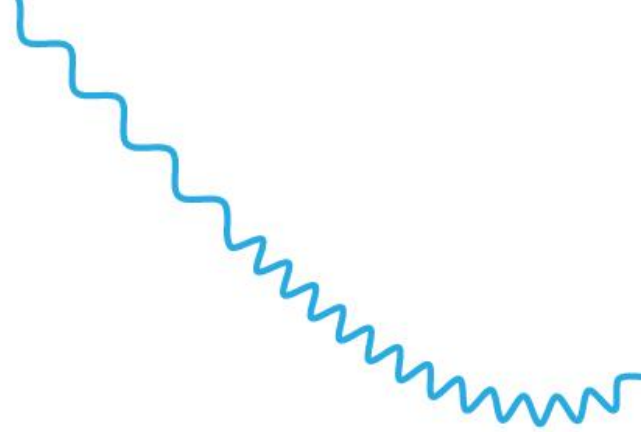




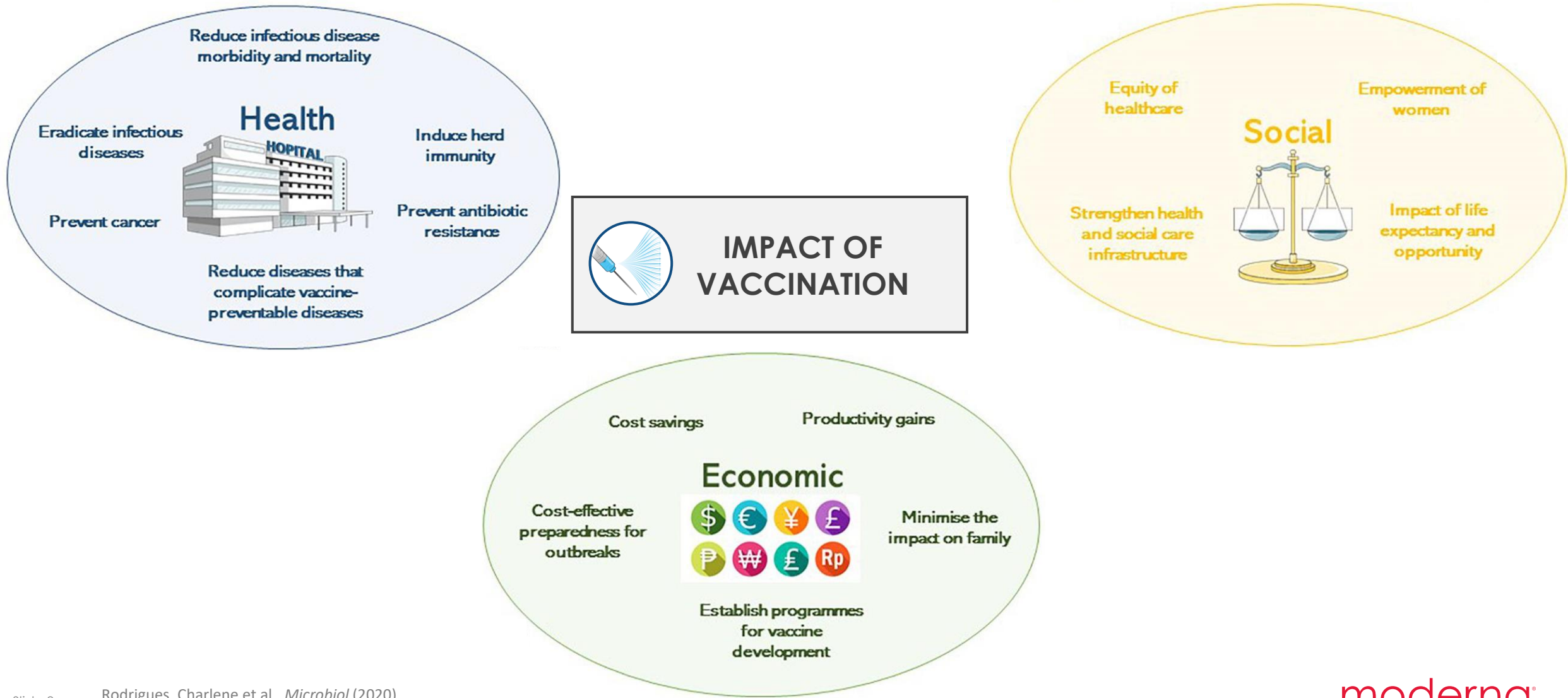
Third Annual Vaccines Day

Thursday, March 24th, 2022

Forward-looking statements and Disclaimer

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including statements regarding: the impact of vaccination on global health, economies and social welfare; the return on healthcare investment in vaccines; the potential for the Company's mRNA platform to disrupt the traditional vaccines market; the Company's ability to produce combination vaccines and bring many vaccines to market; the Company's ability to expand its portfolio and address critical unmet medical needs with its mRNA platform; the Company's plans to expand its portfolio of global public health vaccines to 15 total programs, and the timing for advancing these vaccine programs; the timing for a transition into the endemic phase of the COVID-19 pandemic; the expected seasonal impact on future sales of vaccines; the Company's development of vaccines against COVID-19, including efforts to develop variant-specific and multivalent vaccines against variant strains of SARS-CoV-2 and for booster doses; use of the Company's COVID-19 vaccine in adolescents and pediatrics, the status of testing and approvals for these populations and the potential for mRNA-1273 to provide protection from COVID-19 in vaccine recipients down to 6 months of age; the Company's plans to move forward with regulatory submissions for authorization of mRNA-1273 for primary vaccination of infants and children both in and outside of the U.S.; the safety and tolerability of mRNA-1273 in pediatric populations; the Company's plans to evaluate a booster dose for all pediatric populations and adolescents; the potency and effectiveness of mRNA-1283 and timing for commencement of a Phase 3 study; the ability of mRNA-1283 to facilitate distribution and administration by healthcare providers; timing for expected start of a Phase 3 study of mRNA-1010 and the potential of mRNA-1010 as an annual booster; the potential for lower doses of mRNA-1283 to show strong immunogenicity; the potential for superiority of mRNA-1010 to standard dose vaccine for influenza A strains and non-inferiority to standard dose vaccine for influenza B strains; expected enrollment in the Company's Phase 3 portion of its study of mRNA-1345; expected enrollment in the Company's Phase 3 study of mRNA-1647; the Company's plans to evaluate mRNA-1647 against long-term impacts in Phase III trials; timing of mRNA-1073 entering the clinic; the ability of the Company's mRNA platform to develop vaccines against latent viruses and to provide long-term health benefits; the potential ability to leverage the Company's platform to address "Disease X"; the Company's *mRNA Access* initiative to allow researchers access to Moderna's mRNA platform; the Company's commitment not to enforce its COVID-19 patents in the Gavi COVAX AMC 92 low- and middle-income countries; the potential for mRNA vaccines to elicit autologous neutralizing antibodies in humans, and to be safe and well-tolerated by HIV-uninfected individuals; expected enrollment in the Phase 1 trial of mRNA-1574; the buildout of the Company's manufacturing capacity and commercial footprint; the potential total addressable market for respiratory vaccines, including the expected addressable population; the potential volume of doses in an endemic COVID-19 market; the commercial outlook for Spikevax® in 2022, including anticipated vaccine deliveries under advance purchase agreements and options in 2022 and the associated dollar amounts to be received, which should not be construed as expected 2022 revenue; orders for delivery of Spikevax in 2022 and 2023 and the Company's discussions for additional 2022 and 2023 orders with countries from around the world, including the U.S.; the size of addressable markets for vaccines against latent viruses, and the sales potential of vaccines against latent viruses; the Company's agreements and ongoing discussions with countries regarding service/subscription contracts; and the Company's plans to construct an mRNA manufacturing facility in Kenya. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "could," "expects," "intends," "plans," "aims," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. The forward-looking statements in this presentation are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond Moderna's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties, and other factors include, among others, those risks and uncertainties described under the heading "Risk Factors" in Moderna's most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) and in subsequent filings made by Moderna with the SEC, which are available on the SEC's website at www.sec.gov. Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this presentation in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna's current expectations and speak only as of the date hereof.

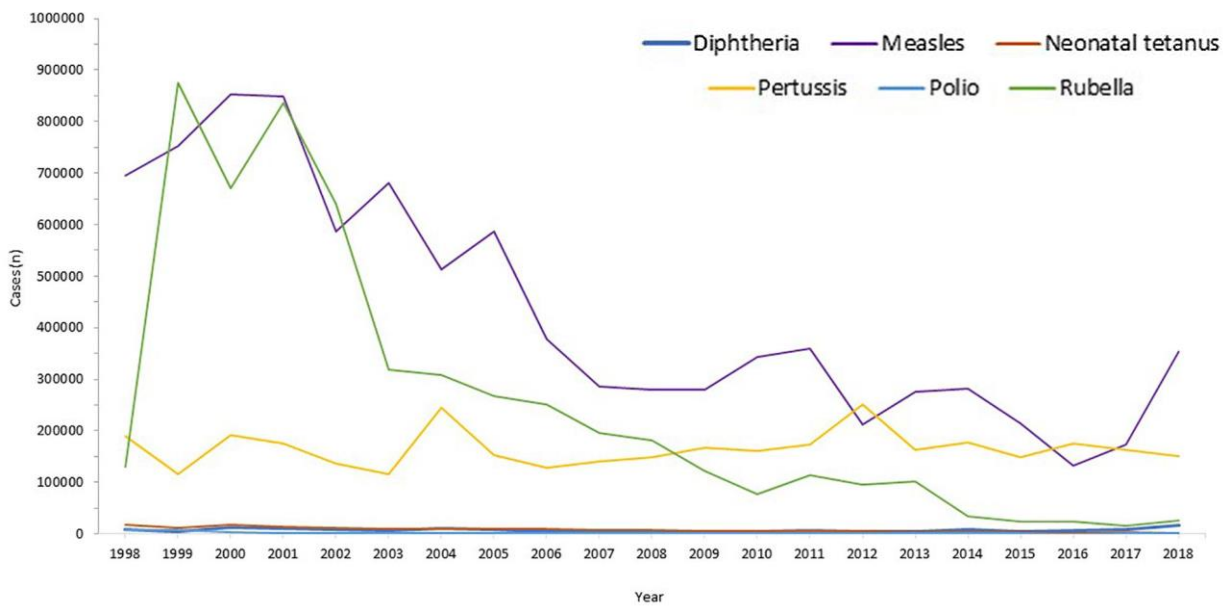
The impact of safe and effective vaccines on global health, economies and social welfare is undeniable



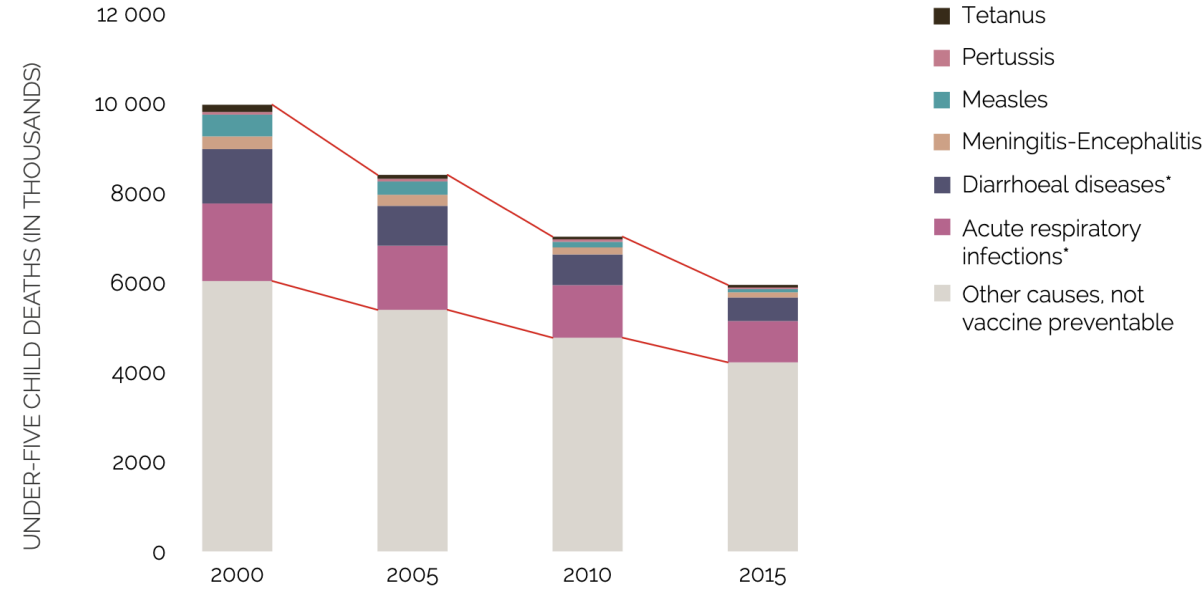
Safe and efficacious vaccines have contributed substantially to global health

Reduction in infectious diseases globally

Across all world regions (WHO), last 20 years



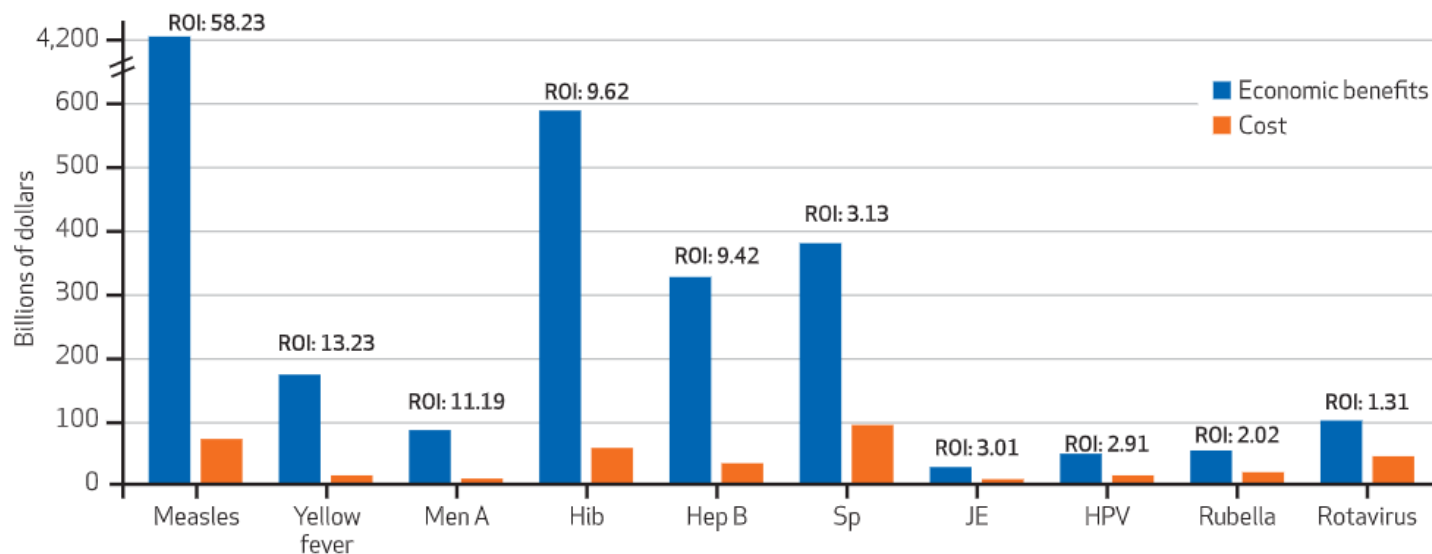
Vaccines have been key contributors to the global reduction in under-five mortality since 2000



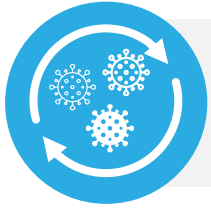
Vaccines can provide a significant return on each healthcare dollar invested

- Every dollar invested in vaccination between 2011-2020 **resulted in a net return of 44 times the cost** in 94 low-and middle-income countries across ten antigens¹
- CDC estimates of vaccination impact on children born between 1994-2013 (US) in the Vaccines for Children (VFC) program²
 - **\$1.3 trillion saved** in total societal cost
 - **322 million illnesses prevented**
 - **732,000 deaths prevented**

Estimated Costs, Economic Benefits Based On Costs Of Illnesses, And Return On Investment For Immunization, By Antigen, In 94 Low- And Middle-Income Countries, 2011–20



We can do better and we should expect more from vaccines



Over **225** viruses known to infect humans across the world¹

Since 1980, more than 80 new viruses have been discovered², helped by major developments in the technology of virus discovery (PCR and high throughput sequencing)

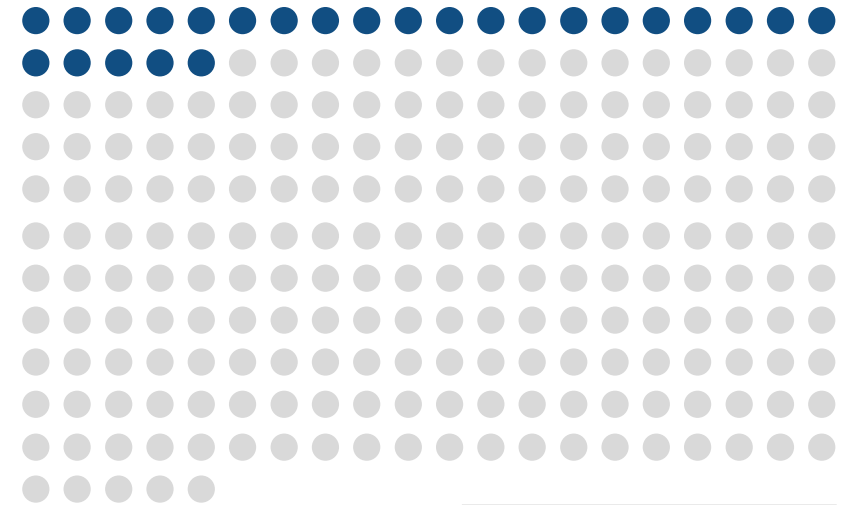


Only **~25** viruses have available vaccines³

Only 4% of the viruses discovered since 1980 have available vaccines; some viruses with available vaccines also have unmet needs (e.g. influenza)

There are many viruses without effective vaccines

Illustrative



● Virus with available vaccine
● Virus with no vaccine

(1) Woolhouse, Mark et al., *Philos Trans R Soc Lond B Biol Sci* (2012), <https://doi.org/10.1098/rstb.2011.0354>

(2) Sources found at [Moderna Vaccines Day 2021](#)

(3) WHO, <https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases>

We believe Moderna's mRNA vaccine platform will disrupt the traditional vaccines market



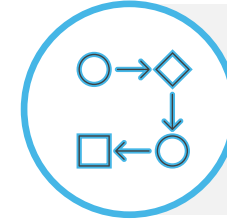
mRNA technology advantages

- ✓ mRNA technology can move faster in updating vaccines
- ✓ Ability to do combination vaccines
- ✓ Ability to develop vaccines against difficult viral targets



Moderna's mRNA platform: Accelerated R&D

- ✓ mRNA vaccine antigens with high biological fidelity
- ✓ Higher probability of success
- ✓ Ability to go from sequence to approved product in record time

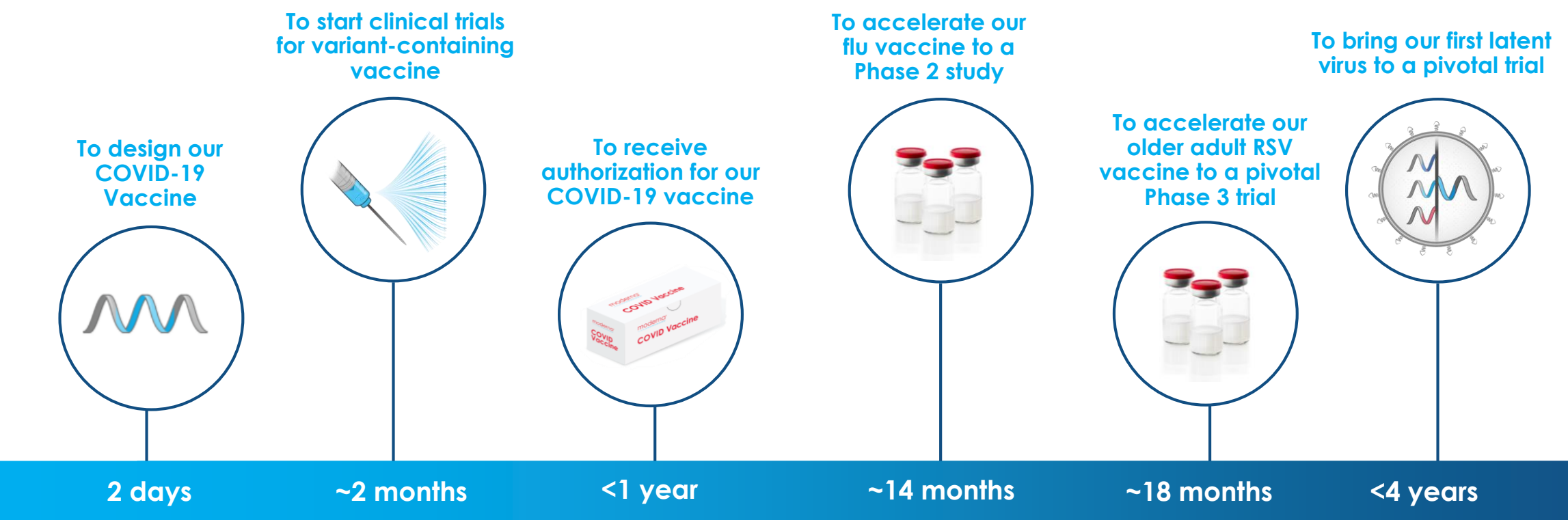


Capital efficiency

- ✓ Greater manufacturing flexibility
- ✓ No need for dedicated plants (mRNA vaccines and mRNA therapeutics using the same process)

Our vaccine development speed has been demonstrated in recent years

Recent examples include:



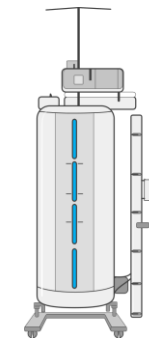
Our platform technology allows for productive manufacturing at scale

- With first commercial product, ability to produce >800M doses in first year (with fewer than 1,500 manufacturing employees)
- mRNA vaccines and mRNA therapeutics use the same process, same equipment, same people and 95% of the same raw materials

Moderna

**Clinical
Manufacture**

**Commercial
Manufacture**



moderna

We expect to bring many more vaccines to market

Moderna's mRNA platform enables us to rapidly develop many vaccines, potentially allowing us to address significant unmet medical needs

In our prophylactic vaccine modality, we have:

31 development programs

19 in the clinic

4 in Phase 3

1 approved product

Our mRNA vaccine technology advantages facilitates development of:

9 viruses with unmet needs (no vaccines available)

8 combination vaccines

7 vaccines against latent viruses

Today we are sharing clinical data updates across our current vaccines pipeline and reviewing two new development programs

Sharing data across multiple development programs

Program (mRNA #)	Phase	Age
COVID-19 Vaccine (mRNA-1273)	3	Pediatrics (<6 years)
Next-generation COVID-19 vaccine (mRNA-1283)	1	Adults
Flu vaccine (mRNA-1010)	2	Adults
RSV vaccine (mRNA-1345)	1	Adults
hMPV/PIV3 vaccine (mRNA-1365)	1	Adults
CMV vaccine (mRNA-1647)	2	Adults

Announced new development programs

COVID + Flu +
RSV combination
respiratory
vaccine

mRNA-1230

Endemic human
coronavirus
vaccine

mRNA-1287

Today's speakers from Moderna



Stephen Hoge, M.D.
President



Jacqueline Miller, M.D.
Senior Vice President,
Therapeutic Area Head,
Infectious Diseases, Moderna



Raffael Nachbagauer, M.D., Ph.D.
Senior Director, Infectious Disease
Development



Sumana Chandramouli, Ph.D.
Director, Infectious
Disease Research

Today's Agenda

Introduction

Stéphane Bancel, *CEO*

Development Strategy

Stephen Hoge, *M.D., President*

Vaccines Against Respiratory Viruses

- COVID
- Flu
- RSV
- Combination strategy

Jacqueline Miller, *M.D., SVP, Therapeutic Area Head, Infectious Diseases*

Shane Crotty, *Ph.D., La Jolla Institute for Immunology*

Raffael Nachbagauer, *M.D., Ph.D., Senior Director, Infectious Disease Development*

Ali Ellebedy, *Ph.D., Washington University School of Medicine*

Coffee Break (5 minutes)

Vaccines Against Latent Viruses

- CMV
- EBV
- Other latent viruses (HIV, HSV, VZV)

Jacqueline Miller, *M.D., SVP, Therapeutic Area Head, Infectious Diseases*

Anthony Cunningham, *AO,FAHMS, Centre for Virus Research; The University of Sydney*

Sumana Chandramouli, *Ph.D., Director, Infectious Diseases*

Alberto Ascherio, *M.D., DrPH, Harvard School of Public Health, Harvard Medical School*

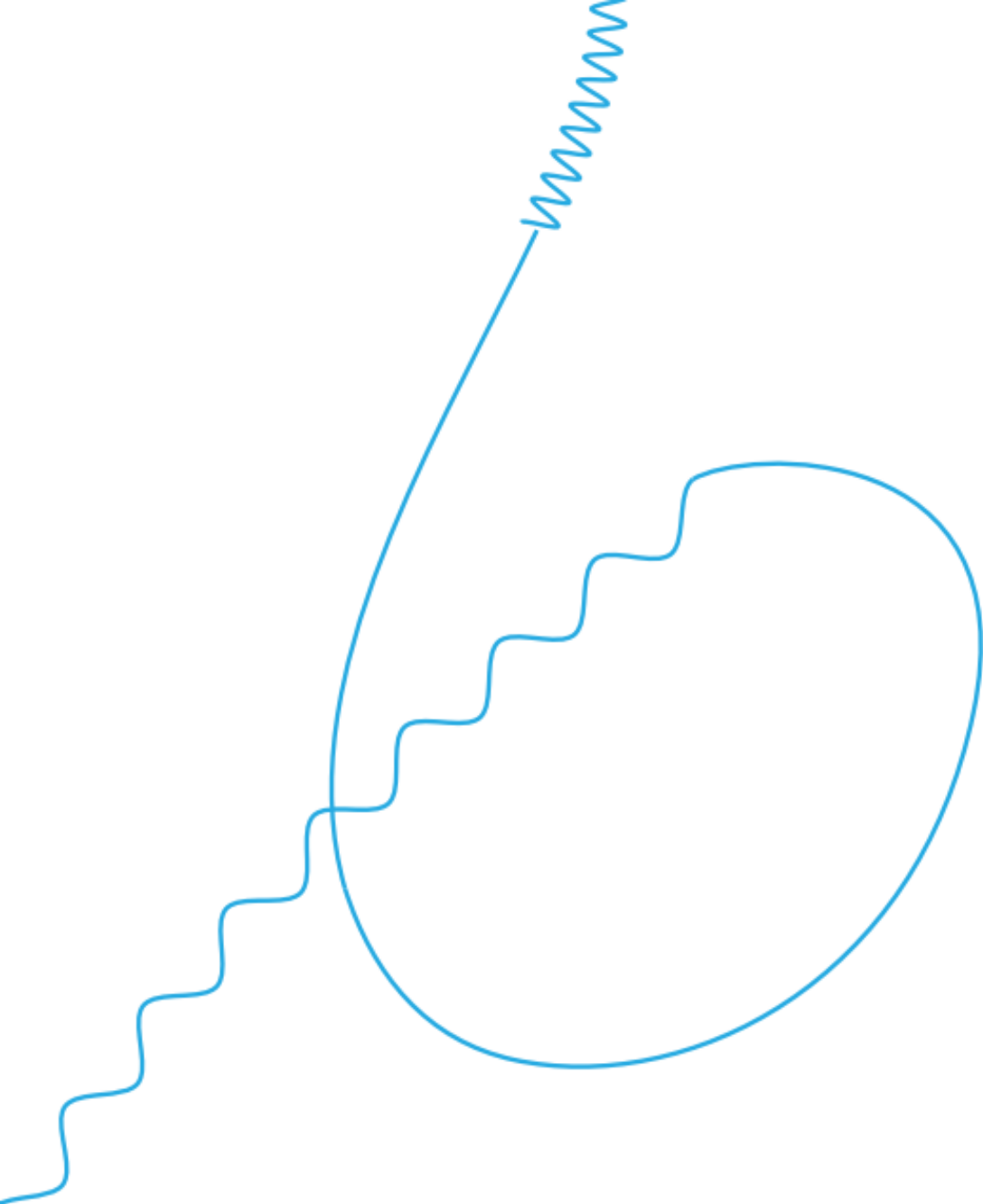
Global Health Vaccines & mRNA Access

Stephen Hoge, *M.D., President*

Conclusion – Expect More From Moderna

Stéphane Bancel, *CEO*

Q&A



Vaccine Development Strategy

Stephen Hoge, M.D., President

What have we learned in the past year about our mRNA platform?

Highly effective

mRNA vaccines have demonstrated the highest efficacy in published Phase 3 clinical trials and highest effectiveness seen in observational trials

Significant immunity

Spikevax[®]/mRNA-1273 **induces significant antibody-mediated immunity** (neutralizing antibodies generated)

Spikevax[®]/mRNA-1273 **induces significant cellular responses** (T-cell responses)

Unique agility

Updated and rapidly advanced variant-containing vaccine candidates into the clinic on multiple occasions, including:

- **3** variant-specific vaccines (Beta, Delta, Omicron)
- **3** bivalent vaccines (Beta/wild-type, Beta/Delta, Omicron/wild-type)
- **1** next-generation vaccine in Phase 2 (mRNA-1283)

Munro, Alasdair et al., *The Lancet* (2021), [https://doi.org/10.1016/S0140-6736\(21\)02717-3](https://doi.org/10.1016/S0140-6736(21)02717-3)

UK Health Security Agency, Technical Briefing 34.

Sharif, Nadim et al., *Front Immunol.* (2021), <https://doi.org/10.3389/fimmu.2021.714170>; Heinz, Franz et al., *npj Vaccines* (2021), <https://doi.org/10.1038/s41541-021-00369-6>; Heath, Paul et al., *N Engl J Med* (2021), <https://doi.org/10.1056/NEJMoa2107659>

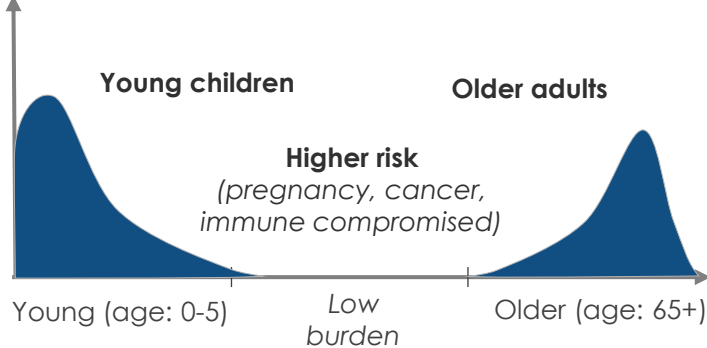
Significant unmet need in vaccines

1

Respiratory viruses

- Highest burden in the young, old and immunocompromised
- Respiratory infections are a top cause of death globally

Burden of Respiratory Viruses (illustrative)

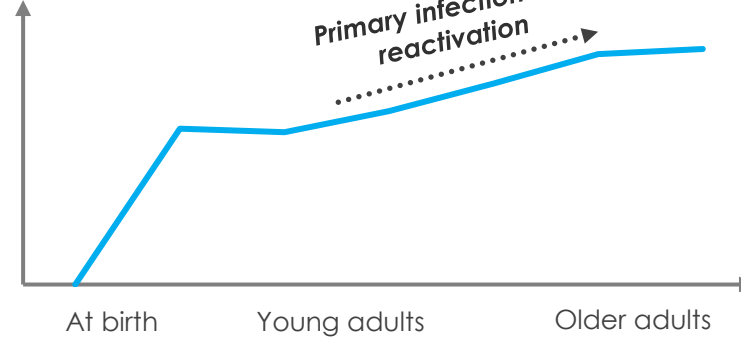


2

Latent viruses

- Immediate impact of infection (e.g., birth defects, mono)
- Long-term sequelae from latent infections (cancer, autoimmune)

Percent of Population Infected (illustrative)



3

Global health threats

- Persistent global health threats (e.g., Malaria, Zika) among WHO/CEPI priority pathogens
- Pandemic preparedness

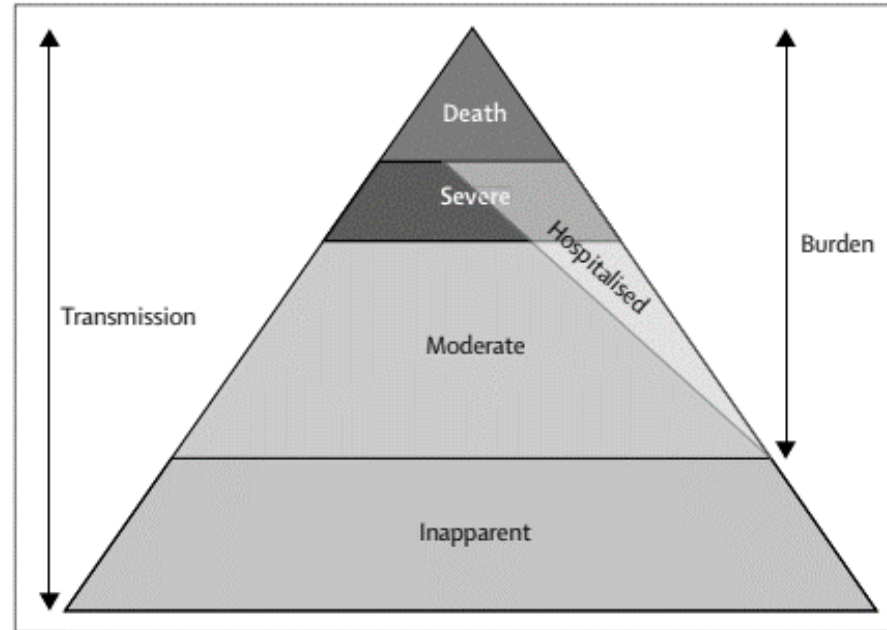


Disease burden from acute viral respiratory infections is not limited to hospitalization and death

1

Respiratory viruses

- Highest burden in the young, old and immunocompromised
- Respiratory infections are a top cause of death globally



Directly measurable

- Mortality
- Hospitalizations and outcomes (e.g., ICU, length of stay, mechanical ventilation)
- Lower respiratory tract infections (LRTIs) & upper respiratory tract infections (URTIs)

More difficult to quantify

- Disability
- Loss of productivity
- Quality of life

Prevention through vaccination has large indirect societal benefits beyond prevention of severe disease

Respiratory vaccines have a large impact on global health

1

Respiratory viruses

- Highest burden in the young, old and immunocompromised
- Respiratory infections are a top cause of death globally

COVID in the pandemic setting has caused >6M deaths globally

The **global population of older adults is projected to double** between now and 2050

Estimates of the global burden attributed to LRTIs among older adults*

	2000	2016	2050**
Deaths	794,349	1.08M	~2.2M
Mortality rate per 100K	278.1	267.4	~267
DALYs	9.8M	13.2M	~26M
Population >70	269M	404M	~810M

DALY: Disability-adjusted life year; LRTI: lower respiratory tract infection
* Defined as diseases of the lower airways, primarily pneumonia and bronchiolitis; includes viral and bacterial LRTIs
** Projected estimates from internal analyses

Latent viruses have short-term and long-term health impact

2

Latent viruses

- Immediate impact of infection (e.g., birth defects, mono)
- Long-term sequelae from latent infections (cancer, AI)

Virus (program)	Associated disease conditions
CMV (mRNA-1647)	Leading infectious cause of birth defects (12-20K congenital CMV cases annually in the U.S. alone) ¹ Major driver of immune dysfunction with aging
EBV (mRNA-1189/95)	>160K deaths attributed to EBV-related malignancies (2017) ² Major driver of Multiple Sclerosis risk (>30x increase)
HIV (mRNA-1644/1574)	Cause of AIDS, resulting in approximately 700,000 deaths worldwide annually (2020) ³ Developing vaccines with IAVI, NIAID, and Gates Foundation
HSV (mRNA-1608)	HSV-2 establishes life-long latent infections within sensory neurons from which it can reactivate, leading to genital herpes Globally, ~5% of the population in the 18-49 range is HSV-2 seropositive ⁴
VZV (mRNA-1468)	Declining immunity in older adults leads to reactivation of the virus from latently infected neurons, causing painful and itchy lesions Herpes Zoster occurs in 1 out of 3 adults in the U.S. in their lifetime ⁵

(1) Lanzieri, Tatiana, CDC, <https://www.hhs.gov/sites/default/files/2018-9-13-nvac-exploringthepipeline-cmvvaccines.pdf>
(2) Khan, Gulfaraz et al., *BMJ Open* (2020), <https://doi.org/10.1136/bmjopen-2020-037505>
(3) Global HIV/AIDS epidemic, <https://www.hiv.gov/hiv-basics/overview/data-and-trends/global-statistics>
(4) Looker et al, *BMJ Global Health* (2020), <https://doi.org/10.1136/bmjgh-2019-001875>
(5) CDC, Shingles, <https://www.cdc.gov/shingles/about/index.html>

Global public health needs

3

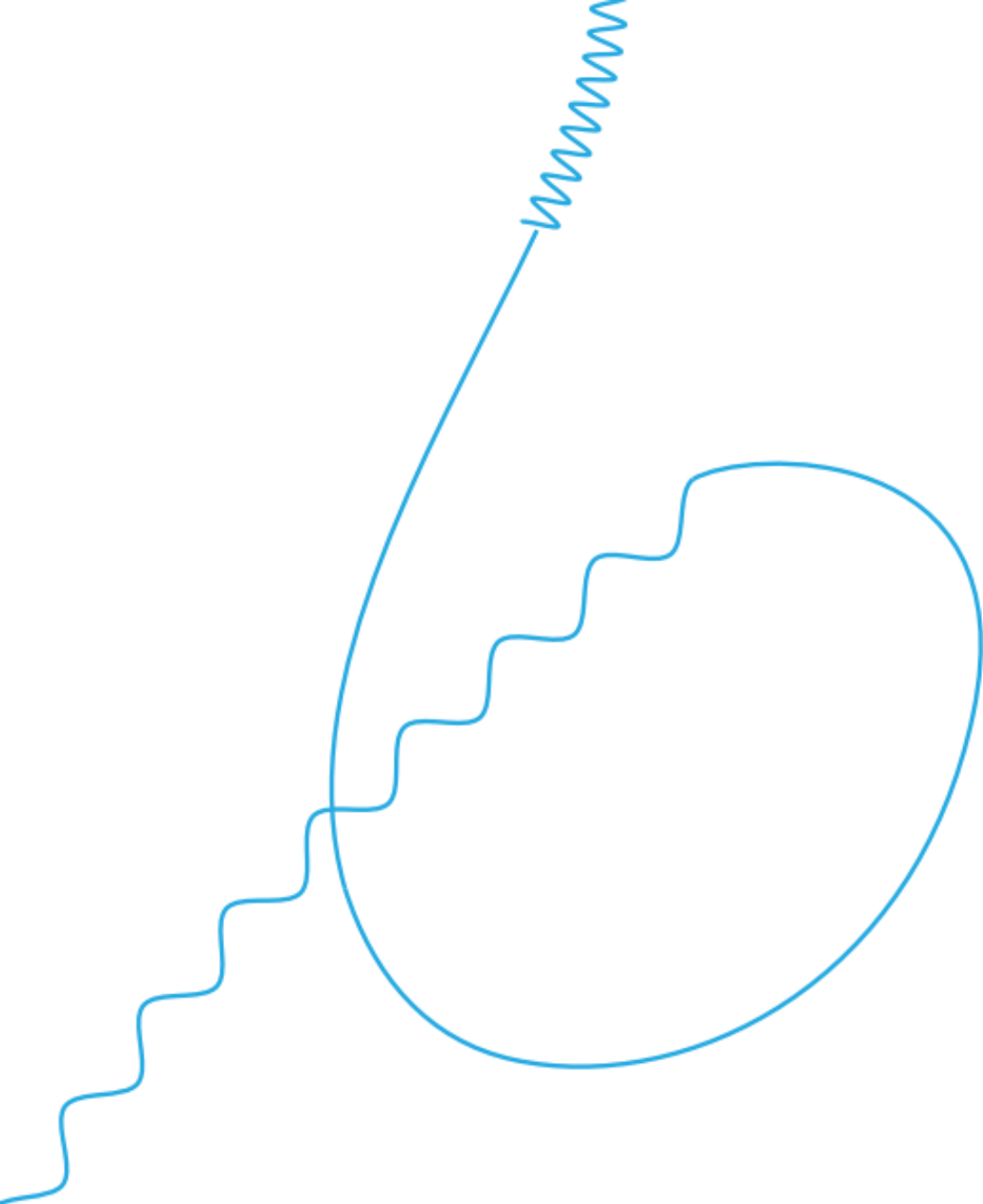
Global health threats

- Persistent global health threats (e.g., Malaria, Zika) among WHO/CEPI priority pathogens
- Pandemic preparedness

Two development programs:

- **Zika (mRNA-1893)** – Major arthropod (mosquito) driven epidemic in 2016; Phase 2 ongoing
- **Nipah (mRNA-1215)** – Outbreak potential with 40 to 75% risk of death; expected to enter Phase 1 this year¹

Commitment to **advance vaccines targeting 15 priority pathogens into clinical studies by 2025**, identified by WHO and CEPI

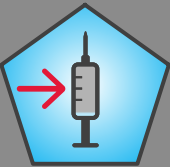


Moderna Vaccines Introduction

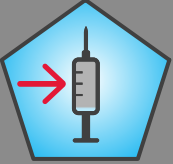
Jacqueline Miller, M.D.

*Senior Vice President, Therapeutic Area
Head, Infectious Diseases, Moderna*

Moderna's Respiratory Vaccines

Modality	Program	ID #	Preclinical development	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
Adults  Prophylactic vaccines	COVID-19 vaccine	mRNA-1273/Spikevax®						Worldwide
		mRNA-1273.351	Beta variant					Worldwide
		mRNA-1273.617	Delta variant					Worldwide
		mRNA-1273.211	Beta variant + wild-type					Worldwide
		mRNA-1273.213	Beta + Delta variant					Worldwide
		mRNA-1273.529	Omicron variant					Worldwide
		mRNA-1273.214	Omicron variant + wild-type					Worldwide
		mRNA-1283	Next generation (2-5 °C)					Worldwide
	Flu vaccine	mRNA-1010				Phase 3 prep		Worldwide
		mRNA-1011						Worldwide
		mRNA-1012						Worldwide
		mRNA-1020						Worldwide
		mRNA-1030						Worldwide
	Older adults RSV vaccine	mRNA-1345						Worldwide
	COVID + Flu vaccine	mRNA-1073						Worldwide
	Influenza + SARS-CoV-2 + RSV vaccine	mRNA-1230						Worldwide
	Pan HCoV vaccine	mRNA-1287						Worldwide
Adolescents & Pediatrics	COVID-19 vaccine (adolescents)	mRNA-1273	TeenCOVE					Worldwide
	COVID-19 vaccine (pediatrics)	mRNA-1273	KidCOVE					Worldwide
	Pediatric RSV vaccine	mRNA-1345						Worldwide
	Pediatric hMPV + PIV3 vaccine	mRNA-1653						Worldwide
	Pediatric RSV + hMPV vaccine	mRNA-1365						Worldwide

Moderna's Latent & Global Health Vaccines

Modality	Program	ID #	Preclinical development	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
Latent vaccines  Prophylactic vaccines	CMV vaccine	mRNA-1647						Worldwide
	EBV vaccine (to prevent infectious mononucleosis)	mRNA-1189						Worldwide
	EBV vaccine (to prevent EBV sequelae)	mRNA-1195						Worldwide
	HSV vaccine	mRNA-1608						Worldwide
	VZV vaccine	mRNA-1468						Worldwide
	HIV vaccines	mRNA-1644						Worldwide <i>IAVI/others funded</i>
		mRNA-1574						Worldwide <i>BMGF/NIAD/others funded</i>
Global health vaccines	Zika vaccine	mRNA-1893						Worldwide <i>BARDA funded</i>
	Nipah vaccine	mRNA-1215						Worldwide <i>NIH funded</i>

Dr. Shane Crotty, La Jolla Institute for Immunology



Shane Crotty, Ph.D.
La Jolla Institute for Immunology

Dr. Crotty's lab studies the fundamental immunology underlying vaccine functions. Initially trained in molecular virology and then viral immunology, Crotty's laboratory focuses on both the basic immunology of T follicular helper (Tfh) CD4 T cells (Science 2009, Immunity 2019), viral immunology including SARS-CoV-2 (Cell 2020), B cell immunodominance (Science 2016, Immunity 2018, Science 2019), and the central roles of germinal centers and memory in vaccine immunology (Cell 2019, Nature Medicine 2020). Dr. Crotty was a Pew Scholar and a 2016-2019 Highly Cited Researcher. His recent COVID-19 immunology work has become the highest attention getting Cell paper ever (Cell 2020; Nature Reviews Immunology 2020).

Understanding adaptive immunity and immune memory to SARS-CoV-2 and COVID-19 vaccines

Shane Crotty, Ph.D.

Professor, Center for Infectious Disease and Vaccine Research

**La Jolla
Institute**
FOR IMMUNOLOGY

UCSD School of Medicine
Dept. of Medicine



Disclosures

Dr. Crotty was not financially compensated for this presentation.

Dr. Crotty's consulting disclosures:

Nutcracker Therapeutics, University of California, California State Universities, United Airlines, and Adagio.

Do people develop immunity to COVID-19?

Article

Shane Crotty & Alex Sette

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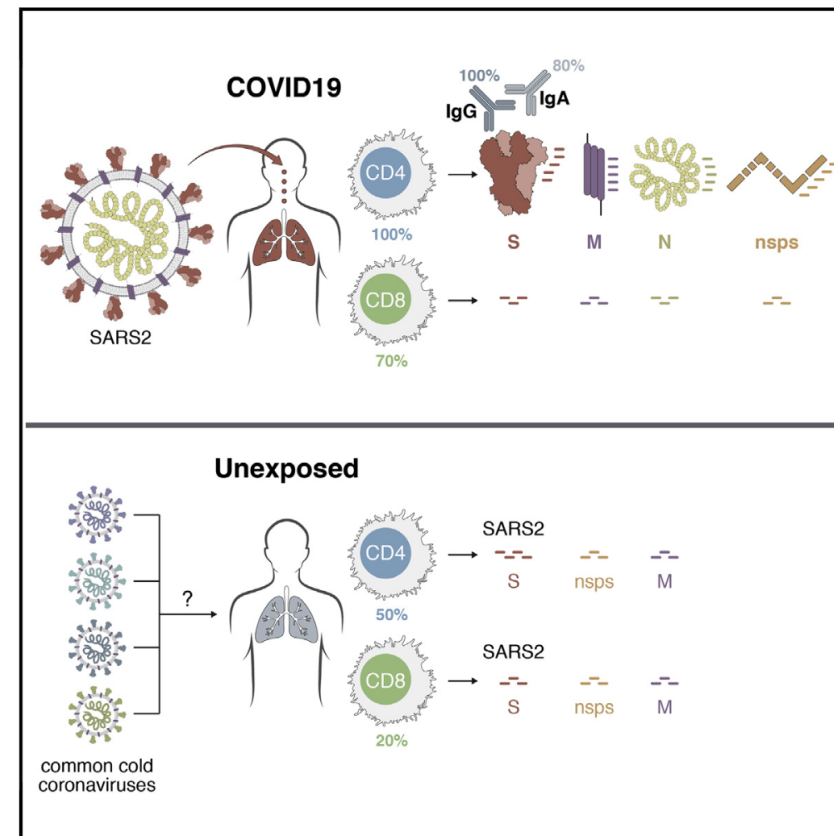


Alessandro Sette

Cell

Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals

Graphical Abstract



Authors

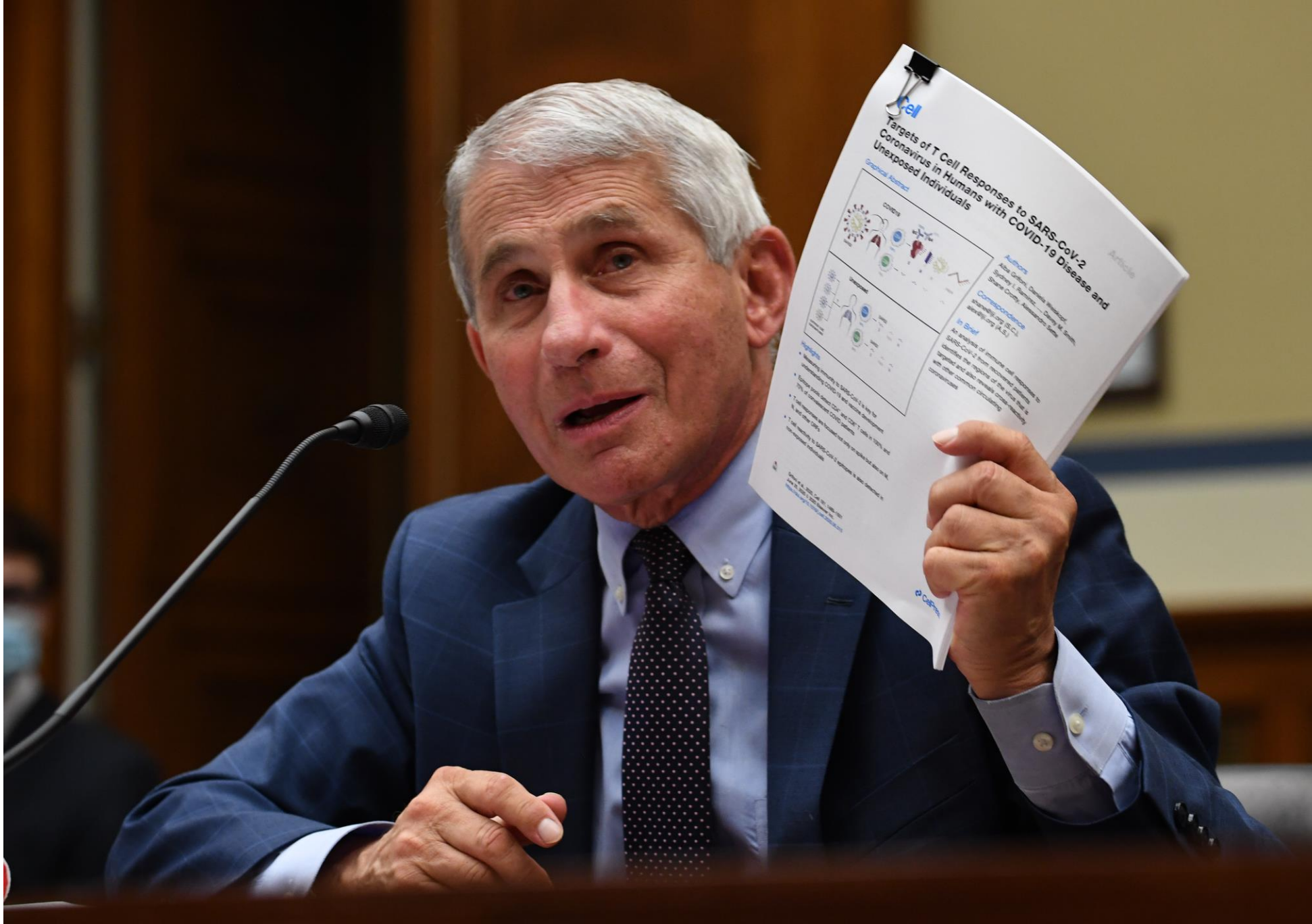
Alba Grifoni, Daniela Weiskopf,
Sydney I. Ramirez, ..., Davey M. Smith,
Shane Crotty, Alessandro Sette

Correspondence

shane@lji.org (S.C.),
alex@lji.org (A.S.)

In Brief

An analysis of immune cell responses to SARS-CoV-2 from recovered patients identifies the regions of the virus that is targeted and also reveals cross-reactivity with other common circulating coronaviruses



Tony Fauci. Congress, July 31, 2020

T cell and antibody responses in 'average' cases of COVID-19

- ❖ SARS-CoV-2 causes acute infections that resolve/cure in most humans
- ❖ What kind of immunity is important against COVID-19?



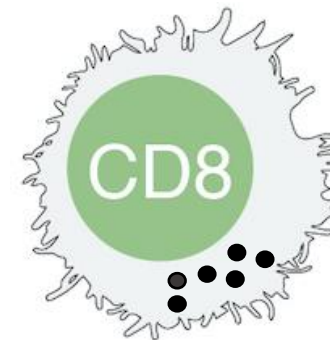
Antibodies
(from B cells)

- ❖ Important in almost all currently licensed human vaccines



CD4 T cells
Helpers

- ❖ Critical for antibody responses
- ❖ Protect independent of antibodies in SARS mouse model

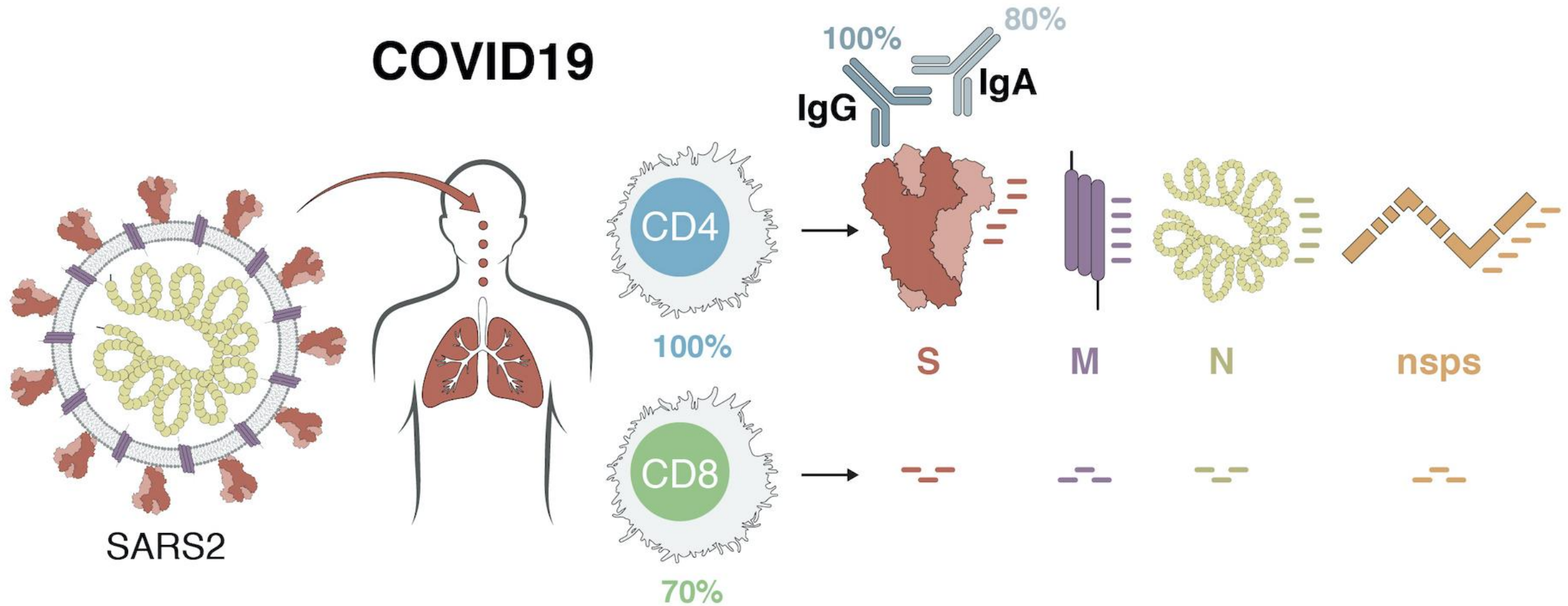


CD8 T cells
Killers

- ❖ Important in many viral infections

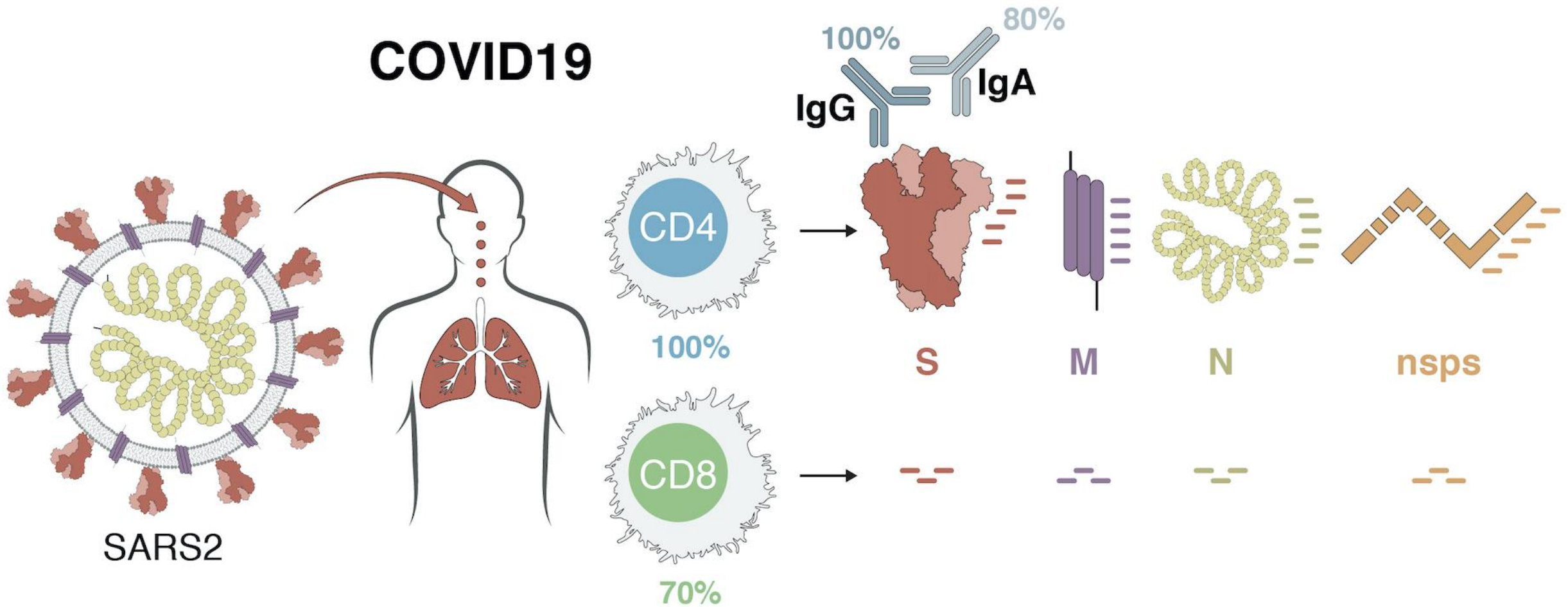
Study of immune responses of 'average' COVID-19 cases

To establish a benchmark of COVID-19 T cell and antibody responses

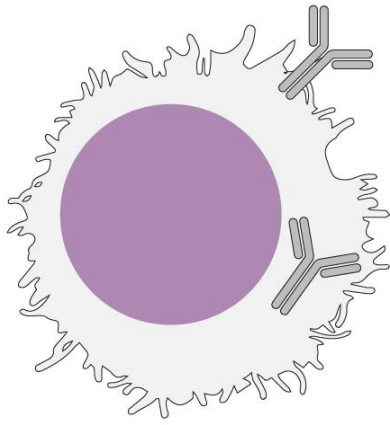


Good news!

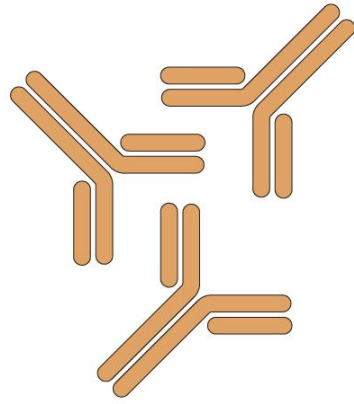
Antiviral immunity that largely matches expectations



How long does immunological memory to SARS-CoV-2 last?



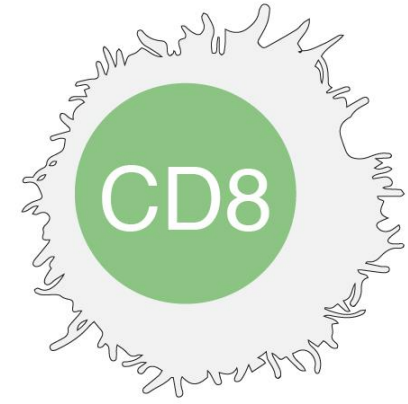
Memory
B cell



Antibodies



CD4⁺ T cells

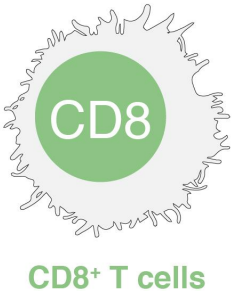
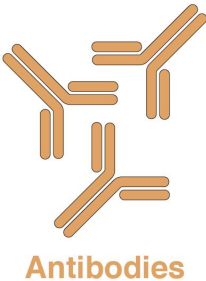
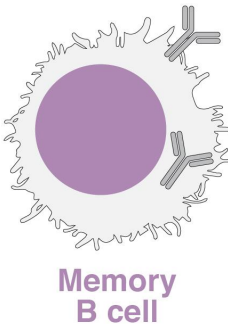


CD8⁺ T cells

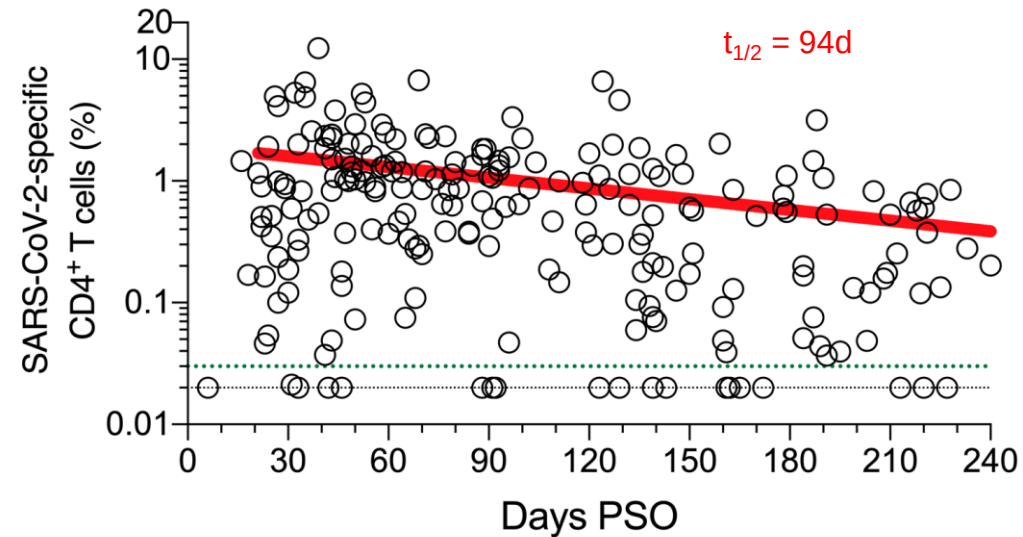
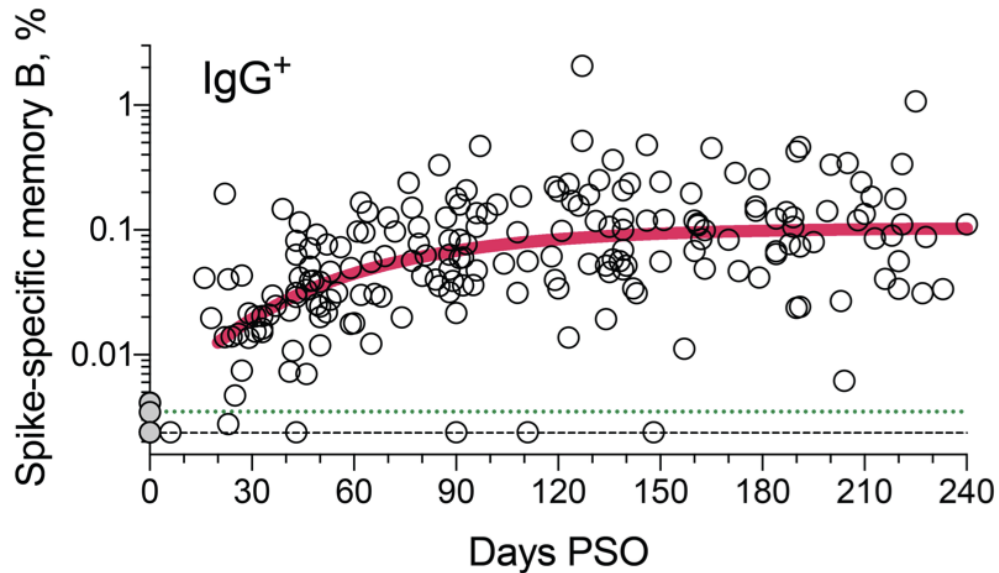
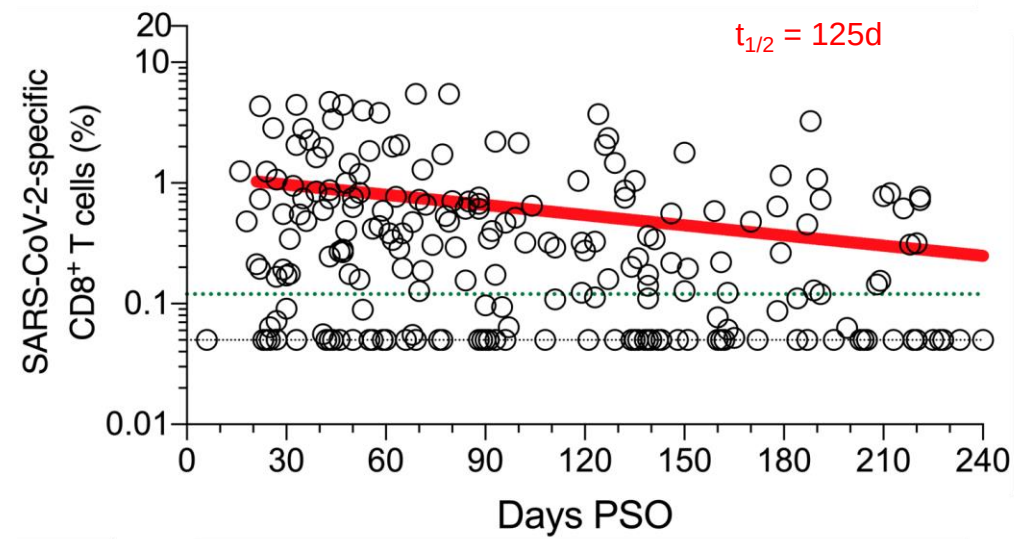
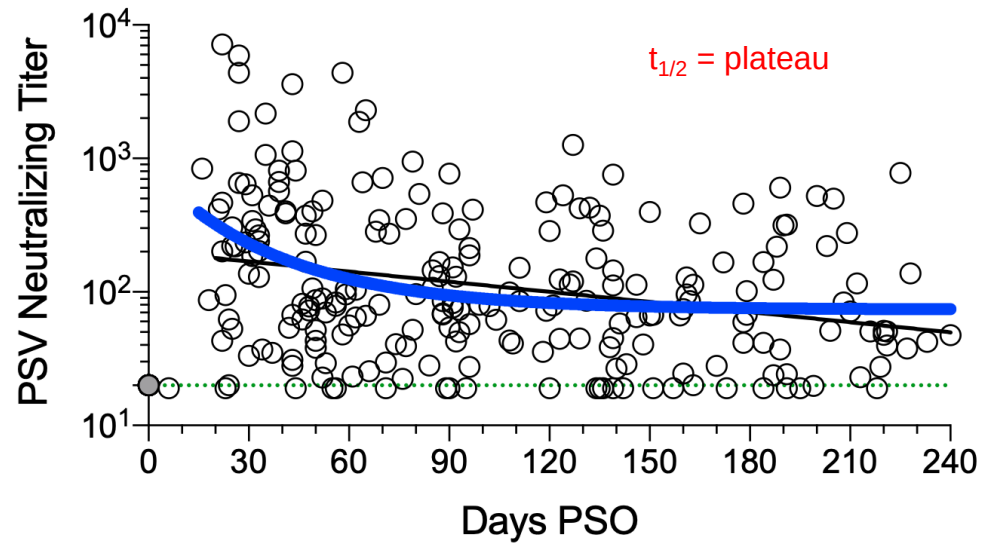
How long does immunological memory to SARS-CoV-2 last?

	COVID-19 (n = 188)
Age (years)	19 - 81 [Median = 40]
Gender	
• Male (%)	43% [80/188]
• Female (%)	57% [108/188]
SARS-CoV-2 PCR positivity	
• Positive	77% [145/188]
• Not performed	20% [37/188]
• Negative	1% [2/188]
• Unknown	2% [4/188]
Peak disease severity	
• Asymptomatic	2% [4/188; 2F, 2M]
• Mild	90% [170/188; 100F 70M]
• Moderate	3% [6/188; 3F, 3M]
• Severe	4% [7/188; 3F, 4M]
Days post symptom onset at collection (n = 254)	6– 240 [Median = 88] 8 months

SARS-CoV-2 specific



How long does immunological memory to SARS-CoV-2 last?



How long does immunological memory to SARS-CoV-2 last?

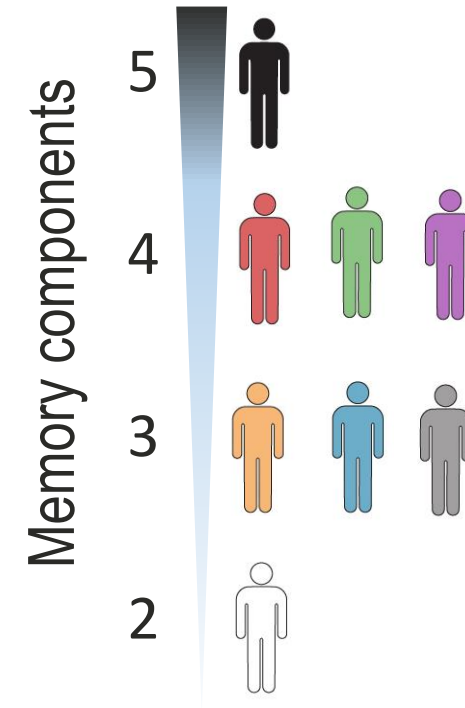
“**G**”, RBD IgG

“**B**”, RBD-specific memory B cells

“**4**”, SARS-CoV-2 specific CD4+ T cells

“**8**”, SARS-CoV-2 specific CD8+ T cells

“**A**”, Spike IgA.



How long does immunological memory to SARS-CoV-2 last?



❖ ~6 months after COVID-19, ~95% of individuals still positive for ≥ 3 of 5 immune memory responses

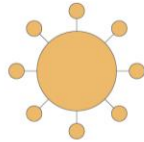
Low dose Moderna COVID-19 vaccine

Low-dose mRNA vaccine (25 μ g)

MEMORY



v. NATURAL
IMMUNITY



FULL DOSE
(100 μ g)



AGE



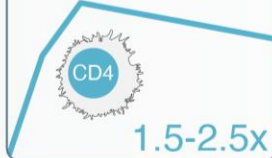
PRE-EXISTING
T CELLS



Antibodies



CD4 T cells



CD8 T cells



D1 → D209

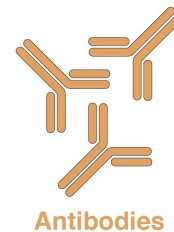
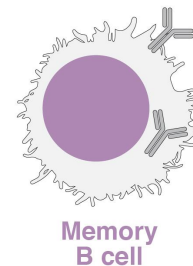


Asst. Prof.
Daniela Weiskopf

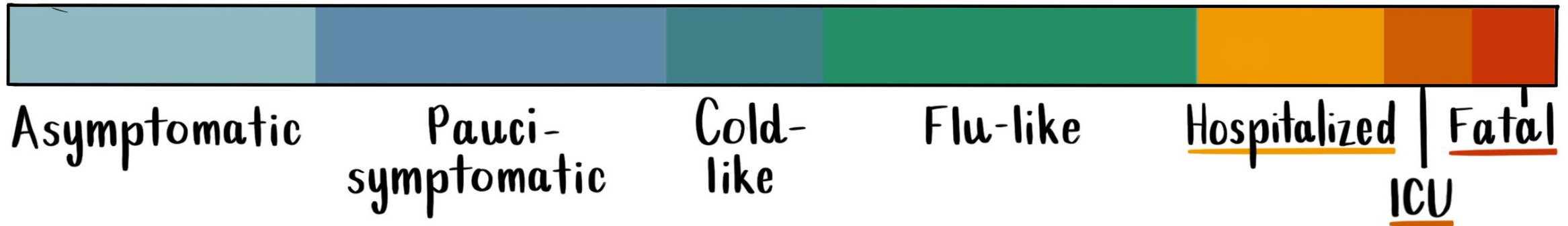
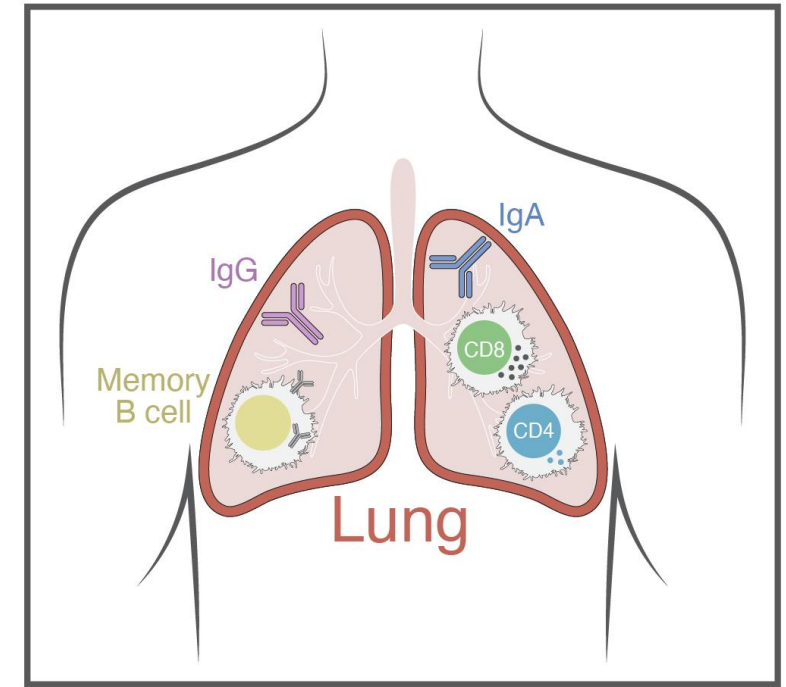
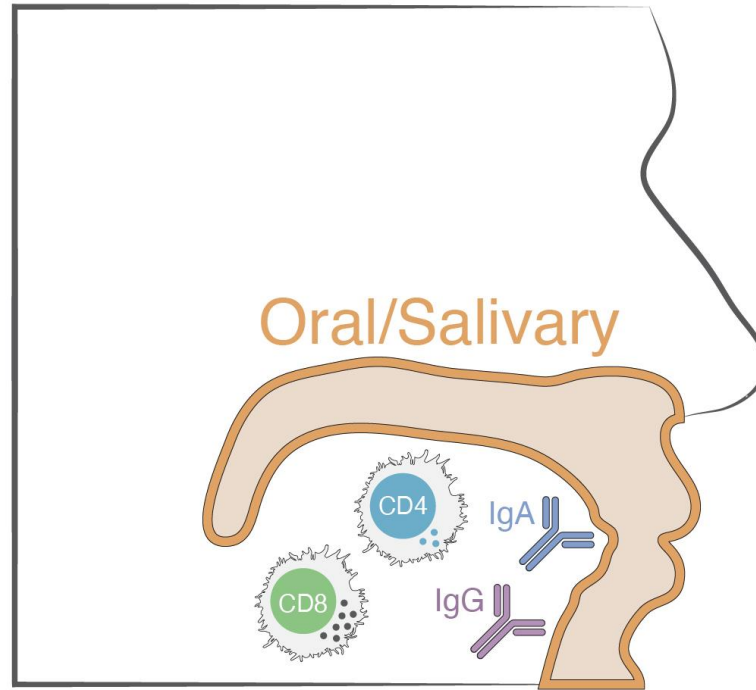
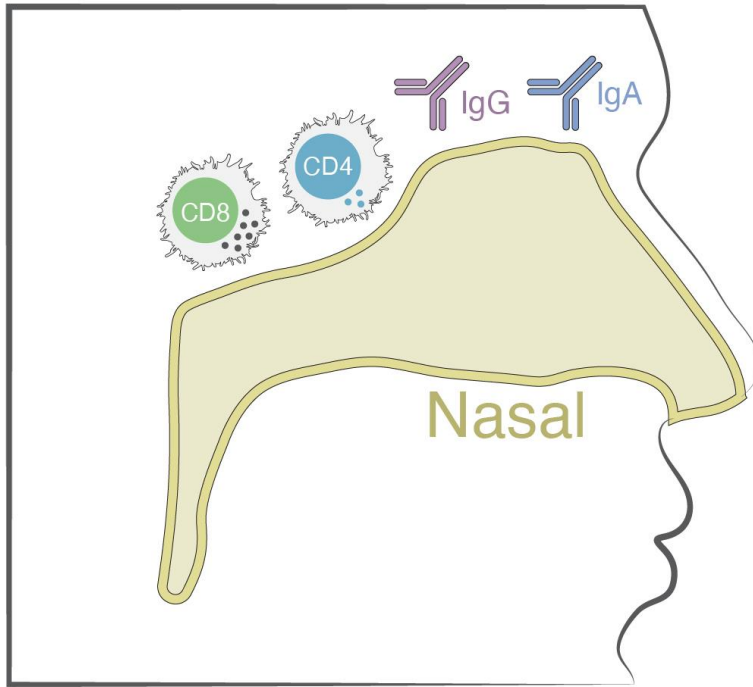
Mateus et al.
Science. Oct 2021.
pmid: 34519540

What are mechanisms of protective immunity against COVID-19?

- ❖ The simplest option for any vaccine development is high level, long lasting, neutralizing antibodies.
- ❖ Various lines of evidence point to protective contributions of T cells against COVID-19
- ❖ It is reasonable to consider that hospitalization-level COVID-19 is prevented by any decent combination of antibody, memory B cells, CD4 T cells, and CD8 T cells.



Anatomy of adaptive immunity to SARS-CoV-2



It is all a race

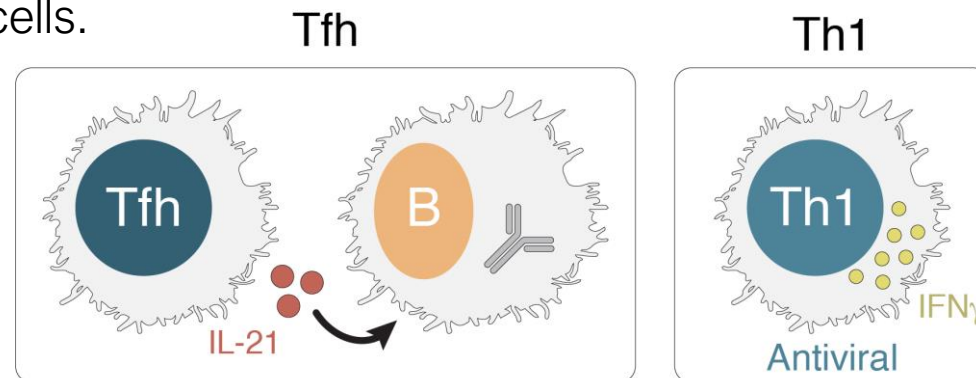
A race between the virus and your immune system.

