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JongerenCommunicatie

Chemie

Woudschoten Chemie Conferentie

Hoe biochemie een cruciale rol speelde in het bestrijden van de corona crisis – *Het Pfizer vaccin verhaal van binnen uit*

Marc Kaptein – Medisch Directeur, Pfizer Nederland



— Wie hebben jullie voor je?

- Geboren in Losser, getogen in Wierden
- Pius X college Almelo
- Geneeskunde VU Amsterdam 88'
- Verloskunde&Gyn Haarlem/Utrecht 96'
- Organon NL 00'
- Organon USA 02'
- Eli Lilly NL 08'
- MyTomorrows NL 14'
- Pfizer NL 16'

- Voormalig voorzitter *NVFG*, Bestuurslid *HollandBIO*, Angel Investor *EV BioTech*
- Getrouwd, vader van twee dochters
- Hobbies; wielrennen en koken



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Van nul naar één



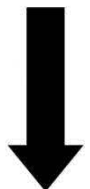


DNA



mRNA

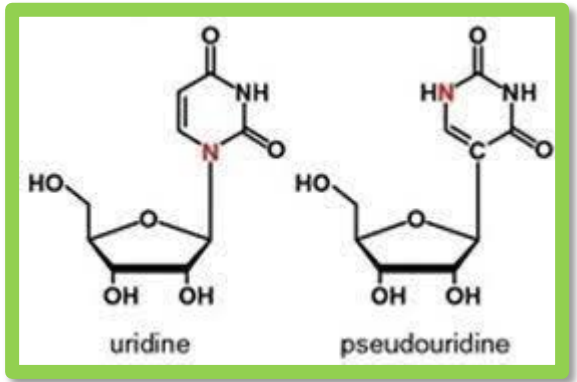
CGGAAGUGA CGGUAGUGAUCUAGUA CAU UUC GA



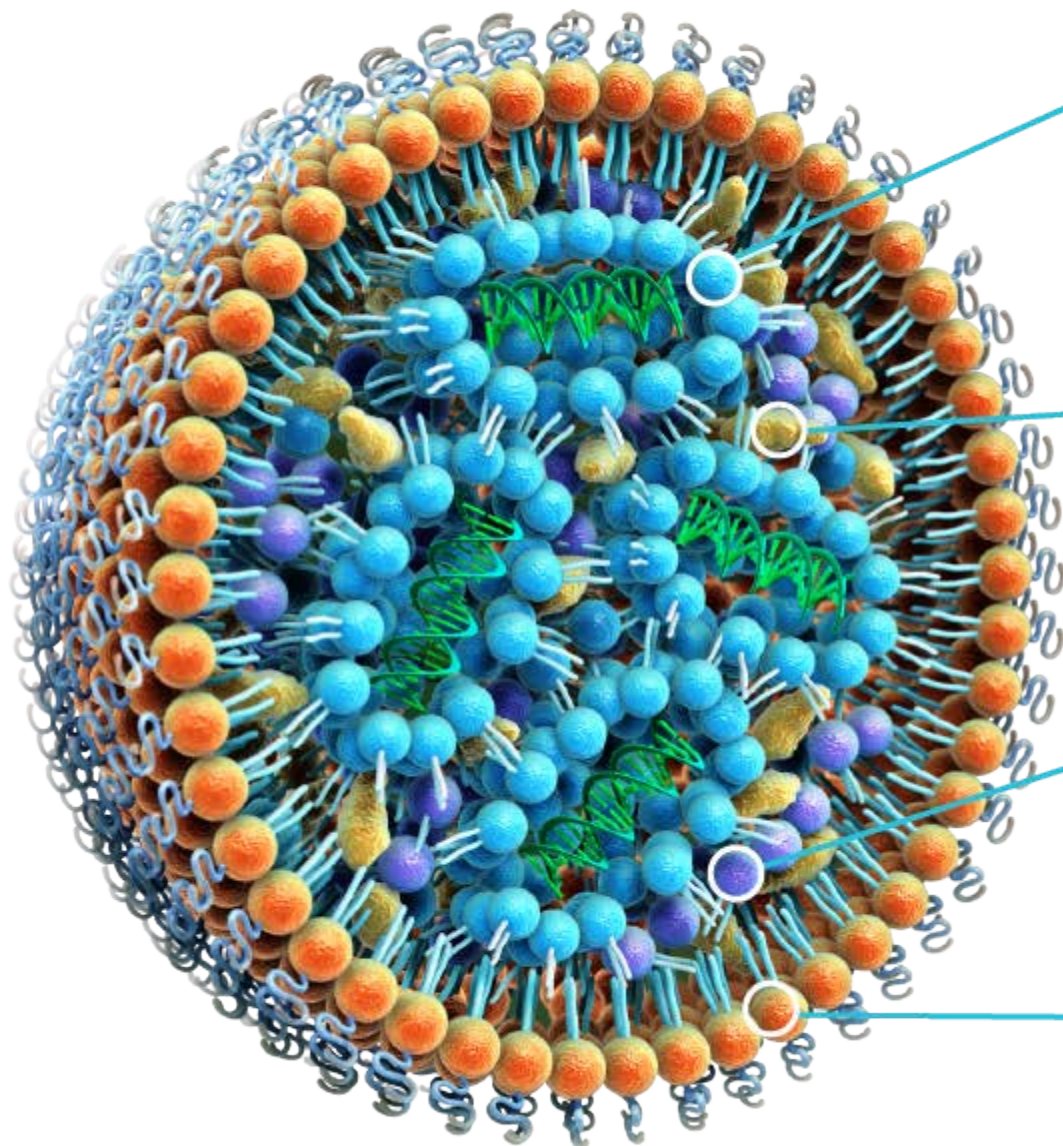
Transcription

mRNA

CGG AAG UGA CGG UAG UGA UCU AGU ACA







Ionizable Cationic Lipid

- Binds & Protects RNA
- Facilitates Endosomal Escape
- Neutral Charge at pH 7.4

Cholesterol

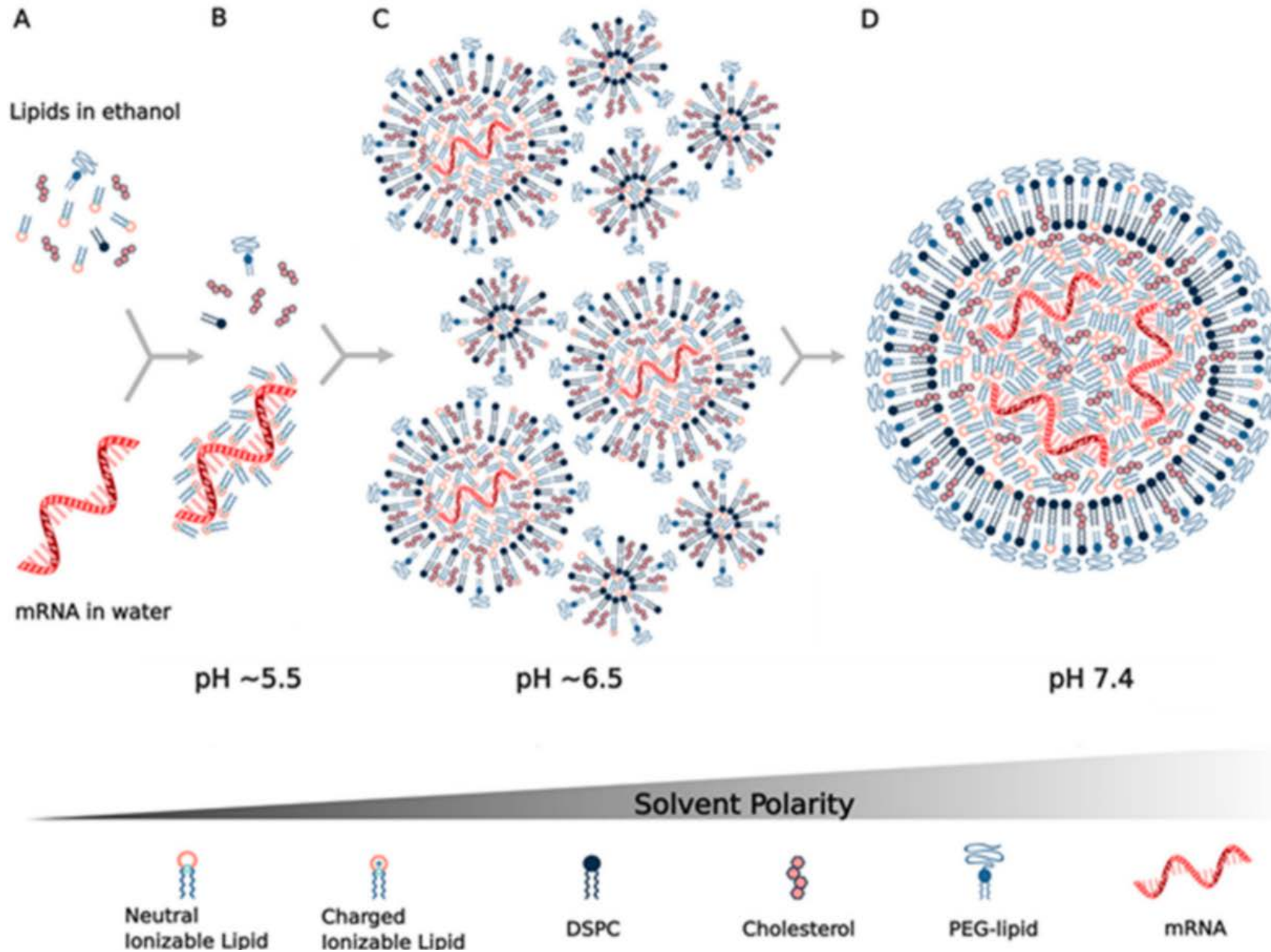
- Important for endocytosis via LDL receptor and ApoE

Helper Lipid

- Structural

Stabilizer

- Stabilizes Particle
- Protect from opsonization





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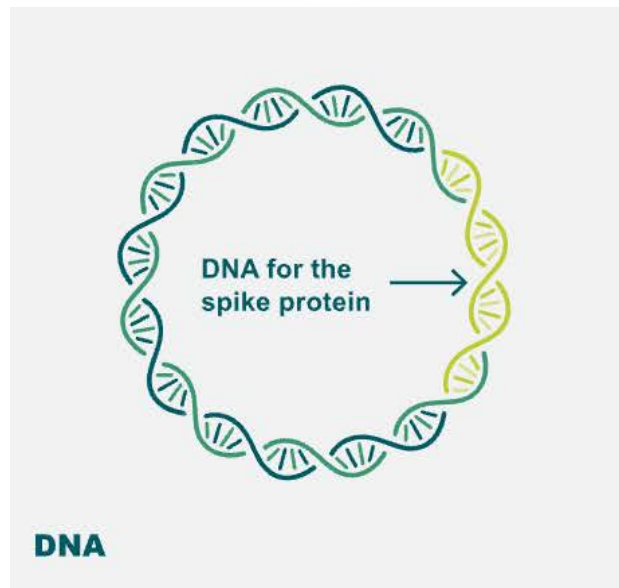
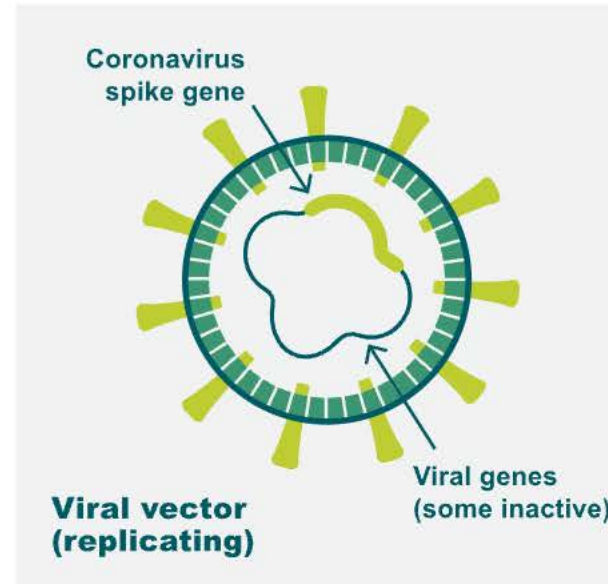
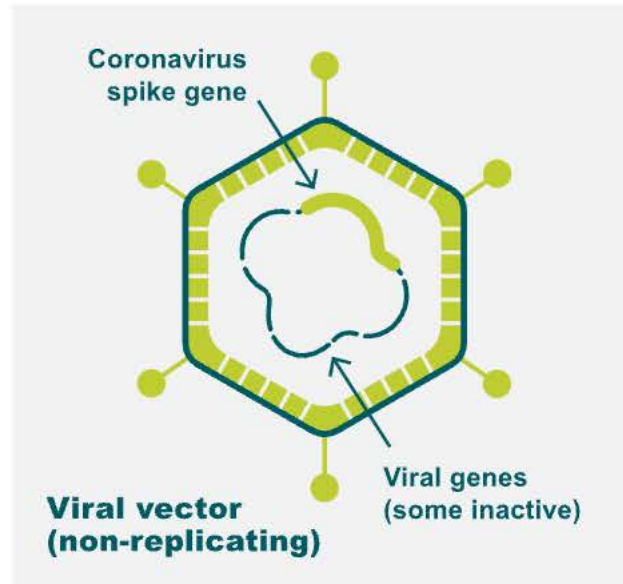
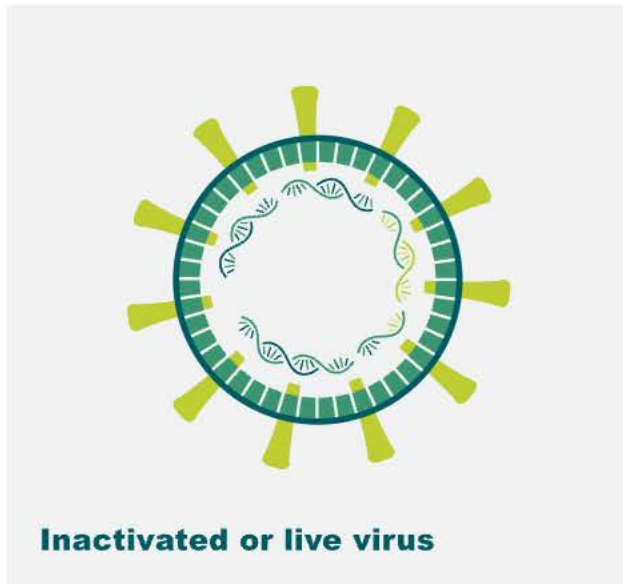
Van één naar duizend



