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Chula Vaccine Research Center
Faculty of Medicine, Chulalongkorn University

School of Global Health
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Vaccine Technology Platforms and Vaccine Development

Kiat Ruxrungtham

Professor of Medicine,
Chula Vaccine Research Center,
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Chulalongkorn University;

Pre-COVID-19 Pandemic – Before 2019

Vaccine Technology Platforms

Whole Pathogen Vaccine

Live-attenuated

Inactivated

Protein-based Vaccine

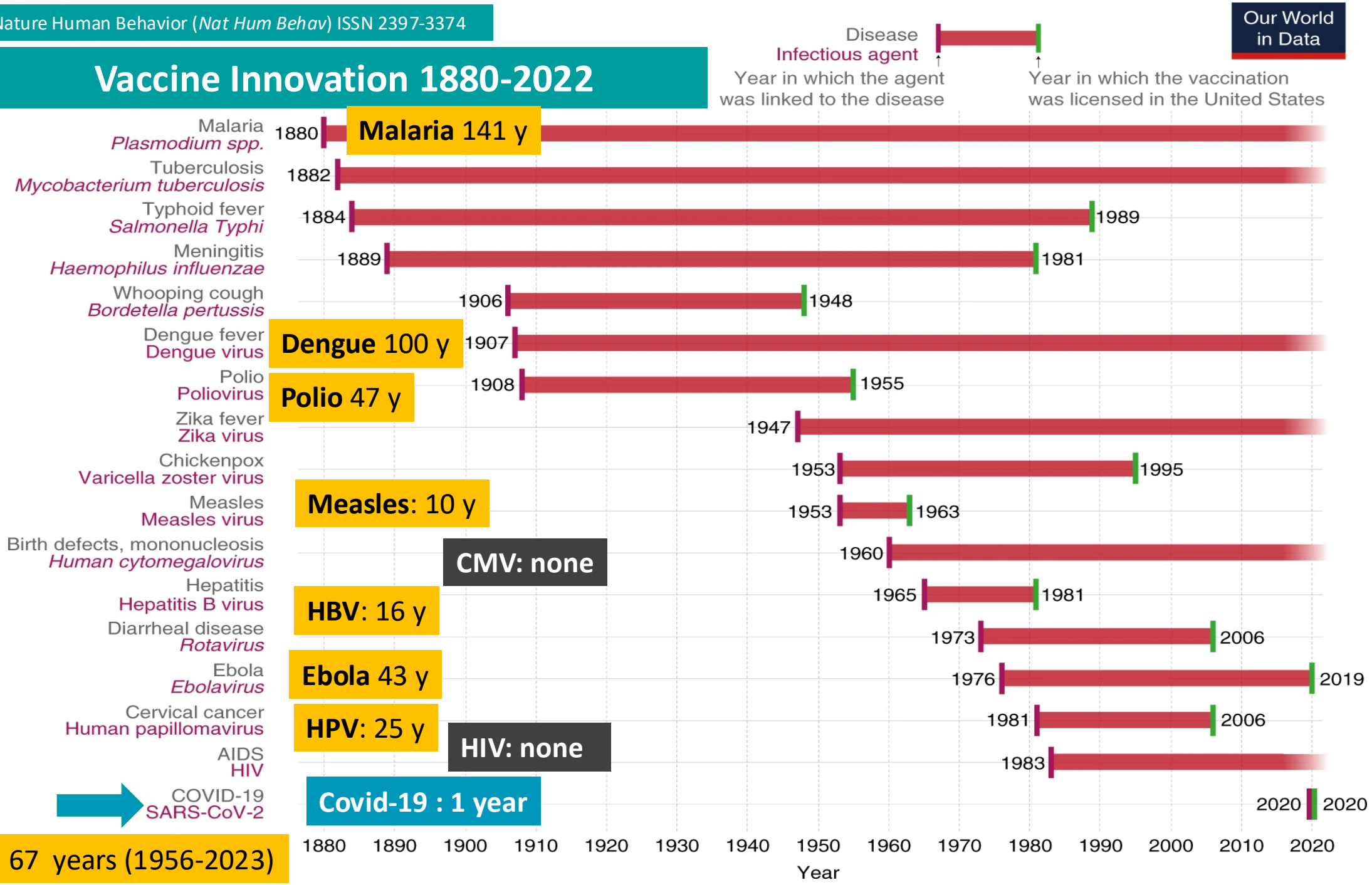
Purified

Recombinant Protien

VLP

Nature Human Behavior (*Nat Hum Behav*) ISSN 2397-3374

Vaccine Innovation 1880-2022



RSV: 67 years (1956-2023)




COVID19 Pandemic

since 1 Jan 2020



Total Cases

7 July 2024

Total Death

775,673,955

7,053,524

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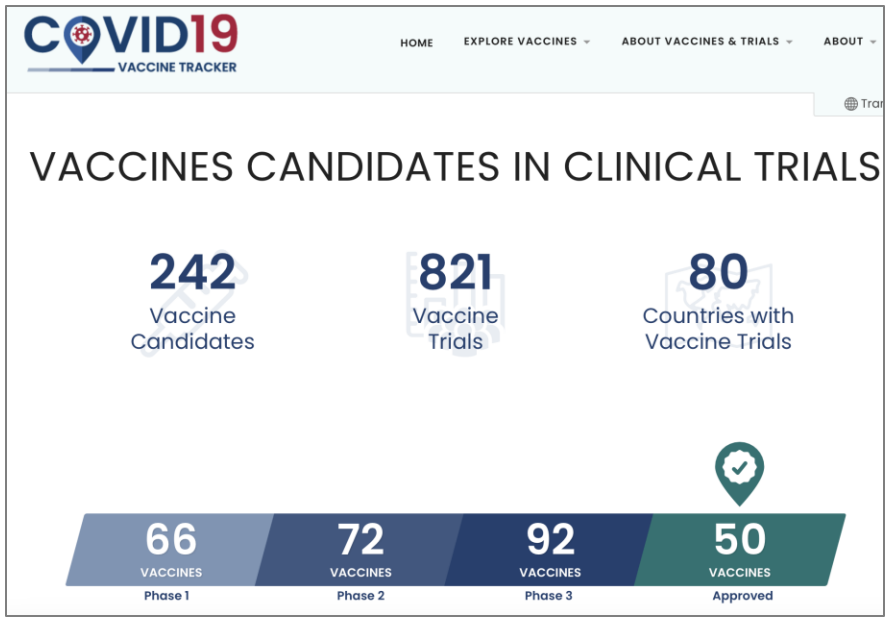
Record-Breaking Covid19 Vaccine



https://covid19.trackvaccines.org/vaccines/

>240 Candidates
>820 Clinical Trials
>80 Countries
50 Approved

World Record

- Speed
- Number/types
- Efficacy
- Rolling out >13.6 Billion Doseas

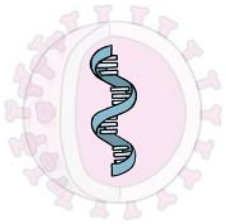
However, Inequity remains an issue !!

Global Covid-19 Vaccine Approved (partially Listed)

NewTechnology

Viral Vector

ASTRAZENECA/OXFORD
J&J
Covidshield
GAMALEYA
CANSINO BIO

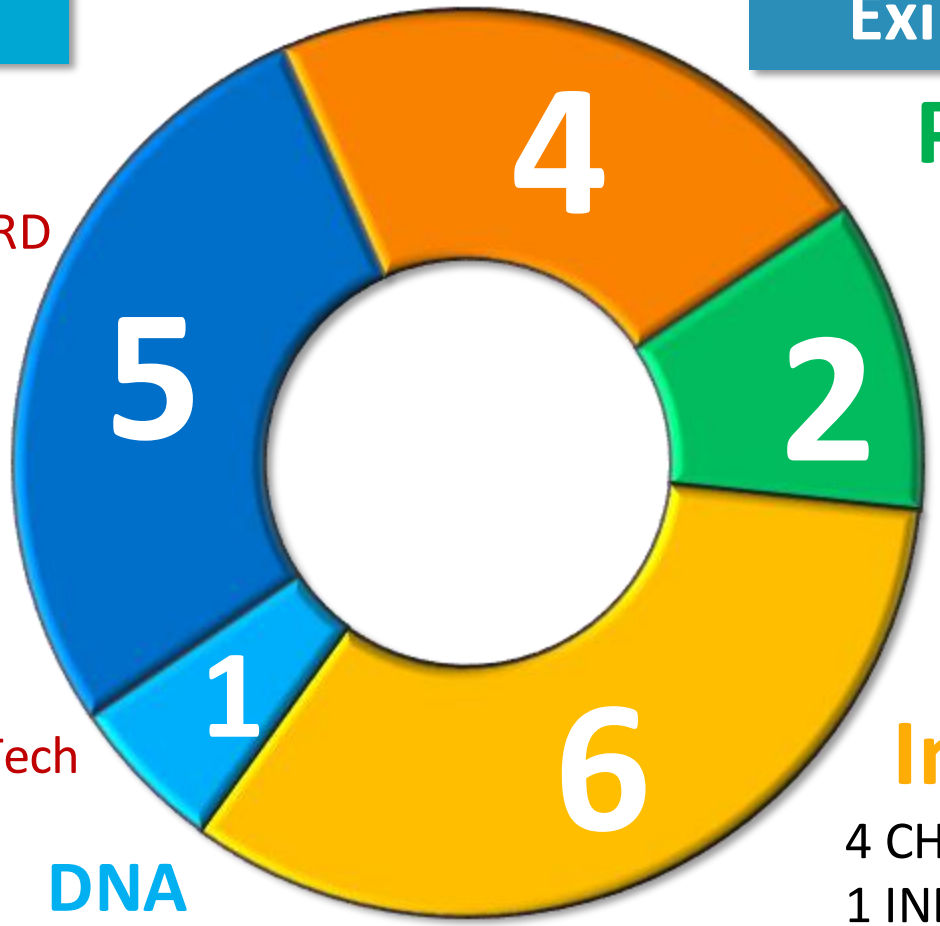


mRNA

Pfizer/BioNTech
MODERNA
China
Japan
India

DNA

Zydus



Exisiting Technology

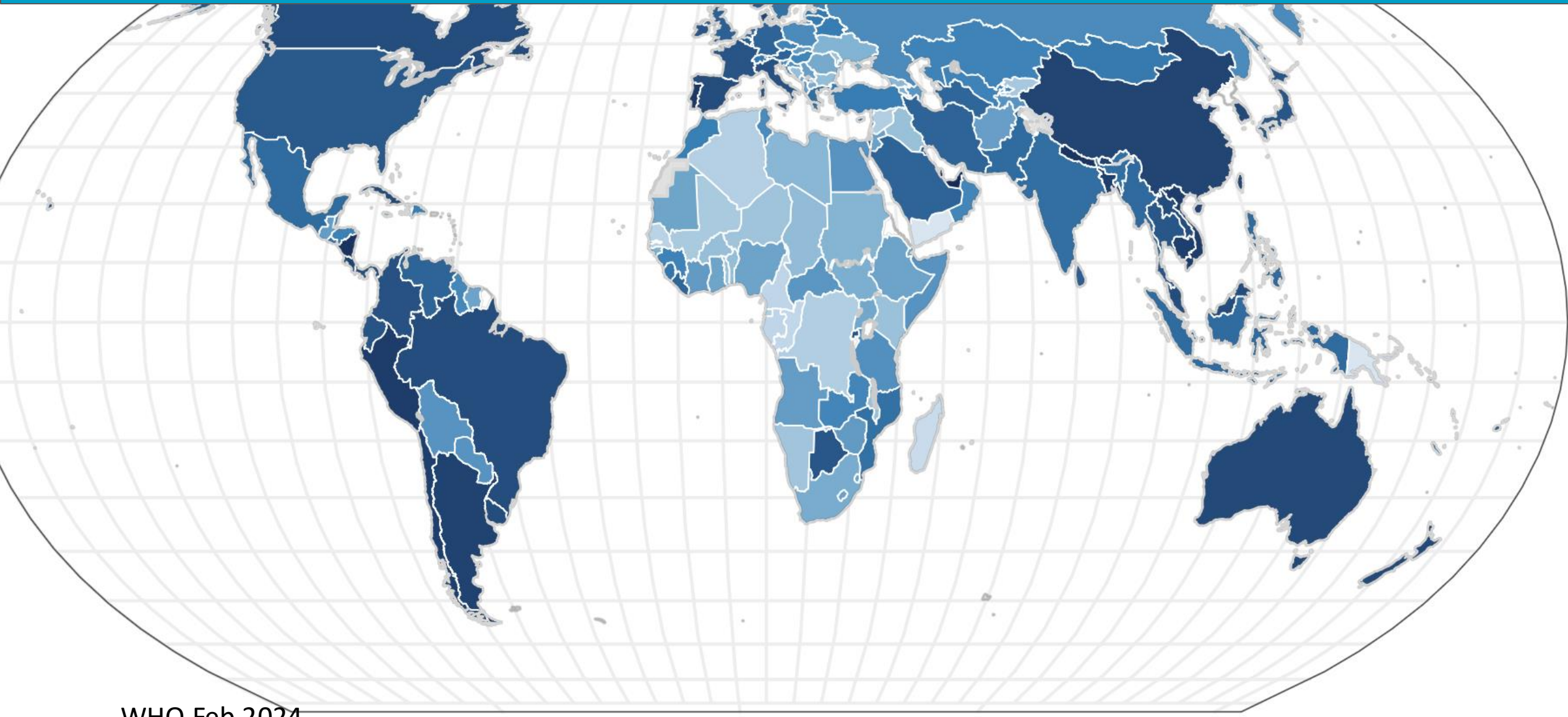
Protien

NOVAVAX
Sanofi/GSK

Inactivated

4 CHINA: BIBP, Sinovac, Sinopharm, IMB
1 INDIA: BHARAT
1 Thailand (GPO): NDV-HXP-S

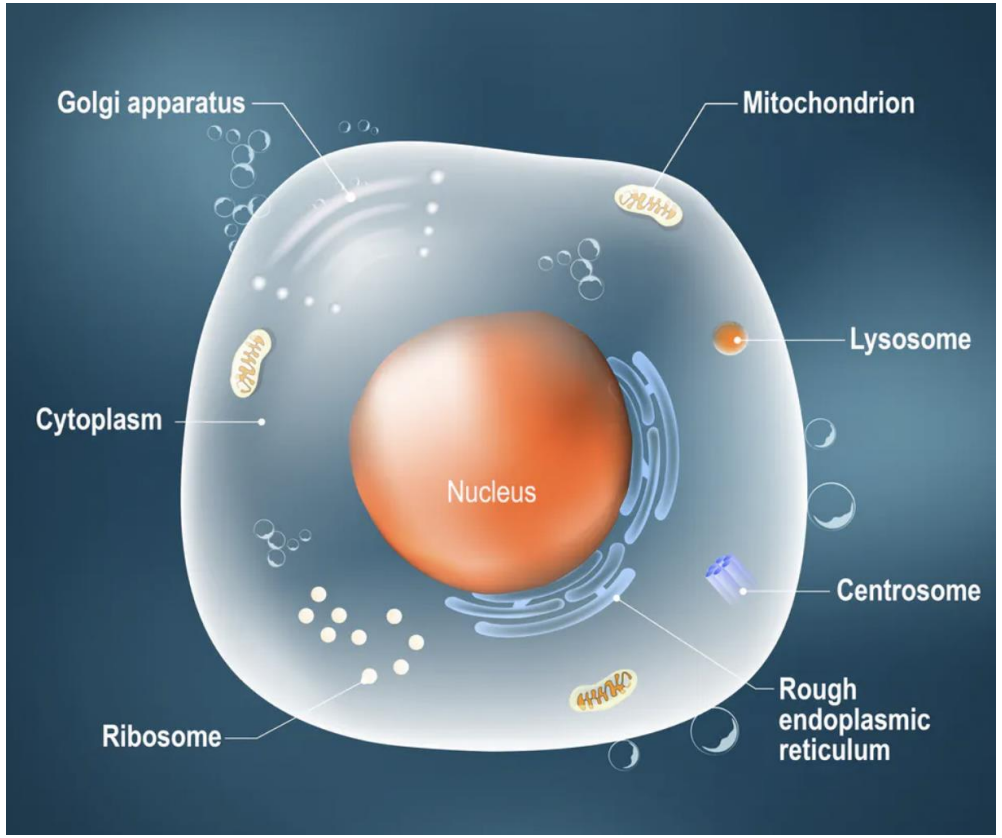
Covid Vaccine >13.6 Billion Doses Given Worldwide

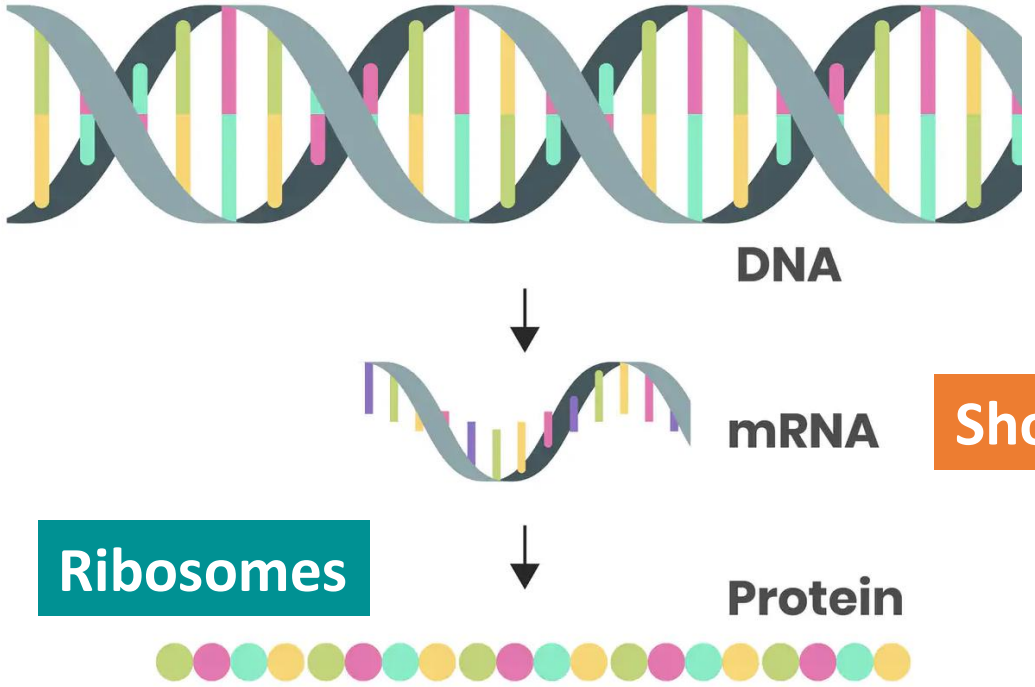


WHO Feb 2024

Nature is Super Amazing

messanger RNA (**mRNA**)