Vaccines change the race. You then have the headstart instead of the virus.

What are mechanisms of protective immunity against COVID-19?

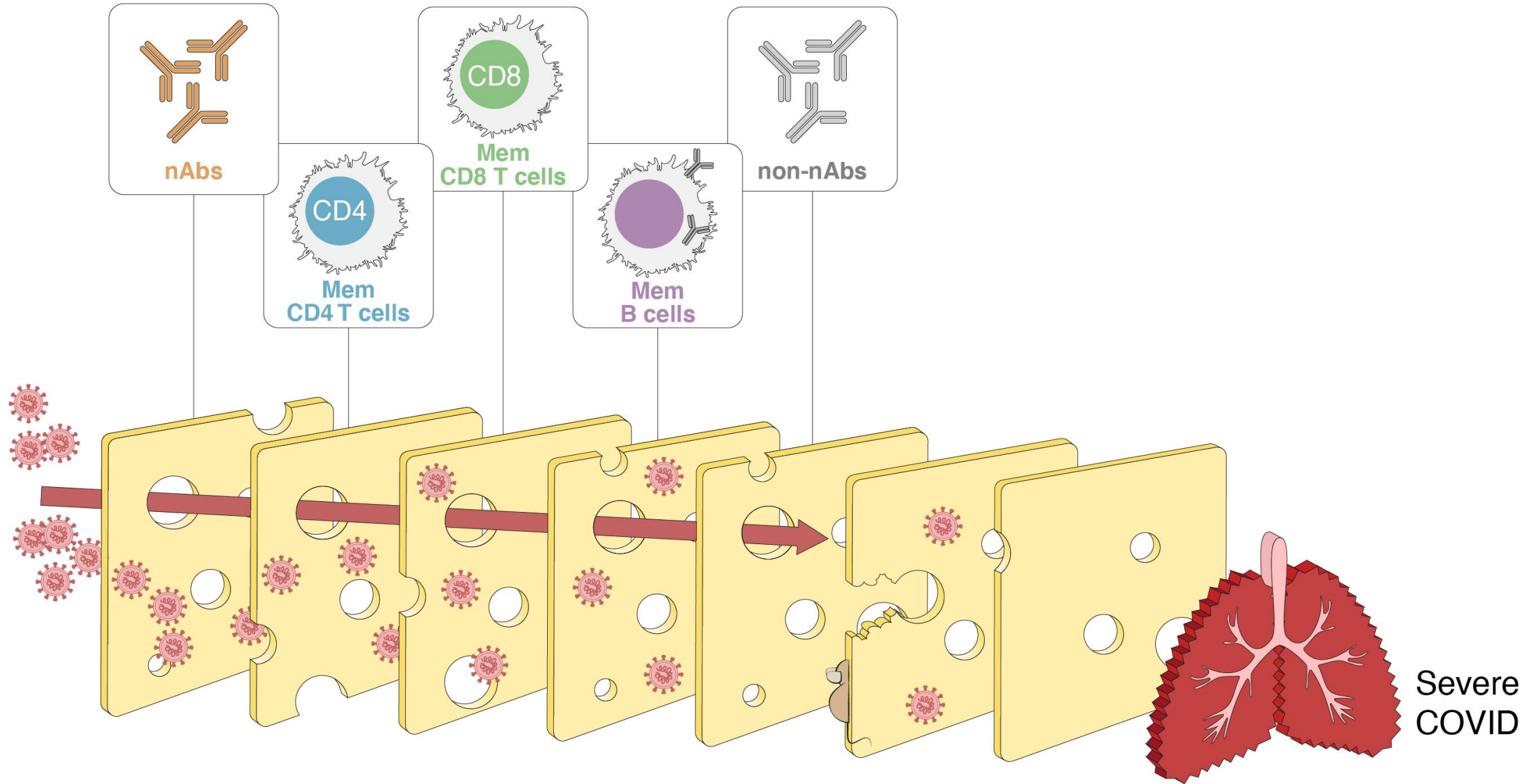
The simplest option for any vaccine development is high level, long lasting, neutralizing antibodies.

- This virus is clearly susceptible to neutralizing antibodies.
- Antibodies can clearly protect against COVID-19 in humans and animal models when present before infection. (Monoclonal antibody studies)
- Antibodies are the only mechanism that can provide truly sterilizing immunity.
- Antibodies correlate with protection from symptomatic COVID-19 in multiple human vaccine studies.
- Antibodies are a correlate of CD4 T cells: Neutralizing antibodies almost always depend on CD4 T cells. Thus, antibodies are usually a surrogate marker of vaccine-specific CD4 T cells, at least T follicular helper (T_{FH}) cells.



Layered defenses

Or the swiss cheese model of immunity



Do T cells help control SARS-CoV-2 infection?

- ❖ Coordinated adaptive immunity is protective immunity
 - T cells appear to be major contributors to controlling SARS2 infection
 - The adaptive immune system has three branches in the armamentarium for good reasons
 - We observed no convincing evidence of likely causal negative associations of adaptive immunity with disease severity
- ❖ Age is a major COVID-19 risk factor, and adaptive immunity shortcomings are part of that problem
 - Poorly coordinated T cell responses
 - Limited naive T cell repertoire



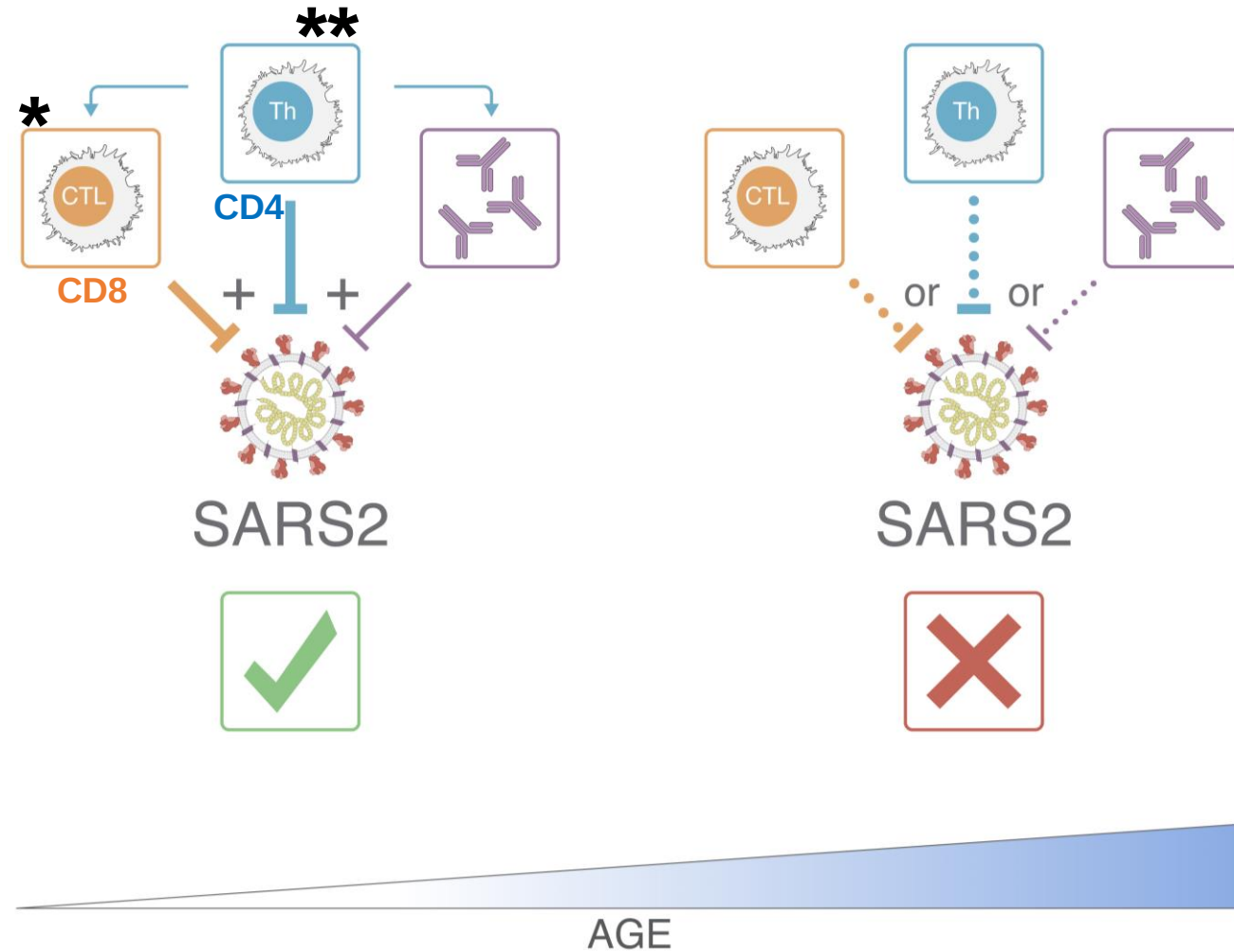
Carolyn Rydyznski
Moderbacher, PhD



Sydney Ramirez,
MD/PhD

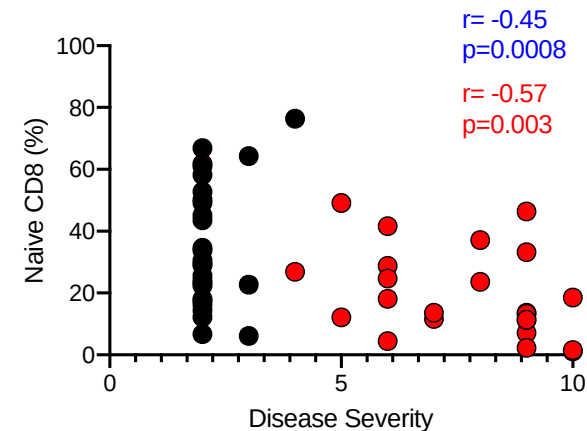
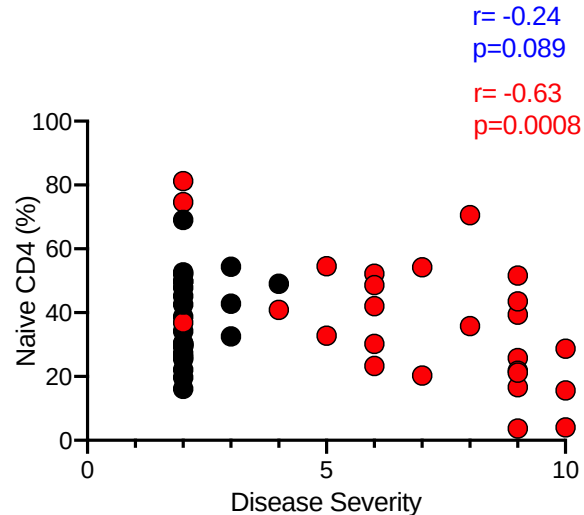
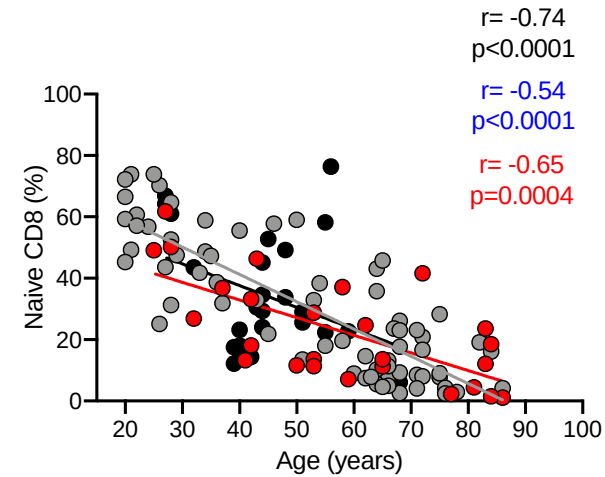
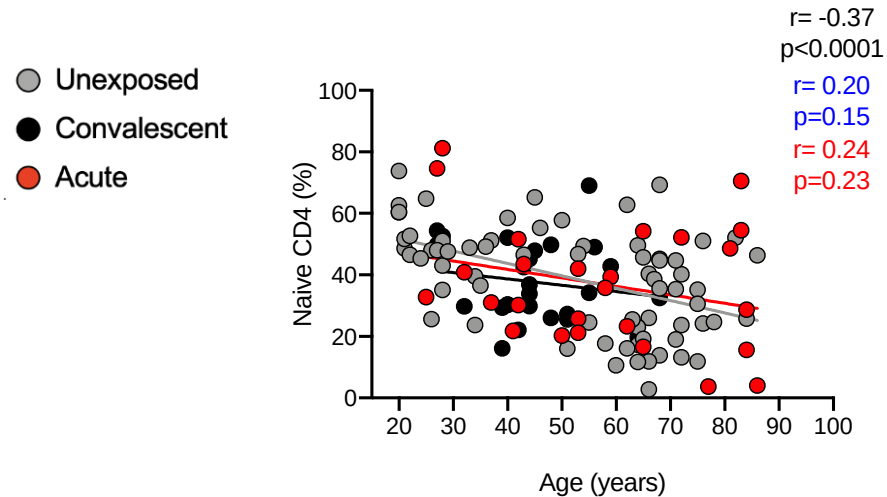


Asst. Prof. Jen Dan
MD/PhD



Age is a major COVID-19 risk factor

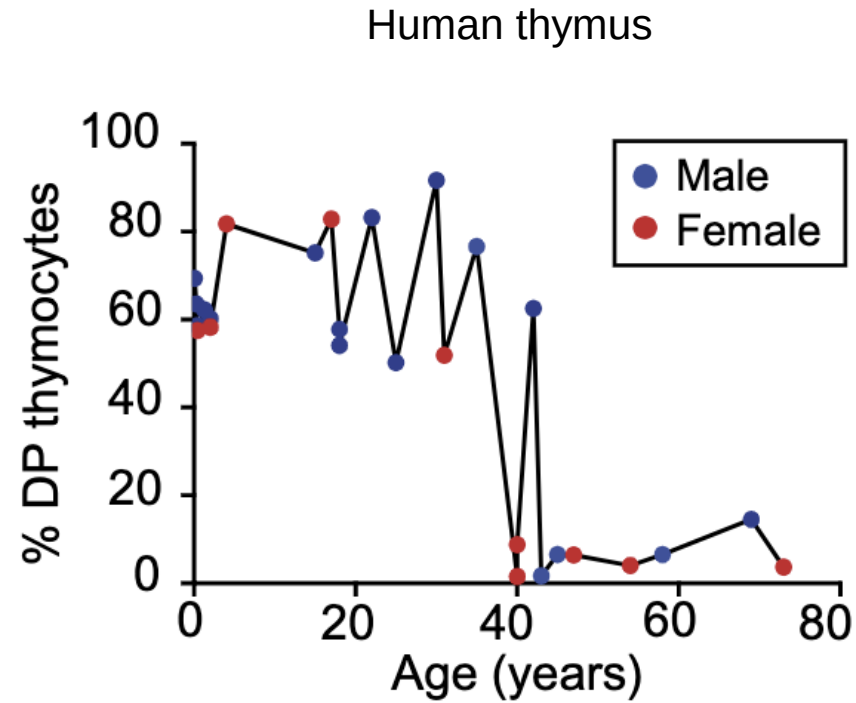
Naive T cell abundance is one immunological component of that risk



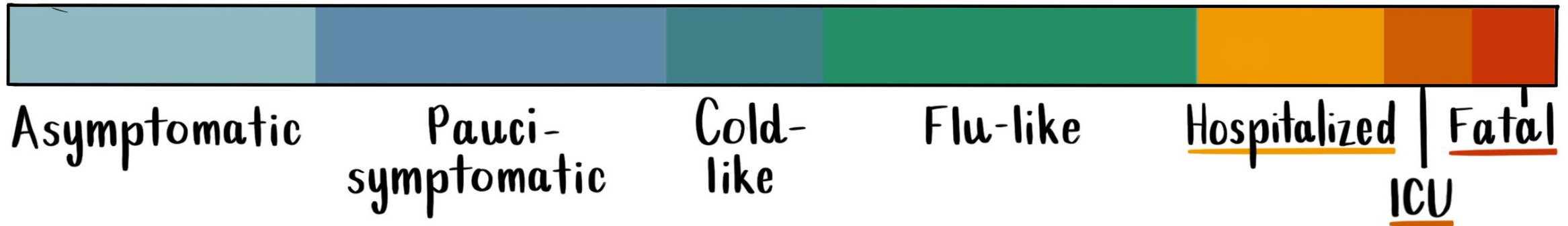
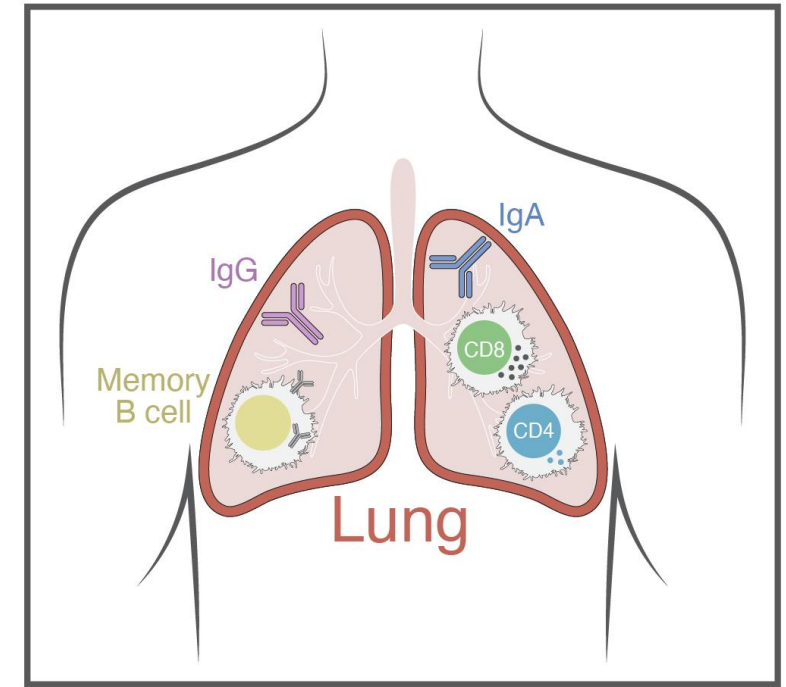
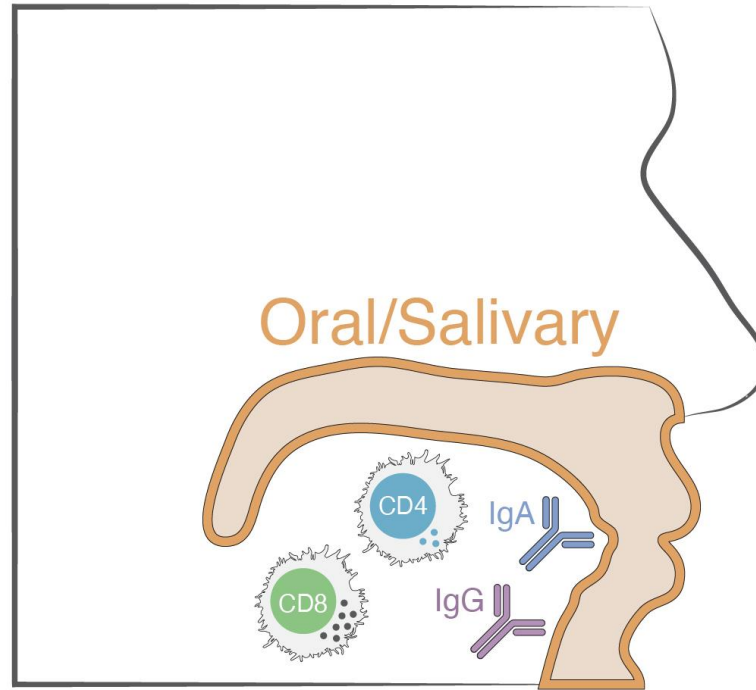
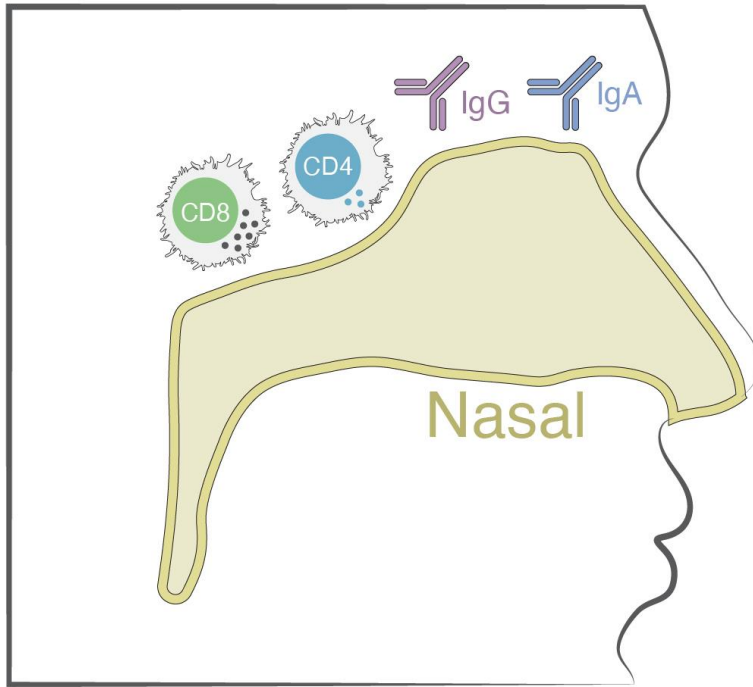
Statistics

Full data set (Ac, Co, Unexp)
COVID-19 disease (Ac, Co)
Acute COVID-19

Decline in naive T cell production with age



Anatomy of adaptive immunity to SARS-CoV-2



It is all a race

A race between the virus and your immune system.

Vaccines change the race. You then have the headstart instead of the virus.

What are mechanisms of protective immunity against COVID-19?

Various lines of evidence point to protective contributions of T cells

- T cell responses correlate with better outcomes and lower viral loads in SARS-CoV-2 infection
- CD8 T cells provide control in monkeys
- Regeneron and Lilly outpatient and inpatient monoclonal antibody clinical trials. Modest impact on viral loads
- Agammaglobulinemic and B cell depleted individuals
 - moderately increased risk of hospitalization with COVID-19
 - COVID-19 in ocrelizumab-treated people with MS is predominantly mild
- 1-dose of Moderna or Pfizer vaccine provided substantial protection in the absence of detectable neutralizing antibodies in most individuals
- T cell responses to vaccines in NHPs correlate with better outcomes and lower viral loads
- T cells can be measured as potential correlates of immunity, and have been correlates in two non-human primate studies, but have not been studied for any human COVID vaccine.
- Kinetics and tissue distribution of SARS-CoV-2

SCIENTIFIC
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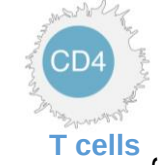
PUBLIC HEALTH

Your Immune System Evolves To Fight Coronavirus Variants

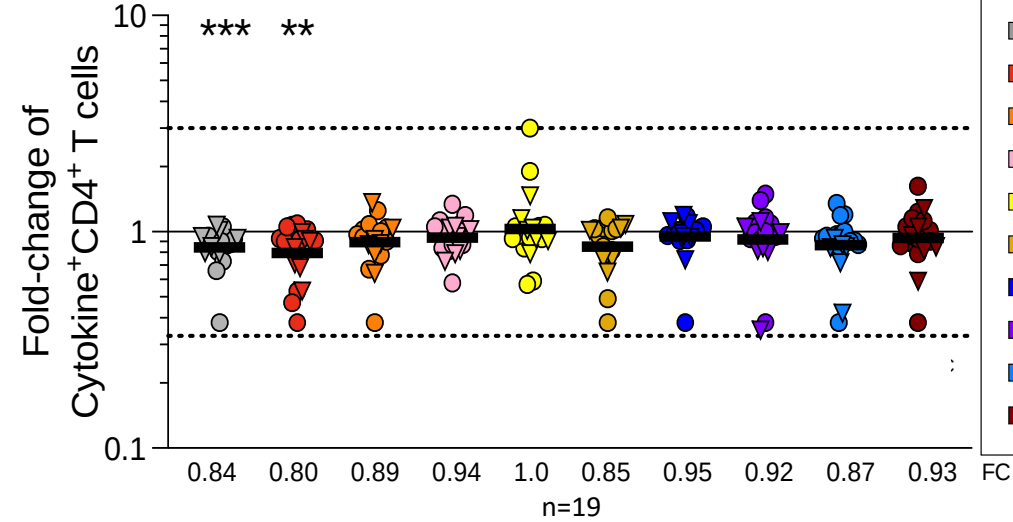
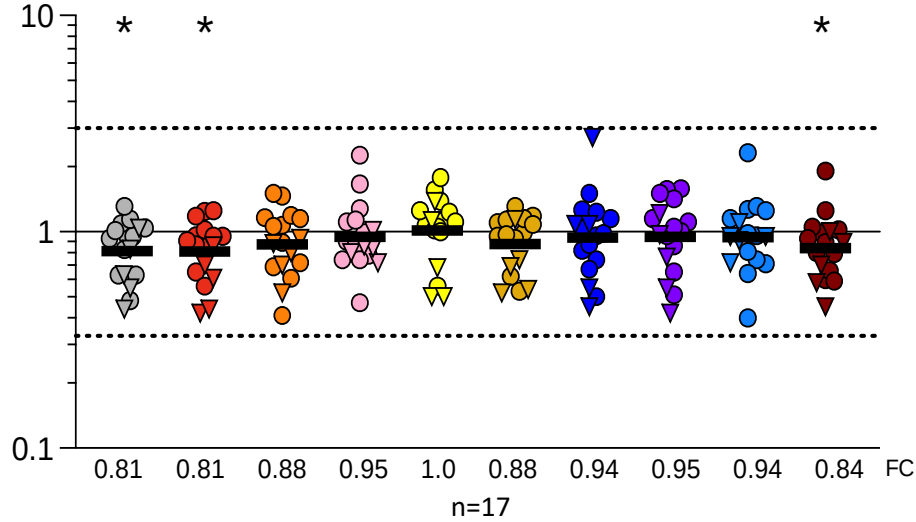
Antibodies can change to counter new forms of the shape-shifting virus, research hints



T cell recognition of Omicron is preserved



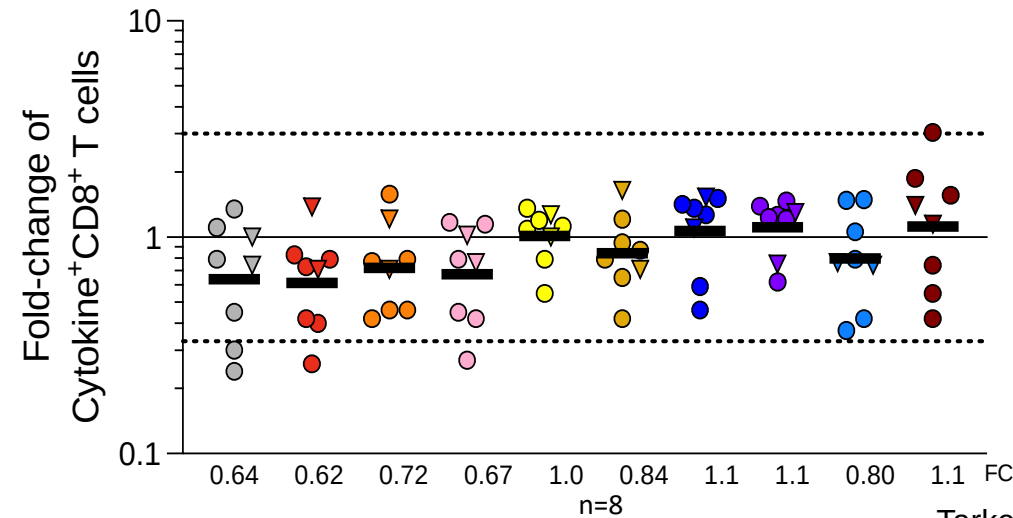
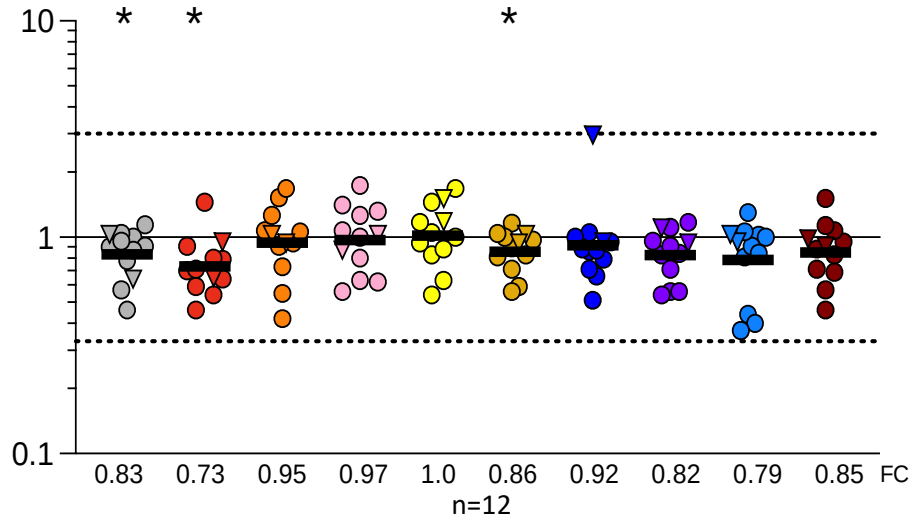
Fold-change of
AIM⁺CD4⁺ T cells



SARS-CoV-2 variant:

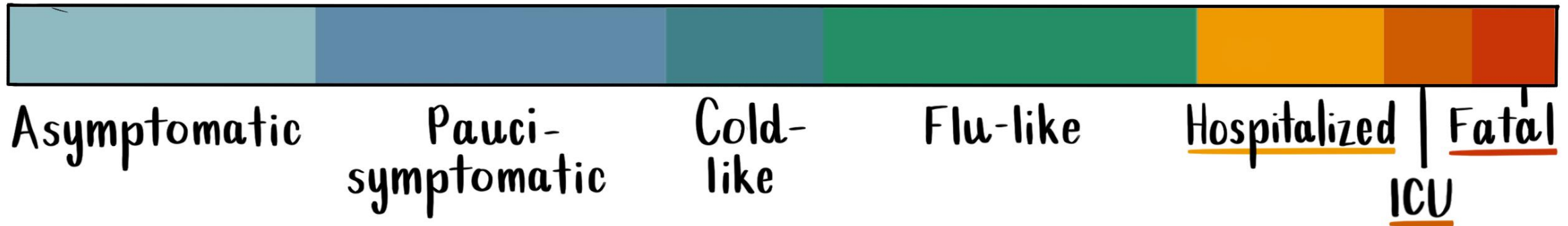
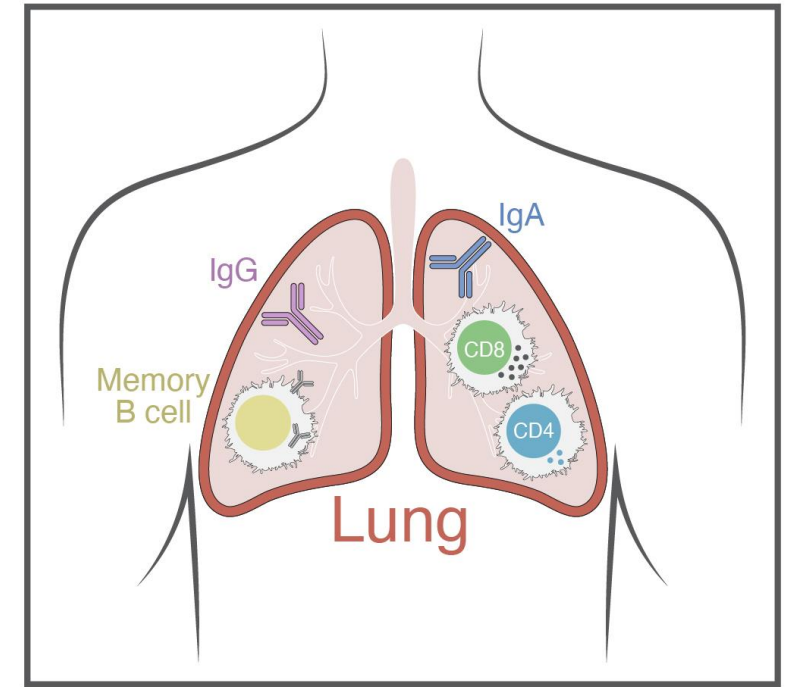
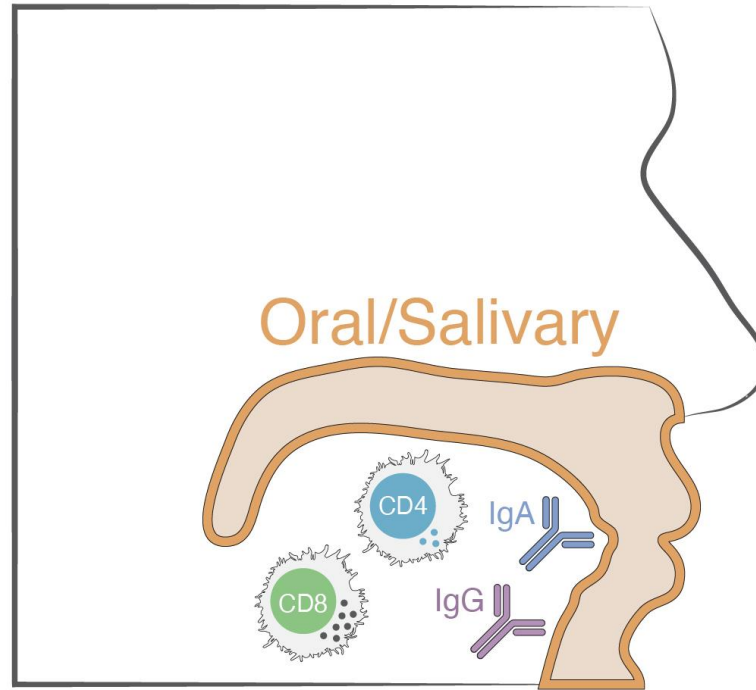
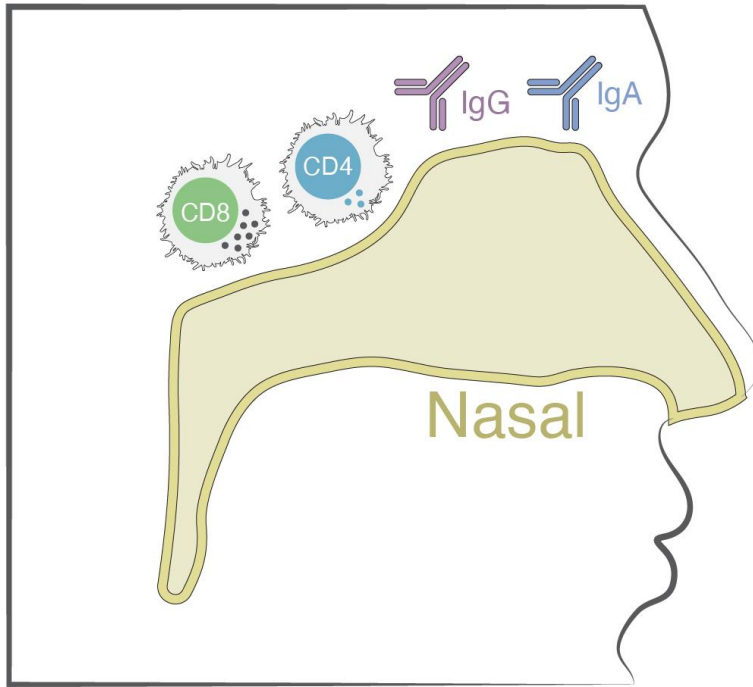
- Alpha (B.1.1.7)
- Beta (B.1.351)
- Gamma (P.1)
- B.1.1.519
- Kappa (B.1.617.1)
- Delta (B.1.617.2)
- Lambda (C.37)
- R.1
- Mu (B.1.621)
- Omicron (B.1.1.529)

Fold-change of
AIM⁺CD8⁺ T cells



Alba Grifoni, PhD

Anatomy of adaptive immunity to SARS-CoV-2

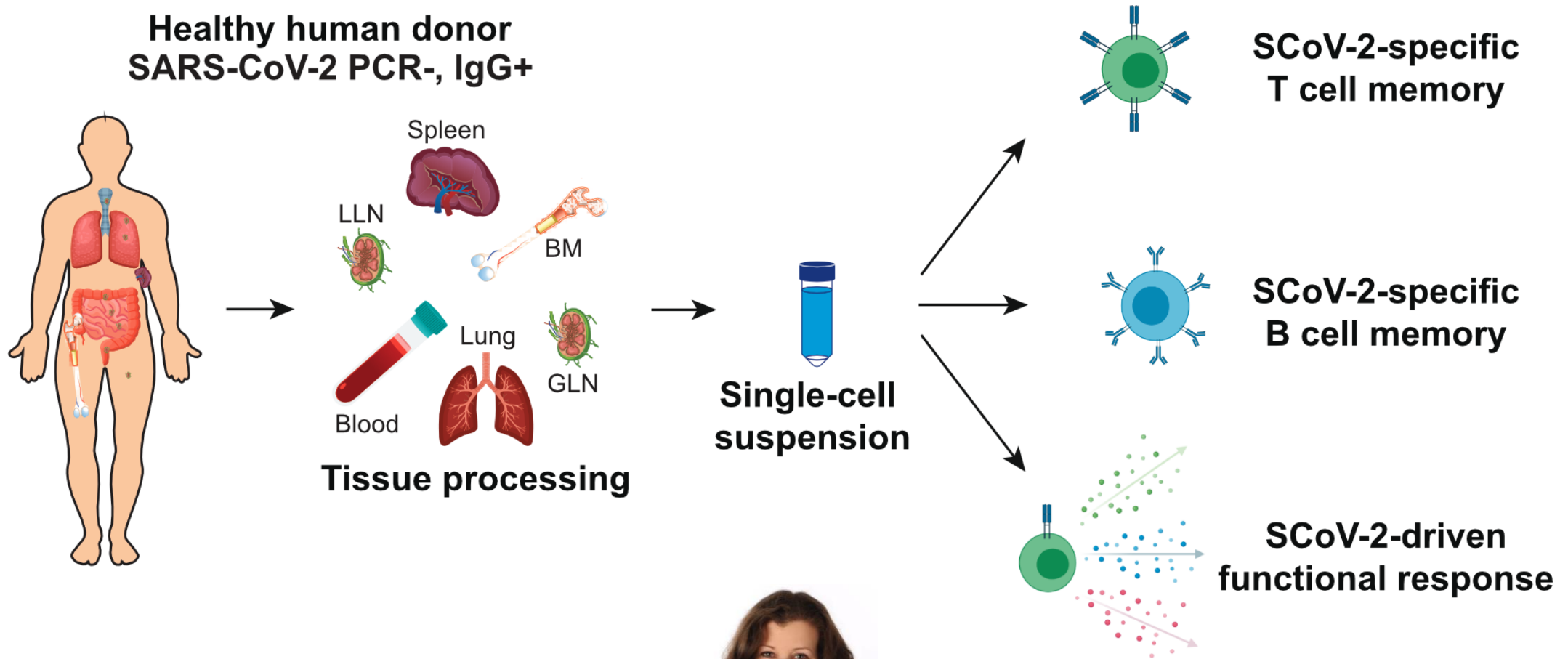


It is all a race

A race between the virus and your immune system.

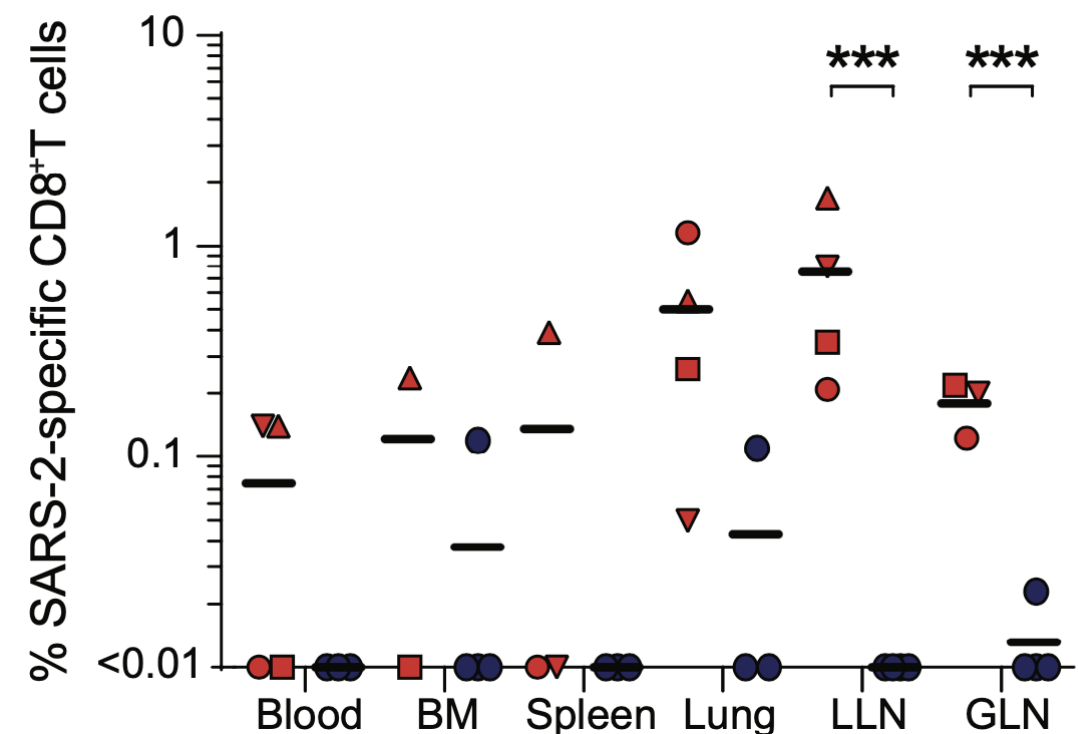
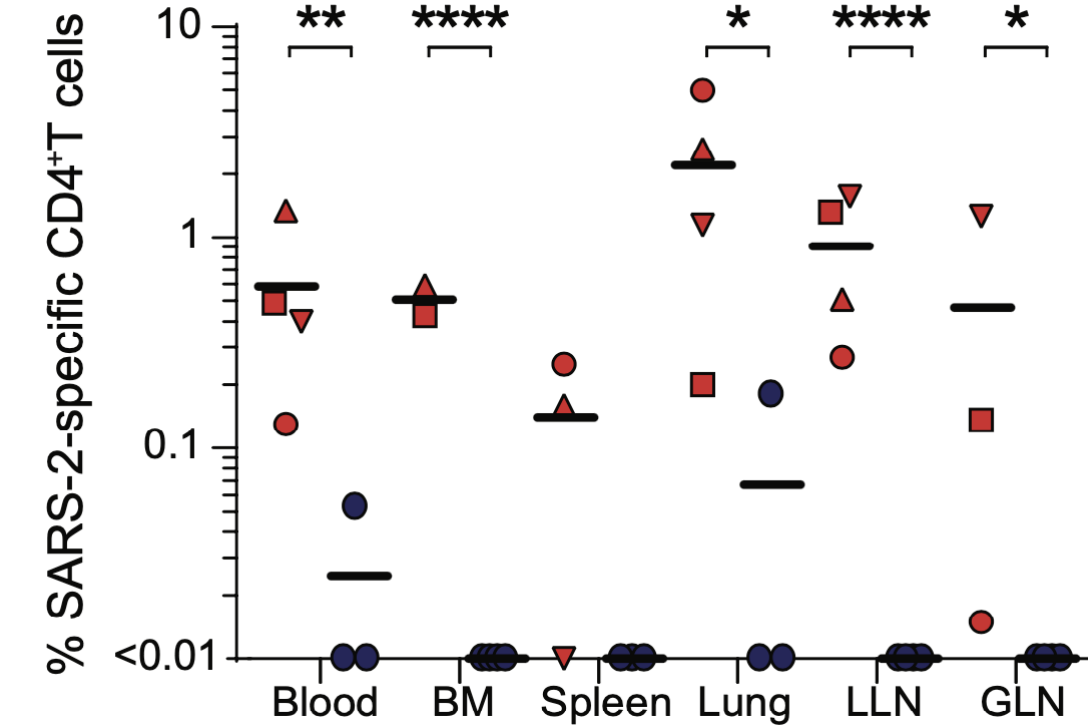
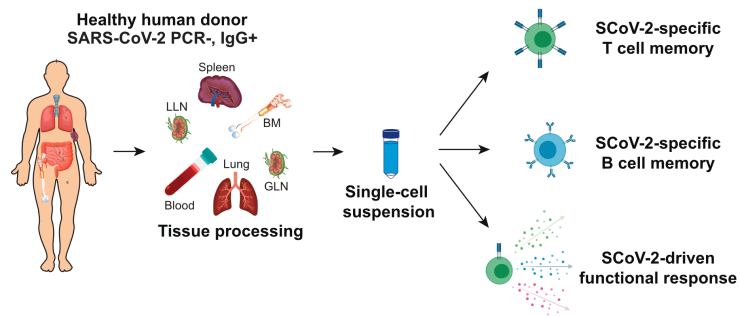
Vaccines change the race. You then have the headstart instead of the virus.

SARS-CoV-2 infection generates tissue-localized immunological memory in humans

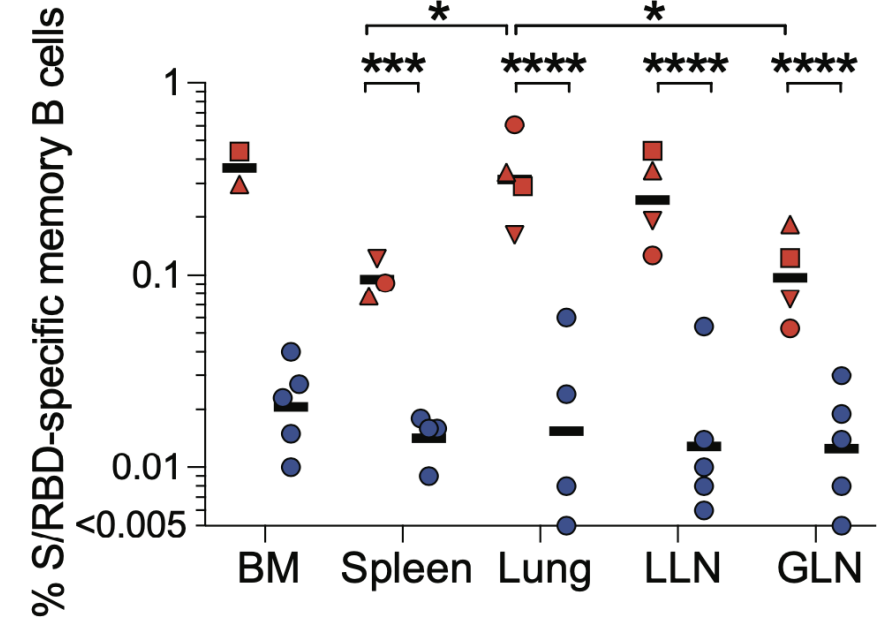
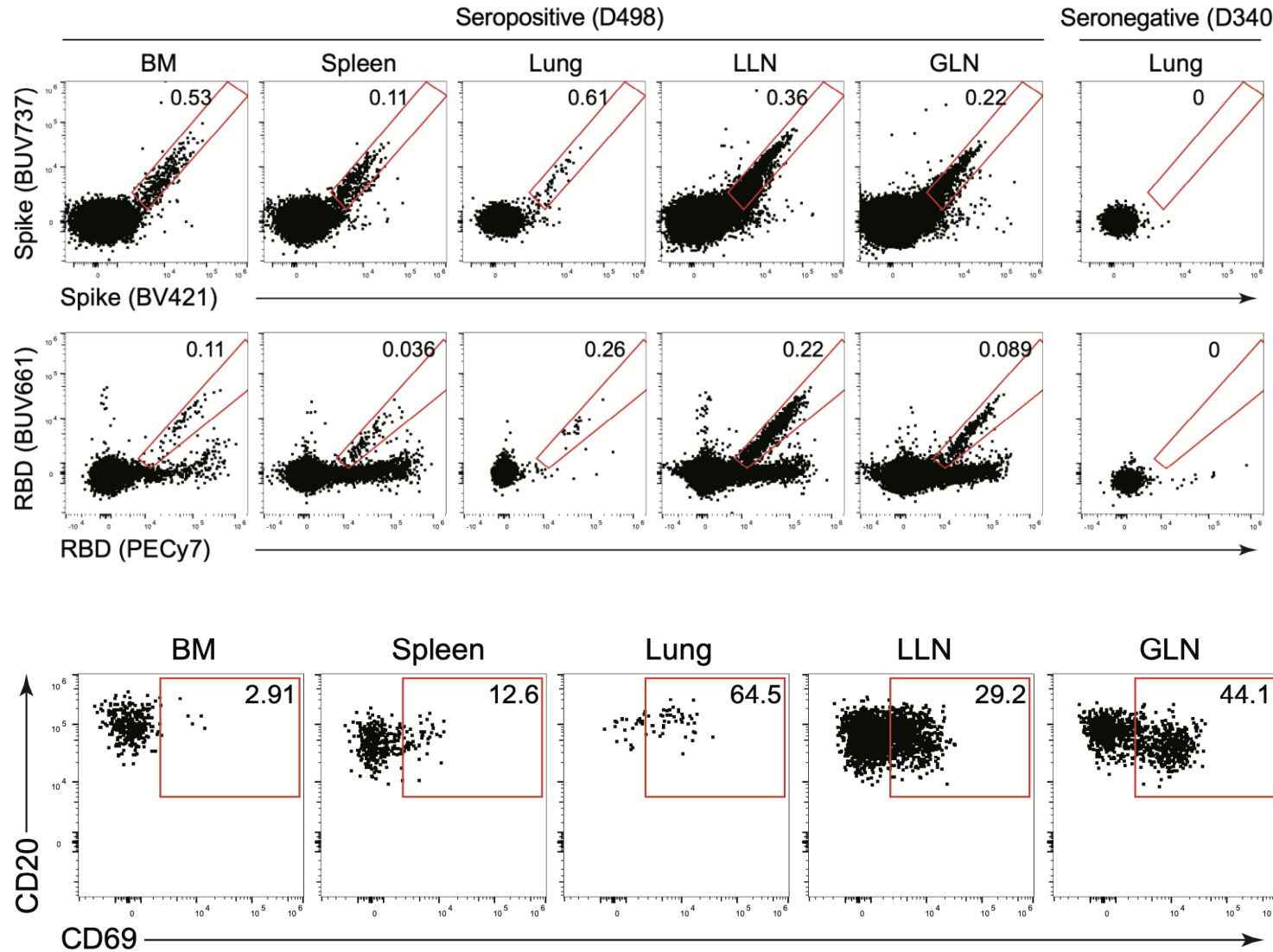


Donna Farber

SARS-CoV-2 infection generates tissue-localized immunological memory in humans

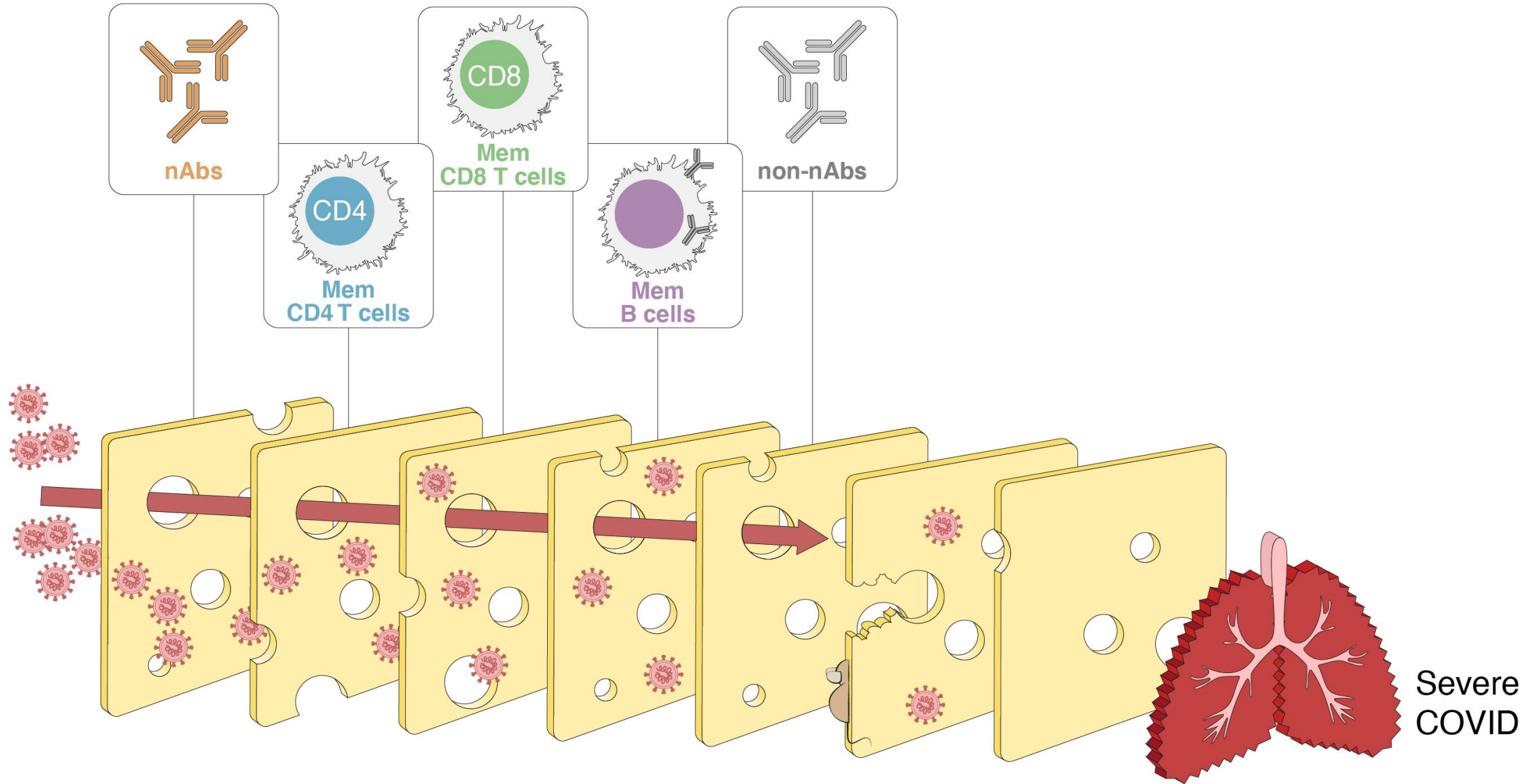


SARS-CoV-2 infection generates tissue-resident memory B cells (B_{RM}) in humans



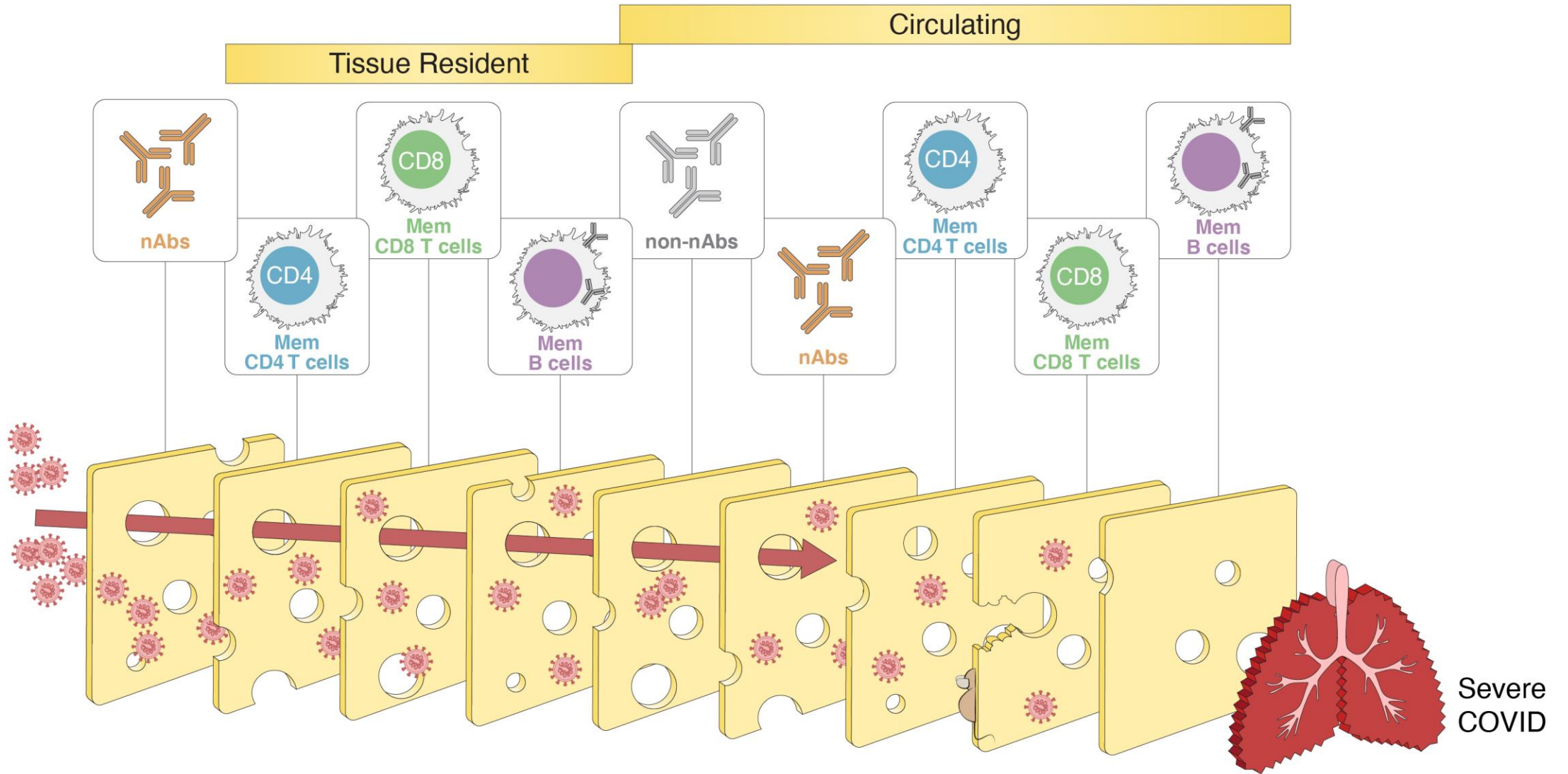
Layered defenses

Or the swiss cheese model of immunity

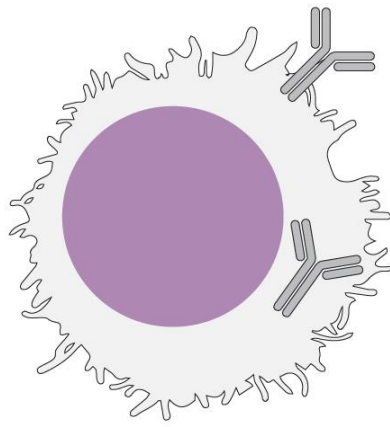


Layered defenses

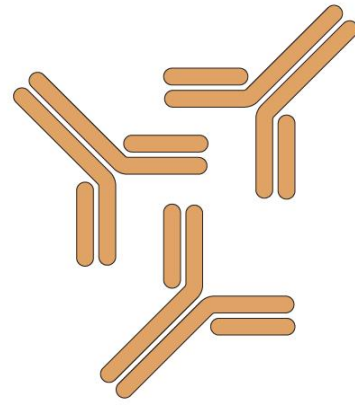
Or the swiss cheese model of immunity



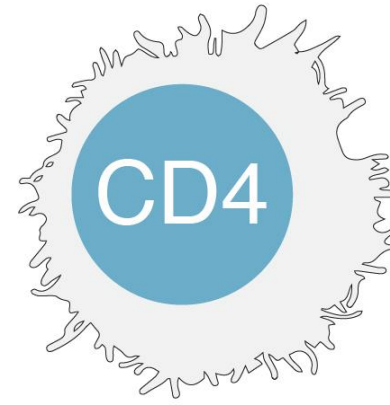
What are mechanisms of protective immunity against COVID-19?



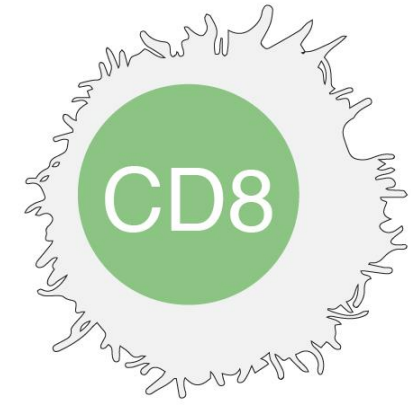
**Memory
B cell**



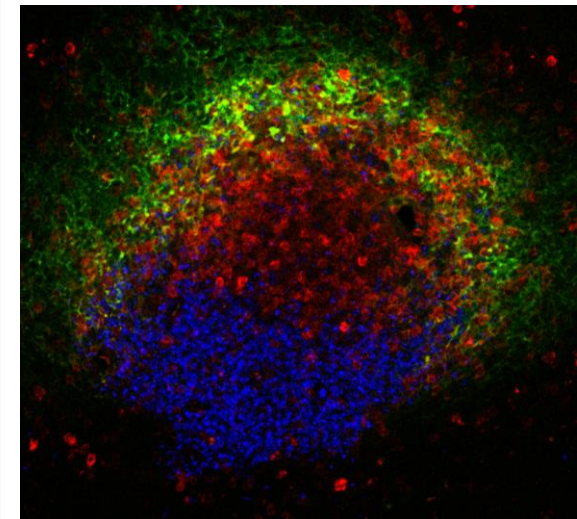
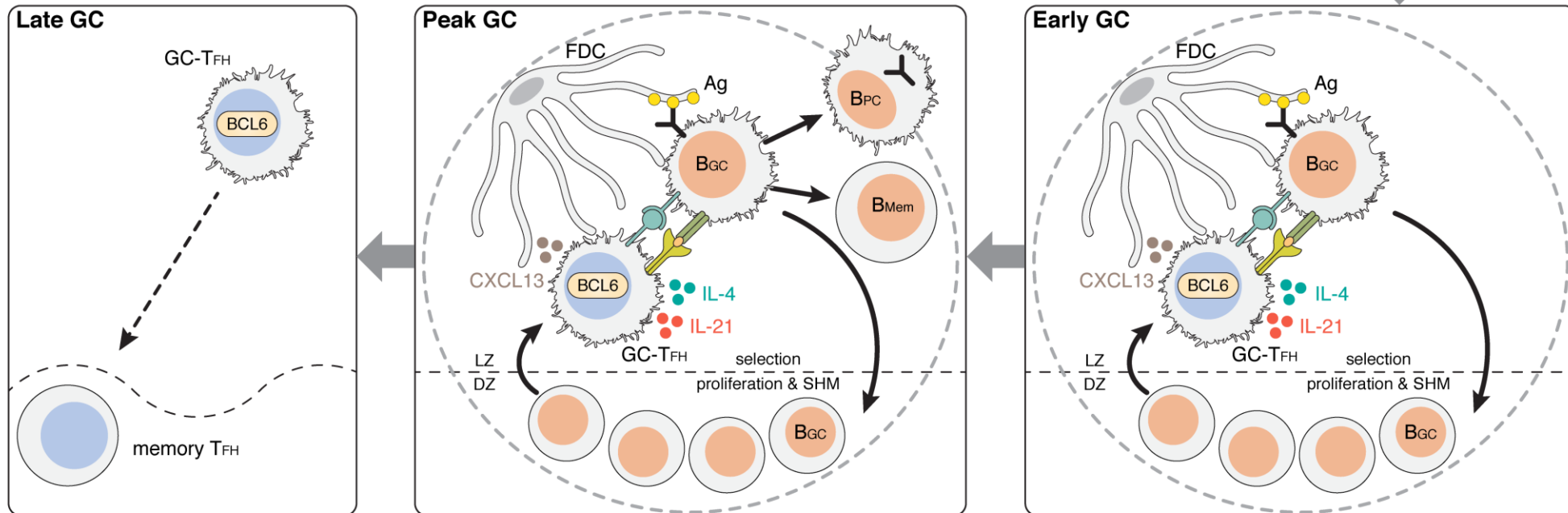
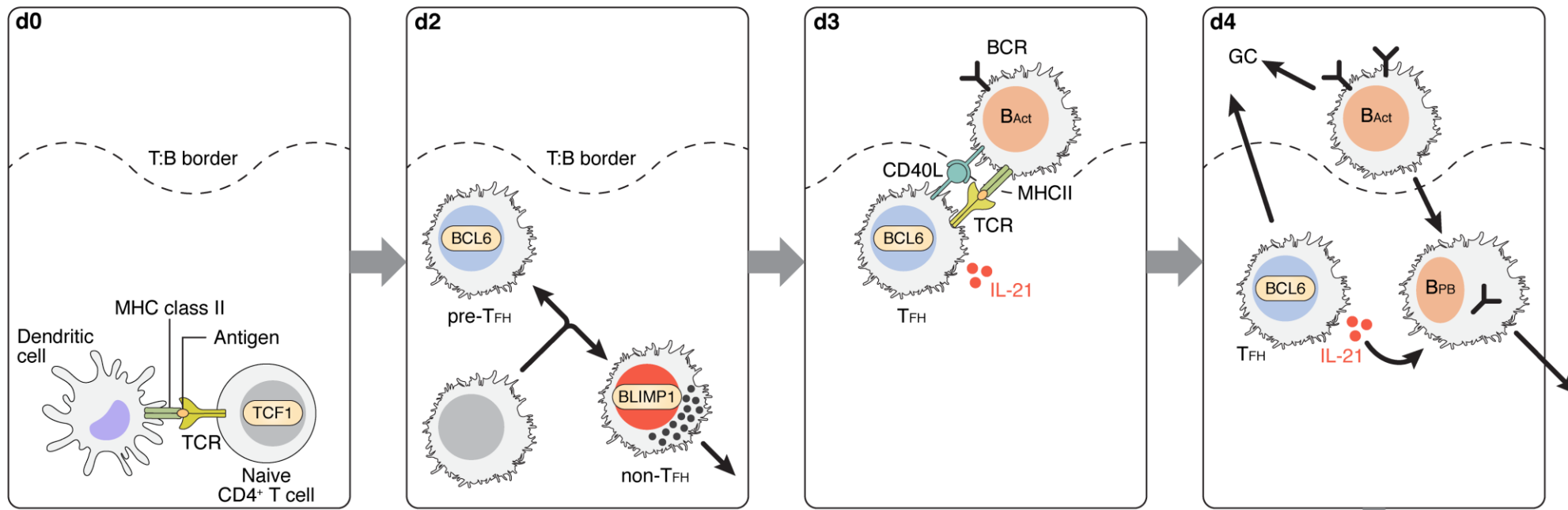
Antibodies



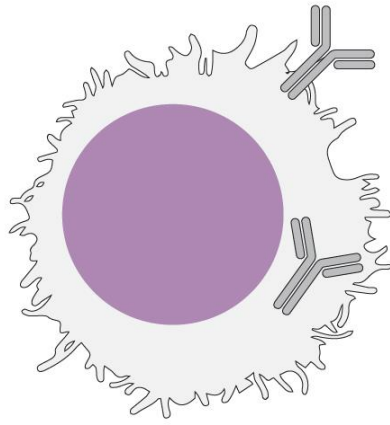
CD4⁺ T cells



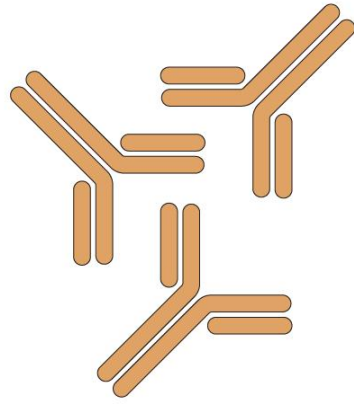
CD8⁺ T cells



What are mechanisms of vaccine protective immunity?



