

# Duke CHAVD Clinical Trials: Results and Plans

**Barton Haynes, MD for the CHAVD SLG  
IAS Meeting  
March 26<sup>th</sup>, 2026**

# Discovery Medicine Clinical Trials Testing Different Vaccine Designs And Concepts

## Platform/Adjuvant focused

- HVTN 137 (BG505 Tr + Adj Comp)
- HVTN 302 (BG505 MD39.3 Tr soluble<sup>^</sup>mb<sup>^</sup>CD4KO mRNA)
- HVTN 304 (DNA NLT-AB05 => Tr 4571 + 3M-052-AF/AI)
- HVTN 318 (CD40.HIVRI.Env + Hiltonol) in ex-Mosaico ppts

## CD4bs

### CH103 lineage

- \* HVTN 115 (CH505TF & Sq gp120 + GLA-SE)
- \* HVTN 135 (CH505 TF + GLA-SE) - **infant**
- \* HVTN 300 (CH505TF Tr + 3M-052-AF ± AI)

### VRC01 lineage

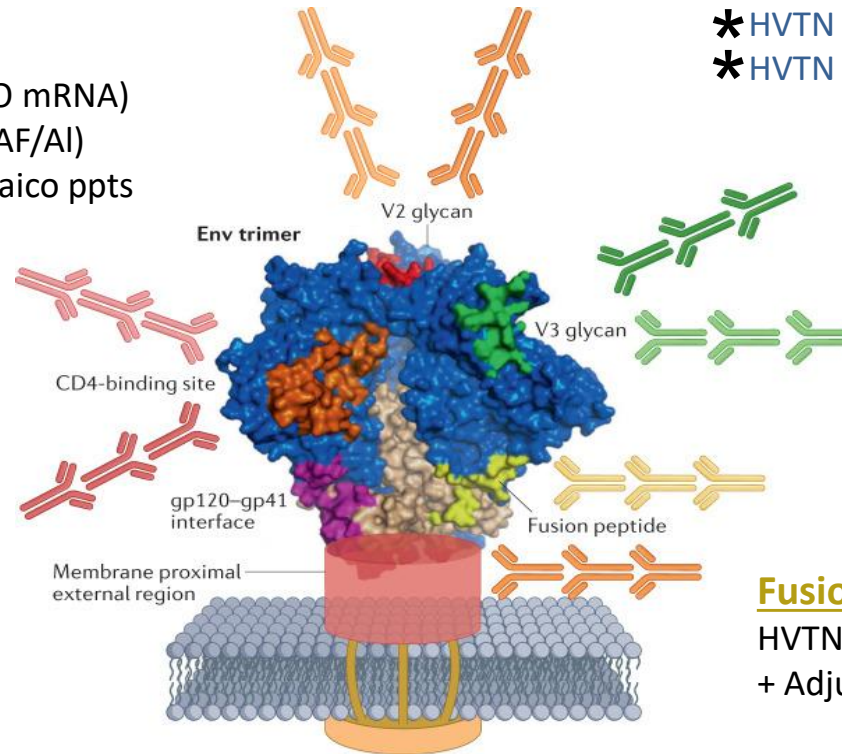
- HVTN 301 (426c NP/GT1.1 + 3M-052-AF/AI)
- HVTN 320 (426c NP/HxB2 +3M-052-AF/AI)
- HVTN 325 (426c NP/HxB2/ConM + SMNP)
- HVTN 807 (426c NP + 3M-052-AF/AI) - **PLWH ATI**
- HVTN 316 (426c NP + 3M-052-AF/AI) - **infant**
- HVTN 305 (DNA GT8 + IL12=>Tr 4571 + 3M-052-AF/AI)

### CH235 lineage

- \* HVTN 312 (CH505M5/CH505TF/CH505w24 mRNA-gp160)
- \* HVTN 324 (DV901/DV902 Sortase Fe-NP + eLNP =>

### Lineage Agnostic

- HVTN 313 (Ad4-Env145NFL & NFLΔGly4 Tr/Tr 4571 + 3M-052-AF/AI)
- HVTN 319 (BG505 UFO-NP + 3M-052-AF/AI)
- HVTN 310 (Lusso mRNA)



## V2 Apex

- \* HVTN 322 (DV201P/DV202B1 mRNA)
- \* HVTN 326 (DV200P-protein NP/DV202B1 mRNA)

## V3 glycan

### DH270 lineage

- \* HVTN 307 (CH848 Fe-NP + eLNP<sup>^</sup>3M052-AF/AI => CH848-Tr2/DV702B2 mRNA)

### BG18-like lineage

- HVTN 144 (N332-GT5 + SMNP)