DNA

mRNA

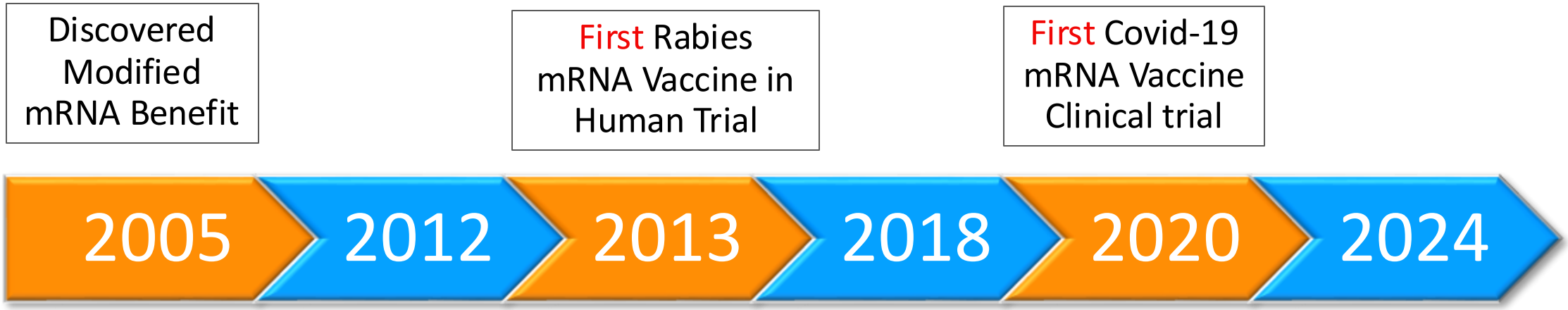
Short-half life

Protein

https://theconversation.com/what-is-mrna-the-messenger-molecule-thats-been-in-every-living-cell-for-billions-of-years-is-the-key-ingredient-in-some-covid-19-vaccines-158511

Highlights the History of mRNA Vaccine

1961 mRNA discovered (>**60** years)
1965 Liposome
2001 Lipid nanoparticles



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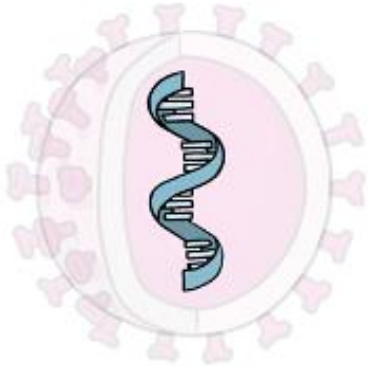
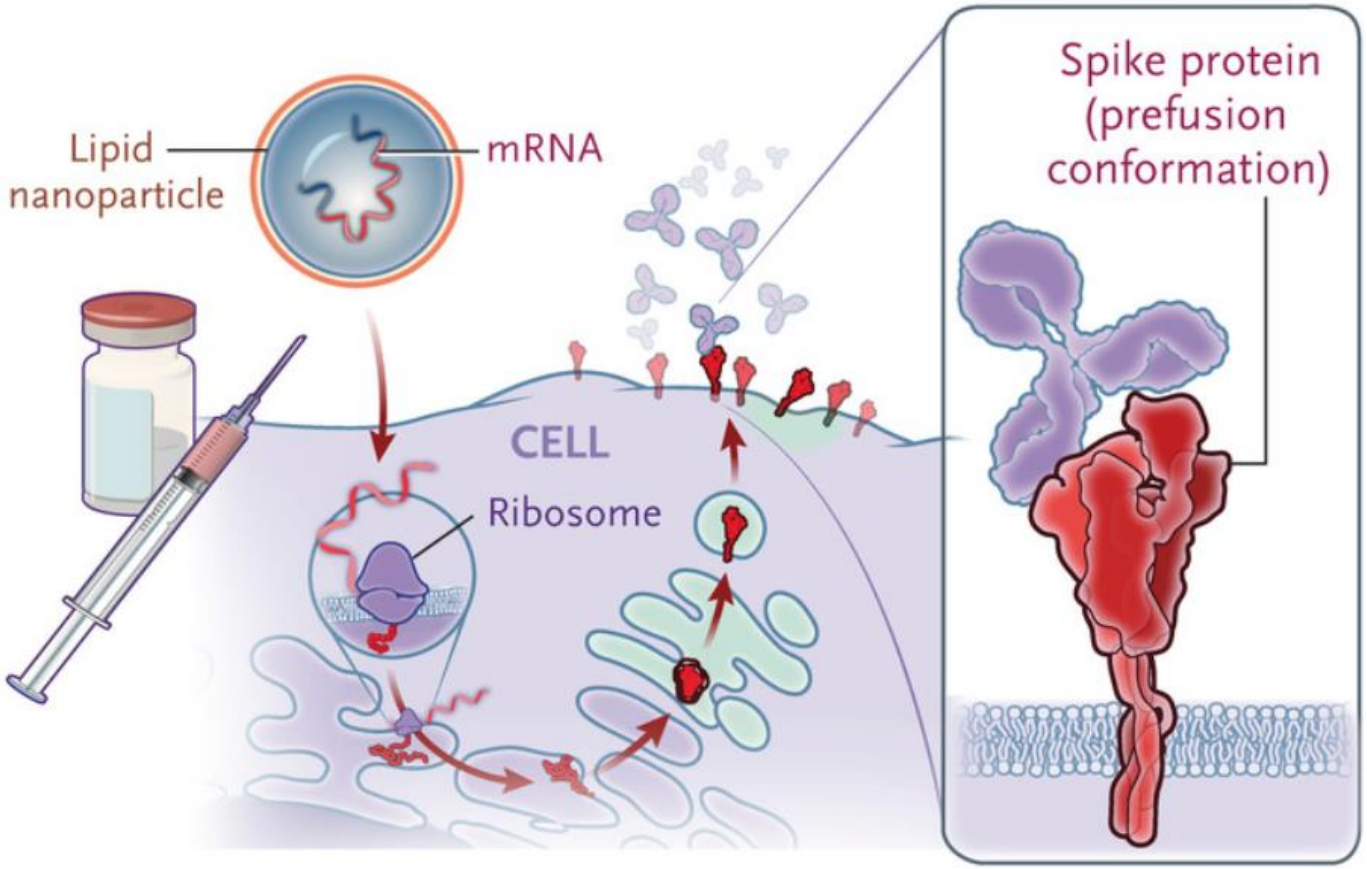
Adapted from Elie Dolgin. Nature | Vol 597 | 16 September 2021

COVID-19 mRNA Vaccine



mRNA

not the whole virus

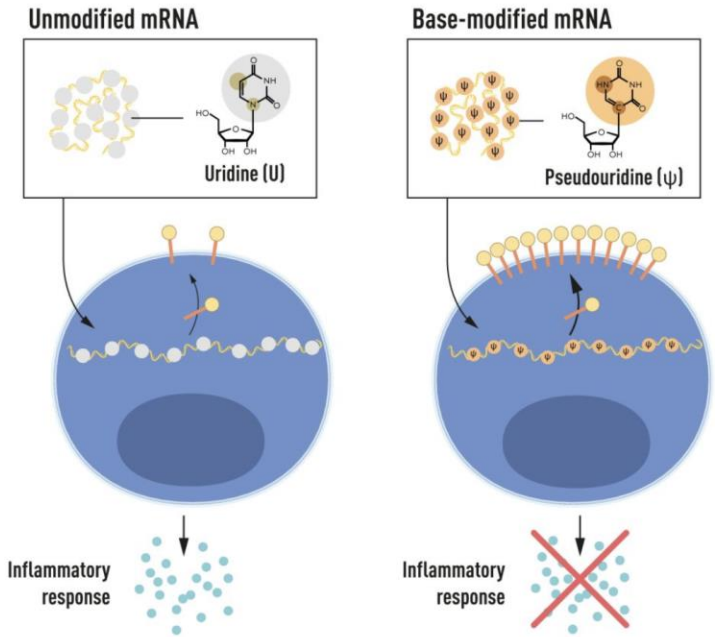


1. mRNA vaccine in general will be eliminated within few days
2. No entering to the nucleus

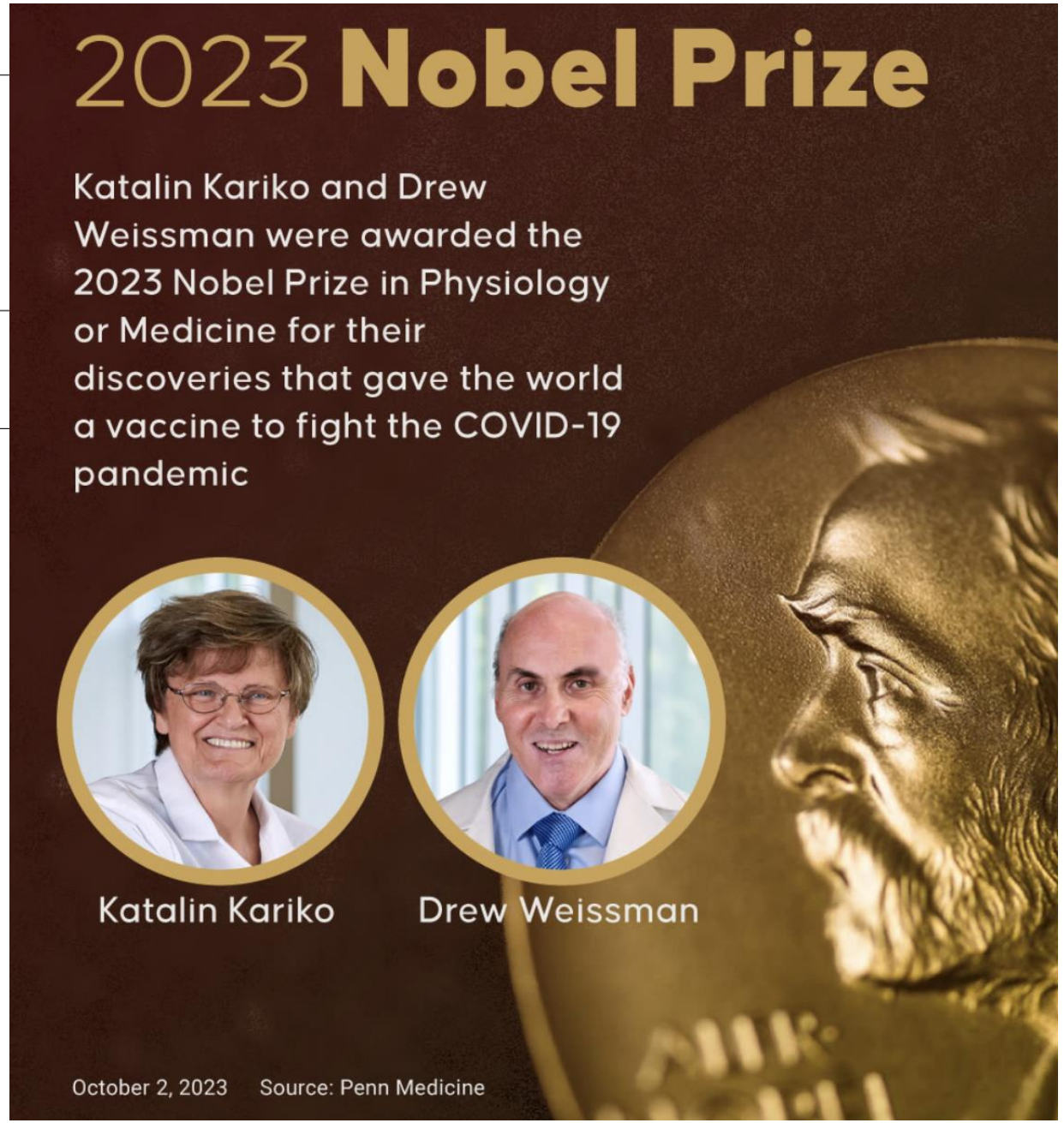
Polack et al. N Engl J Med 2020; 383:2603-2615

PIONEERS OF MRNA COVID VACCINES WIN MEDICINE NOBEL

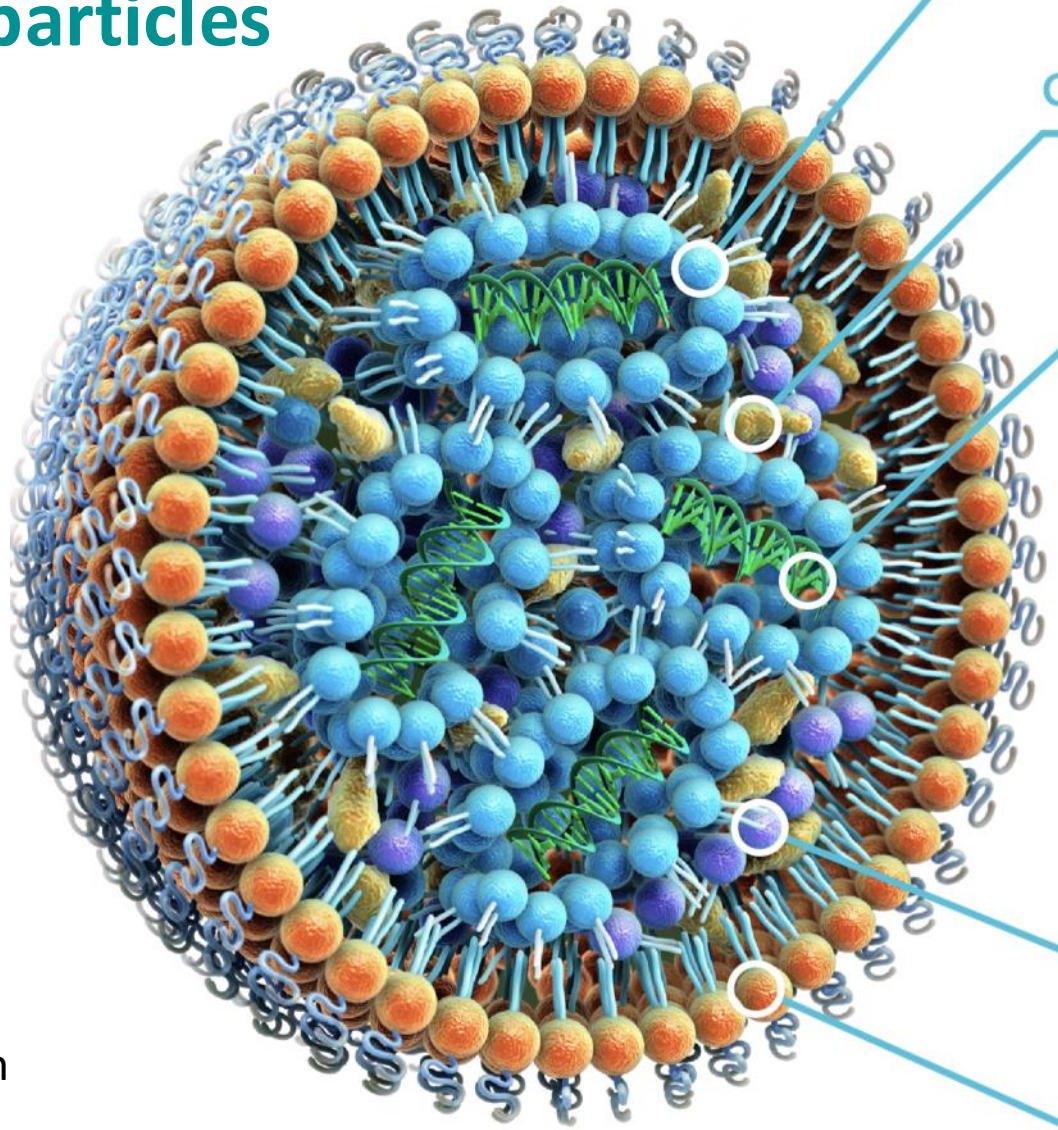
Molecular tweak laid the groundwork for jabs that have saved millions of lives.