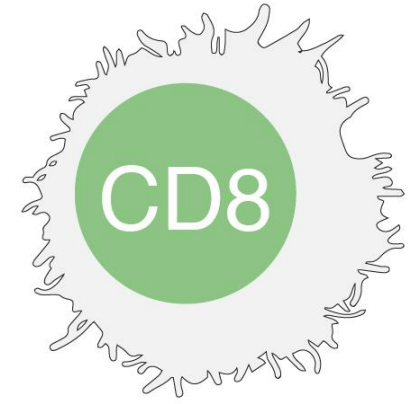
**Memory
B cell**



Antibodies



CD4⁺ T cells



CD8⁺ T cells

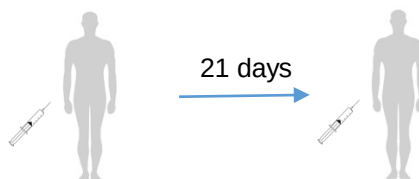
Comparison of immune memory to four COVID-19 vaccines



mRNA-1273-100 µg



BNT162b2-30µg

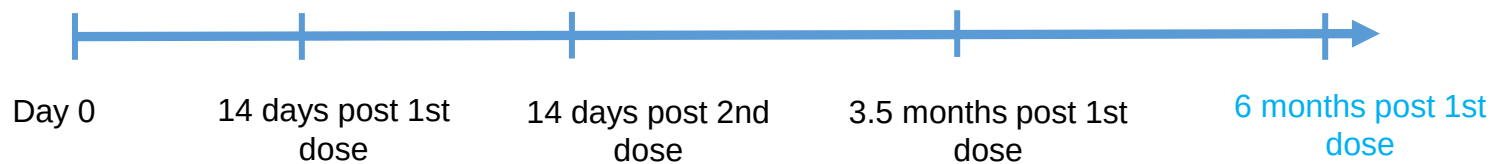


NVX-CoV2373

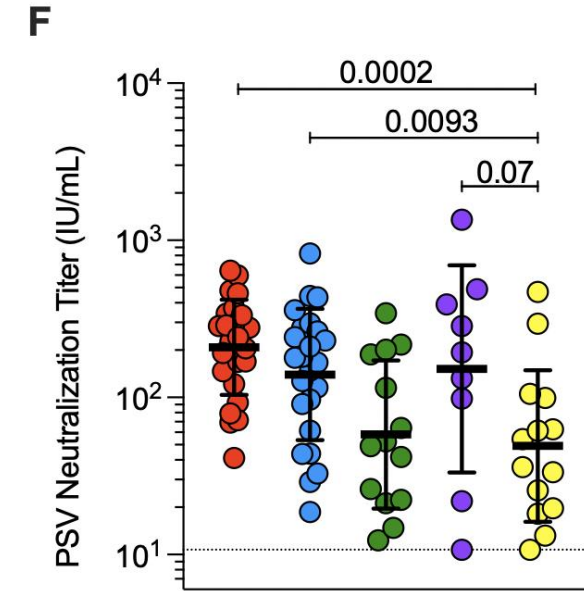
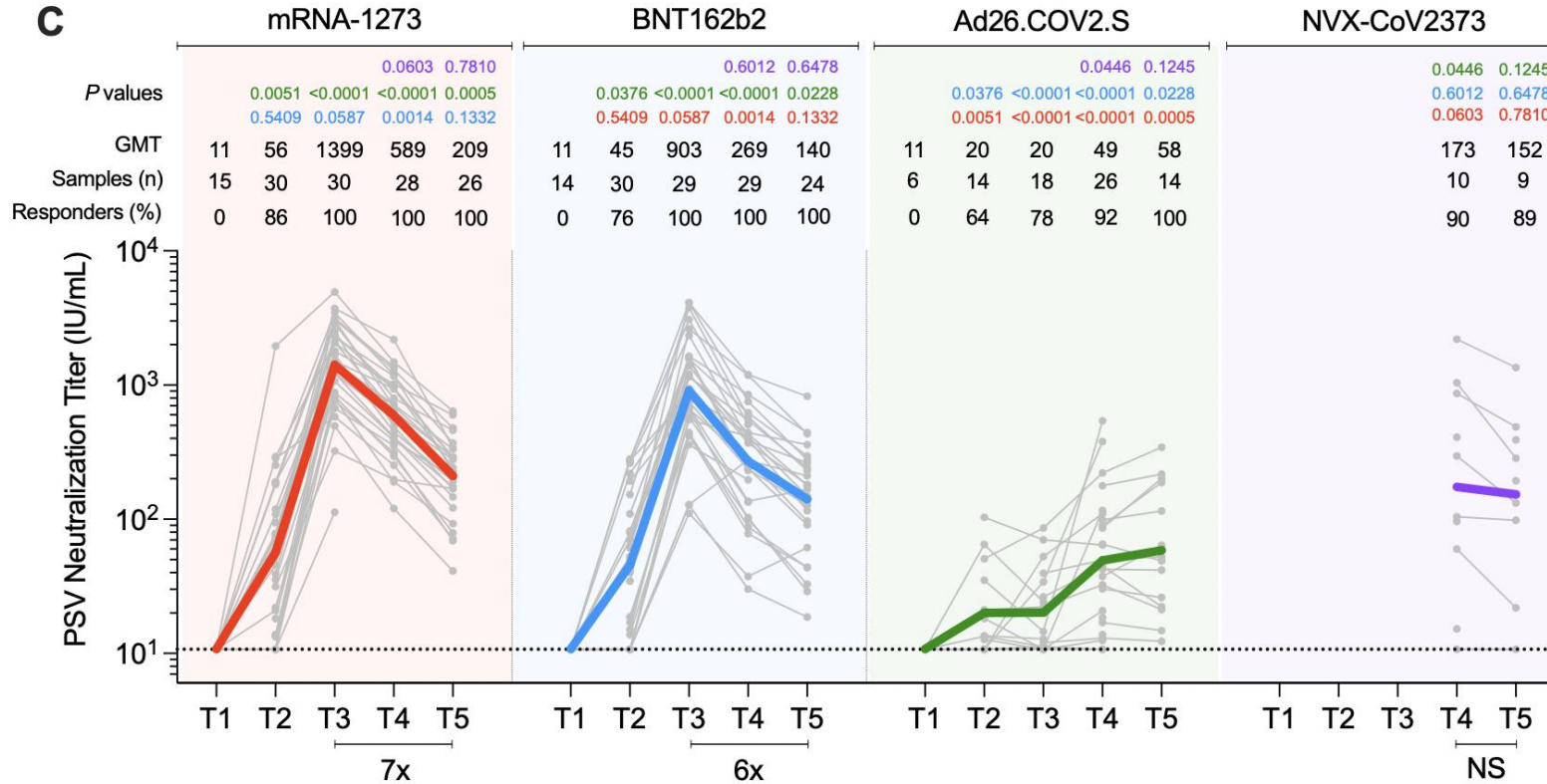


J&J

Characteristic	mRNA-1273 Moderna	BNT162b2 Pfizer	Ad26.COV2.S Janssen	NVX-CoV2373 Novavax
Donors, n	30	30	30	12
Gender, n (%)				
Male	12 (40%)	11 (37%)	11 (37%)	6 (60%)
Female	18 (60%)	19 (63%)	19 (63%)	4 (40%)
Age, years (mean ± SD)	43.6 ± 13.9	43.2 ± 17.4	45.6 ± 14.9	38.3 ± 18.0
Race or ethnicity, n				
Asian	3	9	2	0
White	24	16	24	11
Hispanic or latino	9	5	5	1
Days post-vaccination (mean ± SD)				
T2	15 ± 4	15 ± 2	15 ± 3	-
T3	45 ± 6	37 ± 3	47 ± 8	-
T4	105 ± 6	106 ± 4	108 ± 7	120 ± 19
T5	185 ± 9	184 ± 8	185 ± 3	185 ± 11



Comparison of immune memory to four COVID-19 vaccines

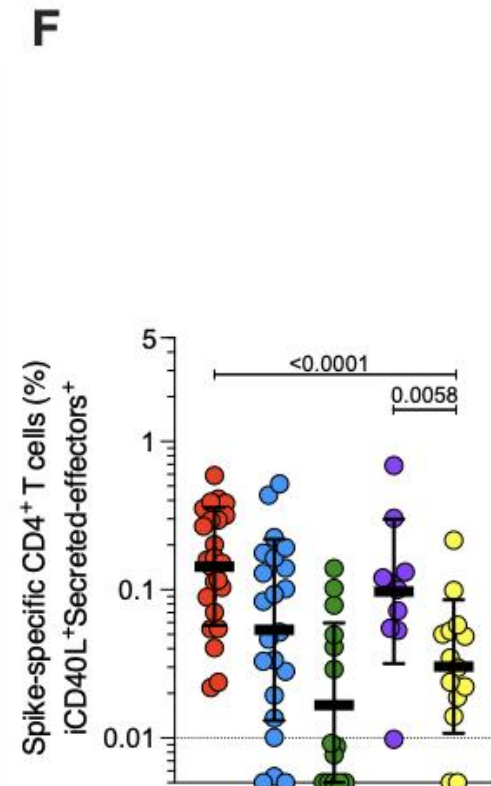
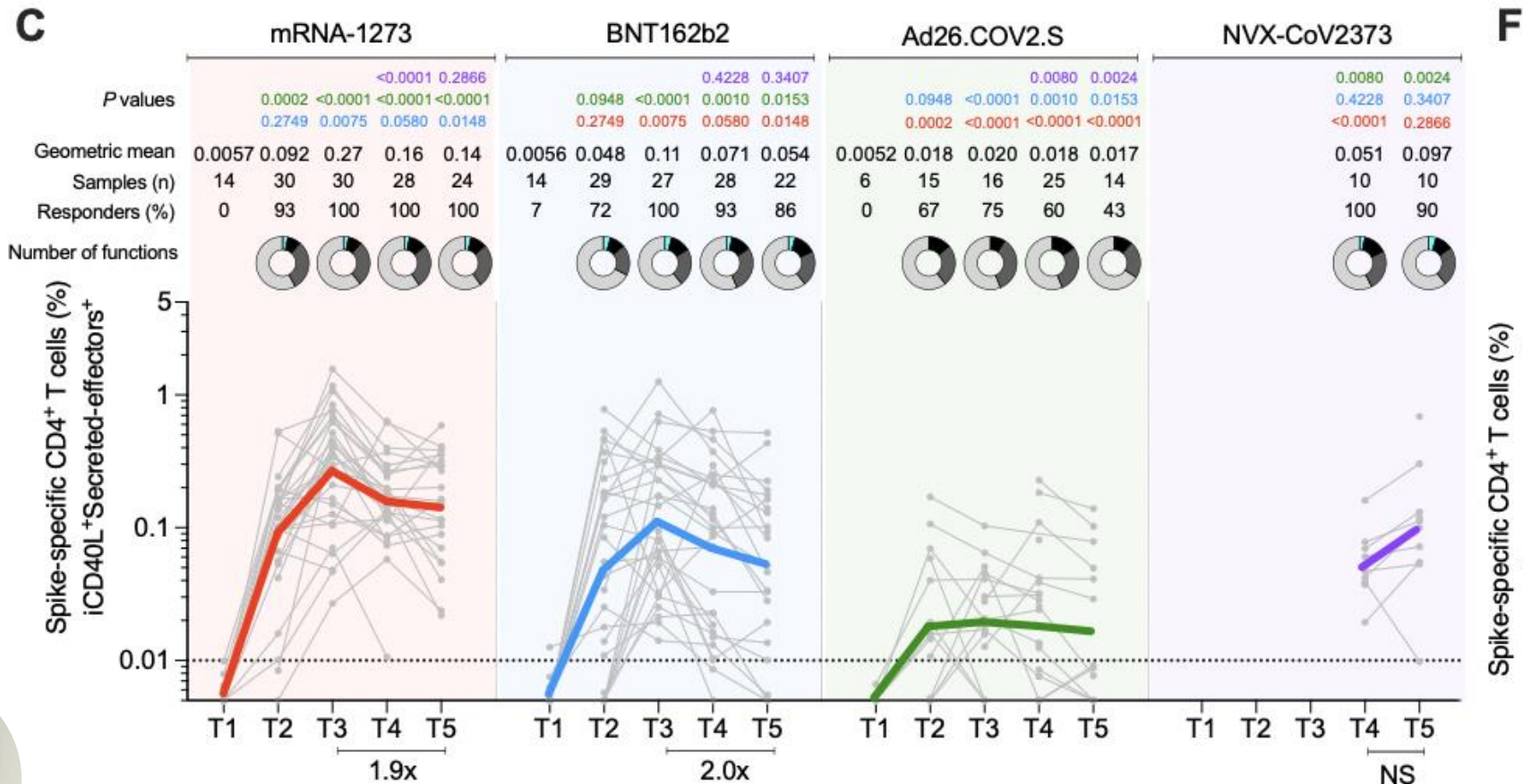


Zeli Zhang, PhD



Jen Dan, MD/PhD

Comparison of immune memory to four COVID-19 vaccines

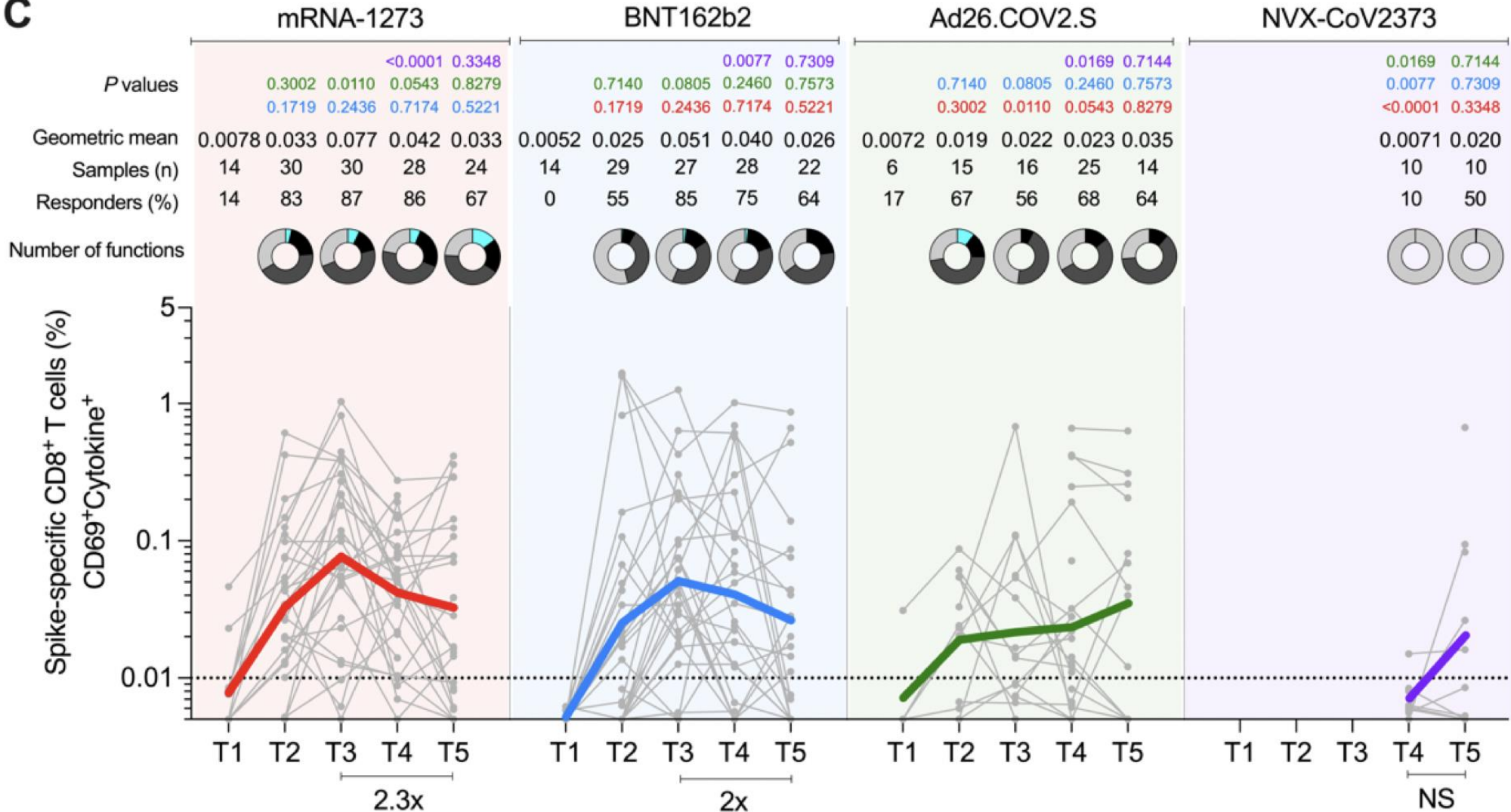


Carolyn Rydyznski
Moderbacher, PhD

Comparison of immune memory to four COVID-19 vaccines

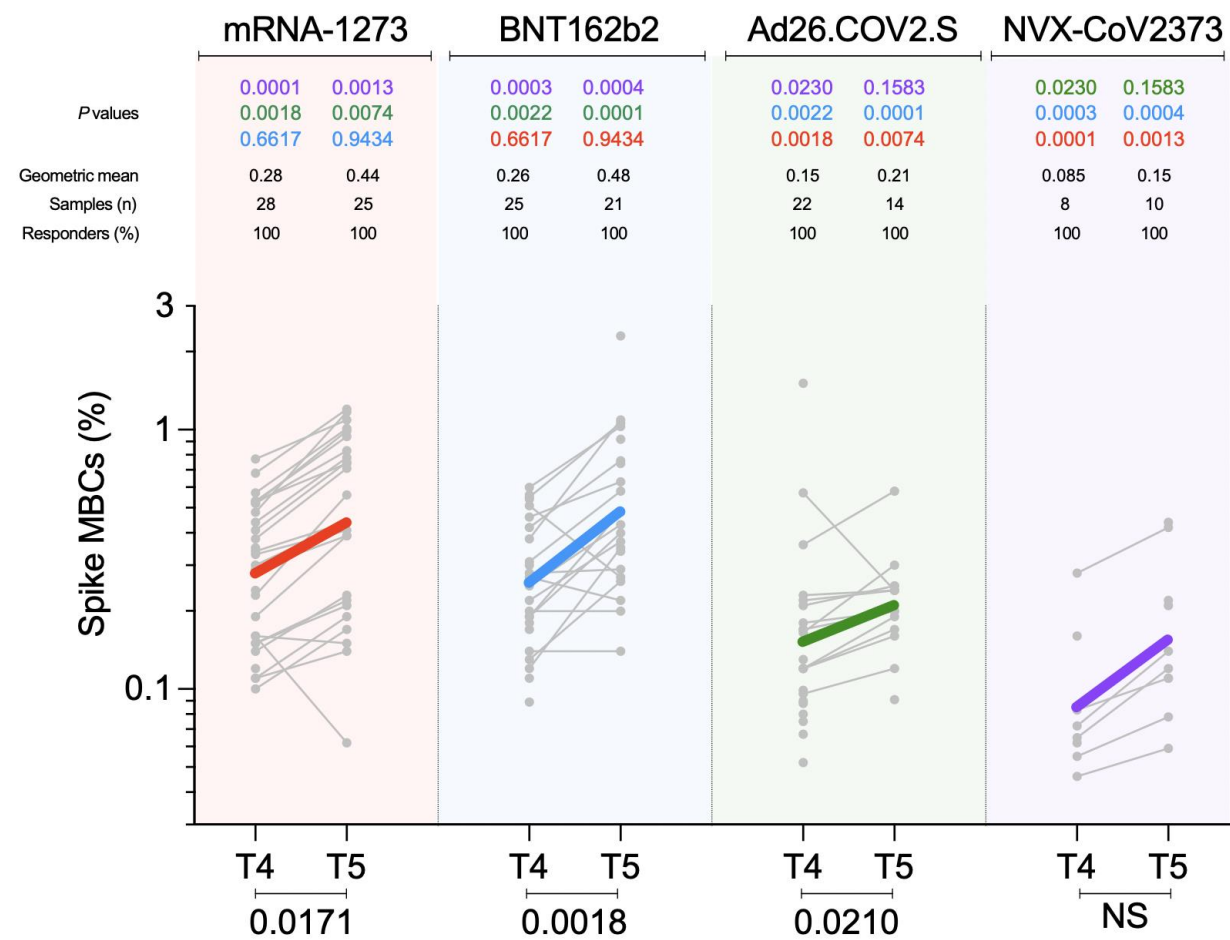
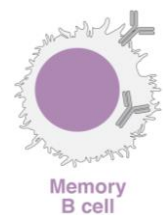


C



Jose Mateus, PhD

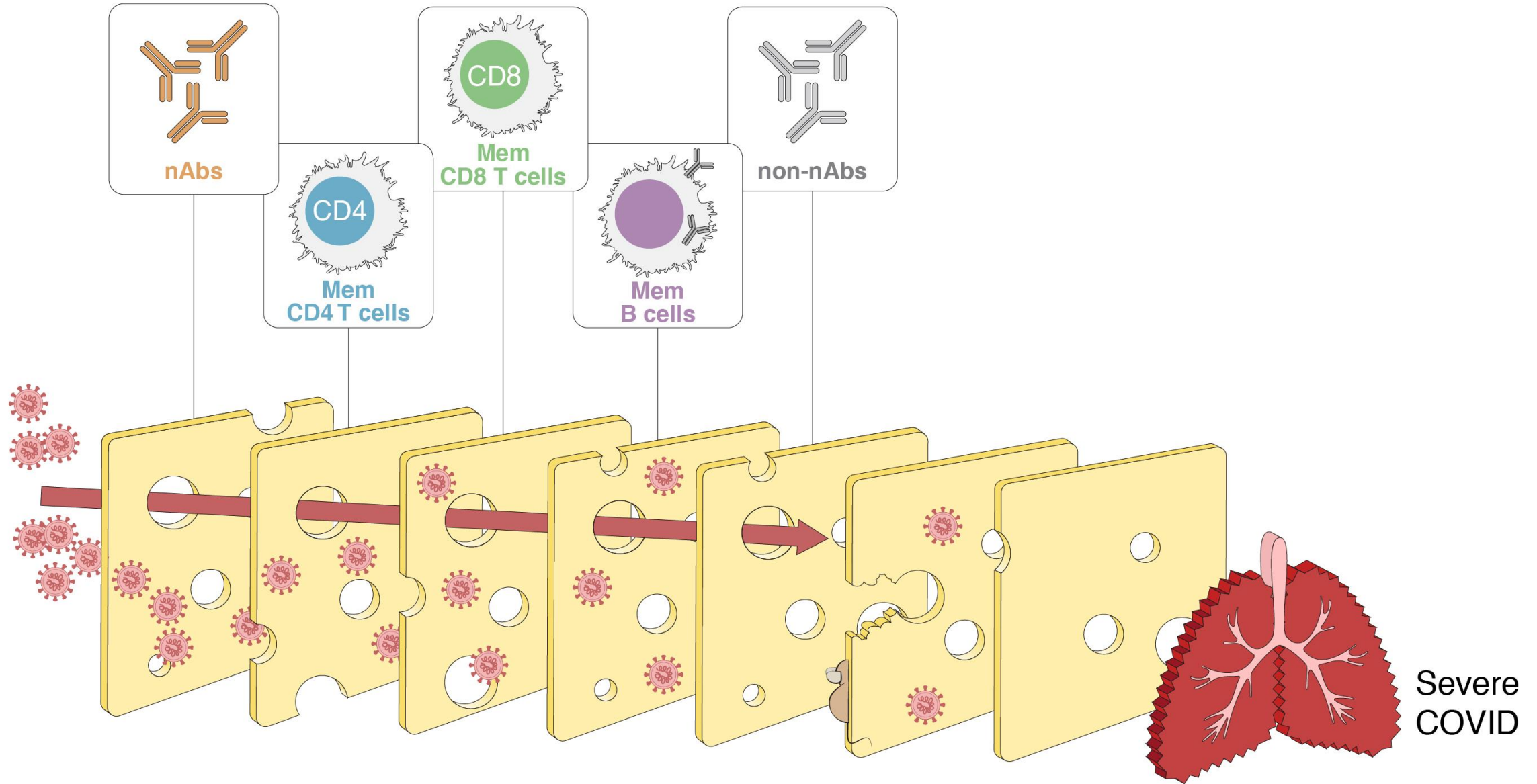
Comparison of immune memory to four COVID-19 vaccines



Camila Coelho, PhD

Layered defenses

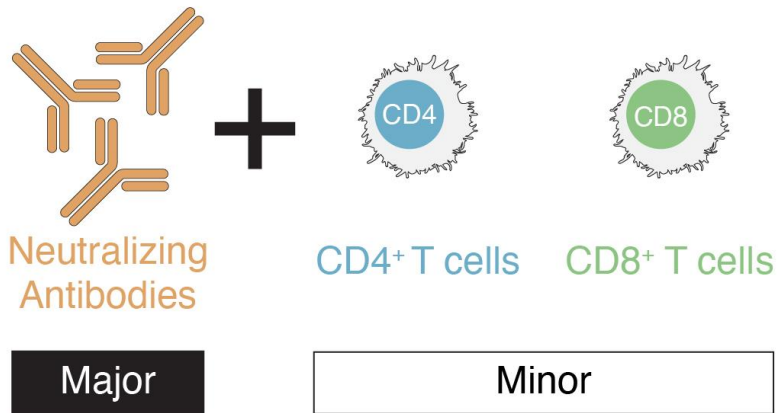
Or the swiss cheese model of immunity



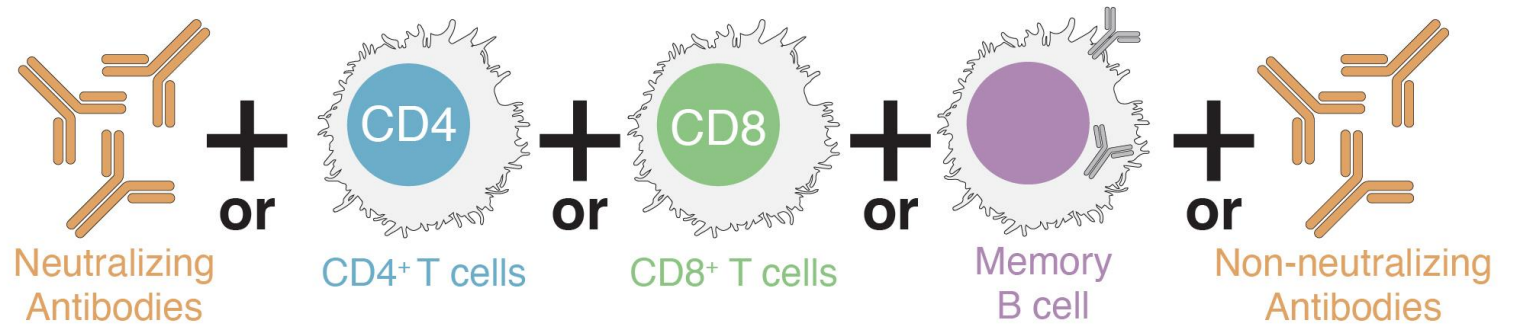
Vaccine protection against SARS-CoV-2



Protection against detectable infection



Protection against hospitalizations and deaths

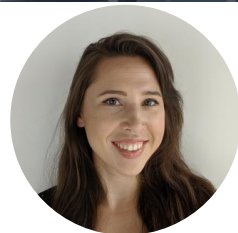


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Carolyn Rydyznski
Moderbacher, PhD



Sydney Ramirez,
MD/PhD



Prof. Jen Dan
MD/PhD



Yu 'Alex' Kato, PhD



Zeli Zhang, PhD



Donna Farber



Alison Tarke,
PhD student



Prof. Alex Sette



Alba Grifoni, PhD



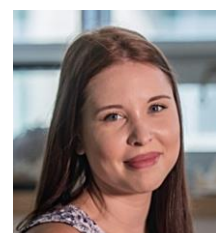
Prof. Daniela
Weiskopf



Jose Mateus, PhD



Maya Poon



Ksenia Rybkina



Camila Coelho, PhD

Crotty Lab

Carolyn Rydyznski
Moderbacher
Sydney Ramirez
Prof. Jennifer Dan
Yu 'Alex' Kato
JH Lee
Harry Sutton
Simon Belanger

Robert Abbott
Katia Faliti
Christina Kim
Eleanor Crotty
Jinyong Choi
Sonya Haupt
Zeli Zhang
Nate Bloom
Ben Goodwin

Sette Lab

Alba Grifoni
Alison Tarke
Esther Yu
Ricardo Da Silva
Antunes
Nils Methot
Jenna Memollo
April Frazier

Weiskopf Lab

Jose Mateus
James Chang

Farber Lab

Maya Poon
Ksenia Rybkina

Saphire Lab

Kathryn Hastie
Erica Ollmann
Saphire

Peters Lab

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Clinical Studies Core

Gina Levi
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Quinn Bui
Jasmine Cardenas

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Vanderbilt University

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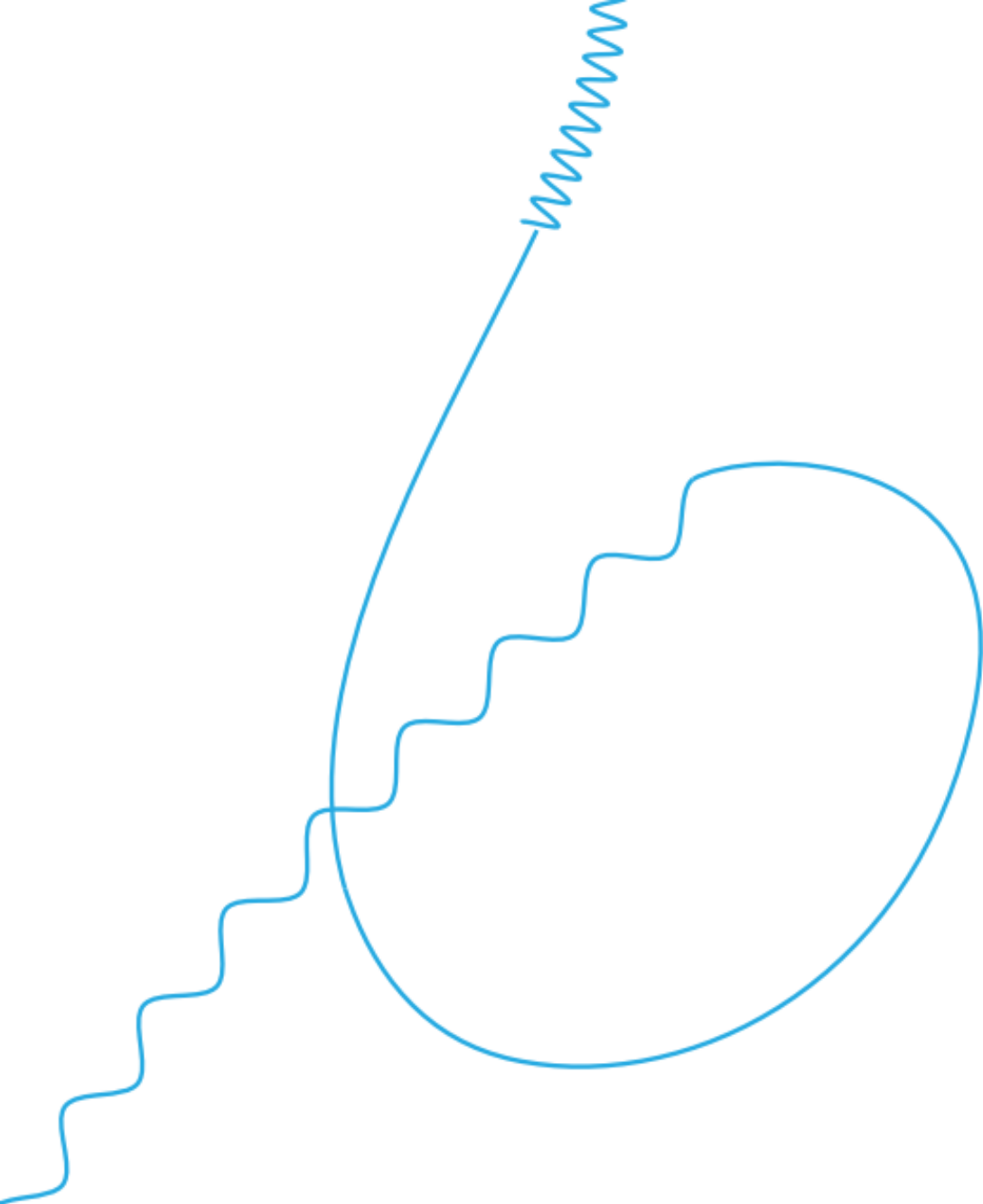
JCVI

Richard Scheuermann



Anonymous Philanthropic Support





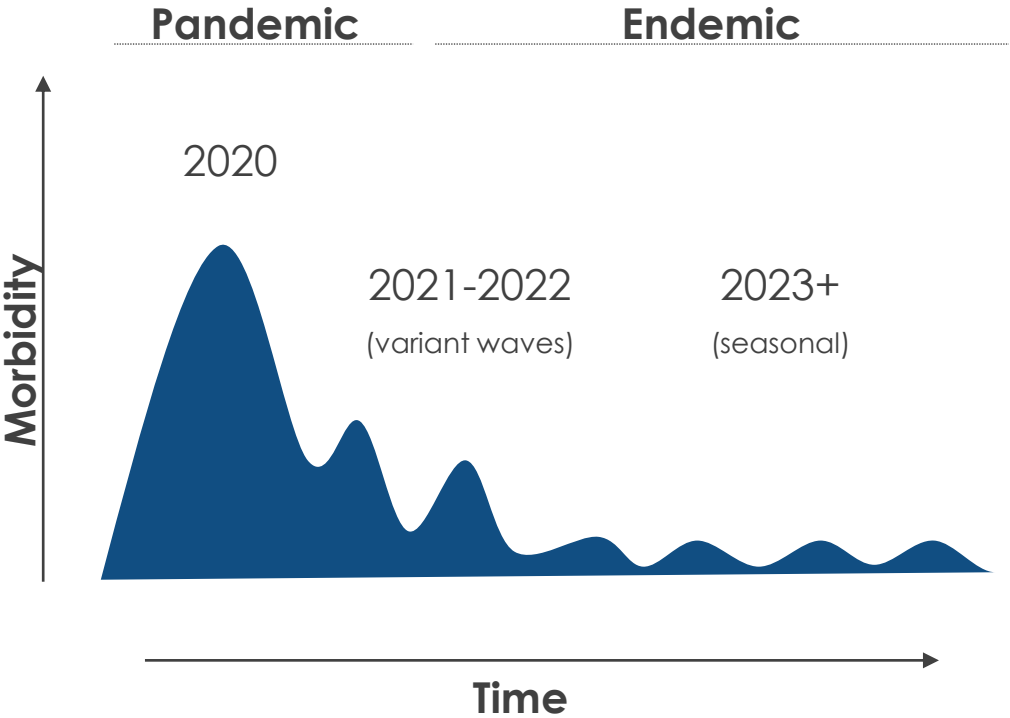
Moderna's COVID Strategy

Jacqueline Miller, M.D.

*Senior Vice President, Therapeutic Area
Head, Infectious Diseases, Moderna*

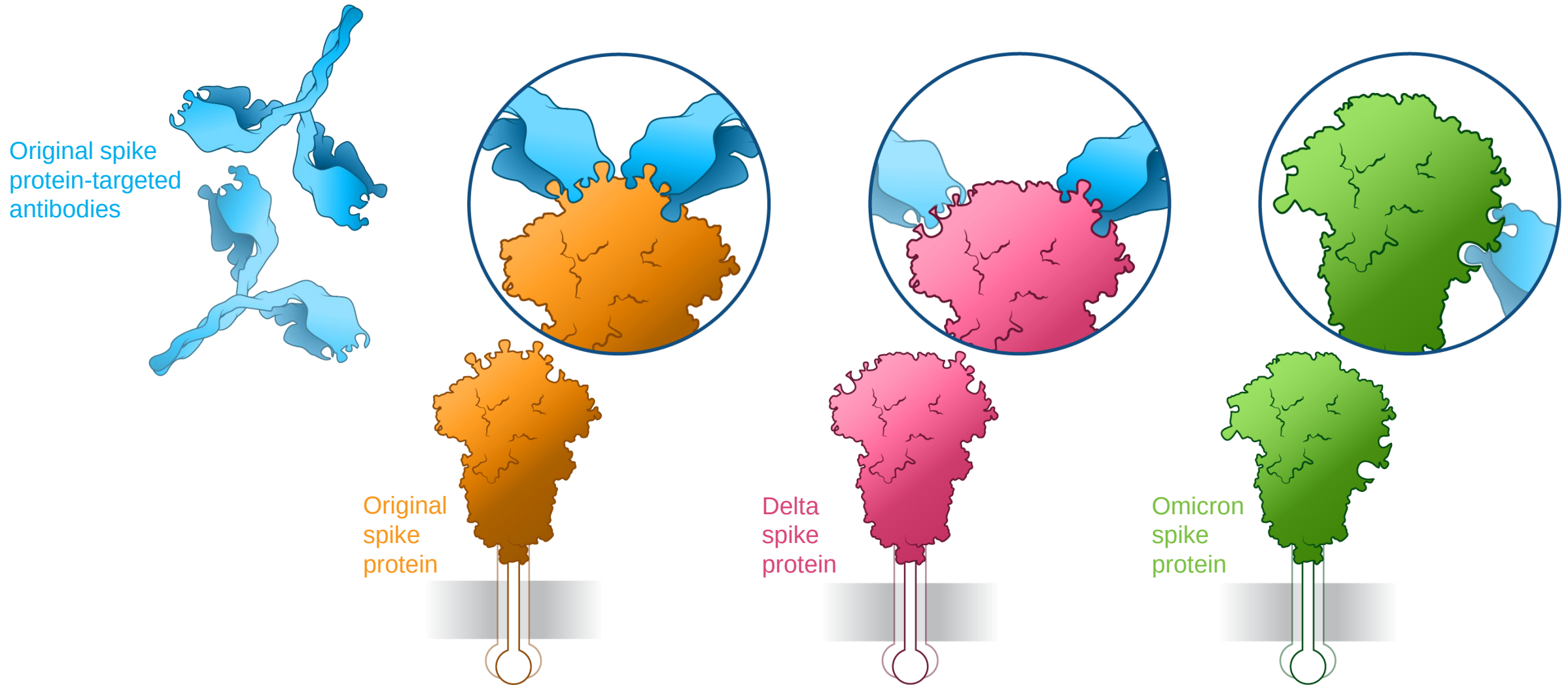
Transitioning into an endemic phase

ILLUSTRATIVE



Stage	Focus for vaccines
Pandemic <i>Initial waves</i>	• Heavy focus on protecting high-risk populations • Mostly ancestral virus vaccine
Variant <i>Reinfection waves</i>	• Focus on suppressing transmission of variants • Speed & adaptability are critical
Endemic <i>Seasonal</i>	• Focus on seasonal protection against waning immunity in high-risk • Multi-valent approaches with broadest immunity

We need to evaluate variant-containing boosters due to mutations in the RBD region



Moderna's booster strategy: Pursuing Omicron-containing boosters for adults aged 18+

1

Prototype booster (mRNA-1273)

- Prototype
- 50 µg dose

2

Omicron-specific booster (mRNA-1273.529)

- Omicron
- 50 µg dose

3

Bivalent booster (mRNA-1273.214)

- Prototype + Omicron
- 50 µg dose (25 µg of prototype, 25 µg of Omicron)

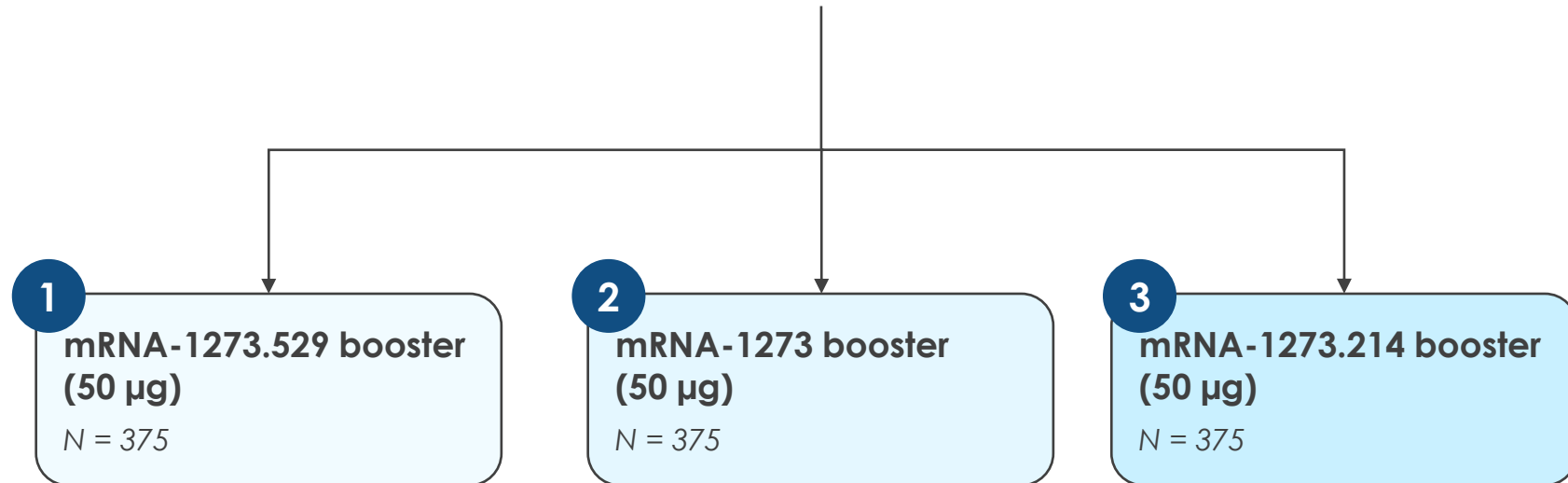
Moderna's booster strategy: Pursuing Omicron-containing boosters for adults aged 18+



U.S. Phase 2 (P205)

- Evaluating Omicron-specific candidate (.529) and Omicron-containing candidate (.214) as a *third or fourth dose*, compared to mRNA-1273 booster as a *fourth dose*
 - .529 also evaluated as a third dose in some participants
- Omicron-specific candidate (.529) group and mRNA-1273 group fully enrolled
- Currently enrolling and dosing .214 group

Recipients who previously received an mRNA-1273 primary series followed by an mRNA-1273 booster dose at least 3 months prior



Moderna's booster strategy: Pursuing Omicron-containing boosters for adults aged 18+



U.K. Phase 3 (P305)

Recipients who previously received any primary series (heterologous, incl. non-mRNA) with or without a booster dose

- Evaluating Omicron-containing candidates as a *third or fourth* dose compared to compared to mRNA-1273 booster as a *fourth* dose in individuals who received any primary series (heterologous, incl. non-mRNA)
- Currently enrolling both cohorts

1

mRNA-1273.529 OR mRNA-1273.214 booster (50 µg)

N = 1400

2

mRNA-1273 booster (50 µg)

N = 1400

Individuals previously received primary series vaccination +/- a booster dose (90% with 3 prior doses, 10% with 2 prior doses)

*Boosting of recipients of an adenovirus-vector vaccine with an mRNA vaccine permitted
≥3-month interval required between most recent dose & study vaccine*

Primary series and booster update in adolescent and pediatric populations

Spikevax®/Moderna COVID-19 Vaccine in ages <18

- **In adolescents aged 12-17 years:**
 - Primary series (2 dose, 100 µg) authorized/approved in more than 40 countries
 - Preparing to submit data for 50 µg booster
- **In children aged 6-11 years:**
 - Primary series (2 dose series, 50 µg) authorized/approved in Australia, Canada and the EU
 - Evaluating 25 µg dose as a primary series
 - Evaluating a booster dose
- **In children aged 6 months to <6 years:**
 - Primary series (2 dose, 25 µg) met primary endpoint
 - Moving forward with global regulatory submissions
- Working with the FDA on updating/filing data across all three age groups



Overall summary for pediatric data (6 months to <6 years old)

- **Two doses of 25 µg of mRNA-1273 met primary endpoint for infants (6m to < 2y) and young children (2-<6y)**
 - Reactogenicity: Acceptable for both age groups and generally consistent with what is seen in young adults, adolescents, and older children (6-<12 yr)
 - Safety: Profile favorable with ≥ 2 months follow up post-dose 2 in 2249 young children and 1288 infants
 - Immunobridging: 2 doses of 25 µg in infants and young children meet non-inferiority (NI) vs 100 µg in young adults (18-25y) in P301
 - Further supported by efficacy estimates in this age group
- **We will move forward with regulatory submissions for infants and young children both in US and outside of the US, for primary series of two doses of 25 µg**

Immunogenicity of mRNA-1273 is consistent across age groups

Age group	N	Dose	Neutralizing Ab GMT		GMR compared to young adults (18-25yo)
Adults: >18yo (P301)	1,053	100 µg	1027 (968, 1089)		N/A
Young adults: 18-25y (P301)	295	100 µg	Duke lab: 1301 (1177, 1439)	PPD lab*: 1391 (1262, 1532)	N/A
Adolescents: 12-17y (P203)	340	100 µg	1402 (1276 to 1539)		1.08 (0.94 to 1.24)
Young Children: 2-5y (P204)*	264	25 µg	1410 (1274, 1561)		1.01 (0.88, 1.17)
Infants: 6m-23m (P204)*	230	25 µg	1781 (1606, 1974)		1.28 (1.12, 1.47)

Safety summary <6 years – Primary endpoint

- Reactogenicity observed is consistent with known profile of mRNA-1273
- Solicited ARs were generally mild to moderate and more frequently reported after dose 2 than dose 1
 - Fever ($\geq 38^{\circ}\text{C}$) rates after dose 2 were observed to lower in the young children (17.0%) and infants (14.6%) than was seen in the older children (23.9%)
 - Fevers $> 40^{\circ}\text{C}$ PD2 were seen in 0.2% of children in both the young children and infants; 10 events occurred in mRNA-1273 PD2, and 5 were associated with URI symptoms
 - Fever after mRNA-1273 occurs predominantly on Day 1 or 2 and usually resolves within 1 day
- No study pause rules were met, safety profile favorable
- No deaths, no myocarditis/pericarditis and no MIS-C reported
- One related SAE, within 28 days of any vaccination, of (unwitnessed) febrile seizure, recovered with no sequelae
- Safety profile is consistent with other pediatric vaccines administered in this age group

Efficacy summary <6 years – Secondary endpoint

- Secondary endpoint of vaccine efficacy shows statistically significant (lower bound of 95% CI excludes 0) but lower efficacy against symptomatic infection during Omicron wave compared to prior variants
 - Omicron was the predominant variant during the pediatric trials – clinical endpoint efficacy in children
 - Efficacy against Omicron is consistent with two-dose effectiveness observed in adults
- Milder disease in children precludes assessment of efficacy against hospitalizations and/or deaths in a clinical study

We are also developing a next-generation COVID-19 vaccine candidate (mRNA-1283)



Refrigerator-stable

- Refrigerator-stable mRNA vaccine that will **facilitate distribution and administration** by healthcare providers
- mRNA-1283 encodes for the portions of the SARS-CoV-2 spike protein critical for neutralization, **specifically the Receptor Binding Domain (RBD) and N-terminal Domain (NTD)**
- Phase 1 study evaluated **mRNA-1283 as a primary series**
 - Safety, reactogenicity and immunogenicity across 3 dose levels

Phase 1 Trial Design

 D1  D29

Cohort 1 (mRNA-1283, 10 µg)
N=21

 D1  D29

Cohort 2 (mRNA-1283, 30 µg)
N=22

 D1  D29

Cohort 3 (mRNA-1283, 100 µg)
N=20

 D1  D29

Cohort 4 (mRNA-1283, 100 µg)
N=18

*Placebo + mRNA-1283
(single-dose arm)*

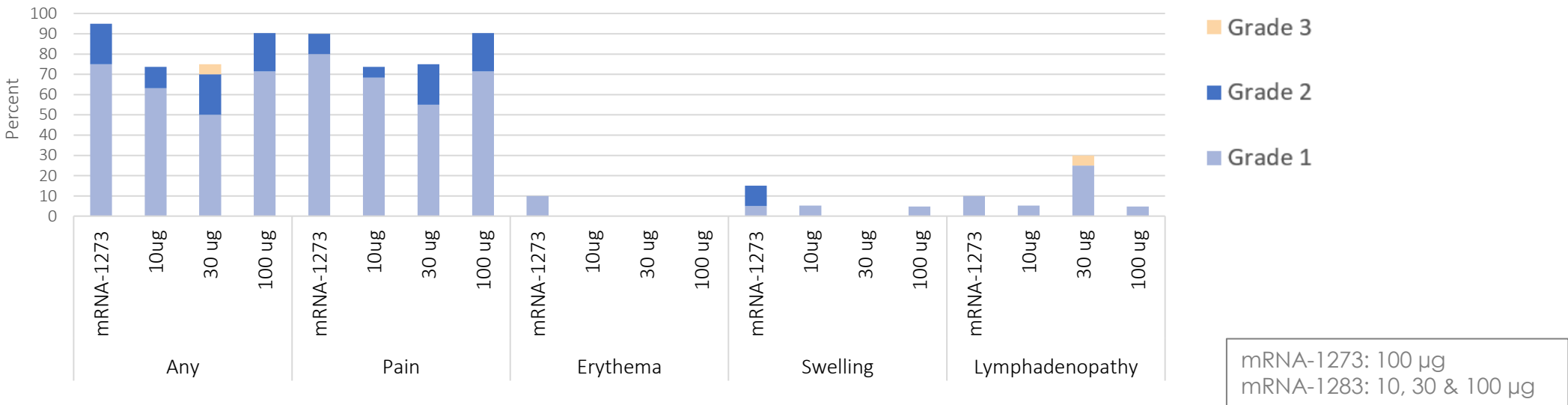
 D1  D29

Cohort 5 (mRNA-1273, 100 µg)
N=22

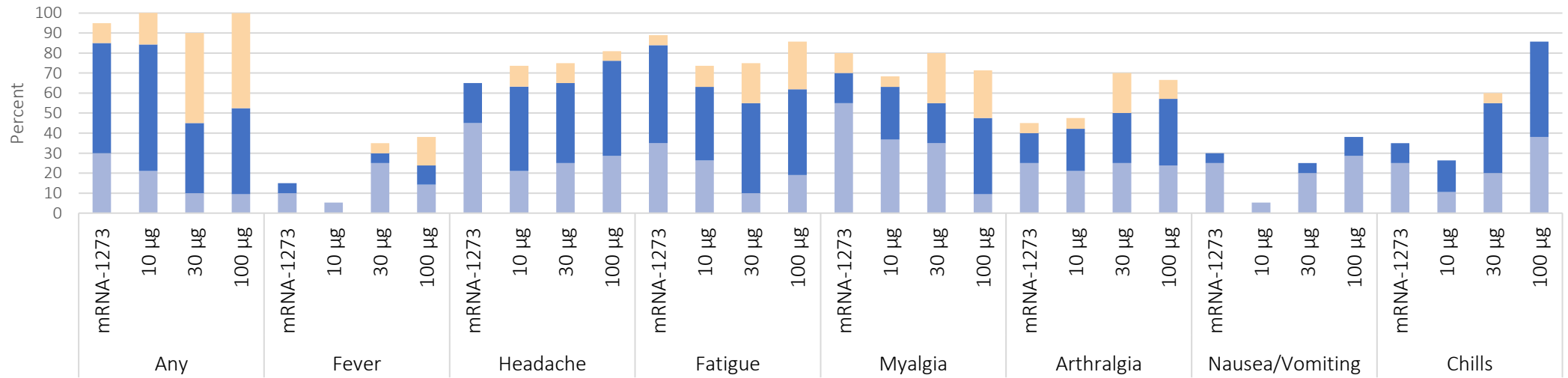
*Moderna COVID-19
Vaccine primary series*

Next-generation COVID-19 vaccine (mRNA-1283): Local & systemic adverse reactions (ARs) after the second dose

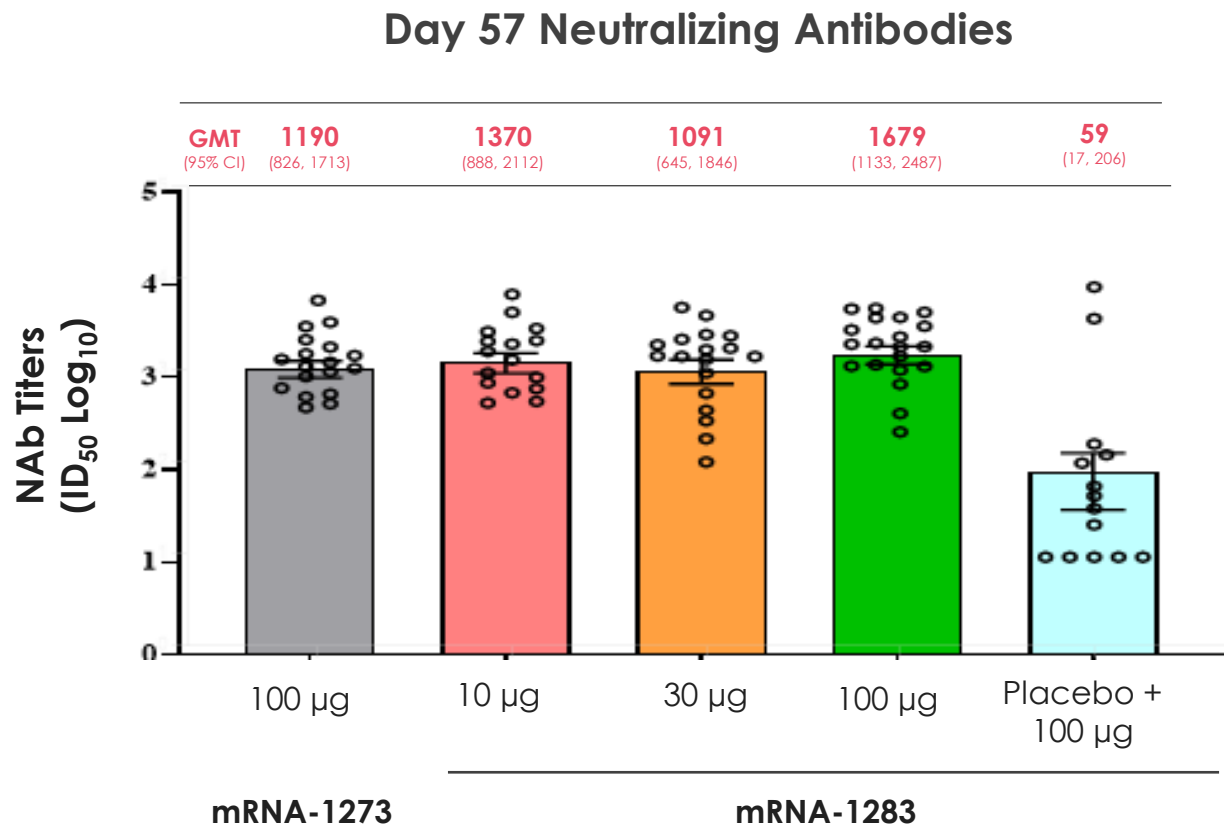
Local ARs within 7 days after second dose



Systemic ARs within 7 days after second dose

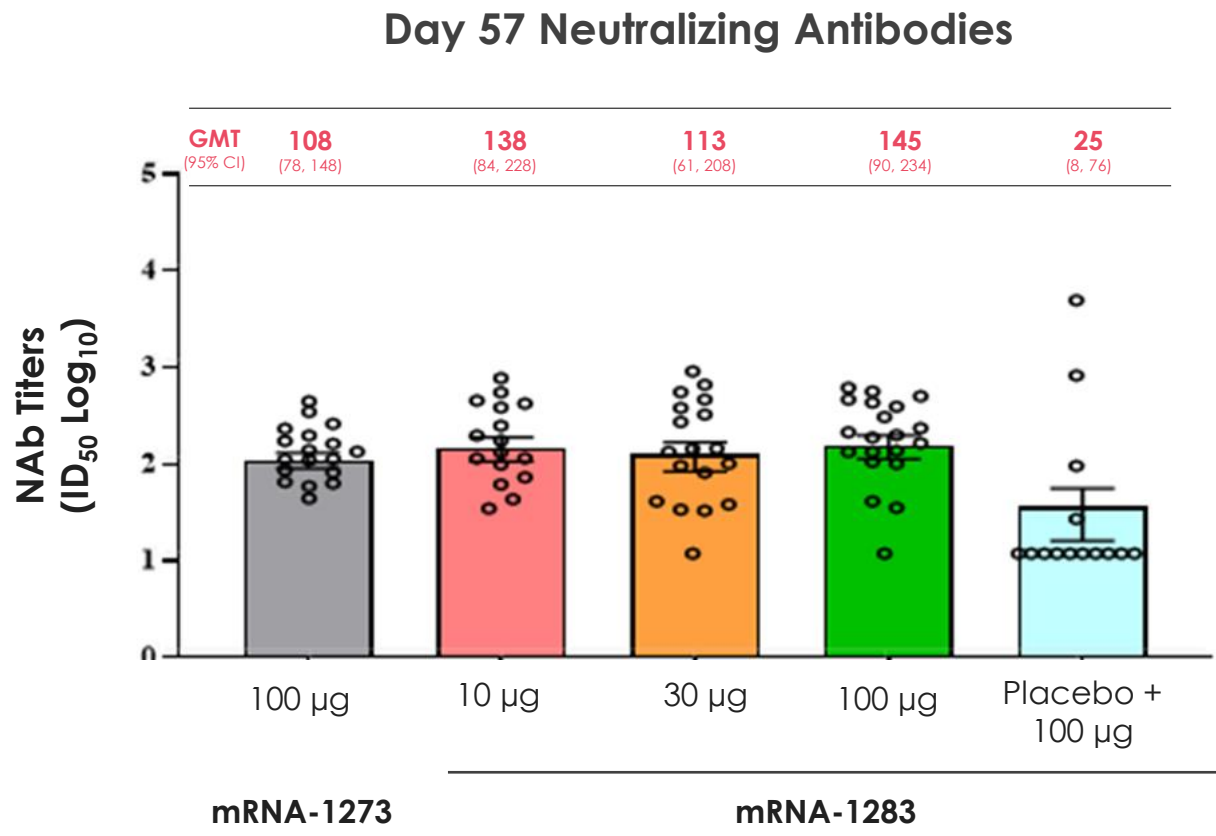


mRNA-1283 (two doses) elicits comparable levels of **ancestral SARS-CoV-2 neutralizing antibodies** compared to mRNA-1273



- Day 57 results indicate that the mRNA-1283 primary series induce **similar or numerically higher neutralizing antibody levels compared to the 100 µg mRNA-1273** primary series against the ancestral SARS-CoV-2 with the D614G mutation
- The unadjusted geometric mean ratio (GMR) of 1283 vs. 1273 at each dose level:
 - 10 µg was 1.2x
 - 30 µg was 0.9x
 - 100 µg was 1.4x

mRNA-1283 (two doses) elicits comparable levels of **Beta neutralizing antibodies** compared mRNA-1273



- Day 57 results indicate that the mRNA-1283 primary series **induce similar neutralizing antibody levels compared 100 µg mRNA-1273** primary series against the Beta (B.1.351) variant
- The unadjusted geometric mean ratio (GMR) of 1283 vs. 1273 at each dose level :
 - 10 µg was 1.3x
 - 30 µg was 1.1x
 - 100 µg was 1.3x

Next-generation COVID-19 vaccine (mRNA-1283): Phase 1 summary

- These preliminary results indicate that, when administered as primary series at lower doses levels (10 µg, 30 µg), **mRNA-1283 elicits a robust anti-SARS-CoV-2 neutralizing antibody response comparable to the 100 µg mRNA-1273 primary series**
- The frequency of local and systemic solicited adverse reactions of the **mRNA-1283 primary series administered at lower dose levels (10 µg, 30 µg) was overall comparable to mRNA-1273**
 - Most common local solicited adverse reaction was injection site pain
 - Most common systemic solicited adverse reactions were headache, fatigue and myalgia
- **Based on these results, we are investigating lower mRNA-1283 doses in a Phase 2 booster vaccine study**

We are currently evaluating mRNA-1283 in a **Phase 2 booster study**

- Part 2: Randomized, observer-blind study of a first booster dose of 1283, 1283.211 (prototype/beta variant), and 1283.529 (omicron), and mRNA-1273 (prototype)
- Enrollment is complete across all groups
- Phase 3 to potentially evaluate other multivalent mRNA-1273 candidates, such as ancestral SARS-CoV-2/Omicron

Phase 2 Trial Design

Part A: Booster dose after mRNA-1273 primary series (100 µg) >6 months

Cohort 1 (mRNA-1283, 2.5 µg)
N=~57

Cohort 2 (mRNA-1283, 5 µg)
N=~57

Cohort 3 (mRNA-1283, 10 µg)
N=~57

Cohort 4 (mRNA-1283.211, 5 µg)
N=~57

Cohort 5 (mRNA-1283.211, 10 µg)
N=~57

Cohort 6 (mRNA-1273 comparator, 50 µg)
N=~57

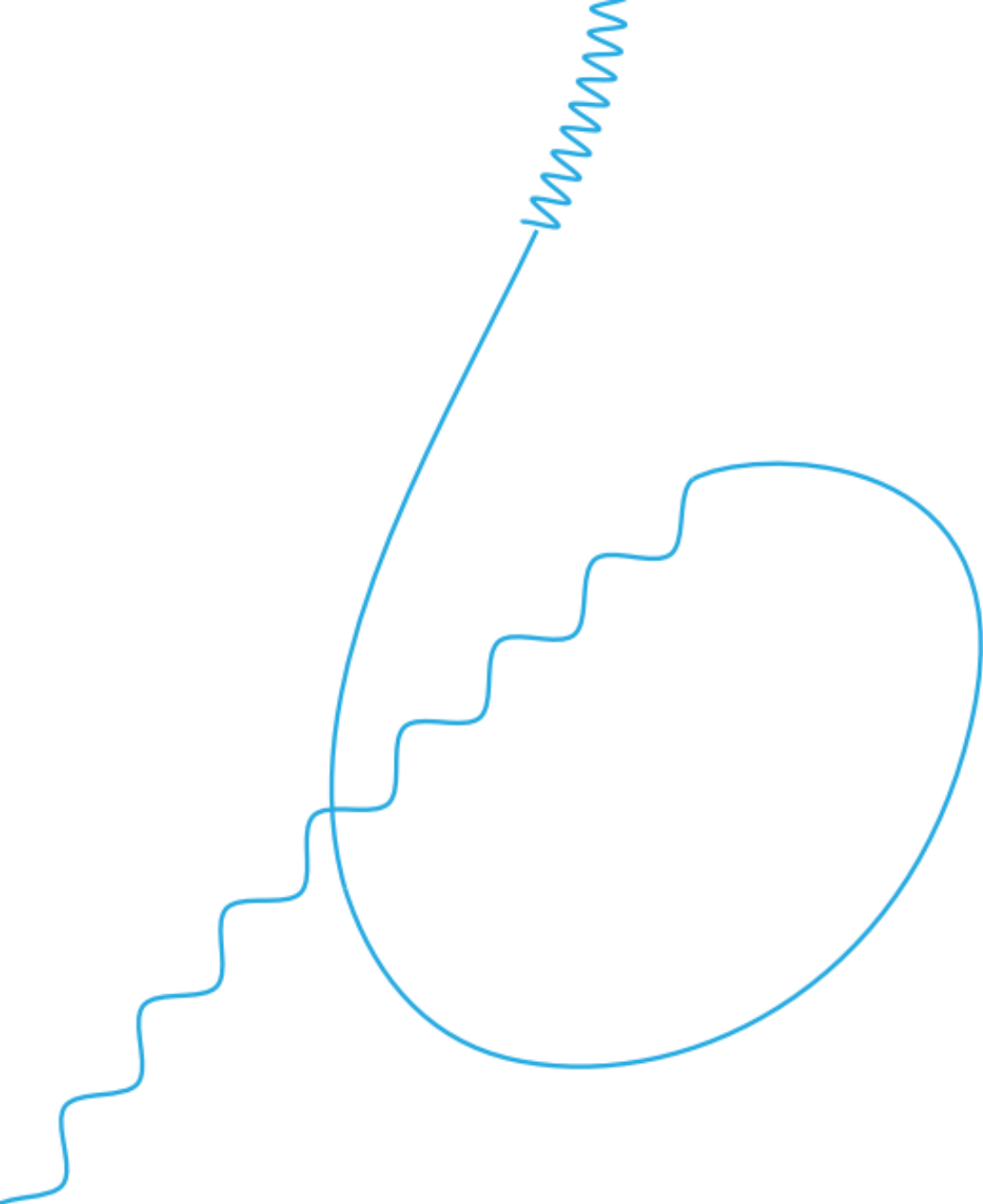
Part B: Booster dose after mRNA-1273 primary series (100 µg) and mRNA-1273 booster dose (50 µg) >3 months

Cohort 7 (mRNA-1283.529, 5 µg)
N=~100

Cohort 8 (mRNA-1283.529, 10 µg)
N=~100

mRNA-1283.211: SARS-CoV-2/Beta bivalent

mRNA-1283.529: Omicron monovalent



Moderna's Influenza Strategy

Jacqueline Miller, M.D.

*Senior Vice President, Therapeutic Area
Head, Infectious Diseases, Moderna*

Seasonal influenza (flu) overview

Seasonal influenza (influenza A and influenza B) occurs seasonally and varies in severity each year, causing respiratory illnesses and placing a substantial burden on healthcare systems

Disease burden:

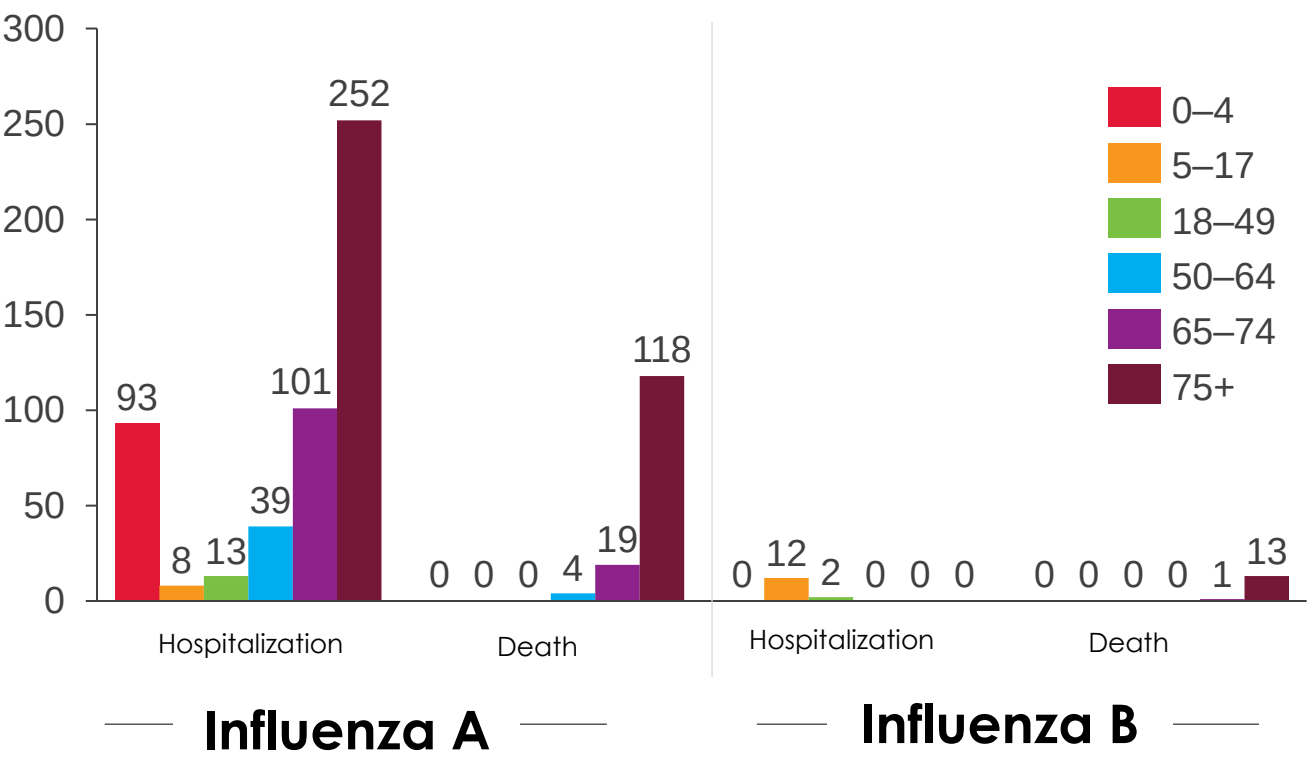
- Worldwide, influenza leads to 3-5M severe cases of influenza and 290-650K influenza-related respiratory deaths annually¹
- About 8% of the US population experiences symptoms from influenza each year, with 140-710K hospitalizations and 12-52K deaths per year²
- Peak influenza activity is seen in temperate climates during fall to winter and is reflected in increased outpatient visits, urgent care visits, and hospitalizations

Influenza symptoms & complications	
Symptoms	Fever Cough Sore throat Nasal congestion Fatigue Vomiting/diarrhea (more common in children)
Complications	Pneumonia (viral and/or bacterial) Ear infections Sinus infections Exacerbation of chronic conditions (e.g. asthma, heart failure)

1. World Health Organization. Influenza (Seasonal). WHO. 2018. [https://www.who.int/news-room/fact-sheets/detail/influenza-\(seasonal\)](https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal))
2. Centers for Disease Control and Prevention. Disease burden of influenza. Available at: <https://www.cdc.gov/flu/about/burden/index.html>

Influenza A strains lead to >95% of flu-related hospitalization in adults

Mean Seasonal Hospitalization and Mortality rates per 100K people in the UK (1997-2007)¹



- **Influenza A strains are the major driver of influenza-related hospitalizations and deaths**
- Recent study of VE from 2004-2015 found average VE of 33% against illnesses caused by H3N2 viruses, compared with 61% against H1N1 and 54% against influenza B virus illnesses²
- Lower vaccine efficacy (VE) against A(H3N2) viruses may contribute to the higher medical burden for Influenza A

1. Matias et al. BMC Public Health (2016), <https://doi.org/10.1186/s12889-017-4177-z>
2. Belongia et al. The Lancet (2016), [https://doi.org/10.1016/S1473-3099\(16\)00129-8](https://doi.org/10.1016/S1473-3099(16)00129-8)

Moderna's seasonal influenza vaccine strategy



Seasonal quadrivalent flu vaccine (mRNA-1010)

Using WHO recommended
strains

Speed to market approach
Established regulatory pathway
(subject to discussions with
regulators)



Beyond quadrivalent flu vaccines (mRNA-1011/1012)

Adding Hemagglutinin (HA)
antigens (e.g. H3N2, H1N1) to
expand strain matching

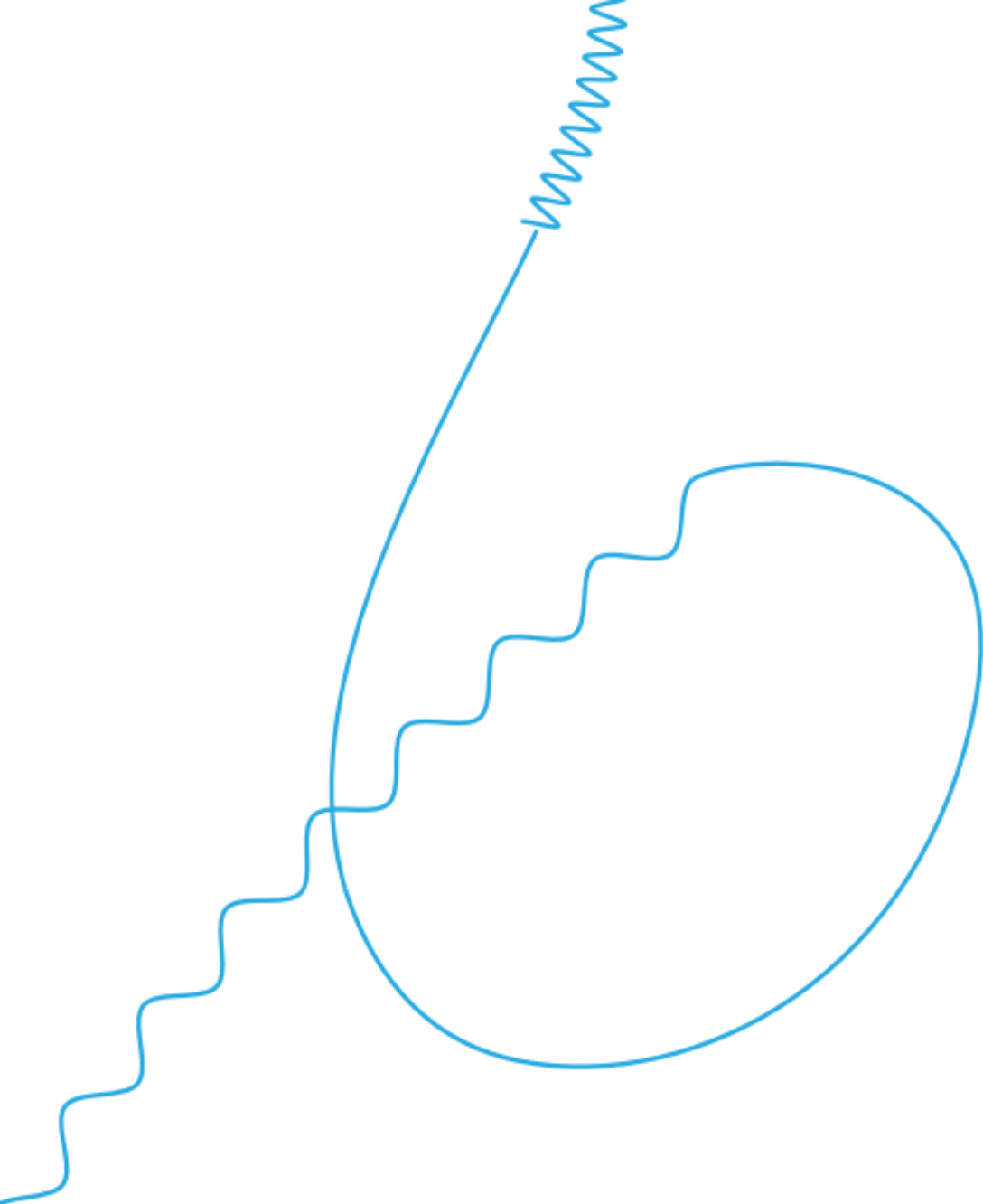
Provide an enhanced antigen
selection opportunity to public
health authorities; potential for
regional variation



Broader antigen flu vaccines (mRNA-1020/1030)

Adding Neuraminidase (NA)
antigens

Improve immunity by targeting
more conserved antigens



Moderna's Phase 2 Influenza Data Review

Raffael Nachbagauer, M.D., Ph.D.

*Senior Director, Infectious Disease
Development*

Influenza vaccine (mRNA-1010) Phase 2 trial overview

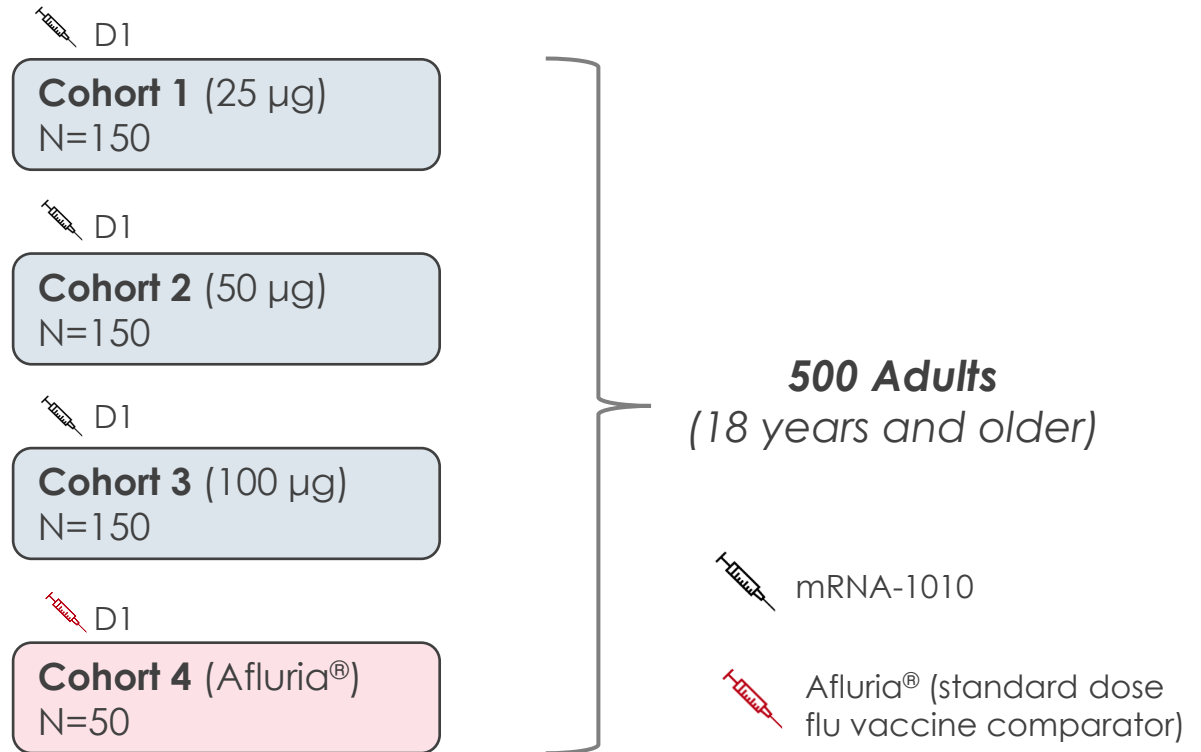
Trial Overview

- Evaluating safety and immunogenicity of different dose levels of the mRNA influenza vaccine
- Testing the Northern Hemisphere strains for the 2021/22 NH influenza season

Primary Outcome Measures

- Safety and immunogenicity at Day 29

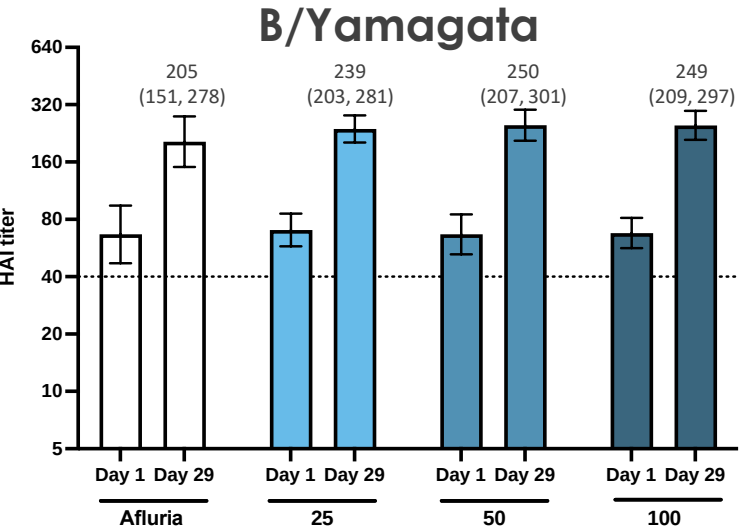
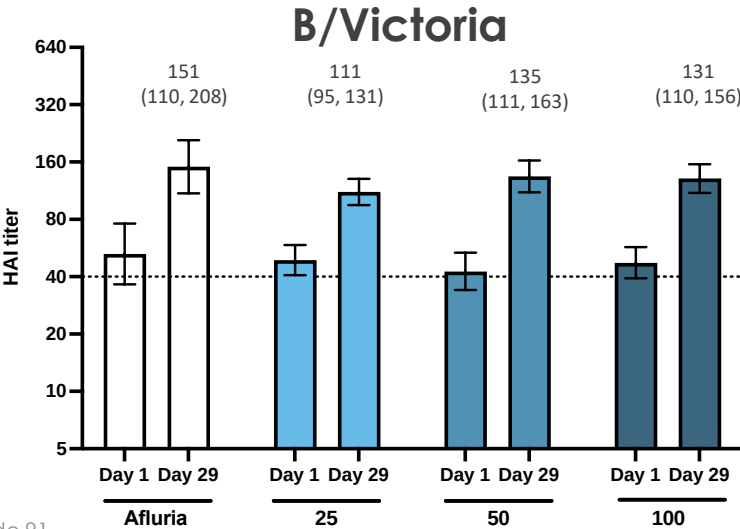
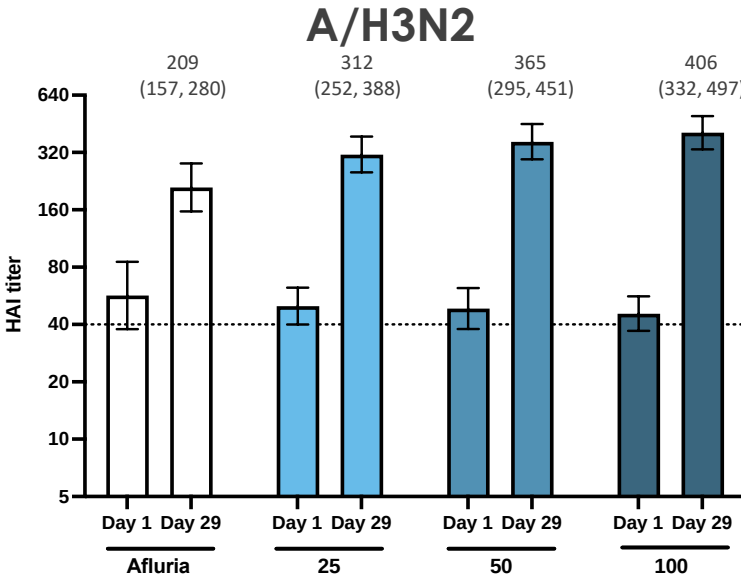
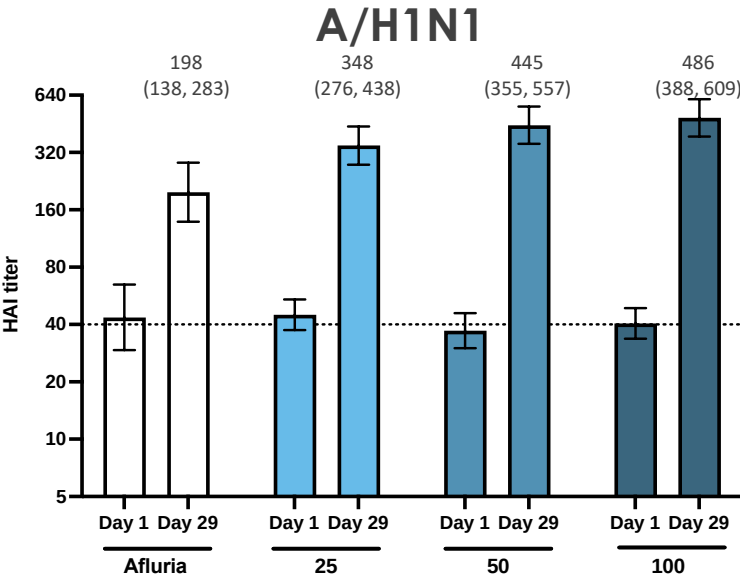
Phase 2 Trial Design



mRNA-1010 Phase 2 demographics

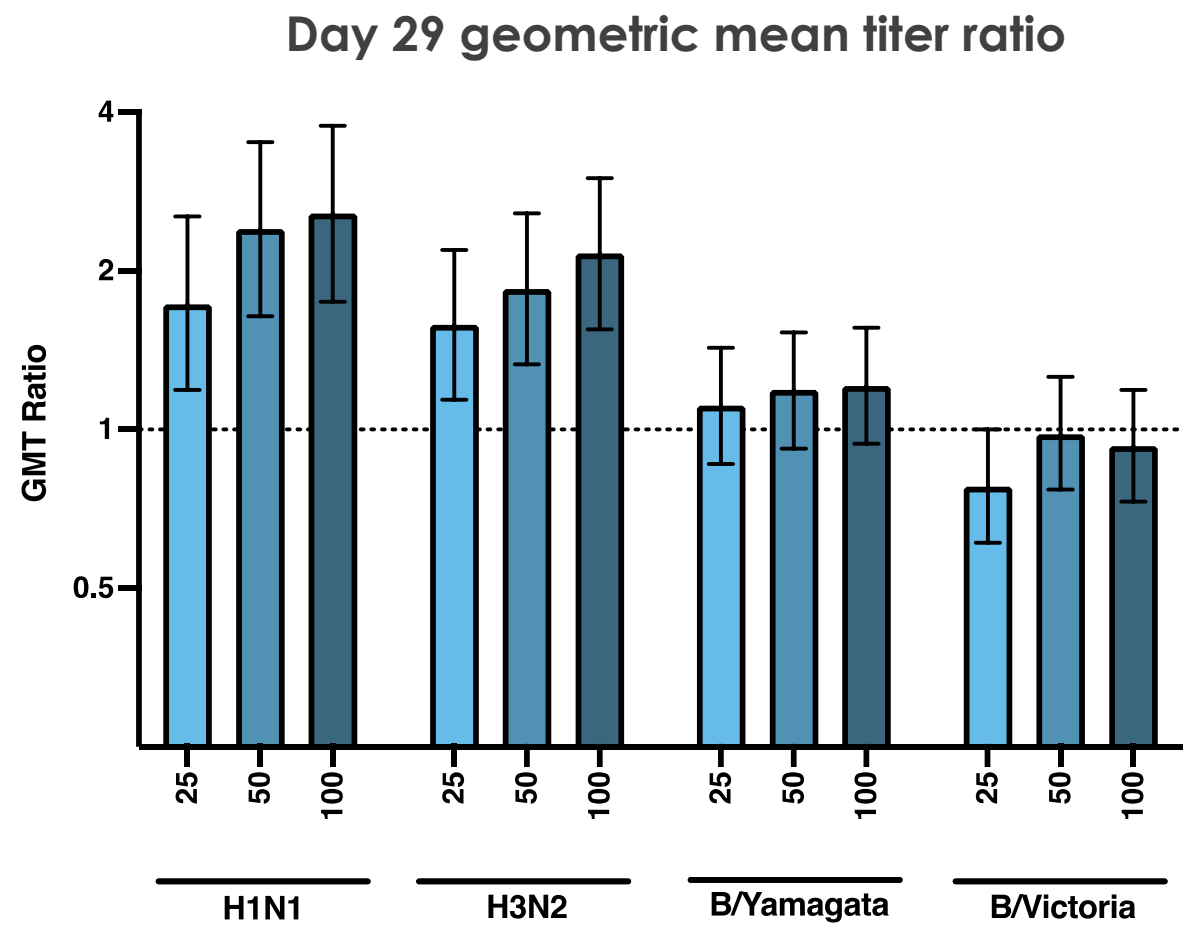
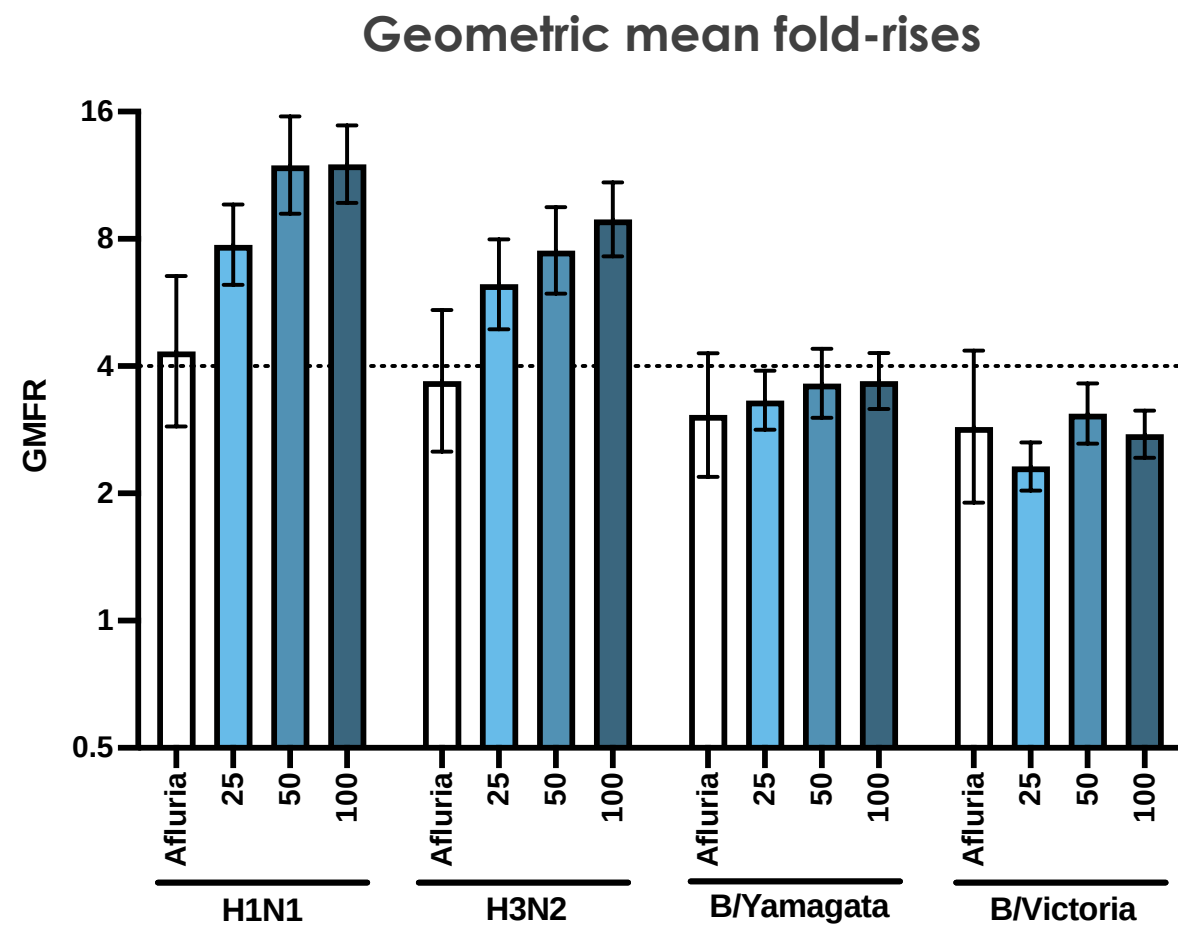
Group	18 to 49 years old				50 to 64 years old				65+ years old			
	Afluria	mRNA-1010 25 µg	mRNA-1010 50 µg	mRNA-1010 100 µg	Afluria	mRNA-1010 25 µg	mRNA-1010 50 µg	mRNA-1010 100 µg	Afluria	mRNA-1010 25 µg	mRNA-1010 50 µg	mRNA-1010 100 µg
N	21	60	58	59	20	60	57	57	12	31	32	31
Age (Mean, Min, Max)	35.9 (20, 49)	34.3 (18, 49)	34.5 (19, 49)	32.4 (18, 47)	56.0 (50, 64)	56.0 (50, 64)	54.9 (50, 64)	56.3 (50, 64)	73.8 (66, 86)	70.5 (65, 86)	71.1 (65, 81)	71.7 (65, 82)
% Female	57.1	55.0	56.9	55.9	45	58.3	49.1	64.9	66.7	67.7	59.4	51.6
% Male	42.9	45.0	43.1	44.1	55	41.7	50.9	35.1	33.3	32.3	40.6	48.4
% White	71.4	76.7	77.6	81.4	80	85	75.4	78.9	100	90.3	87.5	83.9
% Black or African American	14.3	13.3	19	11.9	15	8.3	8.8	14.0	0	9.7	6.3	9.7
% Asian	0	3.3	1.7	1.7	0	0	1.8	1.8	0	0	3.1	0
% Other	14.3	6.7	1.7	5	5	6.7	14	5.3	0	0	3.1	6.4

