

# Progress toward eliciting bnAbs in humans

Bill Schief

VP, Protein Design, Moderna

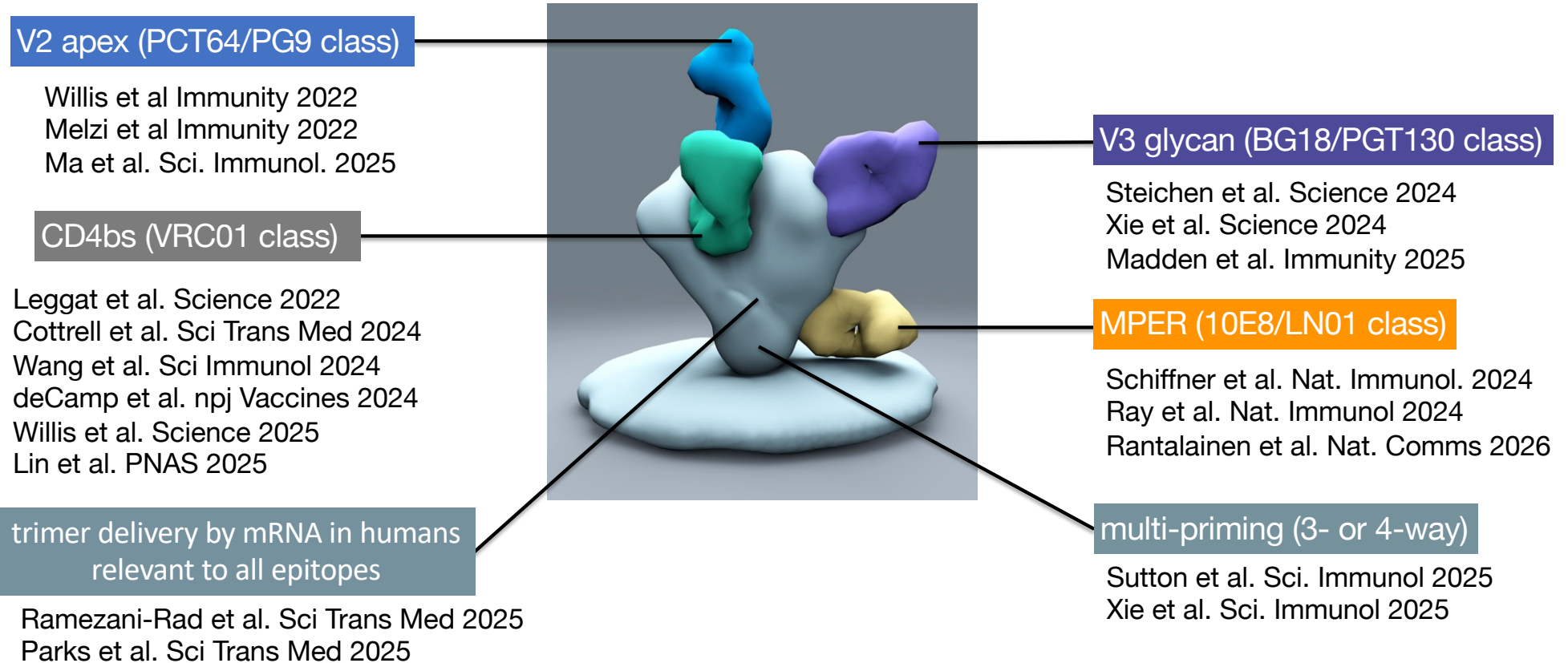
Professor, Immunology and Microbiology, Scripps

