

Inducing HIV-1 bNAbs by vaccination

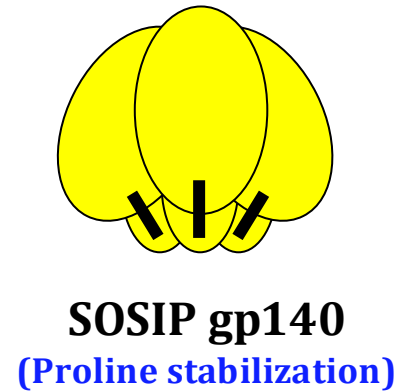
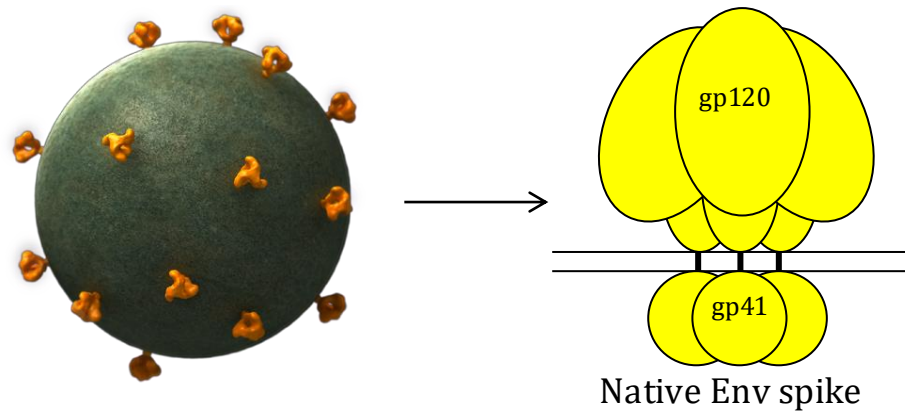
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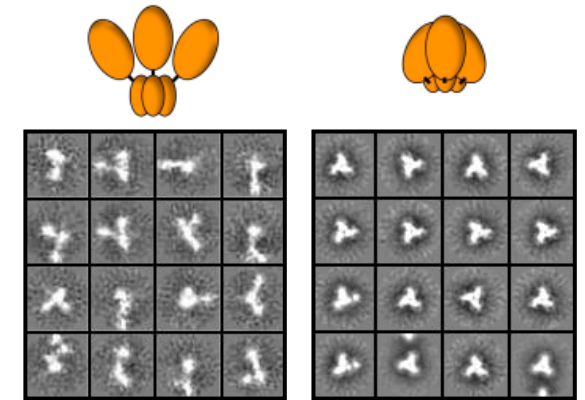
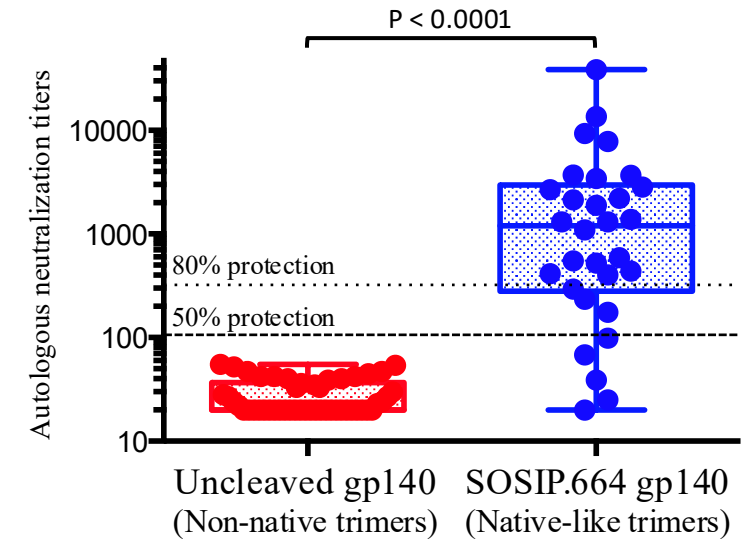
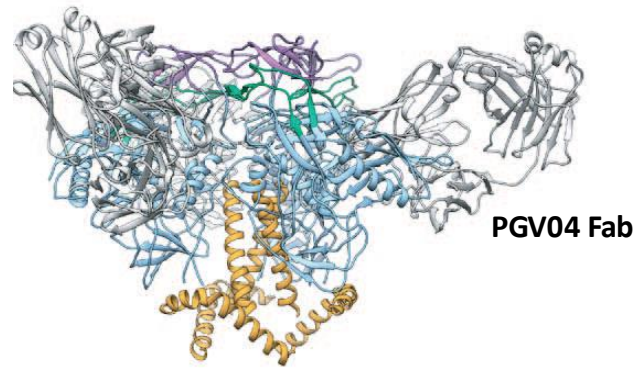
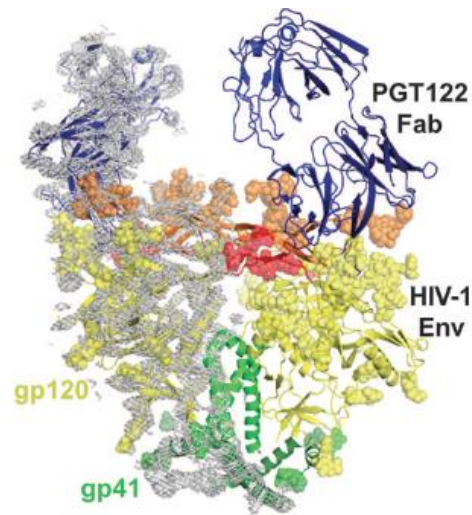
IAS webinar, March 26th, 2026



Stabilized envelope glycoprotein (SOSIP) trimers induce neutralizing antibodies (NAbs)