Geometric mean titers (GMTs) across all ages

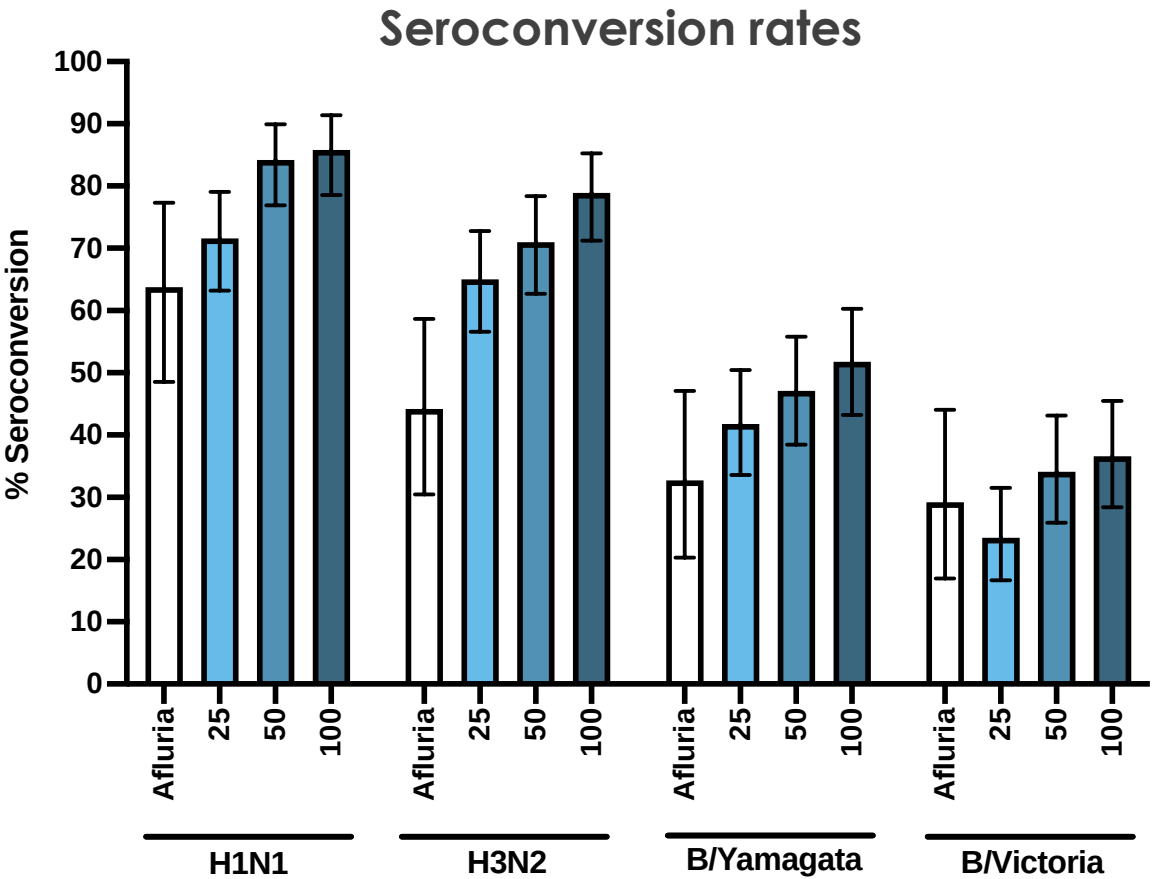


- mRNA-1010 elicits high HAI antibody titers, substantially exceeding 1:40 threshold associated with a 50% reduction in risk of infection
- Day 29 antibody levels are comparable to Afluria for influenza B and higher than Afluria for influenza A strains

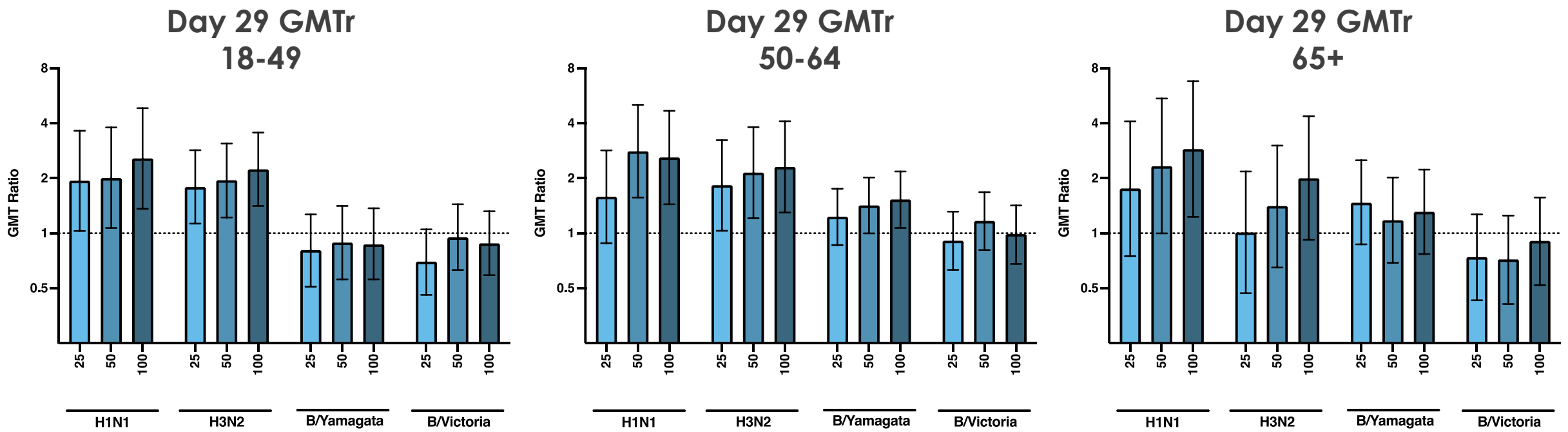
Geometric mean fold-rises (GMFRs) and geometric mean titer ratios (GMTrs) across all ages



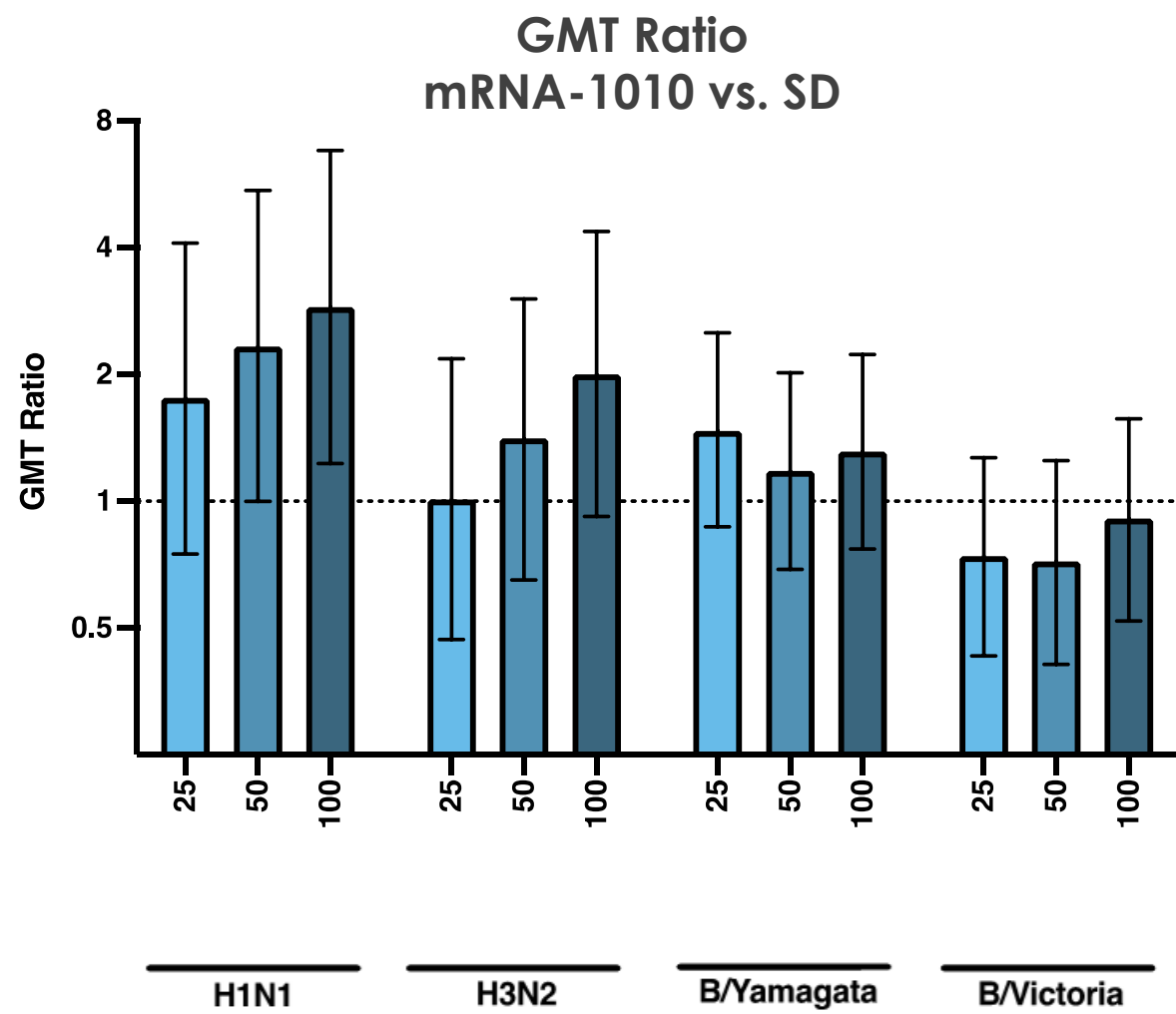
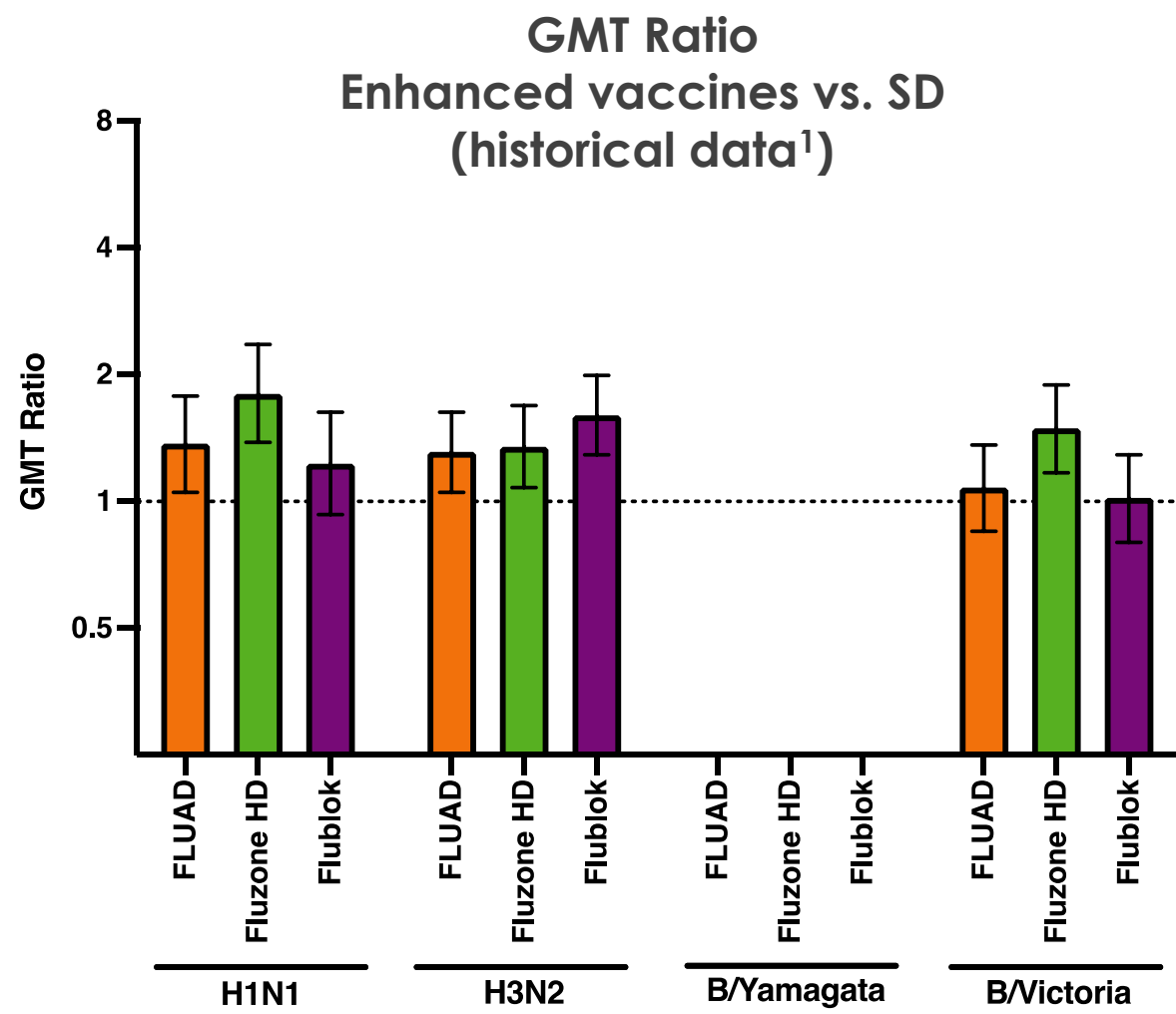
Seroconversion rates across all ages



mRNA-1010 responses were generally consistent across all ages: GMTs by age group



GMT ratio of enhanced vaccines vs. SD vaccine (historical data) compared to mRNA-1010 vs. SD vaccine in older adults



(1) Cowling, Benjamin et al., *Clin Infect Dis* (2020), <https://doi.org/10.1093/cid/ciz1034>

mRNA-1010 Phase 2 interim analysis: **Solicited local adverse reactions**

	18 to 49 years old				50 to 64 years old				65+ years old			
Solicited Adverse Reaction	Afluria % (N=21)	25 µg % (N=60)	50 µg % (N=57)	100 µg % (N=58)	Afluria % (N=19)	25 µg % (N=58)	50 µg % (N=58)	100 µg % (N=57)	Afluria % (N=13)	25 µg % (N=31)	50 µg % (N=31)	100 µg % (N=30)
Any	42.9%	83.3%	84.2%	93.1%	36.8%	72.4%	84.5%	80.7%	30.8%	67.7%	83.9%	80.0%
95% CI	21.8, 66.0	71.5, 91.7	72.1, 92.5	83.3, 98.1	16.3, 61.6	59.1, 83.3	72.6, 92.7	68.1, 90.0	9.1, 61.4	48.6, 83.3	66.3, 94.5	61.4, 92.3
Grade 1	38.1%	70%	56.1%	39.7%	31.6%	51.7%	55.2%	50.9%	23.1%	58.1%	74.2%	53.3%
Grade 2	4.8%	13.3%	21.2%	37.9%	--	19%	24.1%	21.1%	7.7%	3.2%	9.7%	53.3%
Grade 3	--	--	7%	15.5%	5.3%	1.7%	5.2%	8.8%	--	6.5%	--	6.7%
Grade 4	--	--	--	--	--	--	--	--	--	--	--	--

- No serious adverse events related to the study vaccine or pause rules were observed through Day 29
- The most common solicited local ARs were pain and axillary swelling/tenderness

mRNA-1010 Phase 2 interim analysis: **Solicited systemic adverse reactions**

	18 to 49 years old				50 to 64 years old				65+ years old			
Solicited Adverse Reaction	Afluria % (N=21)	25 µg % (N=60)	50 µg % (N=57)	100 µg % (N=58)	Afluria % (N=19)	25 µg % (N=58)	50 µg % (N=58)	100 µg % (N=57)	Afluria % (N=13)	25 µg % (N=31)	50 µg % (N=31)	100 µg % (N=30)
Any	42.9%	85.0%	73.7%	91.4%	31.6%	68.4%	75.9%	75.4%	38.5%	48.4%	77.4%	76.7%
95% CI	21.8, 66.0	73.4, 92.9	60.3, 84.5	81.0, 97.1	12.6, 56.6	54.8, 80.1	62.8, 86.1	62.2, 85.9	13.9, 68.4	30.2, 66.9	58.9, 90.4	57.7, 90.1
Grade 1	19%	31.7%	24.6%	12.1%	10.5%	33.3%	27.6%	19.3%	38.5%	22.6%	32.3%	30%
Grade 2	23.8%	43.3%	33.3%	56.9%	10.5%	29.8%	37.9%	42.1%	--	25.8%	29%	36.7%
Grade 3	--	10%	15.8%	22.4%	10.5%	5.3%	10.3%	14%	--	--	16.1%	10%
Grade 4	--	--	--	--	--	--	--	--	--	--	--	--

- No serious adverse events related to the study vaccine or pause rules were observed through Day 29
- The most common solicited systemic ARs were myalgia, headache and fatigue

Influenza vaccine (mRNA-1010) Phase 2 safety summary

- **The solicited adverse reactions were higher in the mRNA-1010 groups than in the Afluria group**
 - Most common local solicited adverse reactions were pain and axillary swelling/tenderness
 - Most common systemic solicited adverse reactions were myalgia, headache and fatigue
 - Local and systemic solicited adverse reactions were mostly mild to moderate in severity without any Grade 4 adverse reactions
- **No significant safety concerns were identified at the time of interim analysis;** no AESIs or AEs leading to study pauses; No SAEs that were assessed as related to the study vaccine

mRNA-1010 Phase 2 interim analysis summary

- The immunogenicity data at D29 is consistent with a potential for superiority to standard dose vaccine for influenza A strains (which drive majority of disease in adults)
- The data is consistent with potential for non-inferiority to standard dose vaccine in influenza B strains (primarily a concern in pediatrics)
- Consistent profile across ages; GMTs for influenza A strains in 65+ appear higher than published GMTs for enhanced vaccines
- No major safety concerns/issues; overall reactogenicity is 2-3x standard dose vaccine (appears to mirror immunogenicity)

Moderna's seasonal influenza vaccine strategy



**Seasonal quadrivalent
flu vaccine**
(mRNA-1010)

Using WHO recommended
strains

Speed to market approach
Established regulatory pathway
(subject to discussions with
regulators)



**Beyond quadrivalent
flu vaccines**
(mRNA-1011/1012)

Adding Hemagglutinin (HA)
antigens (e.g. H3N2, H1N1) to
expand strain matching

Provide an enhanced antigen
selection opportunity to public
health authorities; potential for
regional variation



**Broader antigen flu
vaccines**
(mRNA-1020/1030)

Adding Neuraminidase (NA)
antigens

Improve immunity by targeting
more conserved antigens

Ali Ellebedy, Ph.D., Washington University School of Medicine



Ali Ellebedy, Ph.D.

*Washington University School of
Medicine*

Ali Ellebedy is a viral immunologist. He was born in Egypt. He graduated with a B.S. in pharmaceutical sciences from Cairo University in 2004. It was during his time at pharmacy school that he was first exposed to- and became fascinated with- viruses and immunology. In 2006, he moved to the US where he studied influenza viruses at St Jude Children's Research Hospital in Memphis, TN for his Ph.D. studies. He earned his Ph.D. in 2011 and moved to Emory University in Atlanta, GA, where he was a postdoctoral fellow in the laboratory of Rafi Ahmed. At Emory, he studied human B cell responses to influenza. In 2017, Ali joined the Department of Pathology and Immunology at Washington University School of Medicine in St. Louis as an Assistant Professor. His team studies the factors determining the ultimate fate of B cells once they are engaged via virus infection or vaccination. He is now a tenured associate professor and co-director of the Center for Vaccines and Immunity to Microbial Pathogens at Washington University School of Medicine.

Enhancing B cell response to influenza virus vaccination in humans

Ali Ellebedy, Ph.D.

Associate Professor of Pathology and Immunology
Co-Director, Center for Vaccines and Immunity to
Microbial Pathogens (CVIMP)



Moderna

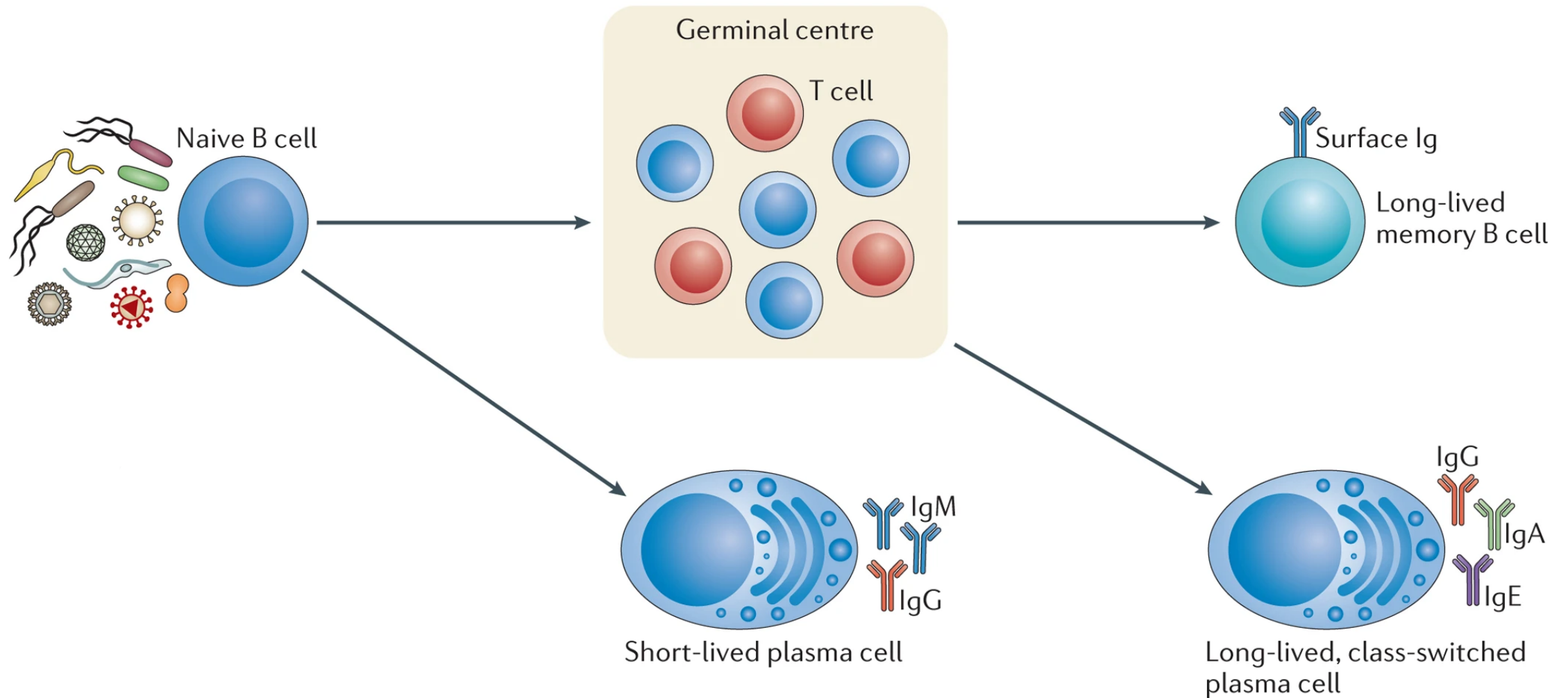
Department of Pathology, Microbiology & Immunology

Thursday, March 24th 2022

Disclosures

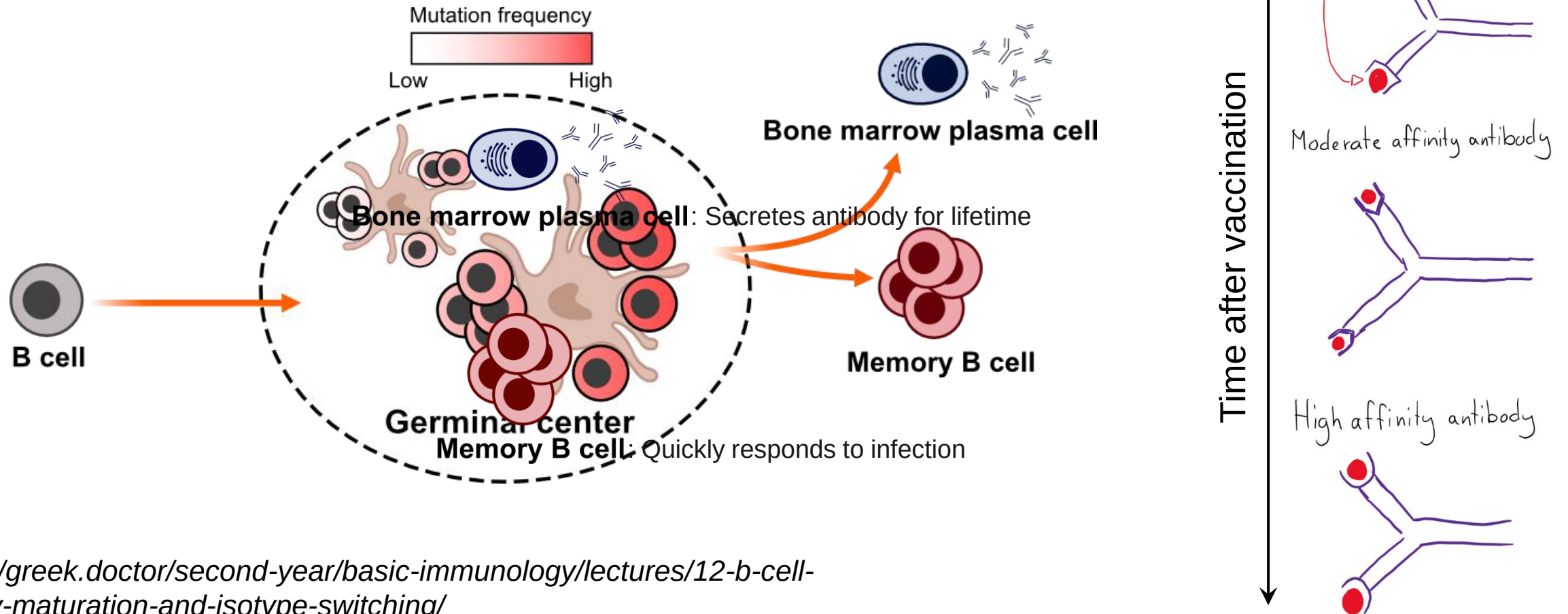
- **Washington University has applied for patents related to some of our anti-influenza virus and anti-SARS-CoV-2 monoclonal antibodies**
- **My laboratory has received funding support in sponsored research agreements from AbbVie, Moderna and Emergent BioSolutions.**
- **I have received consulting fees from InBios International, Inc, Fimbrion Therapeutics, Mubadala Investment Company and Goldman Sachs**

Division of labor in B cell responses

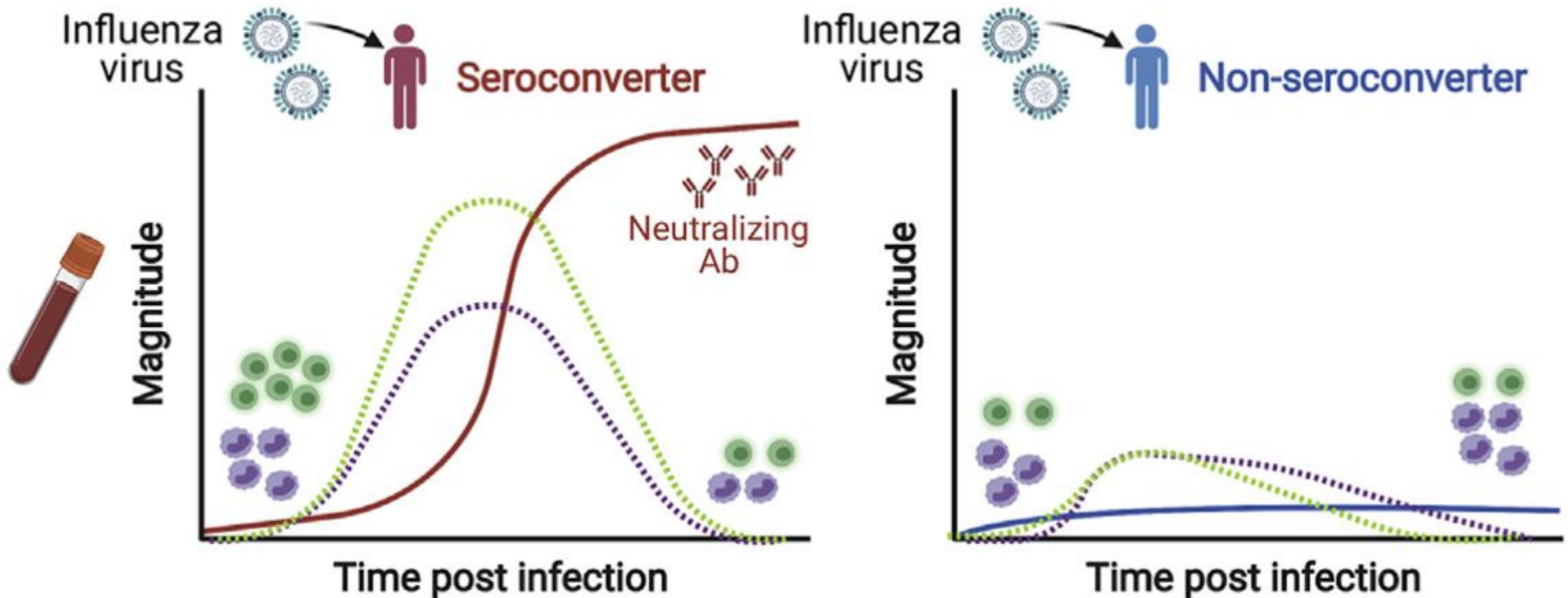


Germinal center reaction is key for affinity maturation of responding B cells

In germinal center, B cells acquire affinity-enhancing somatic hypermutations

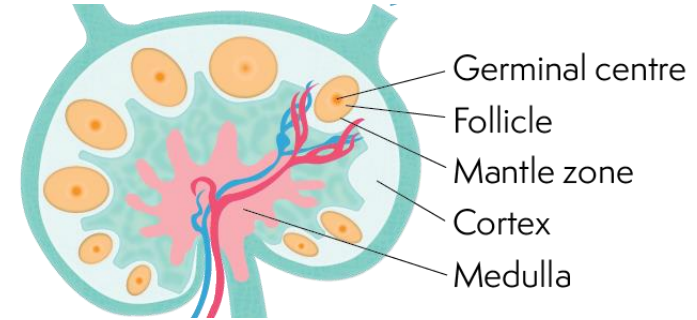
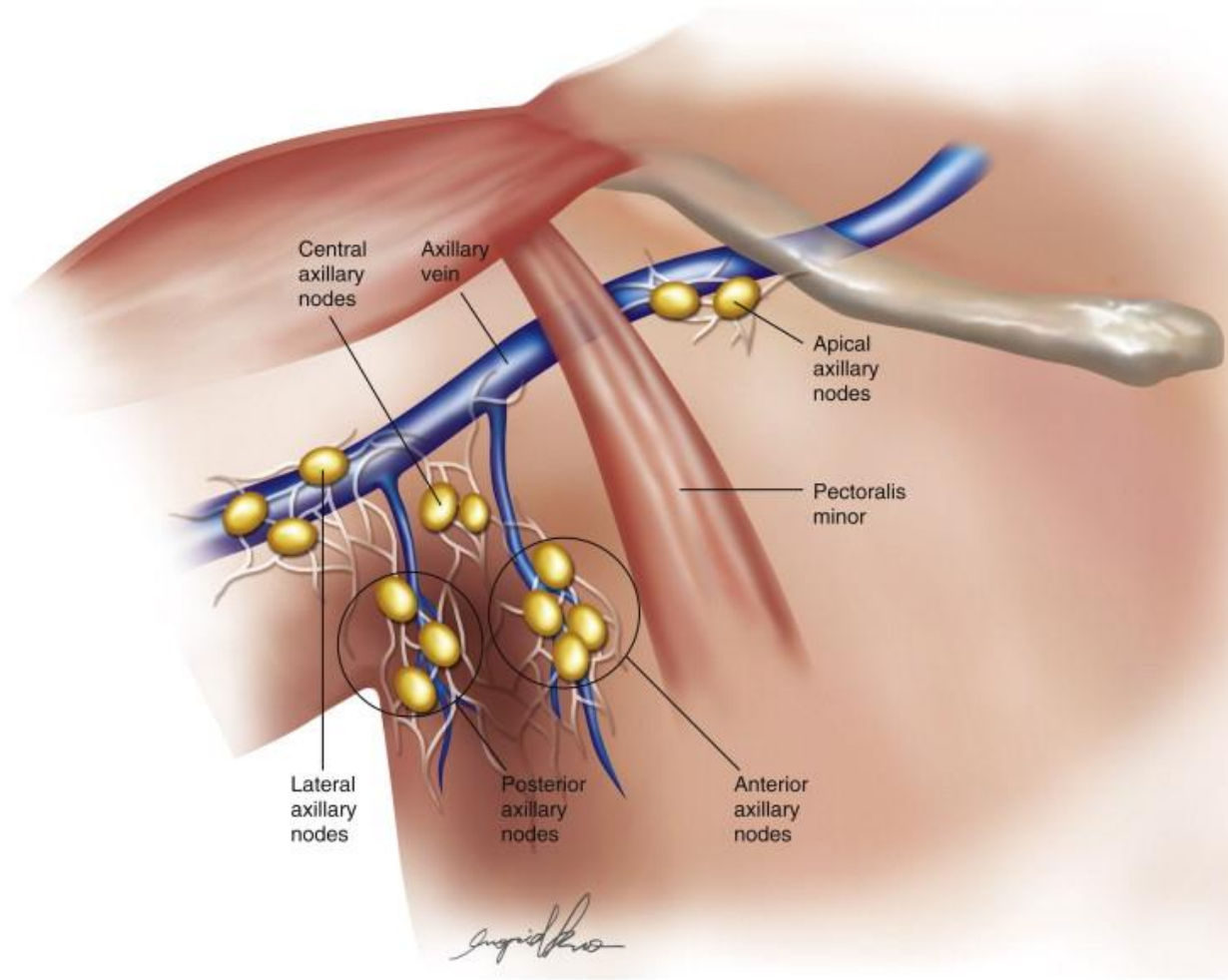


Antibody response to influenza viruses in humans

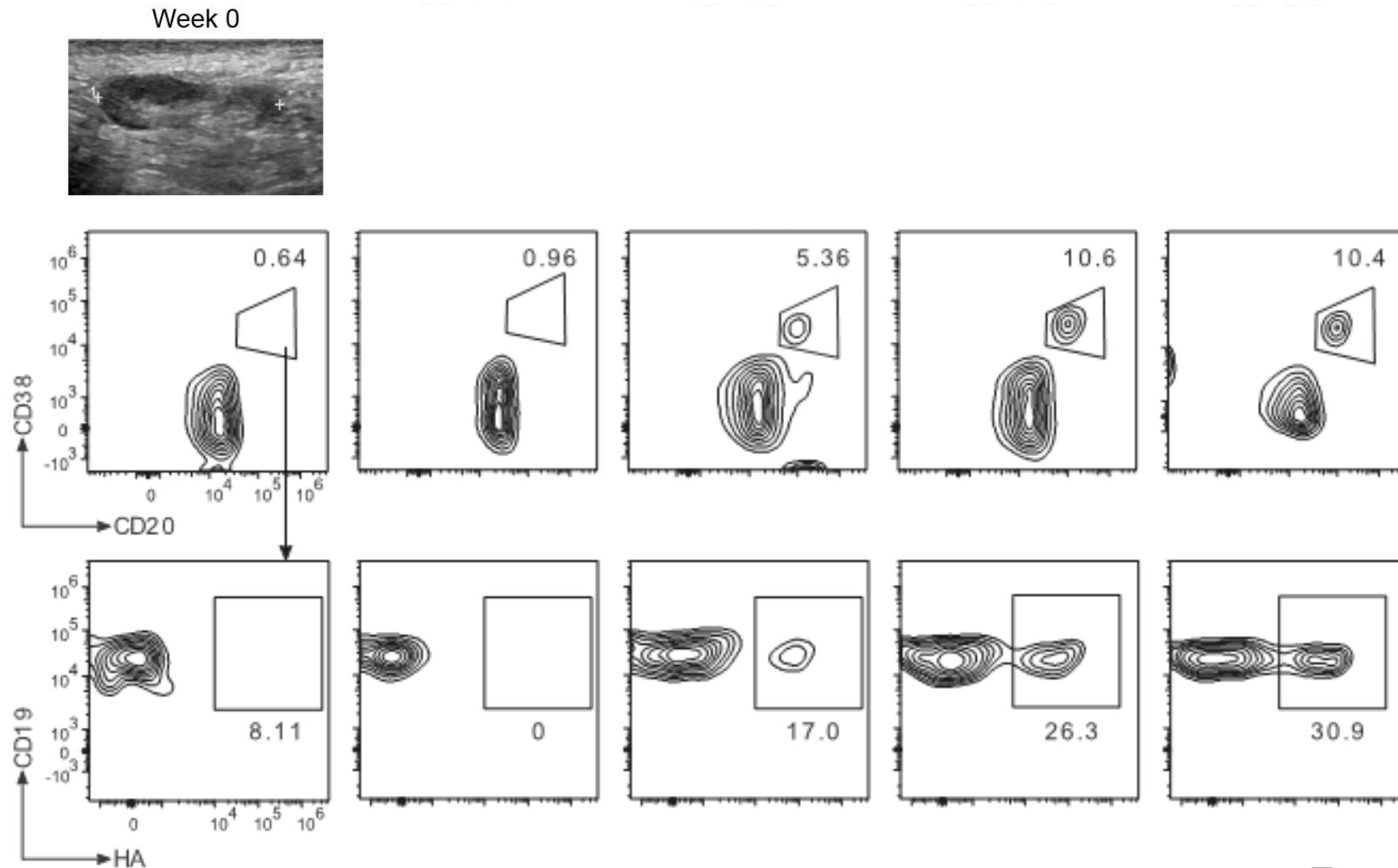


**How to study the germinal center reaction
in humans?**

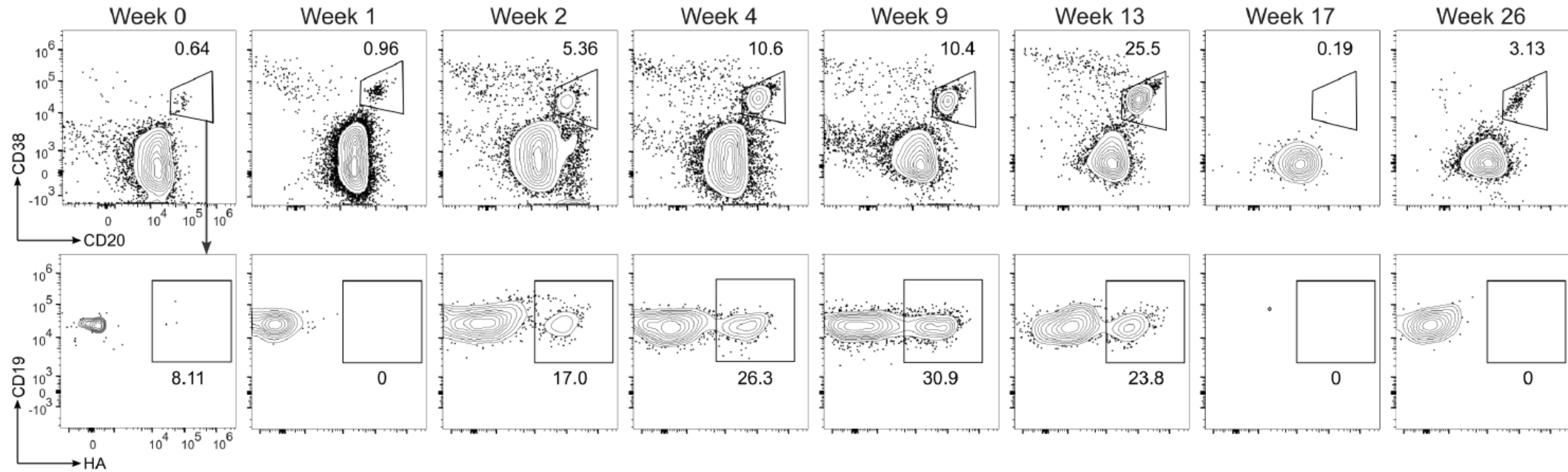
Fine needle aspiration of draining LNs



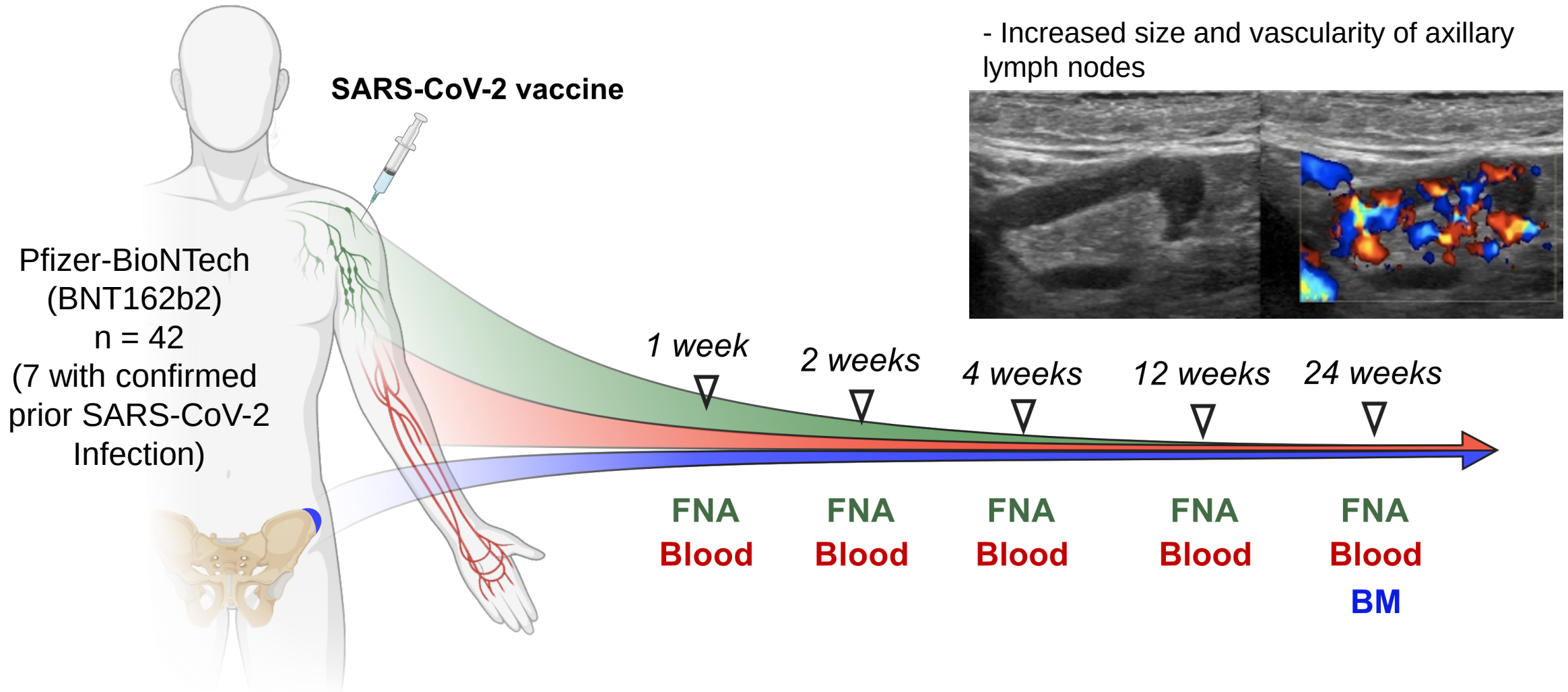
Detection of vaccine-induced GC responses after influenza virus vaccination



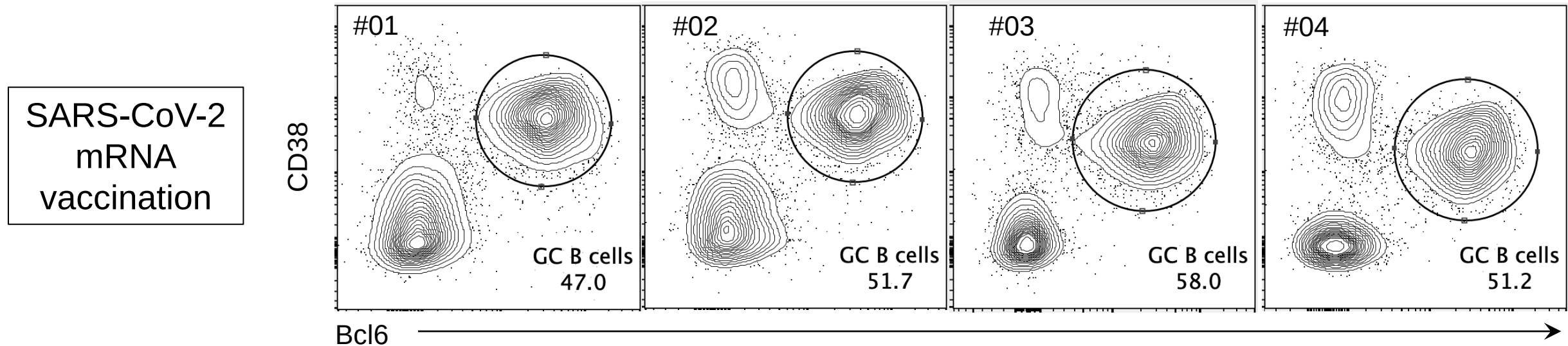
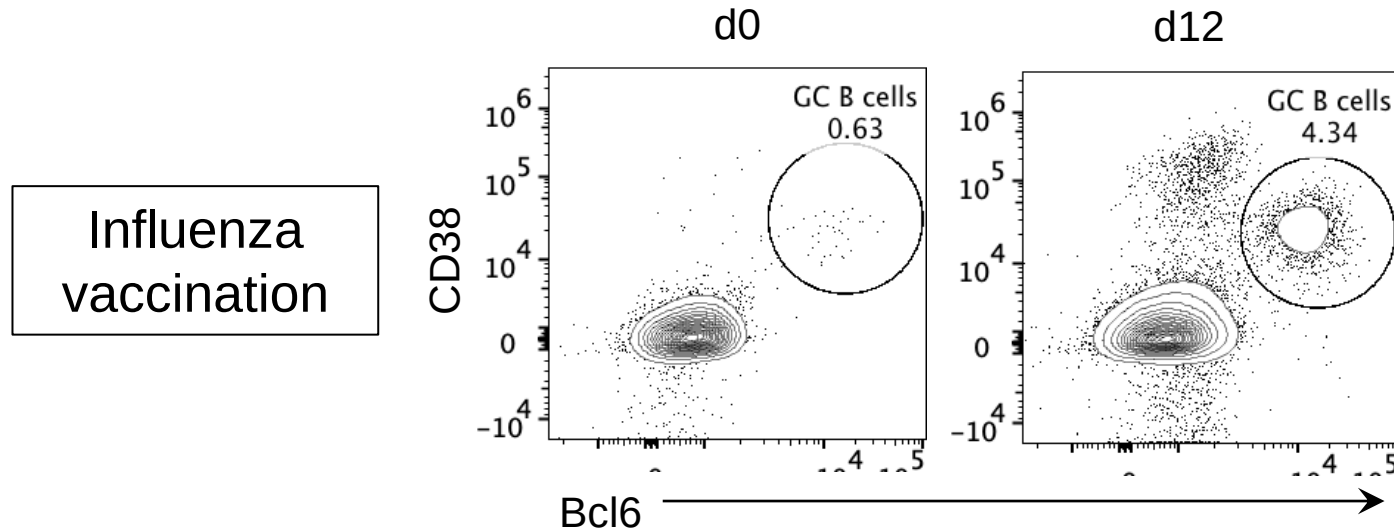
Detection of HA+ GC B cells in 3 out of 7 seasonal influenza vaccine recipients



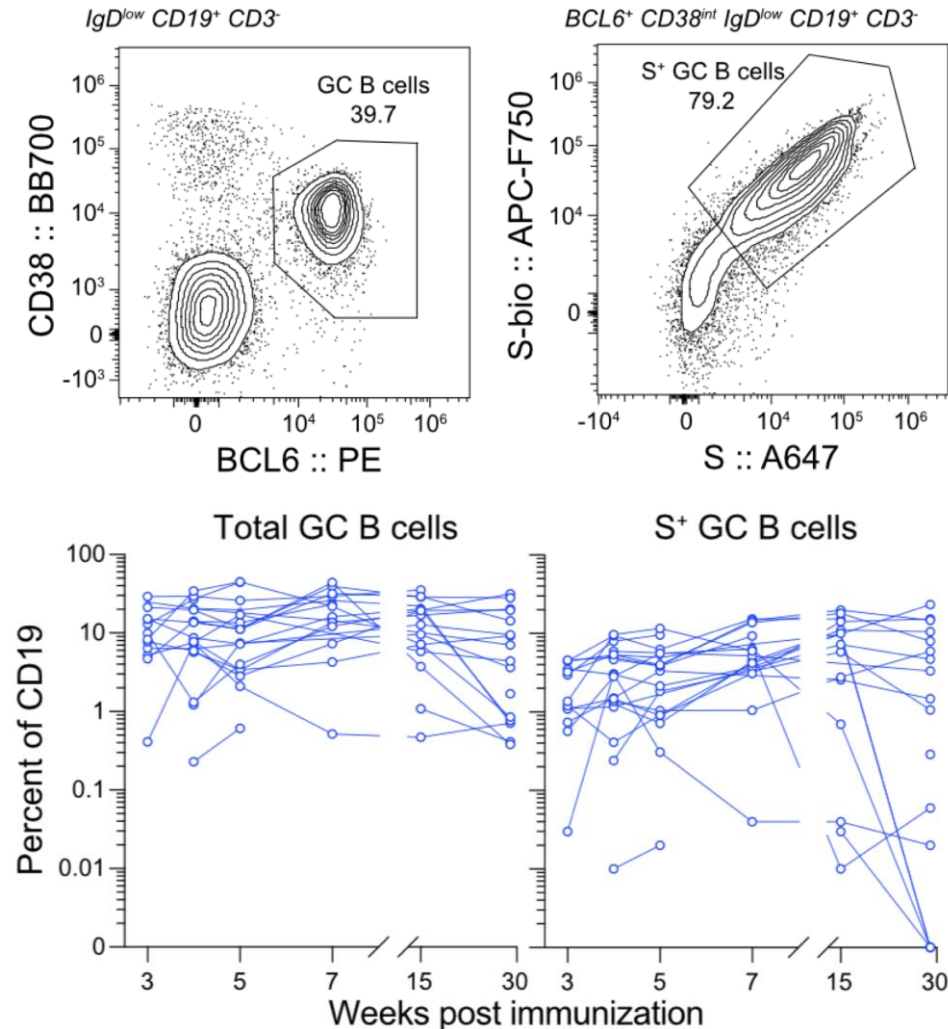
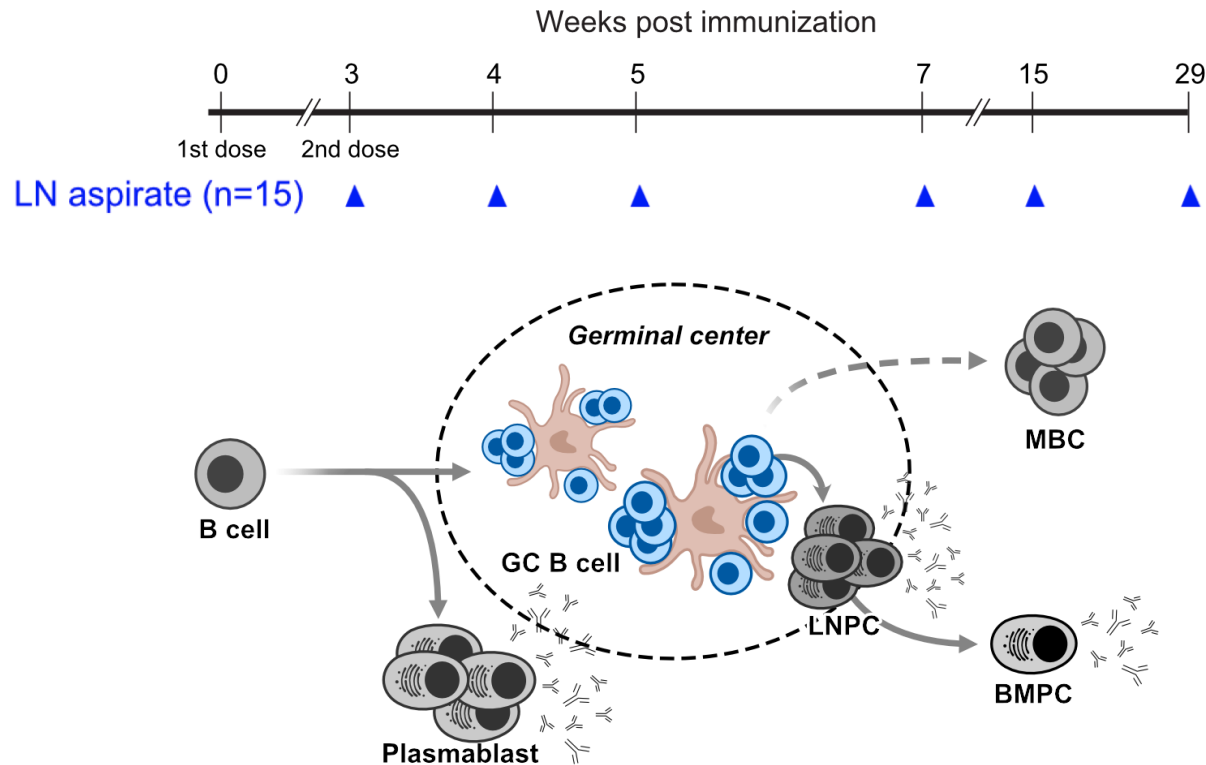
Immune response to SARS-CoV-2 vaccines (Wash U 368 Study)



Greater frequencies of germinal center B cell responses after mRNA vaccination

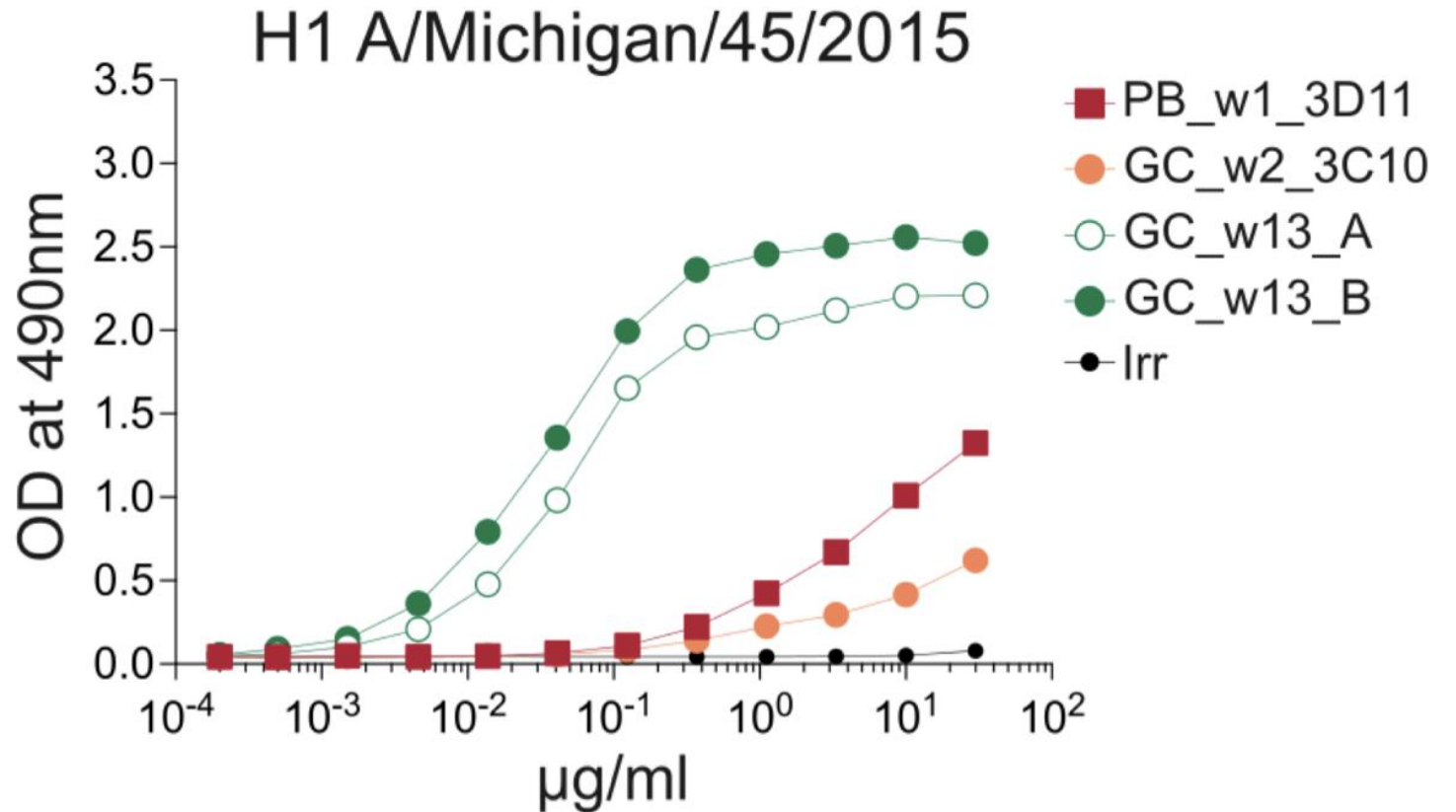
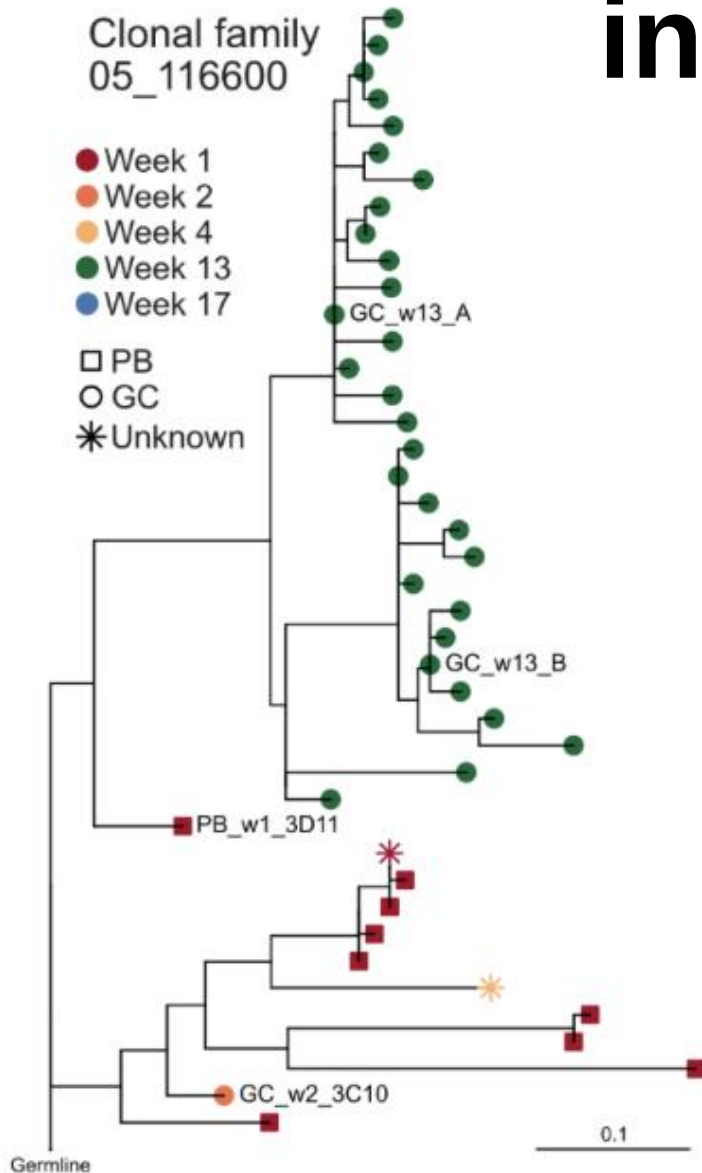


Detection of spike+ GC B cells in humans in ALL vaccine recipients

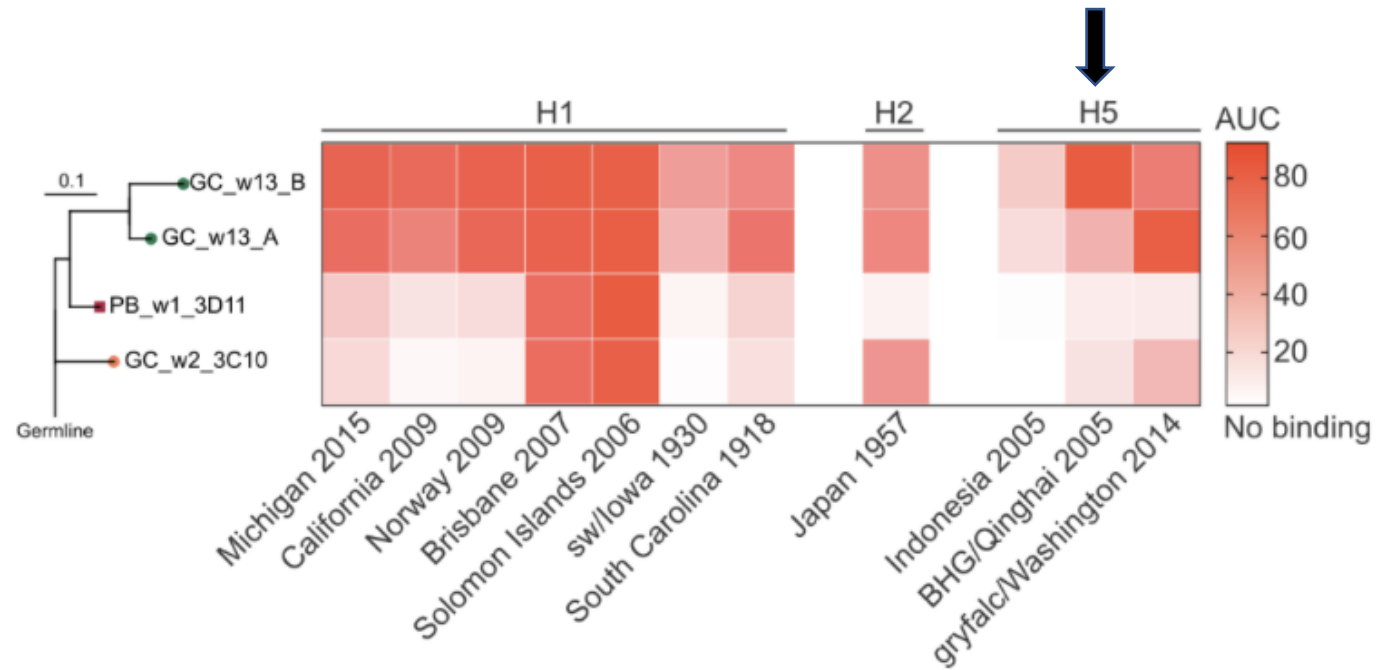
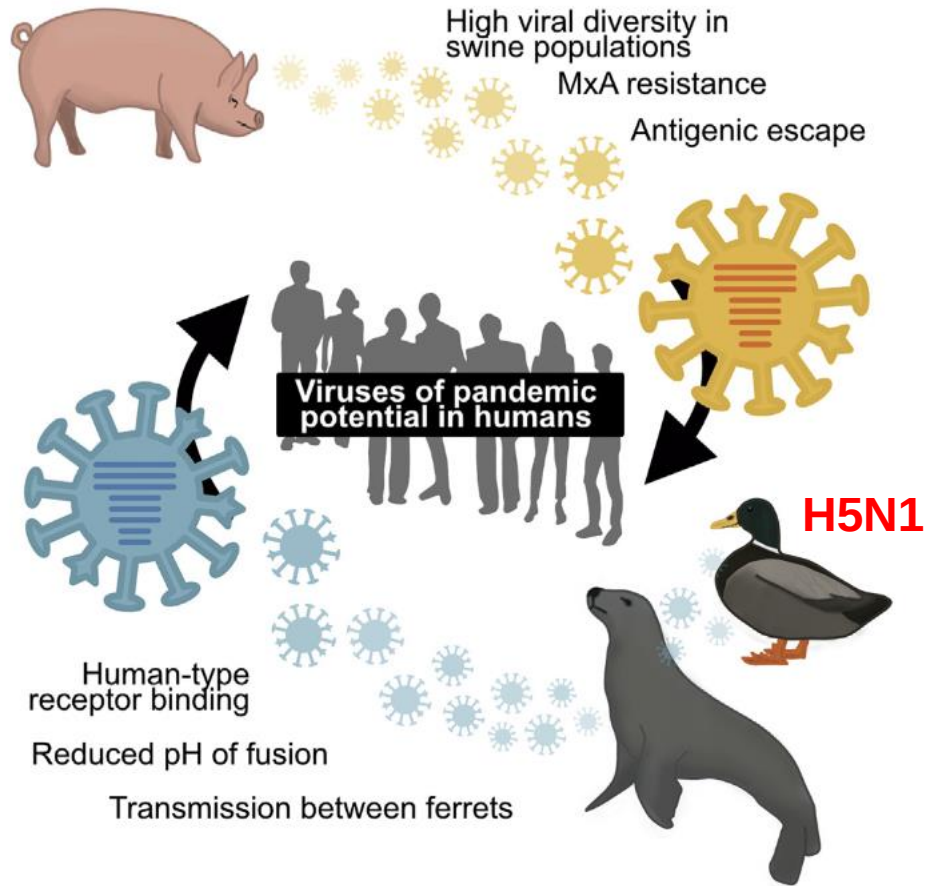


Does it matter to have a robust germinal center response to influenza vaccination?

influenza antibodies

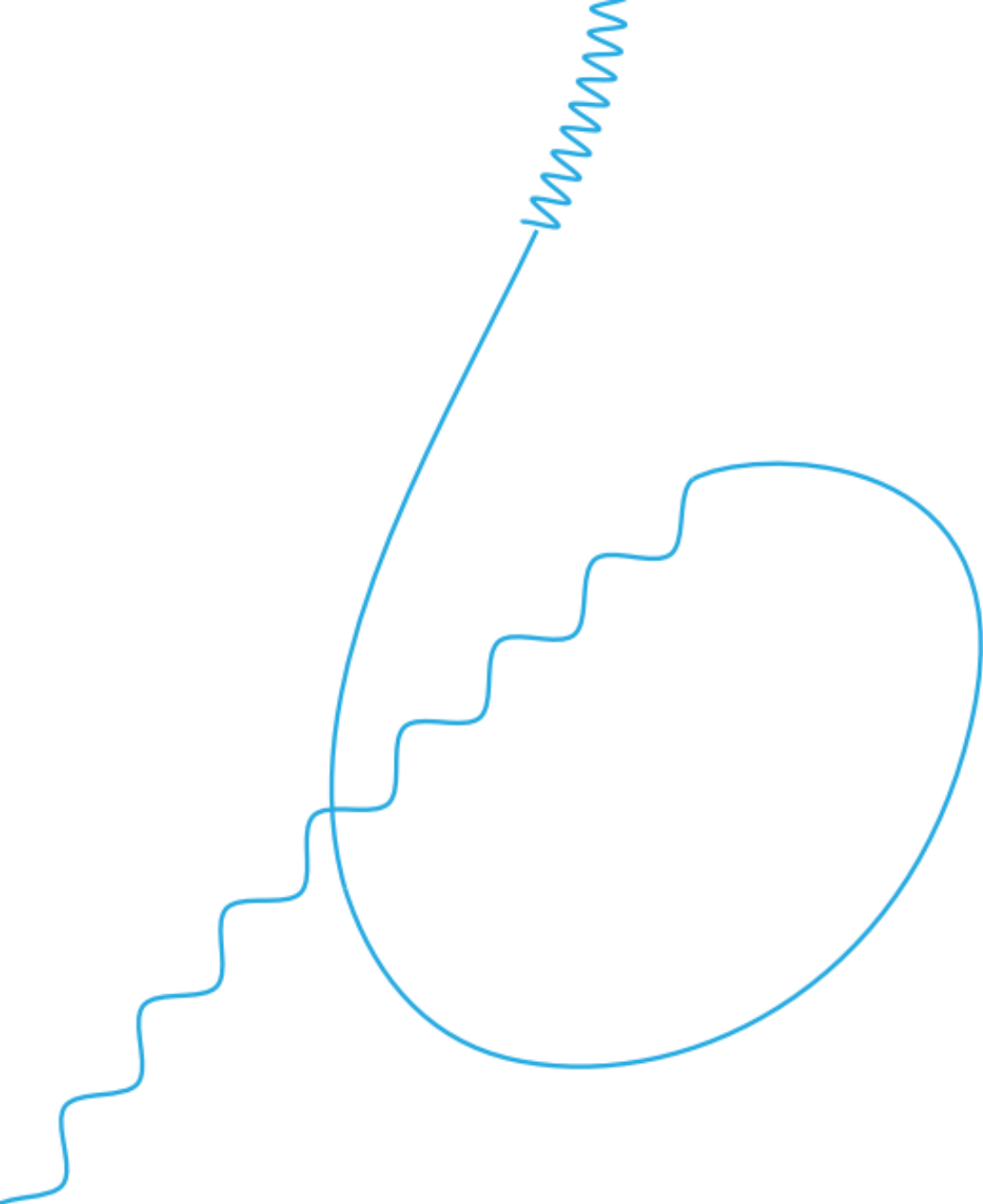


Affinity maturation expands breadth of anti-influenza antibodies



Open questions

- **Can new mRNA-based influenza virus vaccines enhance induced germinal center B cell response in humans?**
 - **Magnitude?**
 - **Breadth?**
 - **Duration?**
- **How about expanding the influenza virus parts targeted by vaccine induced immune responses?**
 - **Neuraminidase?**
 - **T cell responses?**



Moderna's RSV Strategy

Jacqueline Miller, M.D.