Executive Director, Vaccine Design, IAVI

IAS webinar

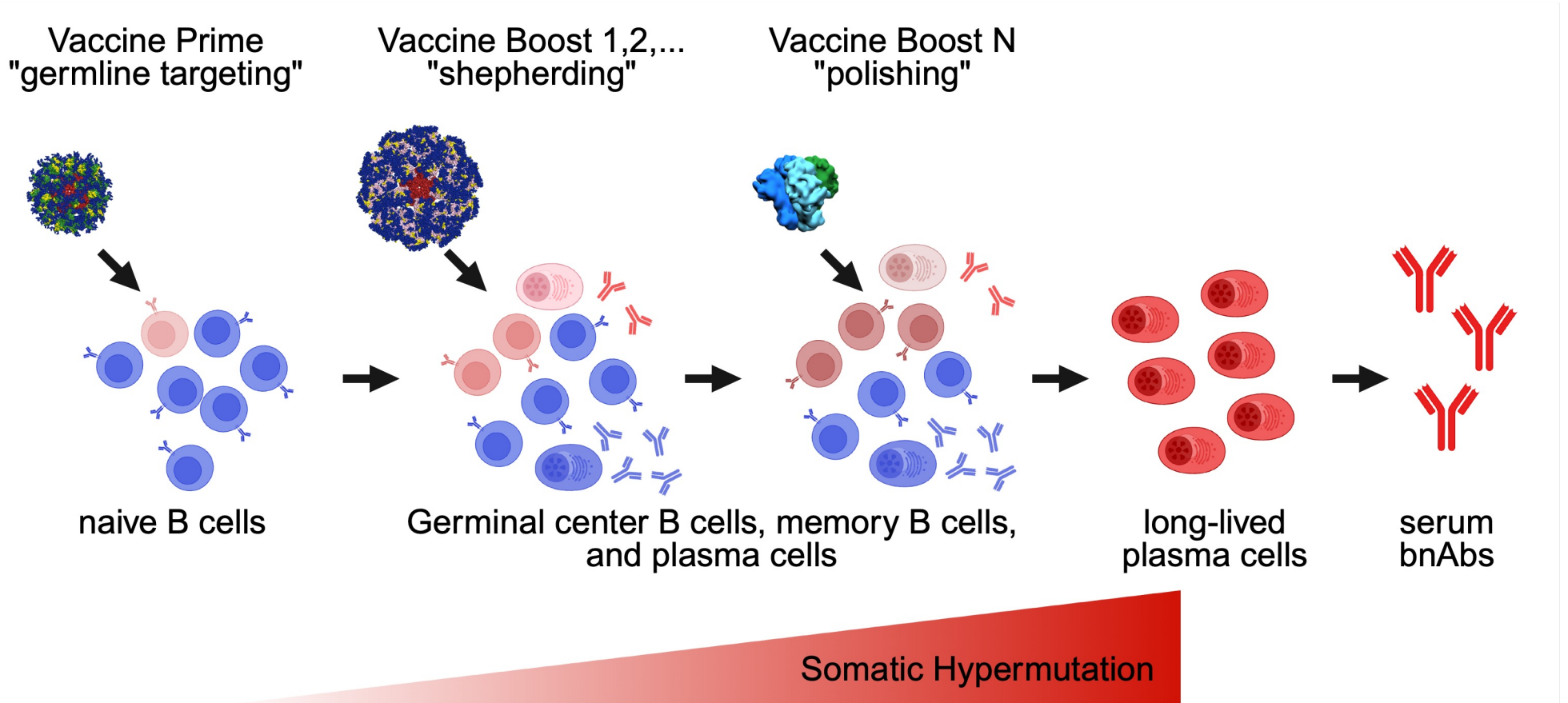
26Mar2026

# We are working to build a multi-bnAb vaccine regimen for high breadth and potency



selected publications from our collaborations

# Strategy to induce bnAbs: Germline-targeting vaccine design

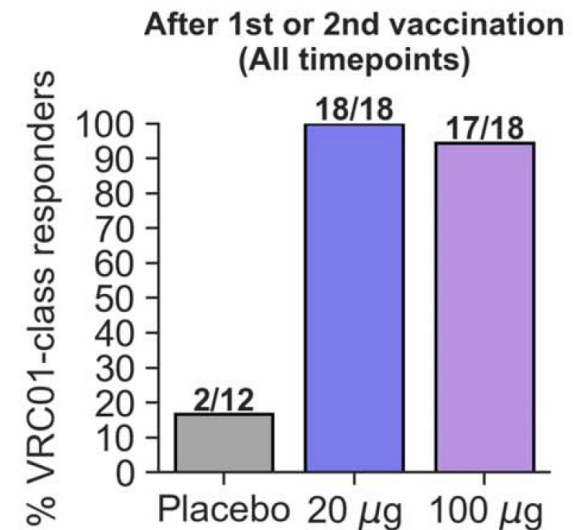