Sanders *et al.* 2002
J.Virol. **76**:8875-8889



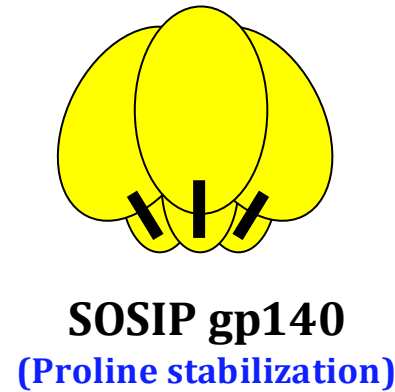
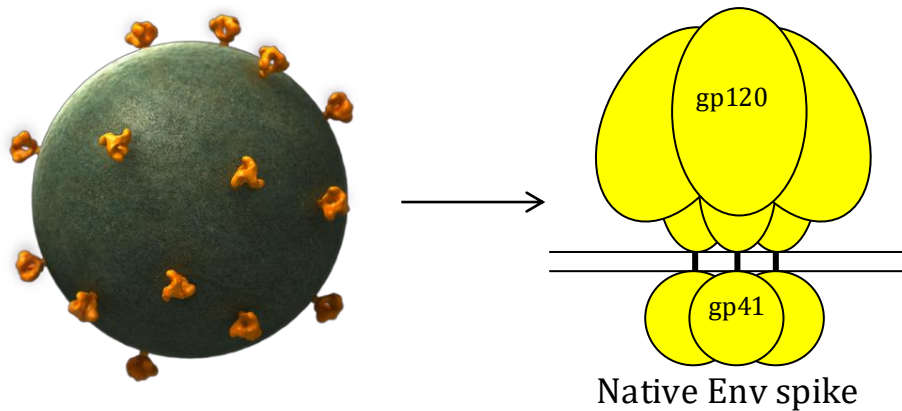
Sanders *et al.* 2015. *Science* **349**: aac4223

Julien *et al.* 2013.
Science **342**:1477-1483

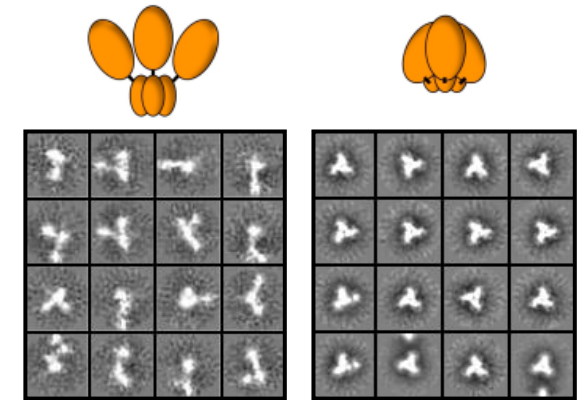
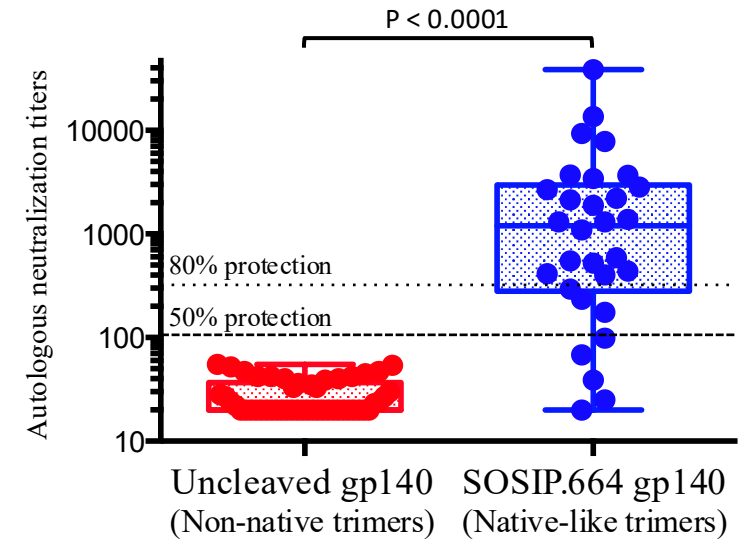
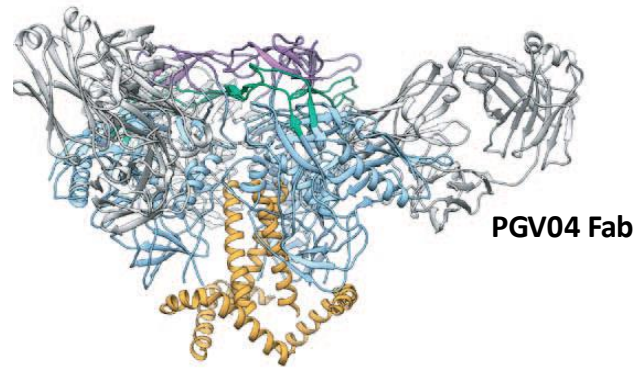
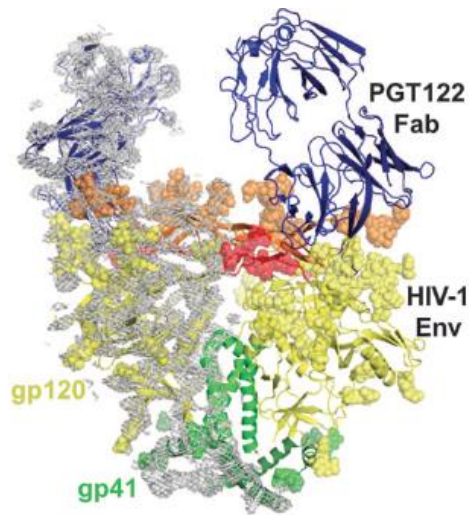
Lyumkis *et al.* 2013.
Science **342**:1484-1490

Sanders & Moore. 2014.
Nature **514**:437-438

Stabilized envelope glycoprotein (SOSIP) trimers induce neutralizing antibodies (NAbs), but not bNAbs