### Multiple lineages

- \* HVTN 321 (DV700P/DV701B1 mRNA)
- \* HVTN 808 (DV700P/DV701B1 mRNA) - **PLWH ATI**

## Fusion peptide

- HVTN 303 (Fusion Peptide/Trimer 4571/Trimer 6931 + Adjuvlex)

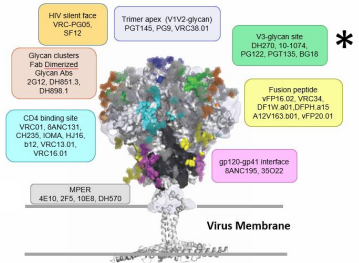
## MPER

- \* HVTN 133 (gp41 MPER Liposome/AI)
- \* HVTN 3XX (gp41 MPER non-PEG Liposome/AI)

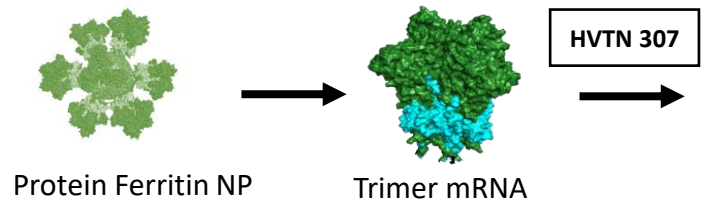
## Mixed Epitope

- \* HVTN 809 (mRNAs -V2 Apex, V3 Glycan & mAbs – VRC07-523, PGT121, PGDM1400 -LS) - **PLWH ATI**

# Duke CHAVD V3-glycan BnAb Preventive HIV Vaccine Portfolio



V3-Glycan

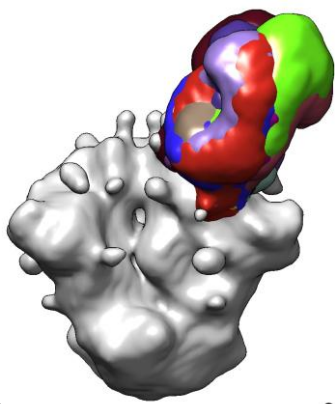


HVTN 307- complete;

- Induced V3-glycan, N332-dependent precursors in 12/14 vaccinees
- After boost #1, isolated the same N332-dependent clones previously primed in 6/14 vaccinees.



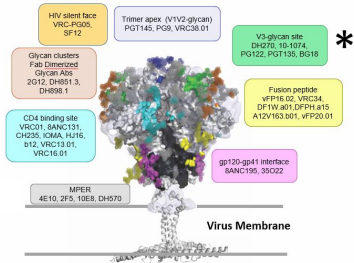
Kevin Saunders Chen-Hao Yeh Daniel Wrapp Davd Montefiori



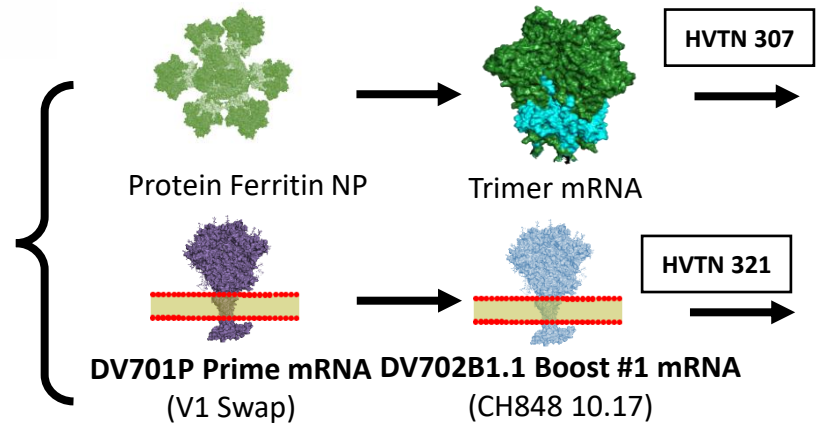
Composite negative stained electron micrograph of 12 different vaccine-induced V3-glycan precursors with the N332, GDIR signature (HCDR3s 20-26 aas)

20 Å

# Duke CHAVD V3-glycan BnAb Preventive HIV Vaccine Portfolio



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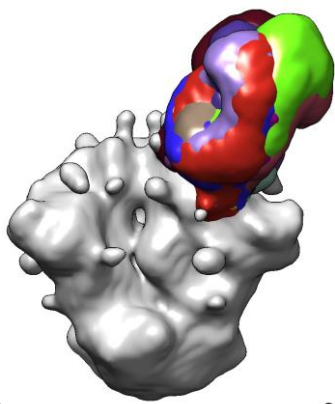
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**HVTN 321- ongoing; designed to induce BG18, DH270 and BF520 types of V3-glycan Abs**



