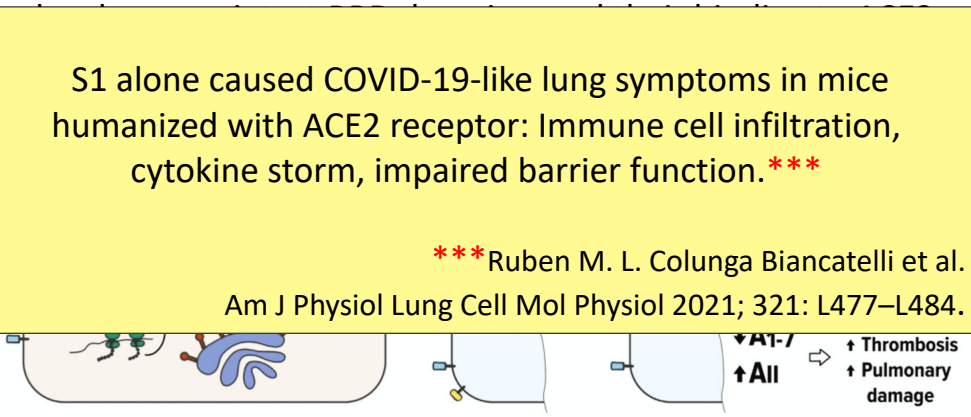
52

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

- S1 [illegible] ay in[illegible]

S1 alone caused COVID-19-like lung symptoms in mice humanized with ACE2 receptor: Immune cell infiltration, cytokine storm, impaired barrier function.***

***Ruben M. L. Colunga Biancatelli et al.
Am J Physiol Lung Cell Mol Physiol 2021; 321: L477–L484.



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

53

"SARS-CoV-2 Spike Protein Impairs Endothelial Function via Downregulation of ACE2"*

- Spike-protein "pseudoviruses" cause endothelial damage by downregulating ACE2
- This increases oxidative stress and impairs mitochondrial function in the endothelial wall lining blood vessels
- Induces vasculitis

*Yuyang Lei et al. Circulation Research 2021; 128: 1323-1326.

54

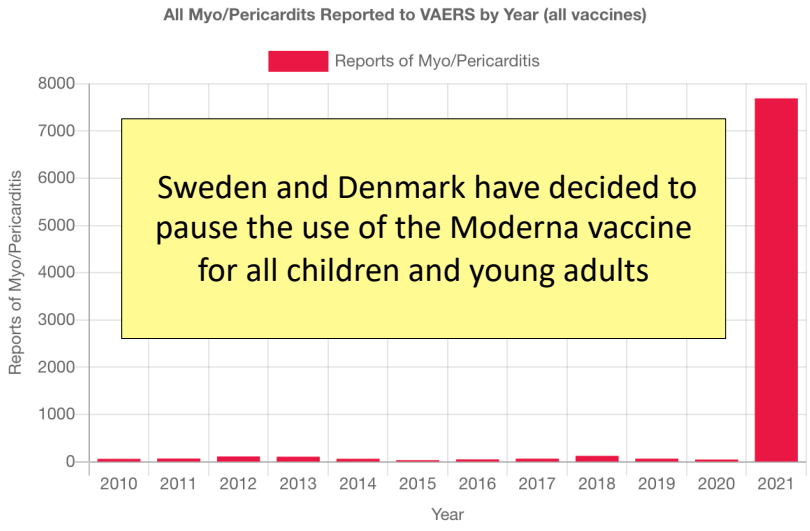
SARS-CoV-2 mRNA Vaccination-Associated Myocarditis in Children Ages 12-17: A Stratified National Database Analysis"*

- Rate of myocarditis after two shots of Pfizer vaccine was 162 cases per million in boys 12-15 years old
  - About 86% required hospitalization
  - May lead to permanent damage and heart failure
- Risk of a healthy adolescent being taken to hospital with COVID-19 in the next three months is 44 per million

*Tracy Beth Høeg et al. medRxiv preprint. August 30, 2021. doi: https://doi.org/10.1101/2021.08.30.21262866