Sanders *et al.* 2002
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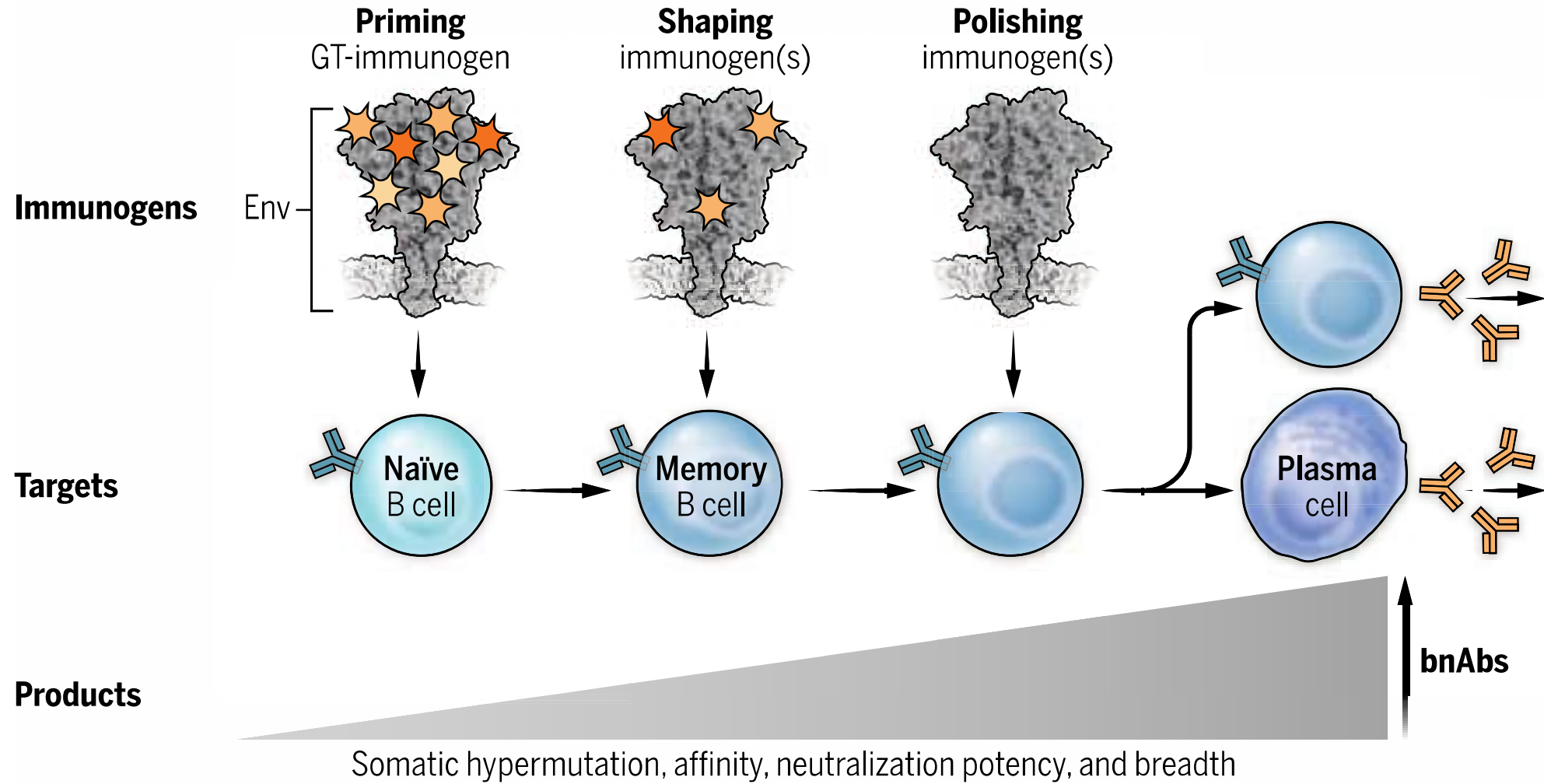
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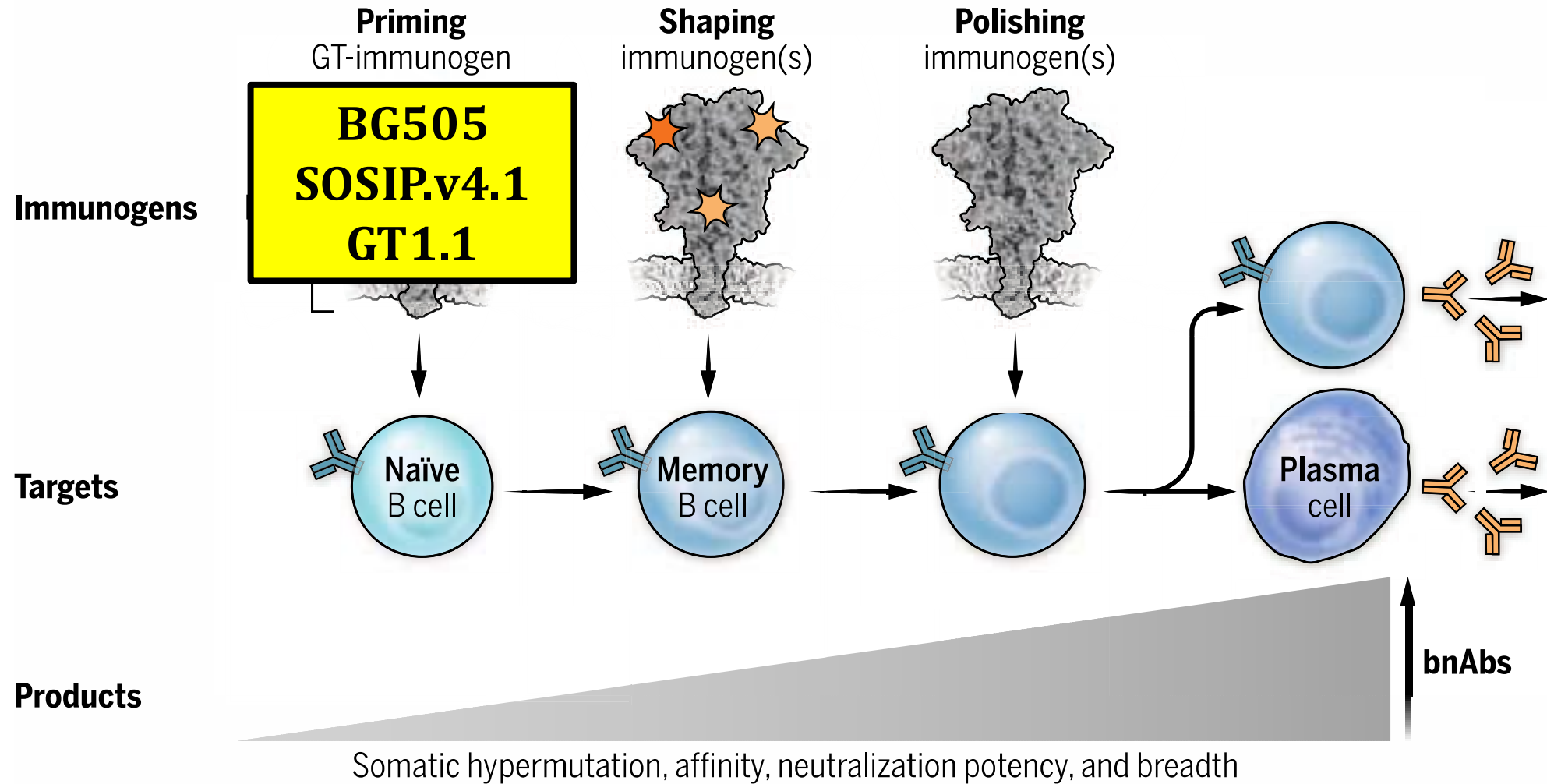
Sanders & Moore. 2014.
Nature **514**:437-438