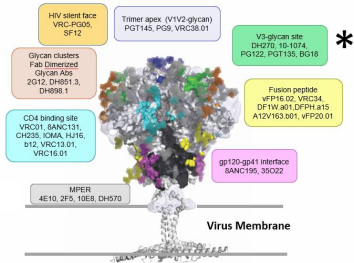
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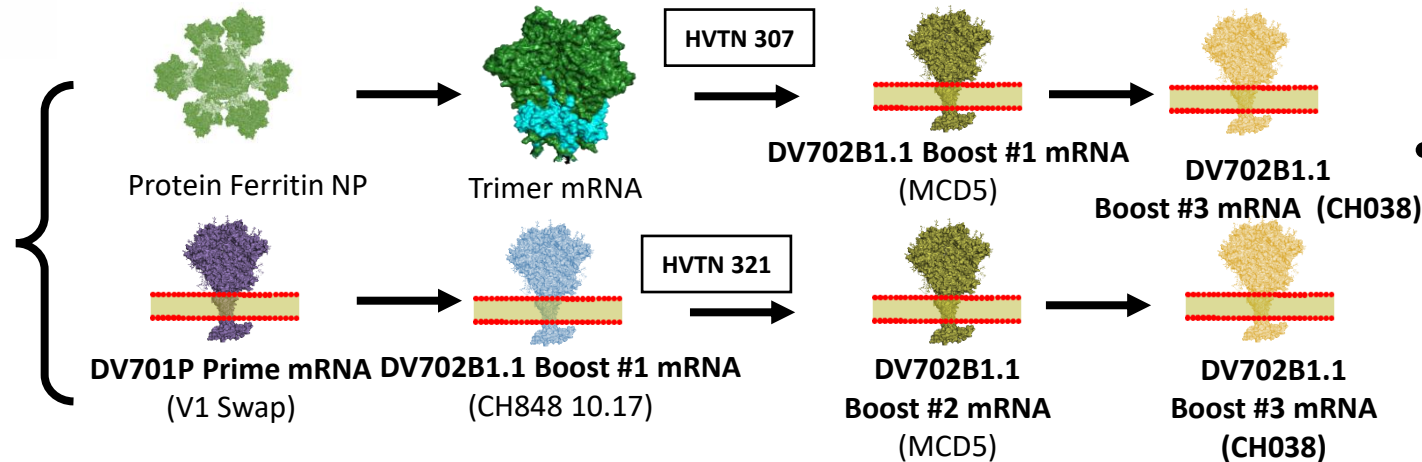
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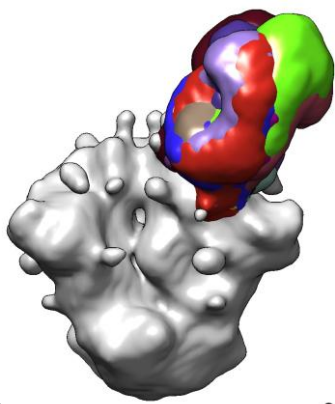
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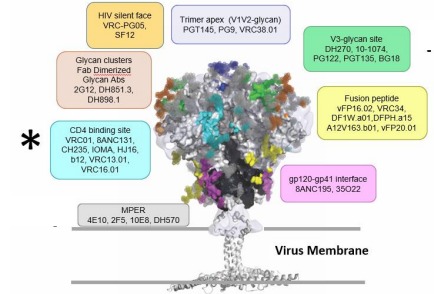
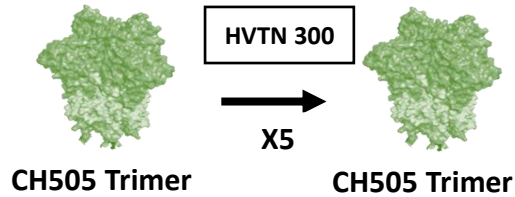


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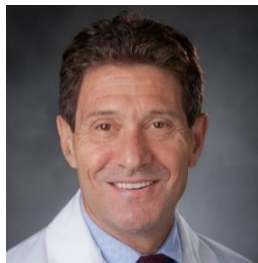
# Duke CD4 Binding Site BnAb CHAVD Preventive HIV Vaccine Portfolio