*Senior Vice President, Therapeutic Area
Head, Infectious Diseases, Moderna*

RSV is the leading cause of respiratory illness in young children and older adults are at high risk for severe RSV infections

Disease burden in pediatrics

- Hospitalization rate in children <5 years old in the U.S.: ~3:1000¹
- Annually ~2 million medically attended RSV infections in children <5 years old in the U.S., more than 86,000 are hospitalized²
- Pediatric RSV results in an estimated ~\$2 billion in annual medical costs in the U.S.
- Almost all children will have had an RSV infection by their second birthday³

Disease burden in older adults

- There are ~177,000 hospitalizations in adults 65+ due to RSV in the U.S. each year, and ~14,000 deaths⁴
- Globally it is estimated that there are ~1.5 million episodes of acute respiratory tract infection and ~336,000 hospitalizations related to RSV each year⁵

Long-term RSV infection sequelae

Pediatric populations⁶

- Recurrent wheeze
- Asthma
- Impaired lung function

Older adults⁷

- Exacerbation of chronic obstructive pulmonary disease
- Higher 1 year mortality after severe illness

(1) Rha, Brian, et al., *Pediatrics* (2020), <https://doi.org/10.1542/peds.2019-3611>

(2) Eiland, Lea., *J Pediatr Pharmacol Ther.* (2009), <https://doi.org/10.5863/1551-6776-14.2.75>

(3) Respiratory Syncytial Virus Infection (RSV), CDC, <https://www.cdc.gov/rsv/about/symptoms.html>

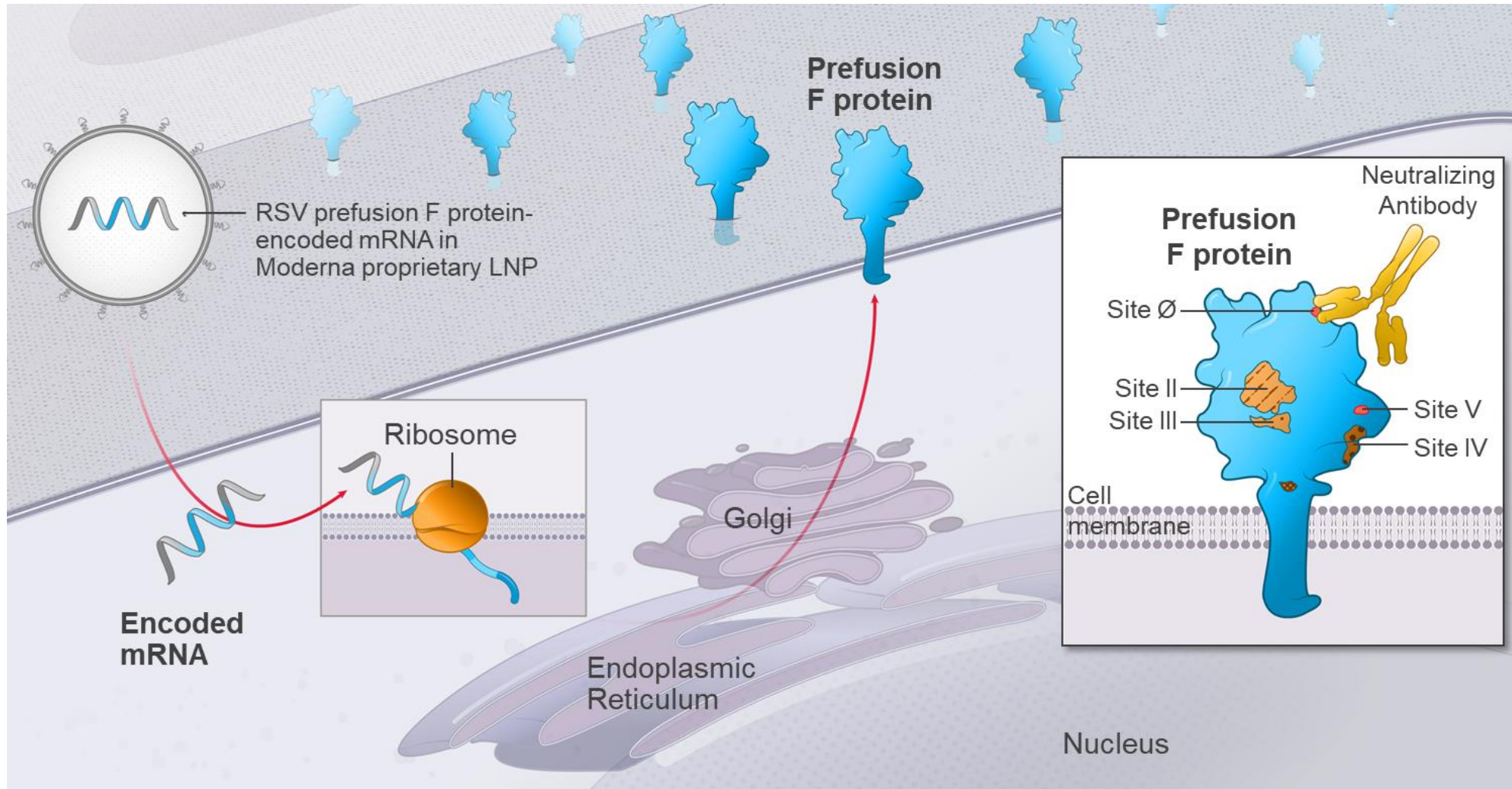
(4) RSV in Older Adults and Adults with Chronic Medical Conditions, CDC, <https://www.cdc.gov/rsv/high-risk/older-adults.html>

(5) Shi, Ting, et al., *J Infect Dis.* (2020), <https://doi.org/10.1093/infdis/jiz059>

(6) Shi, Ting et al., *J Infect Dis.* (2020), <https://doi.org/10.1093/infdis/jiz311>

(7) Ackerson, Bradley et al., *Clin Infect Dis.* (2019), <https://doi.org/10.1093/cid/ciy991>

RSV vaccine (mRNA-1345) encodes for a stabilized prefusion F glycoprotein



RSV vaccine (mRNA-1345) Phase 1 ongoing in pediatric and adult populations

Overview

- Evaluating the tolerability and reactogenicity of mRNA-1345 in younger adults, older adults, children and women of child-bearing potential

Outcome measures

- Safety and immunogenicity
 - Neutralizing antibody titers against RSV

Trial progress

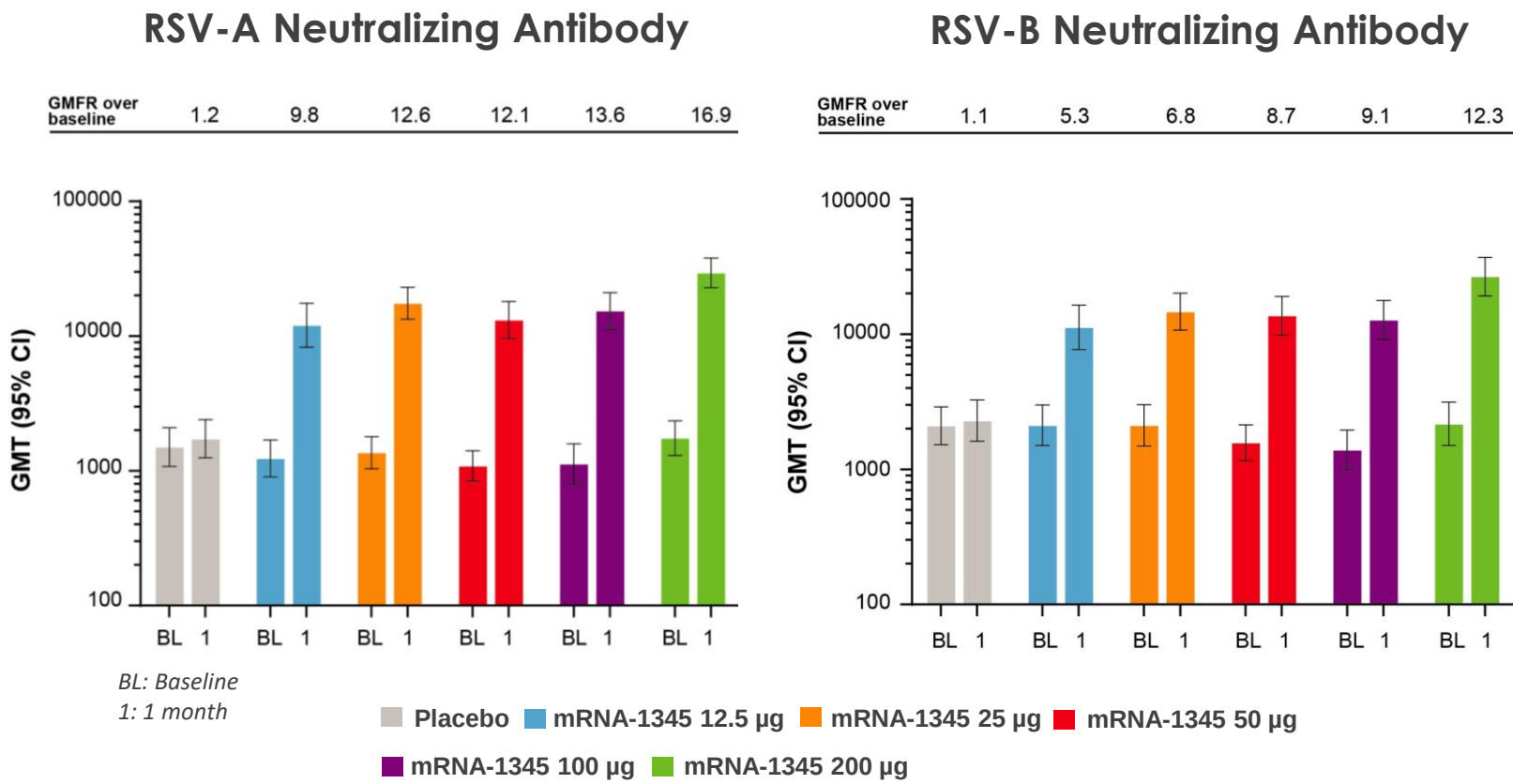
- Younger adults, older adults and women of child-bearing potential cohorts are all fully enrolled
- Enrollment ongoing in RSV seropositive children and Japanese descent older adults

Phase 1 Trial Design

Cohorts 1-4	✓	Younger Adults (18-49 years)
Cohorts 5-6		RSV Seropositive Children (12-59 months)
Cohorts 7-11	✓	Older Adults (65-79 years)
Cohorts 12-14	✓	Women of Child-Bearing Potential (18-40 years)
Cohorts 15		Japanese Descent Older Adults (≥ 60 Years)

✓ Fully enrolled

In older adults, mRNA-1345 boosts RSV neutralizing antibodies

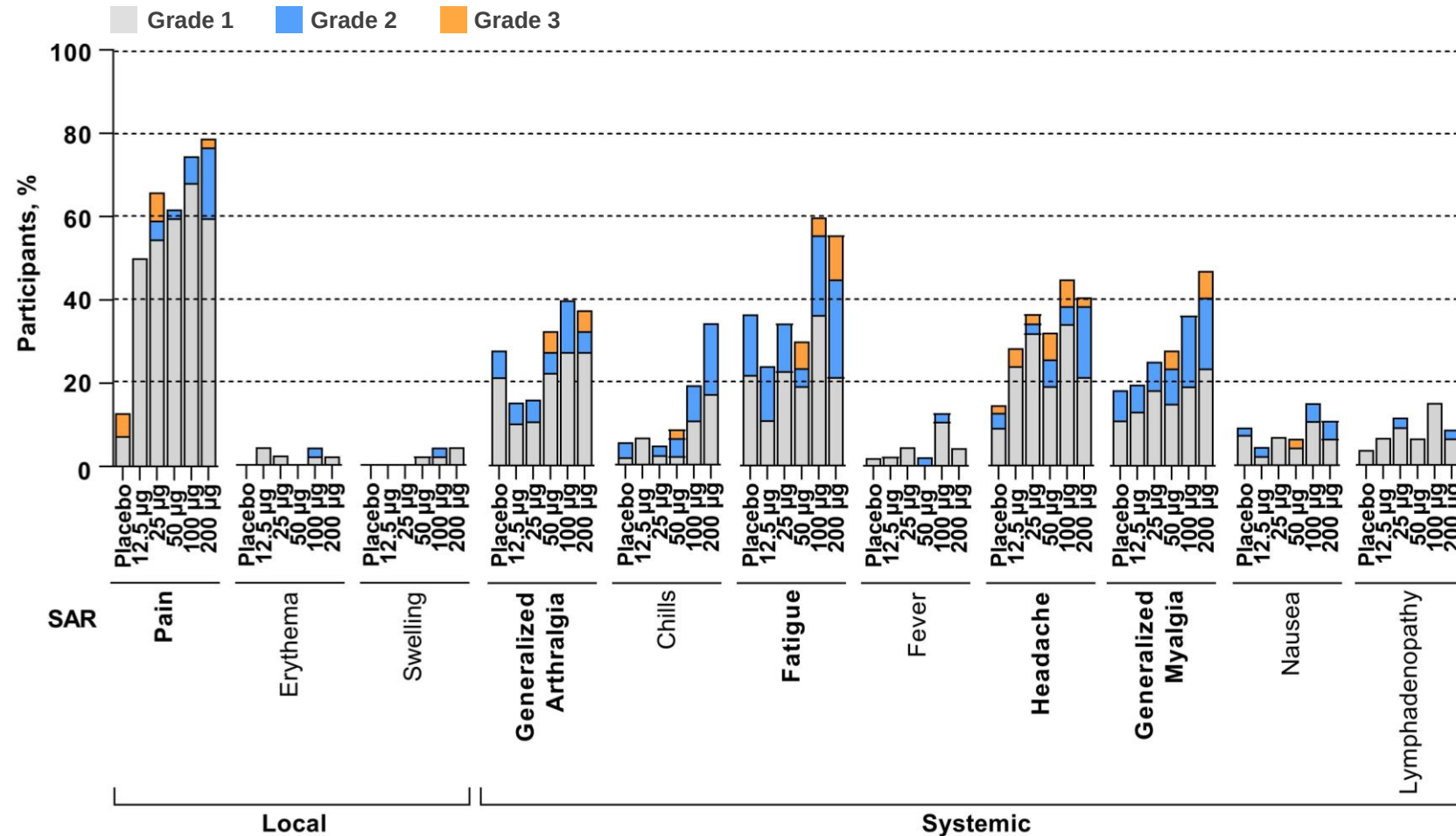


- All participants had nAb against RSV at baseline (BL) before study injections, suggesting prior exposure to RSV
- mRNA-1345 boosted RSV-A and RSV-B nAb GMTs
- GMFR over BL at 1 month were 9.8–16.9 and 5.3–12.3 for RSV-A and RSV-B, respectively
- Minimal dose-response was observed for nAb GMTs

Interim data, Per-Protocol analysis set.
Participants were randomised to receive one dose of mRNA-1345 (12.5, 25, 50, 100, or 200 µg; n=47–48 each) or placebo (n=59). 1/2 of the participants dosed with mRNA will get a booster at the same dose-level as the initial dose, at 12 months

In older adults, mRNA-1345 is well-tolerated at all dose levels

Local and Systemic Solicited Adverse Reactions (SARs) in Older Adults Within 7 Days of Receiving 1 Dose

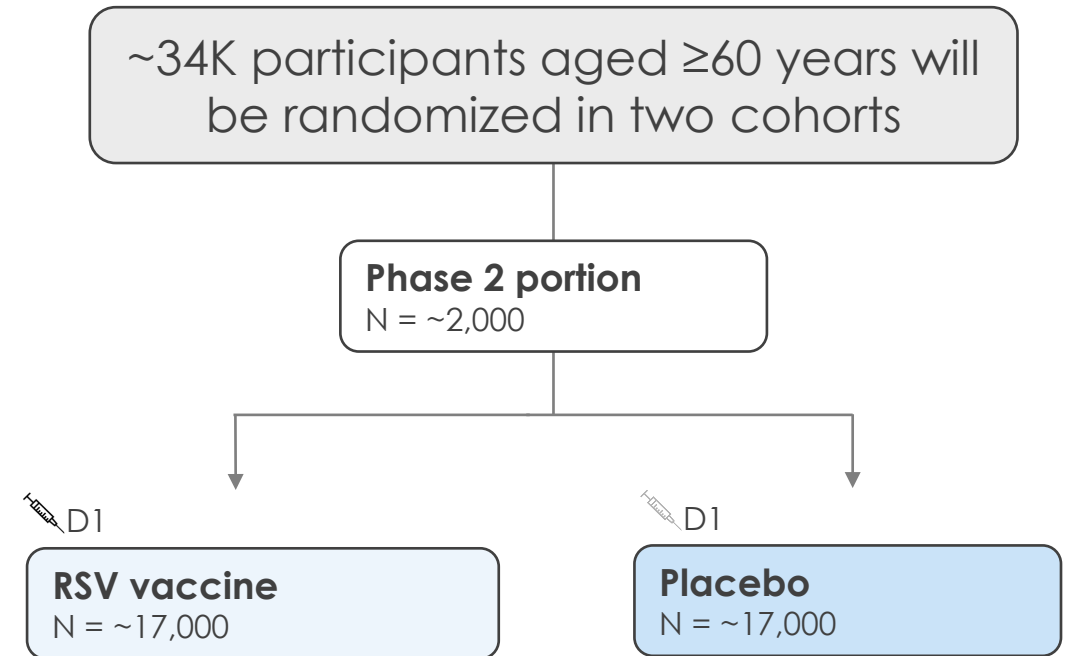


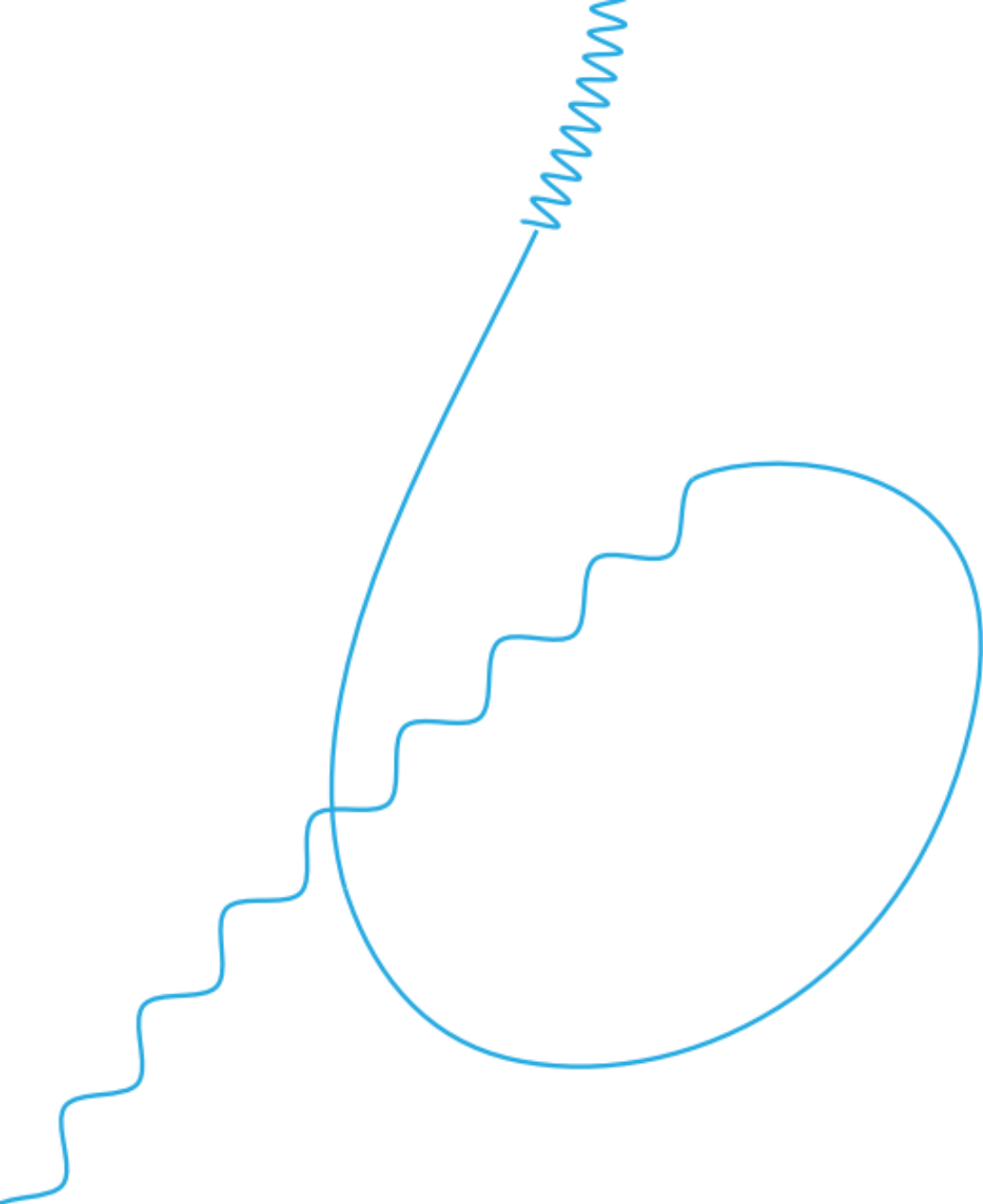
- Local SARs were reported in 50.0%–78.7% and 12.7% of mRNA-1345 and placebo recipients, respectively
 - Pain at the injection site (mostly grade 1) was the most frequently reported
- Systemic SARs were reported in 50.0%–78.7% and 45.5% of mRNA-1345 and placebo recipients, respectively
 - Headache, fatigue, arthralgia, and myalgia were the most frequently reported
- Treatment related unsolicited AEs were reported by 6.7% (16/239) of mRNA-1345 and 10.2% (6/59) of placebo recipients
- Unsolicited severe AEs were reported by 7 (2.9%) of the RNA-1345 recipients with none reported in the placebo group
- No related SAE or AESI were reported

Pivotal Phase 3 trial in older adults ongoing



- Phase 3 portion of pivotal trial started in February 2022 after DSMB review of Phase 2 portion
 - Placebo-controlled, case-driven design
 - Study is in adults ≥ 60 years of age
- Expect to enroll ~34,000 participants in multiple countries; locations influenced by RSV epidemiology
 - Phase 2 portion enrolled ~2,000 participants
- Primary endpoints will be safety and vaccine efficacy
- Primary efficacy analysis will be triggered based on accrual of RSV cases
- Received FDA Fast Track designation for older adults



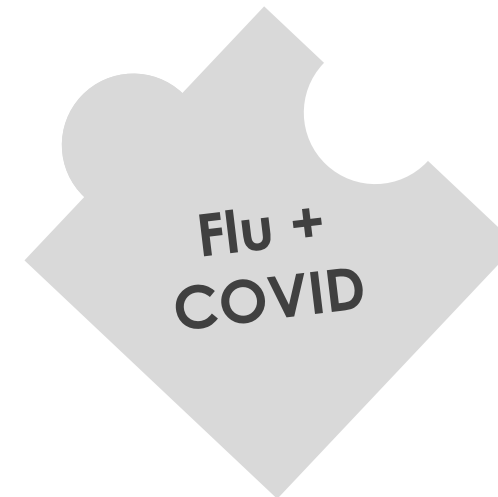
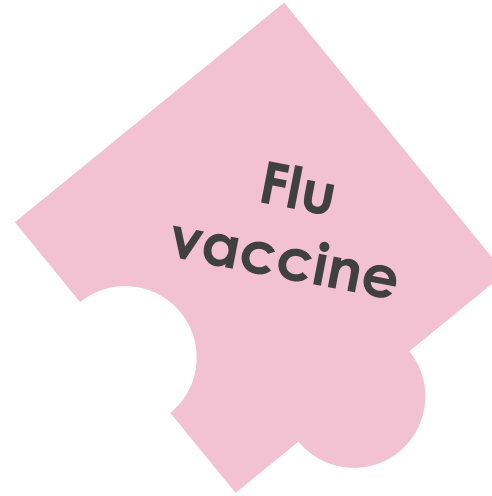


Combination Respiratory Vaccine Strategy

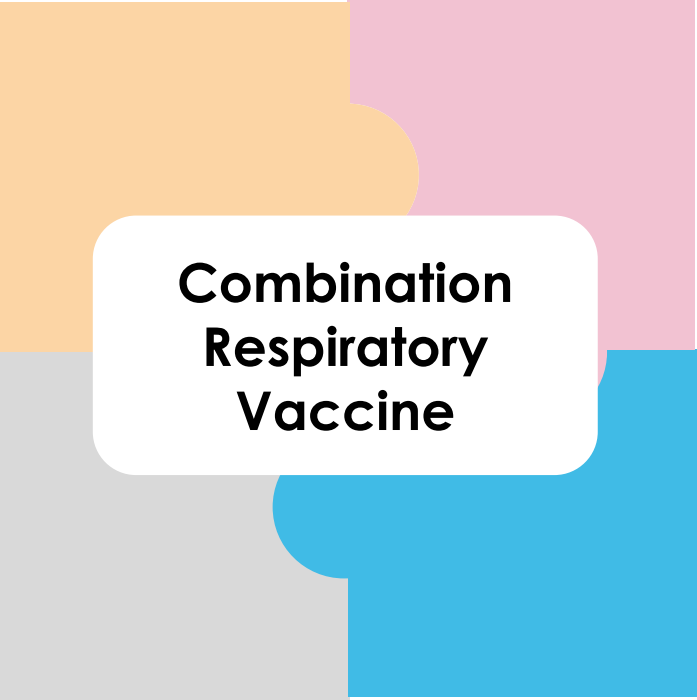
Jacqueline Miller, M.D.

*Senior Vice President, Therapeutic Area
Head, Infectious Diseases, Moderna*

We are developing various “pieces” of our combination respiratory vaccine in parallel



Today we are announcing significant steps towards our combination respiratory vaccine goal



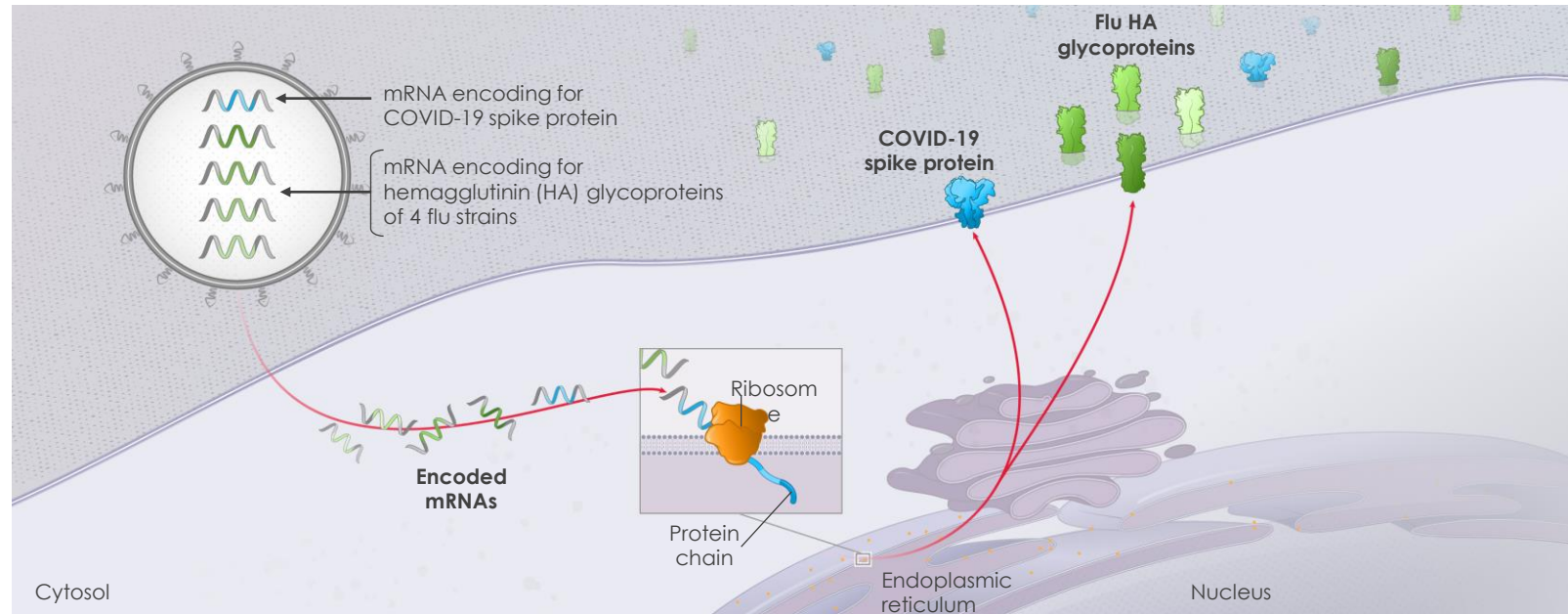
Combination Respiratory Vaccine

Respiratory Combo Vaccine Updates

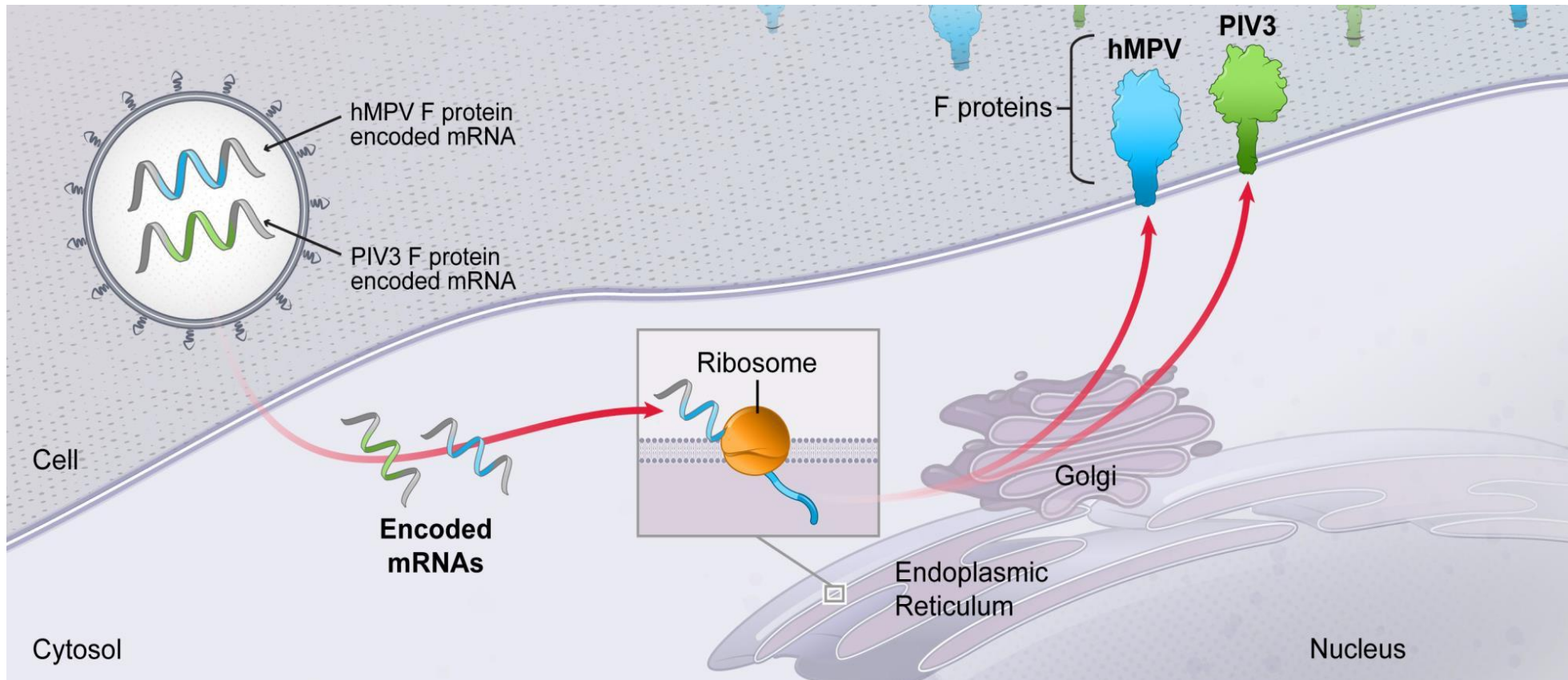
- COVID + Flu vaccine (mRNA-1073) to enter the clinic this year
- New development program for individuals aged 50 years and older (mRNA-1230): COVID booster + Flu + RSV
- New pan human coronavirus program (mRNA-1287): HCoV 229E, NL63, OC43, HKU1

COVID + Flu vaccine (mRNA-1073) expected to enter the clinic this year

- Evaluating mRNA-1073 in healthy adults
- Phase 1 expected to start in 2022
- COVID + Flu vaccine (mRNA-1073) will be compared to COVID vaccine (mRNA-1273) and standalone flu vaccine (mRNA-1010)



We have already shown positive results in a Phase 1 study with a combined vaccine (hMPV + PIV3 vaccine)



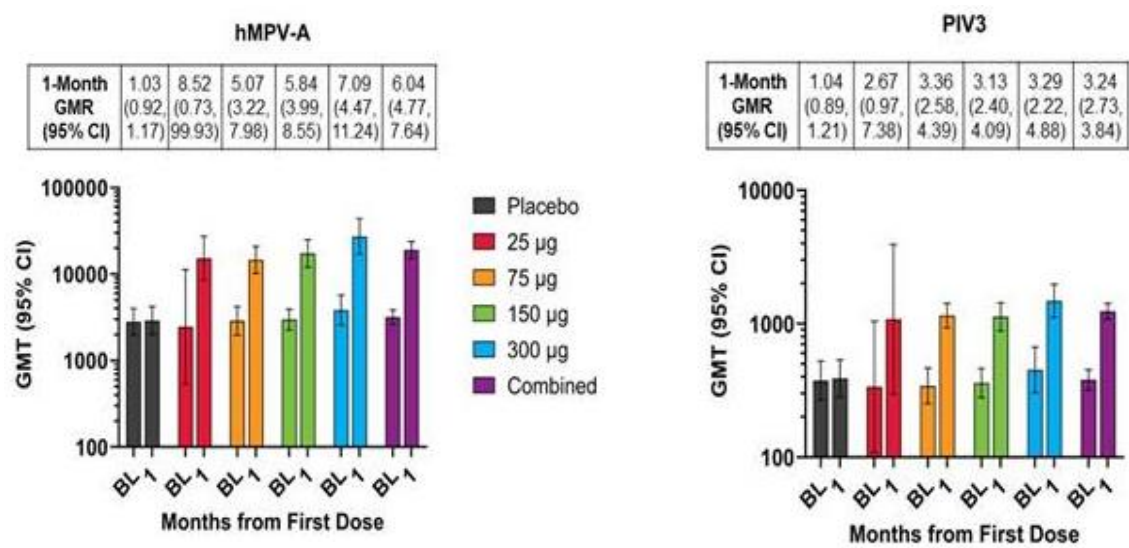
Our combination hMPV/PIV3 vaccine (mRNA-1653) vaccine candidate is safe and elicits neutralizing antibodies to both pathogens

Safety Summary

- **mRNA-1653 combination vaccine has a similar adverse reaction profile as our monovalent vaccine**
 - Injection site pain was the most common solicited local reactogenicity event, which was reported by 80 (85.1%) and 39 participants (70.9%) in the mRNA-1653 treatment groups after doses 1 and 2 (2-dose groups only)
 - Headache, fatigue, and myalgia were the most common solicited systemic reactogenicity events, reported by 48 (51.6%), 44 (47.8%), and 39 (42.4%) mRNA-1653 recipients after dose 1 and by 23 (41.8%), 20 (36.4%), and 24 (43.6%) mRNA-1653 recipients after dose 2

Immunogenicity Summary

- After dose 1, mRNA-1653 increased neutralizing antibody titers against hMPV-A, hMPV-B, and PIV3 for all dose levels (25, 75, 150, and 300 µg), with no apparent increase in titers with escalating dose levels



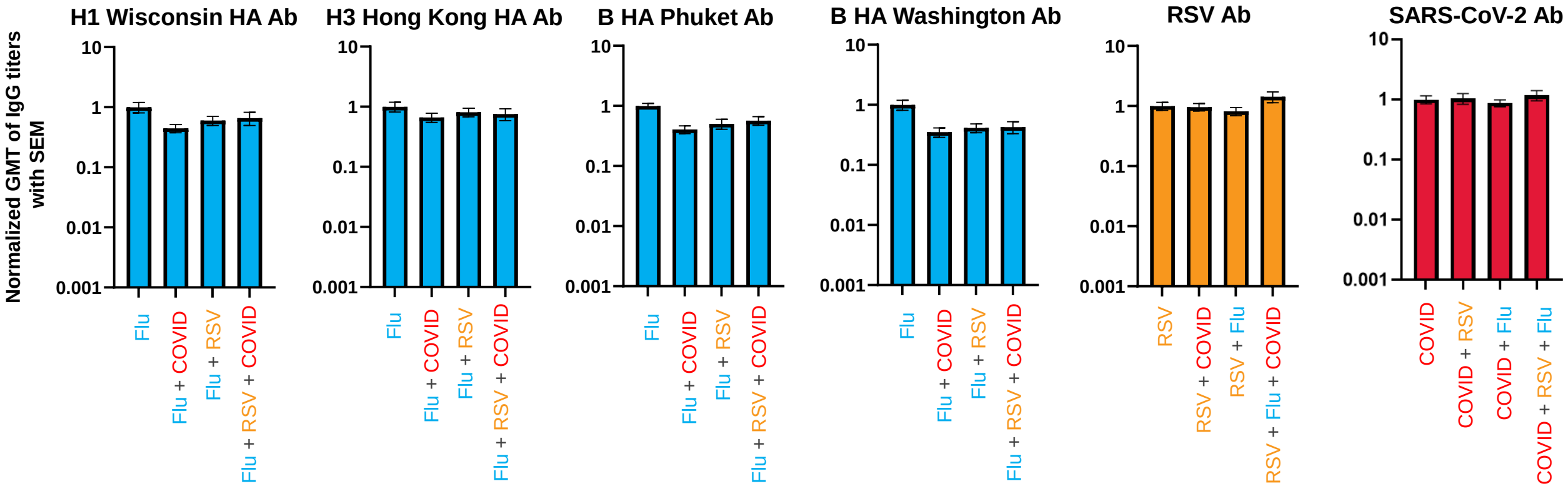
A Flu, RSV and SARS-CoV-2 combo vaccine induces robust antibody responses to all components in mice

Flu vaccine (mRNA-1010) encodes for **4 antigens** (HA)

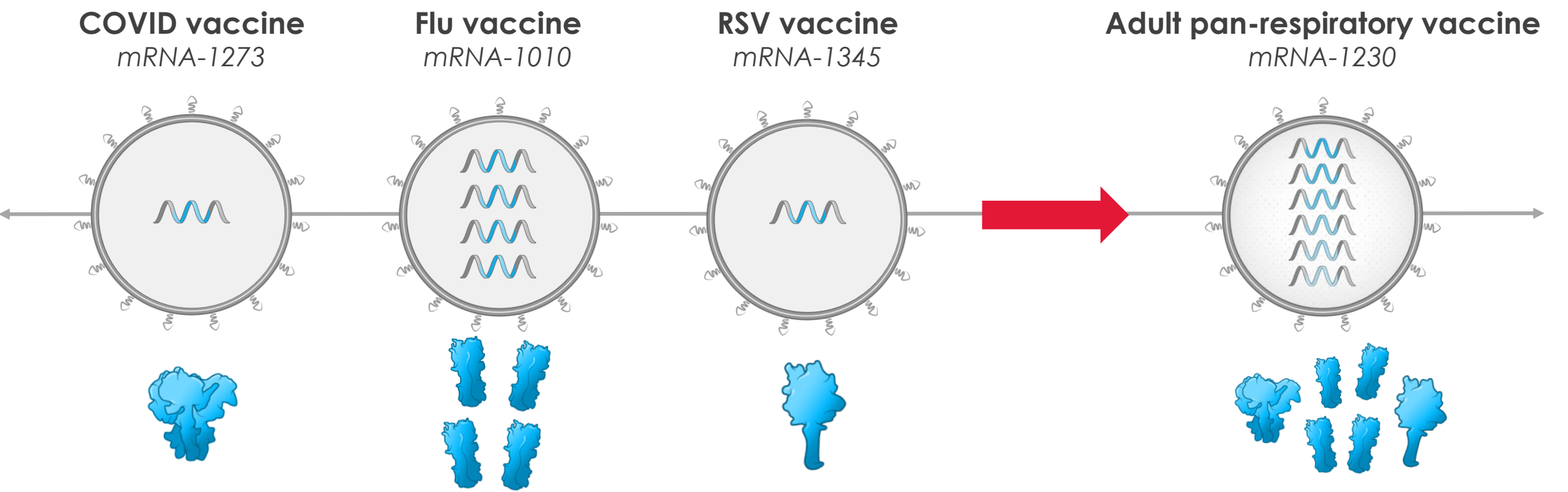
COVID-19 vaccine (mRNA-1273) encodes for **1 antigen** (spike protein)

RSV vaccine (mRNA-1345) encodes for **1 antigen** (prefusion F protein)

or mRNA-1010 + mRNA-1345 + mRNA-1273



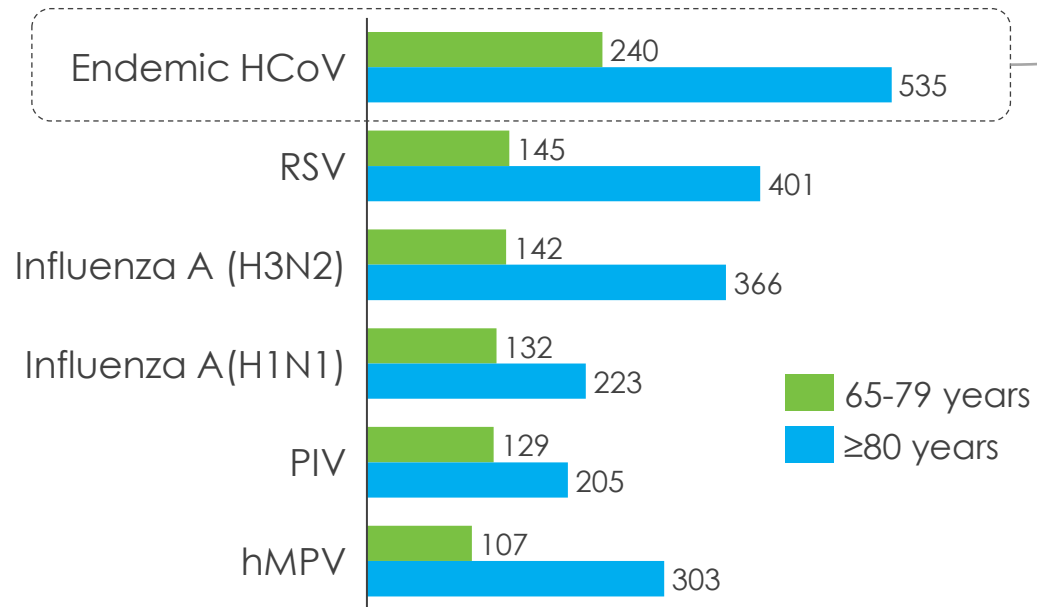
Announcing new older adult pan-respiratory vaccine development program (mRNA-1230)



Announcing new endemic human coronavirus vaccine (mRNA-1287)

Incidence of Community-onset Respiratory Viruses Associated with Hospitalization per 100,000 Persons¹

NYC, 10/2018 – 9/2019



Estimated impact of endemic HCoV in 65+ across OECD markets²⁻⁵

- Over 1 million outpatient visits
- Approximately 350,000 hospitalizations
- Approximately 20,000 deaths
- Four endemic HCoV's account for ~10-30% of upper respiratory tract infections in adults
 - HCoV 229E, NL63, OC43, HKU1

(1) Seiling, William et al., Influenza Other Respir Viruses (2021), <https://doi.org/10.1111/irv.12842>

(2) Person-KFF, Health System Tracker, <https://www.healthsystemtracker.org/brief/potential-costs-of-coronavirus-treatment-for-people-with-employer-coverage/>

(3) Kozak, Robert et al., J Clin Virol (2020), <https://doi.org/10.1016/j.jcv.2020.104338>

(4) Fischer, Natalie et al., Lancet Microbe (2021), [https://doi.org/10.1016/S2666-5247\(20\)30221-4](https://doi.org/10.1016/S2666-5247(20)30221-4)

(5) Gilca, Rodica et al., J Infect Dis (2021), <https://doi.org/10.1093/infdis/jiaa477>

Today's Agenda

Introduction

Stéphane Bancel, *CEO*

Development Strategy

Stephen Hoge, *M.D., President*

Vaccines Against Respiratory Viruses

- COVID
- Flu
- RSV
- Combination strategy

Jacqueline Miller, *M.D., SVP, Therapeutic Area Head, Infectious Diseases*

Shane Crotty, *Ph.D., La Jolla Institute for Immunology*

Raffael Nachbagauer, *M.D., Ph.D., Senior Director, Infectious Disease Development*

Ali Ellebedy, *Ph.D., Washington University School of Medicine*

Coffee Break (5 minutes)

Vaccines Against Latent Viruses

- CMV
- EBV
- Other latent viruses (HIV, HSV, VZV)

Jacqueline Miller, *M.D., SVP, Therapeutic Area Head, Infectious Diseases*

Anthony Cunningham, *AO,FAHMS, Centre for Virus Research; The University of Sydney*

Sumana Chandramouli, *Ph.D., Director, Infectious Diseases*

Alberto Ascherio, *M.D., DrPH, Harvard School of Public Health, Harvard Medical School*

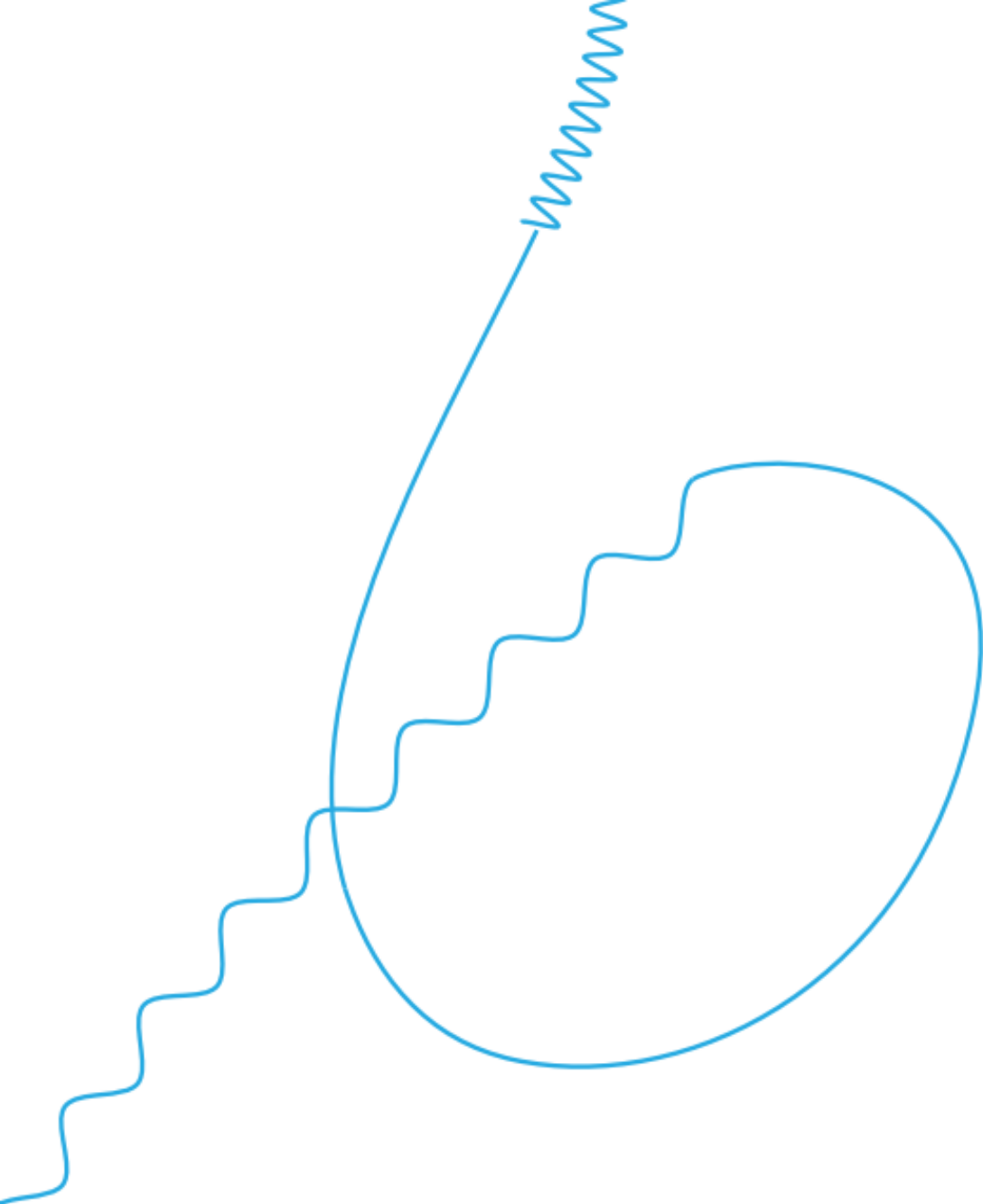
Global Health Vaccines & mRNA Access

Stephen Hoge, *M.D., President*

Conclusion – Expect More From Moderna

Stéphane Bancel, *CEO*

Q&A



Latent Viruses – Introduction

Jacqueline Miller, M.D.

*Senior Vice President, Therapeutic Area
Head, Infectious Diseases, Moderna*

Latent viruses have near-term infection impacts during the active replication phase and long-term health impacts during the latent phase

When a virus is present in the body but exists in a resting (latent) state without producing more virus. A latent viral infection usually does not cause any noticeable symptoms and can last a long period of time before becoming active and causing symptoms¹

Latent viruses have two key phases of infection²

- 1** Active replication: Lytic infection characterized by the release of new progeny (offspring) virus particles
- 2** Latent phase: Virus is 'quiescent' (a state in which the virus is not replicating)

The majority of viruses that can cause latent infections are from the family of *Herpesviridae*

- We believe our **mRNA platform is uniquely positioned to develop vaccines** against latent viruses
- Potential to **protect not only against near-term impacts** (infectious mononucleosis, congenital CMV etc.) **but also provide long-term health benefits** (lower rates of cancer, MS etc.)

Virus	Associated disease conditions ¹
HSV-1 HSV-2	Cold sores, herpetic whitlow, encephalitis, herpetic keratitis, herpes pharyngitis and genital herpes
VZV	Chicken pox and shingles
EBV	Mononucleosis, Burkitt's lymphoma, naso-pharyngeal carcinoma, hairy oral leukoplakia, non-Hodgkin's lymphoma, post-transplant lymphoproliferative disorder (PTLD) and multiple sclerosis
CMV	Congenital diseases, heterophile-negative mononucleosis syndrome, hypertension and atherosclerosis
HHV-6	Roseola
HHV-7	Roseola
KSHV (HHV-8)	Kaposi's sarcoma, primary effusion lymphoma and multicentric Castleman disease

Red = Vaccine program in pipeline

Anthony Cunningham, AO, FAHMS

Centre for Virus Research (WIMR); University of Sydney



Anthony Cunningham, AO, FAHMS
*Centre for Virus Research (WIMR);
University of Sydney*

Professor Anthony (Tony) Cunningham, AO, FAHMS is an infectious diseases physician, clinical virologist and scientist, internationally renowned for his research on the immunobiology of HIV and herpesviruses, his work on vaccine and microbicide development, and as an antivirals expert. He is the Director of the Australian Centre for HIV and Hepatitis Virology Research (ACH2), a Commonwealth Government-funded institute that aims to combat the impact of HIV and hepatitis in Australia and the Asia-Pacific region by bringing together basic researchers with translational scientists and physicians.

Development and trialing of Herpesvirus vaccines

Tony Cunningham

Centre for Virus Research, Westmead Institute,
Sydney Infectious Diseases, University of Sydney



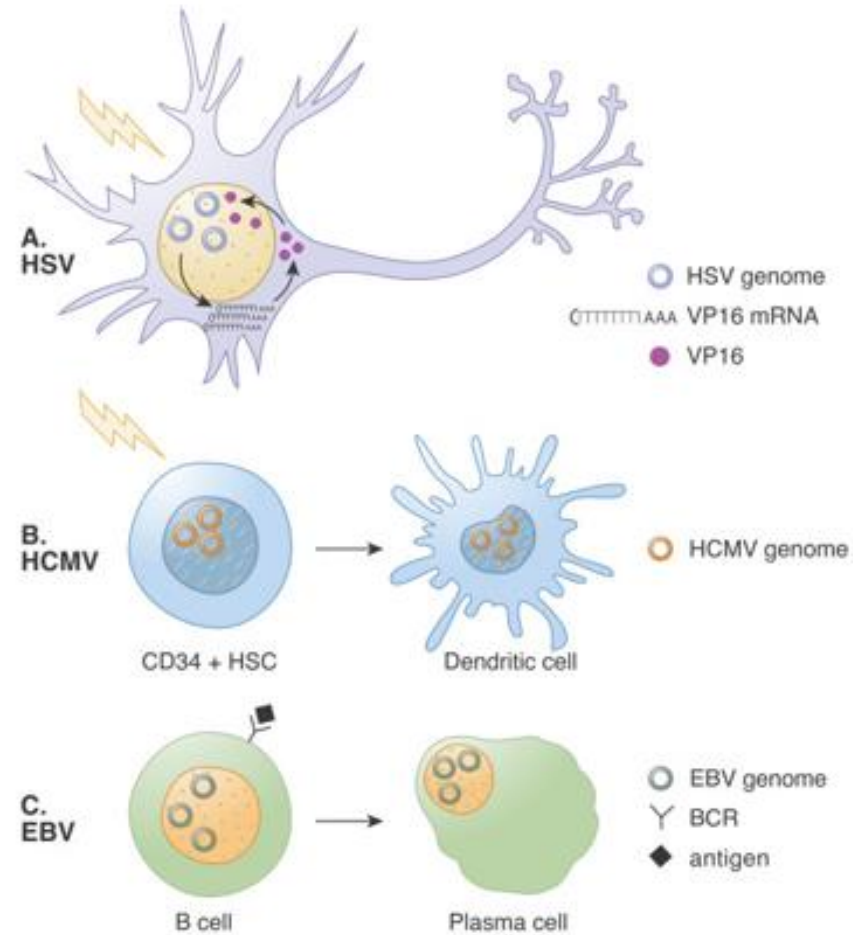
Declarations

- Chair, Publications Committee, GSK Shingrix ZoE50 and ZoE70 trials
- Past Member, Global Adult Vaccine Advisory Board, Merck
- Chair, Zostavax and COVID Vaccine Advisory Boards , Seqirus/BioCSL
- Advisory Board, Astra Zeneca, Australia

Major latent human herpesviruses and their associated diseases

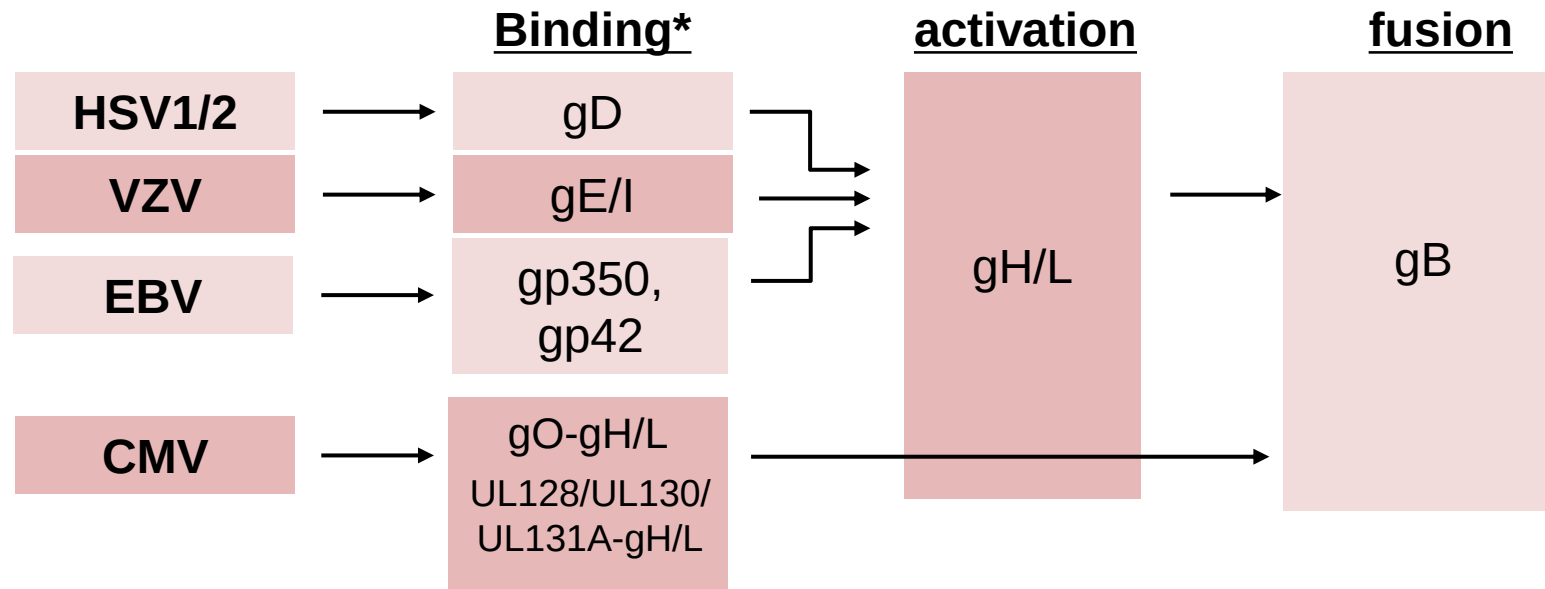
Name	Sero-prevalence	Diseases
Herpes simplex virus -1 (HSV-1)	60-95%	Orolabial, keratitis, encephalitis, Initial genital, neonatal herpes
Herpes simplex virus-2 (HSV-2)	12-70%	Initial and recurrent genital, neonatal, meningitis
Varicella-zoster virus (VZV)	>95%	Varicella (Chickenpox) Herpes zoster (shingles)
Cytomegalovirus (HCMV)	20-70%	Adult Mononucleosis, Severe congenital infection, malformation and deafness. Immune compromised: Hepatitis retinitis, oesophagitis
Epstein-Barr Virus (EBV)	>90%	Infectious mononucleosis Post Tx lymphoproliferative disorder Lymphoma: Hodgkin's, Burkitt's, AIDS Nasopharyngeal and gastric carcinoma Multiple sclerosis

Latency and reactivation of Herpesviruses



Prevention of target cell infection: antibody; Control of their infection: CD4 and CD8 T cells

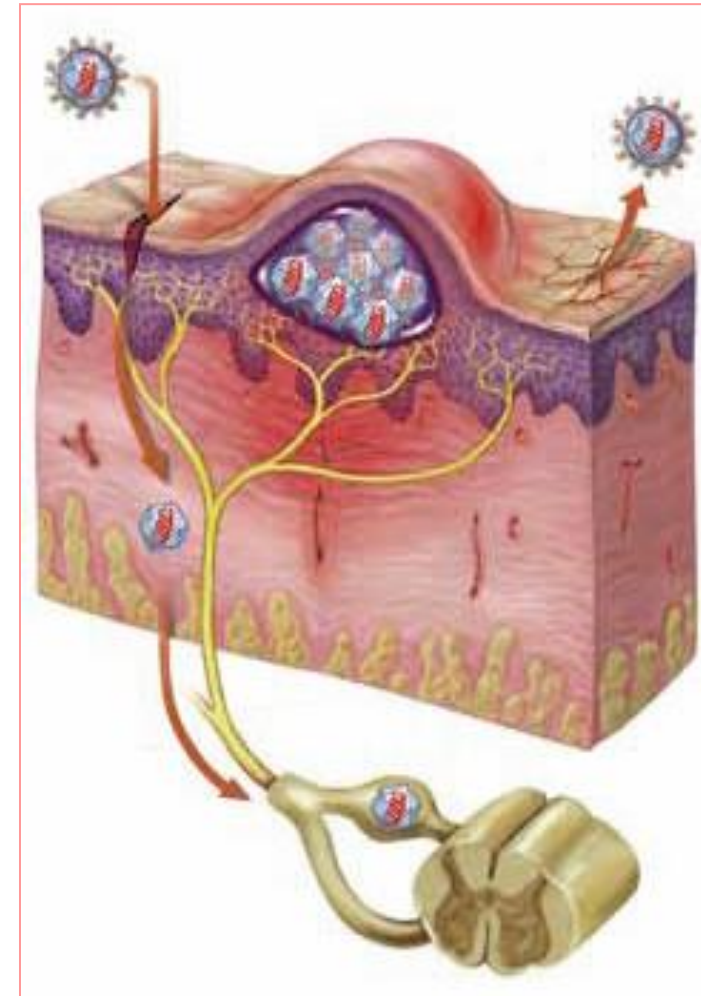
Herpesvirus entry into cells



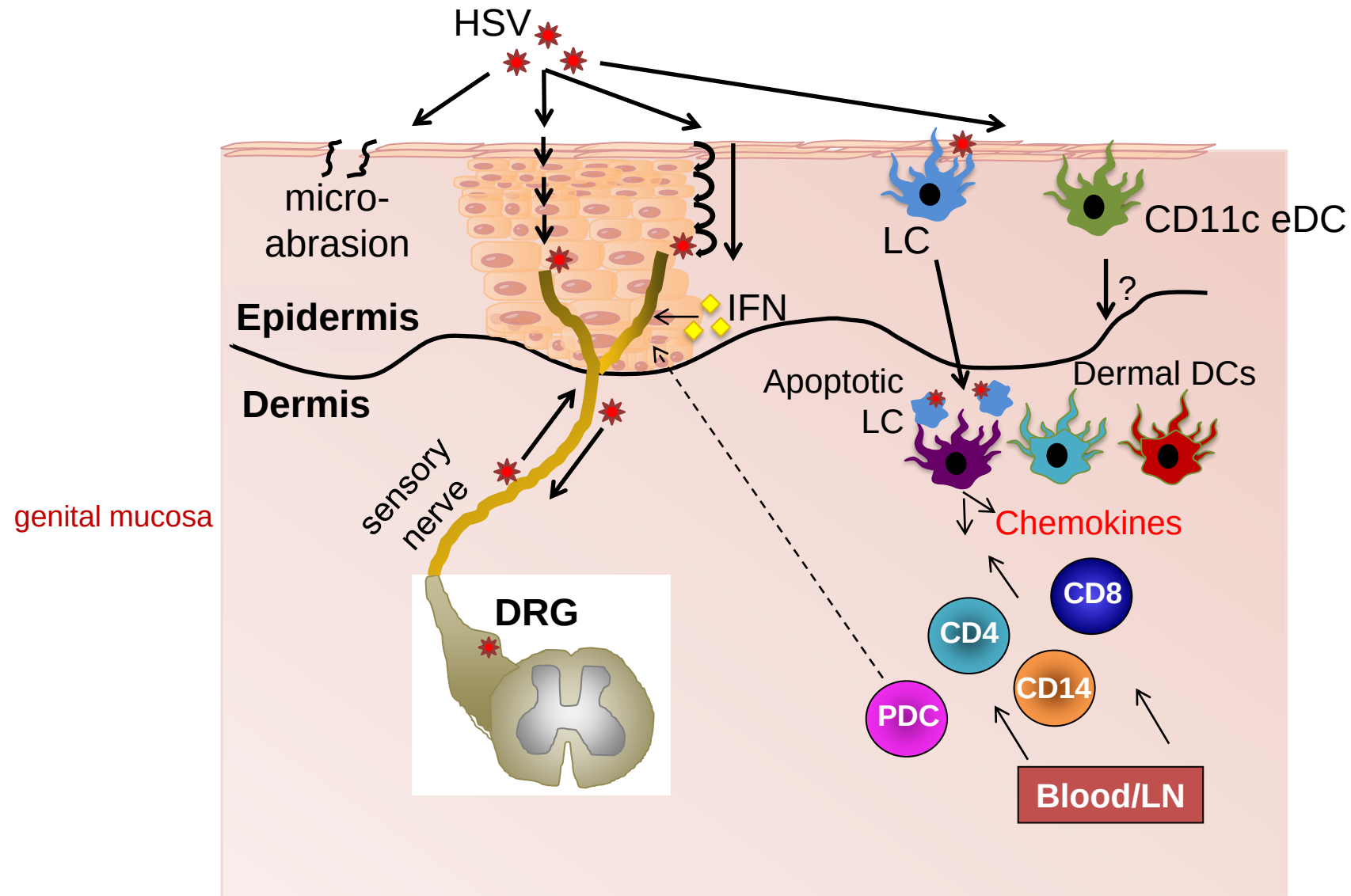
*Viral binding/attachment proteins are targets for neutralizing antibodies induced by vaccines

Herpes Simplex Viruses (HSV) 1& 2

- HSV infects oro/genital skin and enters cutaneous nerves
- Establishes a lifelong dormant infection in DRG that reactivates intermittently back to the epidermis
- HSV infection is restricted to the epidermis



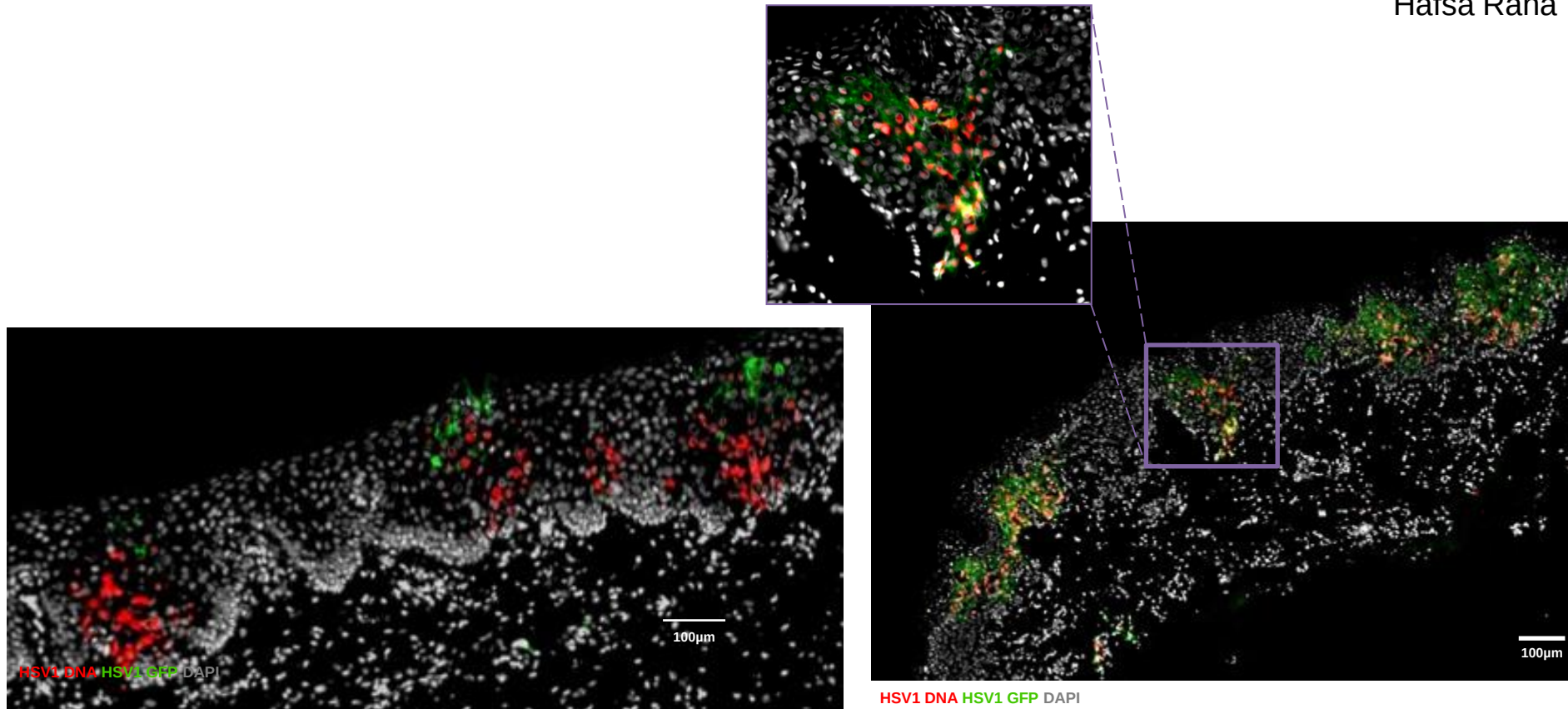
Effective vaccines need to induce antibody and local T cells to combat Herpes Simplex Virus infection



Rapid lateral spread of HSV infection in the epidermis

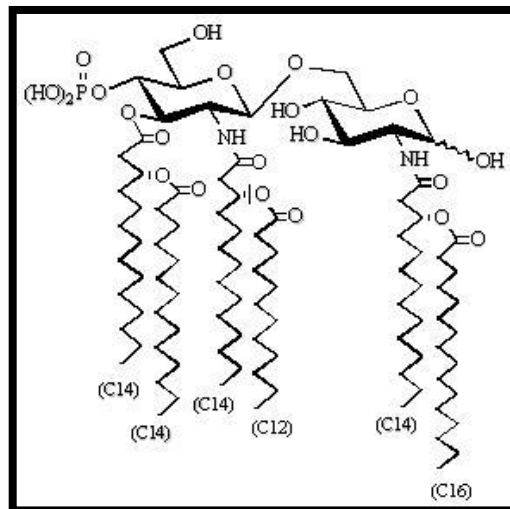


Hafsa Rana



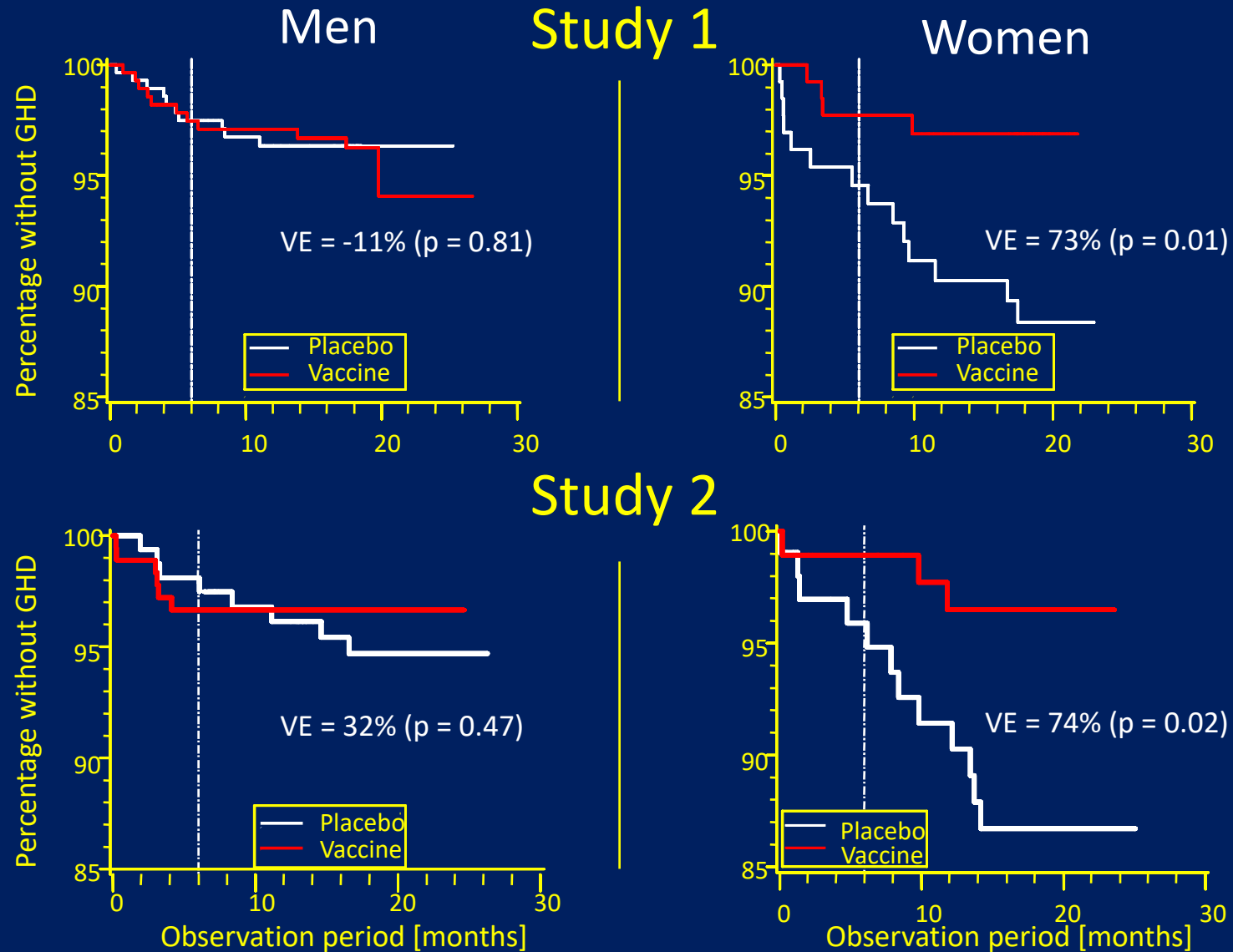
Early vaccine program against HSV2 shows promise

- The first partially successful vaccine candidate for genital herpes was the HSV2 gD/MPL vaccine
- Vaccine construct: recombinant protein antigen + adjuvant
- Antigen glycoprotein D protein + ASO4 adjuvant - Alum and monophosphoryl lipid A (MPL)
- Induces CD4 T cell and antibody response in humans
- Simplirix trial: multicentre, RDBC
 - Consort design: immunize partners of subjects with GHD



MPL

HSV2 gD vaccine prevents disease in female seronegative subjects (Stanberry, Cunningham et al NEJM 2002)

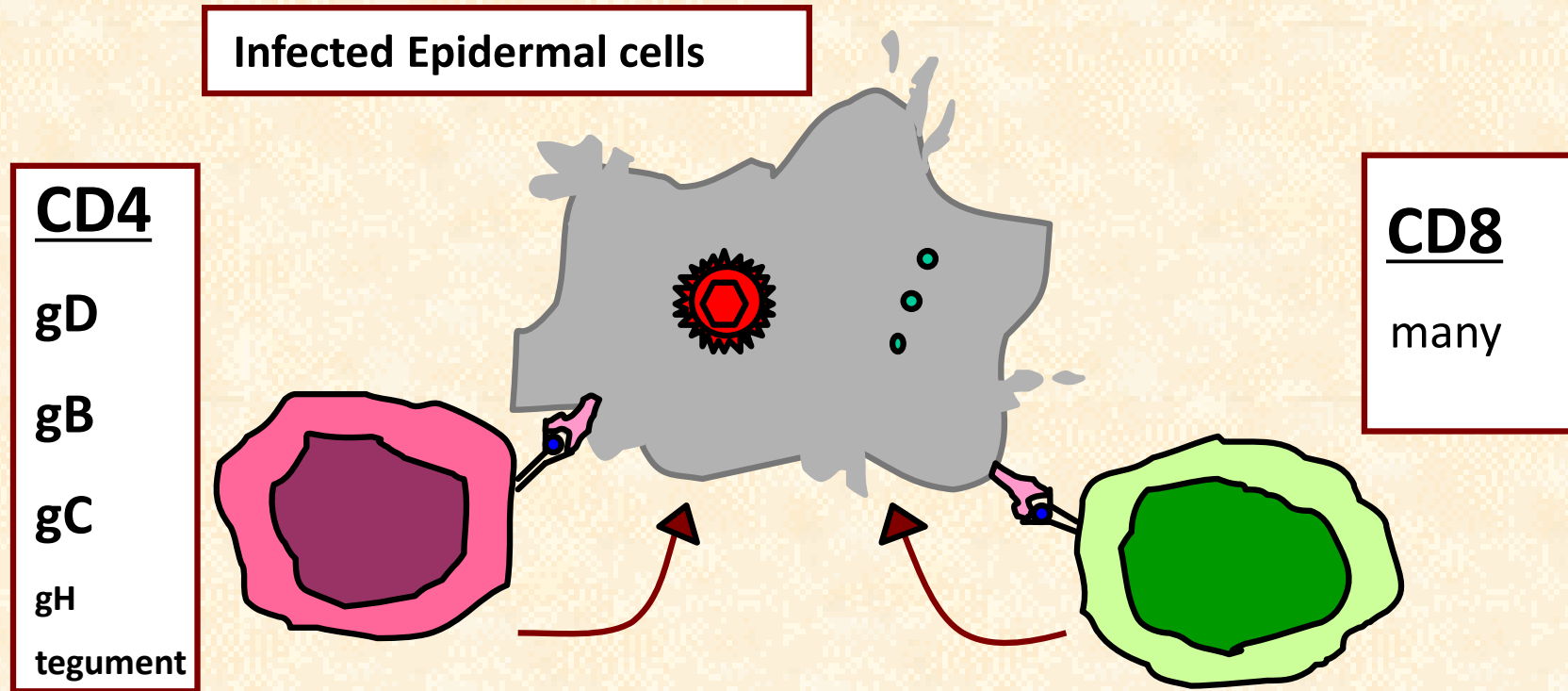


Vaccines and immunotherapy for HSV: Phase III clinical trials

- Recombinant glycoprotein D2 with AS04 adjuvant system (MPL/alum) (GlaxoSmithKline)
 - Stanberry et al NEJM 2002: **73-74% efficacy** in seronegative female consorts of males with recurrent genital herpes
 - Belshe et al NEJM 2012; random seronegative women: **58% efficacy** only in HSV1 genital herpes
 - Vaccine Induced neutralizing antibody, Th1, and Tfh responses, **no CD8+ T cell responses were detected.**
 - **Immunotherapy of recurrent HSV (Genocea):** gD + ICP4 + saponin based adjuvant Matrix M2: 68% reduction in recurrent lesions and 55% in HSV shedding ~ increased memory CD8 T cell responses, also decrease in placebo

HSV Vaccine Candidates

HSV1/2 protein targets for CD4 and CD8 lymphocytes

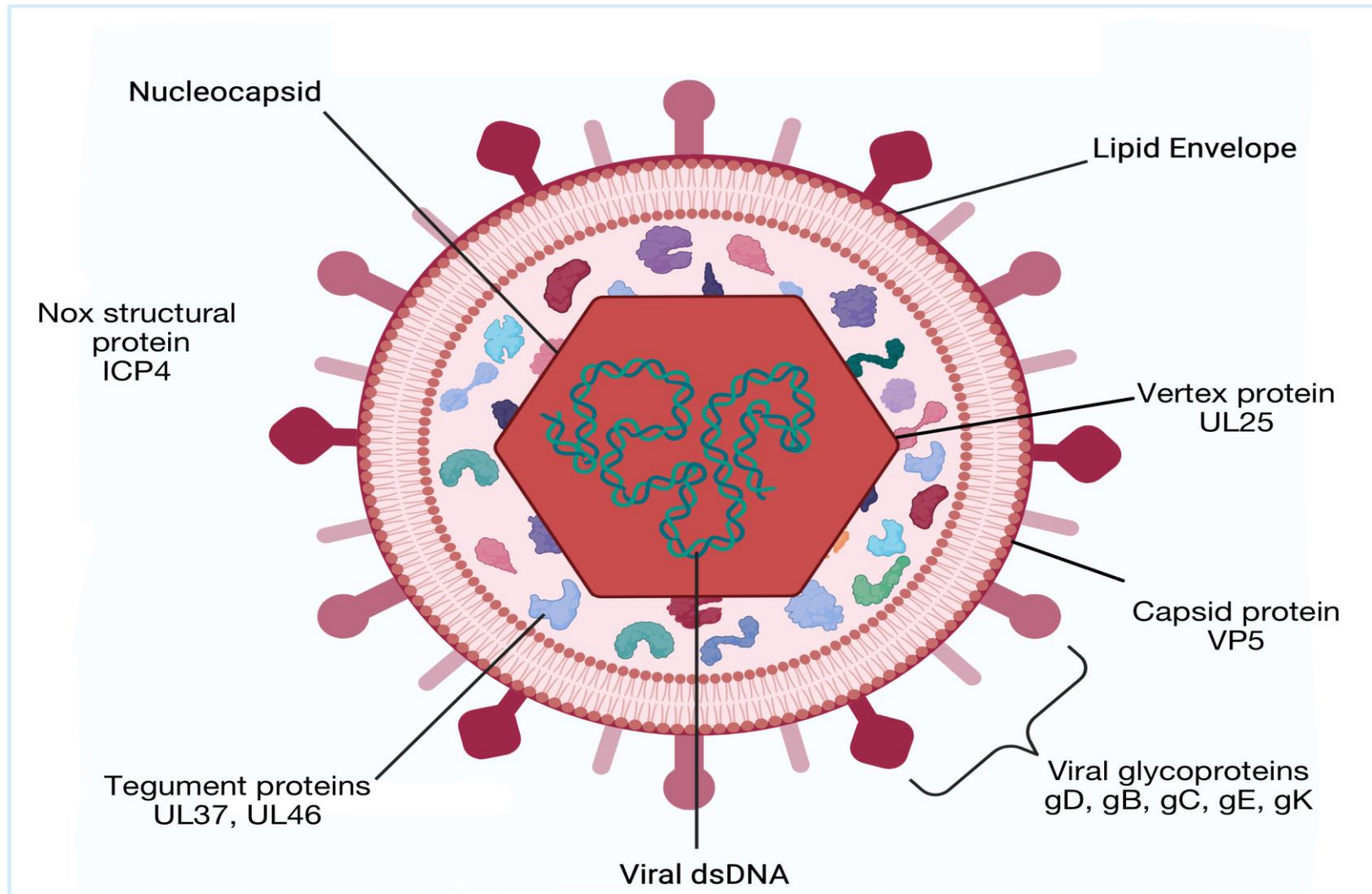


CD4 T cells produce cytokines, support CD8s and antibody production
CD8 T cells kill infected cells, produce antiviral cytokines

Vaccines for Herpes Simplex Virus currently in development

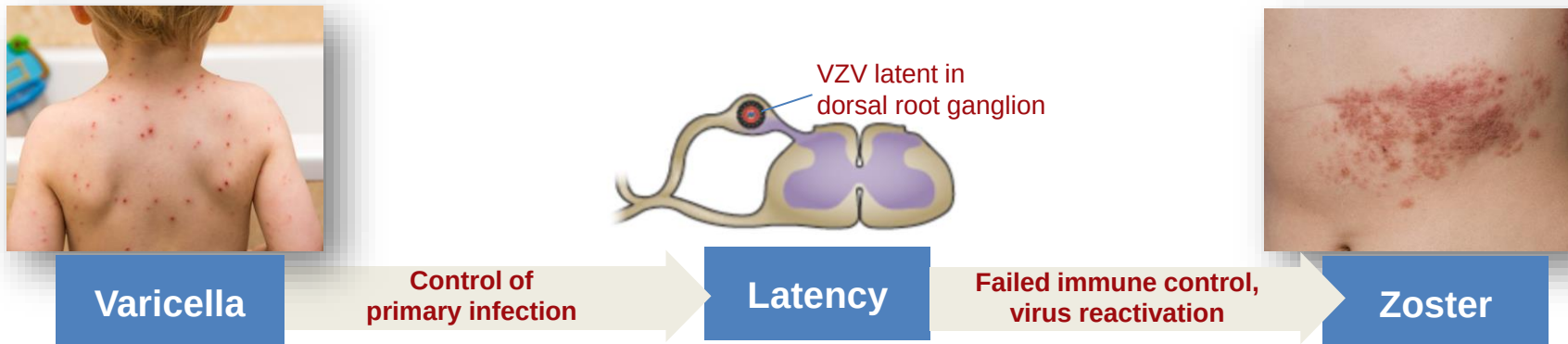
Vaccine candidate	Company	Vaccine constitution	Developmental stage	
Subunit/s + adjuvants				
COR-1	Admedus	gD2 codon optimized DNA vaccine	Phase IIb planned	
NE-HSV2	BlueWillow Biologics	Nanoemulsion with gB2 and gD2 antigens	Pre-clinical, clinical trial planned	
HSV2 trivalent vaccine	University of Pennsylvania	gC2, gD2, gE2 RNA vaccine	Pre-clinical, clinical trial pending	
G103	Immune Design	HSV2 gD, UL19, UL25 + GLA (TLR4 agonist)	Pre-clinical	
Live-attenuated				
HSV529	Sanofi Pasteur	Replication defective HSV2, UL5, UL29 deletion	Phase I trial ongoing	
RVX201	Rational Vaccines	HSV2 ICP0 deletion mutant	Phase Ib/IIa planned	
VC2	Louisiana State University	HSV1 with mutations in gK and UL20	Pre-clinical	
R2	Thyreos LLC	HSV1 with UL37 R2 region mutation	Pre-clinical	
HSV2 ΔgD2	Albert Einstein College of Medicine	HSV2 with US6 (gD) deletion	Pre-clinical	

Current vaccine targets for Herpes Simplex Virus

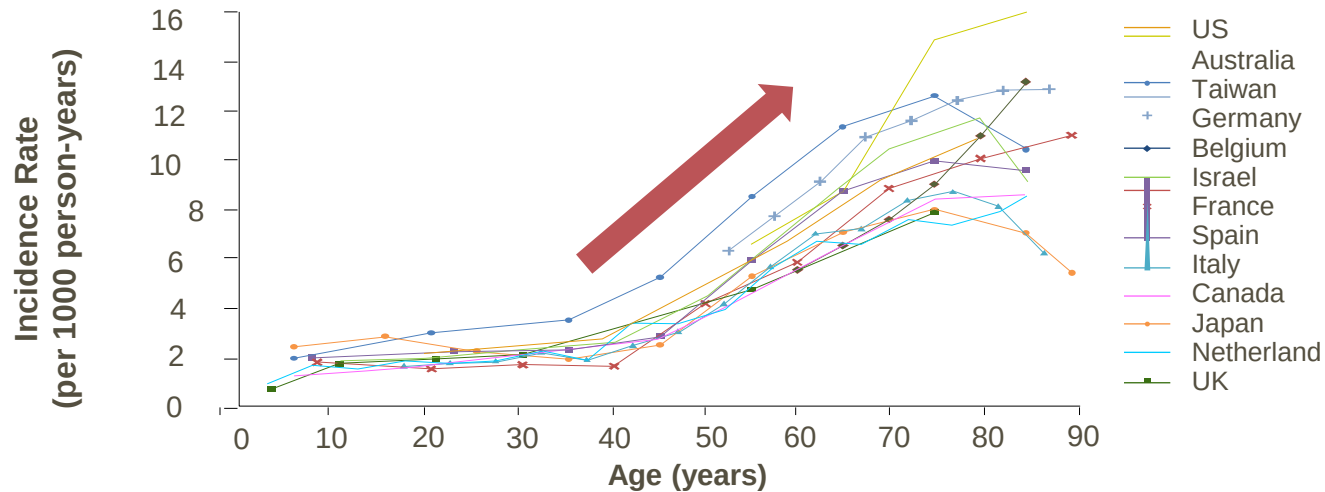


Varicella Zoster Virus (VZV) causes chickenpox and herpes zoster

- Primary infection with VZV causes varicella (chickenpox)
- VZV establishes a lifelong dormant infection in DRG
- Reactivation of VZV causes herpes zoster (shingles) back in the dermis
- 99.5% of adults ≥ 50 years of age are infected with VZV and are at risk for shingles^{1,*}
- 1 in 3 people will develop shingles in their lifetime due to VZV reactivation¹



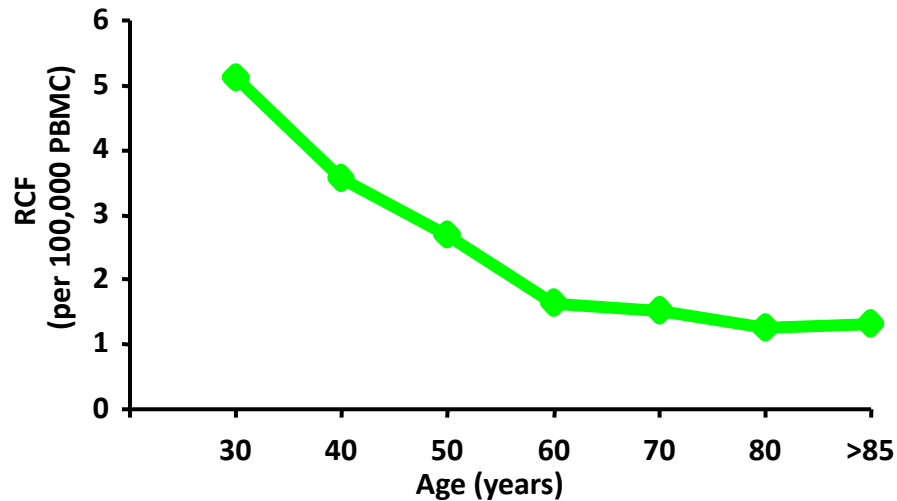
Herpes Zoster: incidence stratified by age