The Nobel Committee for Physiology or Medicine. Ill. Mattias Karlén



mRNA-LNP
Lipid Nanoparticles



1 Ionizable lipid

2 Cholesterol

mRNA

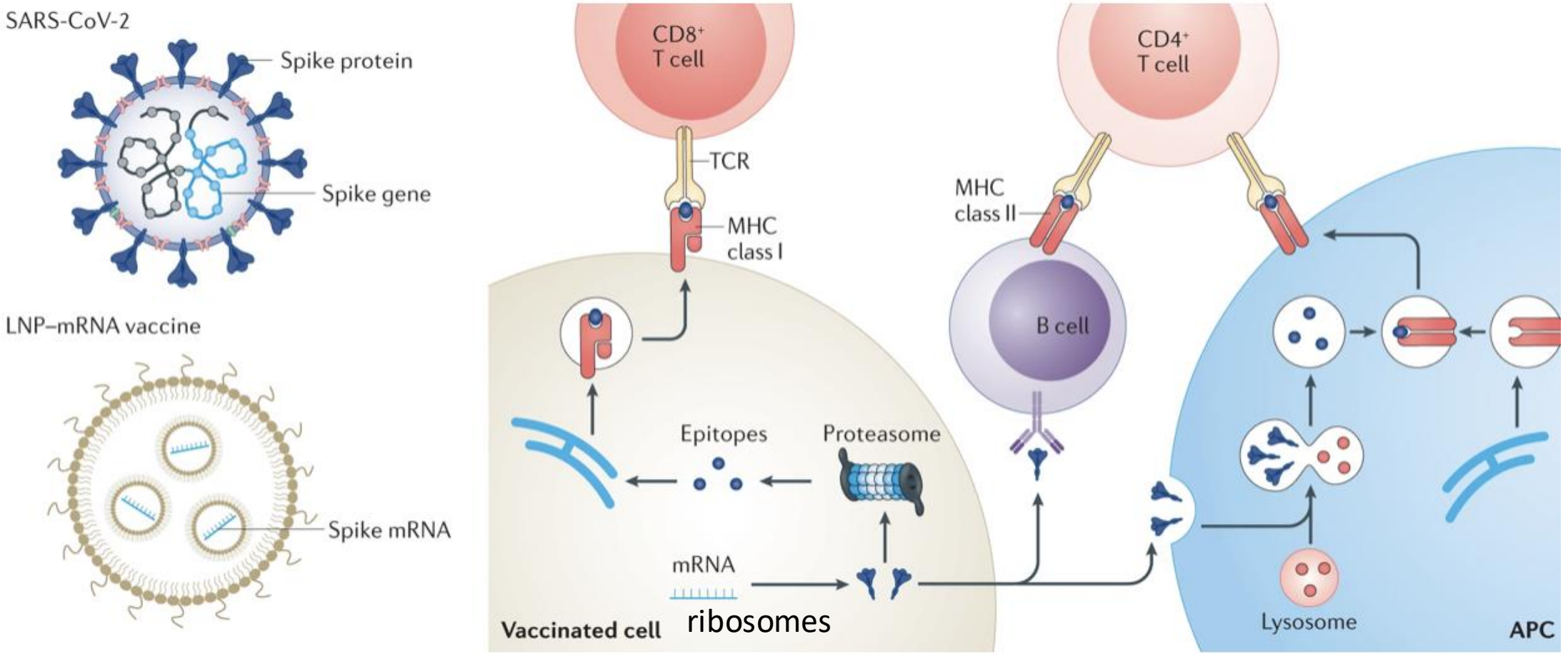
Encapsulated mRNA

3 Phospholipid

4 Pegylated Lipid (PEG)

PrecisionNanosystem

How mRNA Vaccine induces Cellular and humoral immune responses



Hou et al. Nature Reviews Materials (*Nat Rev Mater*) ISSN 2058-8437 (online)

Pros and Cons of mRNA Vaccine

PROS

- Rapid design and development
- Induces high neutralizing antibody
- Induced strong T-cell responses Th1>Th2
- Scalable in a smaller manufacture
- Proven of the highest vaccine efficacy against Covid-19
- Potentially low cost in long-term
- May be a personalizable vaccine or therapy
- >6 Billions of 13.6 Billion doses have been given Worldwide since 2020

CONS

- **Can not produce non-protein antigenic vaccine** : Polysaccharides
- **Needs low temperature cold-chain storing**
  - Some mRNA/LNP vaccine is stable up to 6 months at 2-8 ^{0} C
  - Lyophillizaion can solve this problem
  - **Note**: saRNA with different lipid may be stable >2 yrs at 4-8^{o} C
- **Rare myocarditis AEs concern**
  - 10-20 of 1,000,000 injections
  - **Note:** This may not be a mRNA-specific AEs, as based on a 99 million vaccinees cohort from 8 countries: **Novavax** (protein vaccine) has also shown O/E ratio of >1.5 at various doses up to Dose 4

COVID-19 Vaccine **Efficacy** –

Primary Vaccination - Phase 3 Results

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Vaccine (Company)	Sample Size	Prevent Clinical Covid-19	Preventing Severe Covid-19
CoronaVac (Sinovac) Brazil	12,396	51 %	100 %
AZD122 (AstraZeneca)	17,177	67 %	100 %
Ad26.COV2.S (J & J)	43,783	66 %	85%
NVX-CoV2373 (Novavax)	15,000	89 %	100 %
mRNA-1273 (Moderna)	28,207	94 %	100 %
BNT162b2 (Pfizer)	34,922	95 %	90 %

Modified from Abdool Karim SS, et al NEJM March 24, 2021

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mRNA Vaccine Platforms

Modified Nucleoside mRNA

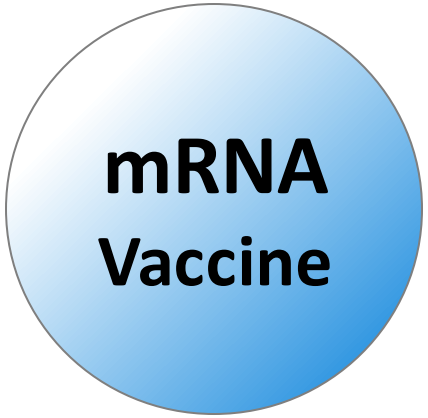
Approved for

Covid-19 Vaccines

- Comirnaty, Pfizer/BNT
- SPIKEVAX, Moderna

RSV Vaccine

- MRESVIA, Moderna



Self-amplifying RNA (saRNA)

Approved for **Covid-19**

- Arturus –Japan
- Gennova -India

Circular RNA (circRNA)

No approved vaccine

Near Future Approval of mRNA Vaccines

Influenza

Phase 3: N=6,000, Moderna –Aug 2023, N=25,000, Pfizer/BNT

Current approved Flu vaccine : Vaccine Efficacy 40-60%

CMV

Phase 3 n=6,900, Moderna

Self-amplifying mRNA Covid Vaccine

The Indian EXPRESS
JOURNALISM OF COURAGE

News / Health And Wellness / India's first mRNA-based Omicron-specific booster vaccine approved

Premium

India's first mRNA-based Omicron-specific booster vaccine approved

Pune's Gennova Biopharmaceuticals gets DCGI approval for its vaccine GEMCOVAC-OM. 'It has demonstrated robust immune responses in phase 3 clinical trials conducted at 20 centres across 13 cities in India. The vaccine is safe and well tolerated and could prevent future waves of the pandemic,' says Dr Sanjay Singh, CEO of the Pune-based Gennova Biopharmaceuticals Ltd

Self-amplifying mRNA Covid-19 Vaccine (saRNA): Gennova

- Low dose 10 ug booster
- Intradermal injection
- Stable at 4-8 °C for ~ 2 years

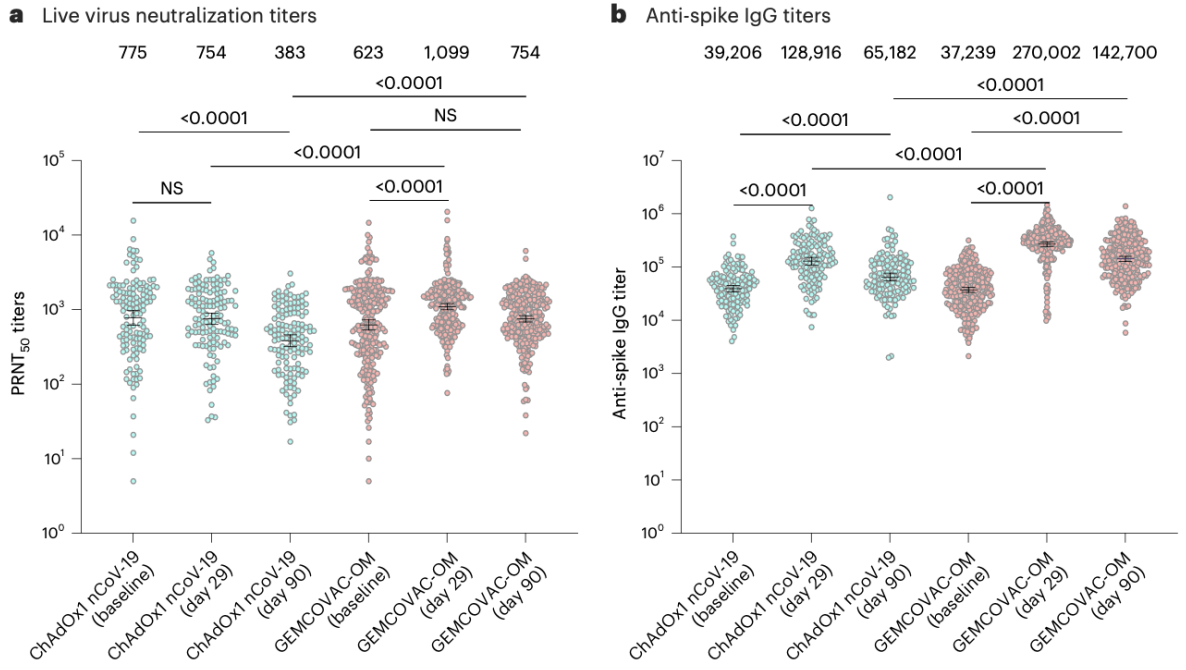
An Omicron-specific, self-amplifying mRNA booster vaccine for COVID-19: a phase 2/3 randomized trial

Amit Saraf, Rohan Gurjar, Swarnendu Kaviraj, Aishwarya Kulkarni, Durgesh Kumar, Ruta Kulkarni, Rashmi Virkar, Jayashri Krishnan, Anjali Yadav, Ekta Baranwal, Ajay Singh, Arjun Raghuwanshi, Praveen Agarwal, Laxman Savergave, Sanjay Singh ✉ & the GEMCOVAC-OM Study Investigators

Nature Medicine **30**, 1363–1372 (2024) | Cite this article

Article https://doi.org/10.1038/s41591-024-02955-2

Gennova –saRNA > Chadox1

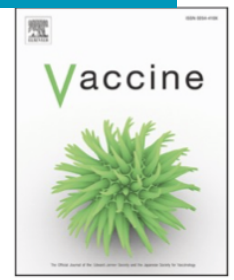


COVID-19 Vaccines – a Multi-countries -Large Scale Cohort Study

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine



GVDN Study
99 Million
Vaccinated
Individuals
8 countries

COVID-19 vaccines and adverse events of special interest: A multinational Global Vaccine Data Network (GVDN) cohort study of 99 million vaccinated individuals

K. Faksova [a,*], D. Walsh [b,c], Y. Jiang [b,c], J. Griffin [c], A. Phillips [d], A. Gentile [e], J.C. Kwong [f,g,h], K. Macartney [d,i], M. Naus [j,n], Z. Grange [k], S. Escolano [l], G. Sepulveda [m], A. Shetty [m], A. Pillsbury [d], C. Sullivan [k], Z. Naveed [j,n], N.Z. Janjua [j,n], N. Giglio [e], J. Perälä [o], S. Nasreen [f,p,x], H. Gidding [d,i], P. Hovi [q], T. Vo [r], F. Cui [s], L. Deng [d], L. Cullen [k], M. Artama [r], H. Lu [b,c], H.J. Clothier [c,m], K. Batty [t], J. Paynter [u], H. Petousis-Harris [c,u], J. Buttery [c,m,v], S. Black [c,u], A. Hviid [a,w]

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[b] *Department of Statistics, University of Auckland, New Zealand*
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[d] *National Centre for Immunisation Research and Surveillance, Westmead, New South Wales, Australia*
[e] *Department of Epidemiology, Ricardo Gutierrez Children Hospital, Buenos Aires University, Argentina*
[f] *ICES, Toronto, Ontario, Canada*
[g] *Public Health Ontario, Toronto, Ontario, Canada*
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K. Faksova et al., Vaccine, https://doi.org/10.1016/j.vaccine.2024.01.100

Supplementary Table 13: All aggregated OE Ratios by last dose, cardiovascular conditions, period 0–42 days, PYRS≥1000, no censoring on observed counts

		MYO		PER	
Dose	Vaccine	OE_Ratio	CI	OE_Ratio	CI
1	AZD	1.36	(1.08,1.68)	1.29	(1.15,1.44)
	BNT	2.78	(2.61,2.95)	1.54	(1.47,1.62)
	MOD	3.48	(3.00,4.01)	1.74	(1.54,1.97)
Dose 1	BIBNT	20.99	(0.53,116.94)	0	
	NVX	20.18	(0.51,112.44)	13.73	(2.83,40.12)
	PBNT	10.41	(4.18,21.44)	1.22	(0.03,6.82)
	BIBP	0		0	
	VGM	0		0	
	JJJ	1.64	(0.87,2.80)	0.81	(0.54,1.18)
	SINO	0		0	
	HMOD	0		0	
2	AZD	1.31	(1.01,1.68)	1.27	(1.12,1.43)
	BNT	2.86	(2.70,3.03)	1.38	(1.32,1.45)
	MOD	6.10	(5.52,6.72)	1.67	(1.50,1.85)
Dose 2	BIBNT	0		0	
	NVX	39.26	(0.99,218.74)	33.99	(4.12,122.78)
	PBNT	8.98	(2.45,22.98)	4.54	(0.94,13.26)
	BIBP	0		0	
	VGM	0		0	
	SINO	0		0	
3	AZD	0		6.91	(3.45,12.36)
	BNT	2.09	(1.88,2.32)	1.19	(1.10,1.28)
	MOD	2.01	(1.60,2.49)	1.39	(1.20,1.59)
Dose 3	BIBNT	0		1.21	(0.03,6.77)
	BIMODO	0		3.00	(0.36,10.85)
	NVX	0		9.72	(2.01,28.42)
	PBNT	0		12.42	(0.31,69.22)
	HMOD	1.80	(0.49,4.61)	0.64	(0.21,1.49)
4	AZD	66.79	(8.09,241.26)	53.41	(14.55,136.75)
	BNT	2.06	(1.47,2.80)	1.55	(1.30,1.83)
Dose 4	MOD	2.91	(1.45,5.21)	2.64	(2.05,3.35)
	BIBNT	1.45	(0.47,3.37)	0.98	(0.56,1.59)
	BIMODO	2.28	(0.92,4.70)	1.63	(1.03,2.45)
	NVX	0		49.87	(6.04,180.15)
5	BNT	11.27	(0.29,62.82)	9.39	(4.29,17.82)
Dose 5	MOD	25.83	(0.65,143.92)	4.14	(0.10,23.06)
	BIBNT	1.73	(0.56,4.04)	2.02	(1.45,2.75)
	BIMODO	2.31	(0.63,5.92)	1.85	(1.19,2.72)
6	BNT	0		41.43	(1.05,230.85)
Dose 6	BIBNT	3.59	(0.09,20.02)	2.35	(0.86,5.11)
	BIMODO	0		0.61	(0.02,3.40)
7	BIBNT	0		0	

AESI: MYO= Myocarditis, PER= Pericarditis

Pfizer/BNT
Moderna
Novavax
Pfizer

Pfizer/BNT
Moderna
Novavax

Astrazeneca
Pfizer/BNT
Moderna
Novavax

Astrazeneca
Moderna

Novavax
Pfizer/BNt

Vaccine abbreviations:

Carditis-OE risk >1.5 AE Special Interest (AESI)

Code	Vaccine brand
AZD	Covishield or Vaxzevria [AstraZeneca or Serum Institute of India]
BNT	Comirnaty or Tozinameran [Pfizer/BioNTech or Fosun-BioNTech]
MOD	Elasomeran or Spikevax or TAK-919 [Moderna or Takeda]
BIBNT	Comirnaty or Riltozinameran or Pfizer/BioNTech COVID-19 Vaccine Bivalent [Pfizer/BioNTech]
NVX	Covovax or Nuvaxoid [Novavax or Serum Institute of India]
PBNT	Comirnaty or Tozinameran Paediatric [Pfizer/BioNTech or Fosun-BioNTech]
BIBP	Covilo or SARS-CoV-2 Vaccine (Vero Cell) [Sinopharm (Beijing)]
VGM	Sputnik V [Gamaleya Research Institute]
JJJ	Janssen [Janssen/Johnson & Johnson]
SINO	CoronaVac or Sinovac [Sinovac Biotech]
HMOD	Elasomeran or Spikevax or TAK-919 Half Dose [Moderna or Takeda]
BIMODO	Spikevax bivalent Original/Omicron [Moderna]

Thresholds for statistical indications of potential signals:

Red: LBCI* >1.5, statistically significant safety signal

Yellow: LBCI* >1 and ≤1.5, statistically significant

Green: LBCI* ≤1.0, not statistically significant

*LBCI: Lower bound of confidence interval

Conditions applied to the analysis of aggregated OE ratios:

- PYRS ≥1000
- No censoring on observed counts

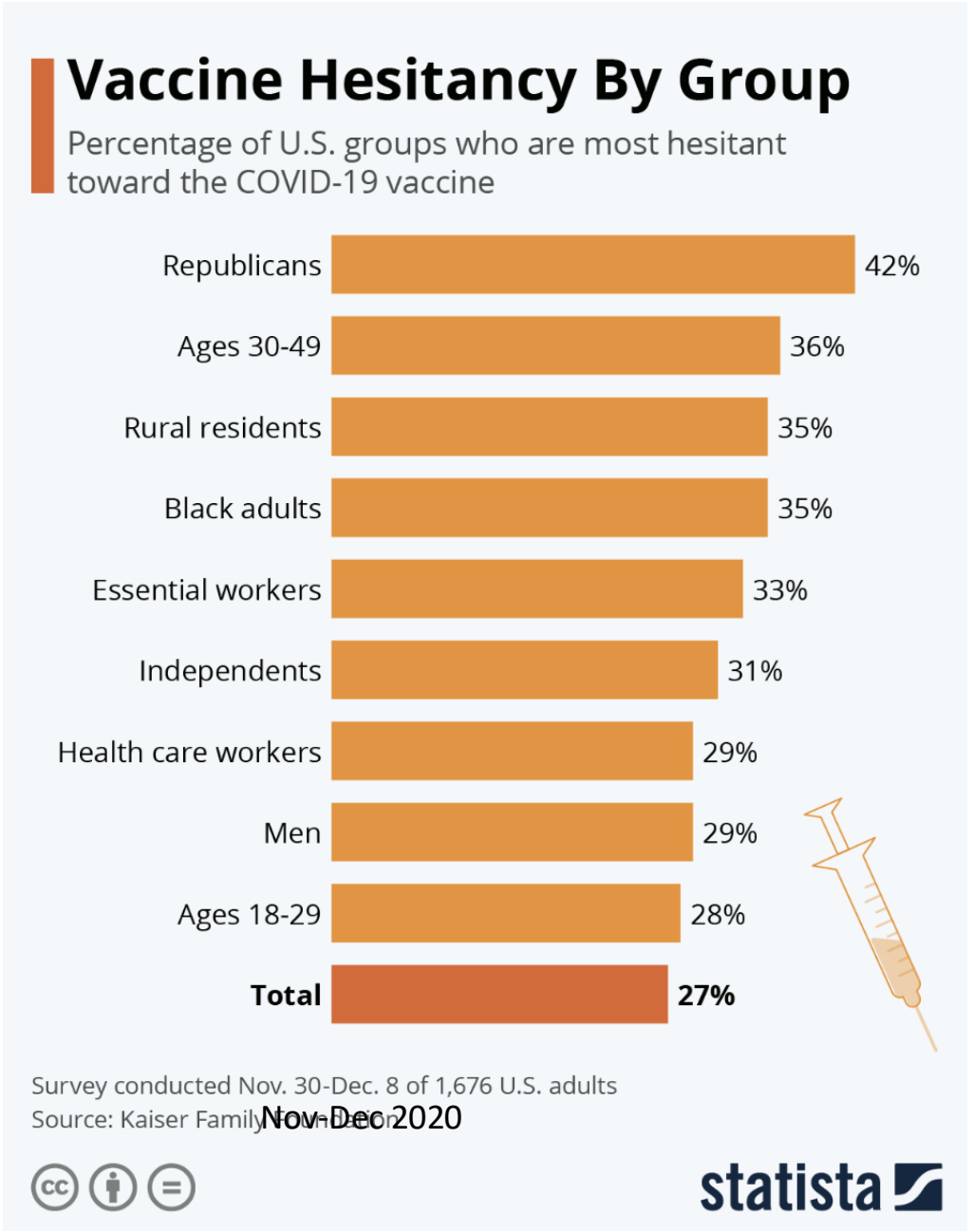
K. Faksova et al., Vaccine, https://doi.org/10.1016/j.vaccine.2024.01.100