CD4bs



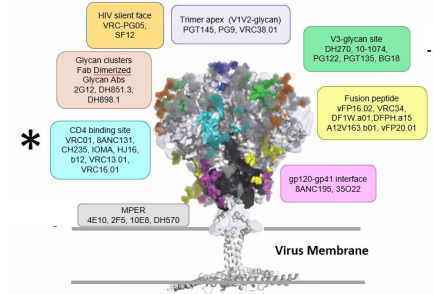
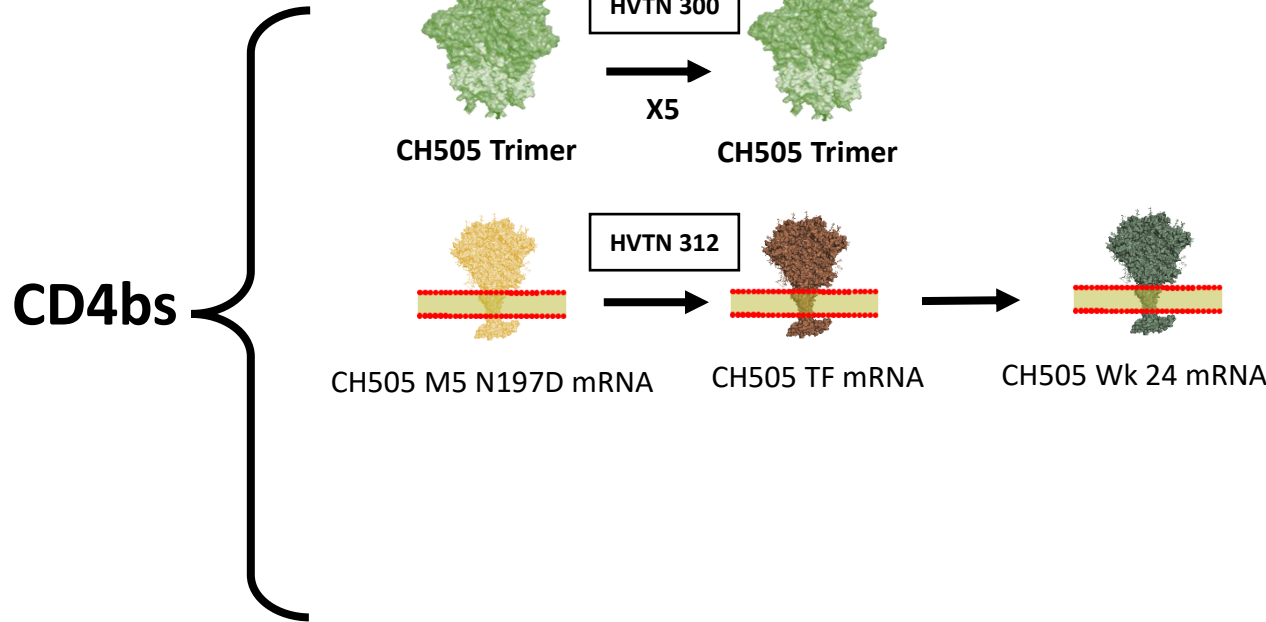
## HVTN 300- Complete

- Induced HCDR3-binder CD4bs precursors in 8/11 vaccinees
- Induced serum CH505 autologous nAbs in 9/11; and isolated heterologous nAb 1/11 (VH4-59, Vκ3-20)