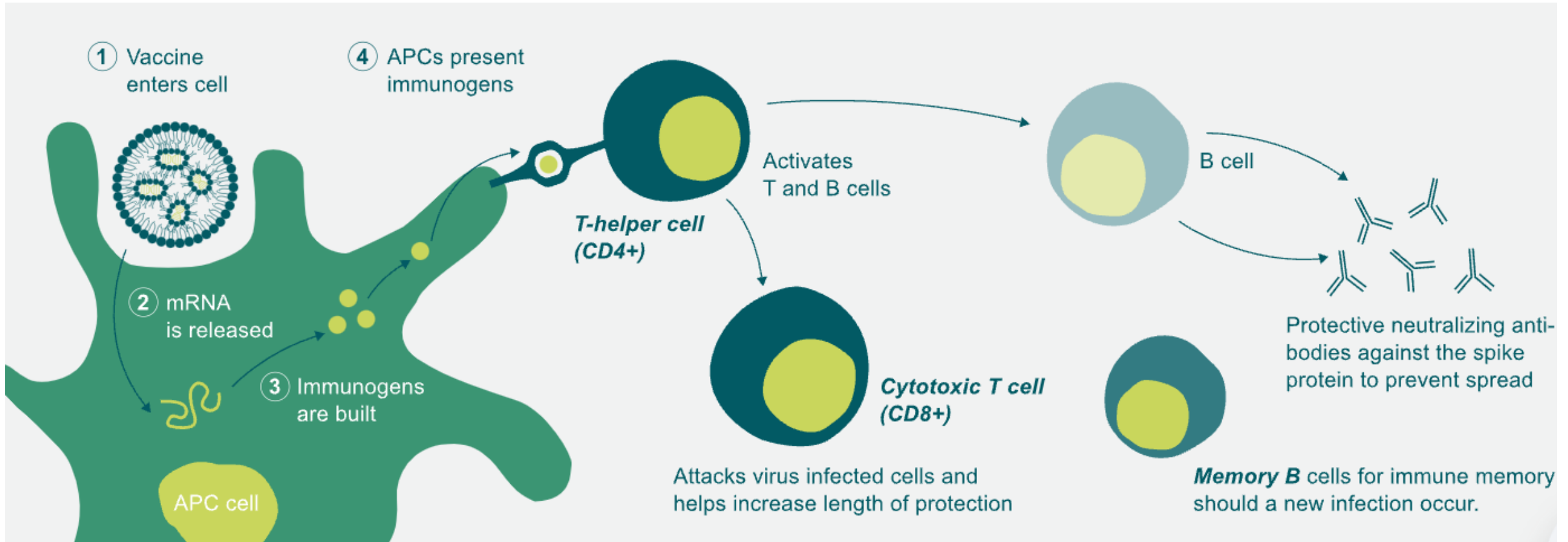




Vaccin platforms



mRNA Vaccin



Unmodified mRNA (uRNA)



RATIONALE

- Intrinsic adjuvant effect expected
- Being tested for tolerability & safety
- Antibody & strong T cell responses expected

Nucleoside-modified mRNA (modRNA)



RATIONALE

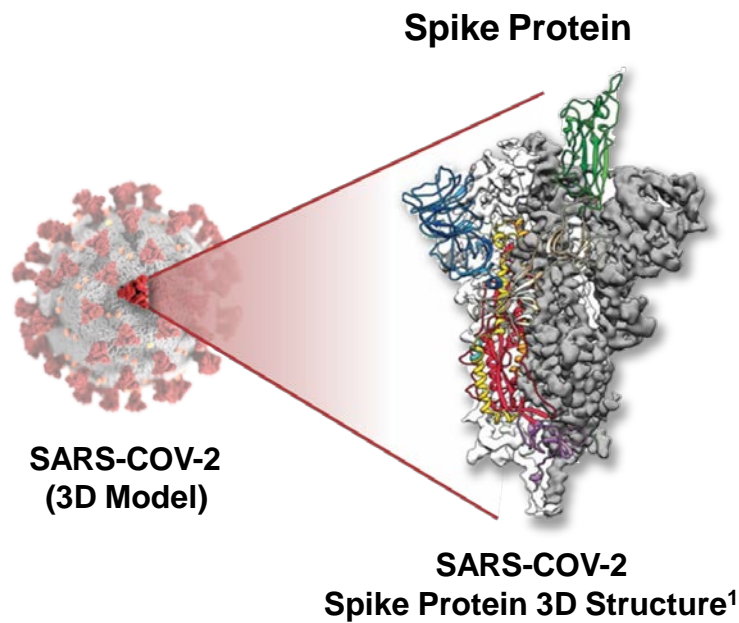
- Less adjuvant effect expected
- Being tested for tolerability & safety
- Strong antibody responses & CD4 T cell response expected

Self-amplifying RNA (saRNA)



RATIONALE

- Long duration of protein expression expected
- Being tested for tolerability and safety
- Higher likelihood for good immune response with only 1x administration than other variants
- Higher likelihood for efficacy with very low vaccine dose than other variants



Initially Four Vaccine Candidates

	Variant	Target	RNA Construct	Regimen
1	162a1	RBD subunit	uRNA	Prime/boost
2	162b1	RBD subunit	modRNA	Prime/boost
3	162b2	P2-mutated* full spike protein	modRNA	Prime/boost
4	162c2	P2-mutated* full spike protein	saRNA	Single injection

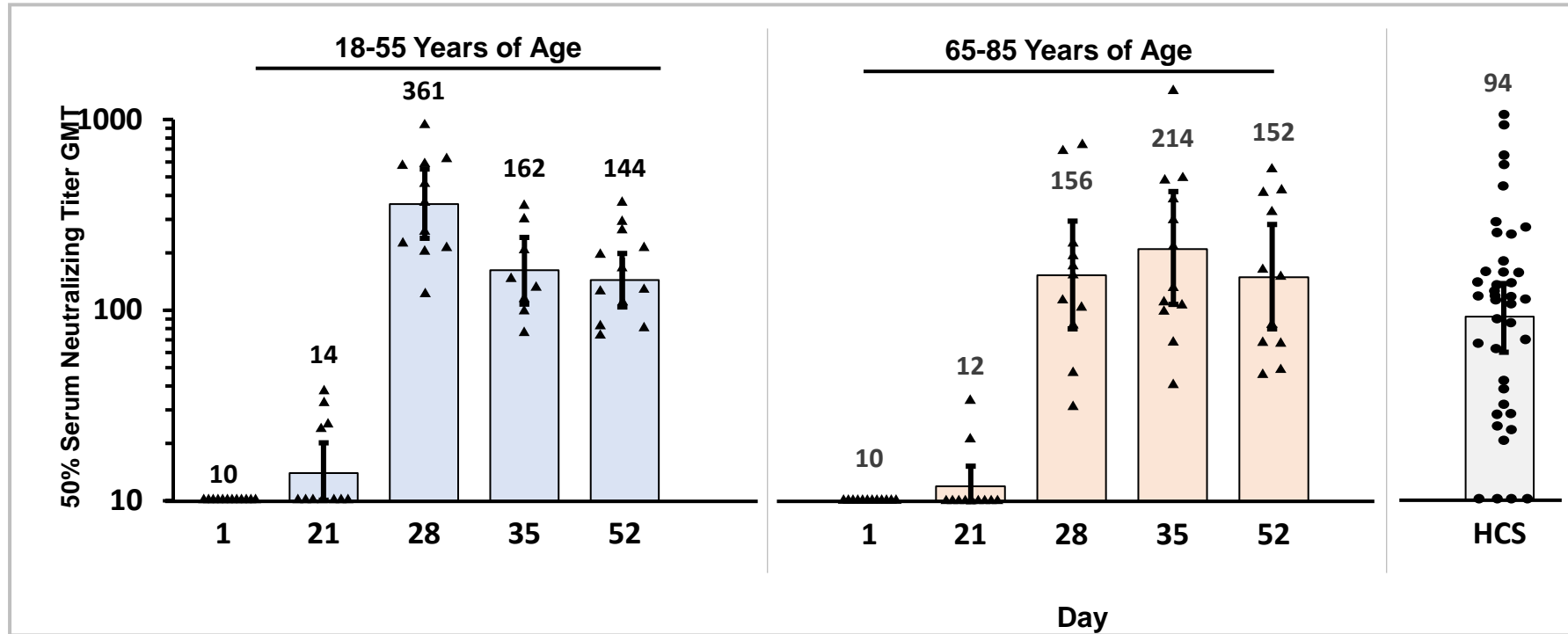
* P2 mutated – two proline mutations to lock the spike protein in the prefusion conformation