VACCINE HESITANCY Global Average **20%** Hesitant

Lazarus. Nature Med 2023

	Vaccine		% change in acceptance	
	% hesitant	% acceptance	2020 to 2022	2021 to 2022
Global average	20.9	79.1	↑ 10.9	↑ 5.2
United States	19.8	80.2	↑ 6.4	↑ 20.4
United Kingdom	19.6	80.4	↑ 12.4	↓ −1.0
Turkey	28.0	72.0	N/A	↓ −2.7
Sweden	20.8	79.2	↑ 21.5	↑ 2.6
Spain	10.1	89.9	↑ 21.0	↑ 4.2
Singapore	7.5	92.5	↑ 36.2	↑ 12.3
South Korea	10.8	89.2	↑ 11.8	↑ 8.4
South Africa	52.1	47.9	↓ −41.3	↓ −21.1
Russia	39.2	60.8	↑ 10.7	↑ 17.8
Poland	35.9	64.1	↑ 13.9	↑ 8.1
Peru	10.4	89.6	N/A	↑ 2.6
Nigeria	28.1	71.9	↑ 10.3	↑ 26.1
Mexico	26.4	73.6	↓ −3.5	↓ −9.4
Kenya	31.2	68.8	N/A	↓ −8.5
Italy	15.4	84.6	↑ 19.5	↑ 6.3
India	1.7	98.3	↑ 31.9	↑ 26.0
Ghana	42.0	58.0	N/A	↓ −13.8
Germany	21.9	78.1	↑ 14.5	↑ 6.0
France	18.3	81.7	↑ 38.7	↑ 28.7
Ecuador	11.4	88.6	↑ 23.2	↑ 12.2
China	3.4	96.6	↑ 9.0	↓ −1.0
Canada	13.0	87.0	↑ 26.6	↑ 9.8
Brazil	12.8	87.2	↑ 2.1	↓ −3.3

Fig. 1 | COVID-19 vaccine acceptance and hesitancy in June 2022, percent change from 2020 and 2021. COVID-19 vaccine acceptance in June 2021 and June 2022 was defined as having received at least one dose of a COVID-19 vaccine and, if not, willingness to take the COVID-19 vaccine when it is available to them. Vaccine hesitancy was defined as having reported 'no' to the question



RSV Vaccine Development History

1956 RSV discovered (>**68** years)
1960's Disastrous clinical trials of inactivated vaccine (ADE phonomenon)
2023 Two subunit vaccines approved
2024 One mRNA vaccine approved

Discovered **RSV**

First Monoclonal antibody approved: palivizumab

2 RSV Subunit Vaccines Approved

RSV mRNA Vaccine Approved

4 disastrous clinical trials of **inactivated vaccines 80% children hospitalized**

ADE phenomenon

Discovery: ADE mechanism and **Virus-NAb binding prefusion F** structure

Ref: Tara Haelle. Scientific America, March 2023

Approved RSV Vaccines

GSK's Arexvy

Sub unit

3 May 2023

Monovalent
Pre-fusion protein F (A)
+ AS01E adjuvant

RSV Vaccine

Pfizer's Abrysvo

Sub unit

31 May 2023

Bivalent
RSV preF (A+B)
no adjuvant

Moderna's MRESVIA

RNA

31 May 2024

Monovalent
RSV preF (A)
mRNA/LNP

RSV Vaccine Efficacy in Older Adults 60+

GSK's Arexvy

+ adjuvant

Sub unit

94% VE Severe Diseases

86% VE Symptomatic Dis.

RSV Vaccine

Pfizer's Abrysvo

no adjvant

Sub unit

86% VE Severe Diseases

67% VE Symptomatic Dis.

Pregnant people

82 %severe RSV in newborns x 3 months

69 % x 6 months

Effectiveness –CDC 2023-2024:

- **AREXVY 77% to 83%**
- **ABRYSVO 73% to 79%**

in preventing RSV-**hospitalization** or **ER** visit in adults 60 and older.

Moderna's MRESVIA

RNA

80.9% VE Severe Diseases at 3.7 months

61 % VE Severe Dis. 8.6 months

RSV Vaccination in Older Adults: Metaanalysis

- Our analysis included five RCTs on five RSV vaccines (RSVpreF, RSVPreF3, Ad26.RSV.preF, MEDI7510, and mRNA-1345). The meta-analysis documented
  - **First RSV Season**: a pooled vaccine efficacy of **81.38%** (95% CI 70.94 - 88.06) for prevention of LRTD with three or more signs/symptoms.
  - **Second Season:** with a pooled VE of **61.15%** (95% CI 45.29 - 72.40)

In conclusion

- adult RSV vaccination was quite effective in preventing LRTD in older adults
- but the overall efficacy rapidly decreased in the second season after the delivery of the vaccine

Ricco M, et al. Vaccines 2024, 12(5), 500

RSV Vaccines –Reported Side Effects

mRNA vs Subunit with adjuvant

RSV mRNA Vaccine
MRESVIA, Moderna

Single dose at 50 ug

AEs reported in 60 yo+

- injection-site pain 55.9%
- Fever 2%
- Fatigue 30.8%
- Headache 26.7%
- Myalgia 25.6%
- Arthralgia 21.7%
- Chill 11.6%
- Axillary swelling or tenderness 15.2%

RSV subunit vaccine with adjuvant
GSK with AS01e

Single dose at 120 ug

AEs reported in individuals 60+

- Injection-site pain 60.9%
- Fever 2%
- Fatigue 33.6%
- Myalgia 28.9%
- Headache 27.2%
- Arthralgia 18.1%

Ref: Package Inserts of each product

RSV Vaccines –Reported Side Effects

mRNA vs Subunit w/o adjuvant

RSV mRNA Vaccine for 60+:
MRESVIA, Moderna

Single dose at 50 ug

AEs reported in 60 yo+

- injection-site pain 55.9%
- Fever 2%
- Fatigue 30.8%
- Headache 26.7%
- Myalgia 25.6%
- Arthralgia 21.7%
- Chill 11.6%
- Axillary swelling or tenderness 15.2%

Ref: Package Inserts of each product

RSV subunit Vaccine: for 60+, Pregnant women
ABRYSVO, Pfizer (divalent, no adjuvant !)

Single dose at 120 ug (60 ug each of RSV A and B pf-F protein)

AEs reported in 60 yo+

- Injection-site pain 10.5%
- Fever 1.4%
- Fatigue 15.5%,
- Headache 12.8%,
- Myalgia 10 %

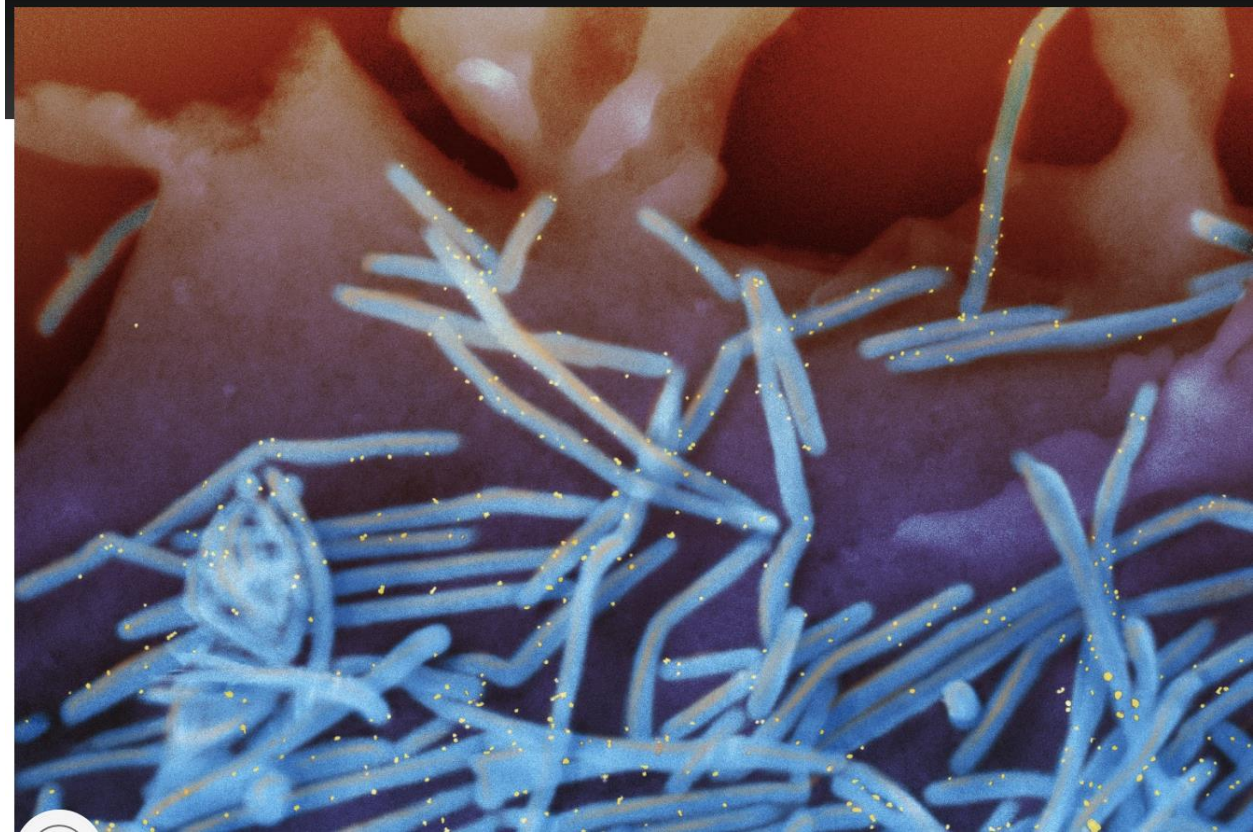
AEs reported in pregnant women

- Injection-site pain 40.6%
- Fever 2.6%
- Fatigue 15%
- Headache 31%
- Myalgia 26.5%
- Nausea 20%

AP

Live updates: Olympics | Donald Trump | Coco Gauff | Simone Biles | Venezuela election

Guillain-Barre syndrome 'more common than expected' with RSV vaccine in older people, CDC reiterates



CDC

Rare GBS Risk of RSV Subunit Vaccines

Morbidity and Mortality Weekly Report (*MMWR*)

Early Safety Findings Among Persons Aged ≥60 Years Who Received a Respiratory Syncytial Virus Vaccine — United States, May 3, 2023–April 14, 2024

Weekly / May 30, 2024 / 73(21);489–494

GBS Risk
4.4 /million Abrysvo
1.8/ million Arexvy

Summary

What is already known about this topic?

The Food and Drug Administration licensed Arexvy and Abrysvo vaccines in May 2023 for prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in adults aged ≥60 years. In trials, Guillain-Barré syndrome (GBS) was identified as a potential safety concern.

What is added by this report?

Findings are consistent with those from trials; reports of GBS (4.4 and 1.8 reports per million doses of Abrysvo and Arexvy vaccine administered,

CDC Recommendations

Adults ages 60 years and older

- CDC recommends an RSV vaccine for everyone ages 75 and older and adults ages 60-74 at increased risk of severe RSV.
- Adults 60-74 who are at increased risk include those with chronic heart or lung disease, certain other chronic medical conditions, and those who are residents of nursing homes or other long-term care facilities.
- RSV vaccine is not currently an annual vaccine, meaning older adults do not need to get a dose every RSV season. That means if you have already gotten an RSV vaccine, you do not need to get another one at this time.
- The best time to get vaccinated is in late summer and early fall — just before RSV usually starts to spread in the community.

Elderly: 75 y or older, 60=74 with clinical risk

Vaccines and Preventable Diseases

Infants and young children

To prevent severe RSV disease in infants, CDC recommends either maternal RSV vaccination or infant immunization with RSV monoclonal antibodies. Most infants will not need both.

Vaccination for pregnant people

- 1 dose of maternal RSV vaccine during weeks 32 through 36 of pregnancy, administered September through January. Pfizer Abrysvo is the only RSV vaccine recommended during pregnancy.

Immunization for infants and young children

- 1 dose of the monoclonal antibody product, nirsevimab, for all infants aged 8 months and younger born during or entering their first RSV season.
- 1 dose of nirsevimab for infants and children aged 8–19 months who are at increased risk for severe RSV disease and entering their second RSV season.
- *Note:* A different monoclonal antibody, palivizumab, is limited to children aged 24 months and younger with certain conditions that place them at high risk for severe RSV disease. It must be given once a month during RSV season. Please see AAP guidelines for palivizumab.

Pregnant women: at 32-36 weeks


ChulaVRC for Vaccine Equity

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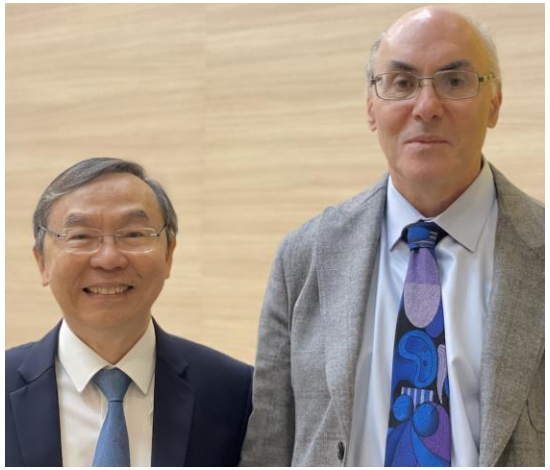
Chula Vaccine Research Center
Faculty of Medicine, Chulalongkorn University



Prof. Drew Weissman, M.D., Ph.D.

The Perelman School of Medicine
University of Pennsylvania

He is a mRNA Pioneer

We started collaborating since **2017**

"[Kiat] worried that any vaccine developed in the West wouldn't be available in Thailand and surrounding low-income countries for years," Weissman said. When Ruxrungtham told him the plan to produce the vaccine for distribution to countries that wouldn't be able to buy one themselves, he said, "that sounded like a beautiful goal."