<https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6333a3.htm>

Rationale for Herpes Zoster Vaccine

- *The frequency and severity of zoster increases with age*
- *T cell responses to VZV decline with aging, while antibody does not*



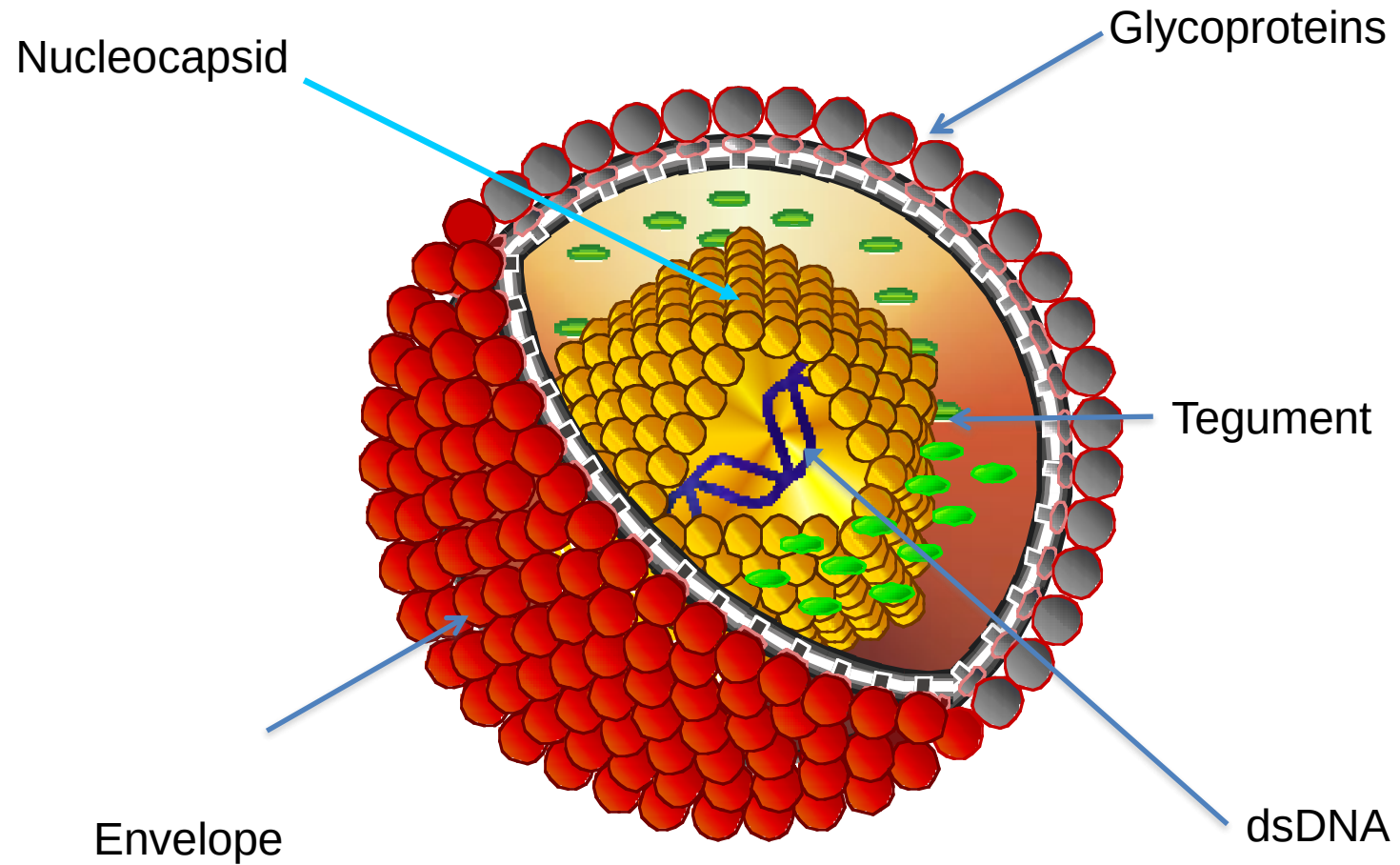
The basis for two hypotheses:

1. the fall in T cell responses to VZV with age to below a threshold permits clinical reactivation of latent VZV

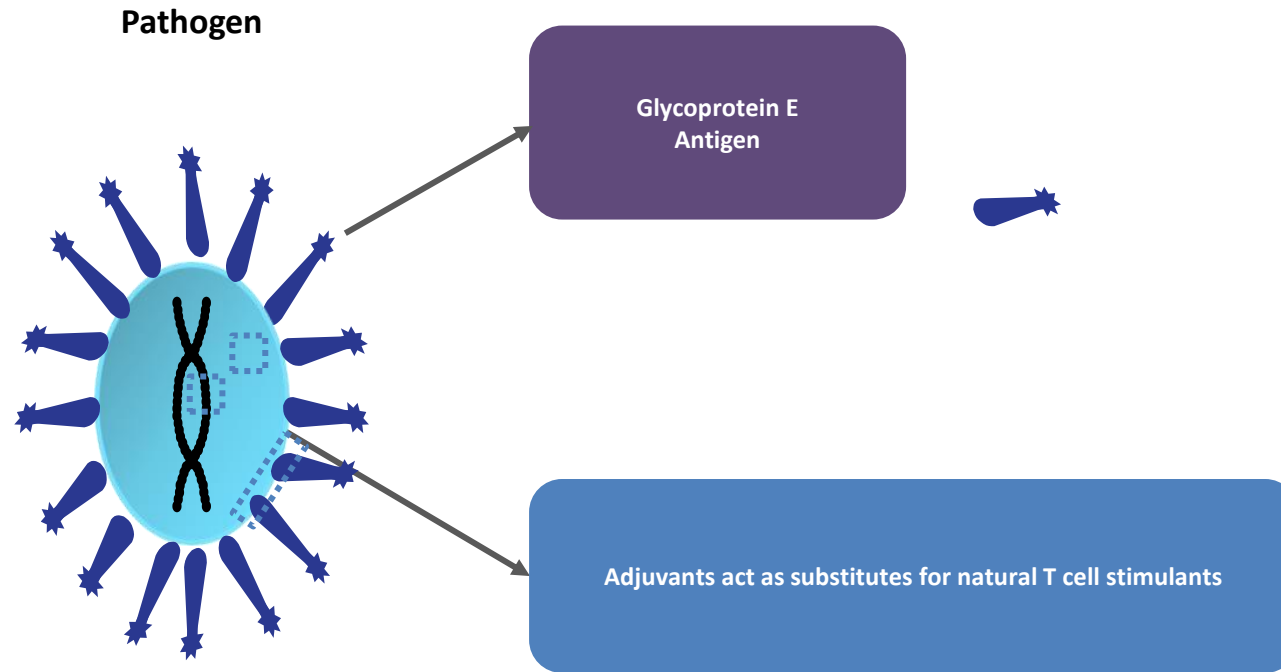
2. increasing the T cell responses to VZV in older people will prevent OR attenuate herpes zoster

-> live attenuated HZ vaccine
VE=51% >60yo (Oxman 2005)

Structure of VZV

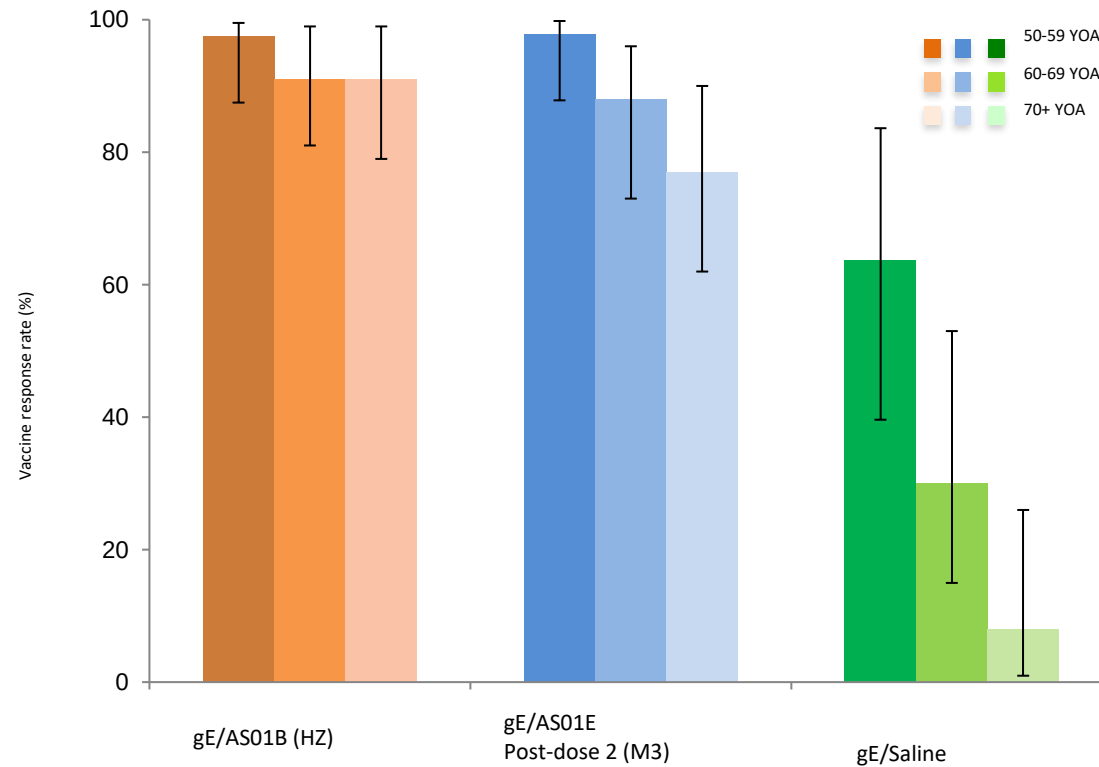


Recombinant Zoster Vaccine (RSV, Shingrix) contains glycoprotein E + T cell adjuvant

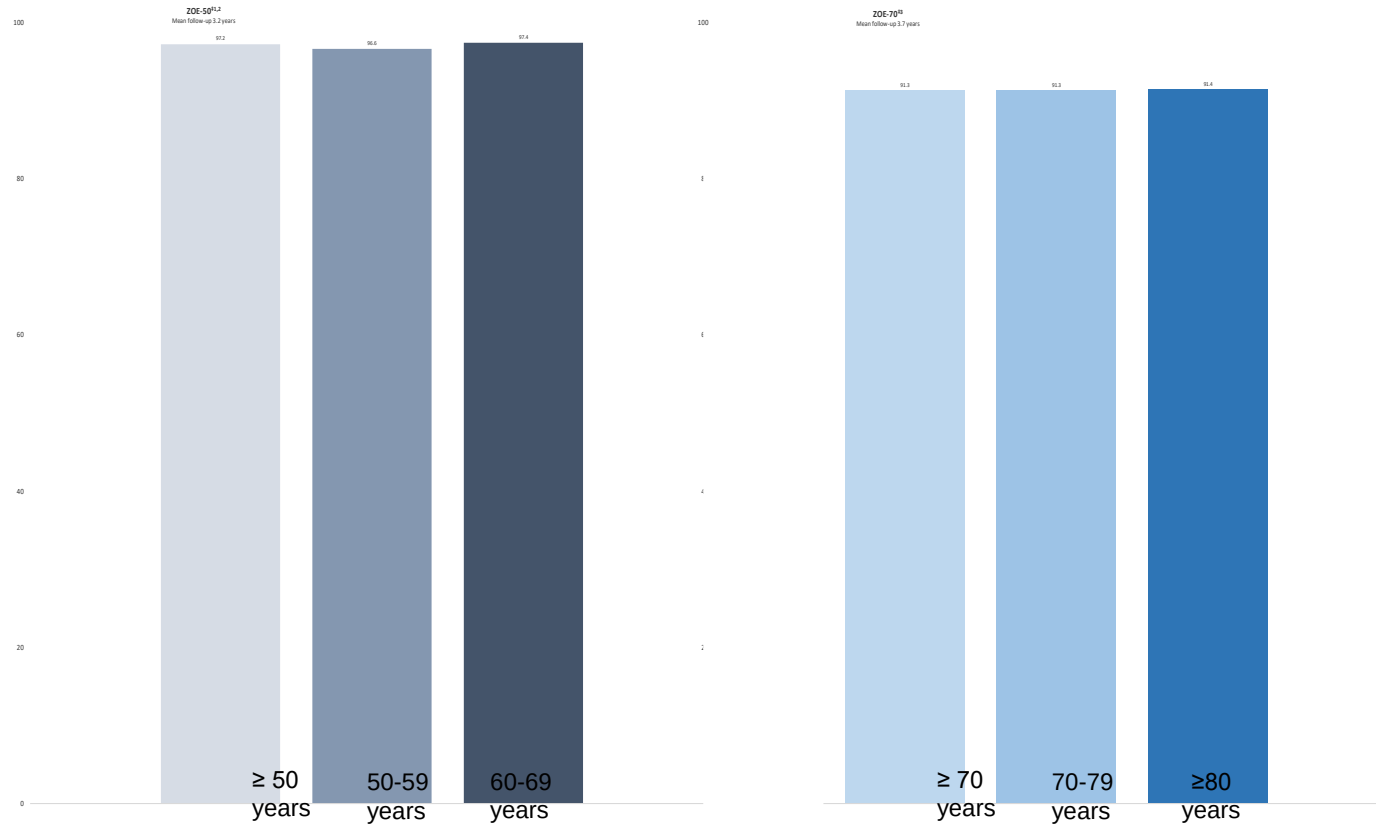


- Viral proteins alone may be insufficiently immunogenic
- Adjuvants act as substitutes for viral immune stimulants enhancing and directing the immune response

Phase I/II: T cell responses to RZV (gE/AS01_B) diminish slower with advancing age than T cell responses to gE antigen alone

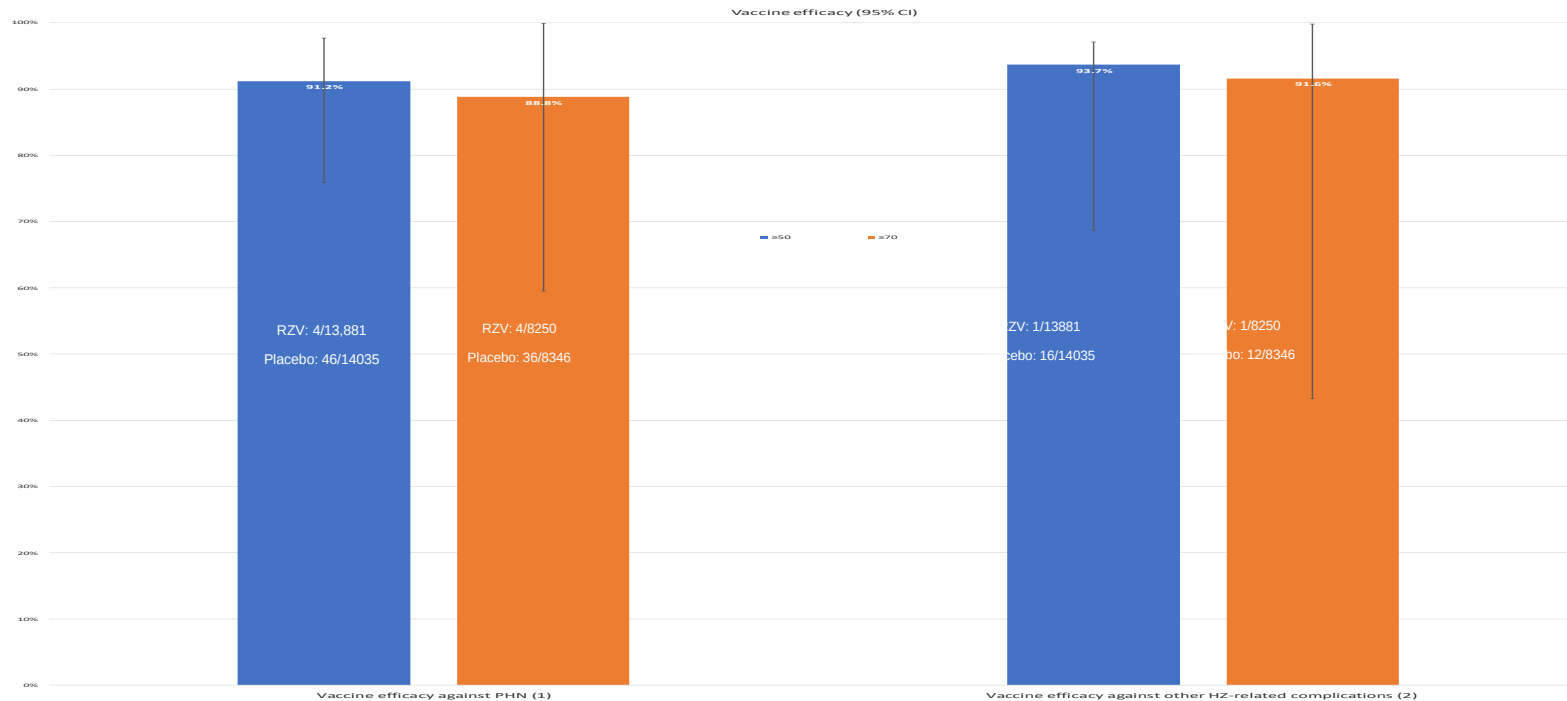


Efficacy of Recombinant Zoster Vaccine (RZV, Shingrix) in subjects >50 and >70YOA



1. Lal H, Cunningham AL et al, *N Engl J Med*, 2015
2. Cunningham AL et al, Heineman T *N Engl J Med*, 2016

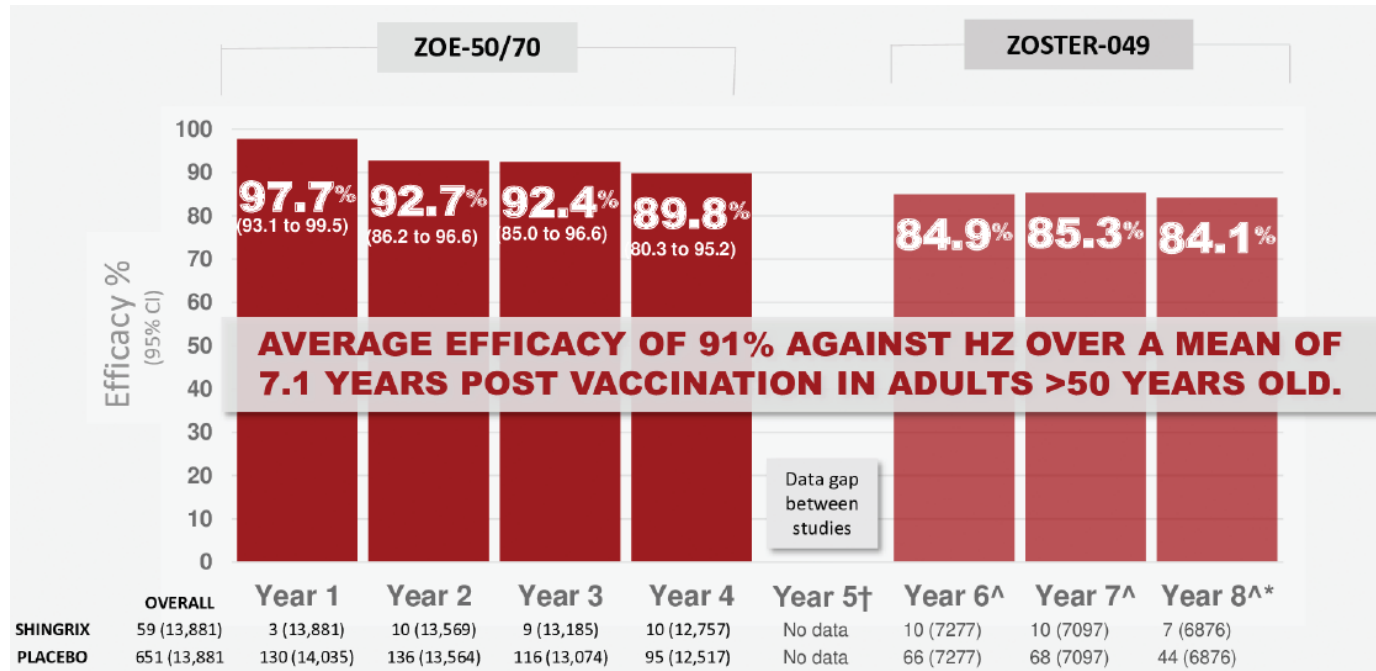
Recombinant Zoster vaccine (Shingrix) significantly reduced risk of PHN and other complications by preventing shingles



PHN is defined as HZ-associated pain rated as ≥ 3 on a 0-10 scale, occurring or persisting for at least 90 days following the onset of rash using the Zoster Brief Pain Inventory questionnaire.¹

Other complications included HZ vasculitis, disseminated disease, ophthalmic disease, neurologic disease, visceral disease, and stroke²

Sustained efficacy against Herpes Zoster in adults ≥ 50 years old for at least 7 years

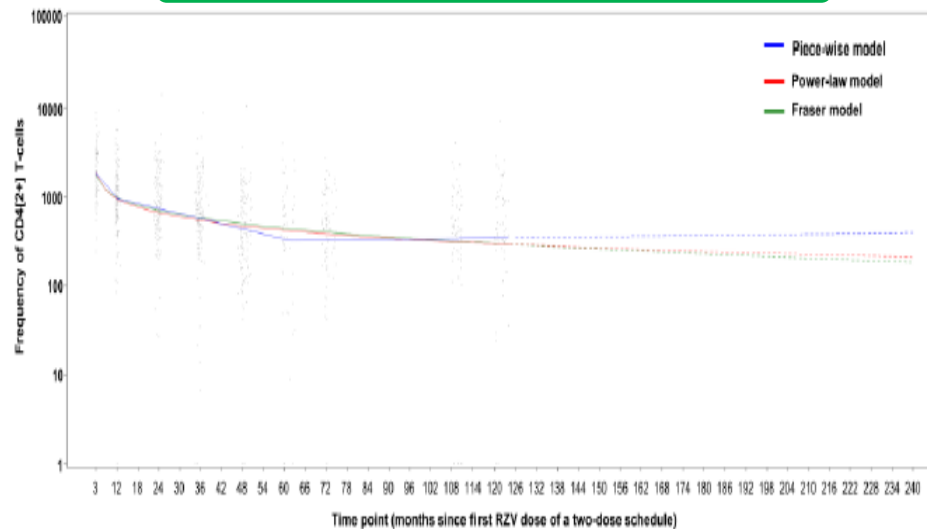


*At the data lock point for the interim analysis in the current follow-up study, data collection for year 8 was still incomplete. † No data are available for Year 5 because that period corresponds to the gap between ZOE-50/70 and the current follow-up study. (N) number of individuals included in each group; n, number of individuals having at least one confirmed herpes zoster. ^ Interim analysis, subset of vaccinees from original ZOE studies, RZV versus matched historical control from the placebo control in the ZOE-50/70 studies, adjusted for age and region at randomization during the ZOE-50/70 studies.

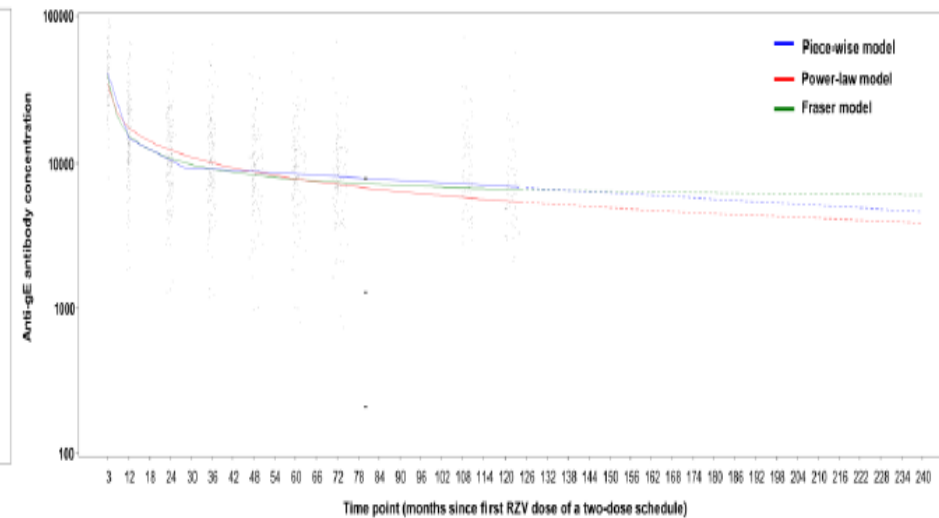
Mathematical modelling of cellular and humoral responses¹

Further Year 10 analysis predicts that mean cellular and humoral immune responses will remain above the observed baseline for at least 20 years after initial vaccination

Cell-mediated immune responses



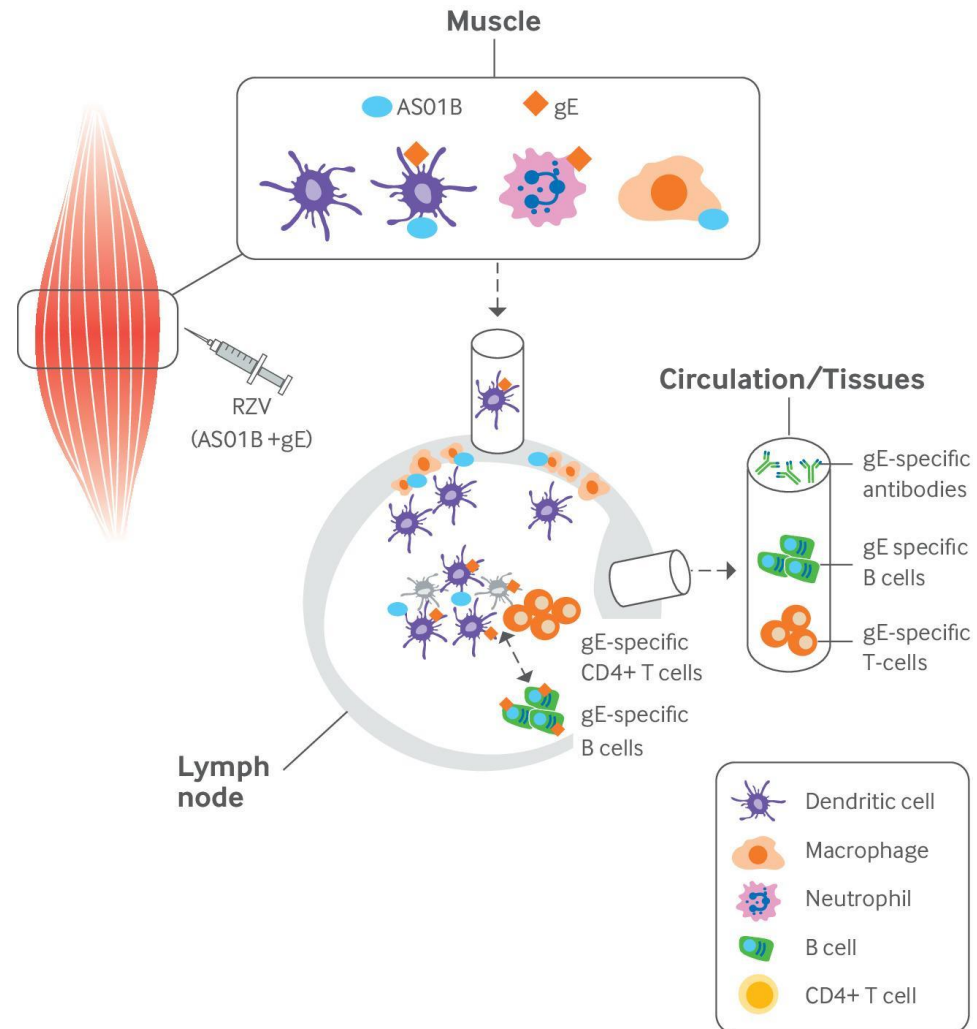
Humoral immune responses



M=month.

1. Hastie A et al. J Infect Dis 2020;10.1093/infdis/jiaa300.

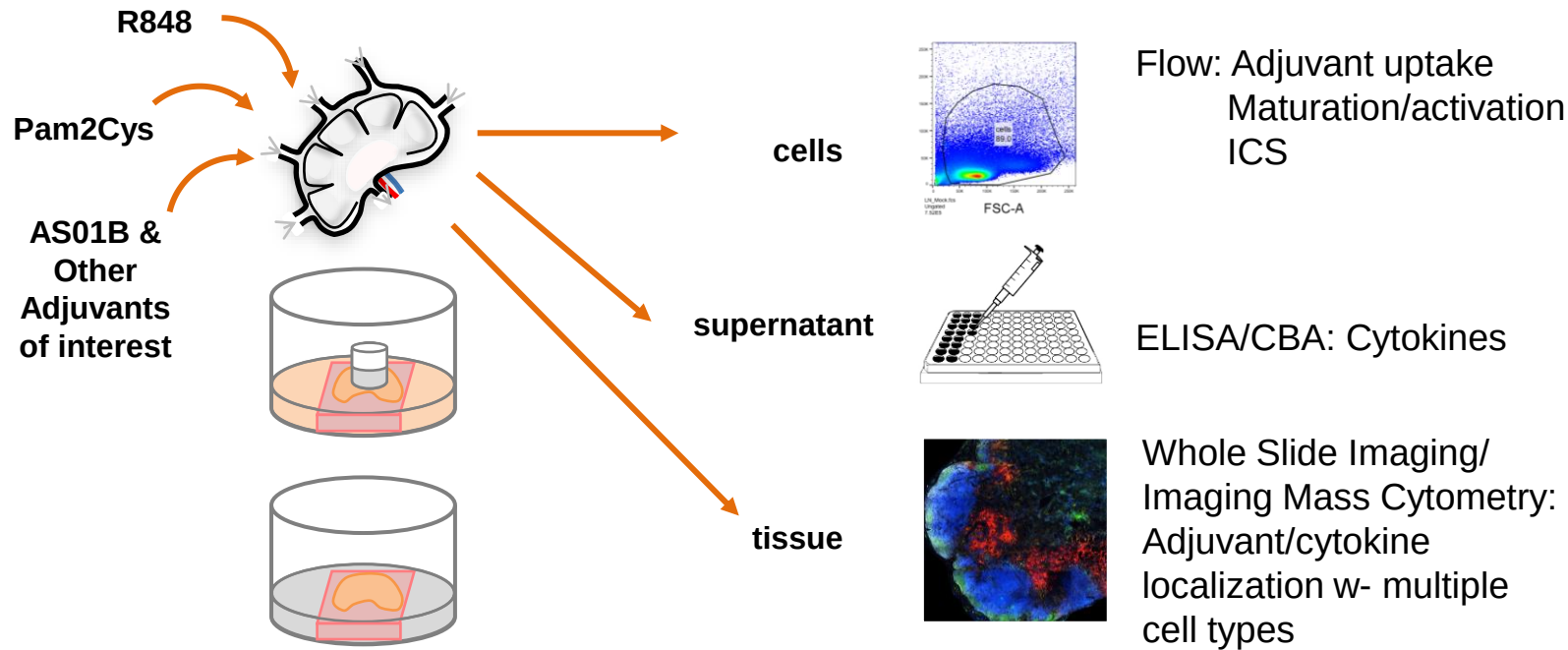
Mechanism of AS01B action in mouse lymph node



Human lymph node models to determine vaccine/adjuvant mechanisms of action



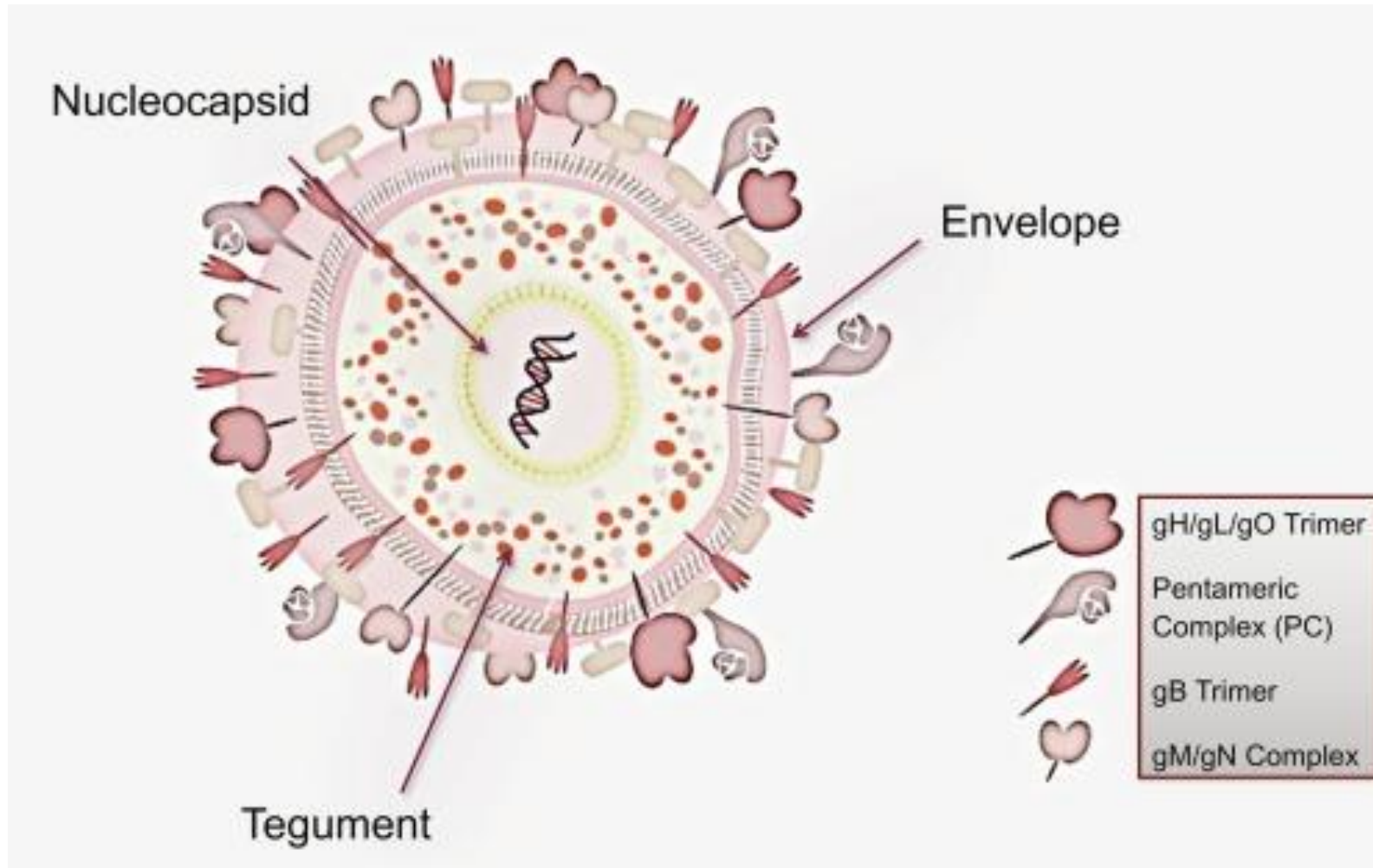
Kerrie Sandgren



AS01 also Stimulates a Cascade of Immune Responses in Human Lymph Nodes

- Human lymph node model was developed for vaccine/adjuvant uptake studies
- Liposomes taken up by Sinus Lining macrophages
- AS01B activates inflammasome in these macrophages then activates DCs and induces T cell interferon gamma production via a cytokine cascade
- **Future:**
 - Compare to mRNA vaccines

Cytomeglovirus attachment proteins: targets for neutralizing antibodies



Pentamer > gB in induction of neutralizing antibody: protects fetus; T cells -> gB

HCMV Vaccine Candidates

HCMV protein targets for CD4 and CD8 lymphocytes

Infected Macrophages, Epithelial or Epithelial cells

CD4

Late

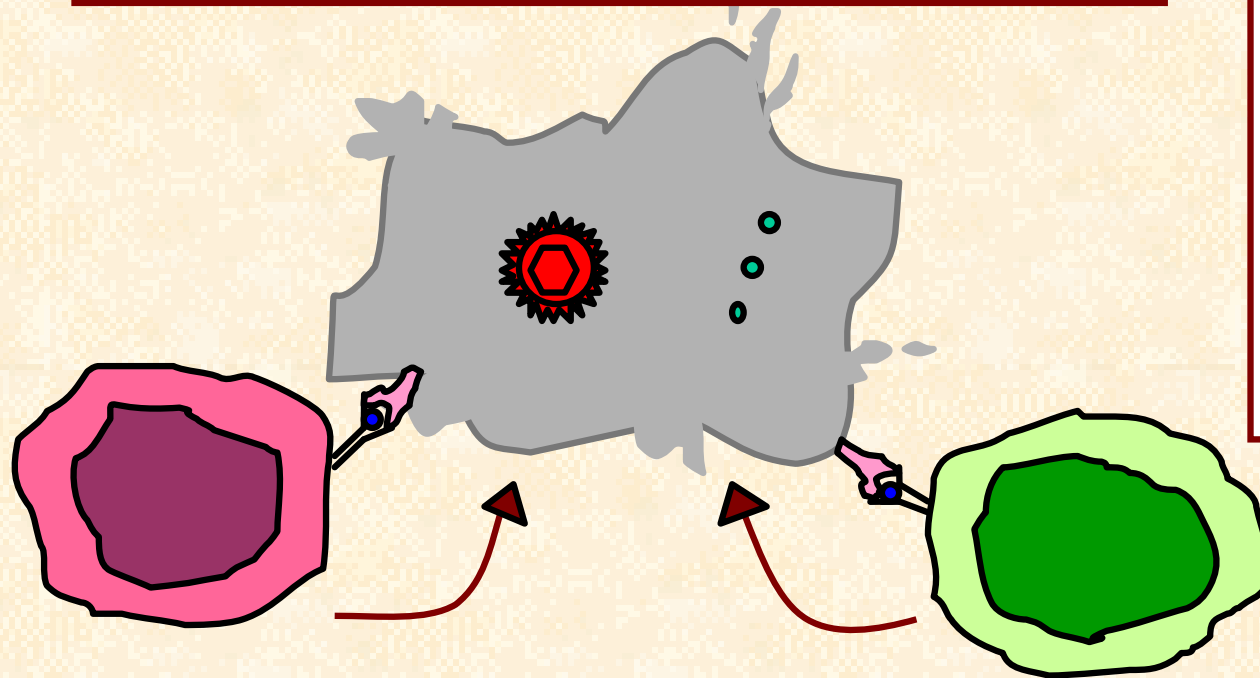
gB

pp65

Early

IE1

IE2



CD8

Late

gB

pp65

Early

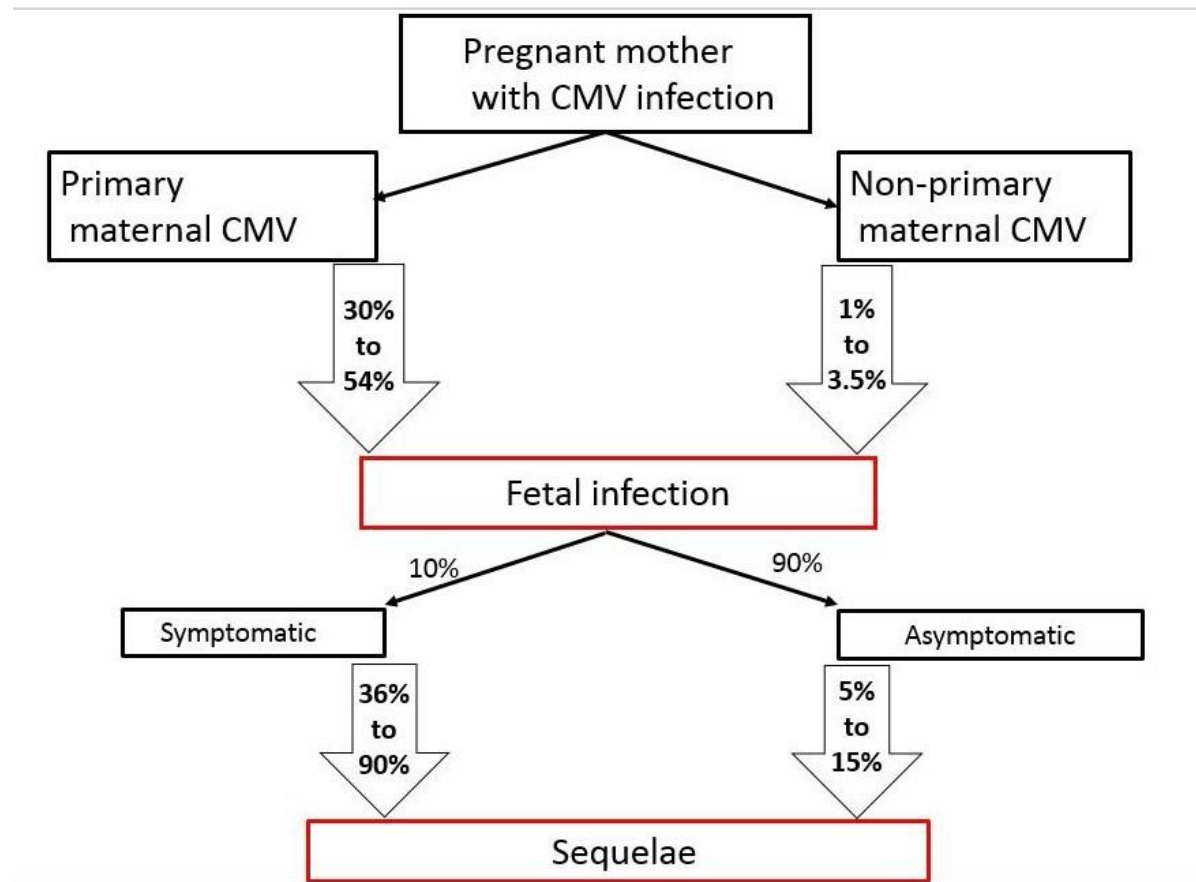
IE1

IE2

Disease Targets for Human Cytomegalovirus Vaccines

- **Congenital CMV syndrome and hearing loss**; 1 in 30/200 newborns
 - ~ Down syndrome and fetal alcohol syndrome
 - most severe in seronegative mothers but there are still sequelae in seropositives
 - >2/3 of all congenital CMV infections occur in seropositives (commoner)
 - 85-90% have no symptoms of birth but 10-15% of these will develop sequelae, especially deafness
- **Post transplant CMV syndromes**
 - Solid organ Tx (SOT): main risk is seronegative patients receiving Tx from seropositive donor: 1/3 develop disease,
+ve -> +ve can develop superinfection with new strain
 - HSCT recipients: seropos -> reactivation from T cells, macrophages, endothelial cells under immunosuppression (needs immunization before and after HSCT)

Rates of fetal infection and sequelae following maternal infection



Historical phase II vaccine trial in congenital Cytomegalovirus

Recent phase II trial:

Sanofi gB/MF59 in seroneg women at 0, 1,6 mo, VE=50% (p=.02)
to CMV infection (Pass R et al NEJM 2009)

Recent correlate of immunity in natural infection suggests:

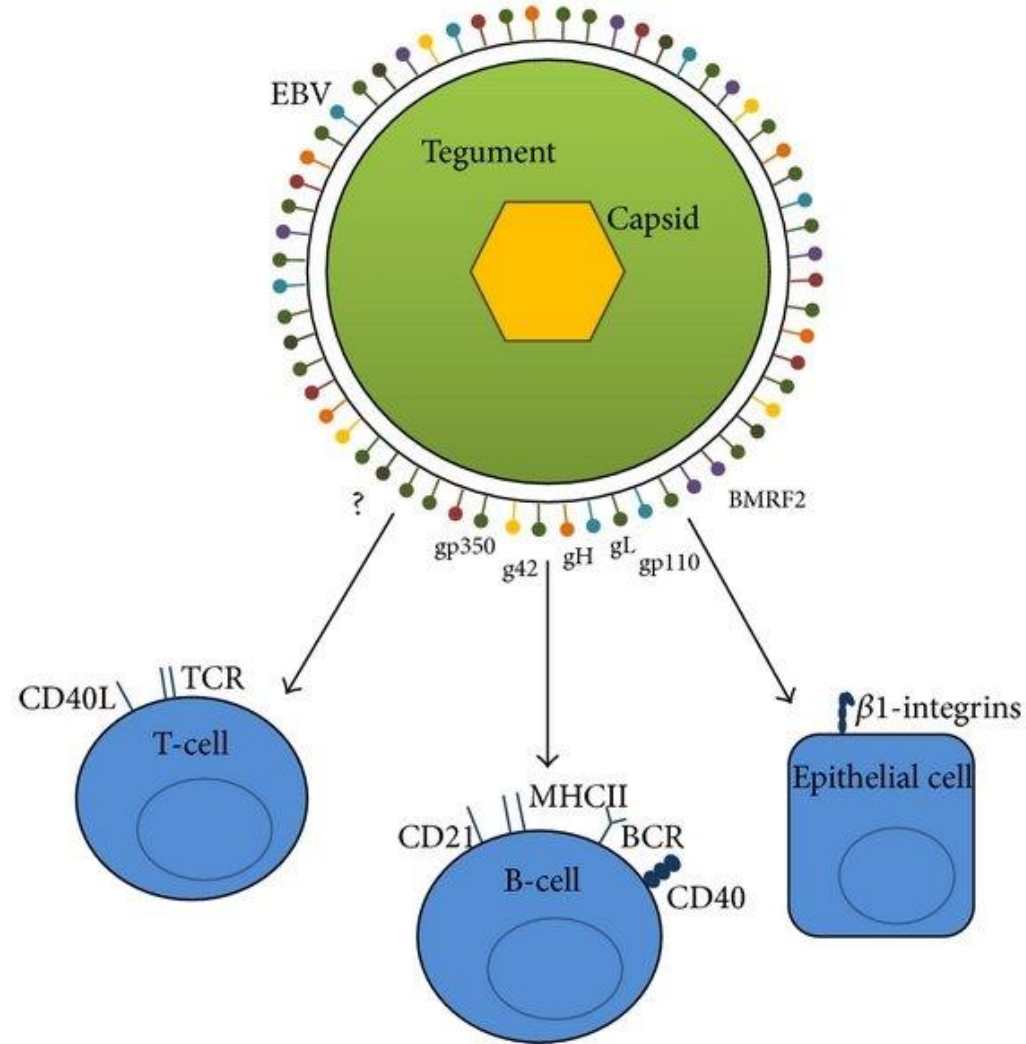
Add pentamer to gB antigens -> for optimal neutralizing antibody levels (ref)

Current Congenital Cytomegalovirus Vaccine

Phase II/III trials

- Merck V160: phase II -> nAb + T cell & memory responses in seronegatives
- Sanofi: trials with gB/pentamer + CD4 adjuvants planned
- **Moderna** commenced gB/pentamer vaccine phase III trial in ~7000 seronegative and seropositive women, primary endpoint is prevention of primary CMV infection in seronegative women

Epstein-Barr virus attachment proteins: targets for neutralizing antibodies

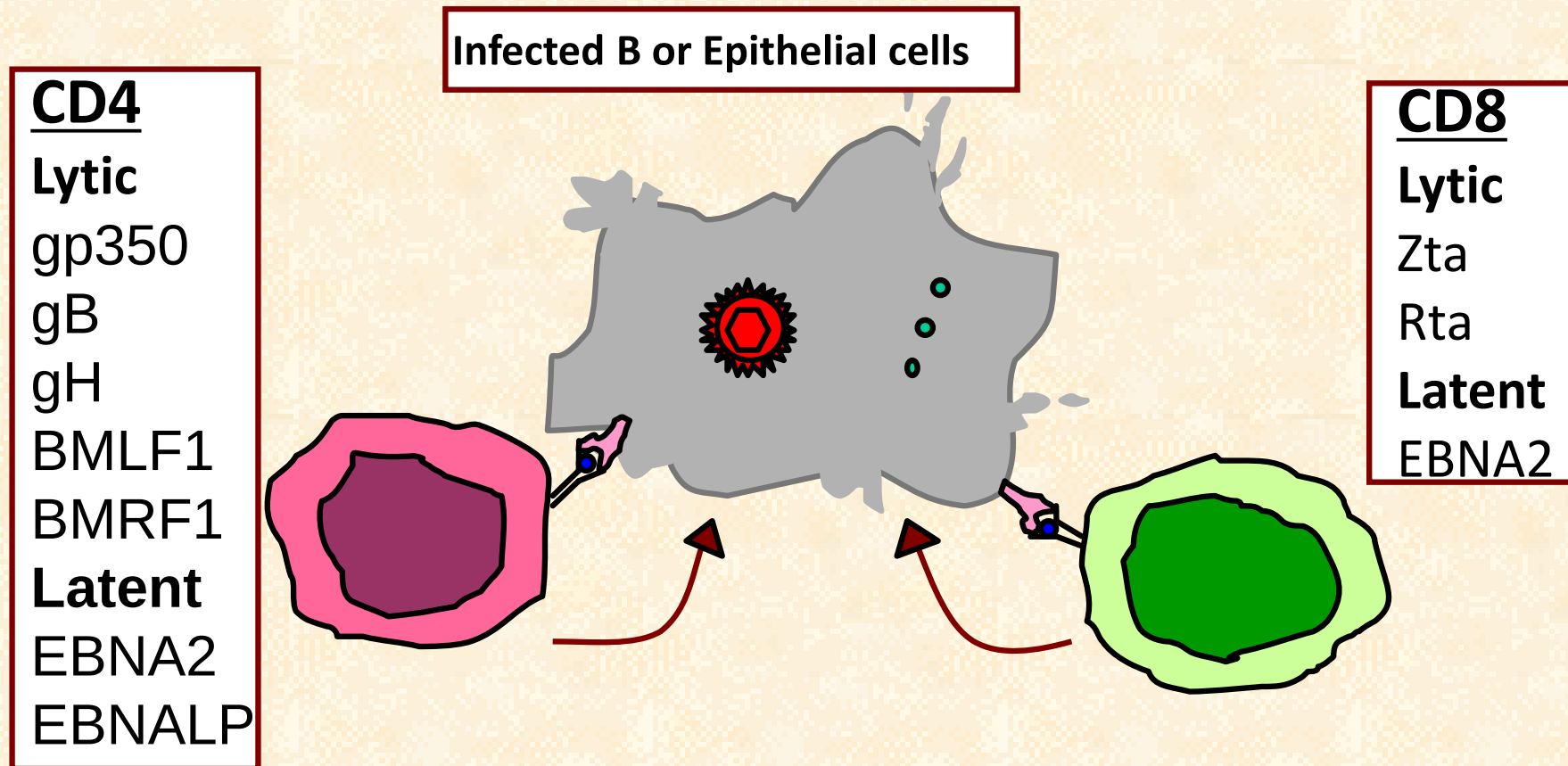


Disease targets for Epstein-Barr virus vaccines

- **Infectious mononucleosis** -> Hodgkin's disease (RR 4.0, median 4.0 years)
-> Multiple sclerosis (RR 2.2, median 5.6 years)
- **EBV post-transplant lymphoproliferative disease**
(within one year post HSCT and <3 years post SOT)
In 6% seroneg Tx recipients: primary infection after Tx -> 30-fold risk
EBV viral load (VL) predictive
- **EBV associated lymphoma in HIV+ patients:** VL also predictive
So even if EBV vaccines don't prevent asymptomatic infection they could reduce VL
- More difficult targets:
 - X linked lymphoproliferative disease: low/short lived response?
 - Burkitt lymphoma (early administration as 50% infected at <1 yr; follow for 5-10 years)
 - Nasopharyngeal/gastric carcinoma: long latency period before cancer develops

EBV Vaccine Candidates

EBV protein targets for CD4 and CD8 lymphocytes



Epstein-Barr virus vaccine trials

- **Infectious mononucleosis:**
 - EBV gp 350 + alum/MPL adjuvant: Phase II dbpc trial in 180 EBV seroneg adults VE =78% (ITT, $p=0.03$ but no effect on asymptomatic infection (Sokal et al 2007)
 - EBNA3A peptide + adjuvants Tet Tox/Montanide ISA720 (oil in water) in HLA-B8 subjects: trend to protection against IM (Rees et al 2009)
- **Nasopharyngeal carcinoma:** EBNA1/LMP2 in MVA (vaccinia); LMP2 peptides; results pending

Future:

Need Phase III trial of gp350 vaccine + adjuvant against IM

In Development:

gp350 tetramers, VLPs, nanoparticles ; gB and gH/L trimers, nanoparticles and VLPs; vectored; mRNA

Epstein-Barr virus vaccines; NIH consensus conference 2011

- **Disease targets:** infectious mononucleosis
EBV associated cancers
- **Need:**
 - EBV malignancy surrogate markers as endpoints
 - immune correlates of protection against both EBV infection and disease
 - epidemiologic studies to define vaccine benefits
 - strategy for academic-government-industry collaborations to accelerate developments

HSV, CMV and EBV vaccine development: overall challenges

- Large viruses, multiple proteins
- Multiple proteins involved in **viral entry** into different cell targets (commonalities being understood):
 - which to target for neutralizing **antibody**/ADCC
- Exact role of **CD4/CD8 T cells**
 - multiple viral protein targets, with individual HLA related heterogeneity -> great complexity in defining immune correlates of protection in multiple diseases
- Selection and development of relevant **adjuvants**
 - according to immune correlates of protection

Acknowledgements



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Hafsa Rana, Nicole Popovic, Orion Tong
Not pictured: Erica Longmuir-Vine

HSV and Vaccine Immunology Group

Dr Naomi Truong, Jacinta Smith, Jason Herbert, **Dr Kerrie Sandgren**,
Dr Monica Miranda-Saksena, Dr Kevin Danastas, Vicki Stylianou

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Vaccines

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Himal Lal

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Surgeons

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Jake Lim

Laith Barnouti

Gavin Sandercoe

Peter Haertsch

Andrew Brooks

Michael Wines

Richard Ferguson

Elizabeth Elder

James French

Obstetrician/Gynaecologist

Gregory Jenkins

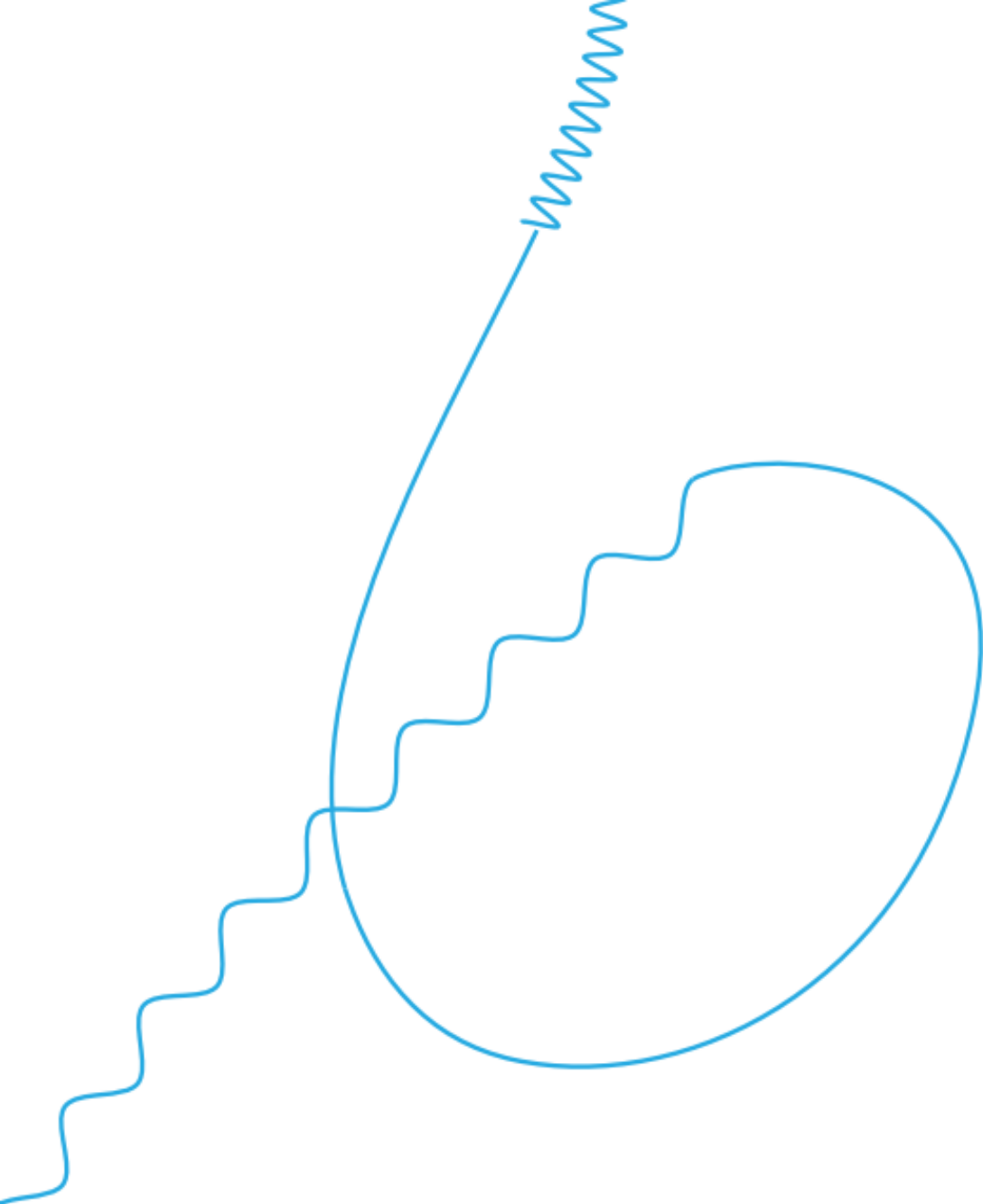
**All patients who kindly consented to
donate tissue**



Dr Kerrie Sandgren



Vicki Stylianou



Cytomegalovirus (CMV) Overview

Jacqueline Miller, M.D.

*Senior Vice President, Therapeutic Area
Head, Infectious Diseases, Moderna*

Learn more about CMV



<https://nowiknowcmv.com/>

Cytomegalovirus (CMV) Overview

Most common
cause of congenital
infection worldwide

>\$1B in annual
healthcare costs¹

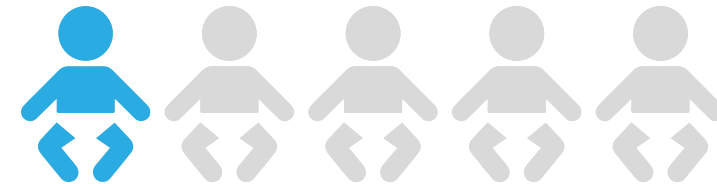
Sequelae include:

- At birth: microcephaly, chorioretinitis, seizures, sensorineural hearing loss
- Long term: cognitive impairment, cerebral palsy, seizure disorder, sensorineural hearing loss



1 in 200

babies in the U.S. are born with a congenital CMV infection (CMV infection is present at birth)



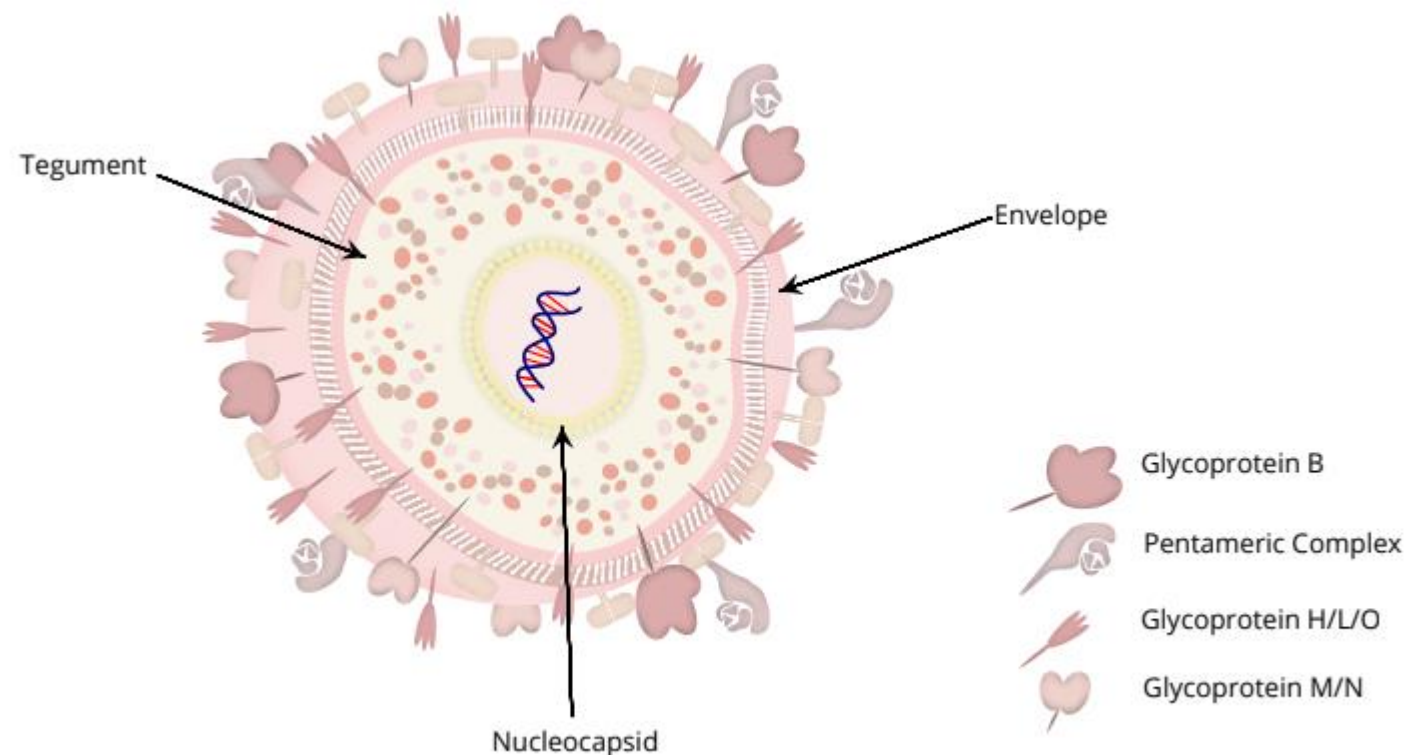
1 in 5

will have severe, life-altering health problems

(1) Grosse, Scott et al. "Economic assessments of the burden of congenital cytomegalovirus infection and the cost-effectiveness of prevention strategies," *Seminars in perinatology*, 2021, <https://doi.org/10.1016/j.semperi.2021.151393>

The Moderna CMV vaccine candidate has two antigens: Glycoprotein B and the Pentameric Complex

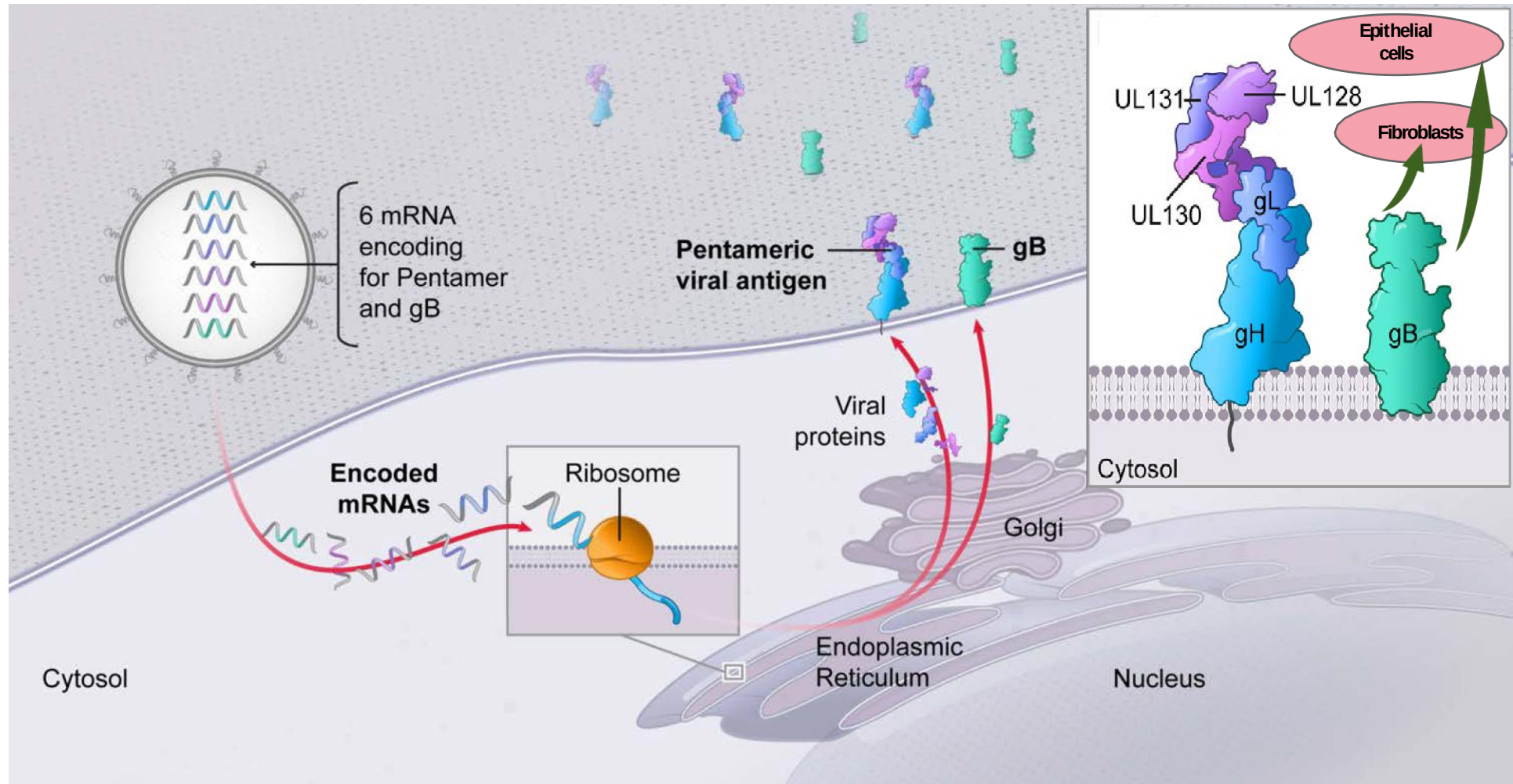
- The CMV virus genome is made up of double-stranded DNA, and the viral DNA and protein is protected by a lipid envelope, which is embedded with virus-encoded proteins¹
- Previous vaccine candidate that targeted the gB protein (with an adjuvant) was able to achieve ~50% efficacy²



(1) <http://cmv.umn.edu/about-cmv>

(2) Pass et al, "Vaccine Prevention of Maternal Cytomegalovirus Infection," *New England Journal of Medicine* (2009), <https://doi.org/10.1056/NEJMoa0804749>

Our CMV vaccine (mRNA-1647) includes 6 mRNAs (five encode the pentamer, the 6th encodes for the gB antigen)



Phase 2 clinical study led to selection of 100 µg dose for evaluation in pivotal Phase 3 trial

Safety Summary

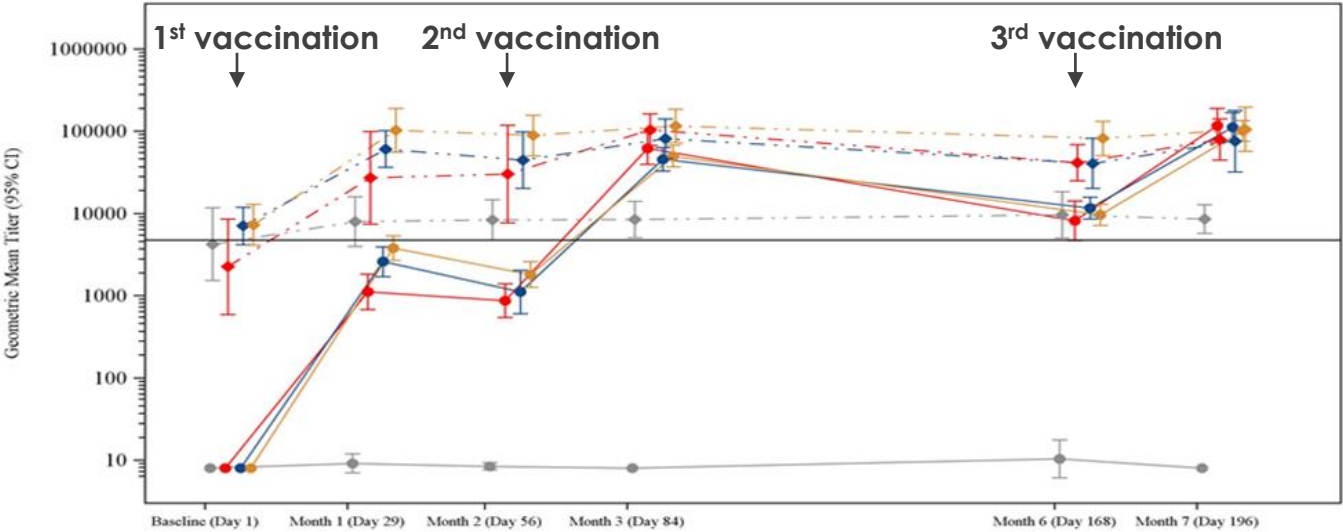
- In the Phase 2 study, which tested 50, 100 and 150 µg dose levels, **mRNA-1647 CMV vaccine was observed to be generally well tolerated:**
 - No treatment-related SAEs and no study pause rules were met
 - Most common solicited local AR was injection site pain
 - Most common solicited systemic ARs were headache, fatigue, myalgia, arthralgia, and chills
 - In general, solicited AR frequency and severity after the 3rd vaccination were similar to or lower compared to the 2nd vaccination

Immunogenicity Summary

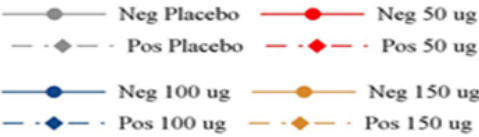
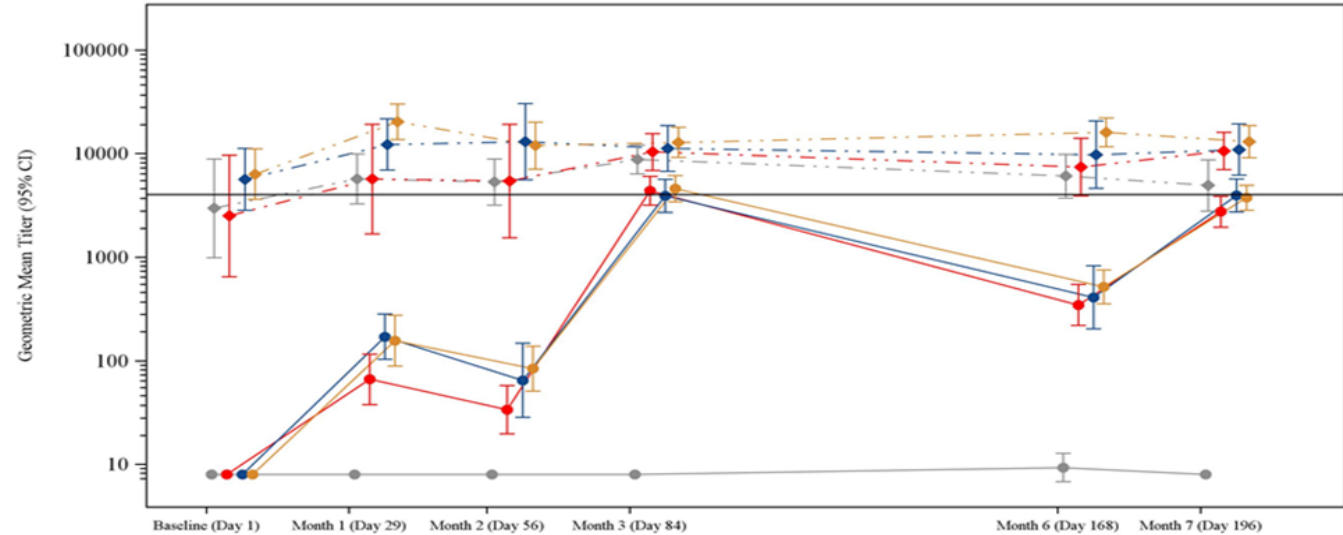
- In both seronegative and seropositive participants, strong immunogenicity seen against epithelial cells and fibroblast cells. After the third dose:
 - nAbs GMT against epithelial cells were 20-fold higher than benchmark in seronegative participants and ~7-fold higher in seropositive participants
 - nAbs GMT against fibroblast cells reached the benchmark in seronegative participants and increased ~2-fold in seropositive participants

mRNA-1647 Phase 2 trial seven-month interim data: Strong immunogenicity seen in both CMV-seronegative and CMV positive participants

Neutralizing Ab Against Epithelial Cell Infection



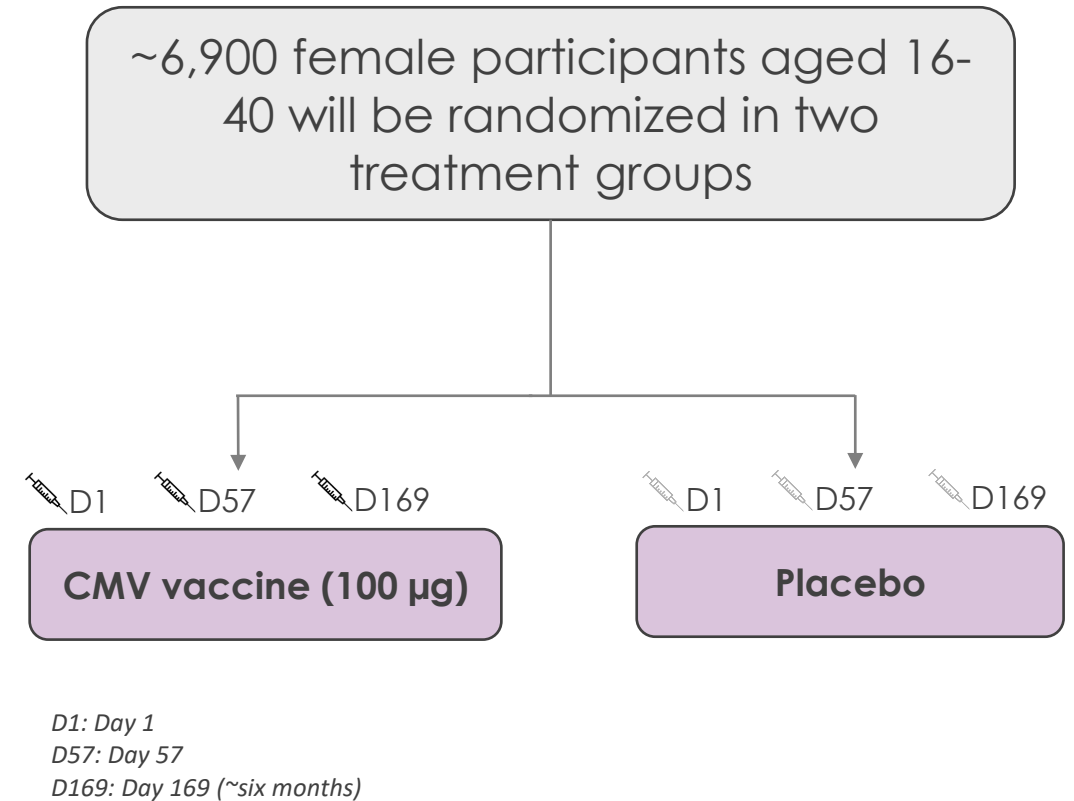
Neutralizing Ab Against Fibroblast Infection



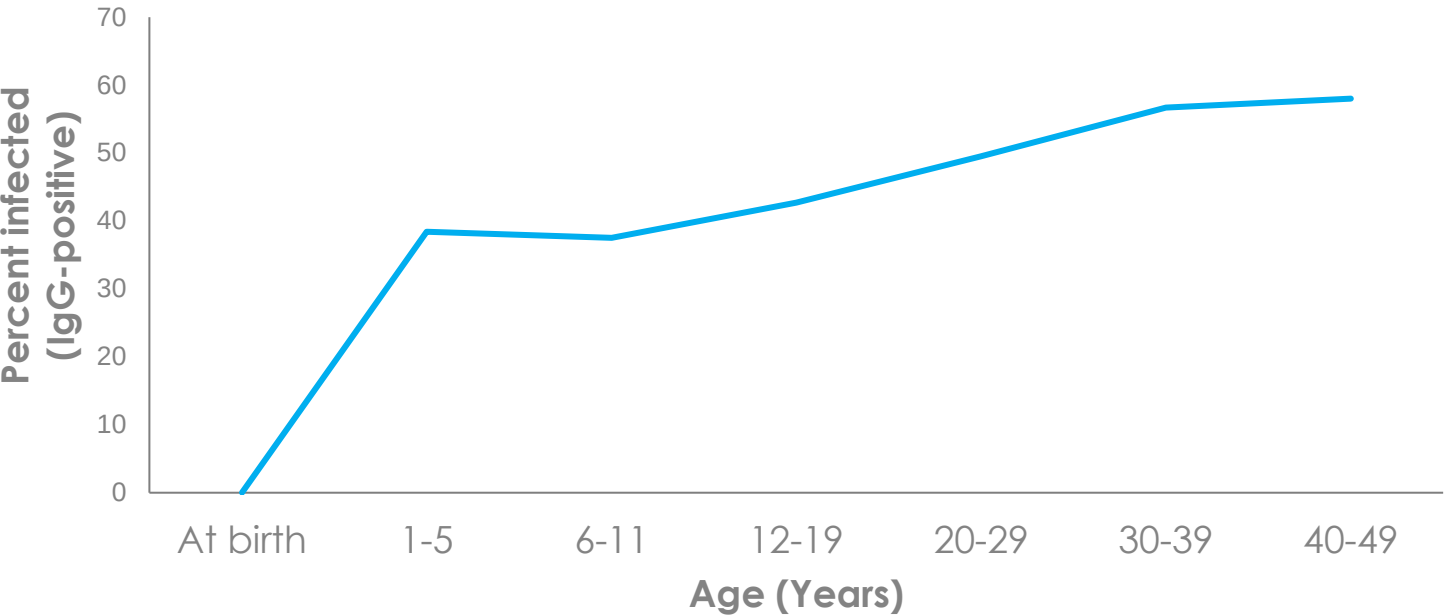
Pivotal Phase 3 trial is ongoing to evaluate mRNA-1647 in women of child-bearing age



- Randomized, observer-blind, placebo-controlled study to evaluate the efficacy, safety and immunogenicity of mRNA-1647 to evaluate prevention of primary infection
- **Enrollment is ongoing in the U.S. and internationally**
 - Expected to enroll up to 6,900 women of childbearing age, from approximately 150 sites globally
- **Participants must be at a higher risk of contracting CMV**
 - Participants aged ≥ 20 years must anticipate having direct exposure (in the home, socially, or occupationally) to at least 1 child ≤ 5 years of age
- **Goal to enroll a diverse group of U.S. participants into the study**, including approximately 42% of participants who are Persons of Color
- **Primary efficacy analysis will be triggered based on accrual of seroconversion cases**; meeting the primary objective will be the basis for filing



But birth defects are not the only impacts of CMV: At each stage of life, CMV may present different long-term outcomes



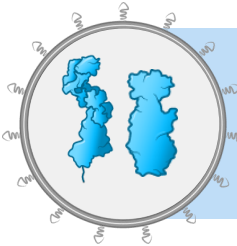
Longer-Term CMV Impacts	
Impaired Influenza vaccination response ¹	Alzheimer's Disease ⁷
Immunosenescence ²	Glioblastoma Multiforme ⁸
Male Infertility ³	Autoimmune Diseases ⁹
Burns, Sepsis, Trauma ⁴	Tuberculosis ¹⁰
Cardiovascular ⁵	Inflammatory Bowel Disease ¹¹
Cognitive Decline ⁶	Organ-specific Complications ¹²

Outcomes listed within this graph are not indicative of every outcome of CMV infection. Additional studies are warranted.