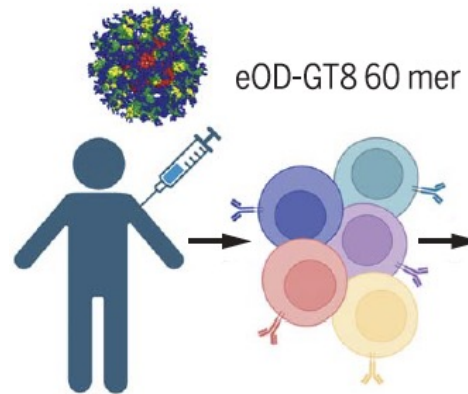


# Proof of concept for GT priming: eOD-GT8 60mer induced VRC01-class precursors in 97% of vaccine recipients in the IAVI G001 clinical trial

## HIV CLINICAL TRIALS

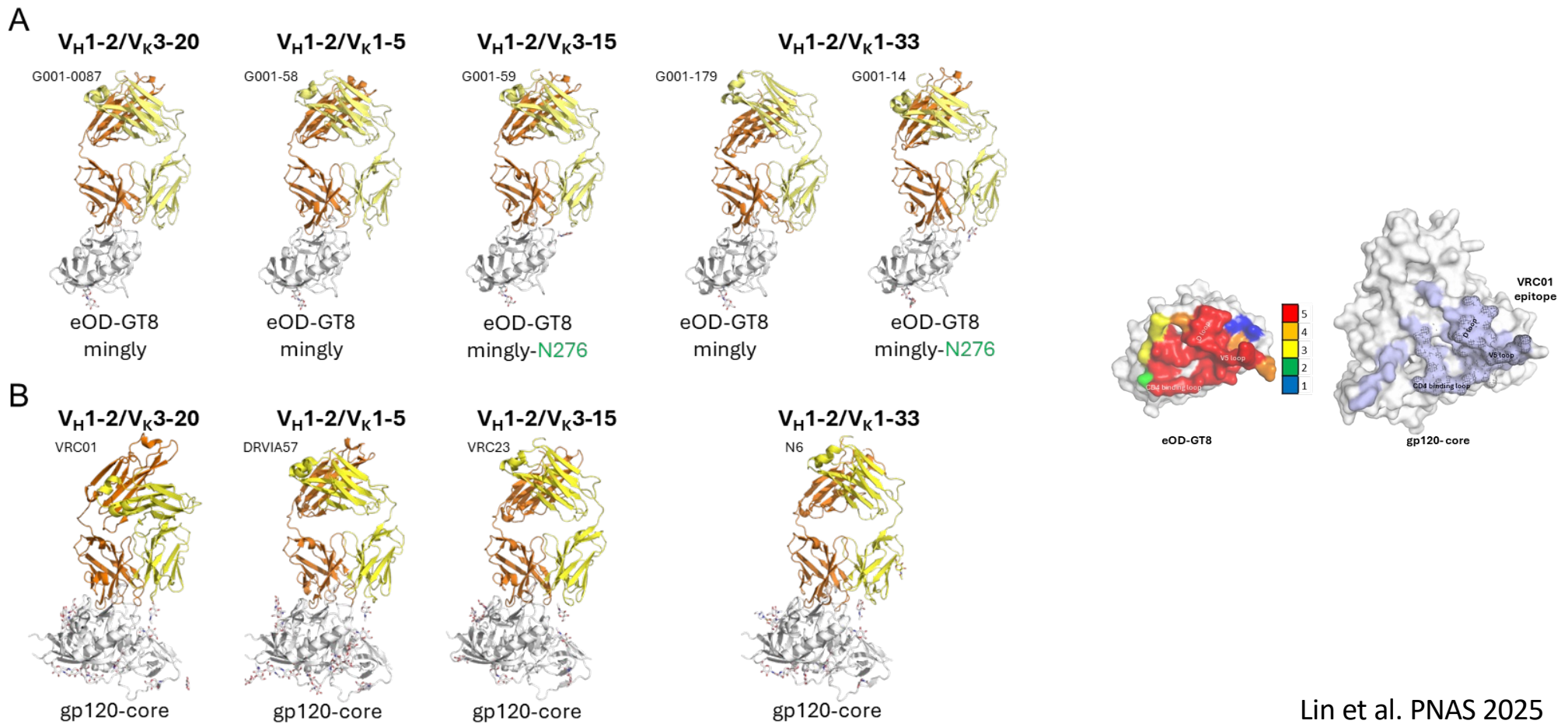
### Vaccination induces HIV broadly neutralizing antibody precursors in humans