Sequential vaccination to promote bNAb development



Sanders & Moore 2024, *Science* 384: 738-739

GT1.1 is a germline-targeting priming immunogen



Sanders & Moore 2024, *Science* 384: 738-739

Phase 1 First-in-human test of GT1.1: IAVI C101

		Months		
Group	N	0	2	6
A	20	30 µg BG505 GT1.1, AS01b	30 µg BG505 GT1.1, AS01b	30 µg BG505 GT1.1, AS01b
	4	placebo	placebo	placebo
B	19	300 µg BG505 GT1.1, AS01b	300 µg BG505 GT1.1, AS01b	300 µg BG505 GT1.1, AS01b
	4	placebo	placebo	placebo
TOTAL	47			

Multi-center, randomized, double-blinded, placebo-controlled, dose-escalation phase 1 clinical trial

PI: Marina Caskey, Rockefeller U (site PIs: David Diemert, GWU; Godelieve de Bree, AUMC)

Sponsor: IAVI; Funder: Bill&Melinda Gates Foundation

Fully enrolled, n=47 (LVLV: July 2023)

No Serious Adverse Events, all Adverse Events were mild to moderate



Gates Foundation



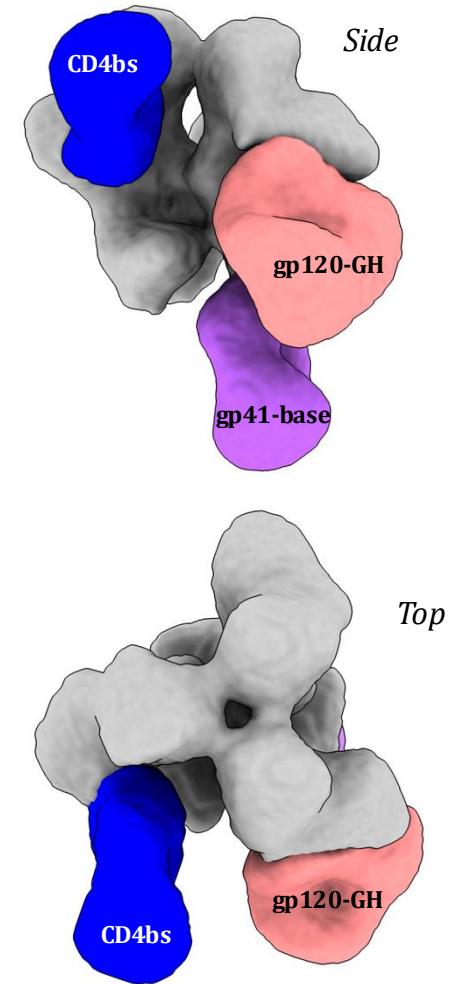
Phase 1 First-in-human test of GT1.1: Highlights

Serum responses

- All vaccine recipients developed detectable GT1.1-binding antibodies after two vaccinations (100% response rate)
- Most recipients developed a dominant CD4bs-directed response as detected by BAMA, signature neutralization and Electron Microscopy Polyclonal Epitope Mapping (EMPEM).

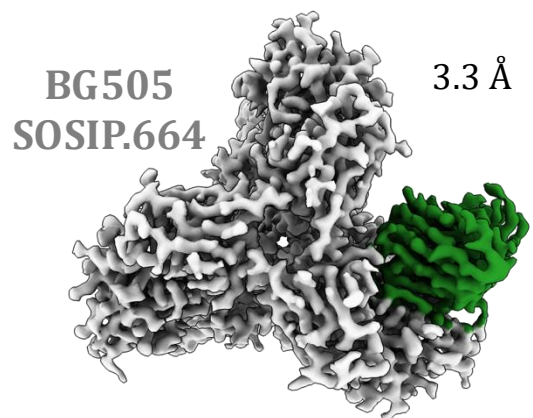
Memory B cell responses

- GT1.1-specific memory B cells constituted 1-10% of all memory B cells (frequency of **~1:30** in the high dose group)
- GT1.1 induced CD4bs-specific memory B cells (frequency of **~1:800** in the high dose group)
- GT1.1 induced VRC01-class memory B cells with VH1-2 and 5 aa CDRL3 (frequency of **~1:2,500** in the high dose group)
- VRC01-class BCRs/MAbs accumulated VRC01-class mutations and selected MAbs bound and neutralized fully glycosylated Env/virus, albeit weakly