David Montefiori Kevin Saunders Drew Weissman

# Duke CD4 Binding Site BnAb CHAVD Preventive HIV Vaccine Portfolio

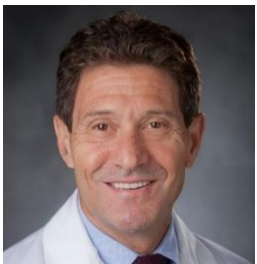


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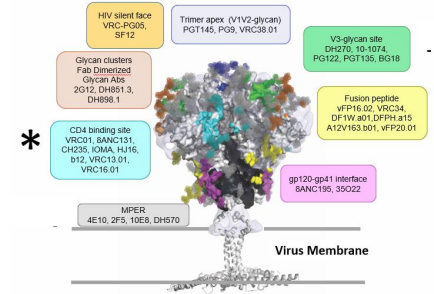
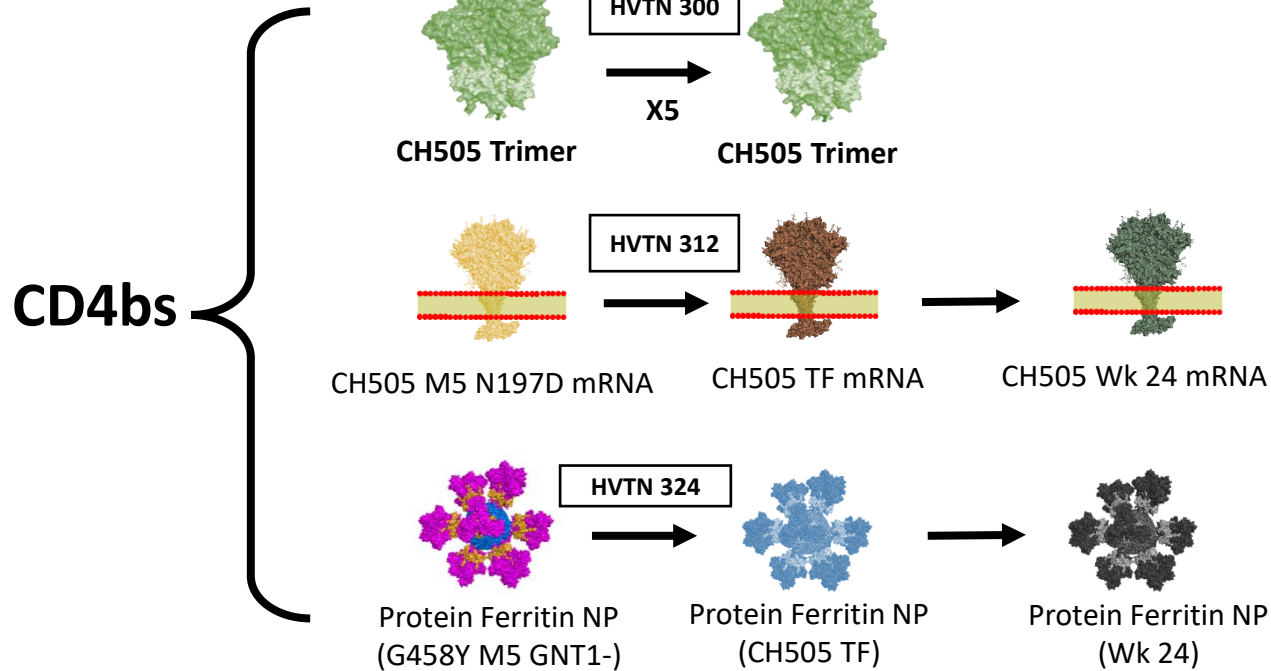
## HVTN 312- VH1-46-class of CD4 mimicking CD4bs bnAbs-Ongoing

HVTN 324- VH1-46-class of CD4 mimicking CD4bs bnAbs- October



David Montefiori Kevin Saunders Drew Weissman

# Duke CD4 Binding Site BnAb CHAVD Preventive HIV Vaccine Portfolio

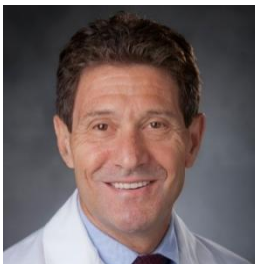


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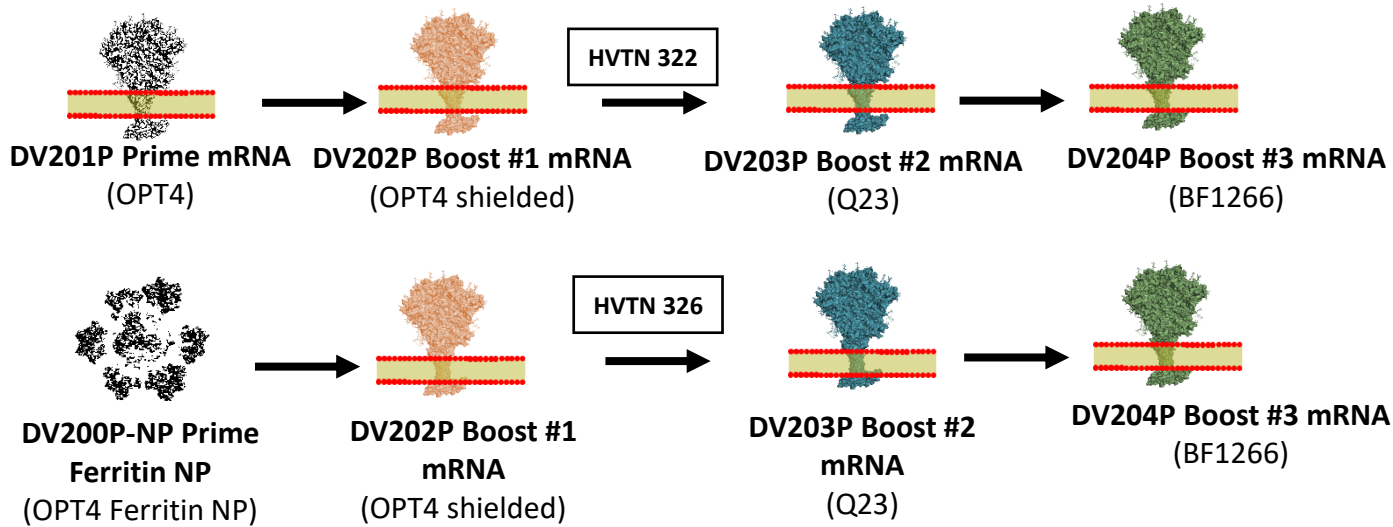
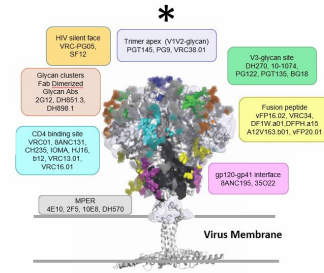
## HVTN 312- VH1-46-class of CD4 mimicking CD4bs bnAbs-Ongoing