uRNA: unmodified mRNA

modRNA: nucleoside modified mRNA saRNA: self-amplifying mRNA

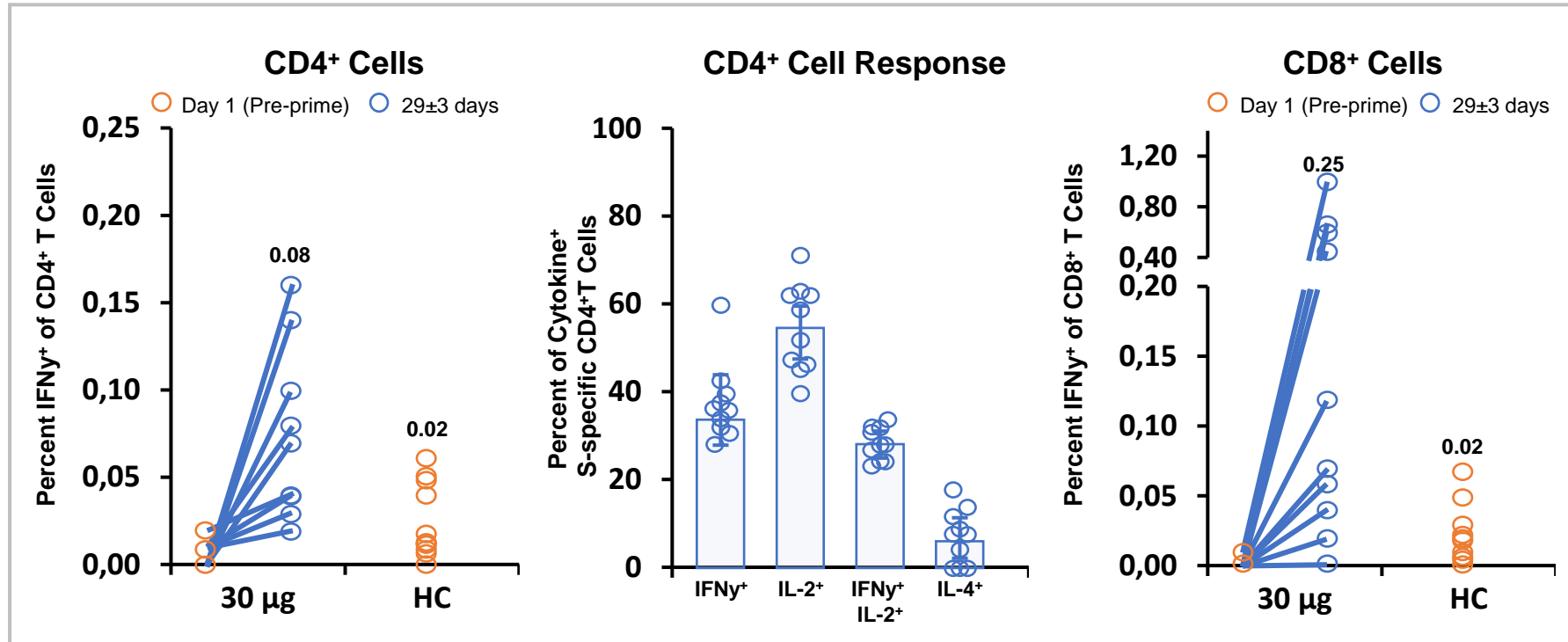
1. Wrapp et al., Science 2020;367:1260-1263.

Phase 1: Two 30 µg Doses of BNT162b2 Induce Neutralizing Antibody Titers Comparable or Higher than Natural Infection (US Study)



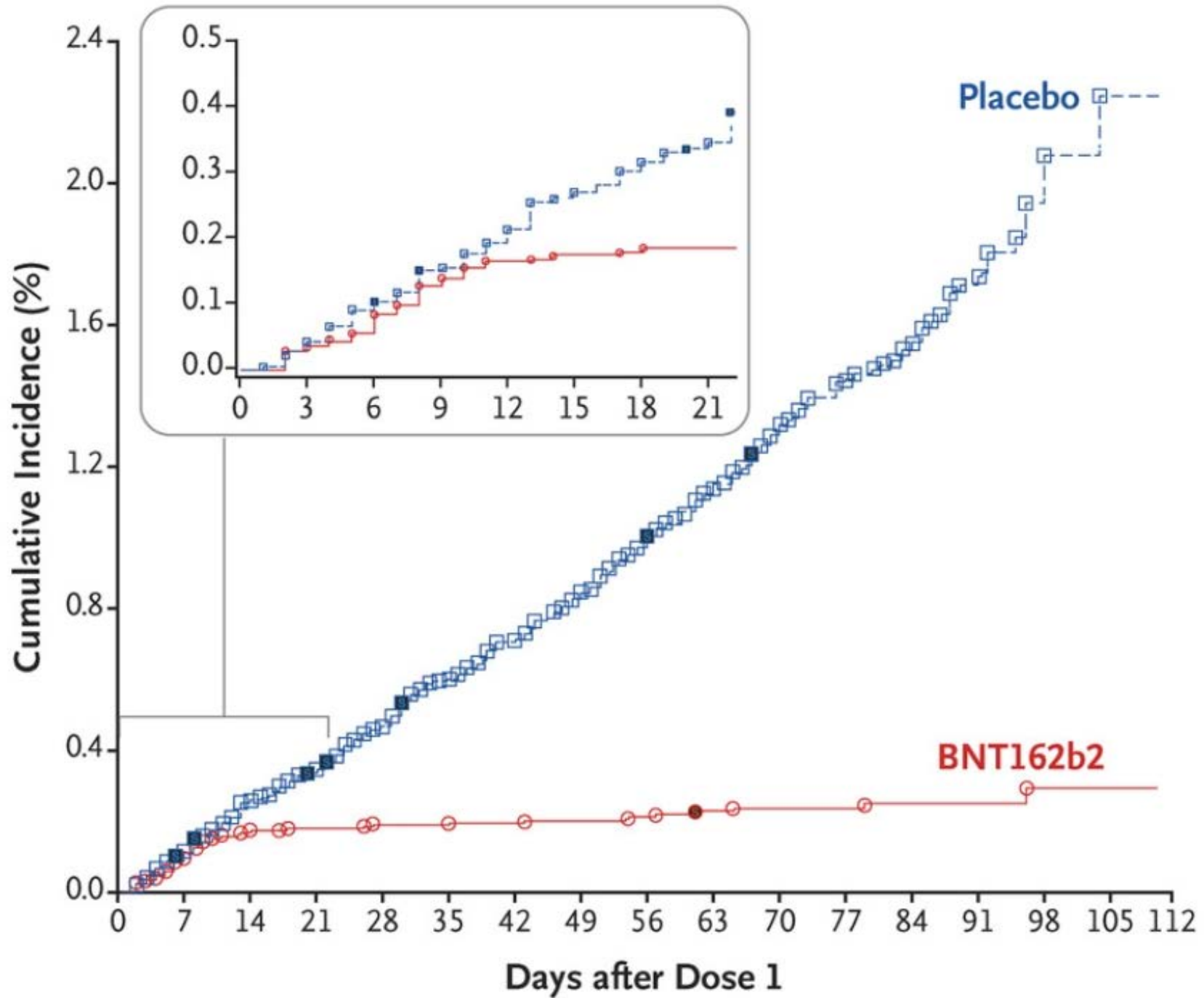
Walsh EE, et al. *N Engl J Med.* 2020

Phase 1 : BNT162b2 Elicits Strong Th1-biased CD4⁺ and CD8⁺ T Cell Responses (German Trial)



Sahin U, Muik A, Vogler I et al, medRxiv preprint doi: <https://doi.org/10.1101/2020.12.09.20245175> link: <https://www.medrxiv.org/content/10.1101/2020.12.09.20245175v1> [preprint]
 Caution: Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information.