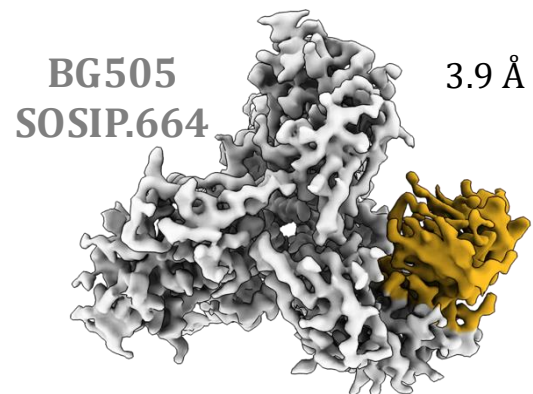


EMPEM analysis of individual SR47-59

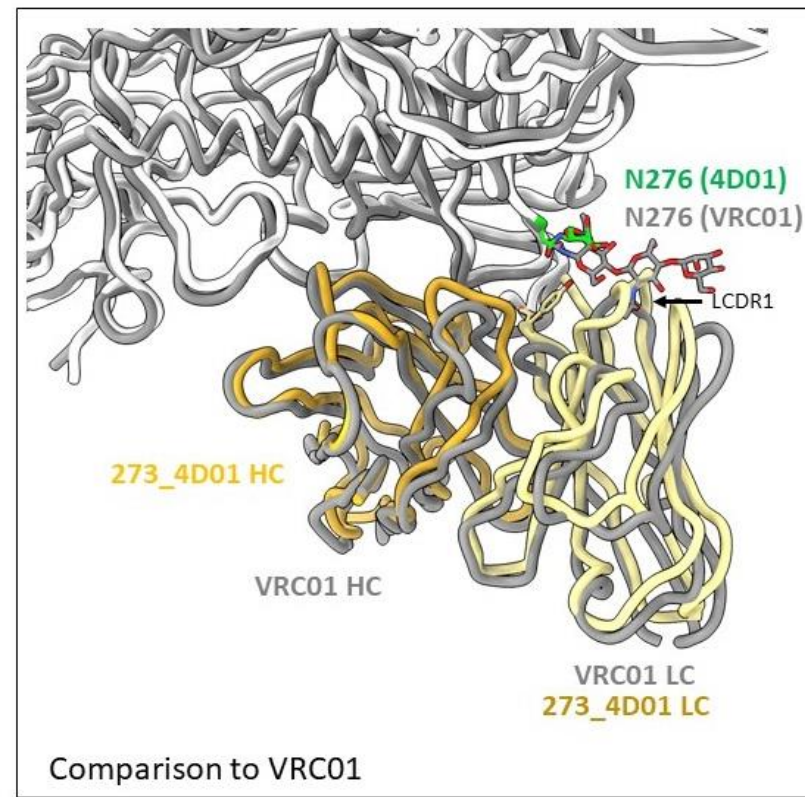
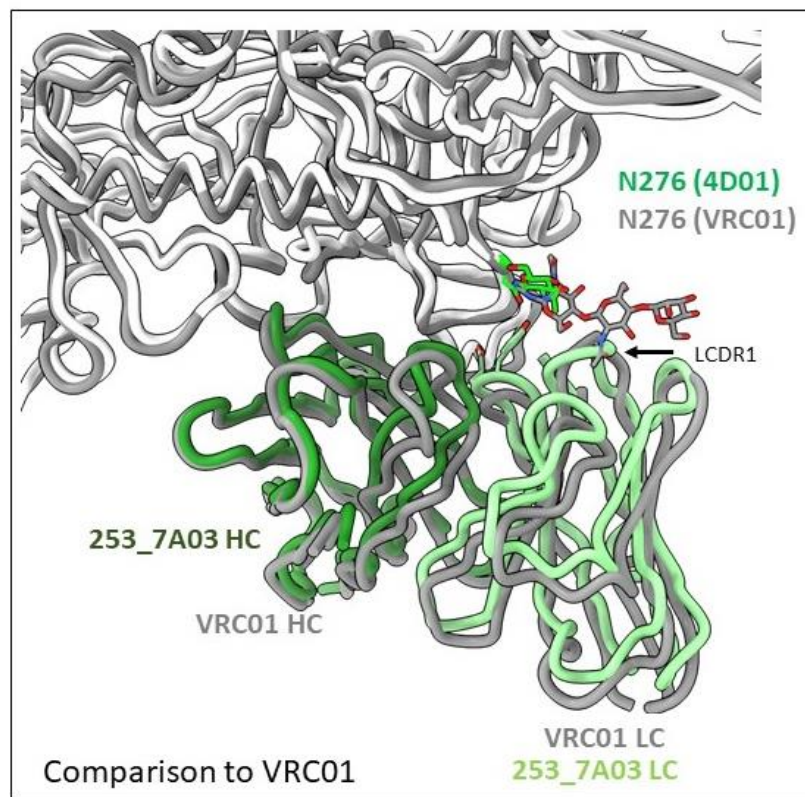
Structures of C101 MAbs are strikingly similar to that of bNAb VRC01