Forbes

CORONAVIRUS | Dec 9, 2020, 06:00am EST | 3,269 views

This Thai Researcher Aims To Make His Country A Covid-19 Vaccine Powerhouse

Caroline Seydel Contributor ⓘ
Health
I write about advances in genetics and biotechnology

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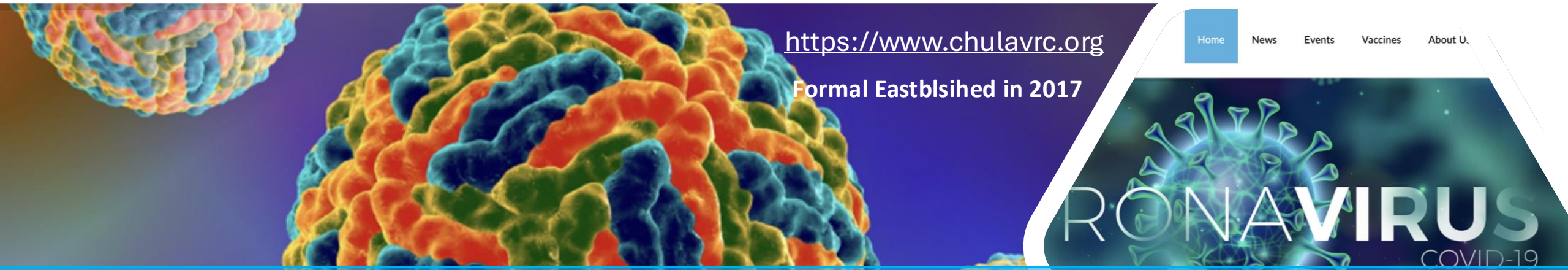
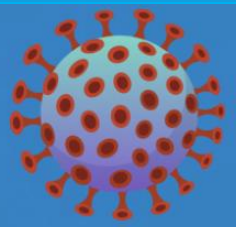
Home | News | Events | Vaccine

https://www.chulavrc.org

Formal Eastblsihed in 2017



Making mRNA Vaccines Accessible in LMICs

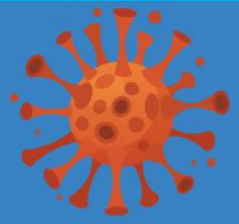


COVID-19

Development of COVID-19 vaccine

Dengue

Development of nanoparticle-based dengue DNA vaccine



HIV

We have been working on HIV DNA vaccine

HDM Allergy

Development of vaccines for prevention and treatment of HDM allergy

Leptospirosis

Development of subunit vaccines against leptospirosis

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The First COVID-19 mRNA Vaccine Produced in Thailand entered Phase 2 Clinical Trials in Thailand and Australia

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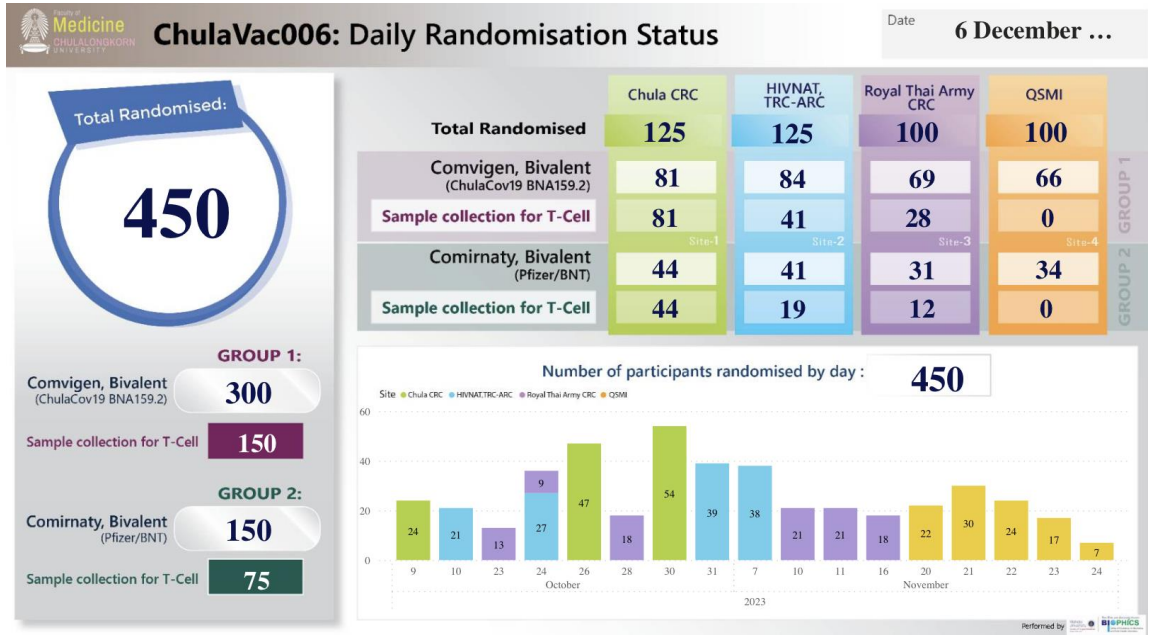
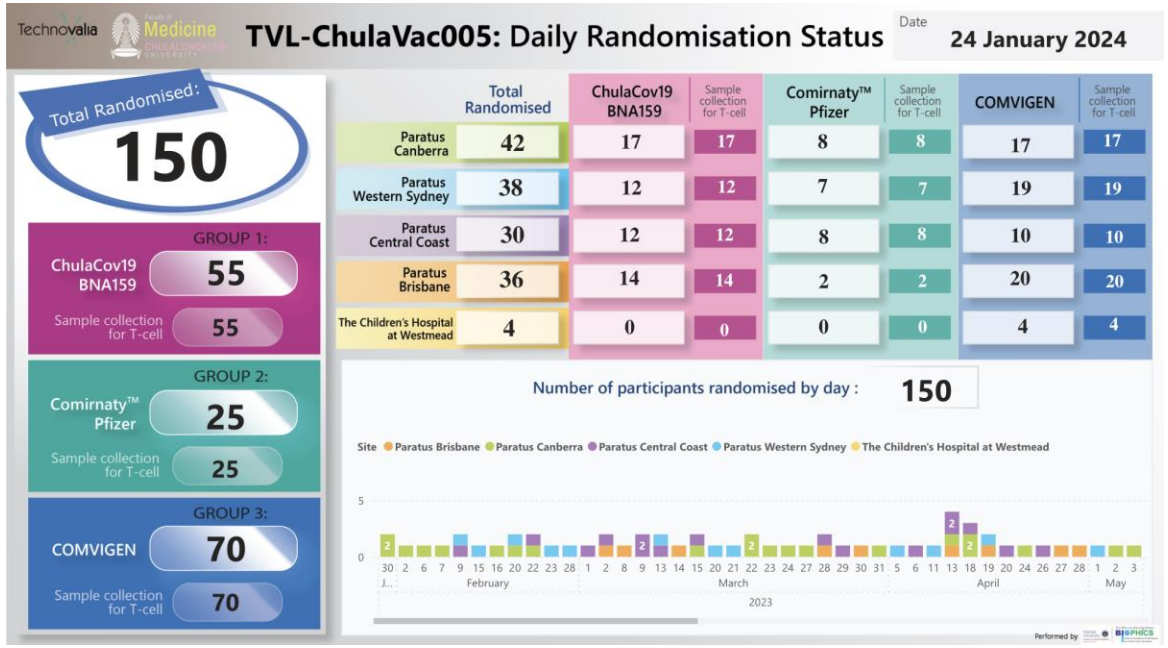
Faculty of Medicine, Chulalongkorn University

Phase 2 Trials of Thai-made ChulaCov19 Bivalent Vaccine COMVIGEN in Thailand and Australia

THAILAND: Booster 450 subjects



AUSTRALIA: Booster 150 subjects



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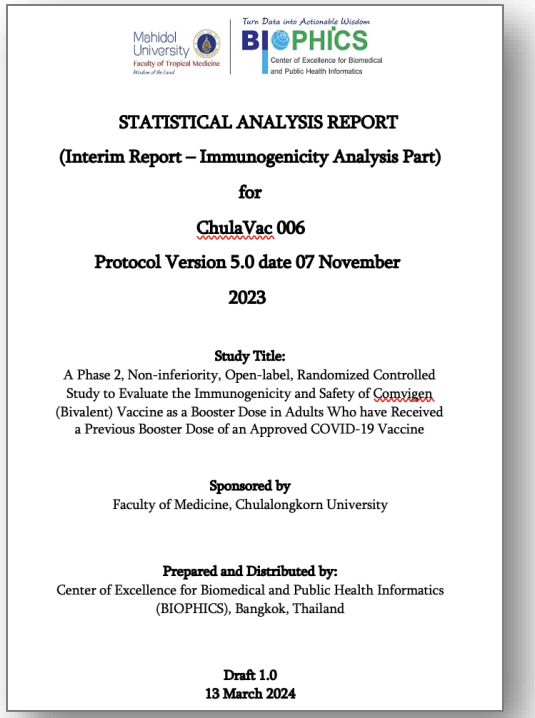
ChulaCov19 “COMVIGEN”: Anti-RBD IgG Titers (mITT)



Mahidol University Faculty of Tropical Medicine
Turn Data into Actionable Wisdom
BIOPHICS Center of Excellence for Biomedical and Public Health Informatics

STATISTICAL ANALYSIS REPORT

(Interim Report – Immunogenicity Analysis Part)

for

ChulaVac 006

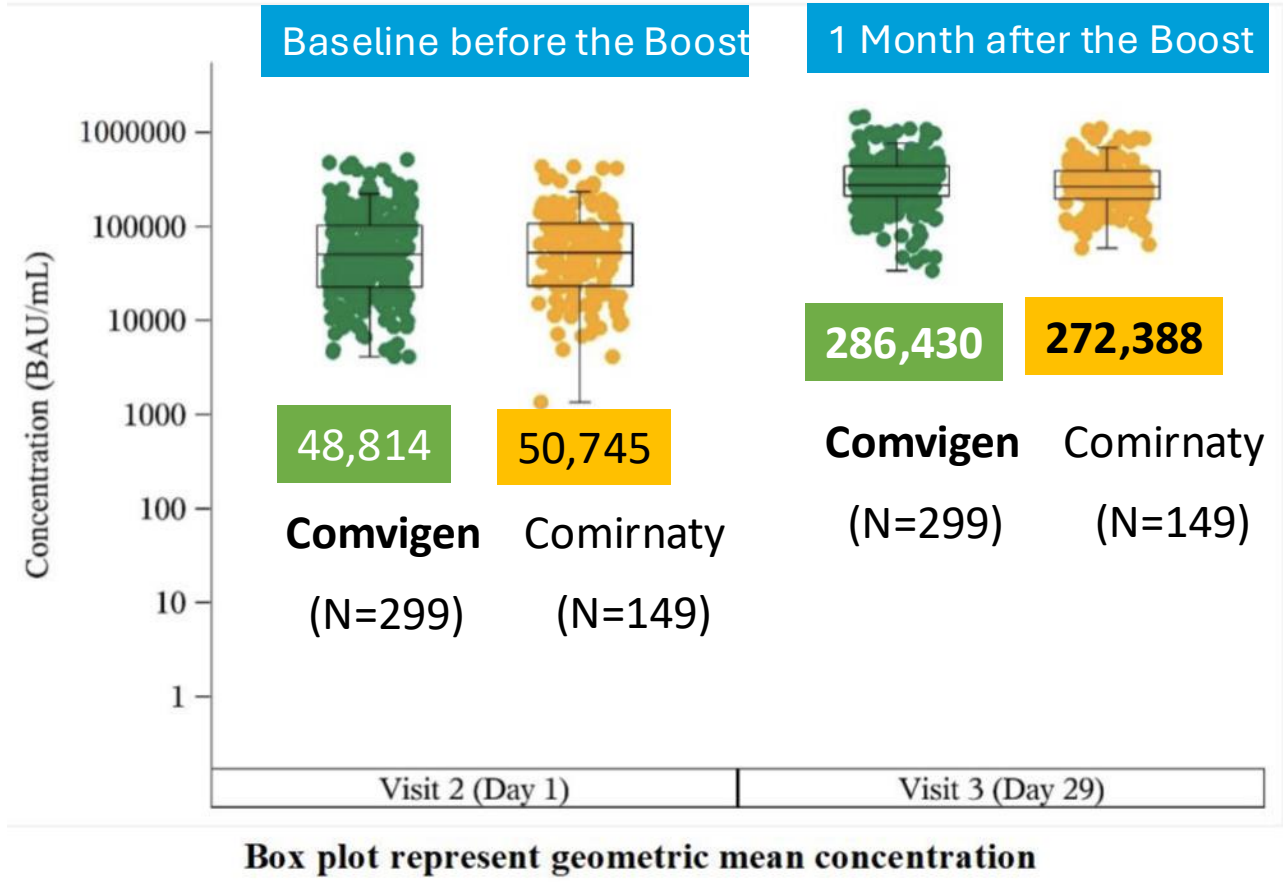
Protocol Version 5.0 date 07 November 2023

Study Title:
A Phase 2, Non-inferiority, Open-label, Randomized Controlled Study to Evaluate the Immunogenicity and Safety of Comvigen (Bivalent) Vaccine as a Booster Dose in Adults Who have Received a Previous Booster Dose of an Approved COVID-19 Vaccine

Sponsored by
Faculty of Medicine, Chulalongkorn University

Prepared and Distributed by:
Center of Excellence for Biomedical and Public Health Informatics (BIOPHICS), Bangkok, Thailand

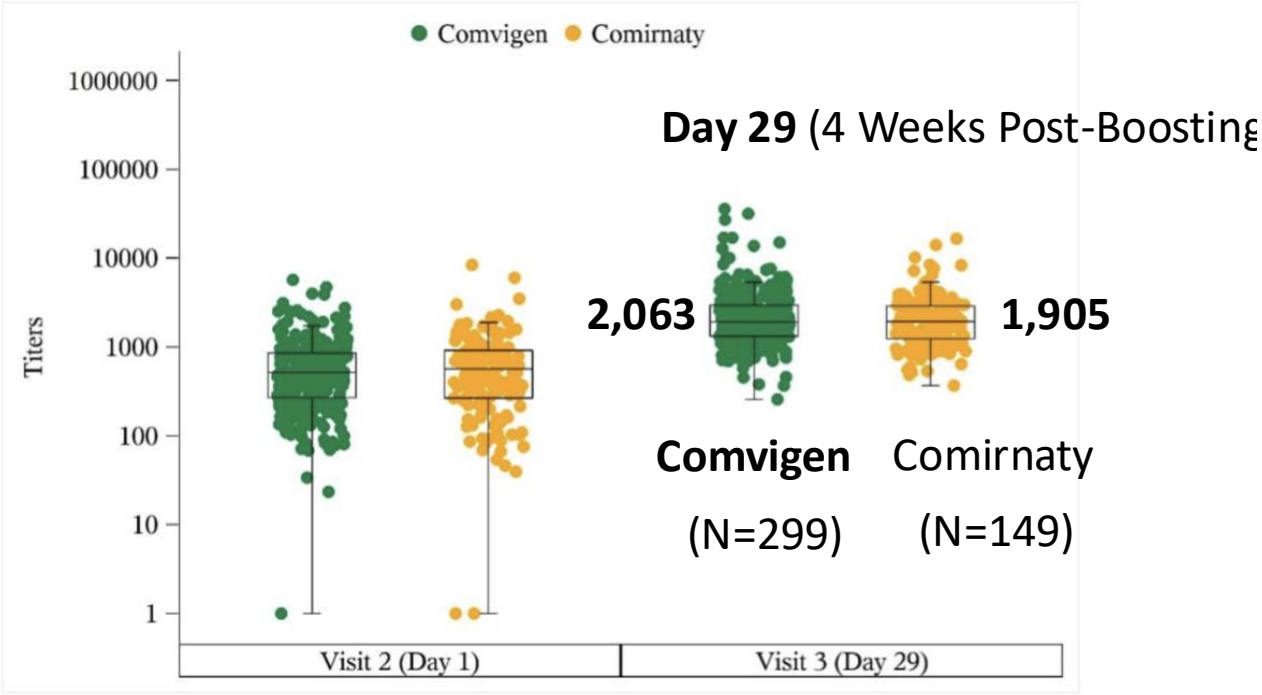
Draft 1.0
13 March 2024



Box plot represent geometric mean concentration

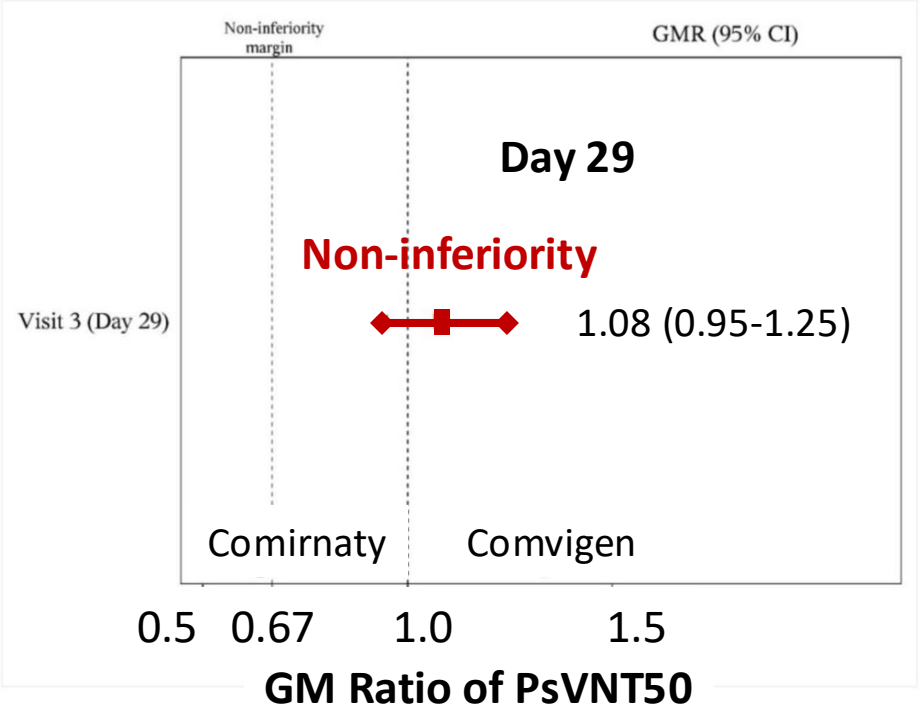
PsVNT50- against SARS-COV-2 Wild-type Results in mITT Population

Figure 5: Geometric Mean Titer (GMT), Geometric Mean Fold Rise of SARS-CoV-2 Pseudovirus Neutralization Test with 50% Inhibition Titer (psVNT50) against Wild Type Virus (WT) in Modified Intent-to-Treat (mITT) Population / Per Protocol Population