55

Myocarditis Reports in VAERS*



Through September 24, 2021

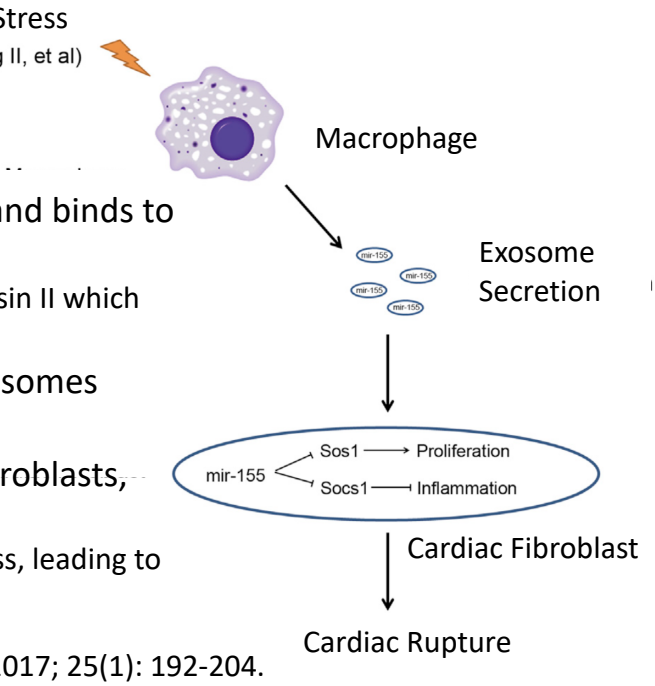
- 16-and-over vaccination began December 14, 2020
- 12-15-year-old vaccination began May 10, 2021

*https://openvaers.com/covid-data/myo-pericarditis

56

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.

57

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 [ventricular rupture] after MI [myocardial infarction] in humans."

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

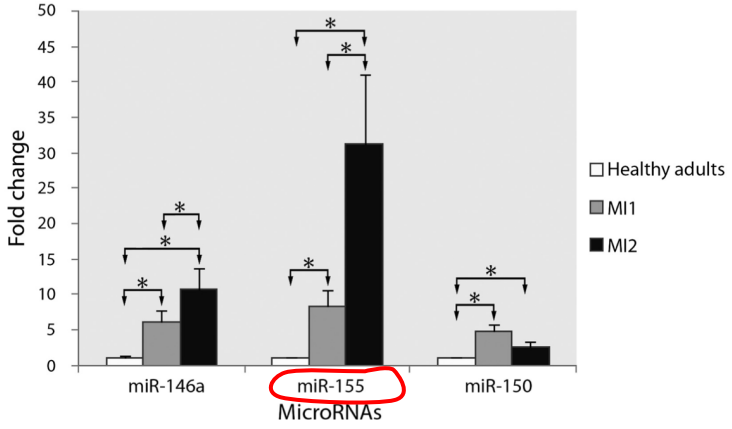


*Figure 1. Nina Zidar et al. Disease Markers 2011; 31: 259-265.

58

Exosomes, microRNAs and Prion Diseases

59

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.

60

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

61

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.

62

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 get internalized by human microglia in the brain"
- "These results uncover a bystander pathway of SARS-CoV-2 mediated CNS [central nervous system] damage through hyperactivation of human microglia"