253_7A03
IGLV2-14

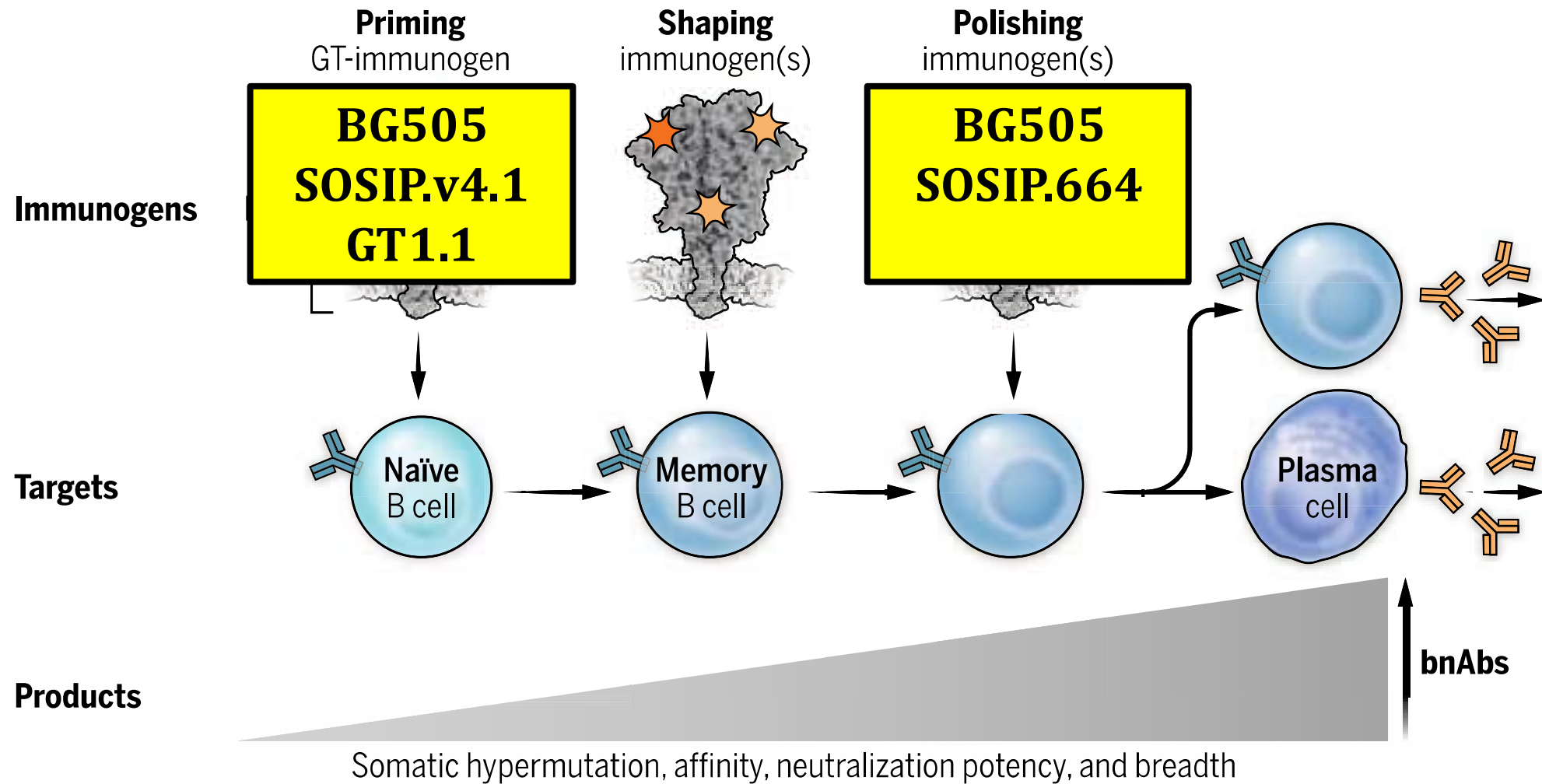


273_4D01
IGKV1-27



Gabe Ozorowski, Swastik Phulera, Andrew Ward

An opportunity-driven sequential study



Sanders & Moore 2024, *Science* 384: 738-739

Boosting GT1.1 recipients with WT Env trimer: IAVI C107&C110

		Months	
Trial	N	0	3
C107	9	100 µg BG505 SOSIP.664 3M-052-AF/Alum	100 µg BG505 SOSIP.664 3M-052-AF/Alum
C110	3	100 µg BG505 SOSIP.664 3M-052-AF/Alum	100 µg BG505 SOSIP.664 3M-052-AF/Alum
TOTAL	12		

C107&C110: Open label phase 1 clinical trials

PI: Marina Caskey, Rockefeller U (site PIs: David Diemert, GWU; Godelieve de Bree, AUMC)

Sponsor: IAVI; Funder: Bill&Melinda Gates Foundation

Fully enrolled, n=12 (LVLV: July 2025), n=10 received both vaccinations

No Serious Adverse Events, all Adverse Events were mild to moderate

Time gap between last (3rd) GT1.1 immunization and first BG505 SOSIP.664 immunization was ~1.5-2 years

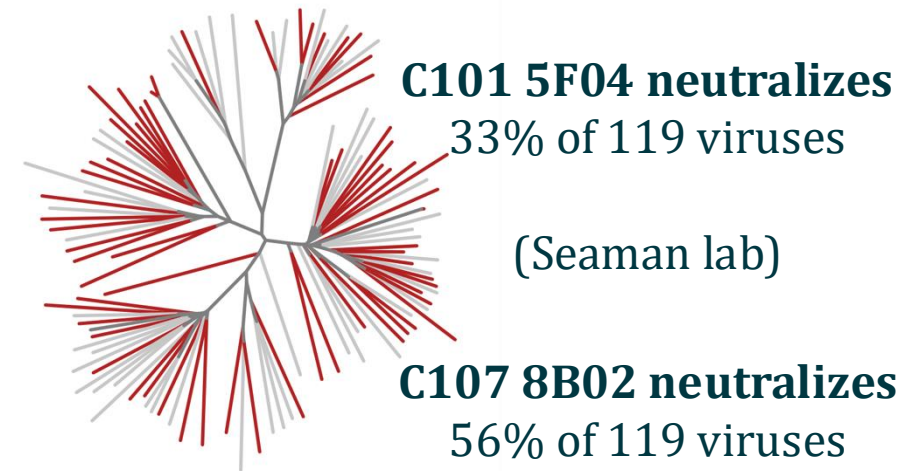
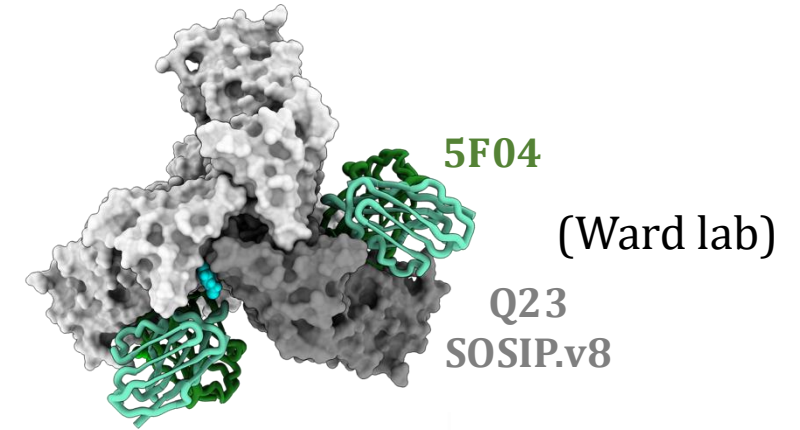