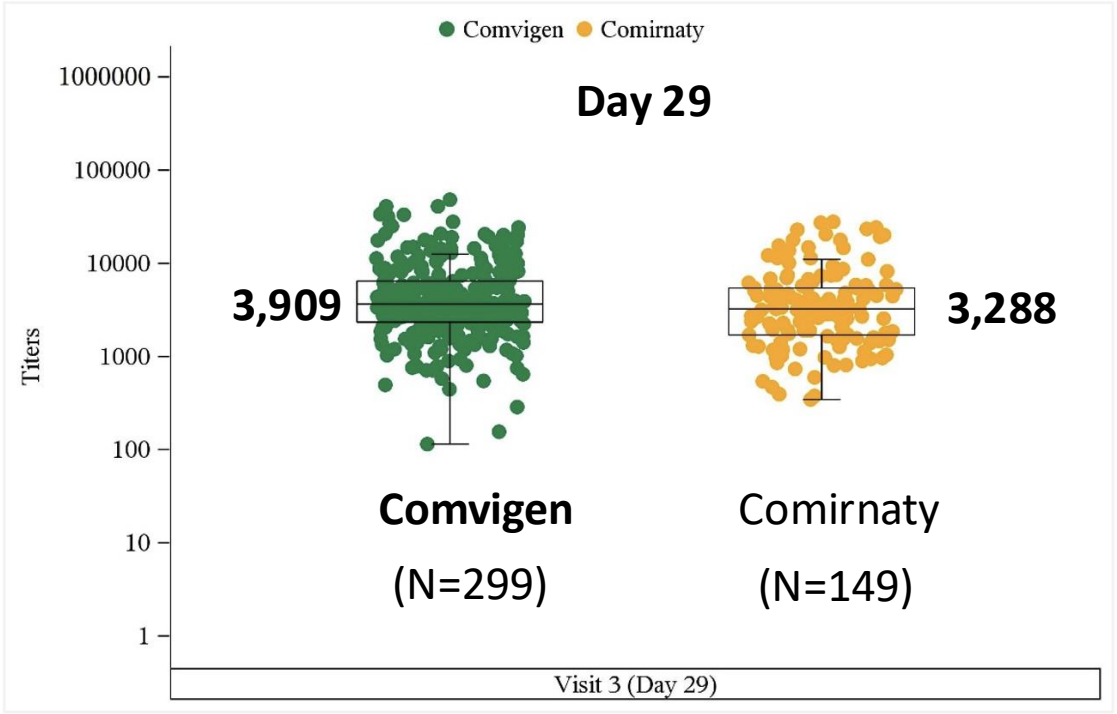


Box plot represent geometric mean titer

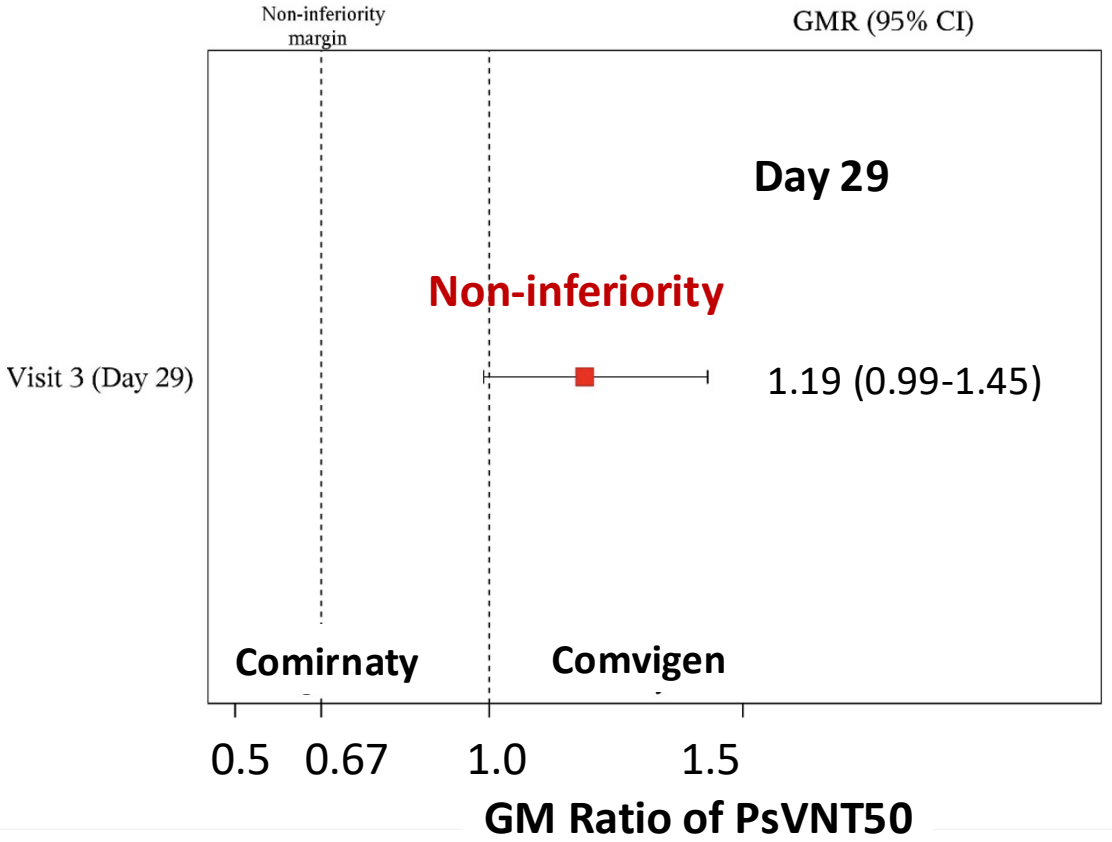
Figure 7: Non-Inferiority Test of Geometric Mean Ratio (GMR) of SARS-CoV-2 Pseudovirus Neutralization Test with 50% Inhibition Titer (psVNT50) against Wild Type Virus (WT) in Modified Intent-to-Treat (mITT) Population / Per Protocol Population



PsVNT50- against Omicron BA.4/.5 Results : mITT



Box plot represent geometric mean titer



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ChulaVRC

Current and Future Capacity

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Faculty of Medicine, Chulalongkorn University

School of Global Health
Faculty of Medicine
Chulalongkorn University

ChulaVRC: R&D Pipelines

For "**Vaccine Inequity Issue**" and **Pandemic Preparedness**

ChulaVRC Initiated Vaccine

Promising in mice
- Dengue vaccine
- HPV Tx vaccine
- Allergy vaccine

In Development
- Leptospirosis
- Avian Flu
- TB
- AMR

Seeking Partner for Phase1 HPV Tx and Allergy vaccine –do have a potential private partner to prusue

Partners Initiated Vaccine

In Animal Testing
- P. *vivax*

In Development
- HFMD
- TB

Major Funder: NVI
Others: Donation Fund and UK-SEA Vax Hub

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ChulaVRC- Joining the Global Network for Vaccine Equity

One of the 4 target vaccines leader

World Health Organization

Vaccine R&D Network

The Co-PI of the new UK-SEA Vax Hub

UK-SEA Vax Hub

U Sheffield –Chula U

South-East Asia Vaccine Manufacturing Research HUB

ChulaVRC

Global Network

for Vaccine Equity

WHO: 4 Diseases Targeted mRNA Vaccines

1. **Dengue vaccine**: ChulaVRC initiative, IVI leads the network
2. **HPV therapeutic vaccine**: ChulaVRC leads
3. **Malaria Vivax**: Trop Med, MU leads, ChulaVRC has made the vaccines for testing
4. **HFMD**: NUS Singapore leads, ChulaVRC will design and make the vaccines for preclinical testing

ChulaVRC Capacity on Vaccine Development: Current and Future

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Faculty of Medicine, Chulalongkorn University

Design & Research Grade Production

Pre-clinical Studies

Clinical Development

Current

1 **Design**
ChulaVRC

2 **DNA**
Outsource

3 **mRNA**
ChulaVRC

4 **LNP**
Encapsulation
In vitro tests
ChulaVRC

5

ChulaVRC
MDCU

7

Chula
NPRC

cGMP

Current:
Outsource
BNA, Thailand

Clinical

Chula-CRC
+ Multicenter
Phase 1-3

Future
Chula GMP

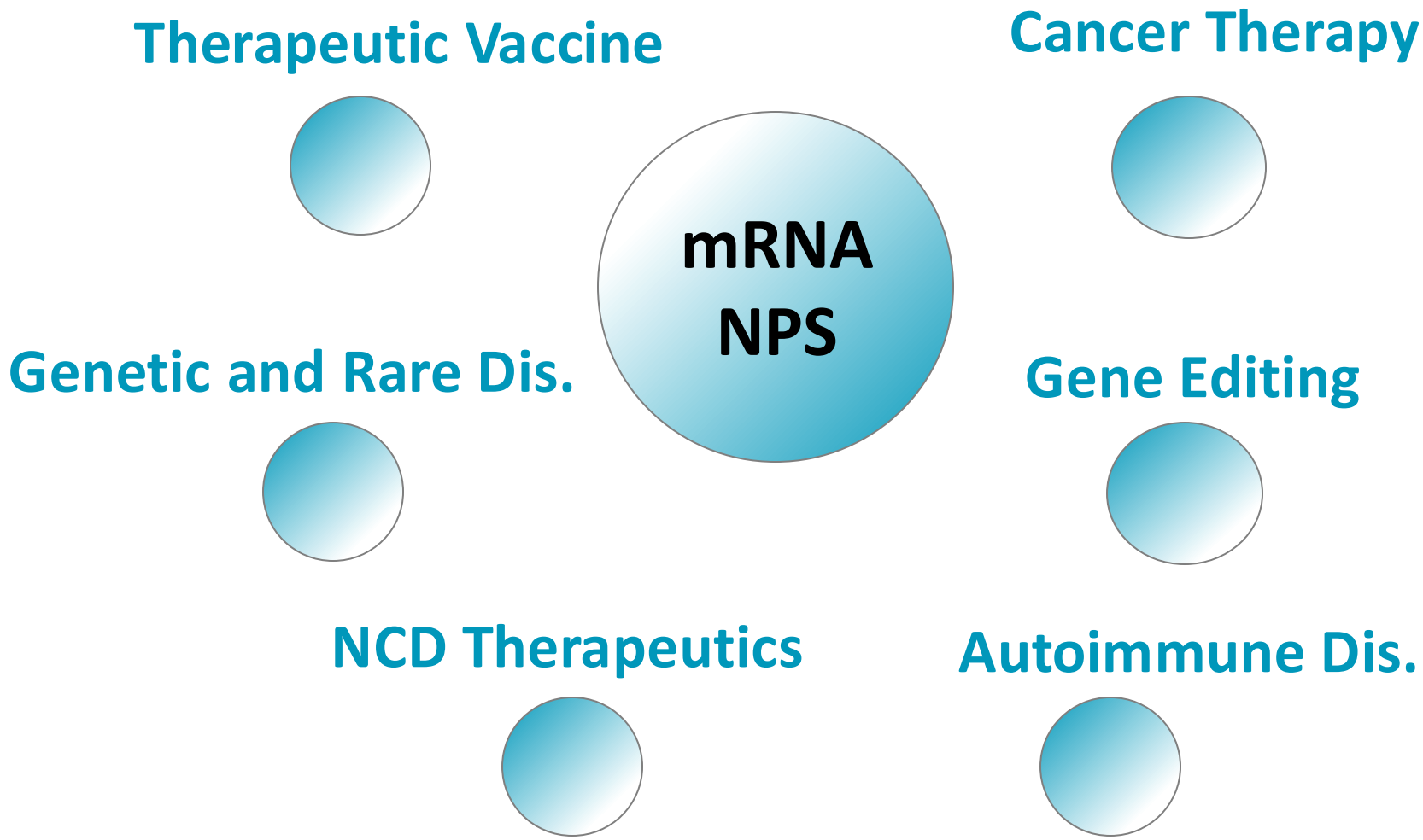
Vaccine Development Pipelines
- ChulaVRC initiative : 6 vaccines
- Collaborator initiative: 3 vaccines


New ChulaVRC
at 12th Floor


New ChulaVRC
at 12th Floor

Near Finished GMP Facilities

mRNA-based Therapeutics



HPV Vaccine

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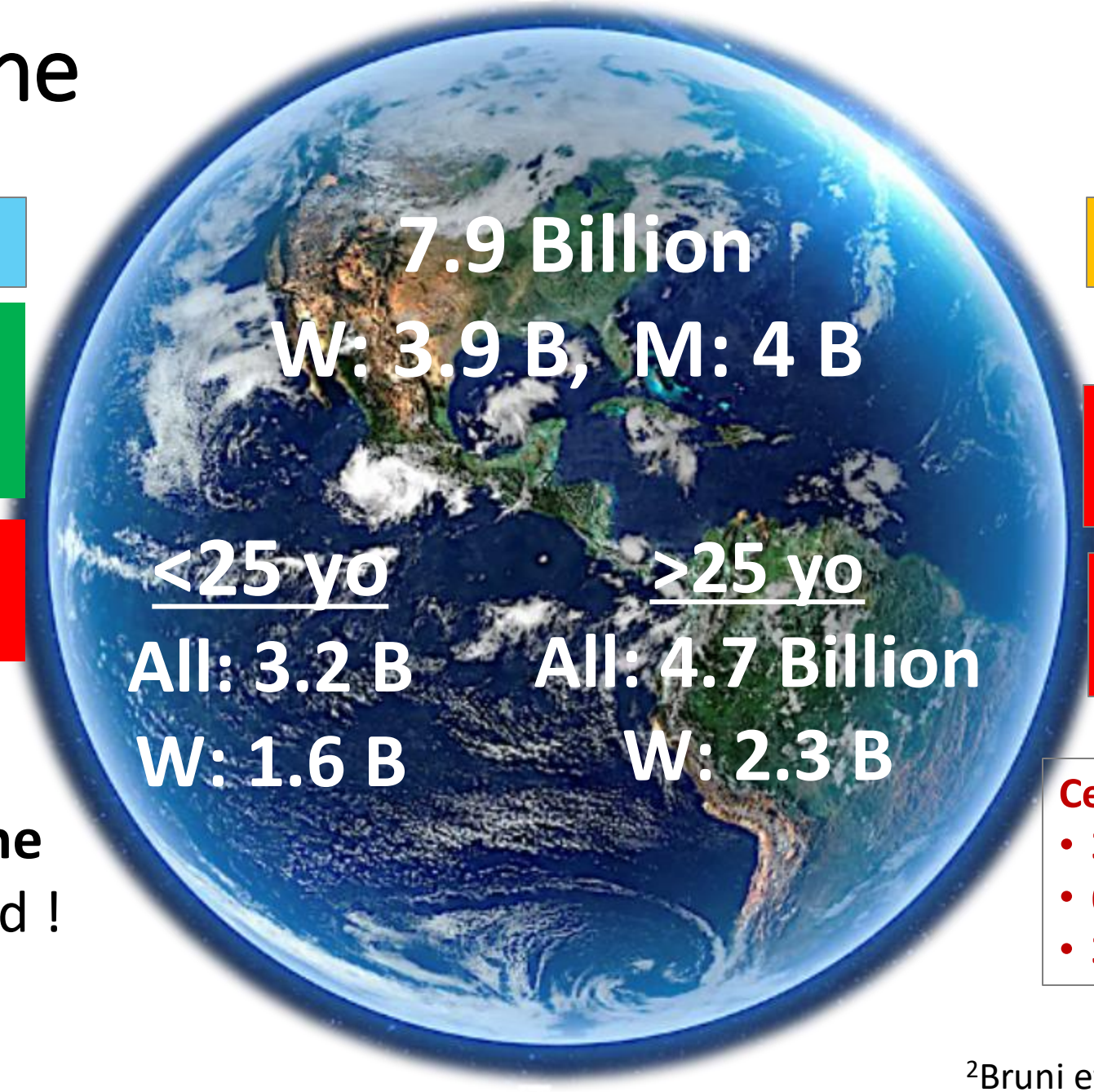
Chula Vaccine Research Center
Faculty of Medicine, Chulalongkorn University

PREVENTIVE

Highly Efffective HPV Vaccine
Avialable since **2014**

Global 2022[1]
21 % coverage !!

L1-VLP
Affordable Vaccine
Is definitely needed !



THERAPEUTIC

Vaccine- not available

291 Million Women are HPV DNA carriers

21% men are HR-HPV Infected[2]

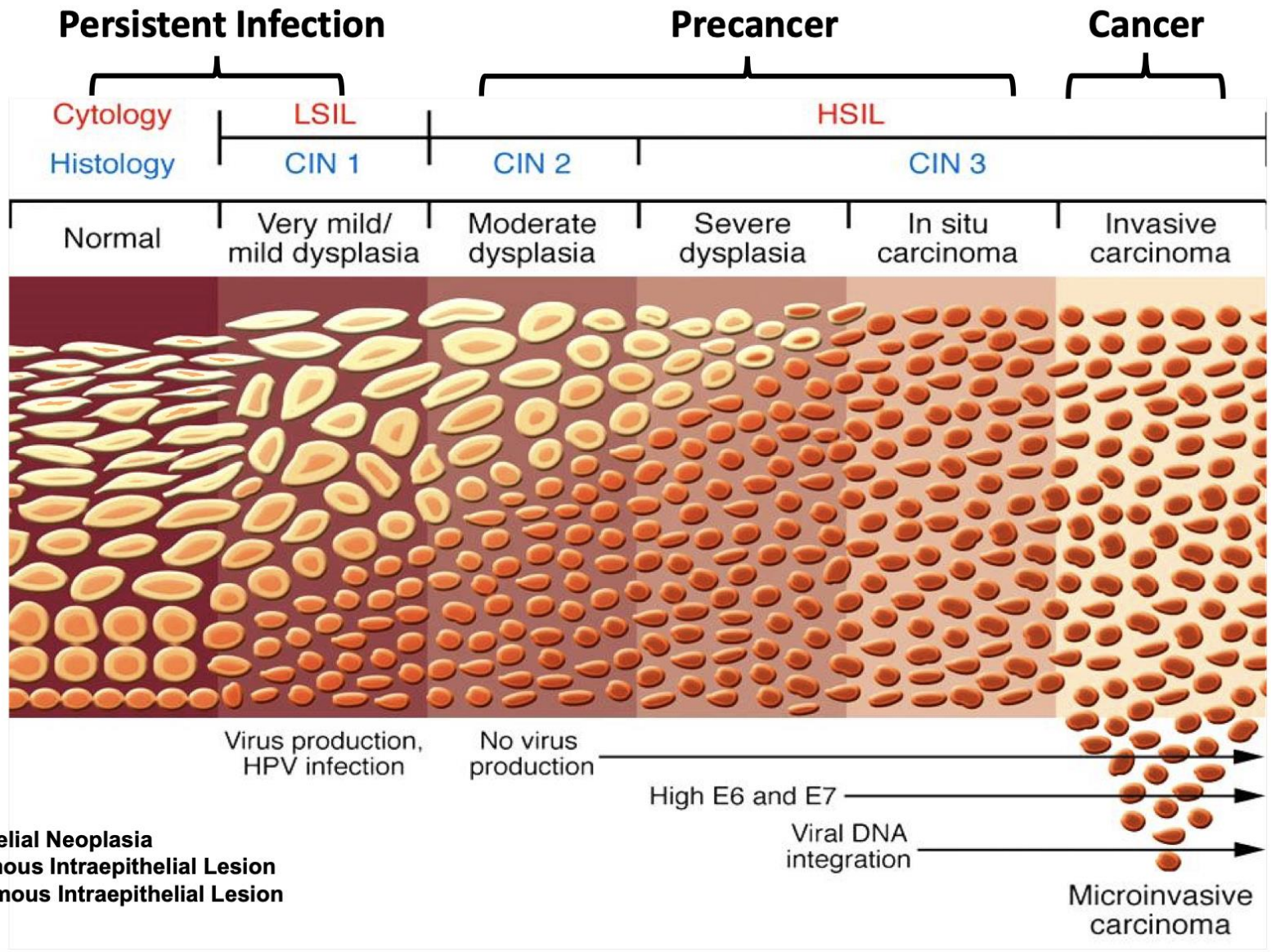
Cervical Cancer
- **3.1%** of all cancers
- **604,127** new cases
- **341,831** deaths annually

[1]WHO, July 2023

[2]Bruni et al. Lancet Global Health 2023

What Stage in HPV Carcinogenesis Should HPV Therapeutic Vaccine Target?