*Ritu Mishra and Akhil C. Banerjea. Frontiers in Immunology 2021; 12:656700

63

Exosome Transfer from Cell to Cell*

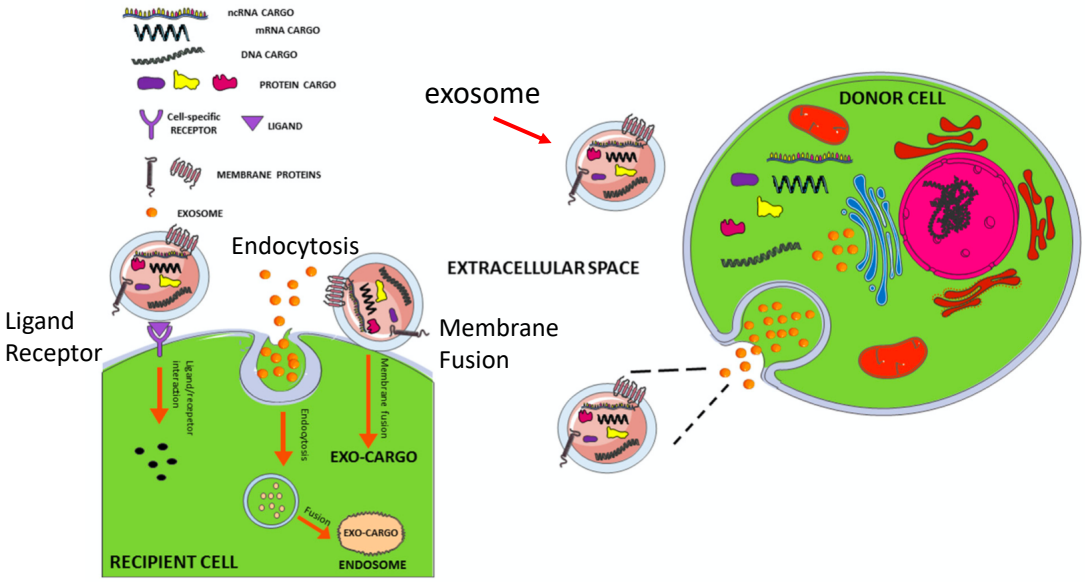
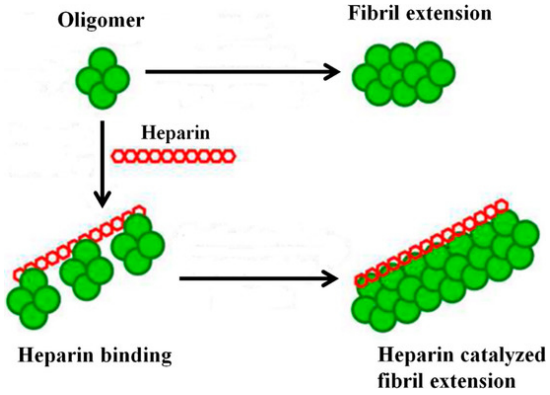


*Figure 1. Marianna D'Anca et al. Front. Aging Neurosci. 28 August 2019; 11: 232.

64

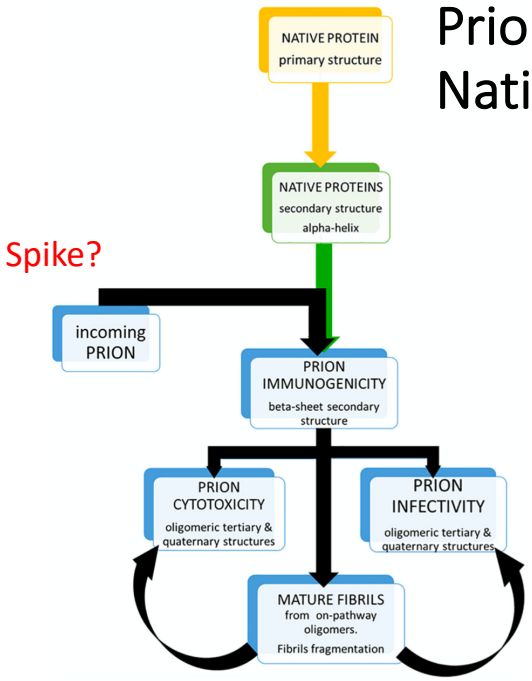
"SARS-CoV-2 spike protein interactions with amyloidogenic proteins: Potential clues to neurodegeneration"*

- 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.

65



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.

66

"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.