1) Nielse, Carolyn et al., *J Immunol.* (2015), <https://doi.org/10.4049/jimmunol.1403080>
2) Khan, Naaem et al., *J Immunol.* (2002), <https://doi.org/10.4049/jimmunol.169.4.1984>
3) Naumenenko, Victor et al., *Herpesviridae* (2011), <https://doi.org/10.1186/2042-4280-2-7>
4) Osawa, Ryosuke et al., *Crit care.* (2009), <https://doi.org/10.1186/cc7875>
5) Simanek, AM et al., *PLoS One* (2011), <https://doi.org/10.1371/journal.pone.0016103>
6) Gow, Alan et al., *Neurobiol. Aging* (2013), <https://doi.org/10.1016/j.neurobiolaging.2013.01.011>

7) Barnes, Lisa et al., *J Infect Dis* (2015), <https://doi.org/10.1093/infdis/jiu437>
8) Rahman, Maryam et al., *Oncoimmunology* (2019), <https://doi.org/10.1080/2162402X.2018.1514921>
9) Gugliesi, Francesca et al., *Viruses* (2021), <https://doi.org/10.3390/v13020260>
10) Heijden, Yuri et al., *Open Forum Infectious Diseases* (2021), <https://doi.org/10.1093/ofid/ofab539>
11) Thorn, Mari et al., *Scandinavian Journal of Gastro Enterology* (2016), <https://doi.org/10.3109/00365521.2016.1156154>
12) Eddleston, M et al., *Clin Infect Dis* (1997), <https://doi.org/10.1093/clinids/24.1.52>

We will evaluate our CMV vaccine (mRNA-1647) against both congenital CMV infection and long-term impacts



CMV Vaccine (mRNA-1647)

Indication

Primary CMV infection
(a necessary precursor
to congenital CMV)

Long-term impacts
(autoimmune disease, cancer,
cardiovascular etc.)

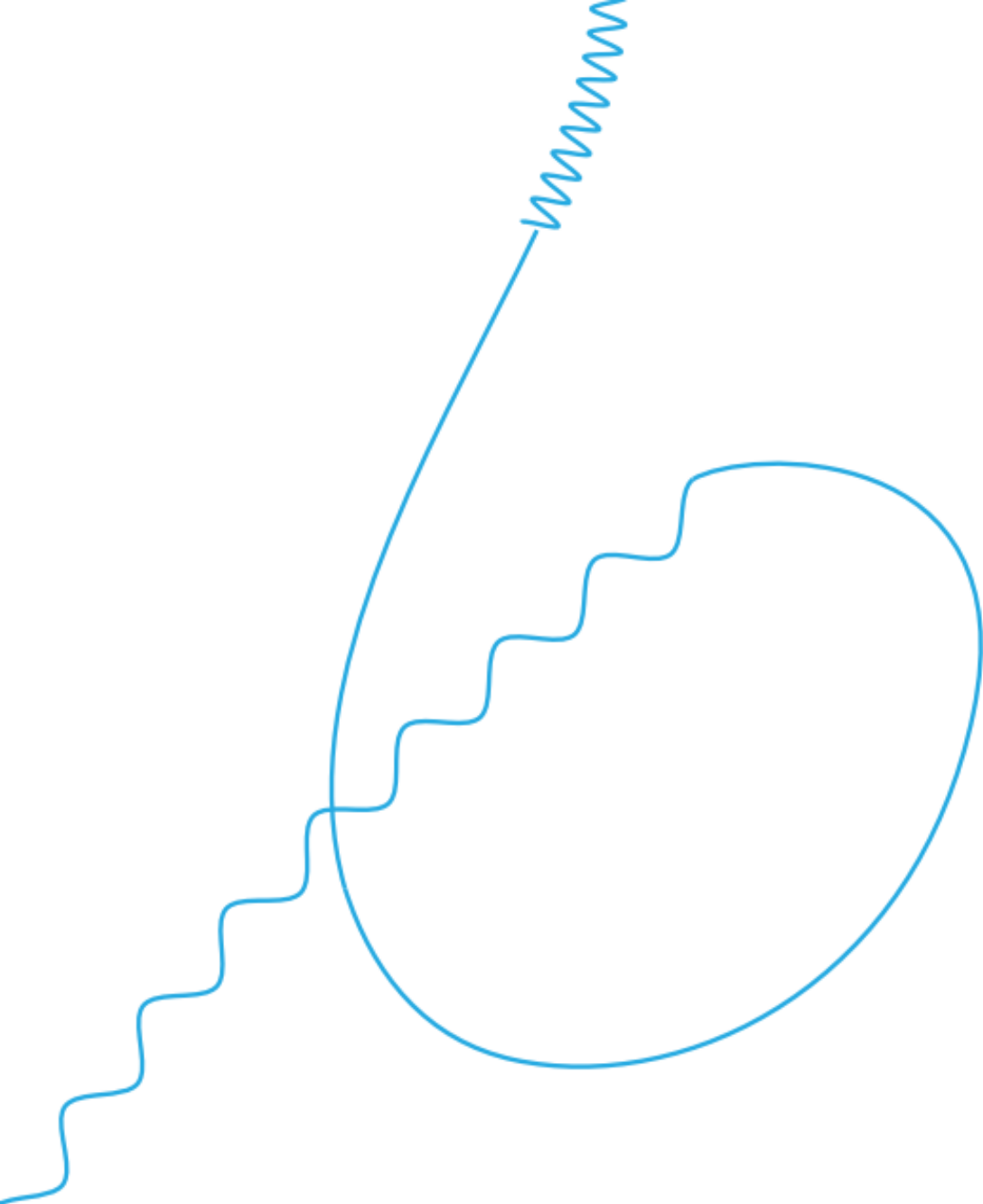
Clinical Trial
Strategy



mRNA-1647-
P301

Phase III Trials
Post-approval studies

Epidemiology studies
Mechanistic studies



Epstein-Barr Virus (EBV) Overview

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Harvard School of Public Health, Harvard Medical School



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*Harvard School of Public Health,
Harvard Medical School*

Alberto Ascherio, MD, DrPH, is a Professor of Epidemiology and Nutrition at the Harvard T. H. Chan School of Public Health and a Professor of Medicine at the Harvard Medical School. Dr. Ascherio trained in internal medicine at the University of Milan, and subsequently practiced medicine and public health in Latin America and Africa. He completed his doctoral degree in epidemiology at the Harvard T. H. Chan School of Public Health. Dr. Ascherio's research is primarily devoted to finding the causes of multiple sclerosis (MS), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS). Since 1997, he has directed the investigation of neurodegenerative diseases in several large cohorts. Among the most notable discoveries to which he has contributed are the key roles of infection with the Epstein-Barr virus, vitamin D insufficiency, and cigarette smoking as risk factors for MS, the importance of vitamin D status as a determinant of MS progression, the role of caffeine consumption and urate as negative risk factors for PD and of urate elevation as a promising therapeutic strategy, and the identification of positive and negative environmental risk factors for ALS.

EBV as a causal factor in multiple sclerosis

Vaccine Day, March 24, 2022

Alberto Ascherio, MD, DrPH
Professor of Epidemiology and Nutrition
Harvard TH Chan School of Public Health
Professor of Medicine, Harvard Medical School
Boston, MA, USA

LECTURES
ON
THE DISEASES OF
THE NERVOUS SYSTEM.

DELIVERED AT LA SALPÊTRIÈRE

BY
J. M. CHARCOT,

PROFESSOR TO THE FACULTY OF MEDICINE OF PARIS; PHYSICIAN TO LA SALPÊTRIÈRE; MEMBER OF
THE ACADEMY OF MEDICINE, AND OF THE CLINICAL SOCIETY OF LONDON; PRESIDENT
OF THE ANATOMICAL SOCIETY, AND EX-VICE-PRESIDENT OF THE
BIOLOGICAL SOCIETY OF PARIS, ETC.

TRANSLATED FROM THE SECOND EDITION BY

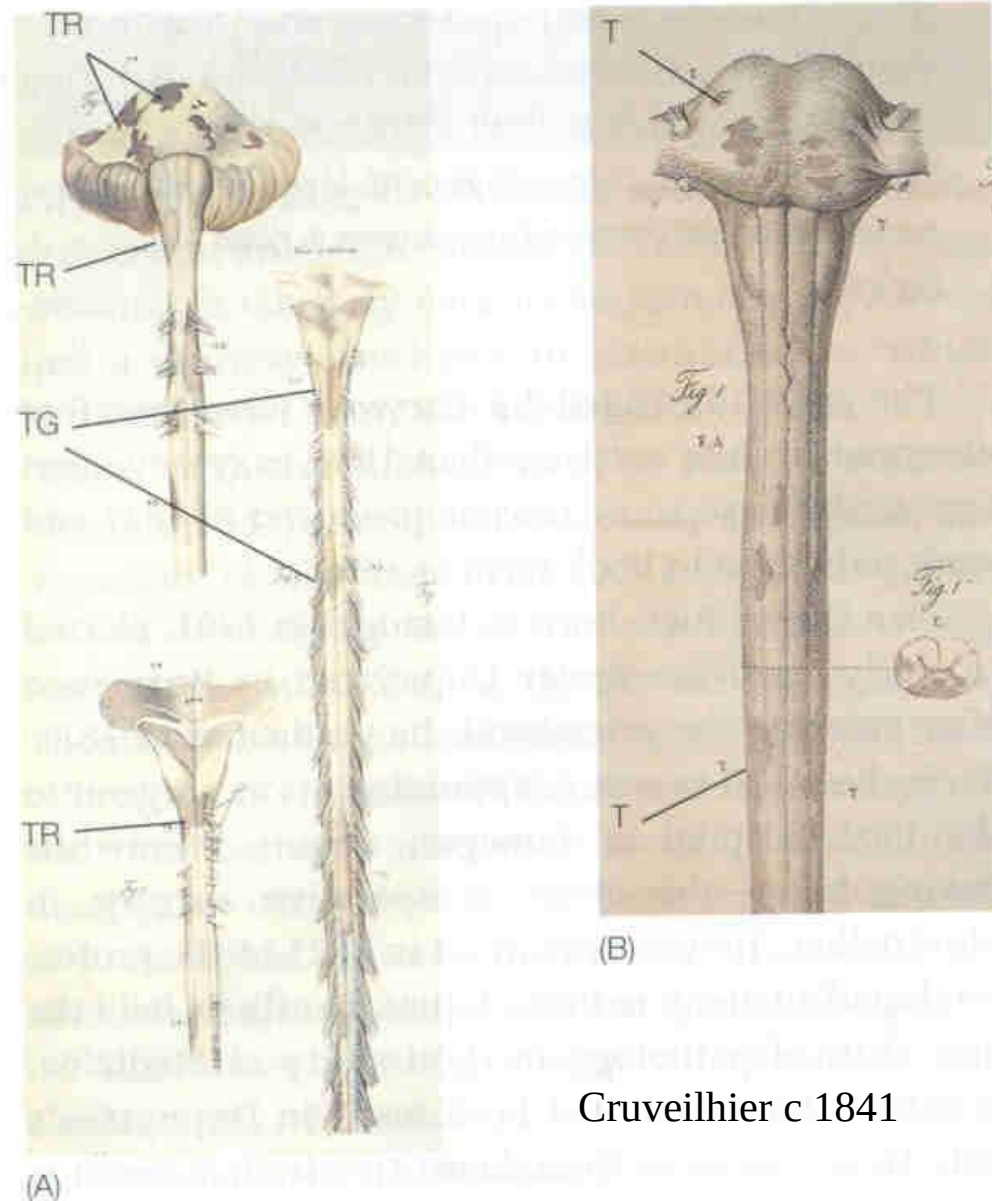
GEORGE SIGERSON, M.D., M.Ch.,

LICENTIATE OF THE KING AND QUEEN'S COLLEGE OF PHYSICIANS; LECTURER ON BIOLOGY AND
EX-DEAN OF THE FACULTY OF SCIENCE, CATHOLIC UNIVERSITY OF IRELAND; FELLOW OF
THE LINNEAN SOCIETY OF LONDON; MEMBER OF THE SCIENTIFIC SOCIETY OF
BELGIUM, AND OF THE ROYAL IRISH ACADEMY, ETC.

WITH ILLUSTRATIONS.



PHILADELPHIA:
HENRY C. LEA.
1879.



Cruveilhier c 1841

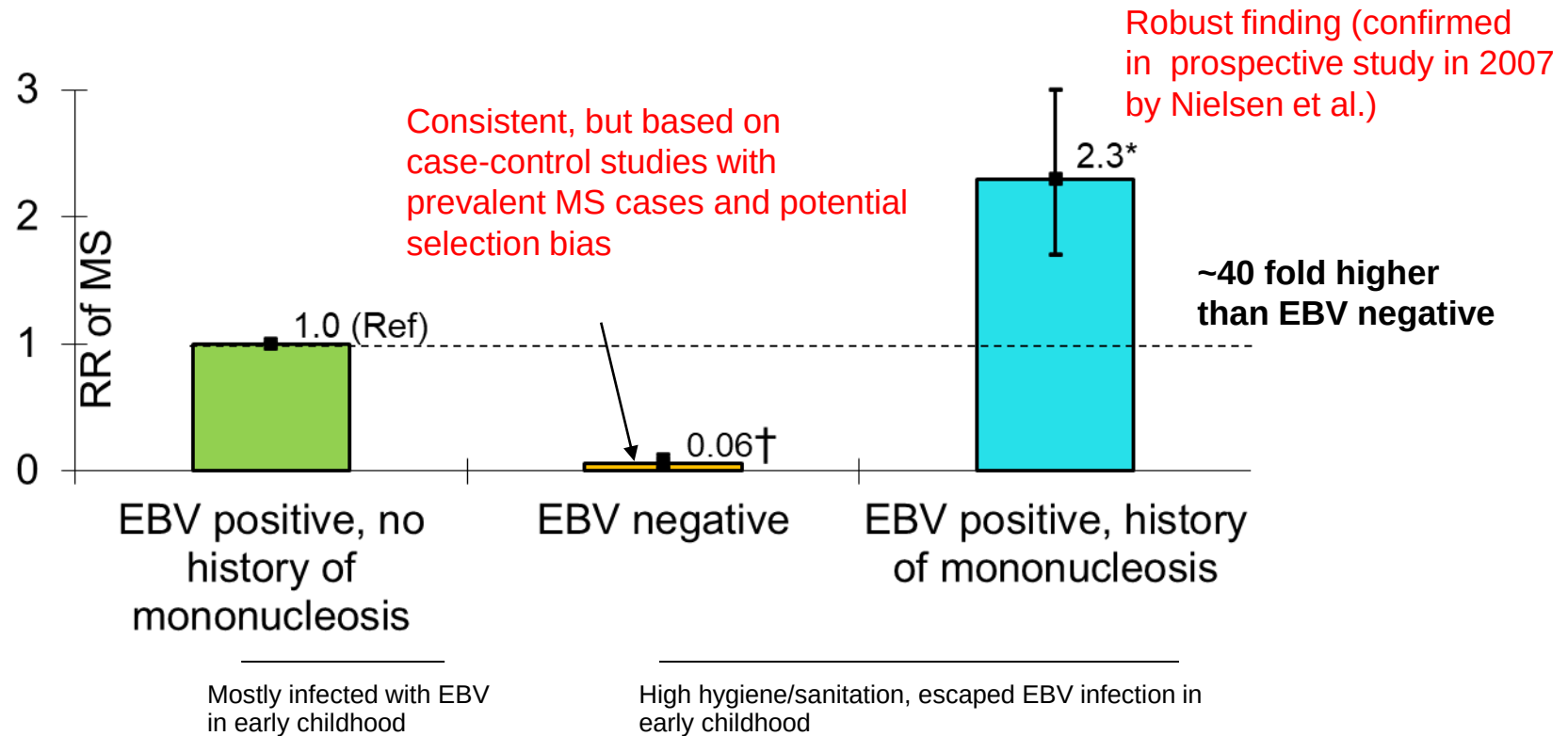
MS Pathology

- Consistent with autoimmune mechanism
- Although CNS infection not excluded, until now defined as “unknown etiology”

MS frequency

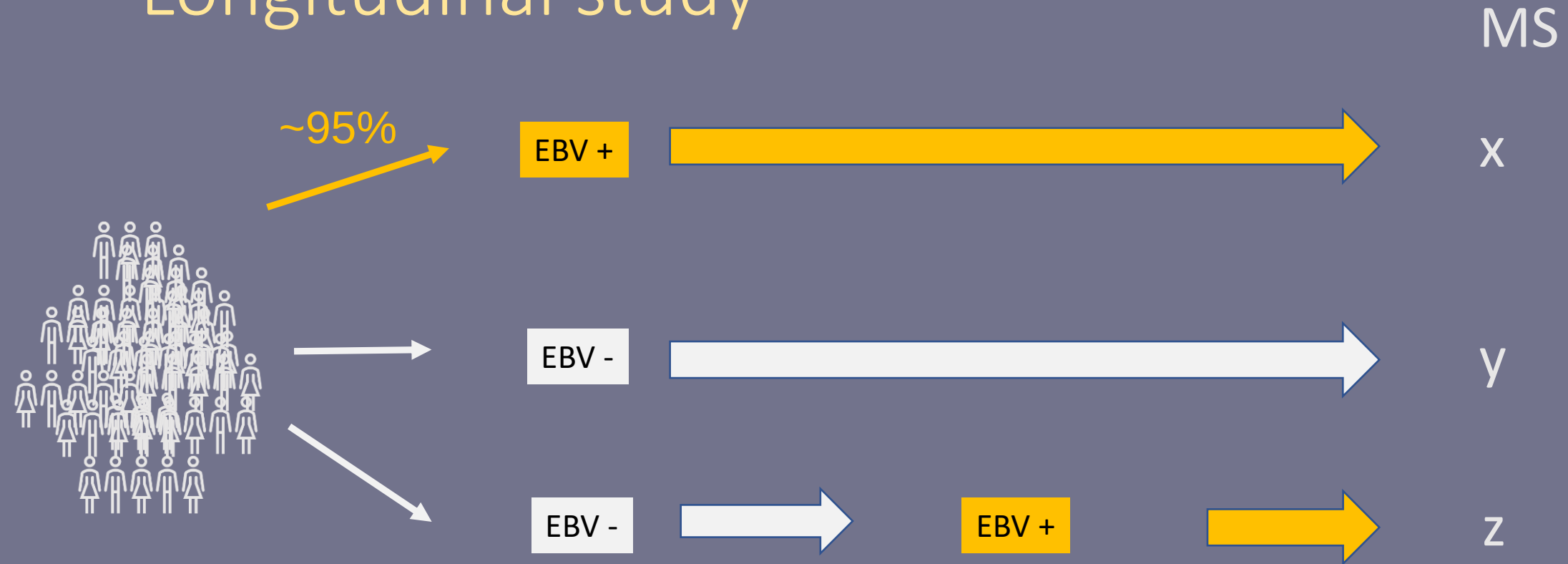
- Most common disabling neurological disease in young adults in US and Europe
- Prevalence 2.8 million worldwide in 2020 and increasing
- Incidence higher in young adults (20-40 yrs)
- More common in women than in men
- Lifetime risk among US women: 4 to 5 / 1,000

MS risk according to EBV infection and history of mononucleosis (= late age at EBV infection)

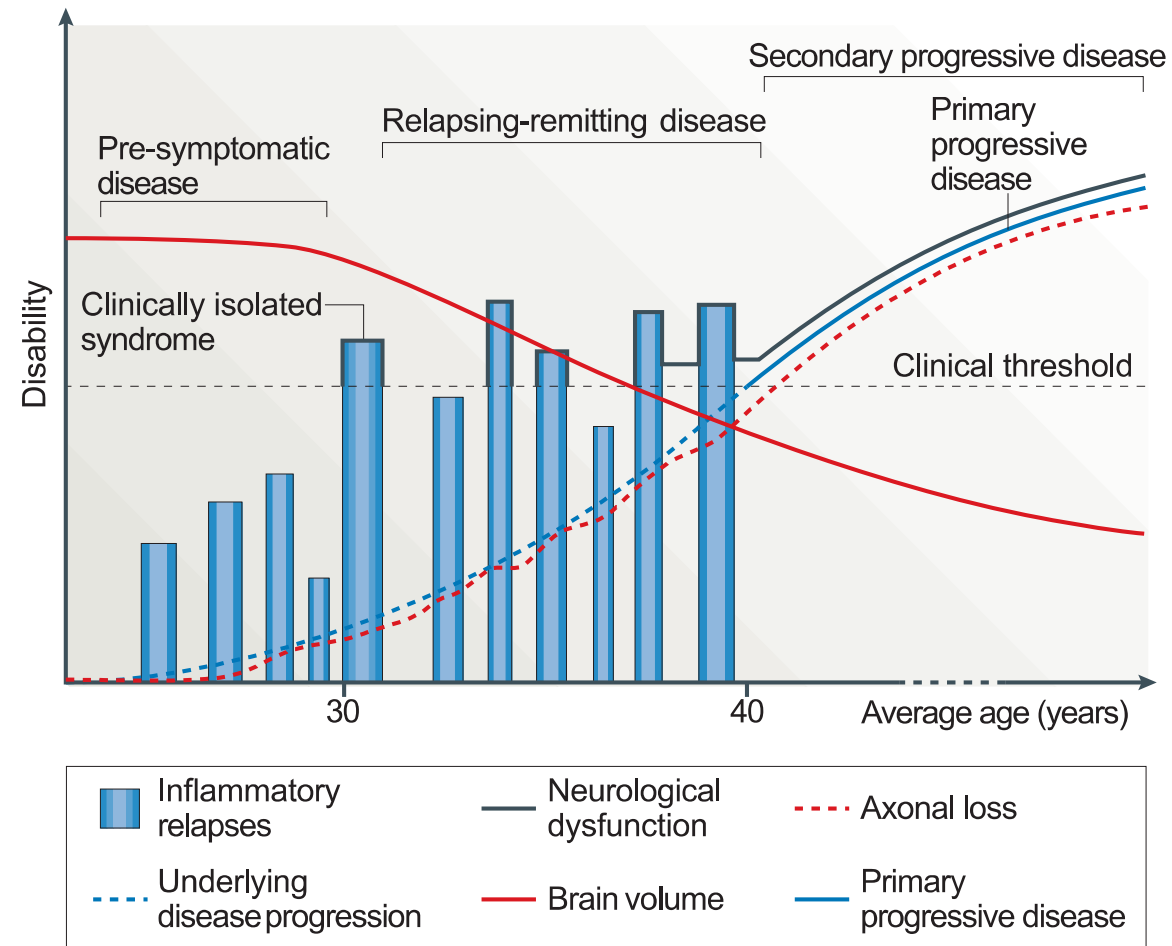


† * Values based on meta-analyses of case-control studies, both $p < 10^{-8}$

Longitudinal study



The presymptomatic phase of multiple sclerosis



1. Dendrou et al. Immunopathology of multiple sclerosis. *Nature Rev Immunol.* 2015.

Objectives of the study:

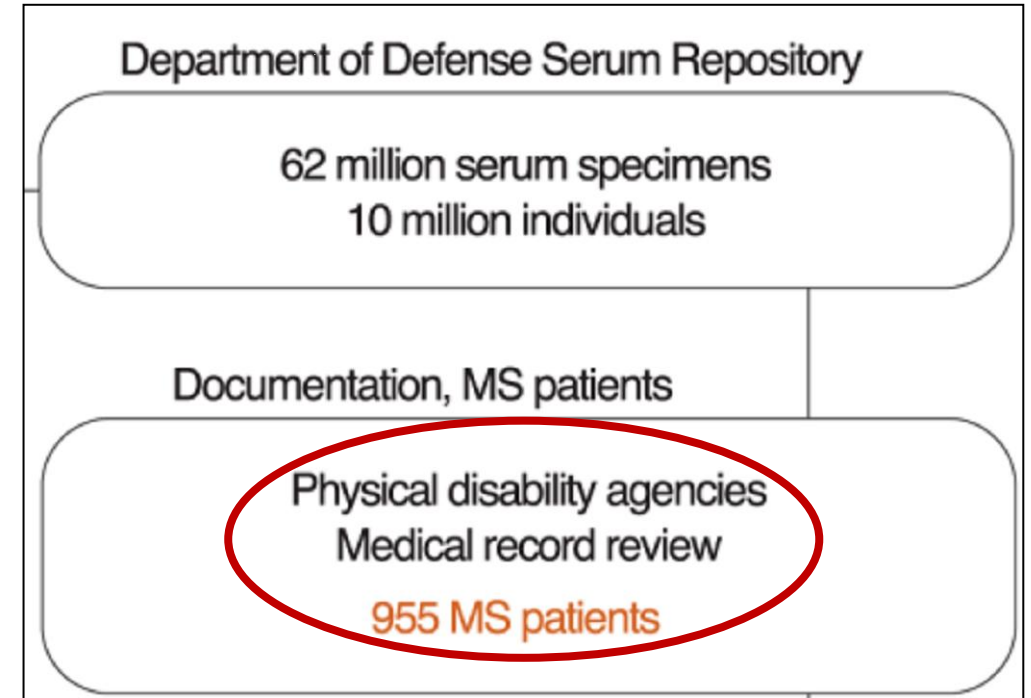
- To determine whether:
 - EBV infection precedes in time:
 - 1) the clinical onset of MS
 - 2) elevation of neurofilament light chain (NfL)
(biomarker of neurodegeneration)
 - Other viral infection occurring after EBV may trigger MS onset

Study population

Cohort of individuals on active-duty in the US military

Why unique?

- Very large cohort
- Repeated blood samples
- MS is a medically disqualifying condition in the US military (searchable code) → Confirmation of diagnoses by medical record review

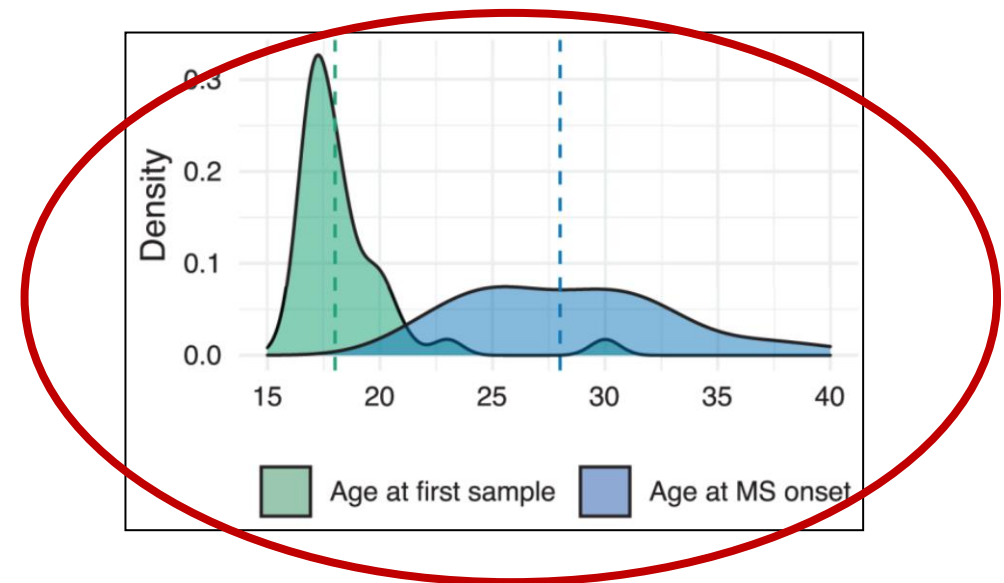
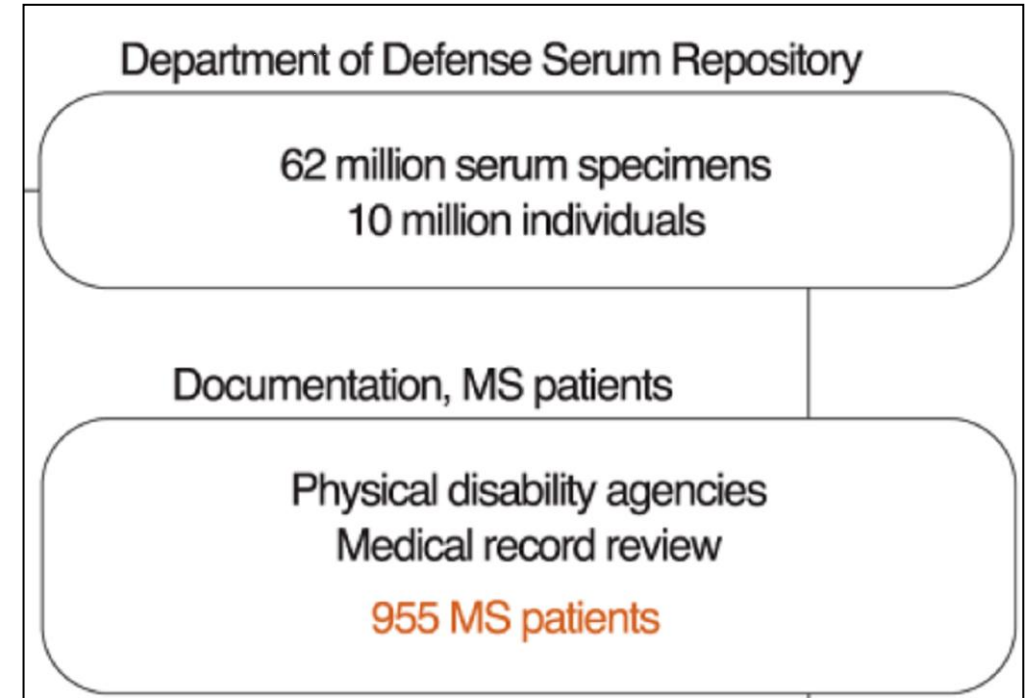


Study population

Cohort of individuals on active-duty in the US military

Why unique?

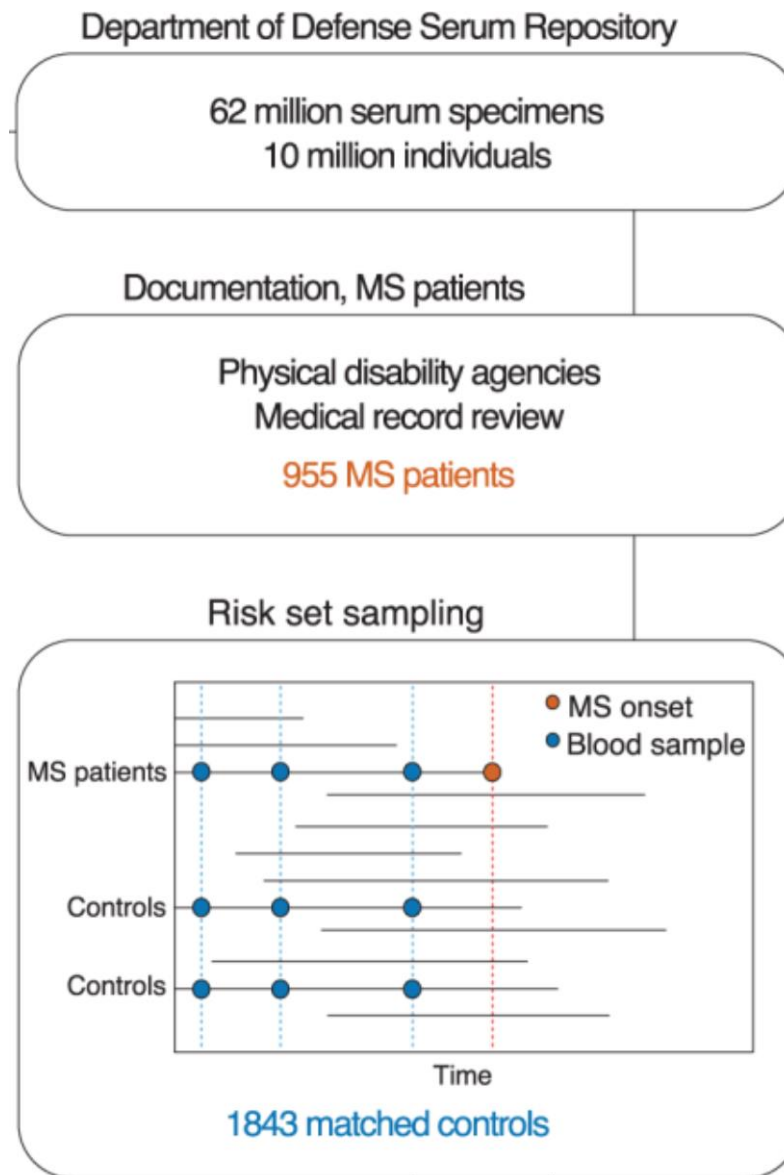
- Very large cohort
- Repeated blood samples
- MS is a medically disqualifying condition in the US military (searchable code) → Confirmation of diagnoses by medical record review
- Age distribution: young adults



Design

Prospective, nested case-control study within this US military cohort

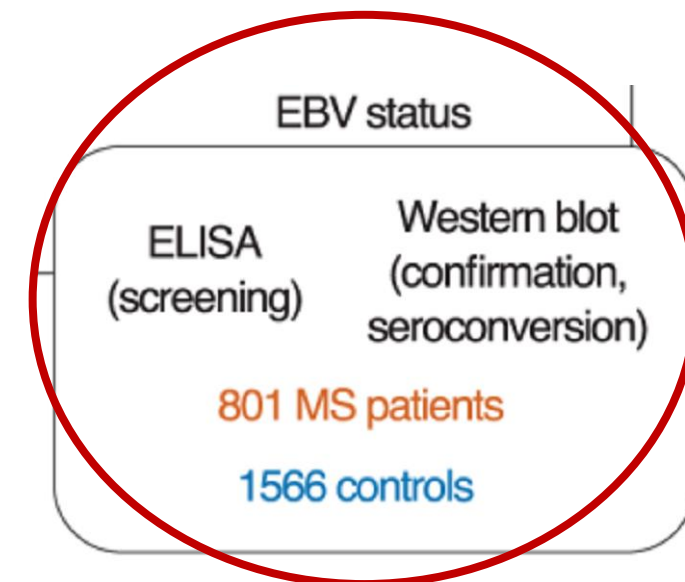
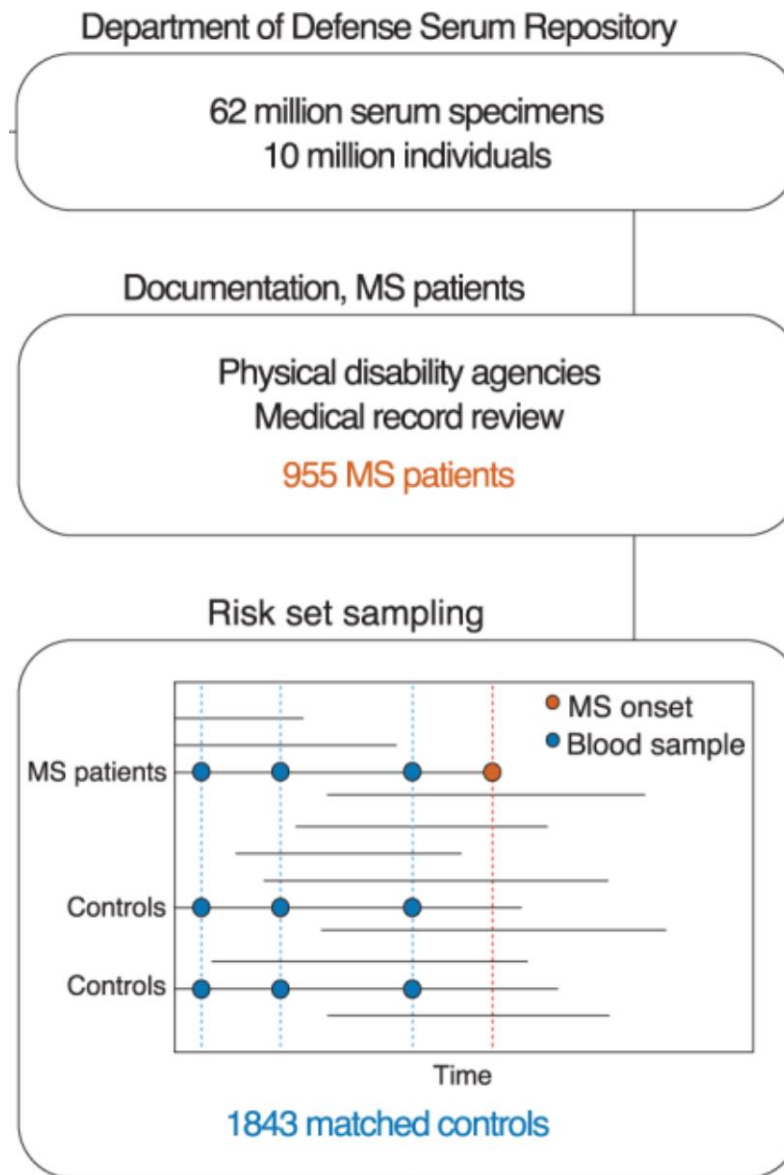
Matched on sex, age,
race/ethnicity, date
of blood collection,
military branch



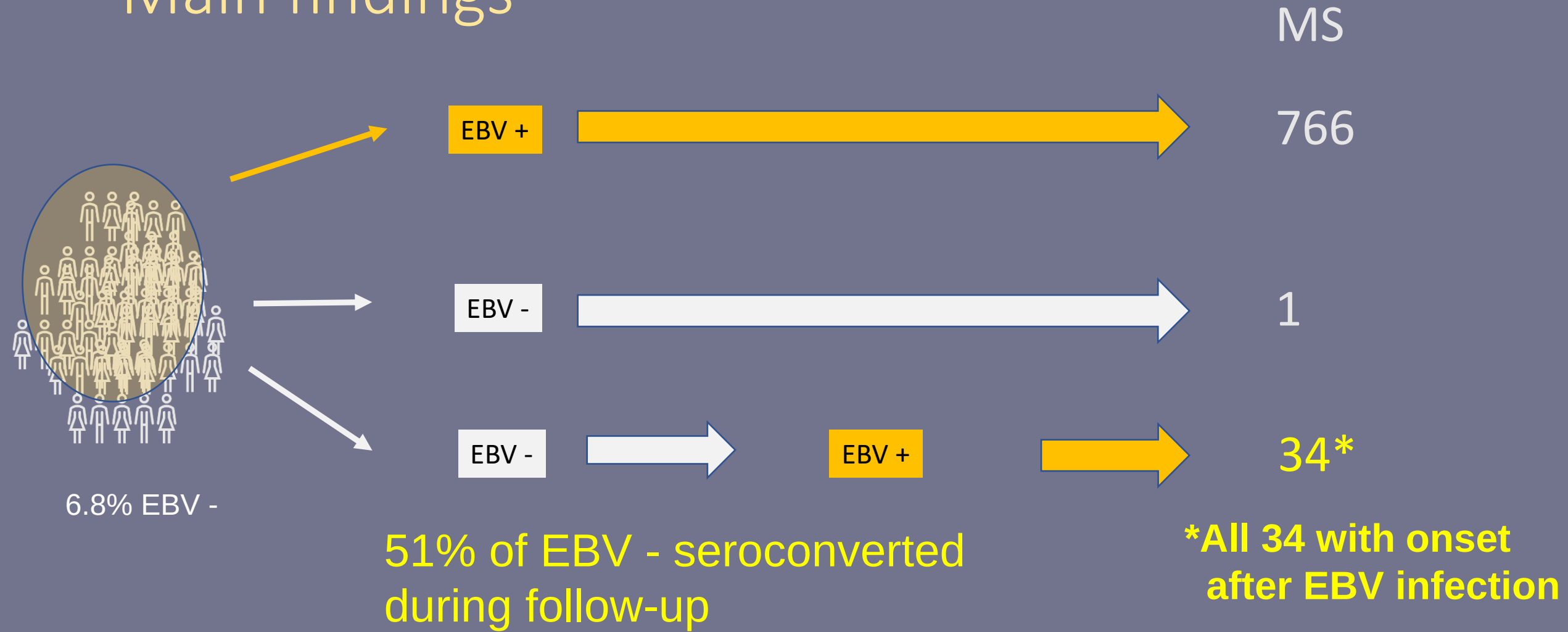
Design

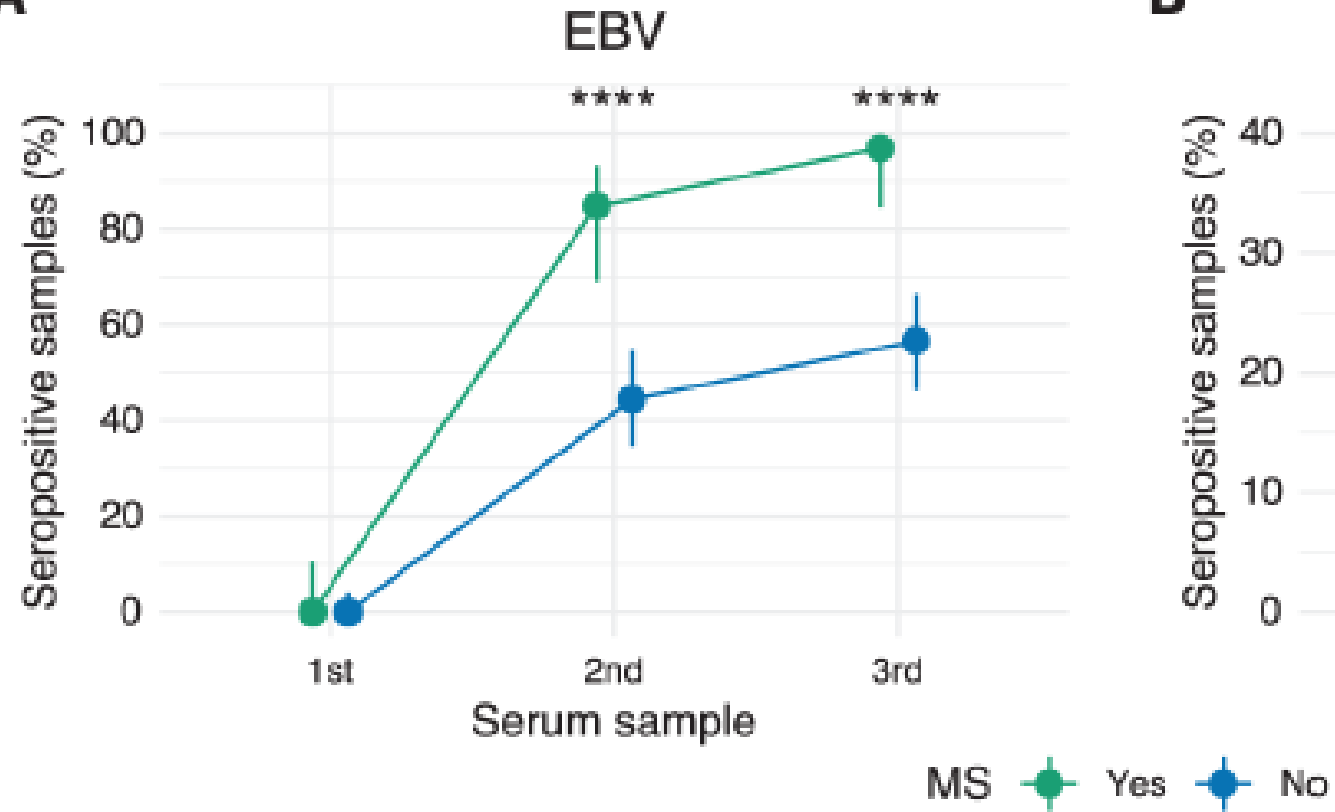
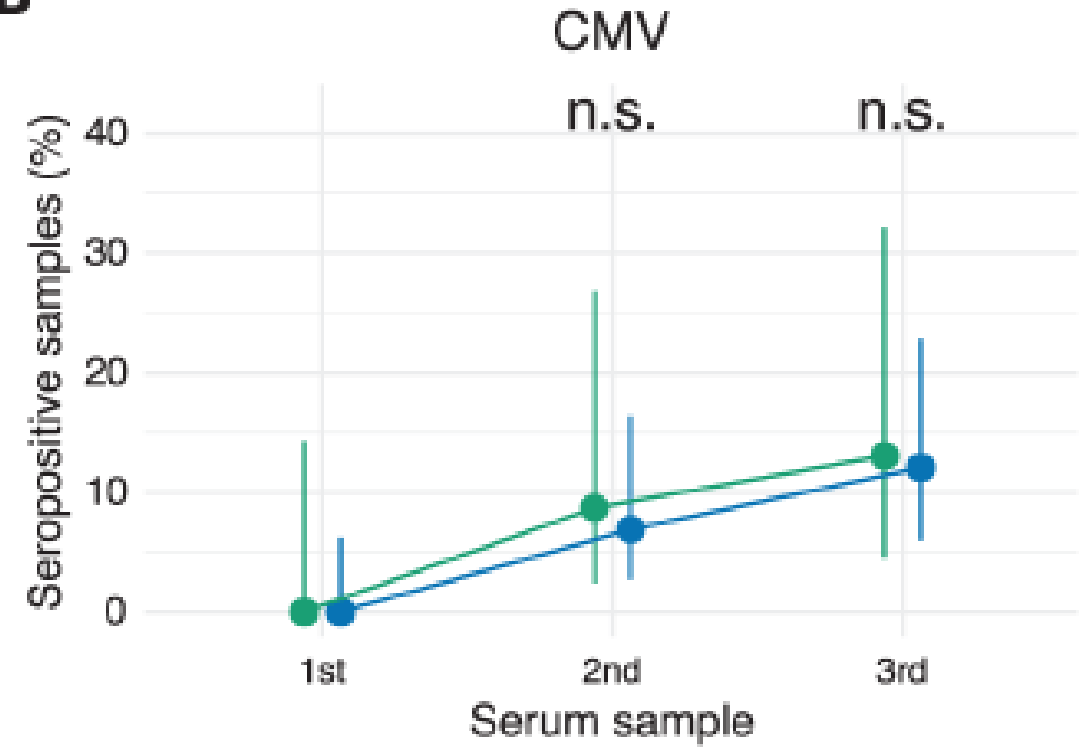
Prospective, nested case-control study within this US military cohort

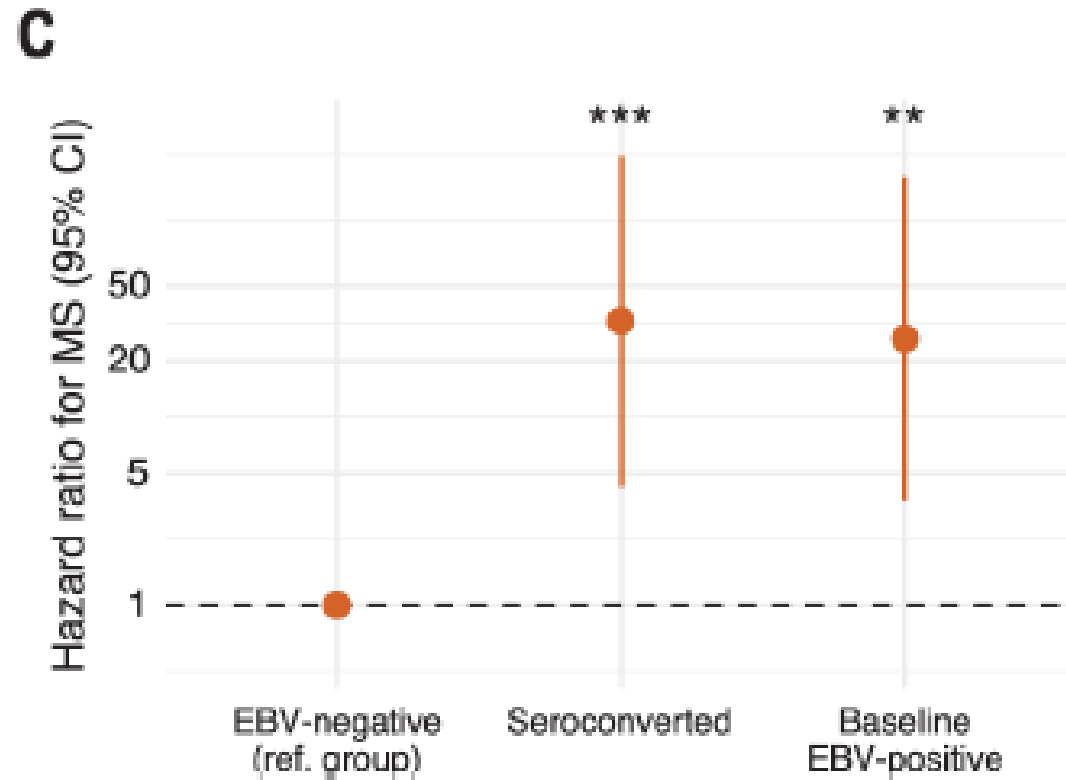
Matched on sex, age, race/ethnicity, date of blood collection, military branch



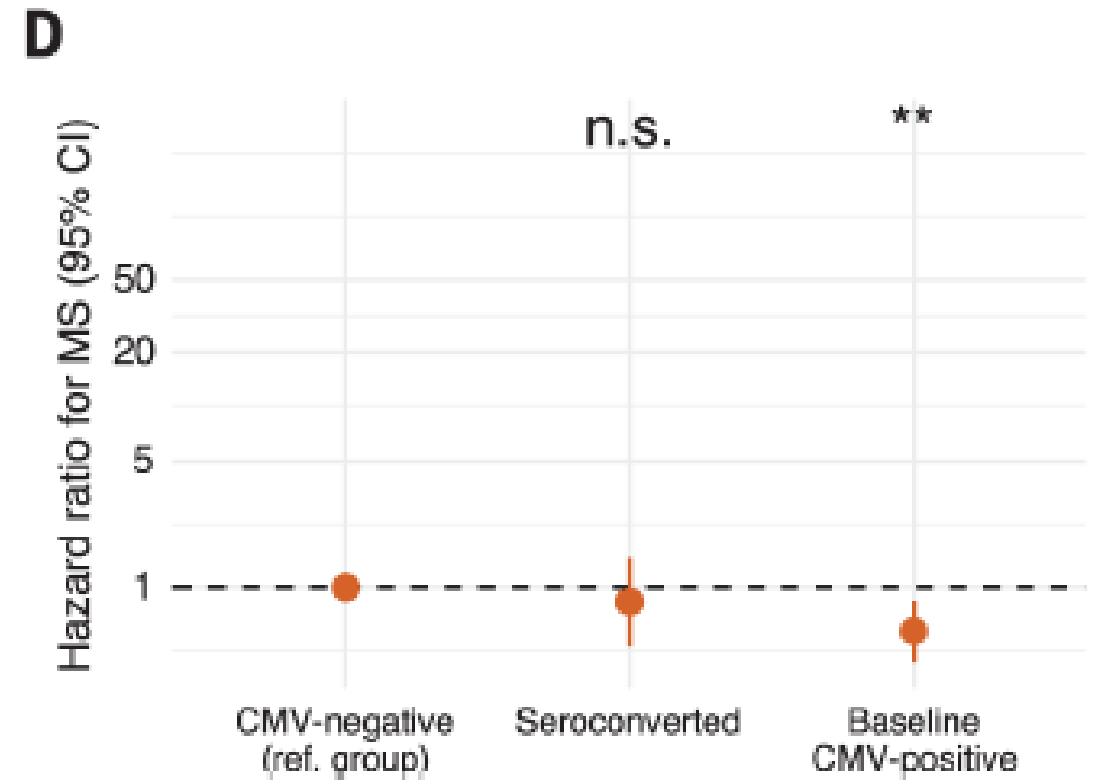
Main findings



A**B**



EBV



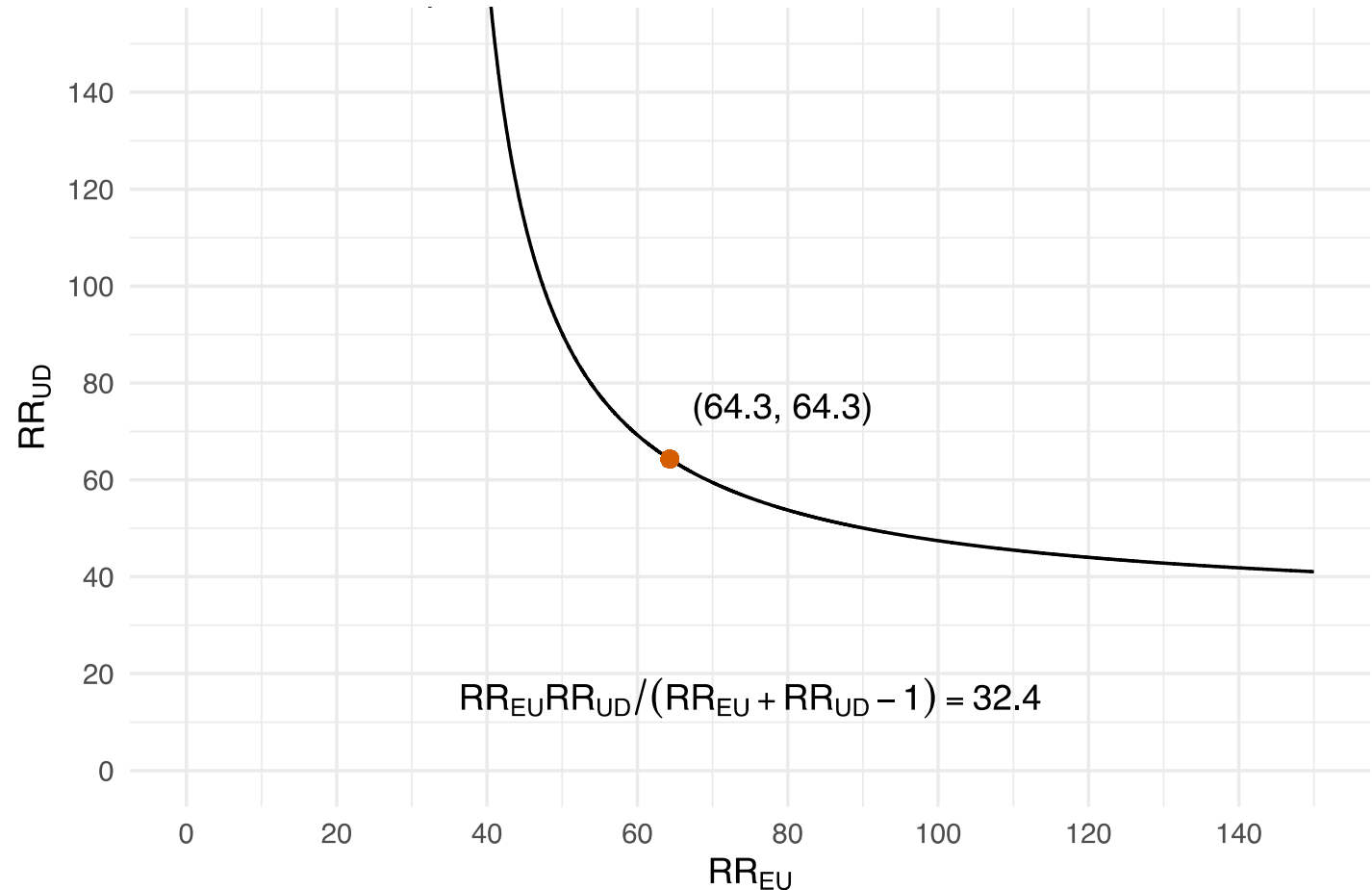
CMV

Other explanations: Confounding ?

Could other known risk factors explain this association?

- Strong estimate cannot be explained by other factors consistently associated with MS
- $RR \sim 1.5-3.0$ (strongest is genetic risk allele HLA-DRB1*1501)

VanderWeele, . Ann Intern Med. 2017



Other explanations: Reverse causality ?

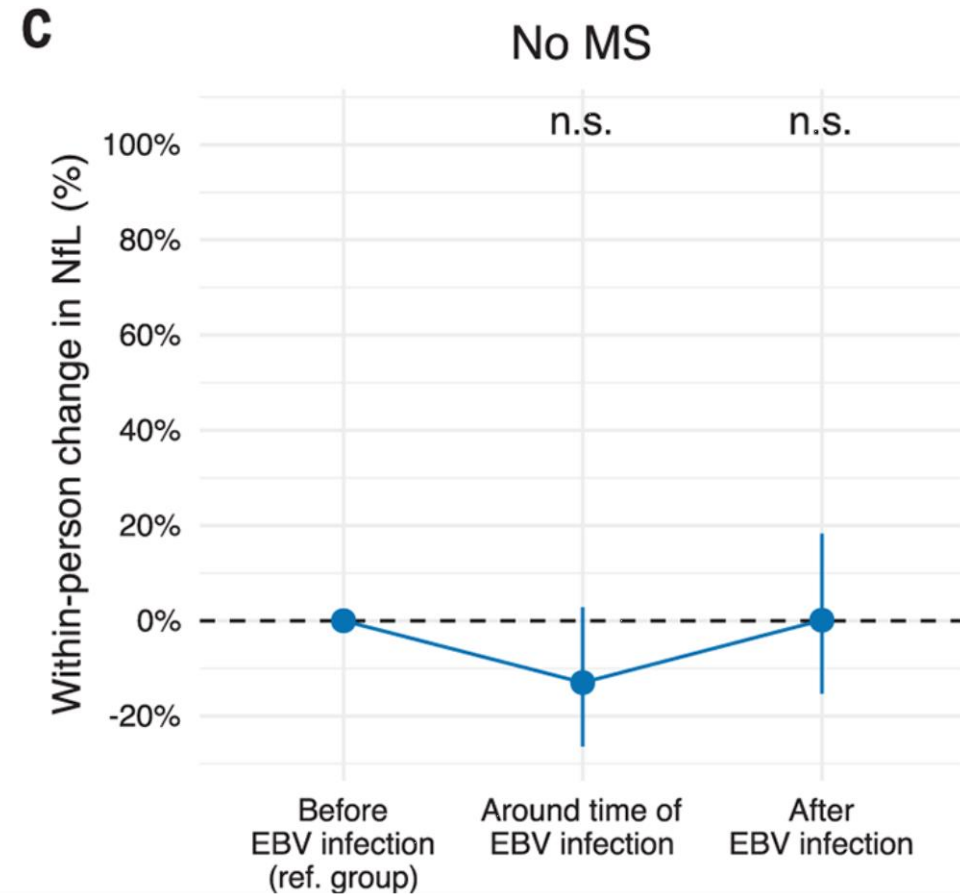
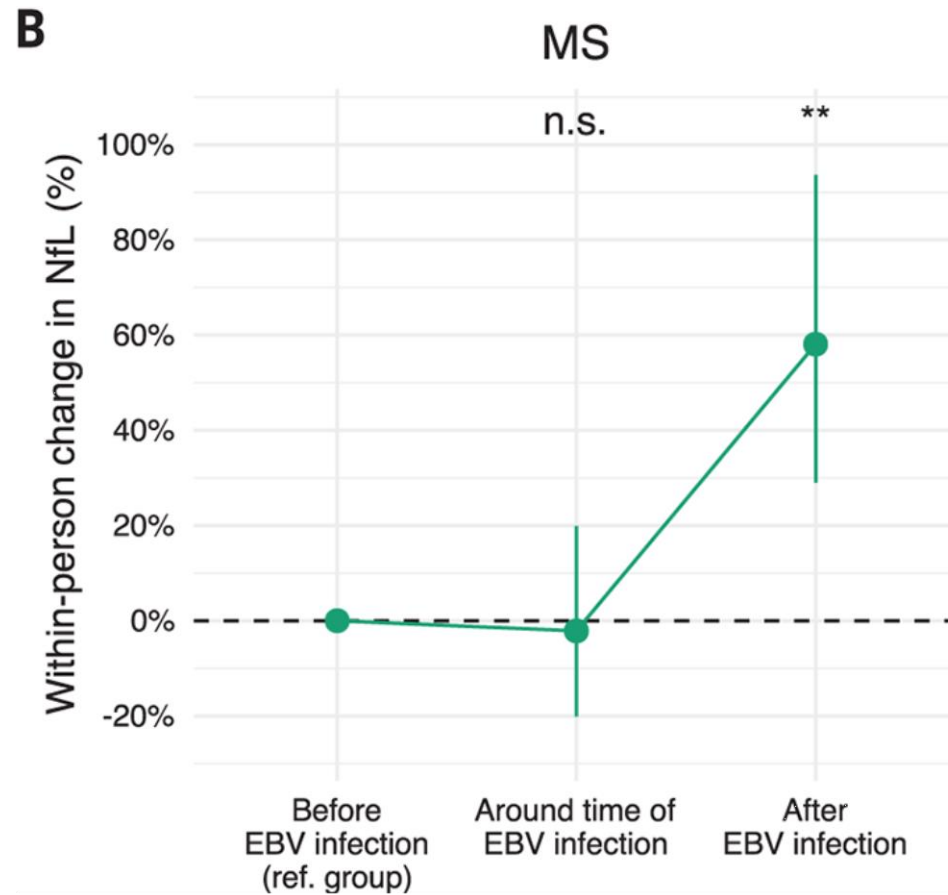
Concern:

Does MS increase the risk of being infected with EBV?

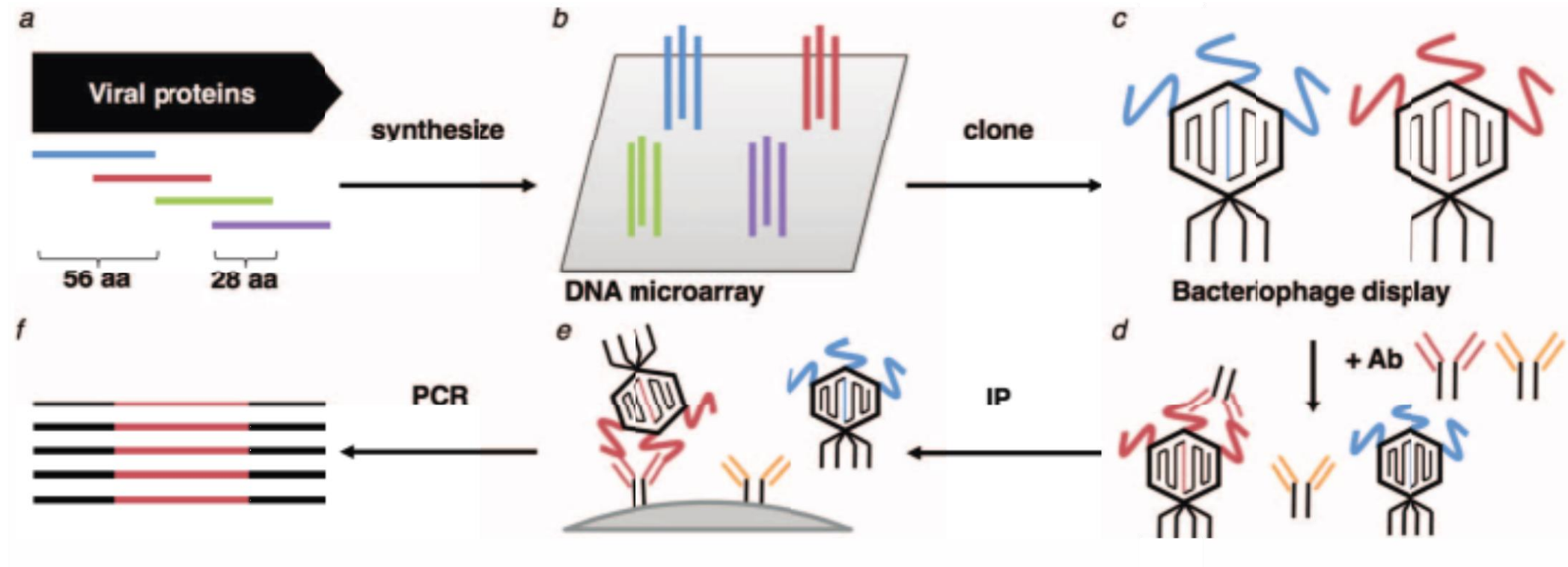
Adressed by:

1. Measuring serum levels of neurofilament light chain (NfL)
 - a sensitive biomarker of neuroaxonal injury, capturing the earliest MS stages before first symptoms
2. Measuring antibody titers against the human virome (VirScan)

Does EBV infection precede NfL increase?

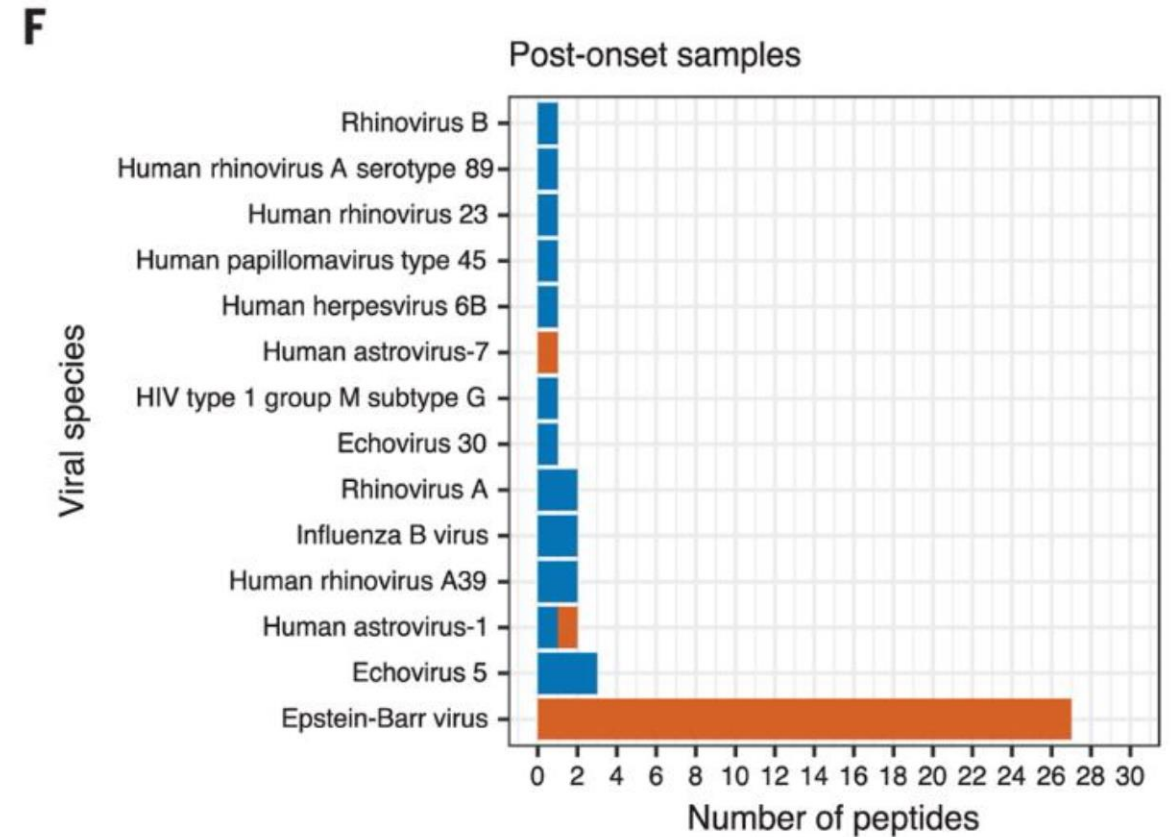
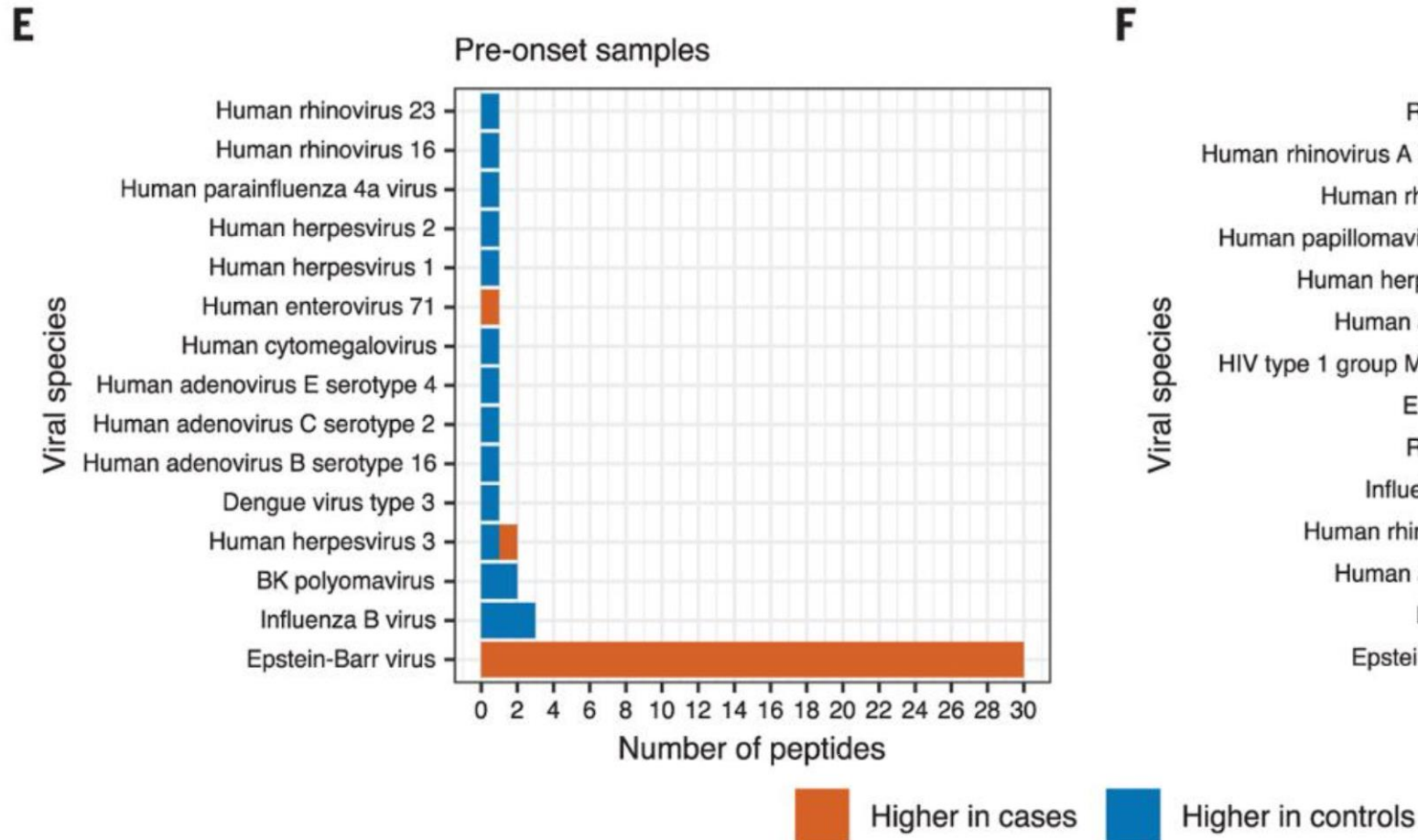


Serological profiling using VirScan



Peptide-specific read counts converted into a Z-score metric, which expresses relative abundance of antibodies against a peptide (relative antibody titer).

No evidence of non-specific immune dysregulation

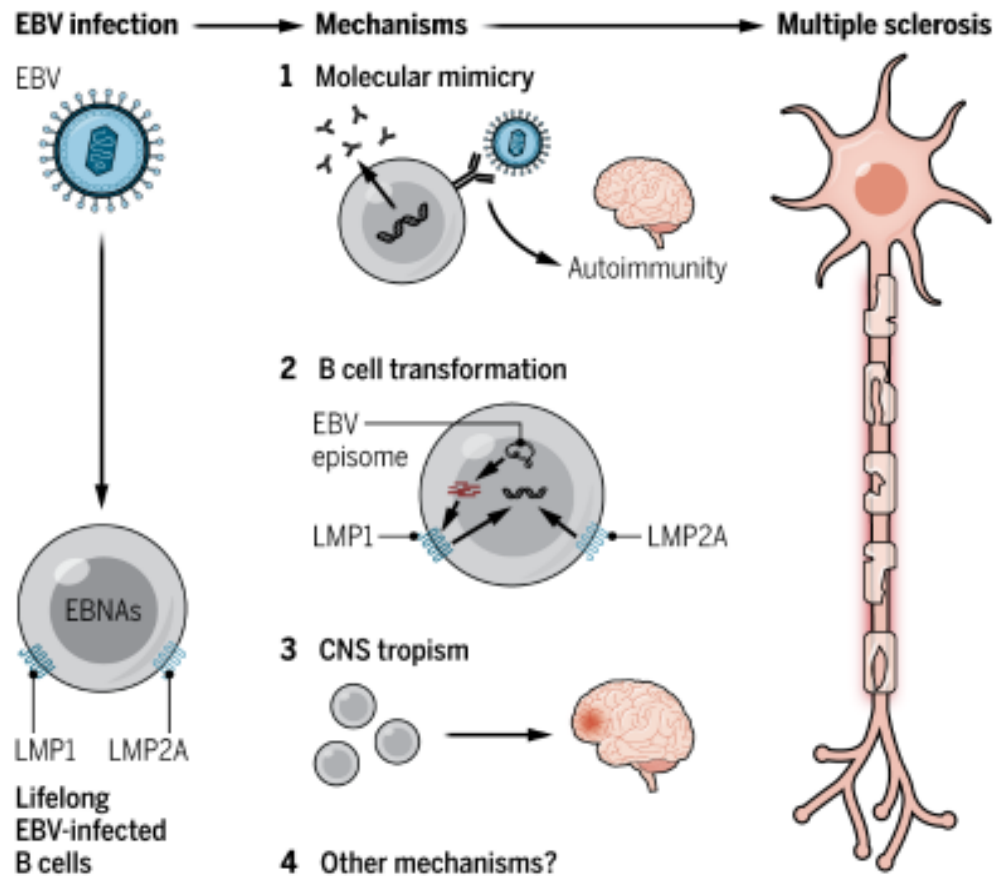


$p < 0.05$ (two-sided Fisher Exact test)

- MS is a rare complication of EBV infection
- Factors that increase risk include:
 - Family history of MS / genotype
 - History of IM (age at EBV infection?)
 - Vitamin D deficiency or insufficiency
 - Tobacco smoking
 - Obesity during adolescence (possibly mediated by low vitamin D)

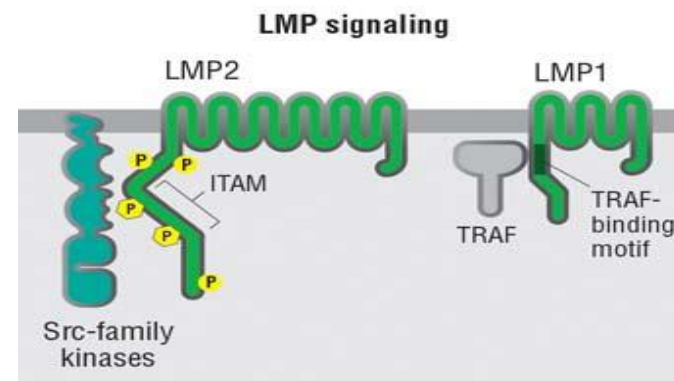
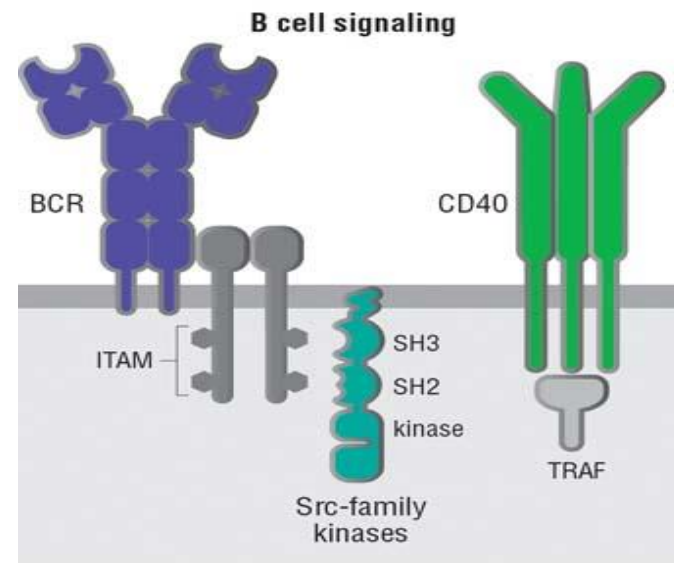
Model for multiple sclerosis development

In at-risk individuals, Epstein-Barr virus (EBV) infection of B cells promotes the development of multiple sclerosis through several possible mechanisms. These include molecular mimicry (1) by EBV nuclear antigen 1 (EBNA-1), B cell transformation (2) through latent membrane protein 1 (LMP1) and LMP2A, induction of B cell trafficking (3) to the central nervous system (CNS), and/or other unknown mechanisms (4).