## HVTN 324- VH1-46-class of CD4 mimicking CD4bs bnAbs- **October**



David Montefiori Kevin Saunders Drew Weissman

# Duke CHAVD Preventive HIV Vaccine V2 Apex BnAb Portfolio



HVTN 322- Opened March 13<sup>th</sup>, 2026

HVTN 326- October, 2026

CHAVD NHP Trials- Serum heterologous bnAbs in 12/12 and 5/5 RMs



Beatrice Hahn



Kshitij Wagh



Bette Korber



George Shaw



Kevin Saunders



Drew Weissman

# MPER: HVTN 133 Trial for Proximal MPER BnAb Induction



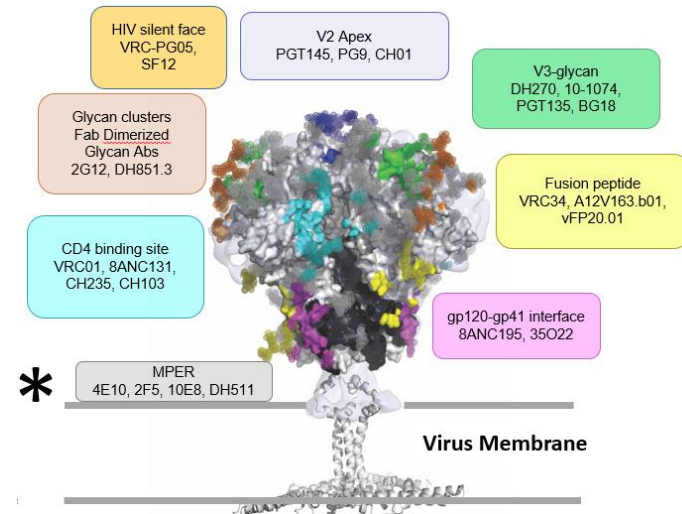
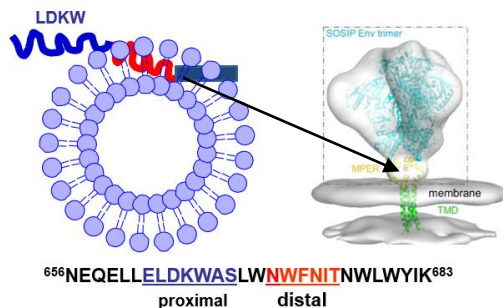
Munir Alam



Wilton Williams



Priyamvada Acharya

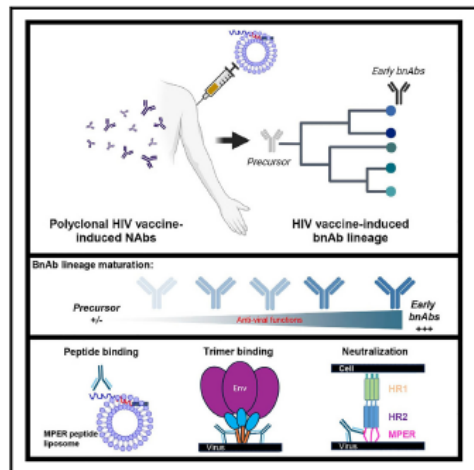


Cell

Article

## Vaccine induction of heterologous HIV-1 neutralizing antibody B cell lineages in humans

Graphical abstract



Authors

Wilton B. Williams, S. Munir Alam, Gilad Ofek, ..., Stephen R. Walsh, Lindsey R. Baden, Barton F. Haynes

Correspondence

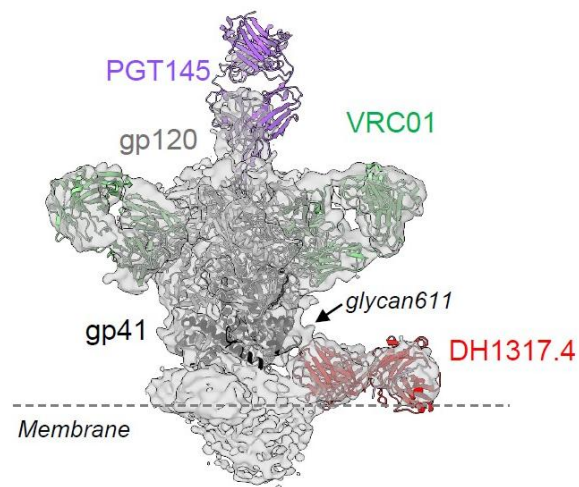
wilton.williams@duke.edu (W.B.W.), munir.alam@duke.edu (S.M.A.), swalsh@bwh.harvard.edu (S.R.W.), lbaden@bwh.harvard.edu (L.R.B.), barton.haynes@duke.edu (B.F.H.)