David J. Leggat<sup>1†‡</sup>, Kristen W. Cohen<sup>2†</sup>, Jordan R. Willis<sup>3,4,5†</sup>, William J. Fulp<sup>2†</sup>, Allan C. deCamp<sup>2†</sup>, Oleksandr Kalyuzhnyi<sup>3,4,5</sup>, Christopher A. Cottrell<sup>3,4,5</sup>, Sergey Menis<sup>3,4,5</sup>, Greg Finak<sup>2</sup>, Lamar Ballweber-Fleming<sup>2</sup>, Abhinaya Srikanth<sup>1§</sup>, Jason R. Plyler<sup>1</sup>, Torben Schiffner<sup>3,4,5¶</sup>, Alessia Liguori<sup>3,4,5</sup>, Farhad Rahaman<sup>6</sup>, Angela Lombardo<sup>6</sup>, Vincent Philiponis<sup>6</sup>, Rachael E. Whaley<sup>2</sup>, Aaron Seese<sup>2</sup>, Joshua Brand<sup>1#</sup>, Alexis M. Ruppel<sup>1</sup>, Wesley Hoyland<sup>1</sup>, Nicole L. Yates<sup>7</sup>, LaTonya D. Williams<sup>7</sup>, Kelli Greene<sup>8</sup>, Hongmei Gao<sup>8</sup>, Celia R. Mahoney<sup>2</sup>, Martin M. Corcoran<sup>9</sup>, Alberto Cagigi<sup>1</sup>, Alison Taylor<sup>1</sup>, David M. Brown<sup>10</sup>, David R. Ambrozak<sup>1</sup>, Troy Sincomb<sup>3,4,5</sup>, Xiaozhen Hu<sup>3,4,5</sup>, Ryan Tingle<sup>3,4,5</sup>, Erik Georgeson<sup>3,4,5</sup>, Saman Eskandarzadeh<sup>3,4,5</sup>, Nushin Alavi<sup>3,4,5</sup>, Danny Lu<sup>3,4,5</sup>, Tina-Marie Mullen<sup>3,4,5</sup>, Michael Kubitz<sup>3,4,5</sup>, Bettina Groschel<sup>3,4,5</sup>, Janine Maenza<sup>2,11</sup>, Orpheus Kolokythas<sup>12</sup>, Nadia Khati<sup>13</sup>, Jeffrey Bethony<sup>14</sup>, Shane Crotty<sup>4,15,16</sup>, Mario Roederer<sup>1</sup>, Gunilla B. Karlsson Hedestam<sup>9</sup>, Georgia D. Tomaras<sup>7</sup>, David Montefiori<sup>8</sup>, David Diemert<sup>14,17</sup>, Richard A. Koup<sup>1</sup>, Dagna S. Laufer<sup>6</sup>, M. Juliana McElrath<sup>2,11\*</sup>, Adrian B. McDermott<sup>1\*†‡</sup>, William R. Schief<sup>3,4,5,18\*</sup>