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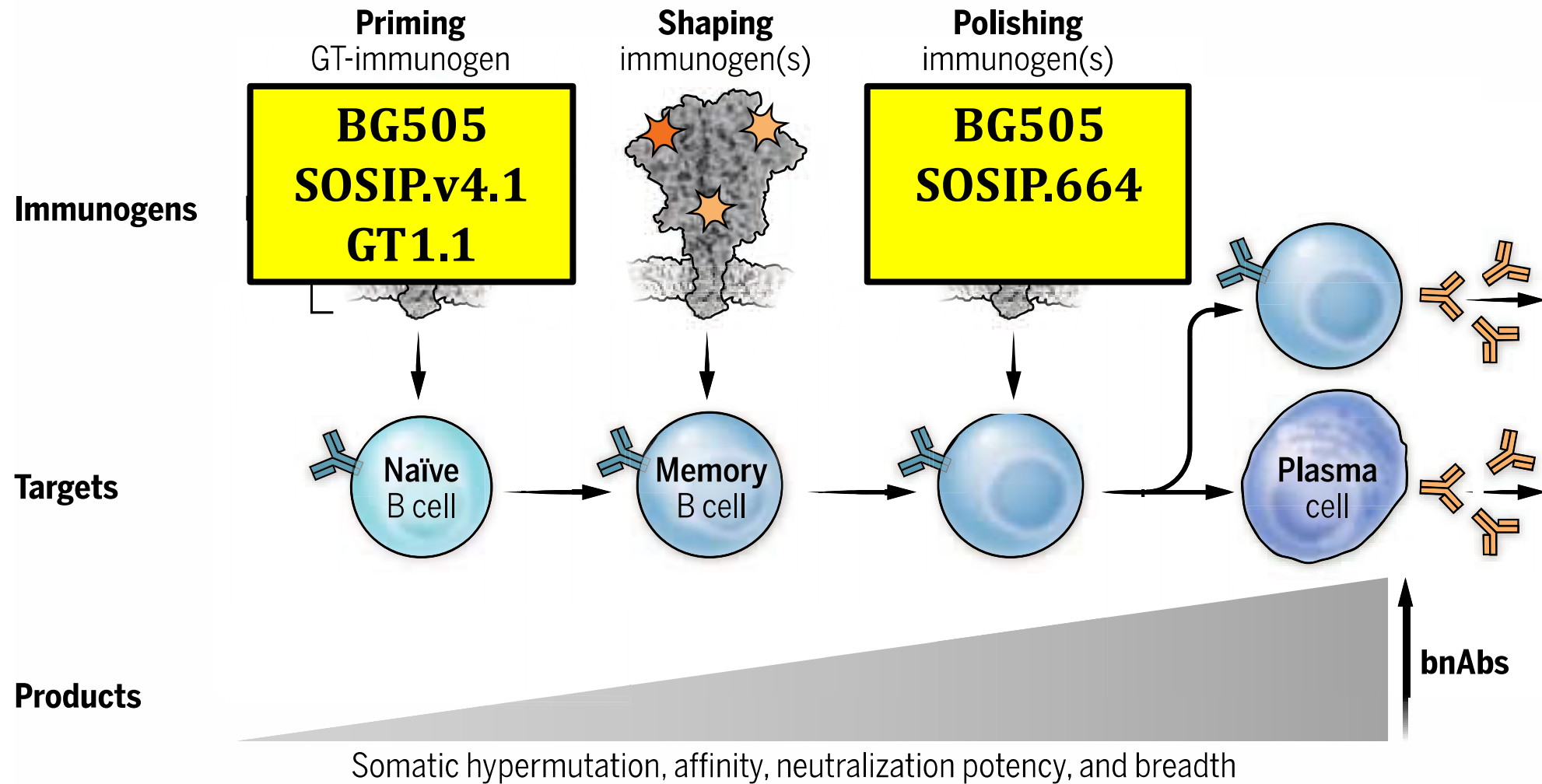


Boosting GT1.1 recipients with WT Env trimer: Highlights

- VRC01-class and other CD4bs-directed memory B cells remained in circulation 1.5-2 years after the last GT1.1 immunization and continued to acquire SHM
- VRC01-class and other CD4bs-directed memory B cells were efficiently engaged and activated by the booster vaccination
- VRC01-class and other CD4bs-directed memory B cells gained the ability to recognize fully glycosylated Env trimers and accommodate the N276 glycan
- VRC01-class other CD4bs-directed MAbs gained the ability to neutralize fully glycosylated virus, including heterologous viruses; some MAbs represent *bona fide* bNAbs (>50% breadth)
- **Proof-of-concept for inducing HIV-1 bNAbs by vaccination in humans**