In brief

The HVTN 133 human clinical trial demonstrated the first success of vaccine induction of polyclonal heterologous HIV-1-neutralizing antibodies that target gp41 MPER. Proximal MPER bnAb precursors can be activated by gp41 MPER peptide-liposomes in humans to neutralize HIV-1.

Induced unusual antibodies that bound both lipids and MPER. **41% clade B, 14% global HIV.**

MPER peptide liposomes reformulated without PEG and lyophilized in a stable form; stable > 1 year.



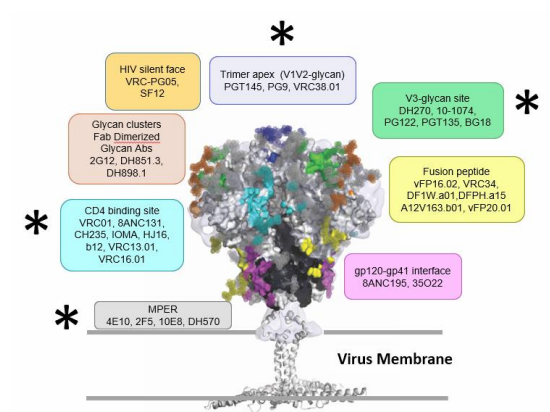
Williams W, et al. Cell, 2024; Nature Communications, under revision



**CHAVID**  
Duke Consortium for  
HIV/AIDS Vaccine Discovery

# Summary-Preventive HIV BnAb Vaccine

- Success in initiation of bnAb B cell lineages and partial heterologous breadth.
- Remaining tasks:
  - Design of boosts that “finish” the maturation of bnAb development. Improve titers, improve breadth.
  - Formulate a practical vaccine. AI, Project 2K.



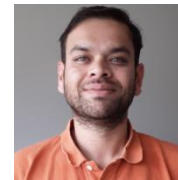
Rory Henderson



Kevin Wiehe



Kevin Saunders



Kshitij Wagh

## Implement Therapeutic Immunization Trials

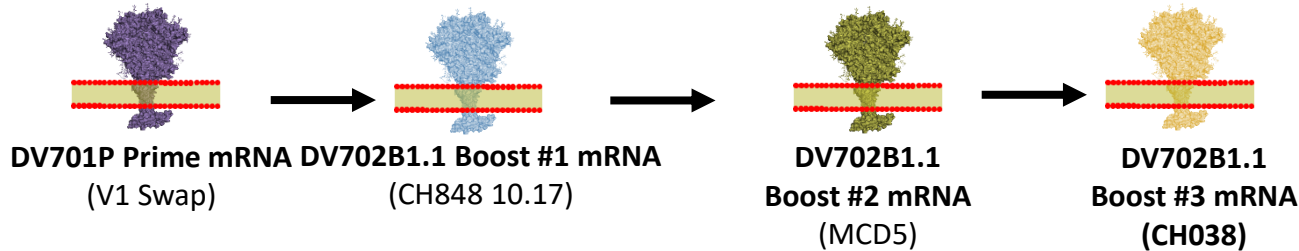


# Duke CHAVD Therapeutic HIV Vaccine Portfolio

## HVTN 808

### V3-Glycan

Nivashnee Naicker  
Juan Montenegro  
Ronnie Gravett  
Chairs



ART → Vaccination → ATI

- Immunogenicity of vaccine
- Effect of rebound virus on bnAb B cells
- Effect on VL and IPDA
- Spring 2026