67

Other Consequences of Vaccine-induced MicroRNAs

68

"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

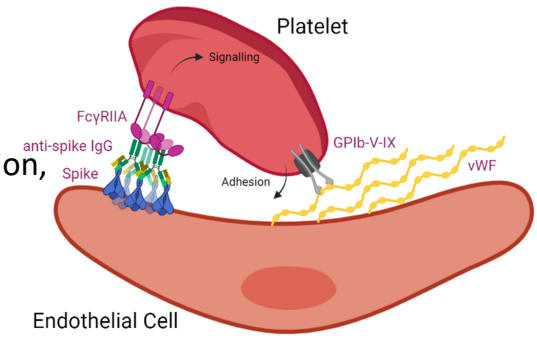
  →increased risk *systemically* to autoimmune disease and cancer

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

69

Thrombocytopenia & miR-148a*

- Platelets have *an Fcγ 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 Fcγ receptor and protects from thrombocytopenia
- miR-148a targets TULA-2 mRNA and downregulates TULA-2 protein expression



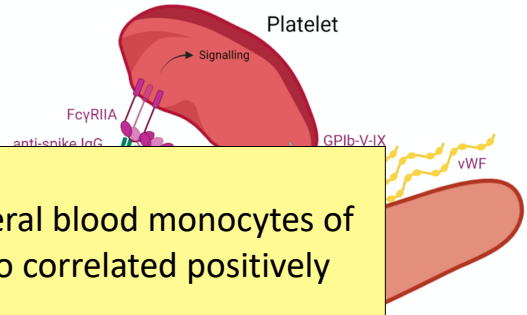
CONCLUSION: miR-148a overexpression can lead to heparin-induced thrombocytopenia (in the absence of heparin)

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

70

Thrombocytopenia & miR-148a*

- Platelets have *an Fcγ receptor* for the constant fragment of immunoglobulin G in antigen-antibody complexes
  - R
    a
- TUL
  plat
  - I
    p
- miR-
  downregulates TULA-2 protein expression



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.

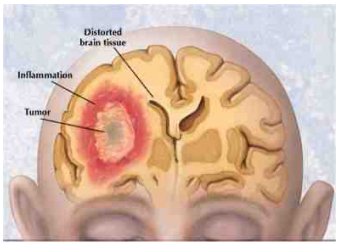
CONCLUSION: miR-148a overexpression can lead to heparin-induced thrombocytopenia (in the absence of heparin)

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

71

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.

72

"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?

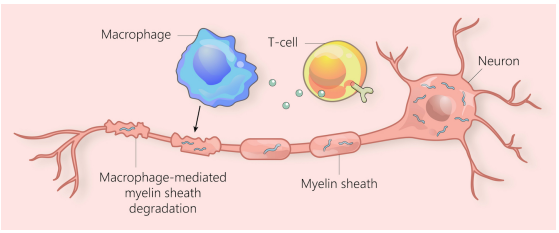
*EH Einstein et al. Cureus 2021; 13(6): e15664.

73

"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.



74

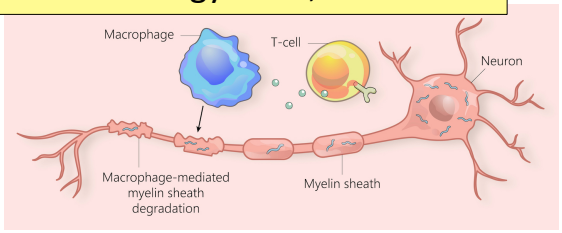
"miR-155 as an Important Regulator of Multiple Sclerosis Pathogenesis. A Review"*

- "miR-155 is among those miRNAs that are *most strongly implicated in au[illegible]*"
  - [illegible]
  - [illegible]
  - [illegible]
- mi[illegible] matter lesions in association with multiple sclerosis compared with healthy controls