Leggat *et al.*, Science, December 2022

# VRC01-class mAbs elicited in G001 bind CD4bs with same angle of approach as bnAbs

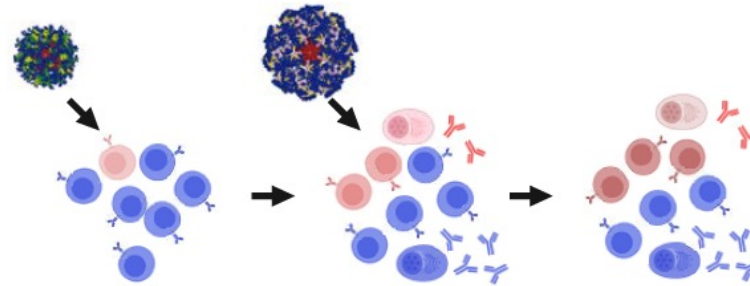


# Now building on the successful prime+boost1 in IAVI G002 and successful priming in Africa in IAVI G003

Two phase 1 clinical trials testing first steps in the strategy with mRNA

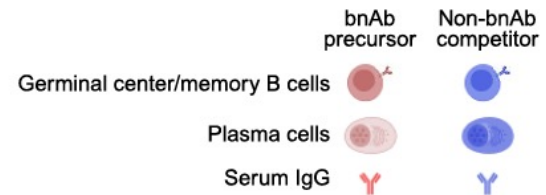
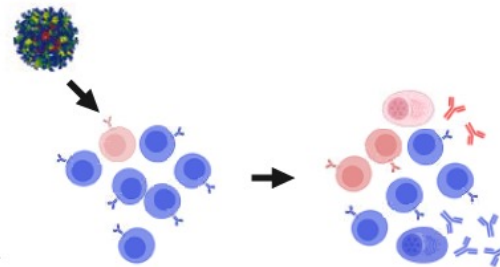
**IAVI G002**