A. MASTIN/SCIENCE

From **Immunity: The Immune Response in Infectious and Inflammatory Disease**
2007-2008 Online Update
 by DeFranco, Locksley and Robertson



© 1999–2008 New Science Press

Robinson & Steinman, Science 2002

Mechanisms

- MS risk not increased with immunosuppression
- EBV viral load in peripheral blood only modestly elevated
- Strong association with serum anti-EBNA titers
- Infected B cells $\ll$ EBV specific T cells
-  **suggest key role of immune response to EBV**

EBV vaccine and MS prevention

- In EBV negative individuals:
 - A vaccine that confers sterile immunity would prevent MS
 - A vaccine that prevents mononucleosis, but not EBV infection *likely* to reduce MS risk
- In EBV positive individuals:
 - In healthy individuals a vaccine could modify immune response to EBV and reduce risk of EBV reactivation and MS (e.g. herpes zoster vaccine)
 - Potential for a **therapeutic vaccine** in individuals with MS

Acknowledgements



KM



KB



MC

Study investigators:

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Kjetil Bjornevik, MD, PhD

Marianna Cortese, MD, PhD

Uniformed Services University of the Health Science

David W. Niebuhr, MD

Ann I. Scher, PhD

Armed Forces Health Surveillance Branch/ Department of Defense Serum Repository

U.S. Army, Navy and Air Force

Brian C. Healy, PhD (BWH – Harvard)

Michael Mina, MD, PhD (BWH – Harvard)

Steven Elledge, MD, PhD (BWH – Harvard)

Yumei Leng, PhD (BWH – Harvard)

Christian Barro, MD (University of Basel)

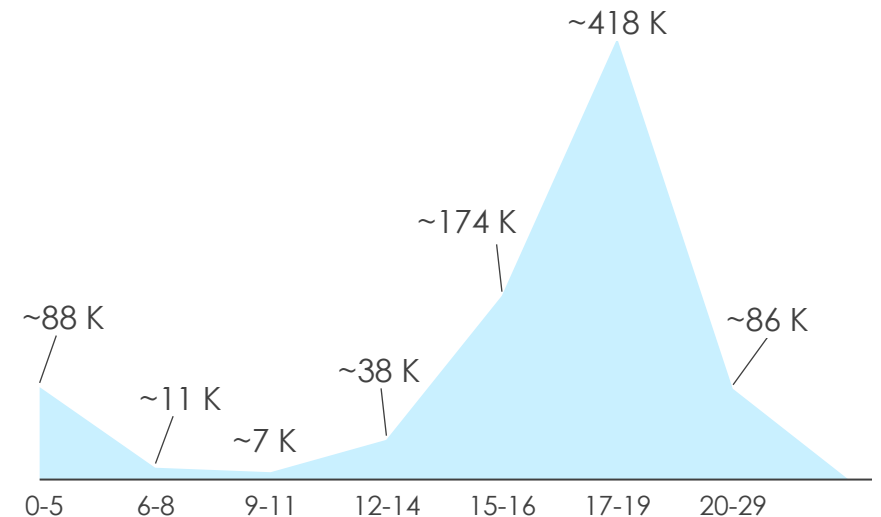
Jens Kuhle, MD, PhD (University of Basel)

Funding: The National Institute of Neurologic Disorders and Stroke

Epstein-Barr virus (EBV) is a major cause of infectious mononucleosis (IM)

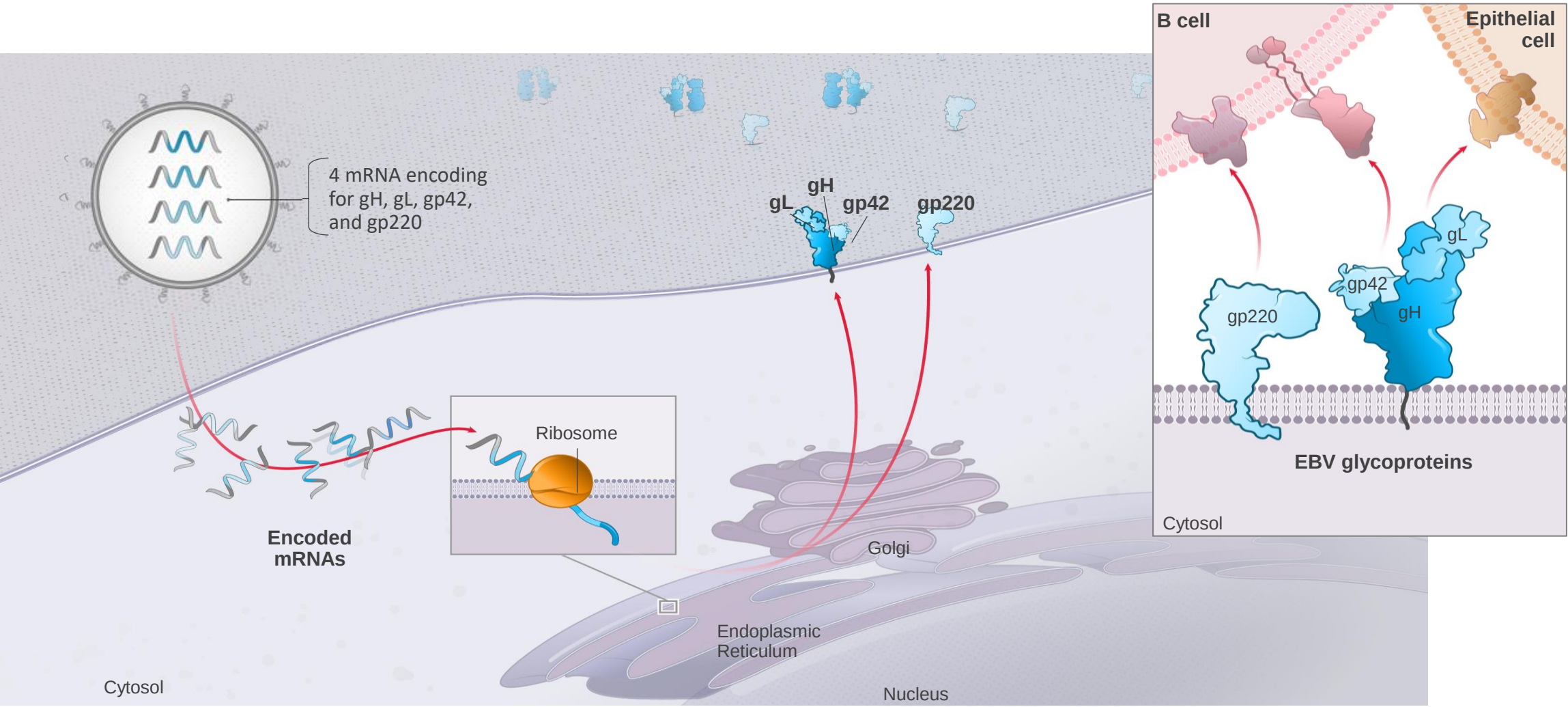
- EBV is spread through bodily fluids (e.g., saliva) and **contracted primarily by young children and adolescents**
- **EBV is a major cause of infectious mononucleosis (IM) in the U.S.**, accounting for over 90% of the ~1+ million cases annually¹
 - IM symptoms includes sore throat, lymphadenopathy, fever, body aches, fatigue and splenic rupture (rare complication)

U.S. Estimated Infectious Mononucleosis Cases By Age Group (<30 years old) Per Year²



Modelling and not actual surveillance; Based on published study that observed Danish population, <30 years old, from 2006-2011

EBV vaccine (mRNA-1189) encodes for four antigens



EBV vaccine (mRNA-1189) Phase 1 trial ongoing with the aim to reduce the rate of IM

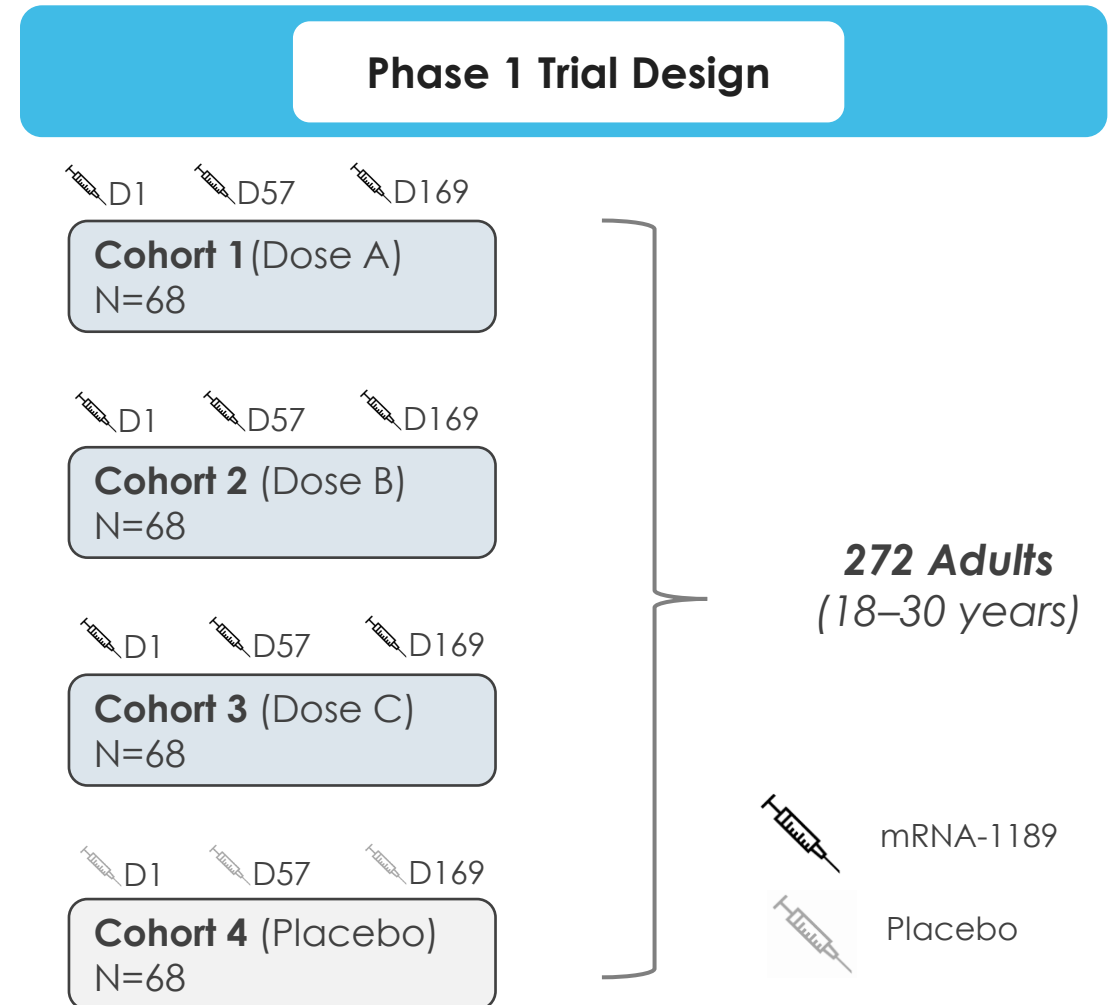
- Evaluating safety and reactogenicity of 3 different dose levels of an EBV vaccine

Outcome measures

- Safety and immunogenicity

Trial progress

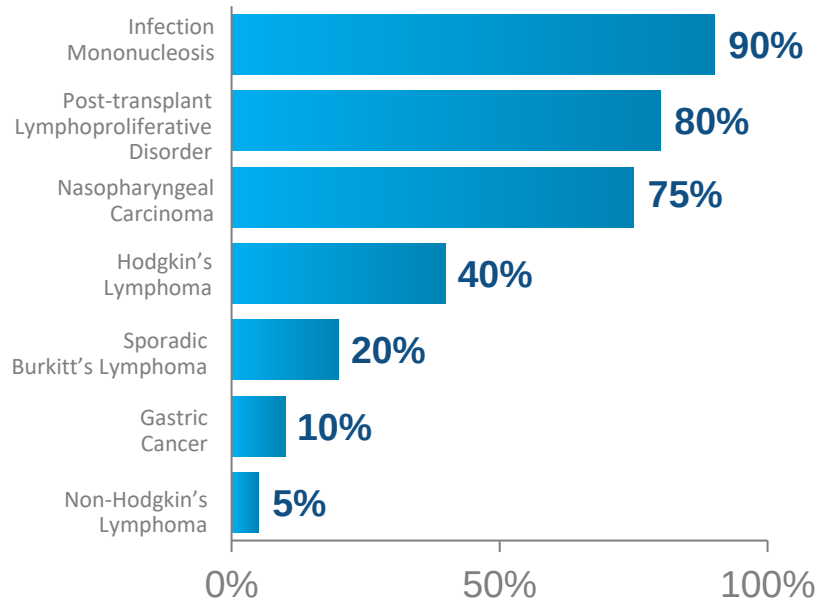
- Enrollment started in December 2021
- Expansion phase ongoing



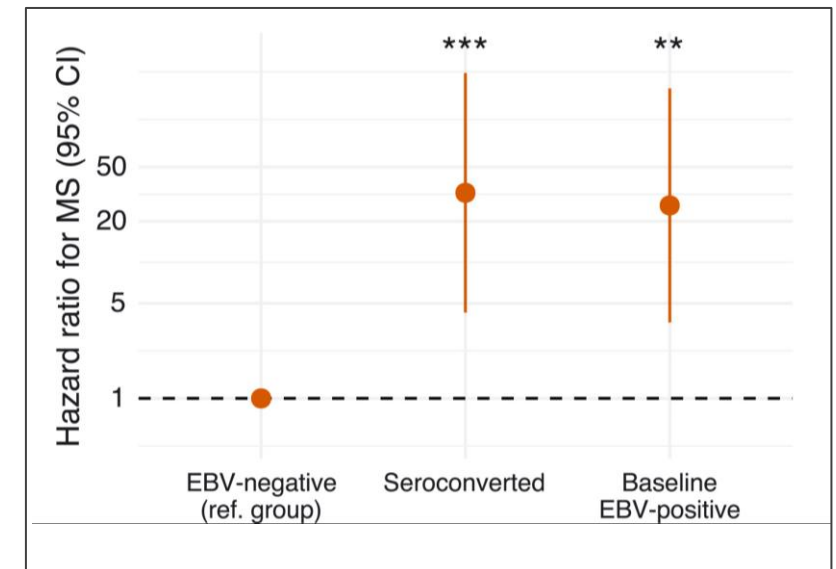
EBV also has significant long-term impacts

- **Lifetime associated risks include:**
 - Associated with certain lymphoproliferative disorders
 - Higher risk of developing cancers and autoimmune diseases
 - Increased risk of developing multiple sclerosis by ~32 fold
- **~90% EBV prevalence** in the U.S.

Association of Epstein-Barr Virus
by Indication in the United States



Hazard ratio for MS in those who are EBV seropositive

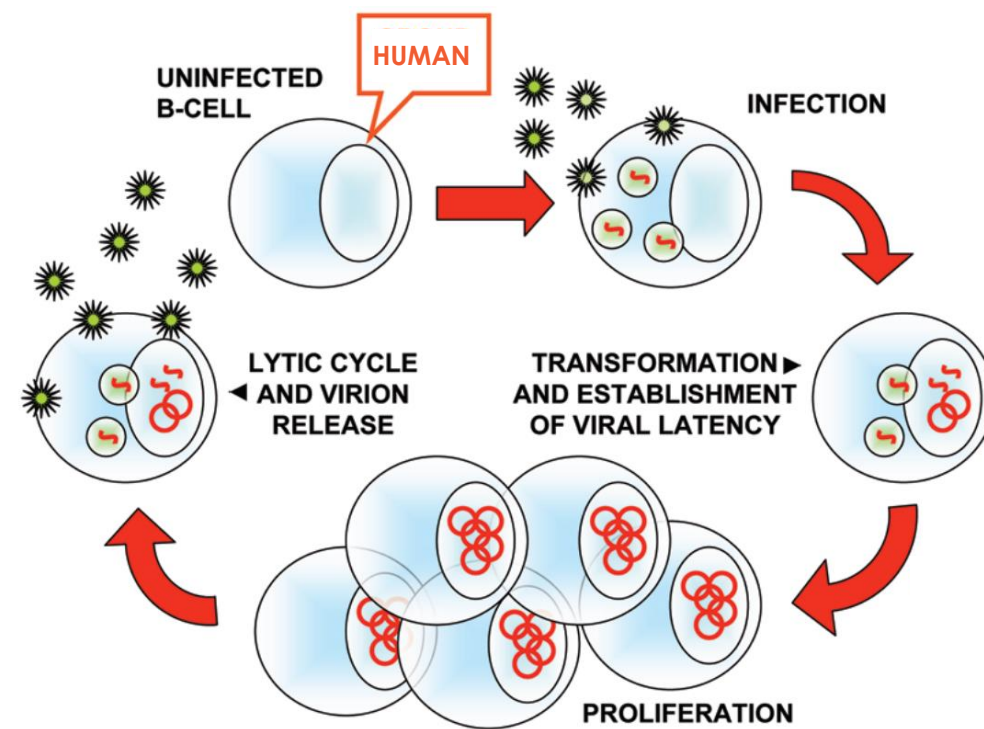


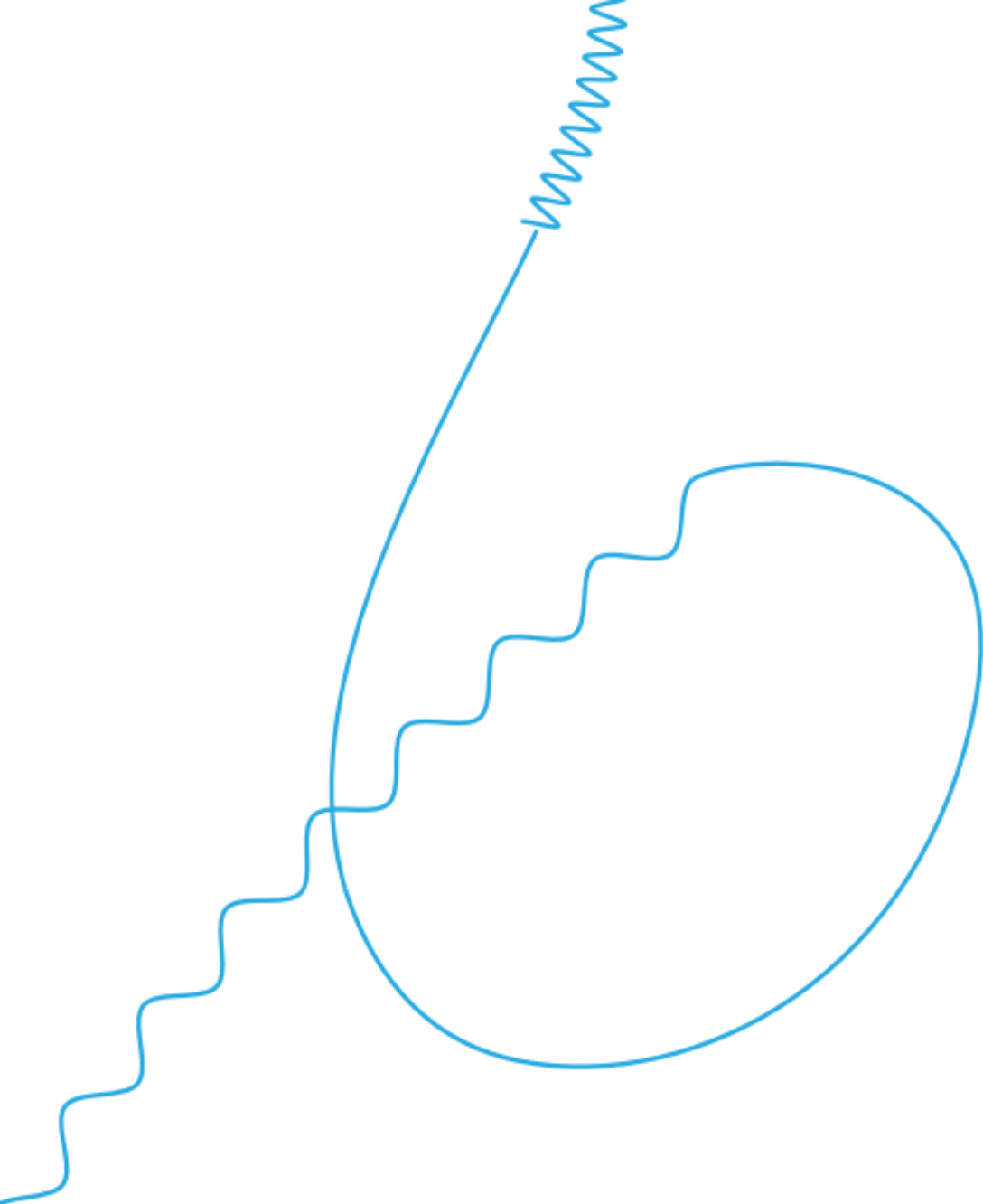
Risk ratio for MS according to EBV status. Sample includes 955 incident MS cases among active-duty military personnel and 1,566 controls matched for demographics; three serum samples were collected before date of MS

We are developing an EBV vaccine (mRNA-1195) against long-term EBV sequelae

EBV Vaccine (mRNA-1195)

- To prevent longer term sequelae of EBV infection
- Encodes for additional latent antigens
- Indications
 - Post-transplant lymphoproliferative disease (80% of PTLD cases can be attributed to EBV)
 - Multiple sclerosis
- In preclinical development





Additional Latent Viruses

Jacqueline Miller, M.D.

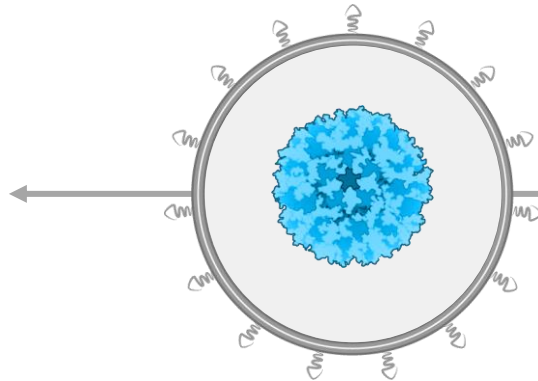
*Senior Vice President, Therapeutic Area
Head, Infectious Diseases, Moderna*

HIV: Two complementary approaches in the clinic that tackle key challenges for making HIV Vaccines

1

Target B cells that produce broadly neutralizing antibodies

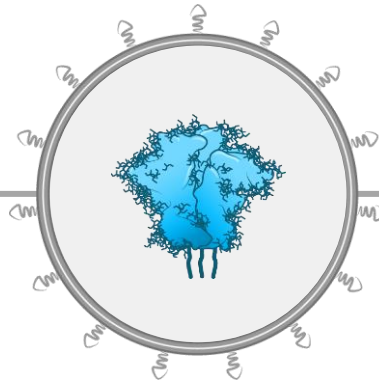
mRNA-1644



2

Native like HIV trimers

mRNA-1574



Iterative Vaccine Design/Test Cycle

IMMUNOGEN DESIGN



mRNA FORMULATION



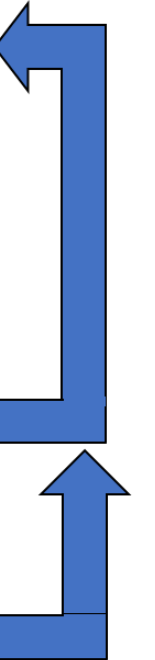
VACCINE TESTING IN
ENGINEERED MICE AND
OTHER MODELS



HUMAN CLINICAL TRIALS



PROTECTIVE VACCINE



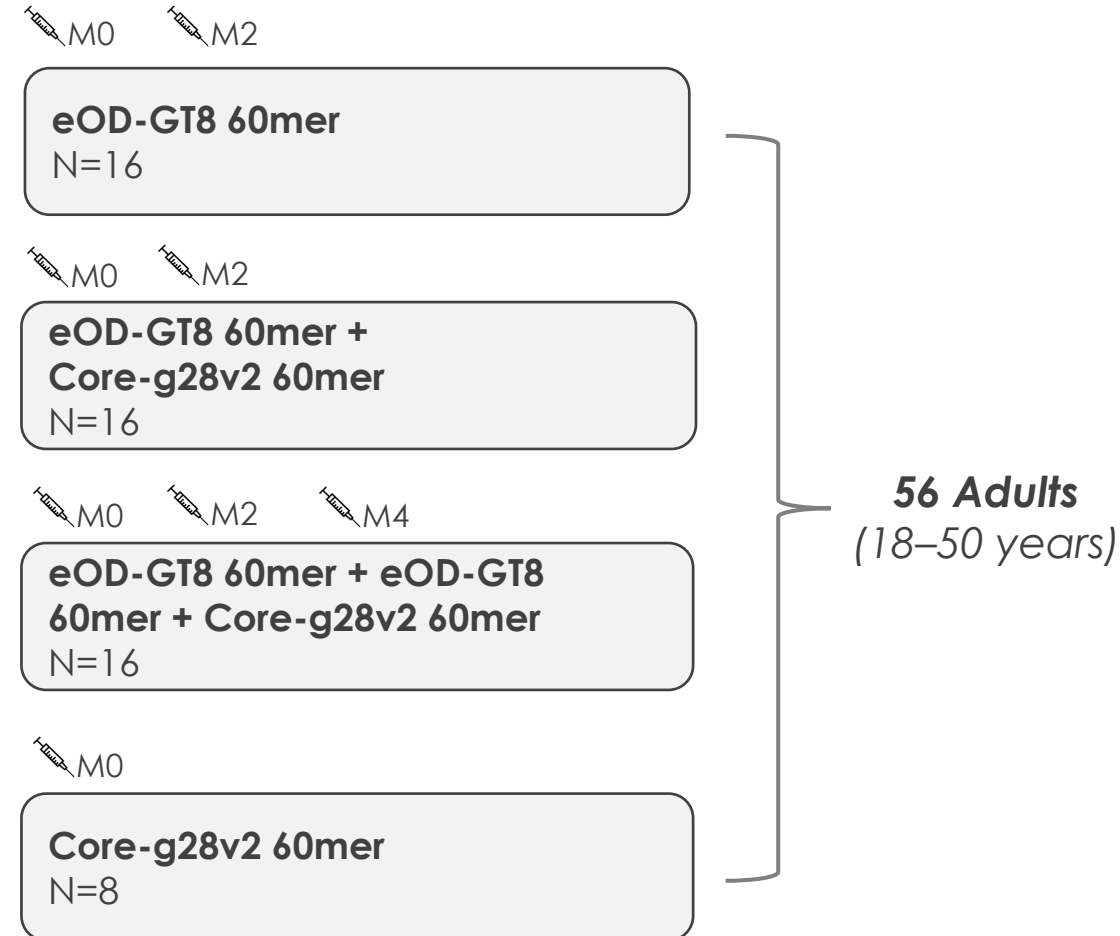
HIV Vaccine (mRNA-1644): Germline targeting approach



mRNA-1644

- Phase 1, randomized, open-label study to evaluate the safety and immunogenicity of eOD-GT8 60mer mRNA Vaccine and Core-g28v2 60mer mRNA Vaccine in HIV-1 uninfected adults
- The induction of bnAbs is widely considered to be a goal of HIV vaccination
- Testing hypothesis that sequential administration of priming and boosting HIV immunogens delivered mRNA can induce specific classes of B-cell responses and guide their early maturation toward broadly neutralizing antibody (bnAb) development
- Immunogens being tested were developed by scientific teams at IAVI and Scripps Research

Phase 1 Trial Design



Dose: 100 µg

HIV vaccine (mRNA-1574): Trimer approach



mRNA-1574

- Open-label, multicenter, randomized Phase 1 study to evaluate the safety and immunogenicity of experimental HIV trimer mRNA vaccines (BG505 MD39.3, BG505 MD39.3 gp151, and BG505 MD39.3 gp151 CD4KO)
- Primary hypothesis is that the soluble and membrane-bound HIV envelope trimer mRNA vaccines will be safe and well-tolerated by HIV-uninfected individuals and will elicit autologous neutralizing antibodies
- Envelope trimers being evaluated in this study were developed by William Schief, Ph.D. (professor at Scripps Research and director at IAVI) and colleagues

Phase 1 Trial Design

Part A

 M0  M2  M6

BG505 MD39.3

Dose: 100 µg, N=18

 M0  M2  M6

BG505 MD39.3 gp151

Dose: 100 µg, N=16

 M0  M2  M6

BG505 MD39.3 gp151 CD4KO

Dose: 100 µg, N=16

Part B

 M0  M2  M6

BG505 MD39.3

Dose: 250 µg, N=18

 M0  M2  M6

BG505 MD39.3 gp151

Dose: 250 µg, N=16

 M0  M2  M6

BG505 MD39.3 gp151 CD4KO

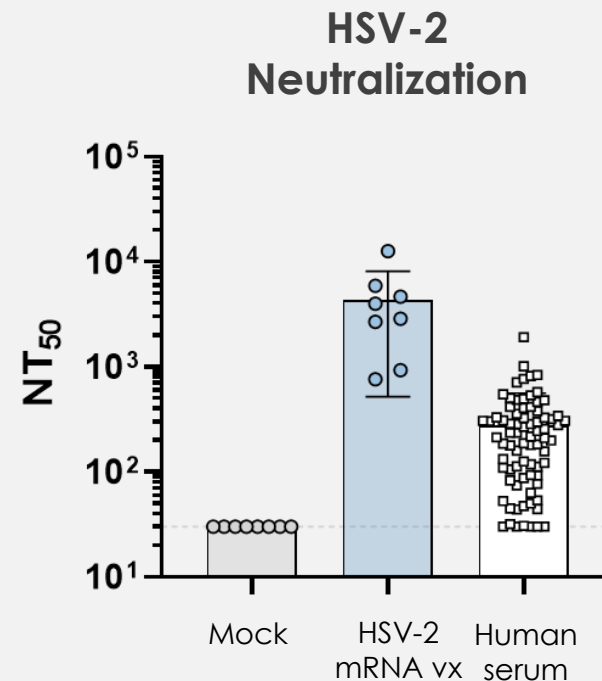
Dose: 250 µg, N=16

HSV: Vaccine against HSV-2 (mRNA-1608)

HSV-2 (Herpes) disease overview

- Herpes simplex virus type 2 (HSV-2) primarily infects the genitals
- HSV-2 establishes **life-long latent infections** within sensory neurons from which it can reactivate
- Significant burden of disease from HSV infections
 - Estimated **18.6 M HSV-2⁺ people** aged 18-49 in the US¹
 - Globally, ~5% of the population in the 18-49 range is HSV-2 seropositive²
- Burden of disease includes a **reduction in quality of life**

mRNA vaccine containing HSV-2 antigens induces strong immune response in preclinical animal studies



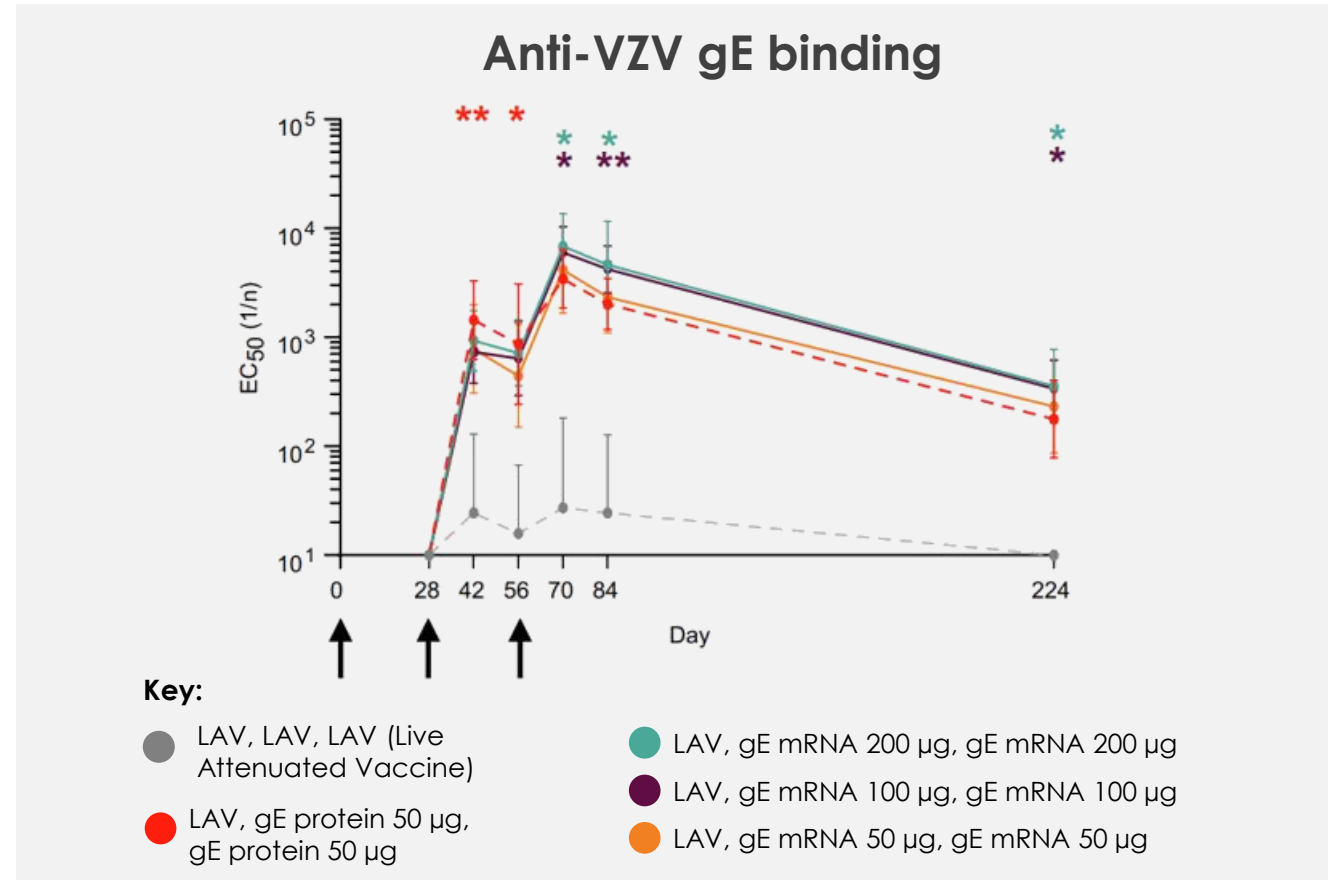
Naïve c57/Bl6 mice were immunized twice at 3 weeks interval with either PBS (mock) or HSV-2 mRNA vaccine. Each group contained 8 animals, and neutralizing activity was measured 2 weeks after the second immunization

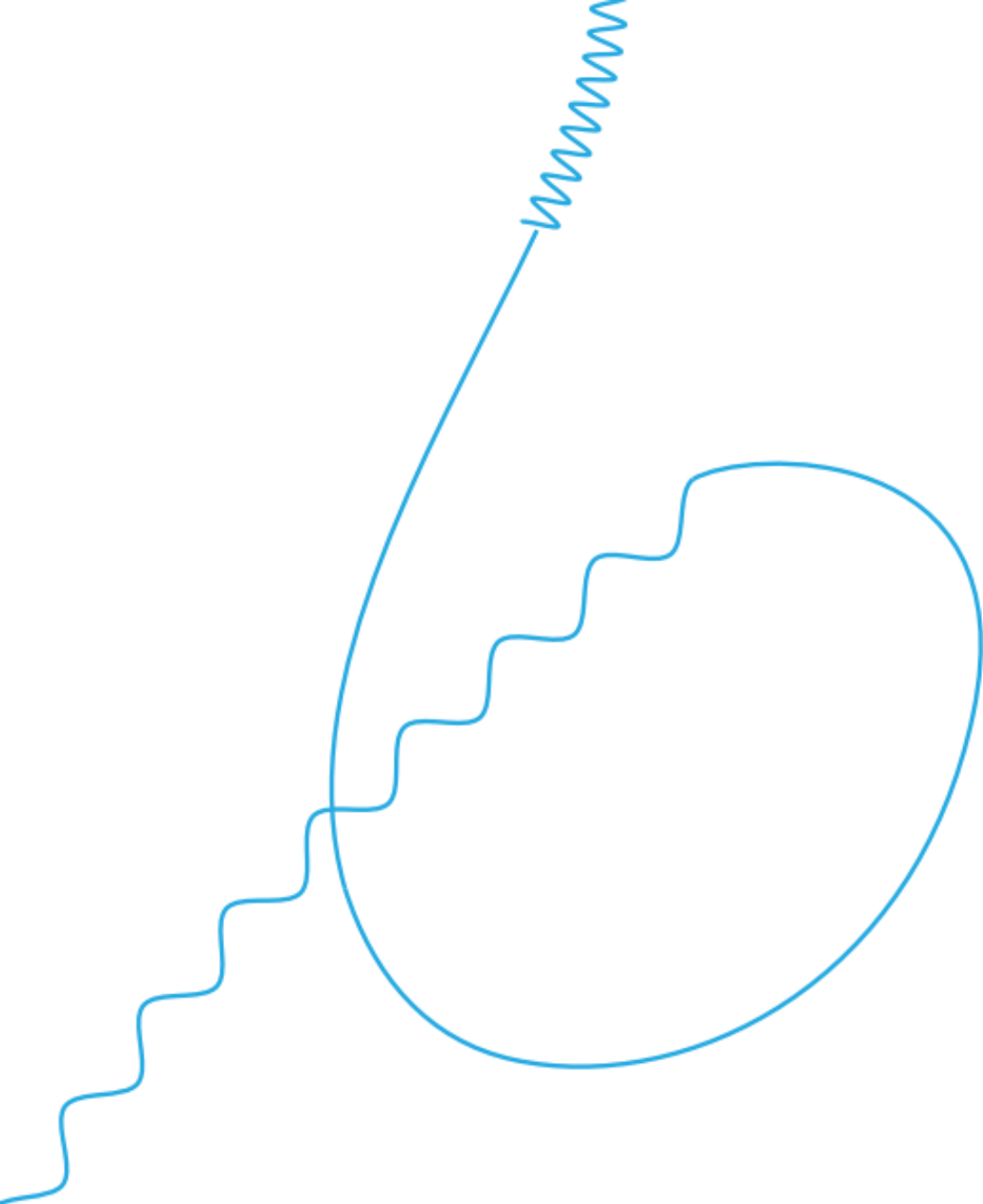
VZV: Vaccine against herpes zoster/shingles (mRNA-1468)

Herpes Zoster (shingles) disease overview

- Herpes zoster is caused by **reactivation of latent varicella-zoster virus (VZV)**
- **Declining immunity in older adults** decreases immunity against VZV, allowing reactivation of the virus from latently infected neurons, causing painful and itchy lesions
- Herpes Zoster occurs in **1 out of 3 adults in their lifetime** and incidence dramatically increases at approximately 50 years of age¹

mRNA vaccine generated similar anti-gE titers compared to an adjuvanted subunit gE vaccine (proxy for Shingrix™)² in NHP





Global Health Vaccines

Stephen Hoge, M.D.

President

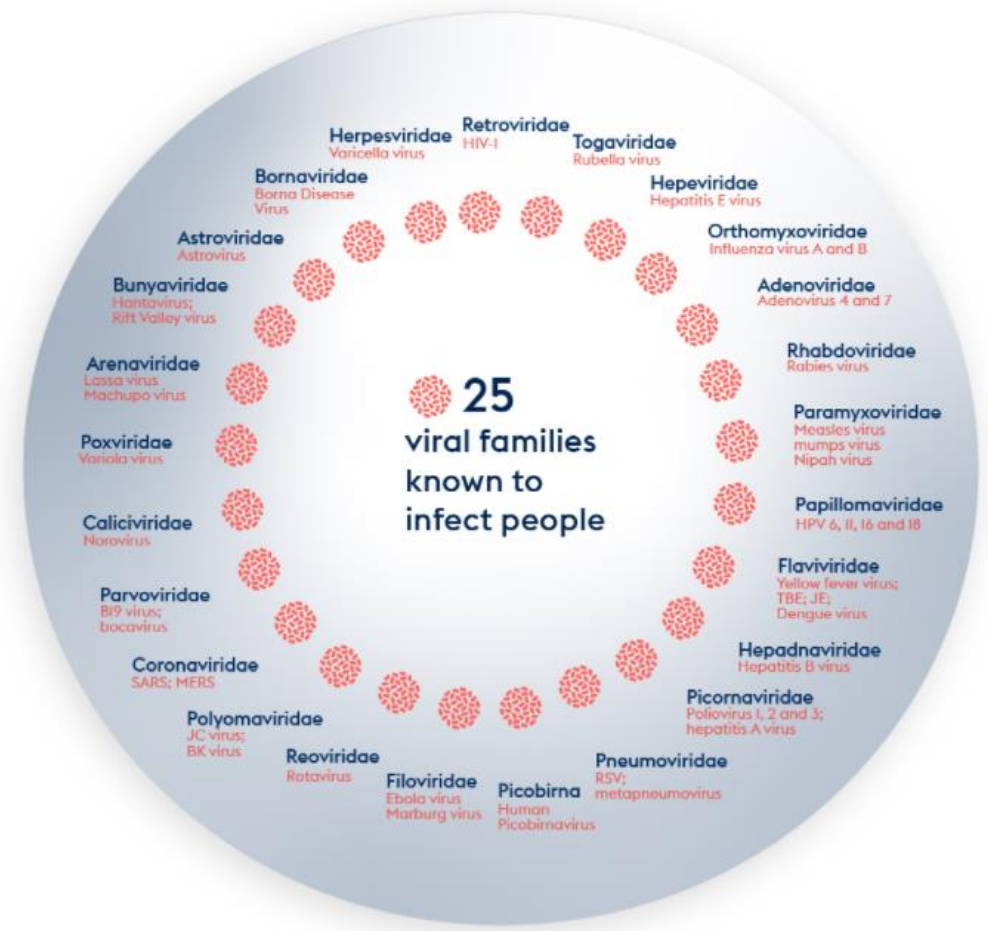
Pandemic and epidemic threats will continue to arise

THE LANCET Infectious Diseases

- Emerging pathogens continue to pose a serious threat to global health. More lives can be saved if medical countermeasures are deployed in time.
- Investments can be made now to accelerate the availability of medical countermeasures during a pandemic.

Disease X represents the knowledge that a serious international pandemic could be caused by a pathogen currently unknown to cause human disease. It was first included in the WHO's list of priority pathogens in 2018. COVID-19 represents the first occurrence of Disease X since its designation was established, emerging much sooner than anticipated.

CEPI



We have been committed to using our mRNA platform for public health since our founding

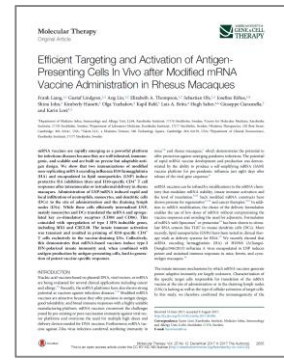


Leading funding & development partners for vaccines

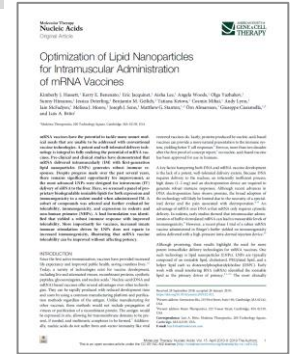


2015
First-in-Human vaccine trial on H10N8 and H7N9 influenza vaccines
Published in 2019: Feldman et al., Vaccine 37 (2019) 3326

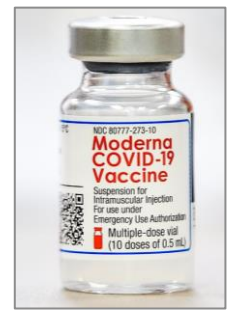
2010
moderna®
Founded



2017
Publication of Moderna's work on mechanistic understanding of mRNA vaccine mechanism of action
Liang et al., Mol. Ther. 25 (2017) 2635



2019
Publication of Moderna's work on vaccine-specific LNP in Nucleic Acids
Hassett et al., Mol. Ther. Nuc. Acids 15 (2019) 1



2020/2021
Development & authorization of mRNA-1273 COVID-19 vaccine



2020/2021
Multiple publications on pre-clinical and clinical results of mRNA-1273



2022
Commitment to advance vaccines targeting 15 pathogens identified as biggest public health risk

2021

2022

nature
The NEW ENGLAND JOURNAL of MEDICINE

moderna®

Three key pillars of our global health strategy

1

Priority Pathogens

Commitment to **advance vaccines targeting 15 priority pathogens into clinical studies by 2025**, identified by WHO and CEPI

2

mRNA Access™

New collaborative access enabling researchers around the world to utilize Moderna's mRNA technology platform to pursue research in their own labs on emerging and neglected infectious diseases

3

Patents

Expands **commitment to never enforce COVID-19 patents in the Gavi COVAX Advance Market Commitment (AMC)** for 92 low- and middle-income countries

Our platform is uniquely suited for rapid response to Disease X

- Committing to advancing into clinical studies **a portfolio of 15 vaccine programs targeting emerging or neglected infectious diseases by 2025**, advancing vaccines that addresses current diseases of significant impact to low- and middle-income countries, and those that prepare for Disease X
- We are prioritizing:
 - HIV
 - Tuberculosis (TB)
 - Malaria
 - Neglected tropical diseases
 - Priority pathogens of the WHO and CEPI

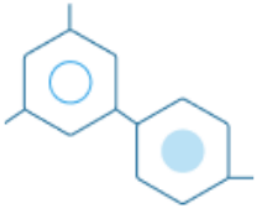
	Persistent Global Health Threats	WHO R&D Blueprint	CEPI Priority Pathogens	Prototype Viral Family
Chikungunya virus			X	Togaviridae
COVID-19		X		Coronaviridae
Crimean-Congo haemorrhagic fever		X		Nairoviridae
Ebola virus disease		X	X	Filoviridae
HIV	X			
Malaria	X			
Marburg virus disease		X		Filoviridae
Lassa fever		X	X	Arenaviridae
Middle East respiratory syndrome coronavirus (MERS-CoV)		X	X	Coronaviridae
Nipah and henipaviral diseases		X	X	Paramyxoviridae
Rift Valley fever		X	X	Phenuiviridae
Tuberculosis	X			
Zika		X		Flaviviridae
"Disease X"		X	X	
Dengue				Flaviviridae
Severe fever with thrombocytopenia syndrome				Phenuiviridae

mRNA Access Powered by Moderna

- Researchers at partnering institutions are invited to take advantage of our mRNA platform to develop mRNA medicines for existing neglected diseases
- These programs will leverage Moderna's Early Development Engine to accelerate vaccine development to the clinic
- mRNA Access will also allow scientists around the world to explore novel vaccine designs against prototype viral families in preparation for Disease X



mRNA Access Powered by Moderna



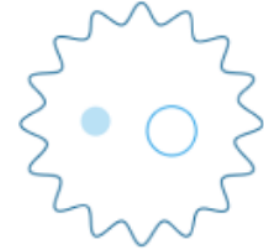
mRNA Design Studio

Our custom mRNA is codon optimized for optimal expression and manufacturability



High-Throughput Production

Optimized mRNA is manufactured using our prophylactic vaccine process, suitable for *in vitro* or *in vivo* testing

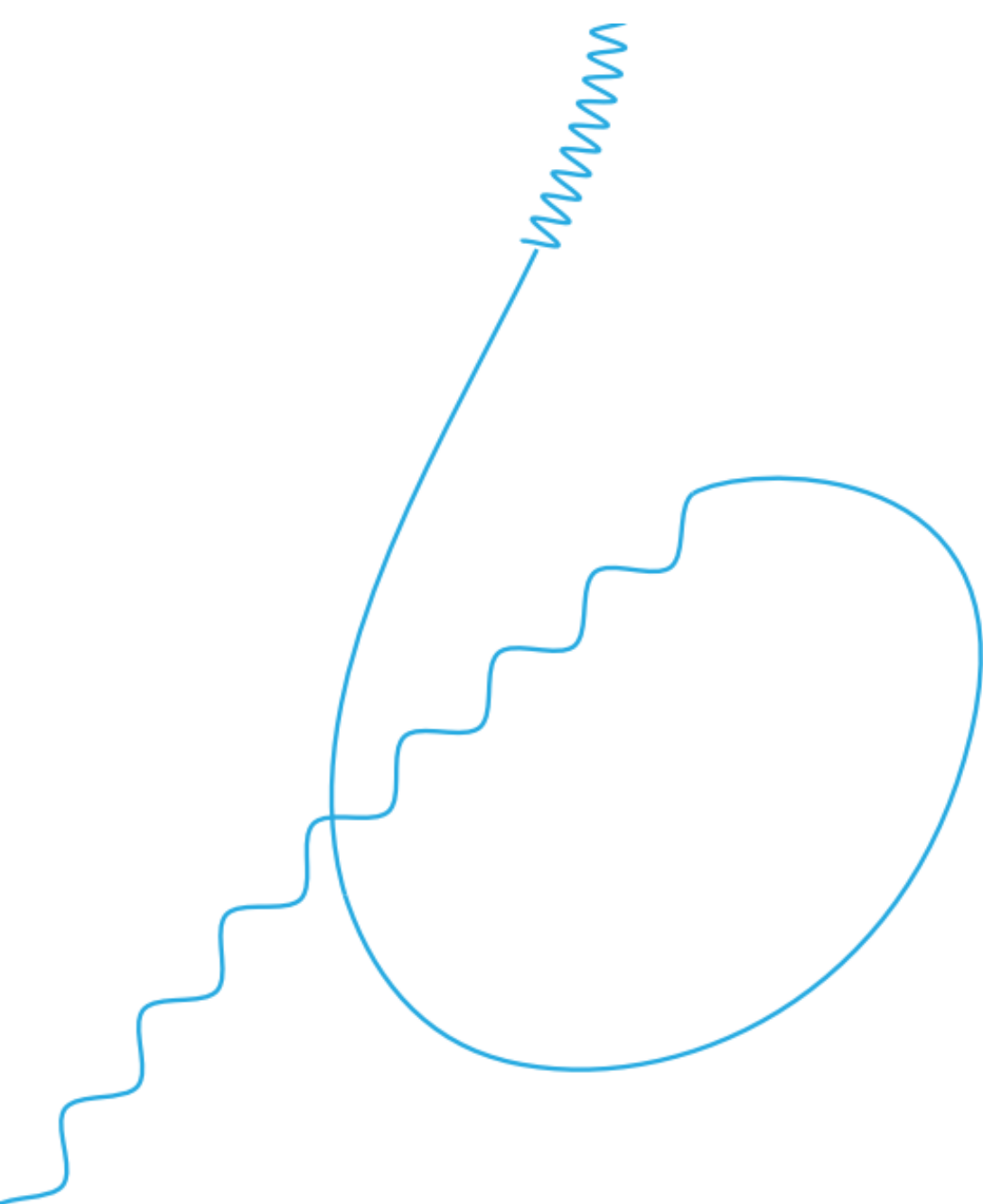


Iterative Research

The speed and flexibility of our platform allows for rapid design-test cycles of antigen design and pre-clinical testing

Example
collaborators





Expect More From Moderna's Vaccines

Stéphane Bancel, CEO

Moderna's commercial vaccine strategy

Respiratory Vaccines

Single virus vaccines

- COVID-19 (mRNA-1273)
 - Variant-containing candidates
- Flu (mRNA-1010)
- RSV (mRNA-1345)

Combination vaccines

- COVID + Flu (mRNA-1073)
- COVID + Flu + RSV (mRNA-1230)
- Endemic HCoV (mRNA-1287)
- Pediatric RSV + hMPV (mRNA-1365)
- Pediatric hMPV + PIV3 (mRNA-1653)

Latent Virus Vaccines

- CMV (mRNA-1647)
- EBV (mRNA-1189/95)
- HSV (mRNA-1608)
- VZV (mRNA-1468)
- HIV (mRNA-1644/1574)

What do we know about the current respiratory vaccine market?

- ✓ Older adult population: High compliance and uptake rate 90%+ in 65+ year old for COVID-19 vaccines
- ✓ Higher prices for highly effective innovative vaccines
- ✓ In flu, slightly higher vaccine efficacy commands higher price

What are latent virus vaccine proxies?

- ✓ Successful vaccines against latent viruses can significantly improve long-term health outcomes
- ✓ These vaccines have multi billion-dollar sales potential (strong growth, annuity-like)

Respiratory viruses: Older adult populations are more susceptible to severe disease

U.S. adults 65+

Respiratory Virus	Within Season Outpatient (Attack Rate per 1,000)	Annual Inpatient (Attack Rate per 1,000)	Inpatient Mortality	US Estimated Annual Cost
Influenza (all)	32	4.3	3-4%	\$5.6 bn
Respiratory syncytial virus (RSV)	19	1.9	5.2%	\$1.5 bn
Human coronavirus (HCoV) excl. SARS-CoV-2	18	2.6	7.3%	\$1.4 bn
Human rhinovirus (HRV)	12	5.9	3.2%	\$4.0 bn
Human metapneumovirus (HMPV)	11	1.6	3.9%	\$1.3 bn
Parainfluenza viruses (PIV)	7	1.5	4.9%	\$1.1 bn
Subtotal	94	17.8	3-7%	~\$15 bn

+ Endemic SARS-CoV-2 will add to these totals

Global implications

Estimated **\$20-40 billion of annual cost globally** from these viruses in adults 65+

Approximately **19 million disability adjusted life-years (DALY)** lost in 2019 alone

Respiratory vaccines: Potential total addressable market (TAM)



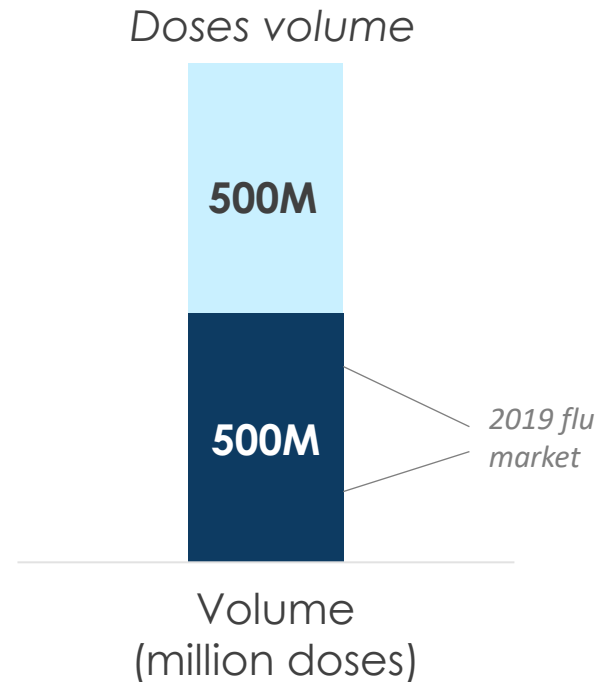
Addressable population with an unmet medical need (high risk adults¹)

>82M individuals in U.S.

>340M individuals in high-income countries

>1.7B individuals in world

Potential volume of doses in endemic COVID market



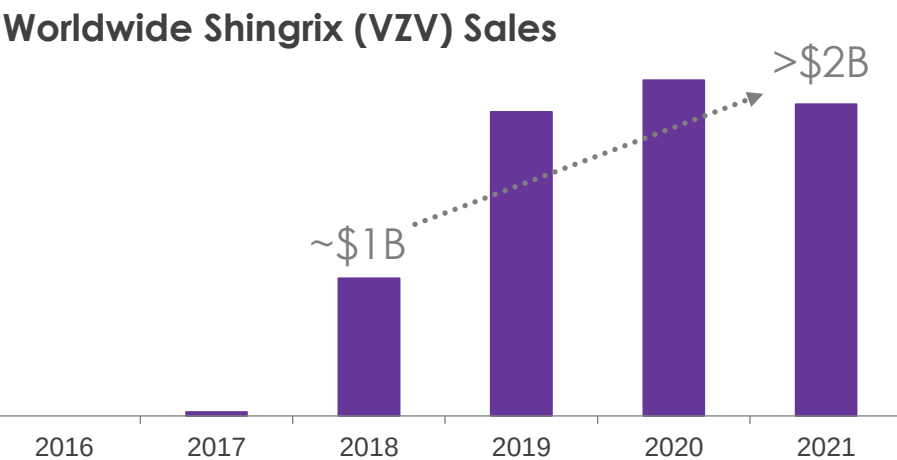
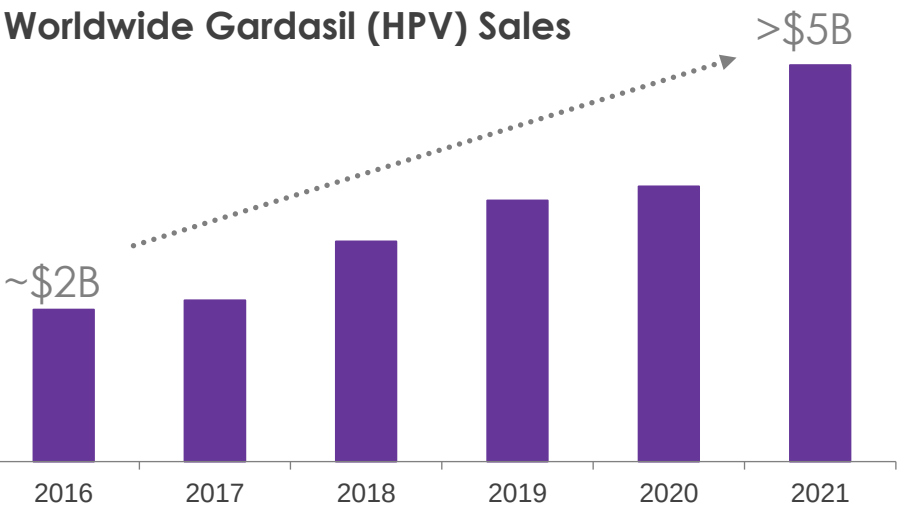
How does COVID change the respiratory vaccines market?

- ✓ Increased awareness of mRNA vaccine efficacy
- ✓ Recognition of vaccines as the gold standard in preventing disease burden and medical costs
- ✓ Economic and social disruption from pandemic
- ✓ Desire to go back to normal

(1) Higher risk due to age 65+ and adults 50-65 with at least one risk factor; CDC, <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html#print>; Ajufo, Ezimamaka et al., *The American Journal of Cardiology* (2021), <https://doi.org/10.1016/j.ajpc.2021.100156>; Clark, Andrew et al., *Lancet Glob Health* (2020), [https://doi.org/10.1016/S2214-109X\(20\)30264-3](https://doi.org/10.1016/S2214-109X(20)30264-3)

Latent viruses vaccines have large addressable markets

Latent Viruses	Moderna Program
Cytomegalovirus (CMV)	mRNA-1647
Epstein-Barr virus (EBV)	mRNA-1189
Herpes simplex virus (HSV)	mRNA-1608
Varicella zoster virus (VZV)	mRNA-1468
Human immunodeficiency virus (HIV)	mRNA-1644/-1574



Source: Evaluate Pharma

First Annual Vaccines Day (April 2020) vaccines pipeline

9 development programs in vaccines 0 commercial 0 Phase 3 1 Phase 2

Program	mRNA #	Phase
Cytomegalovirus (CMV) vaccine	mRNA-1647	Ph 2
Novel coronavirus (SARS-CoV-2) vaccine	mRNA-1273	Ph 1
Zika vaccine	mRNA-1893	Ph 1
Respiratory syncytial virus (RSV) vaccine	mRNA-1172/Merck V172	Ph 1
Respiratory syncytial virus (RSV) vaccine	mRNA-1177	Ph 1
hMPV/PIV3 vaccine	mRNA-1653	Ph 1
Influenza H7N9 vaccine	mRNA-1851	Ph 1
Pediatric respiratory syncytial virus (RSV) vaccine <i>Future respiratory combo</i>	mRNA-1345	Preclinical
Epstein-Barr virus (EBV) vaccine	mRNA-1189	Preclinical

Third Annual Vaccines Day (March 2022) vaccines pipeline

31 development programs
in vaccines

1 commercial

4 Phase 3

9 Phase 2

Program	mRNA #	Phase
COVID-19 vaccine	mRNA-1273/-351/-617/-211/-213/-529/-214 mRNA-1283	Commercial Ph 2/3
Older adults RSV vaccine	mRNA-1345	Ph 3
COVID-19 vaccine (adolescents)	mRNA-1273	Ph 3
COVID-19 vaccine (pediatrics)	mRNA-1273	Ph 3
Flu vaccine	mRNA-1010/-11/-12/-20/-30	Ph 2 Preclinical
Pediatric RSV vaccine	mRNA-1345	Ph 1
Pediatric hMPV + PIV3 vaccine	mRNA-1653	Ph 1
COVID + Flu vaccine	mRNA-1073	Preclinical
Influenza + SARS-CoV-2 + RSV vaccine	mRNA-1230	Preclinical
Pan HCoV vaccine	mRNA-1287	Preclinical
Pediatric RSV + hMPV vaccine	mRNA-1365	Preclinical

Program	mRNA #	Phase
CMV vaccine	mRNA-1647	Ph 3
Zika vaccine	mRNA-1893	Ph 2
EBV vaccine (<i>to prevent infectious mononucleosis</i>)	mRNA-1189	Ph 1
HIV vaccines	mRNA-1644/-1574	Ph 1
EBV vaccine (<i>to prevent EBV sequelae</i>)	mRNA-1195	Preclinical
HSV vaccine	mRNA-1608	Preclinical
VZV vaccine	mRNA-1468	Preclinical
Nipah vaccine	mRNA-1215	Preclinical

Where is the Moderna vaccine pipeline going to be in 2 years?

2020 Pipeline

9 development programs

- 0 commercial
- 0 Phase 3
- 1 Phase 2
- 6 Phase 1
- 2 preclinical

2022 Pipeline

31 development programs

- 1 commercial
- 4 Phase 3
- 9 Phase 2
- 5 Phase 1
- 12 preclinical

2024 Pipeline?

Endemic market dynamics: global sales infrastructure

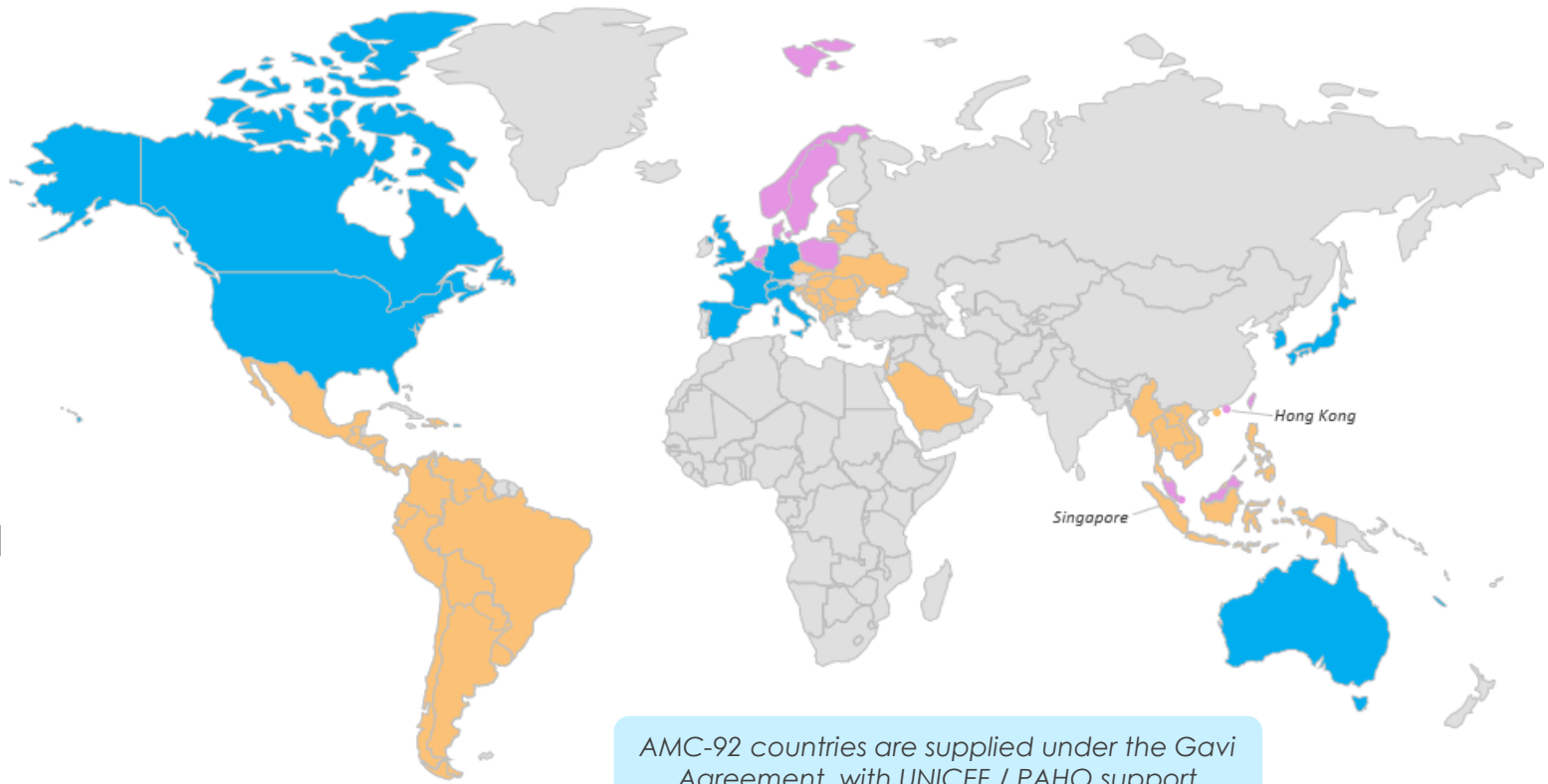
■ Operating commercial subsidiary as of Dec 2021 ■ 2022 new commercial subsidiaries ■ Distributor partnerships as of Feb 2022

Sales and marketing in US is fragmented in normal times (non pandemic):

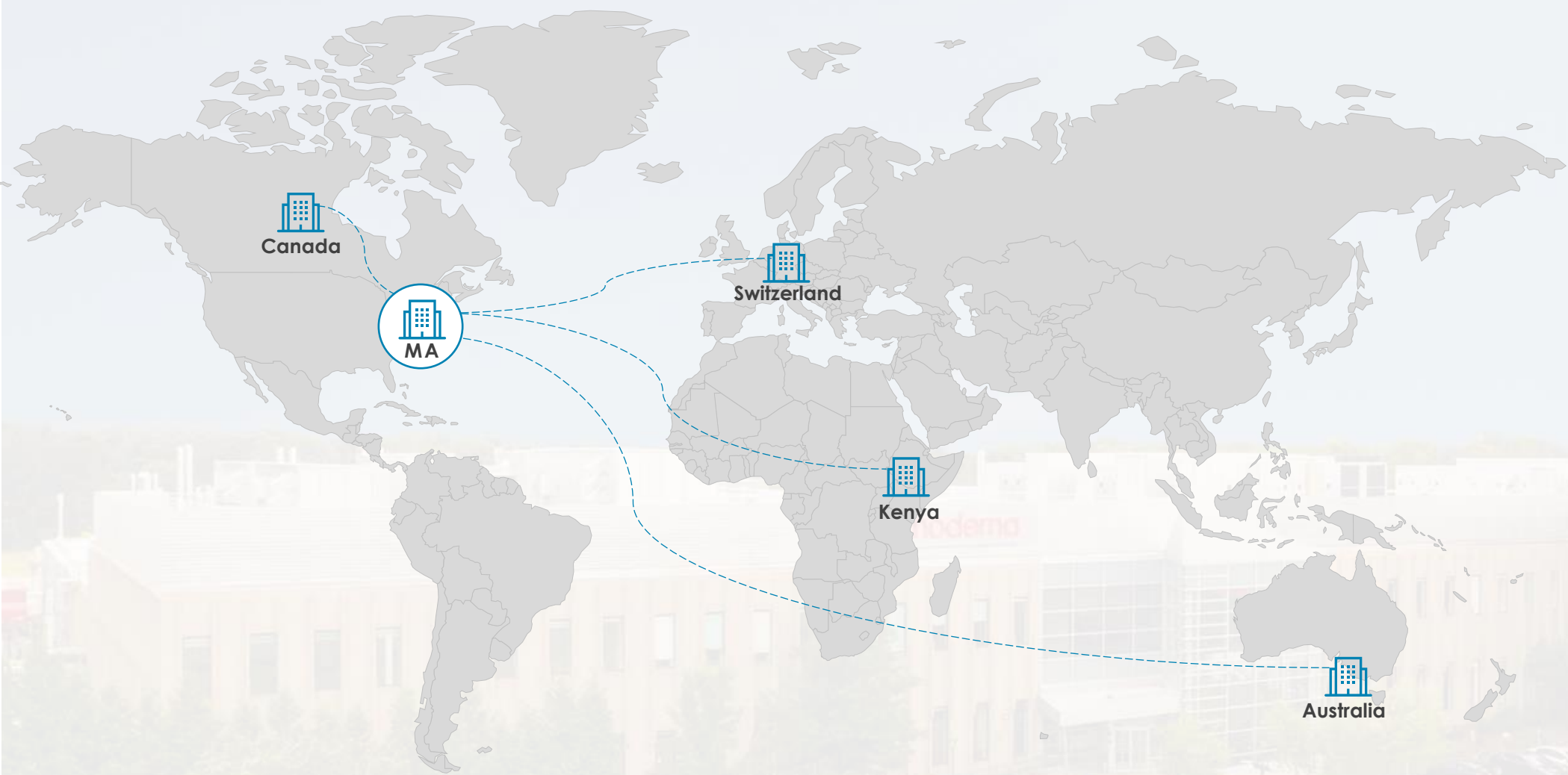
- USG buys for Medicare, Medicaid
- Private insurance health plans (UNH, Cigna, Blue Cross)
- Private commercial market: Development of commercial market to large employers

International markets:

- Typically single payor, reimbursement at government level, national and regional tenders, leverage relationships with health ministers established during Pandemic
- Sizable private market in select countries e.g. South Korea



We are building manufacturing capability to prepare for the future



F/F & Drug
Product Partners

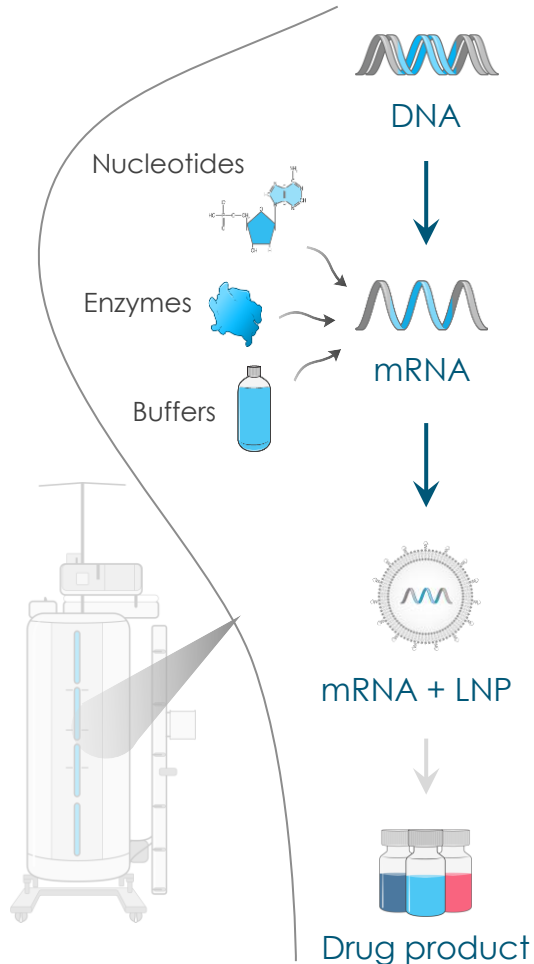
Lonza
ThermoFisher
SCIENTIFIC

Catalent

 **ROVI**
Pharma Industrial Services

..and others!

mRNA manufacturing is flexible and one plant can manufacture multiple vaccines and therapeutics to prepare for the future



- Our manufacturing facilities can manufacture all of our mRNA vaccines
- Initial capacity to be used for our COVID-19 vaccine, but will be expanded as more vaccine products are commercialized
- If/when therapeutics reach the market, they will be manufactured out of our Norwood facility
 - Therapeutics will be administered more frequently (repeat dosing) and at larger doses (mg/kg vs. mcg) compared to vaccines
 - We can make mRNA therapeutics out of our other, worldwide facilities as needed
- Long-term strategic collaborations with Thermo Fisher and Rovi for fill/finish capabilities

Low-income countries are now in excess of vaccine supply since early Q1 2022

African Union

- Asked to delay Q1 option into Q2
- Subsequently asked to delay Q2 into Q3
- Recently asked to cancel option

COVAX

- Asked to delay some of the Q1 shipments
- Did not exercise option for 166M doses in Q3
- Low likelihood that they exercise option for Q4 (166M doses, expires April 1st)

Spikevax[®] commercial outlook in 2022

Spikevax[®] 2022 commercial outlook

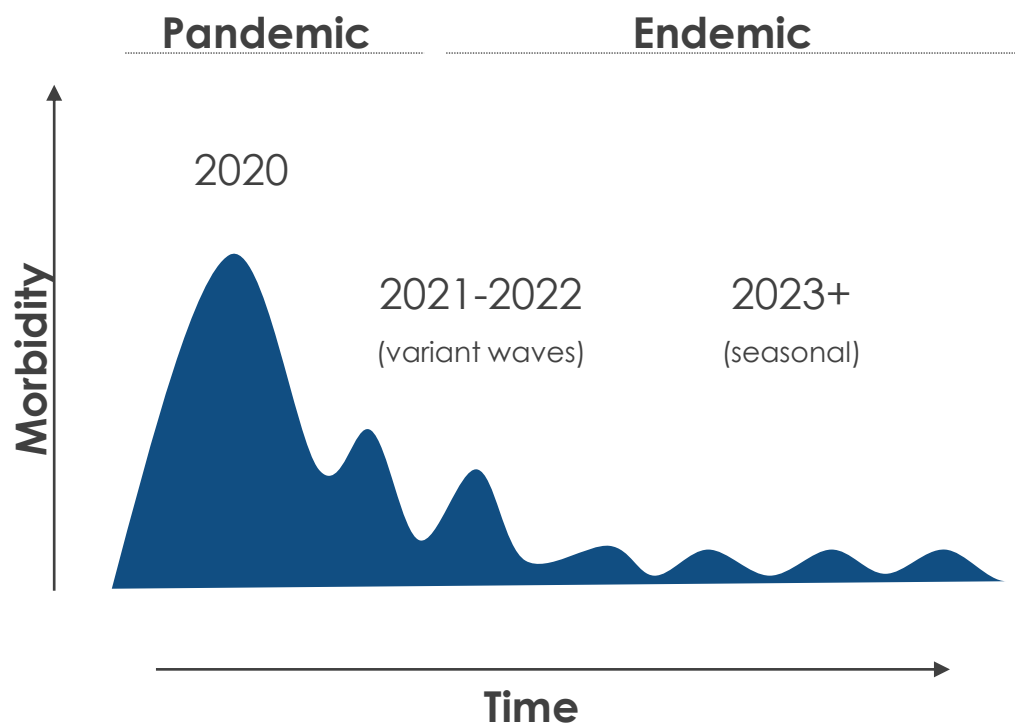
- Signed APA, including recently announced Japan: ~\$21B
- Options (probability weighted): ~\$0.5B
- Discussions ongoing with countries around the world, including the U.S.
- Expect that SARS-CoV-2 will become endemic this year with sales larger in the second half of the year as the Northern Hemisphere enters the Fall/Winter
- Excess of supply in low- and middle-income countries since early Q1 2022

	4Q21 Earnings Call (Feb. 24, 2022)	Vaccines Day (March 24, 2022)
Signed APAs	~\$19B	~\$21B
Options (probability weighted)	~\$3B	~\$0.5B

These 2 numbers assume \$0 from the U.S. for Fall 2022

Spikevax[®] commercial outlook in 2023

ILLUSTRATIVE



2023 Firm Orders

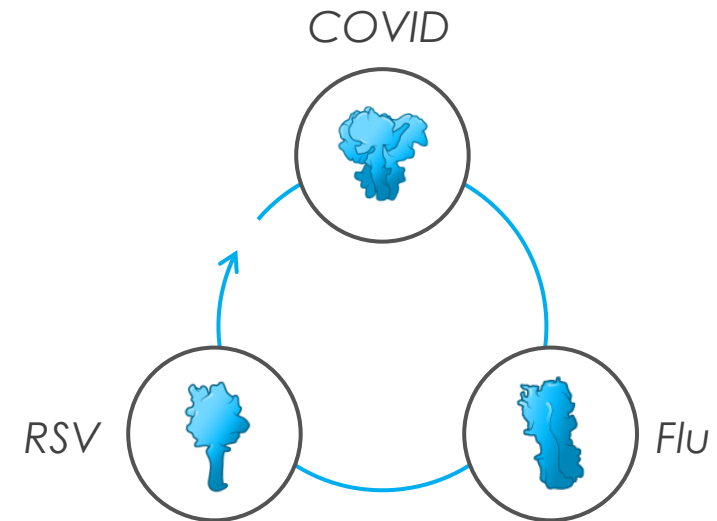
- United Kingdom
- Canada
- Taiwan
- Kuwait
- Switzerland
- In discussions with countries around the world

Service/subscription model for our pan-respiratory franchise

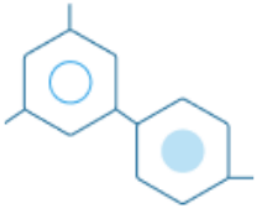
10-year agreements with strategic countries

- **Strategic supply agreements** with governments
- **Committed agreement with Australia;** announced in **principle agreements with Canada** and in discussions with additional countries around the world

Ability to customize respiratory vaccines portfolio



mRNA Access Powered by Moderna



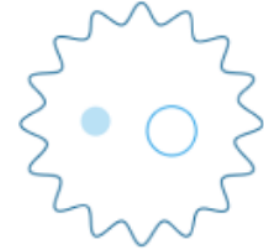
mRNA Design Studio

Our custom mRNA is codon optimized for optimal expression and manufacturability



High-Throughput Production

Optimized mRNA is manufactured using our prophylactic vaccine process, suitable for *in vitro* or *in vivo* testing



Iterative Research

The speed and flexibility of our platform allows for rapid design-test cycles of antigen design and pre-clinical testing

Example
collaborators



Expect more from Moderna



Responsibility to advance our technology, working with governments around the world, to accelerate our vaccines against pathogens that pose a worldwide threat of infection and disease and those that are more regional or endemic in certain parts of the world



Manufacturing facility in Kenya



Country specific pathogens



Populations at risk in center of strategy (customized “pathogen protection”)

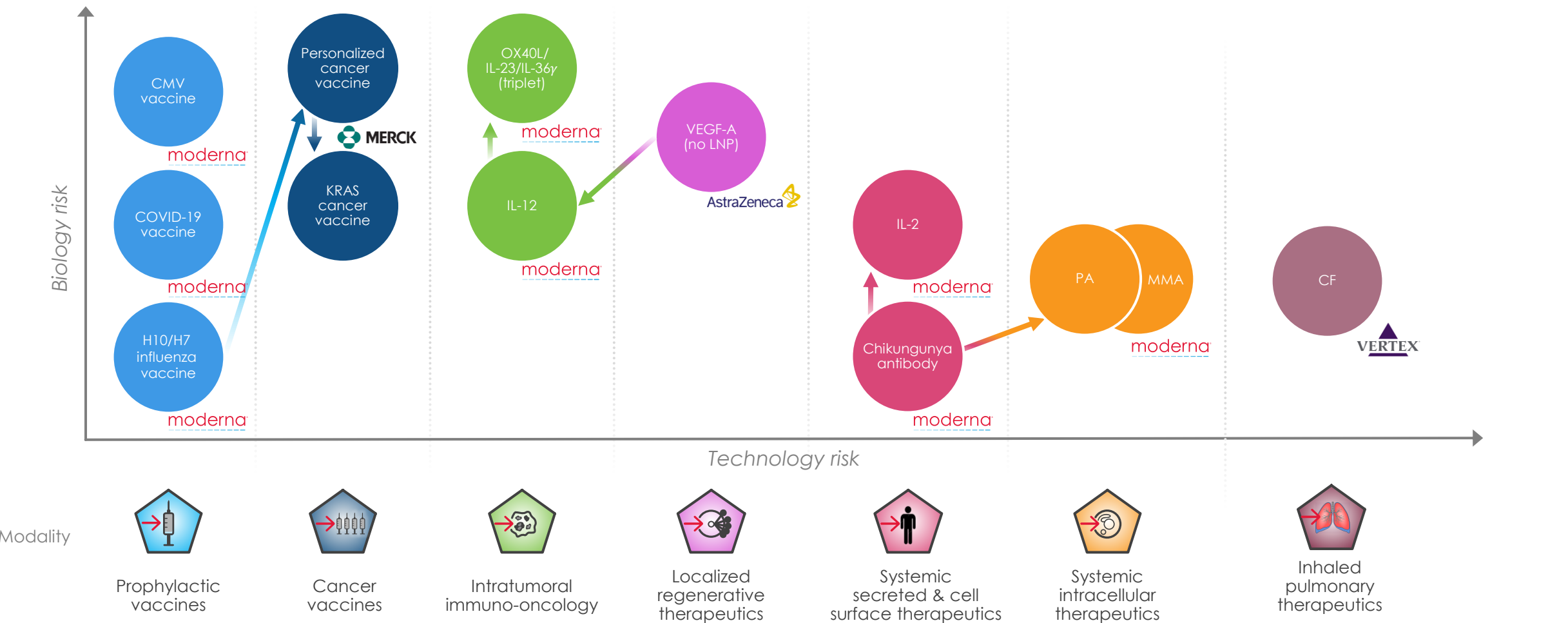


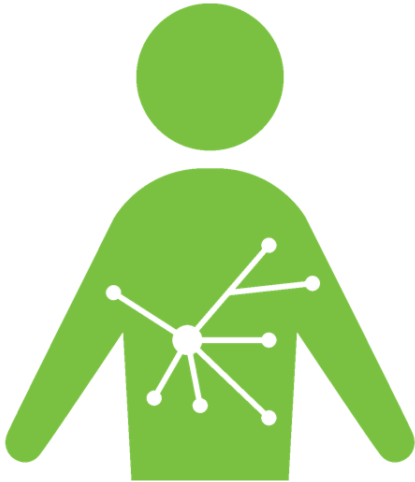
Pandemic preparedness



mRNA Access

Conclusion: Moderna is an information-medicine based platform company





Our mission

To deliver on the promise of mRNA science to create a new generation of transformative medicines for patients.