HIV Database Workshop

www.hiv.lanl.gov

seq-info@lanl.gov

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Additional database staff:

Werner Abfalterer, Kumkum Ganguly, Jennifer Macke, James Szinger, Elena Giorgi, Hyejin Yoon

Contract Officer Representative: Anjali Singh, NIAID, NIH

Theoretical Biology and Biophysics, T-6
Los Alamos National Laboratory

HIV DB Workshop slides:
https://tinyurl.com/HIVDB-2019-IEDB

HIV Immunology Database Workshop

- Yesterday
  - Overview of the HIV Immunology and HIV Sequence Databases
  - T cell epitope data and search interface
  - Peptide tools
- Today
  - Neutralizing Antibody Resources
  - CATNAP
    - neutralization exploration
    - tailored for HIV but pathogen-agnostic
  - Integration of Antibody and Sequence Data (a walk-through)
  - CombiNaber, applicable for any pathogen
  - Glycan shield
  - HIV Genome Browser
  - Vaccine design and evaluation tools

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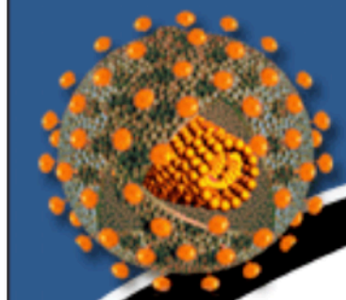


http://hiv.lanl.gov

HIV DATABASES

The **HIV databases** contain comprehensive data on HIV genetic sequences and immunological epitopes. The website also gives access to a large number of tools that can be used to analyze and visualize these data. This project has been funded in whole or in part with Federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under Interagency Agreement No. AAI12007-001-00000. Our content is reviewed by an Editorial Board.

SEQUENCE DATABASE ▸

IMMUNOLOGY DATABASE ▸

OTHER VIRUSES ▸

News:

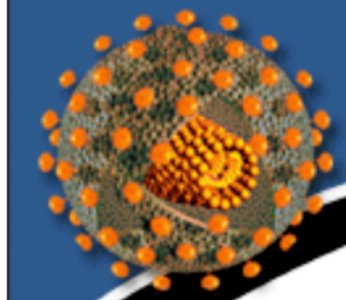
Archived News ▸

2018 Alignments

The 2018 *Web*, *Filtered Web*, and *Super Filtered Web Alignments* are now available online. These curated alignments contain a full range of sequences available through the end of 2018. *08 October 2019*

Questions or comments? Contact us at seq-info@lanl.gov

nos
ATORY



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HIV Molecular Immunology Database

The HIV Molecular Immunology Database is an annotated, searchable collection of HIV-1 cytotoxic and helper T-cell epitopes and antibody binding sites.

Search Interfaces

- CTL/CD8+ search
- T Helper/CD4+ search
- Antibody search
- CTL variant search
- T Helper variant search

- Search help
- Variant search help

Database Products

- All Database products and publications
- Epitope maps
- Epitope tables
- Epitope alignments
- Epitope density plots
- T cell epitope variants and escape mutations
- Neutralizing antibody resources & CATNAP
- The HIV Molecular Immunology Compendium
- About the HIV Molecular Immunology Database
- How to cite this database
- Frequently-asked Questions (FAQ)

Tools and Data Sets

- Tools & Links for immunologists
- SIV Epitopes (PDF) review article summarizing known SIV epitopes
- Identifying HLA-Associated Polymorphisms in HIV-1 (PDF) review article summarizing HIV polymorphism associated with escape mutations. Also a table of polymorphisms.

mmunology Database

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Neutralizing Antibody Resources

www.hiv.lanl.gov/content/immunology/neutralizing_ab_resources.html

Tools

- CATNAP: Compile, Analyze and Tally NAb Panels
  Analysis of panels of antibody data for identification of potential genetic signatures.
  - Database CATNAP analyzes published IC_{50}/IC_{80} data for anti-HIV neutralizing antibodies.
  - Custom CATNAP analyzes any numerical data associated with a protein alignment.
  - Hybrid CATNAP analyzes your neutralization data together with published data.