United States



**IAVI G003**

Rwanda & South Africa



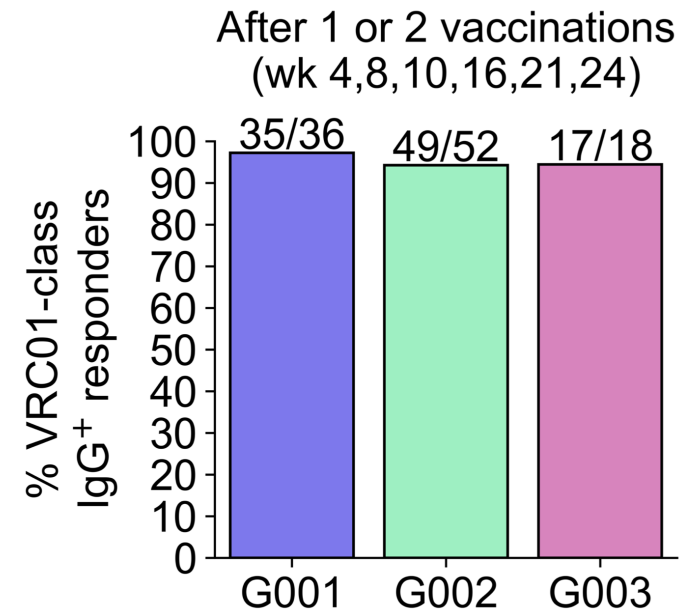
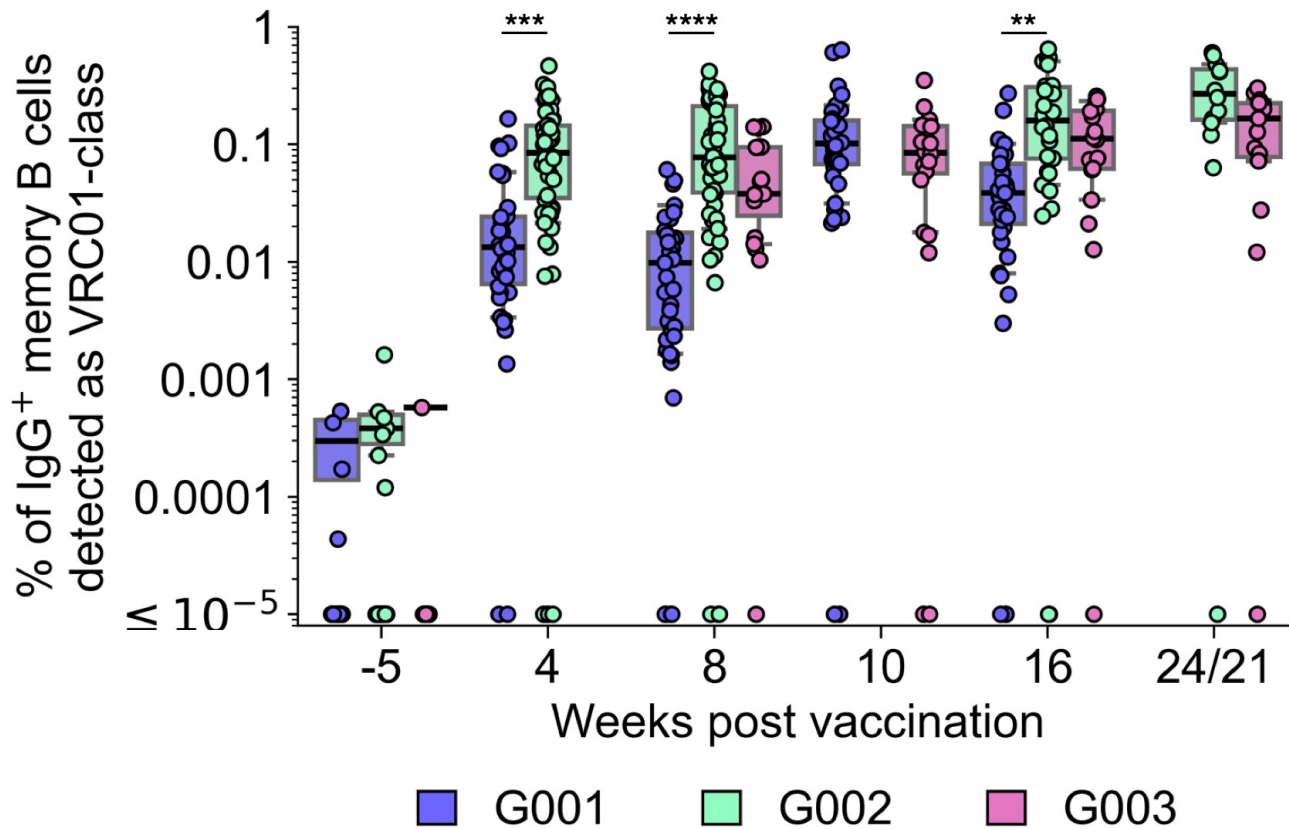
CLINICAL TRIALS

Science 31 JULY 2025

## Vaccination with mRNA-encoded nanoparticles drives early maturation of HIV bnAb precursors in humans

Jordan R. Willis†, Madhu Prabhakaran†, Michelle Muthui†, Ansuya Naidoo†, Troy Sincomb†, Weiwei Wu†, Christopher A. Cottrell†, Elise Landais†, Allan C. deCamp†, *et al.*

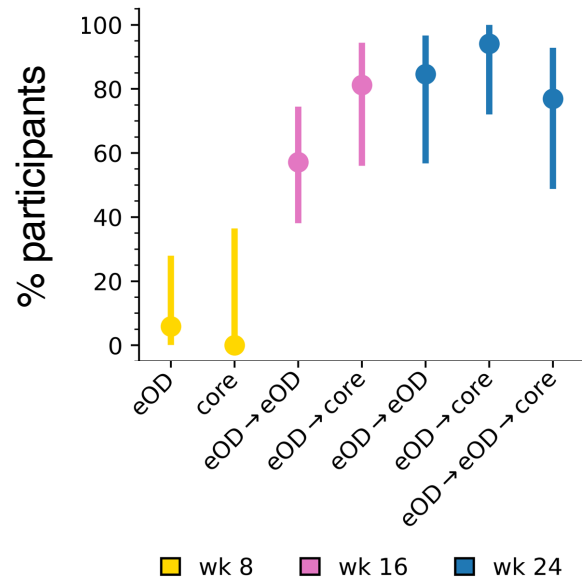
# eOD-GT8 60mer mRNA-LNP primed VRC01-class responses to high frequencies in 94% of vaccinees in IAVI G002 (US) and G003 (Africa)