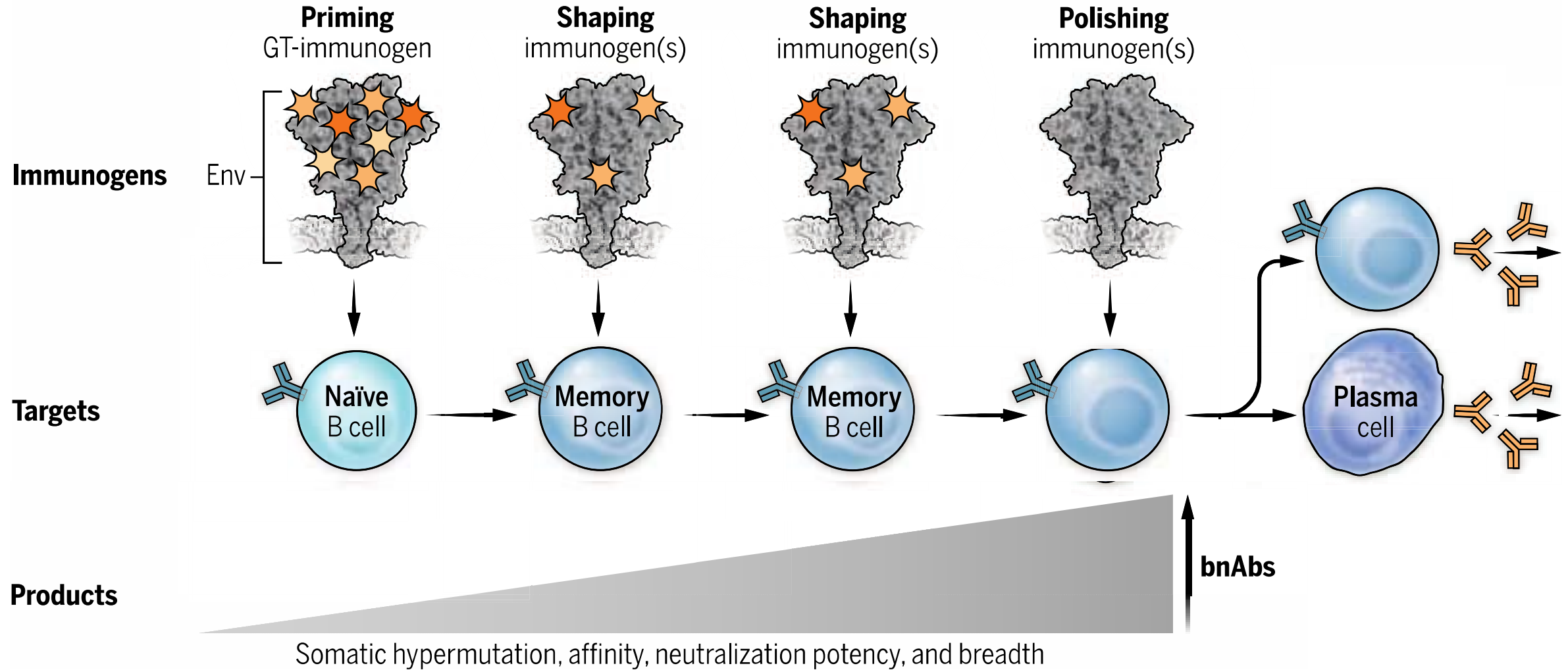


An opportunity-driven sequential study



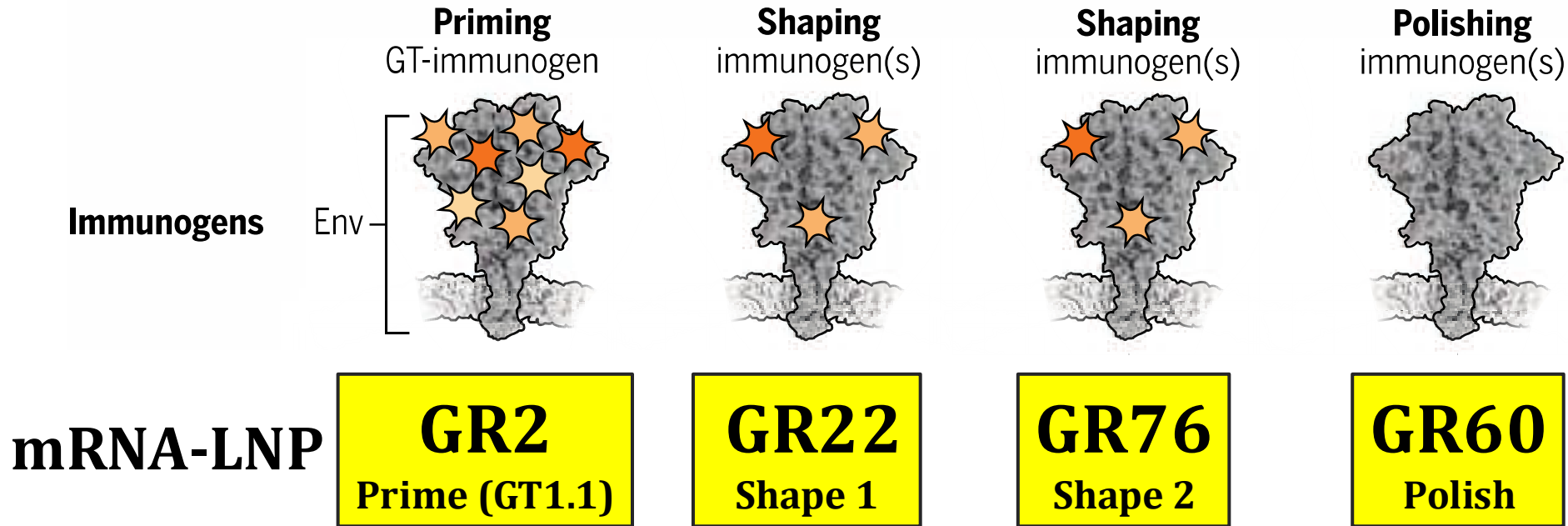
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A designed sequential study: BRILLIANT-002 (Q4 2026)



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A designed sequential study: BRILLIANT-002 (Q4 2026)



Title: A Randomized, Placebo-controlled Phase 1 Trial to Evaluate the Safety and Immunogenicity of Single versus two dose GT1.1 (GR2) mRNA Immunogen prime with shaping and polishing mRNA boost combinations in adults living without HIV (n=60).

Clinical lead: BRILLIANT Consortium, Desmond Tutu Health Foundation (DTHF), Wits Health Consortium

Analysis: University of Witwatersrand

Developer: Amsterdam UMC & Gates Medical Research Institute

Funder: Gates Foundation

Gates Foundation



Glenda Gray, Linda-Gail Bekker, Penny Moore, Nigel Garrett, Fatima Abrahams, Katekani Baloyi-Oseh *et al.*



GT1.1 IAVI C101/C107/C110 Roster

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