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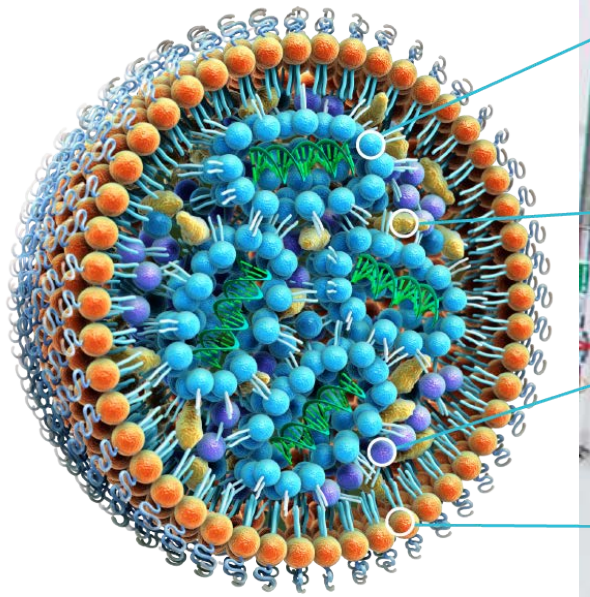
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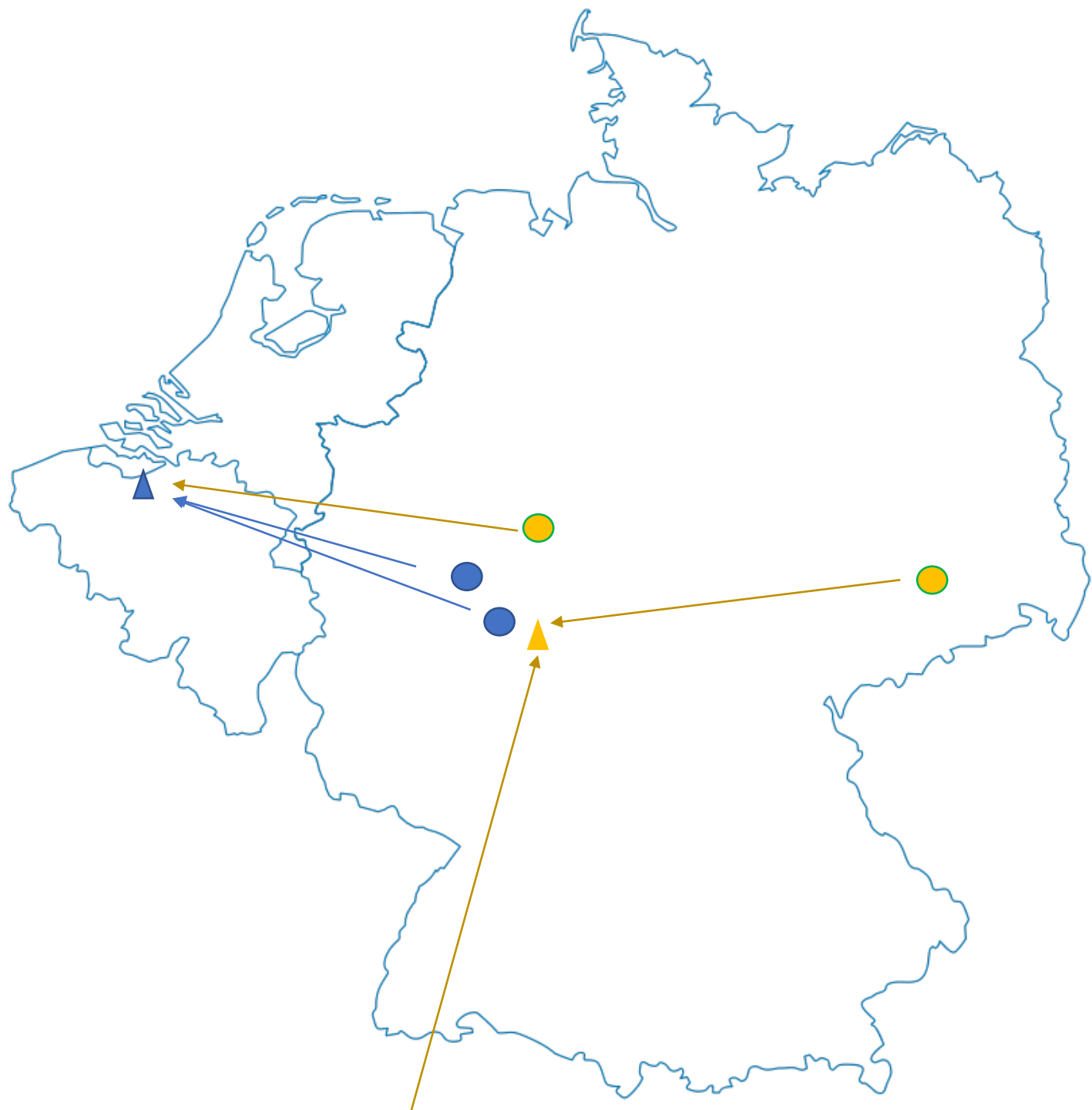
Van duizend naar miljarden