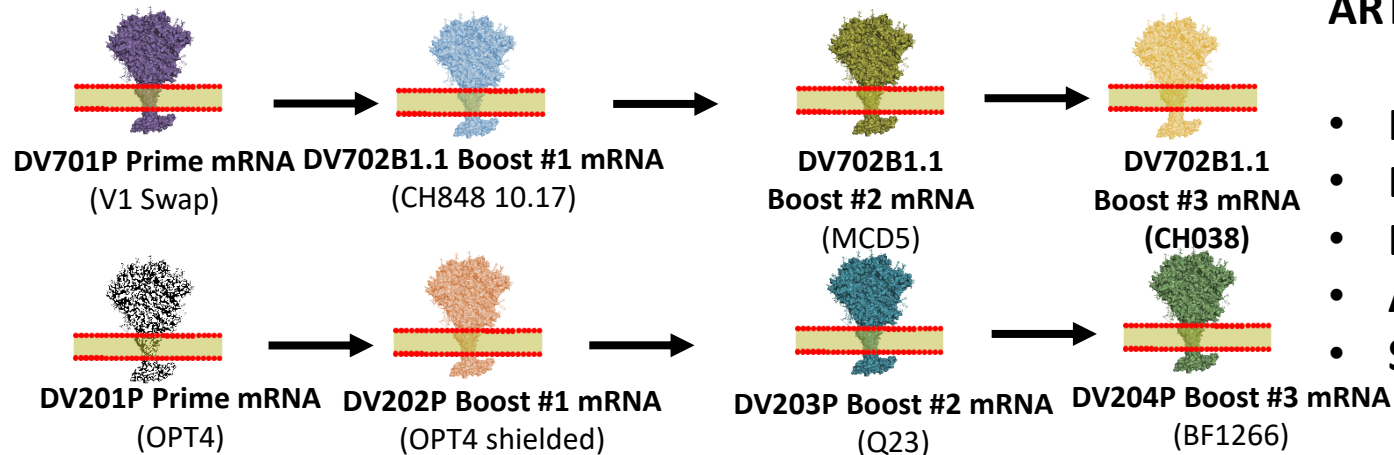
## HVTN 809

### V3-Glycan

+

### V2-Apex

Glenda Gray  
Jorge Gallardo  
Stephen Walsh  
Chairs



ART → BnAbs → Vaccination → ATI

- Immunogenicity of vaccines
- Effect of rebound virus on bnAb B cells
- Effect on VL and IPDA
- Arm in PLWoH
- Spring 2026

# Summary

- **Preventive vaccines have been successful in initiating bnAb B cell lineages in humans and achieved both autologous and weak heterologous neutralizing activity after 1-4 immunizations.**
- **Since PLWH have a permissive immune system for bnAb induction and maturation, use of current HIV vaccines may be more successful in PLWH, and therefore inform preventive vaccine design.**



**CHAVD**

Duke Consortia for HIV/AIDS  
Vaccine Development

# CHAVD Scientific Leadership Group



**George Shaw**  
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**Kshitij Wagh**  
Computational  
Biology



**Andrew McMichael**  
Immunology



**Persephone Borrow**  
T cell biology



**Bette Korber**  
Computational Biology



**Stuart Shapiro**  
SLG DAIDS Program



**Garnett Kelsoe**  
Immunology



**Beatrice Hahn**  
Virology and Env Biology



**Fred Alt**  
B cell Immunology



**Kevin Wiehe**  
Computational Biology



**Kevin Saunders**  
Immunogen Design



**Lindsey Baden**  
Clinical Trials

# Acknowledgements

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Wilton Williams  
RJ Edwards  
Rory Henderson  
Munir Alam  
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Sravani Venkatayogi  
Graham Johnson  
David Montefiori  
Amanda Eaton  
Derek Cain  
RJ Edwards  
Georgia Tomaras  
Garnett Kelsoe  
Chen-Hao Yeh  
Tom Denny  
Todd DeMarco

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Rob Parks, Maggie Barr  
Nicholas Levering, Elise  
Schweer

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Jared Lindenberger, Chipu  
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Nathan Erdmann  
Troy Martin  
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HVTN laboratories and sites  
HVTN trial participants

## Penn

Drew Weissman  
Ted Kreider  
Beatrice Hahn and Lab  
George Shaw and Lab

## Harvard

Fred Alt, Michael Seaman  
Sampa Santra, Ming Tian

## Oxford

Persephone Borrow  
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Isabela Pedroza-Pacheco

## Administration and Program Management

Kelly Cuttle, Laura Sutherland,  
Amanda Newman, Whitney Beck,  
Cynthia Nagle, Chris Todd

# Acknowledgements

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- Benjamin Mildenberg
- Michelle Lifton
- Georgeanna Morton
- Han Tran

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- Laura Sutherland
- Whitney Edwards
- Kelly Cuttle
- Barton Haynes

## University of Pennsylvania

- Mohamad-Gabriel Alameh
- Edward Kreider
- Drew Weissman

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- Ashley Miller
- Jane Fontenot
- Francois Villinger

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- Andrew McMichael
- Tomas Hanke

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- Jenn Kirscherr

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**Center for HIV/AIDS Vaccine Immunology (CHAVI) UM1-AI067854**

**Duke Consortium for HIV/AIDS Vaccine Discovery (CHAVD) UM1-AI144371-**

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**Stuart Shapiro, Angela Malaspina, CHAVD Program Officers**

**Pervin Ankalesaria, Gates Foundation**

**The HIV Vaccine Trials Network, Larry Corey, PI**



**Gates Foundation**