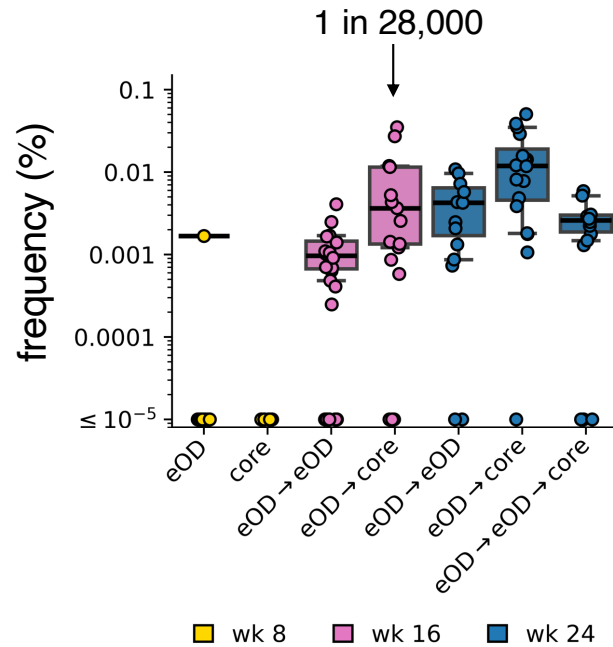
Non-responders all have non-permissive VH1-2 genotype

# Robust vaccine induction of maturation toward bnAb in humans: “Elite” VRC01-class B cells with $\geq 5$ key residues, corresponding to Abs with neutralizing activity, were detected in most participants and had high frequencies and high polyclonality