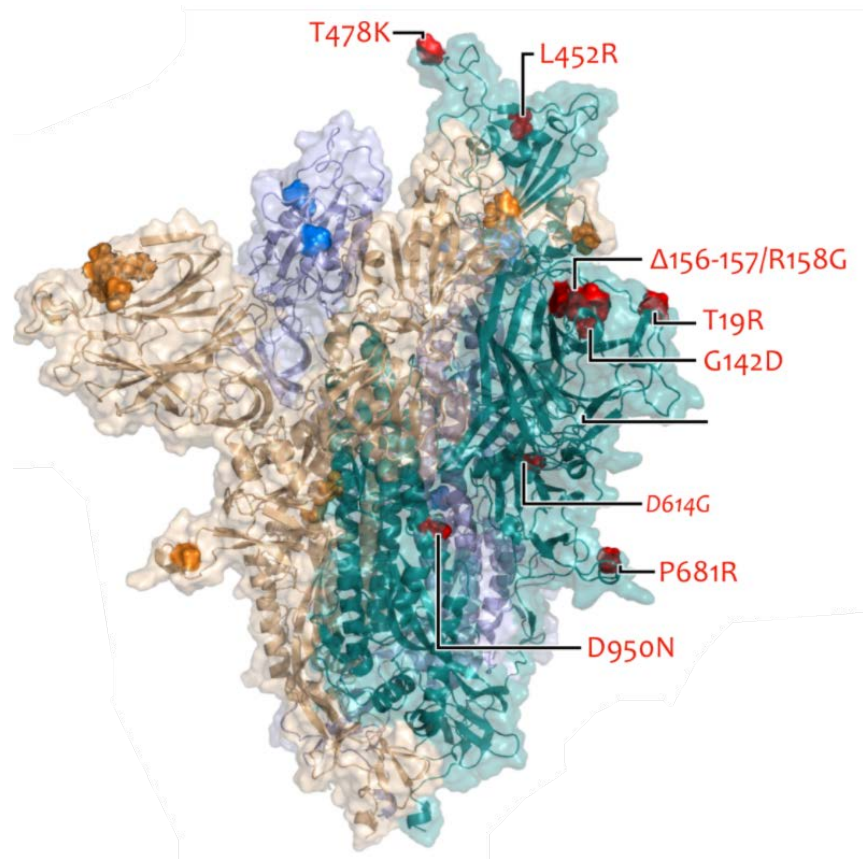


25,5 Million Kilograms

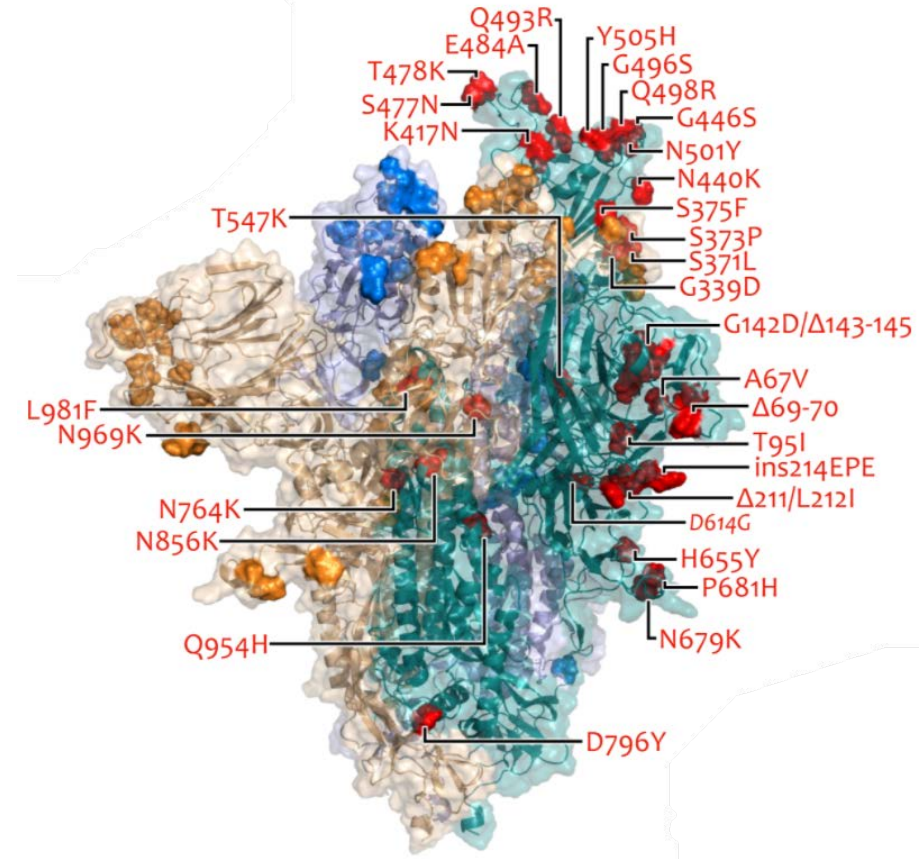


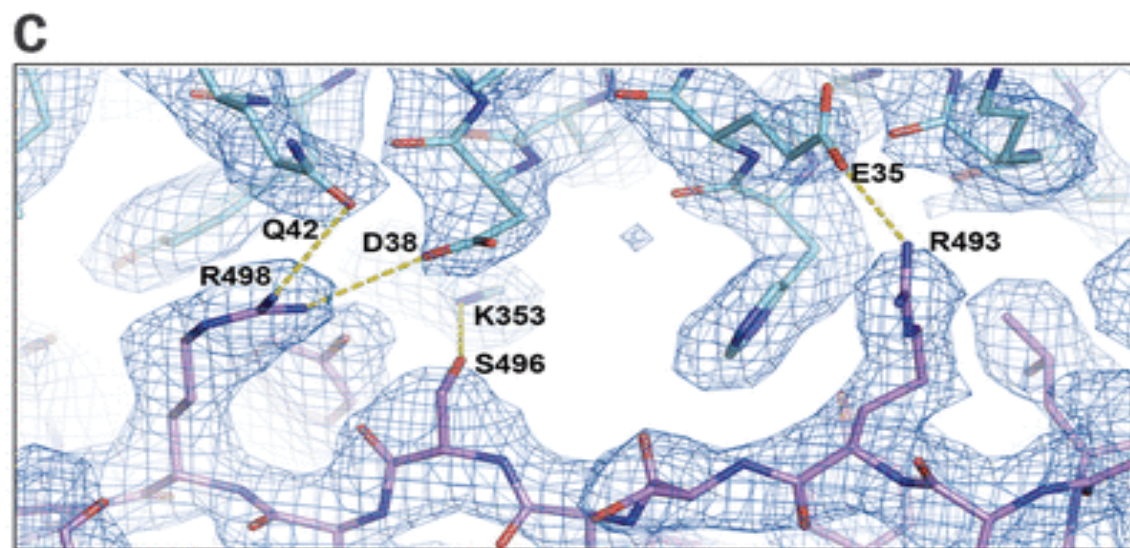
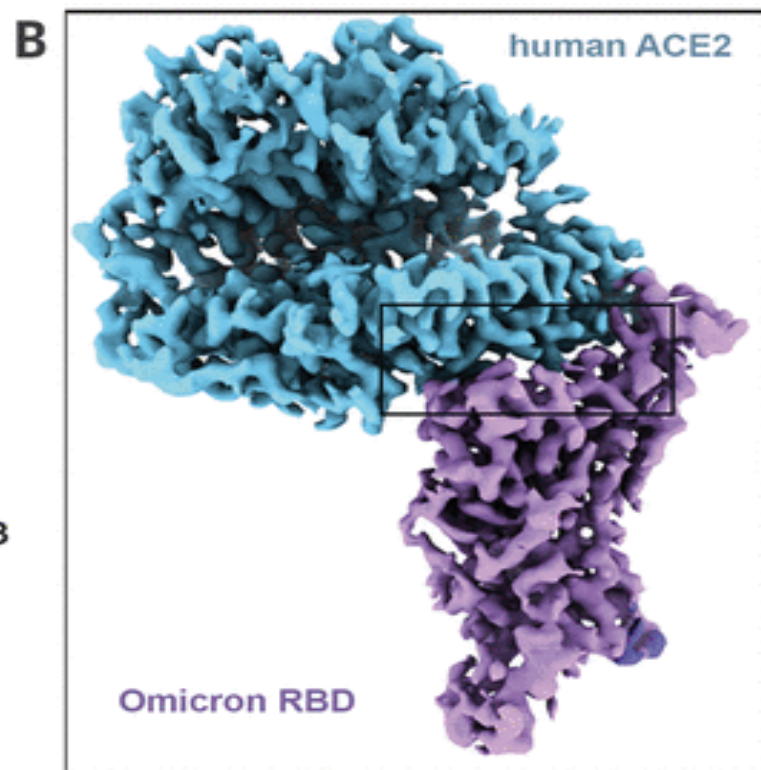
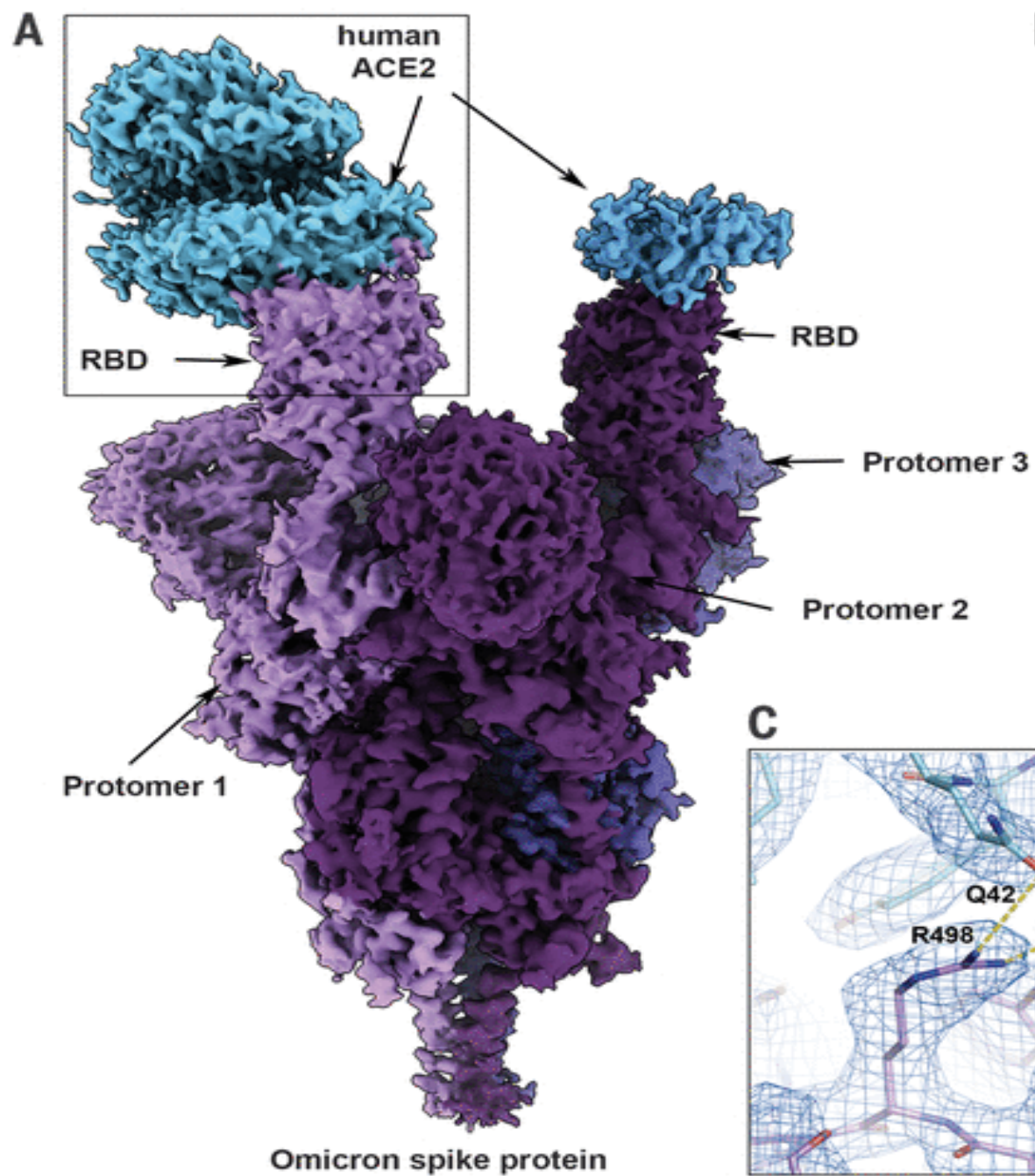
Omicron Ba1, Ba4, Ba5, etc?