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

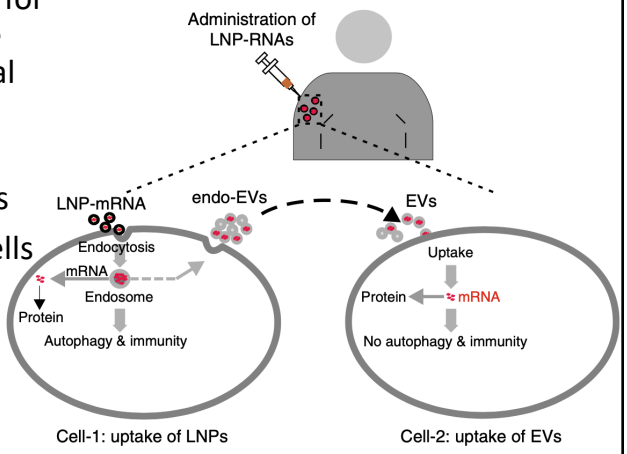
*Karina Maciak et al. International Journal of Molecular Sciences 2021; 22: 4332.



75

mRNA Transfer to Other Cells via Exosomes*

- Lipid nanoparticles containing mRNA coding for a specific protein are taken up by cells at the injection site and repackaged into endosomal vesicles that are then released into the circulation as exosomes
- The cationic lipid is included in the exosomes
- These exosomes can be taken up by other cells which then *translate the RNA into protein*
- EVs= extracellular vesicles = exosomes



*Marco Maugeri et al. Nature Communications 2019; 10: 4333.

76

Spike Antibodies and Autoimmune Disease

77

NEWS FEATURE · 19 JANUARY 2021

Rogue antibodies could be driving severe COVID-19 *

Evidence is growing that self-attacking 'autoantibodies' could be the key to understanding some of the worst cases of SARS-CoV-2 infection.

I predict that a massive vaccination campaign against COVID-19 may result in a dramatic increase in all sorts of autoimmune diseases

*Nature News Feature. https://www.nature.com/articles/d41586-021-00149-1

78

"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

79

"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

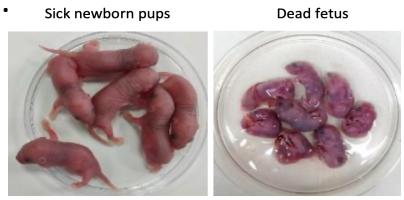
Protein/organelle	Diseases
• transglutaminase	Celiac disease
• extractable nuclear antigens	Scleroderma, lupus
• myelin basic protein	Multiple sclerosis, autism
• mitochondria	Lupus, primary billiary cirrhosis, hepatitis, myocarditis
• nuclear antigen	Sjogren's syndrome, mixed connective tissue disease, 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.

80

"Pathogenic antibodies induced by spike proteins of COVID-19 and SARS-CoV viruses"*

- REGN10987 is a neutralizing IgG antibody produced in response to the spike protein
- Researchers injected the antibody into the peritoneum of pregnant rats
- The offspring of the pregnancy were highly damaged:
  - Acute renal tubular injury
  - Myocardial hemorrhage (heart damage)
  - Inflammation in the brain
  - Many were born dead



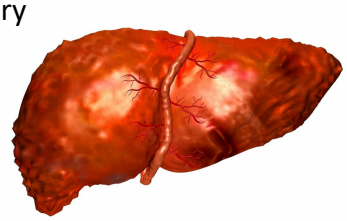
- Antibody also bound broadly to human inflammatory tissues or cancer tissues, likely increasing the severity of preexisting disease

*Huiru Wang et al. Research Square Jun 17, 2021. DOI: 10.21203/rs.3.rs-612103/v2.

81

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.

82

Recapitulation

- 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 multiple 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 heart to induce myocarditis and 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

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Summary

- The novel vaccine technology for COVID-19 prevention is untested and may cause devastating neurodegenerative, autoimmune, oncological and cardiovascular diseases in the vaccinated population
  - A primary mechanism may be through the release of massive numbers of exosomes containing spike protein and specific microRNAs
- The vaccines may be the primary driver behind the emergence of resistant variants like Delta
- Natural immunity is far more protective for a much longer time than vaccine-based immunity
- There is real potential for the vaccines to backfire through ADE
- Antibodies to the spike protein also bind to many human proteins associated with diverse autoimmune diseases through molecular mimicry

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