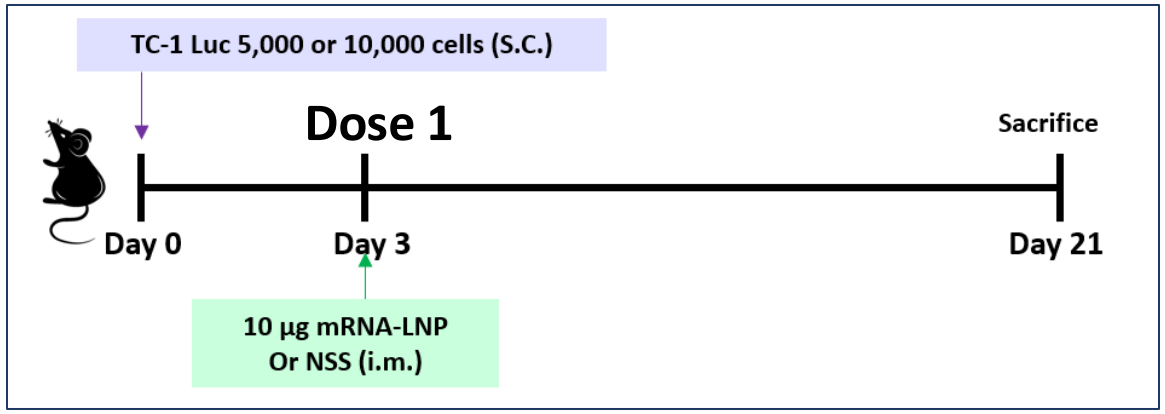
FROM John Schiller, Ph.D., NCI, NIH

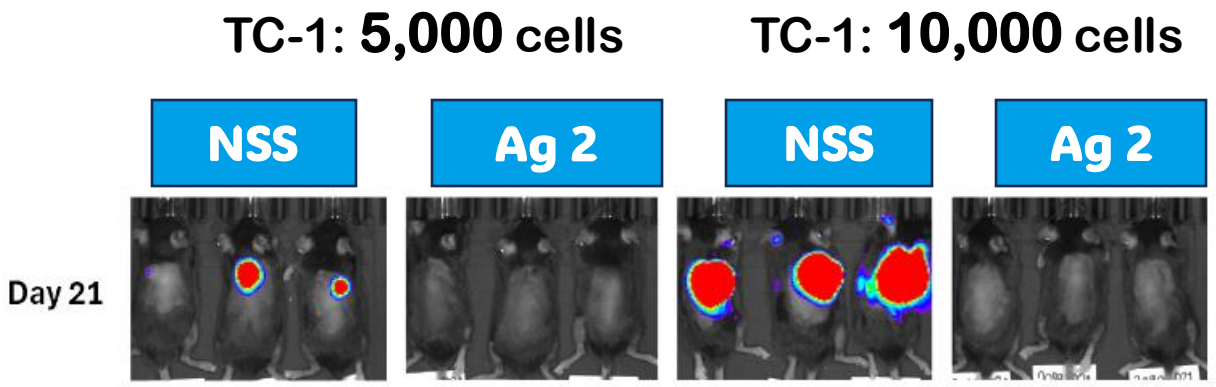


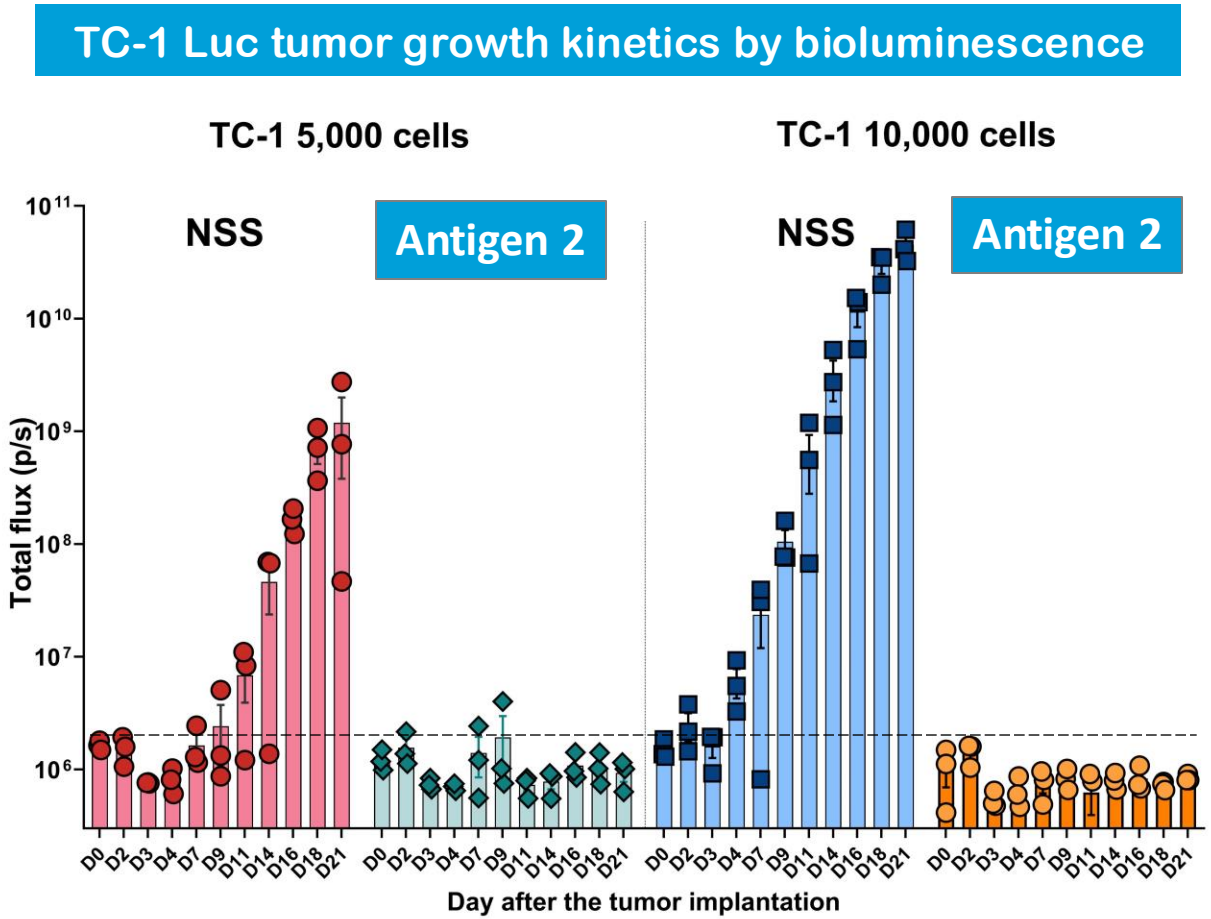
CIN = Cervical Intraepithelial Neoplasia
LSIL = Low grade Squamous Intraepithelial Lesion
HSIL = High grade Squamous Intraepithelial Lesion

HPV Therapeutic Vaccine Results: Single Dose Study

Single Dose of an HPV16-E7 Vaccine Induced Tumor Free in Mice Implanted with HPV-tumor cells

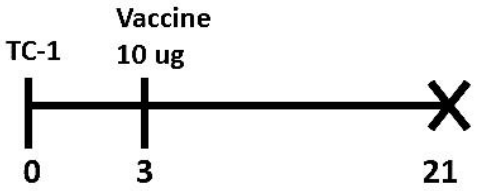


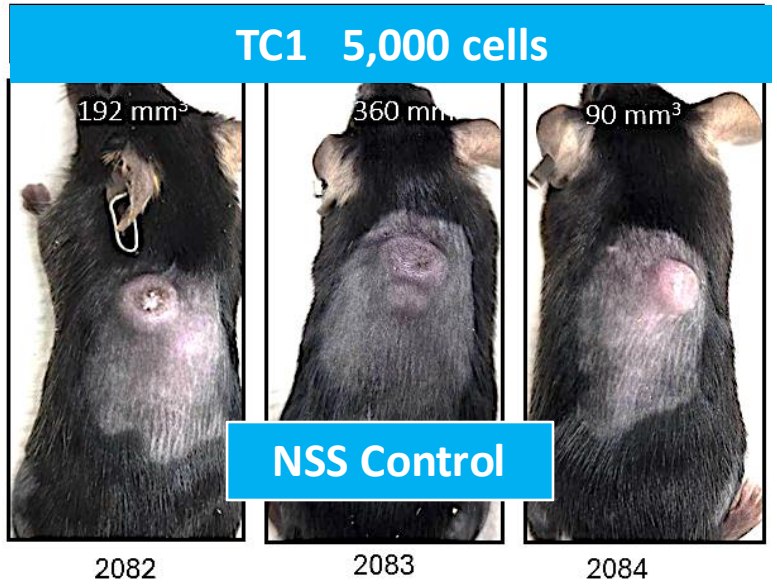


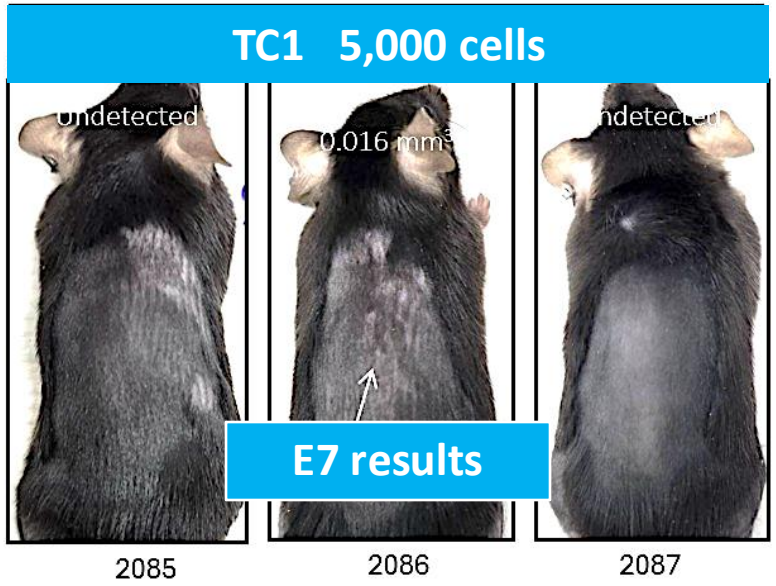


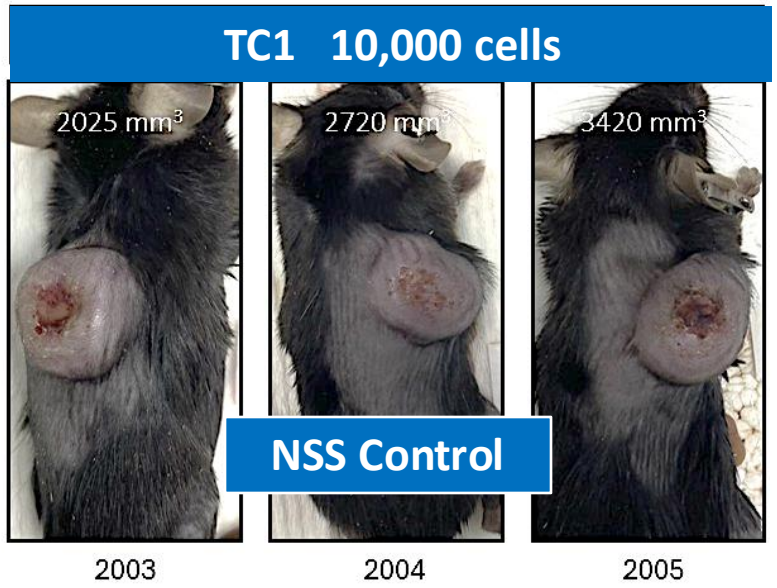
Note: Horizontal line indicates the background of bioluminescence at Day 0 before tumor implantation.

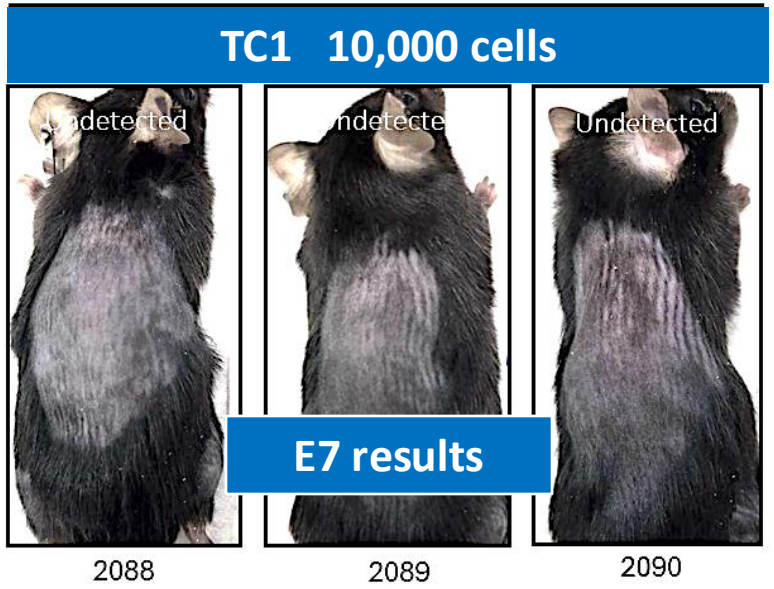
Aim: Tumor regression study (Single does): HPV16 E7 mRNA-LNP



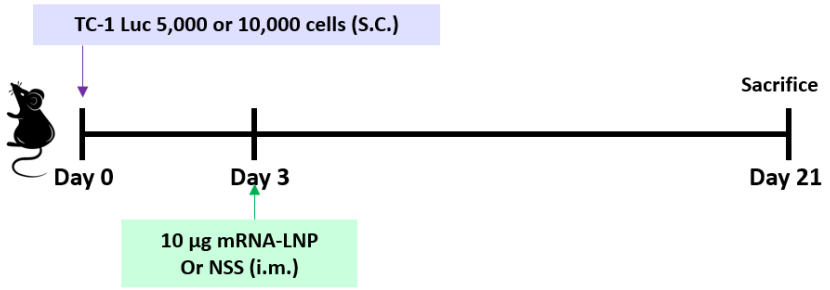


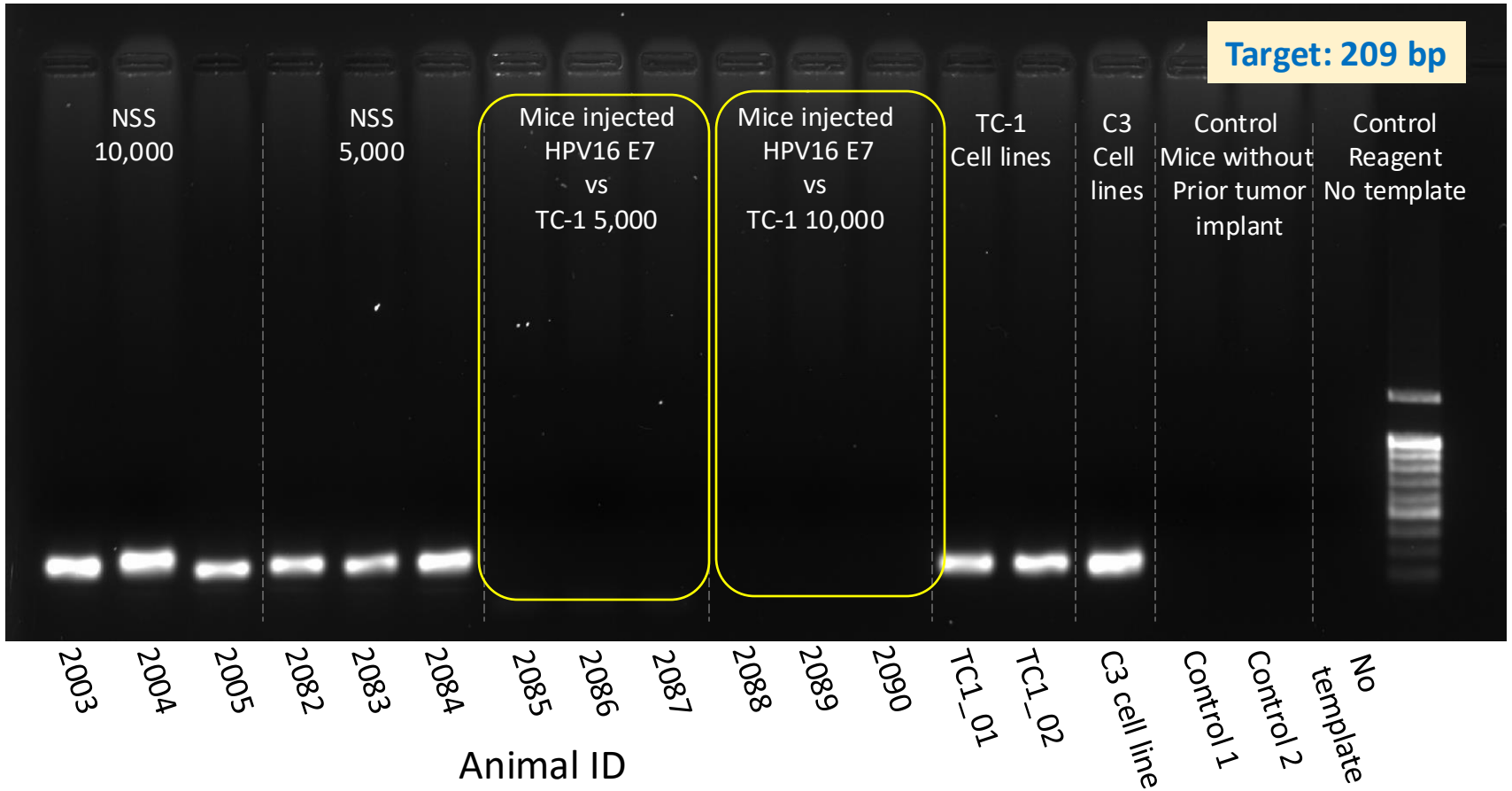






Study: The single dose of HPV16 E7 mRNA vaccine in mice given after 5,000 and 10,000 TC1-Lcu cells implantation