Spike protein mutations
(**Delta**: B.1.617.2)



Spike protein mutations
(**Omicron**: B.1.1.529)





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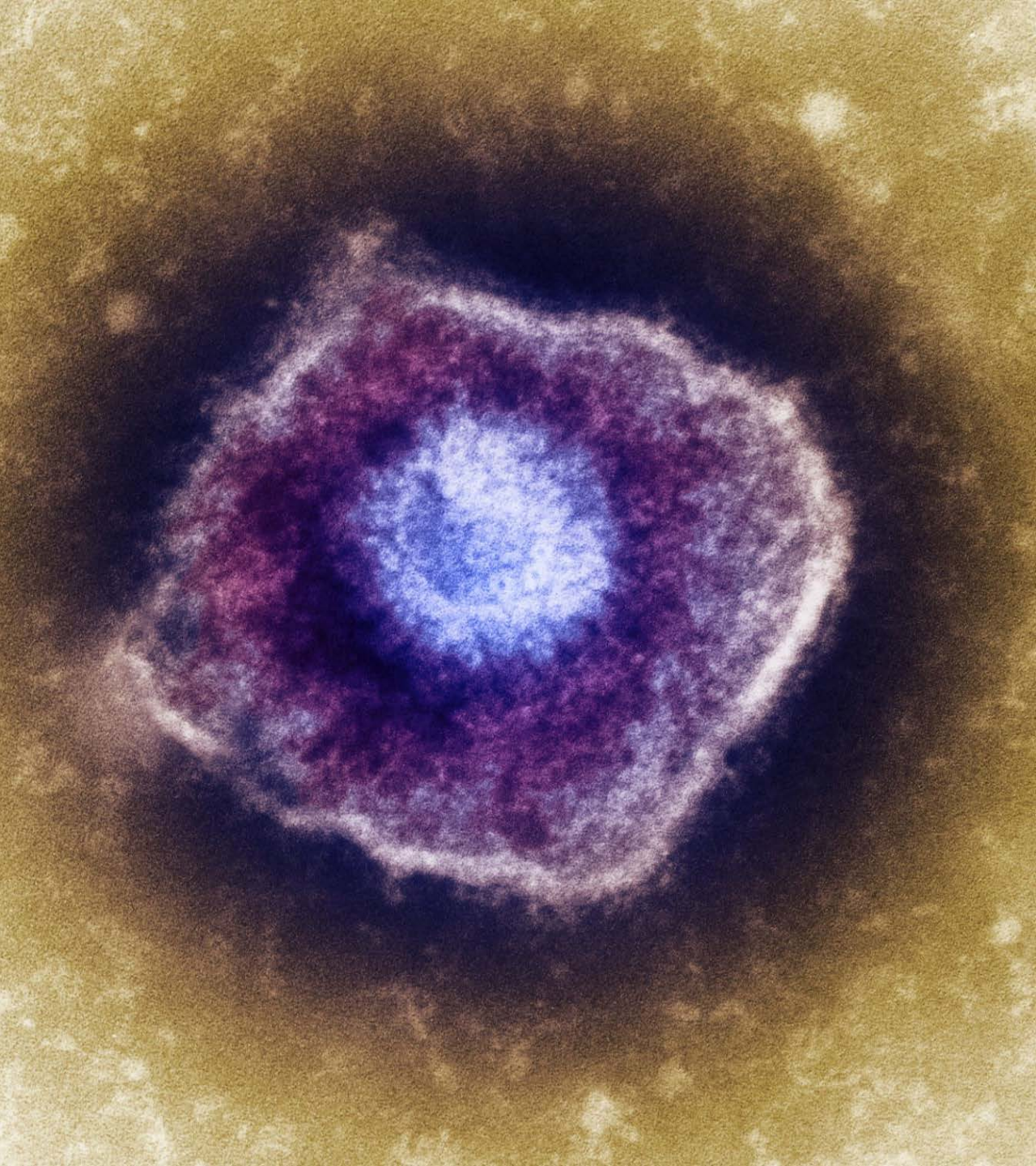
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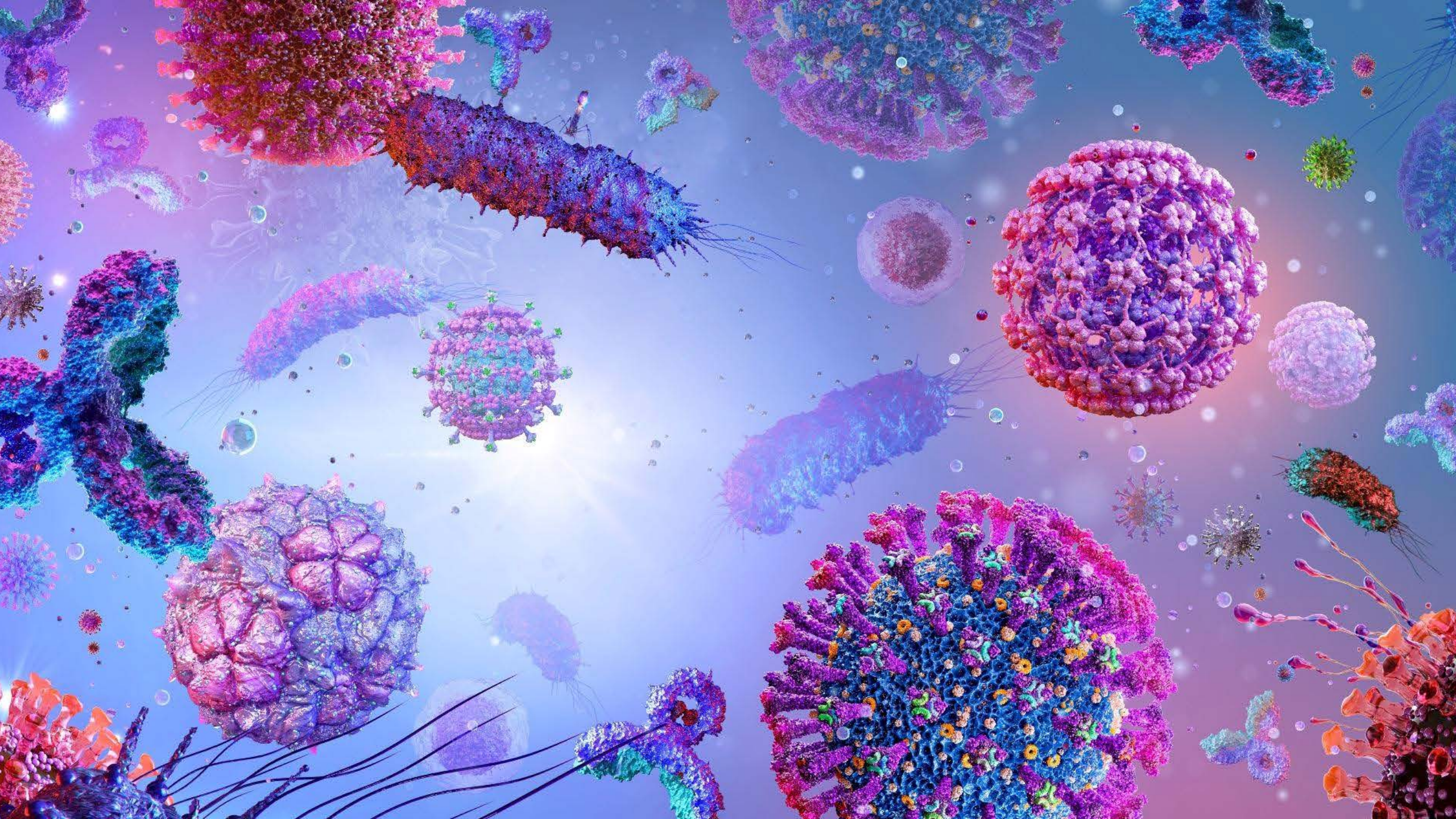
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Bio-optimisme > 2022