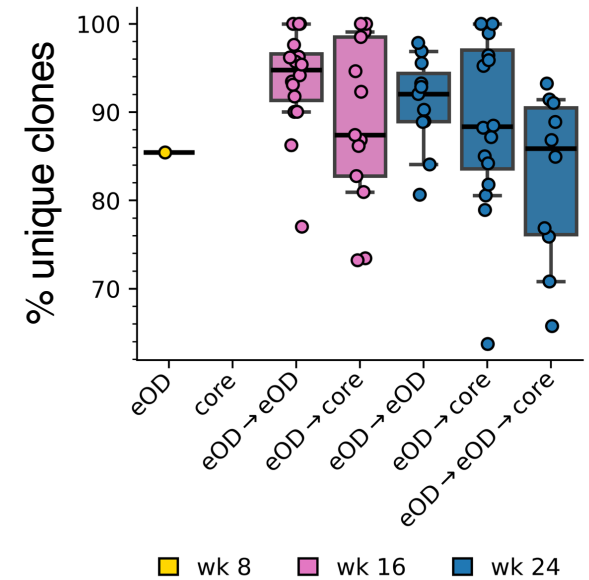
% participants with elite VRC01-class



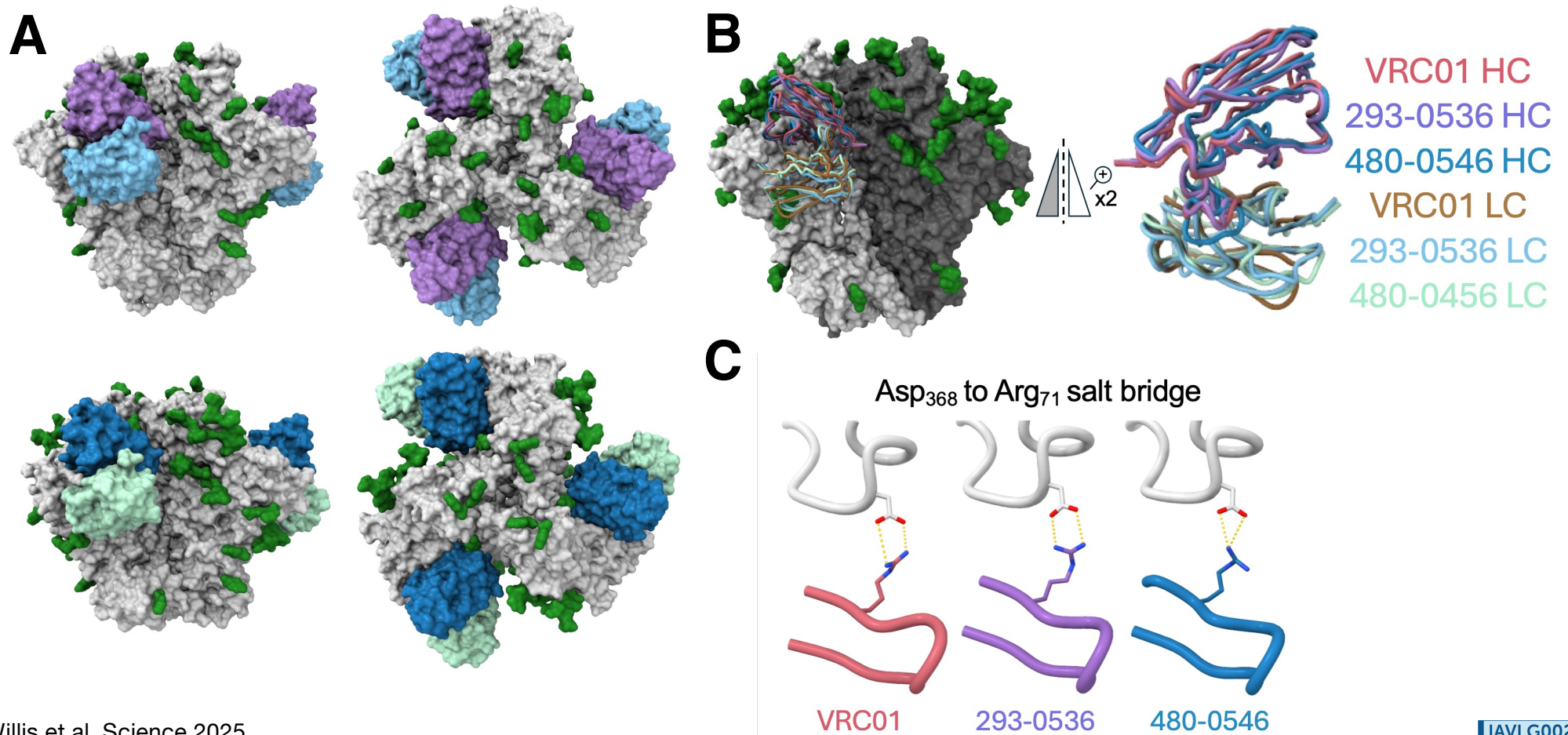
elite frequency in IgG memory B cells



elite polyclonality



# CryoEM shows that VRC01-class BCRs elicited by eOD→core bind trimer with VRC01-class binding mode



## Conclusions from IAVI G002+G003:

- ❖ The immunological results establish clinical proof of concept that heterologous boosting can advance bnAb precursor maturation; demonstrate bnAb priming in Africa, where the HIV burden is greatest; and encourage development of additional boosters to induce bnAbs.
- ❖ The high rate of urticaria in IAVI G002 compared with clinical studies of non-HIV mRNA vaccines suggested a role for the HIV antigens expressed by mRNA, which will require further investigation and mitigation in future studies.

## Current and next steps:

- ❖ IAVI G004 testing lower dose prime-boost regimen from G002 currently ongoing in So.Africa. Also testing BG18-class priming immunogen. All as Moderna mRNA.
- ❖ If safety and immuno from IAVI G004 are acceptable, we aim to conduct a follow on study attempting to induce bnAbs with a full boosting regimen
- ❖ Pre-clinical studies ongoing to finalize bnAb-inducing sequential boosting regimens



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National Institutes of Health



HIV VACCINE TRIALS NETWORK



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As of November 2022



# IAVI G002 & G003 Acknowledgments — People

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IAVI G002

IAVI G003