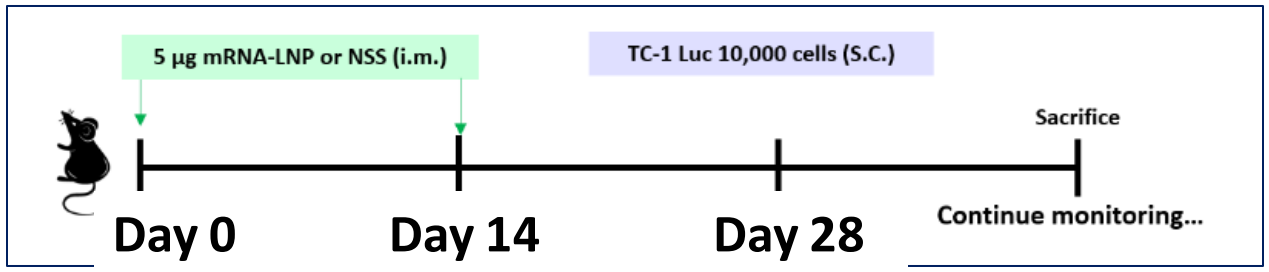


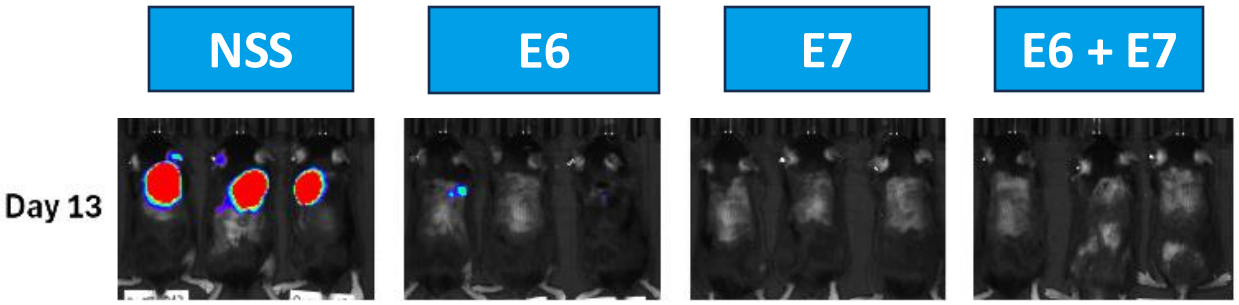


Gr.	Animal ID	Tumor free	Undetectable HPV-DNA
NSS Vs 10,000 cells	2003	✘	✘
	2004	✘	✘
	2005	✘	✘
NSS vs 5,000 cells	2082	✘	✘
	2083	✘	✘
	2084	✘	✘
HPV16 E7 Vs 5,000 cells	2085	✓	✓
	2086	✓	✓
	2087	✓	✓
HPV16 E7 Vs 10,000 cells	2088	✓	✓
	2089	✓	✓
	2090	✓	✓

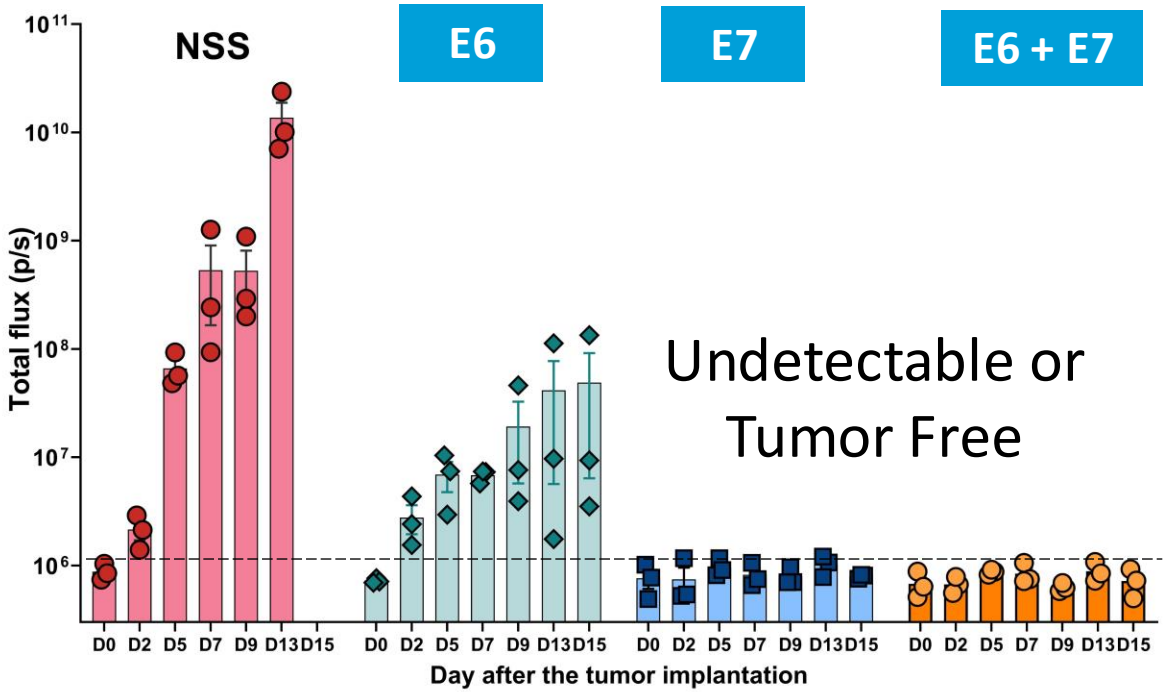
HPV Preventive Vaccine Results

HPV16 –E6, E7 mRNA Vaccine given 2 doses prior to TC1 implantation





TC-1 Luc tumor growth kinetics by bioluminescence



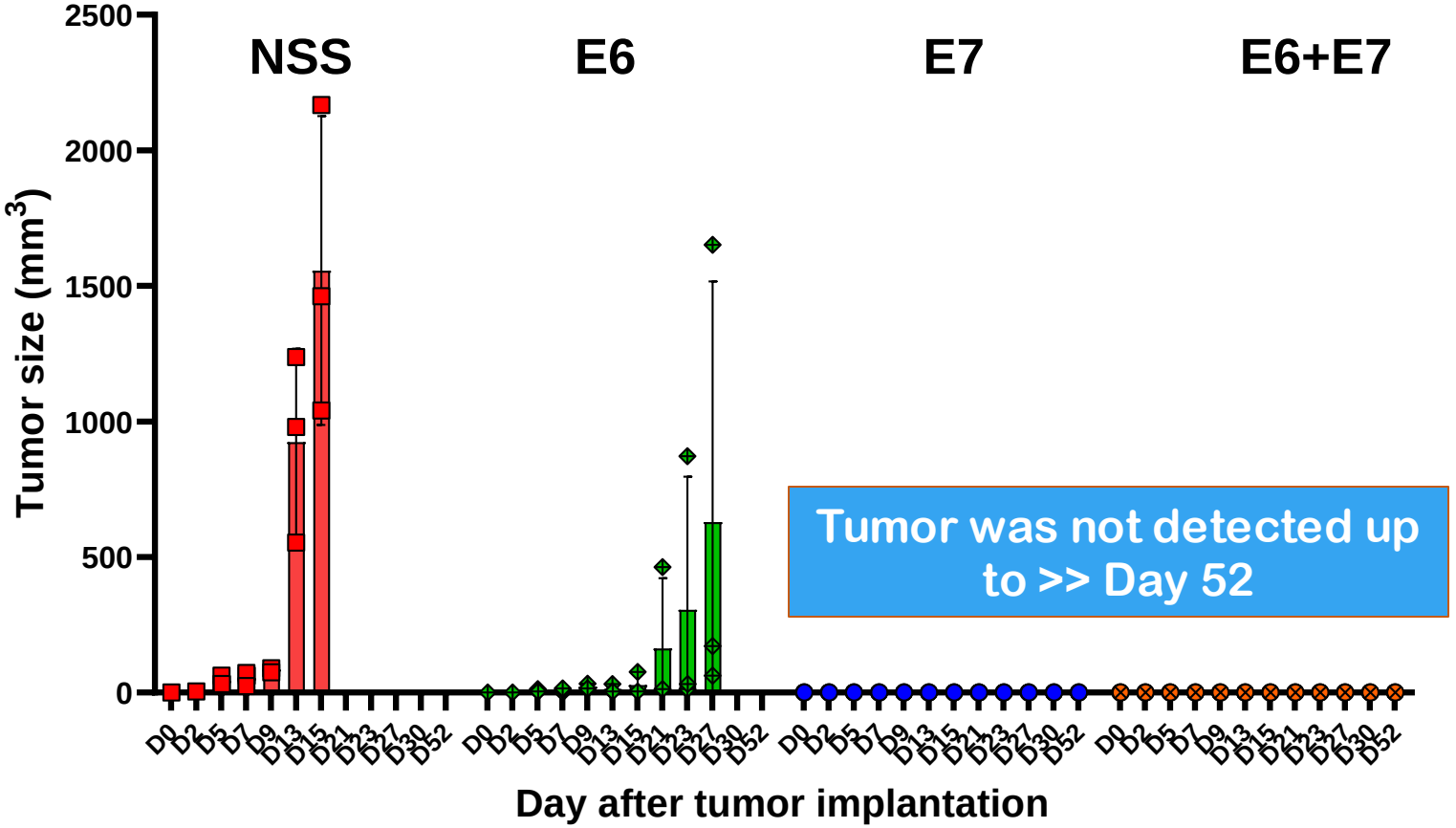
Note: Horizontal line indicates the background of bioluminescence before tumor implantation.

Results of HPV16 – E6, E7 mRNA Vaccine as Prevention

Preventive tumor model
TC-1 10,000 cells

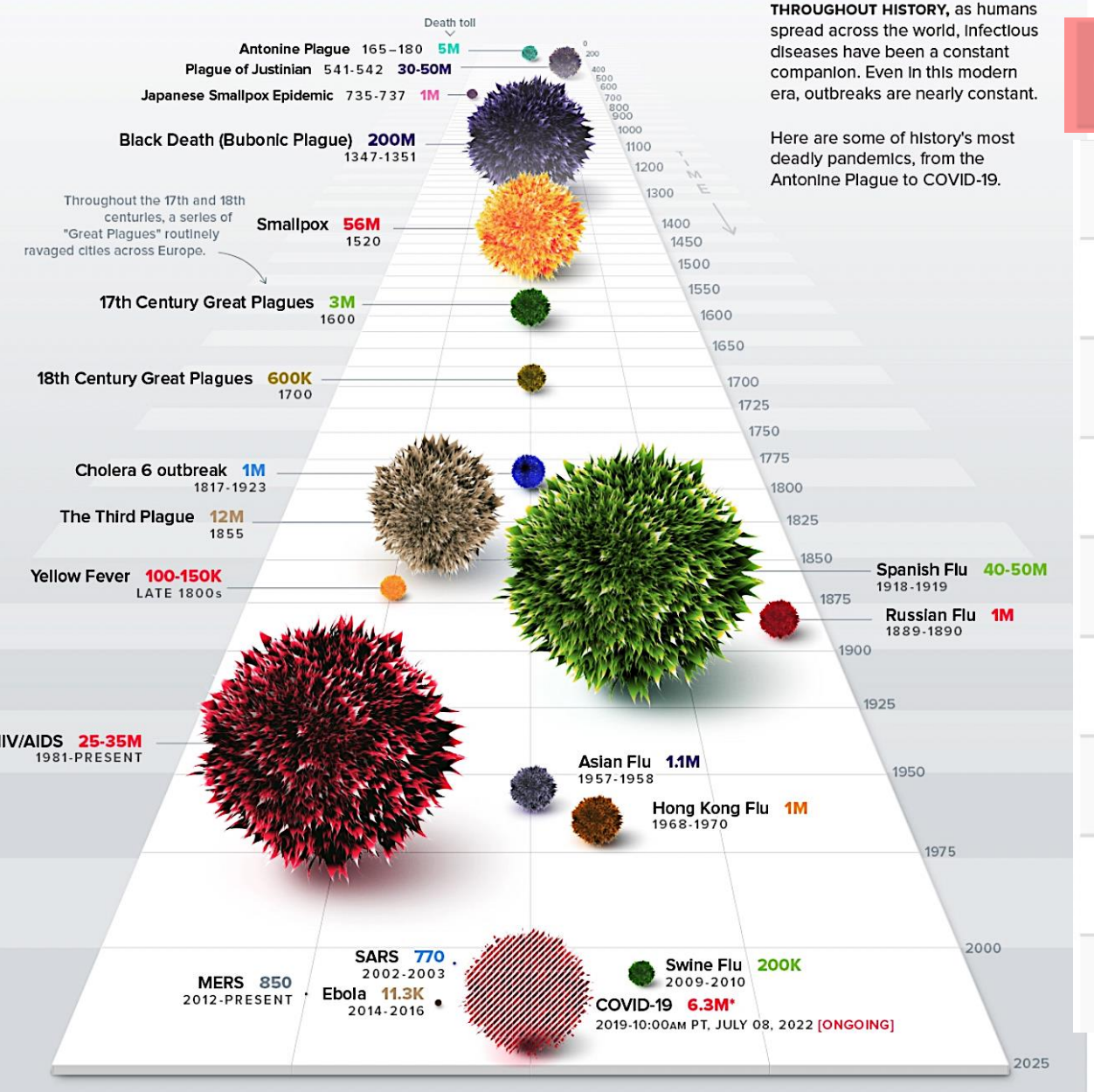
Tumor size (mm^3)

Formula = $(L^2xW)x0.5$



HISTORY OF PANDEMICS

PAN·DEM·IC (of a disease) prevalent over a whole country or the world.



THROUGHOUT HISTORY, as humans spread across the world, infectious diseases have been a constant companion. Even in this modern era, outbreaks are nearly constant.

Here are some of history's most deadly pandemics, from the Antonine Plague to COVID-19.

VISUAL CAPITALIST

Pandemics in the past Century

Name	Time period	Type / Pre-human host	Death toll
Spanish Flu	1918-1919	H1N1 virus / Pigs	40-50M
	38 y		
Asian Flu	1957-1958	H2N2 virus	1.1M
	10 y		
Hong Kong	1968-1970	H3N2 virus	1M
	11 y		
HIV/AIDS	1981-present	Virus / Chimpanzees	25-35M
	28 y		
Swine Flu	2009-2010	H1N1 virus / Pigs	200,000
	21 y		
SARS	2002-2003	Coronavirus / Bats, Civets	770
	11 y		
Ebola	2014-2016	Ebolavirus / Wild animals	11,000
	1 y		
MERS	2015-Present	Coronavirus / Bats, camels	850
	4 y		
COVID-19	2019-Present	Coronavirus – Unknown (possibly pangolins)	6.3M (Johns Hopkins University estimate as of July 8, 2022)

Vaccine Technology Platforms

Profile	Inactivated	Subunit	Viral vector	mRNA
Easy to develop	++	++ / +++	++ / +++	++++
Speed	++	++ / +++	++ / +++	++++
High Cost	++	+++	++	++
Production facility	Large	Large	Large	Small foot print
Efficacy	++ / +++	+++ / ++++	++ / +++	+++ / ++++
Pandemic P	+++	+++	+++	++++

Are Thailand and the Region **Ready for the Next Pandemic** ?

School of Global Health
Faculty of Medicine
Chulalongkorn University

Chula VRC
Chula Vaccine Research Center
Faculty of Medicine, Chulalongkorn University

Fundings for ChulaCov19

Corporate and Public Donors

Funding for HPV Tx vaccine

- DonationFund, and
- UK-SEA Vax Hub, UK

HPV Tx Vaccine : Acknowledgement

ChulaVRC

- Prof. Dr. Kiat Ruxrungtham
- Dr. Supichcha Saithong
- Assoc.Prof. Eakachai Prompetchara
- Assoc.Prof. Chutitorn Ketloy
- Kittipan Tharakhet
- Papatsara Kaewpamg
- Nongnaphat Yostrerat
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- Kunlanan Charsangbong
- Yanisa Sutjaporn
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- Pachara Wangsoontorn
- Patrawadee Pitakpolrat
- Dr. Sunee Sirivichayakul
- Dr. Supranee Buranapraditkun
- Prof. Tanapat Palaga
- Prof. Kanitha Patarakul

Kiat

Supichcha

Eakachai

Chutitorn

Strong international collaborations

- **mRNA Vaccine pioneers and experts**
  - Drew Weissman University of Pennsylvania, USA
  - Mohamad-Gabriel Alameh, Children Hospital, UPenn, USA

Penn
University of Pennsylvania

- **Lipid nanoparticles**
  - James Heyes Genevant Science Corp., Canada

GENEVANT

- **HPV Tumor cell lines**

TC-1 tumor cells

- Kindly provided by T.-C. Wu (Johns Hopkins University)

C3 tumor cells

- Kindly provided by S.H. van der Burg (Leiden University Medical Center, The Netherlands)

ChulVRC Teamwork and Partners

Prof. Kiat Ruxrungtham

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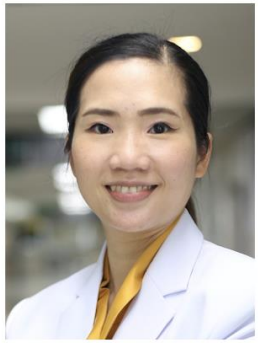
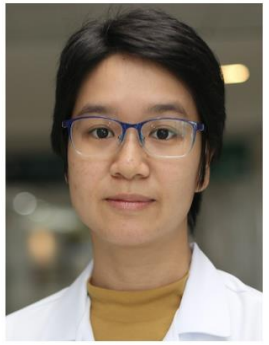
School of Global Health
Faculty of Medicine
Chulalongkorn University

Chula-Vac001 : Clinical Study Teams

Thanyawee Puthanakit



Sivaporn Gatechompol



Wonngarm Kittanamongkolchai

Kanitha Patarakul

Somchai Sriplienchan

Sasiwimol Ubolvam

+ up 50 members involved from **Chula CRC, HIVNAT, SEARCH, MHRP, KCMH, MDCU**

Sarawut Siwamogsatham

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Thanks

Hearts of Volunteers

ChulaCov19 Vaccine