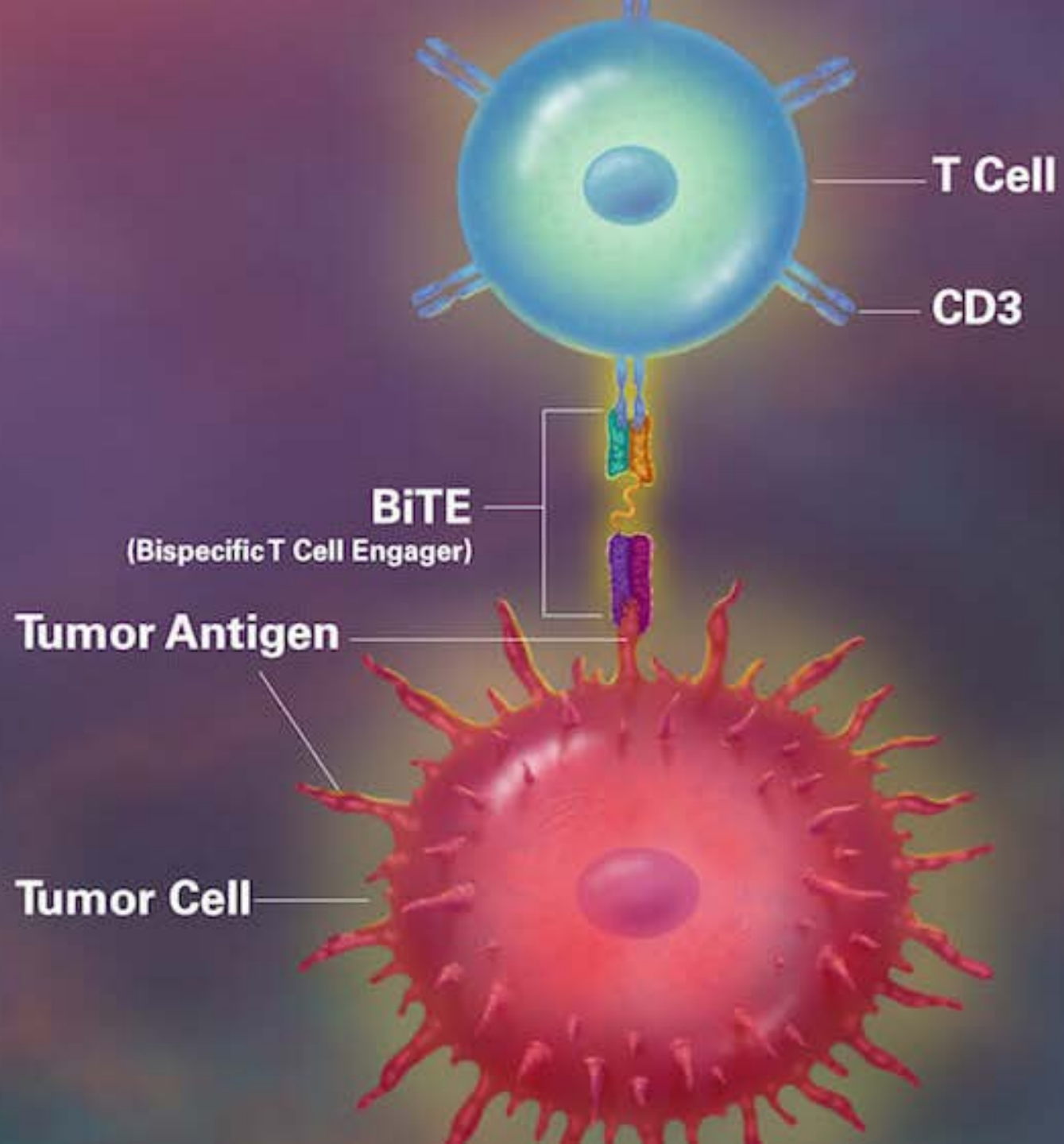




Pfizer and BioNTech Initiate Phase 1 Study of Single Dose mRNA-Based Combination Vaccine Candidate for Influenza and COVID-19

Thursday, November 03, 2022 - 06:45am





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