- HIV Genome Browser
  A customization of jBrowse displaying genome and proteome features of HIV, including epitopes and neutralizing antibody features.
  - Env browser: direct link with Ab contact features shown.

- CombiNAber
  Predict the neutralization of combinations of antibodies

- External Tools for Germline Antibody Reconstruction
  A list of external computational tools for modeling antibody evolution and germ line reconstruction from antibody or T-cell receptor sequence data.

Search interface

- Neutralizing antibody contacts and features database
  Search for antibody contact locations and other HIV-1 Env features.

Tables

- Neutralizing antibody features spreadsheet (.xlsx)
  A summary of selected information from the search interface above, presented in a single spreadsheet. Each row of the table corresponds to one residue of HIV-1 Env, and each column represents a protein feature or set of known binding residues of broadly neutralizing antibodies. Loops and other features of Env are shown.

- Best neutralizing antibodies
  A table presenting many of the most broadly-neutralizing HIV-1 antibodies, with links to papers, neutralization data, notes on breadth of neutralization, locations of Ab contacts or key residues, heavy and light chain composition, and more.

Protocols and Other Data

- Standardized Assessments of Neutralizing Antibodies for HIV/AIDS Vaccine Development Assay protocols from Duke Central Reference Laboratory

- Neutralization Serotype Discovery Panel. A large panel of Env-pseudotyped viruses assayed against plasmas from chronic infection. The panel and plasmas were selected to represent M-group diversity.

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10E8 Contacts

DATABASES SEARCH ALIGNMENTS TOOLS PUBLICATIONS GUIDES Search Site

Neutralizing Antibody Contexts & Features

Purpose: To provide exact coordinates of known neutralizing antibody binding sites and other HIV-1 Env features. The data are also summarized in a spreadsheet (.xls). For details, see Help.

Detailed information available for 242 HIV neutralizing antibodies

MAb name: 10-1074, 10-996, 10E8, 12A12

Antibody class: CD4bs, CD4i, CH4bs, glycan

Env AA position: 315,323

Type: antibody related feature, other Env feature

Reference: Andrabi2015, Balla-Jhagjhoorsingh2013, Bhiman2015, Blattner2014

Database ID: 1, 2, 3, 4

Submit Reset

View Neutralizing Antibody Contexts & Features

ID 18

Description 10E8 contacts

Antibody class MPER

Reference Huang2012a

Type antibody related feature

MAb name 10E8 (Click MAb name to get to Immunology DB notes)

Env pos.	Feature	HXB2 AA	Entropy Group M	Entropy Subtype B	Entropy Subtype C	Annotation
671	gp41	N	0.779	0.669	0.885	10E8 N671 structure and neutralization: key epitope position.
672	gp41	W	0.017	0.023	0.014	10E8 W672 structure and neutralization: key epitope position.
673	gp41	F	0.058	0.065	0.073	10E8 F673 structure and neutralization: key epitope position.
676	gp41	T	0.683	0.610	0.674	10E8 T676 structure and binding: key epitope position.
680	gp41, gp41 transmembrane	W	0.069	0.083	0.081	10E8 W680 structure and neutralization: key epitope position.
683	gp41, gp41 transmembrane	K	0.577	0.499	0.569	10E8 K/R683 structure: key epitope position.

Important position(s) with Hxb2 amino acid: N671 W672 F673 T676 W680 K683

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https://www.hiv.lanl.gov/components/sequence/HIV/featuredb/search/env_ab_search_pub.comp

CATNAP (Compile, Analyze and Tally NAb Panels)

- Compiles published HIV Ab neutralization data (currently >400 Abs and Ab mixtures, and >1000 HIV pseudoviruses)
- Integrates on one screen neutralization and viral sequence data.
- Provides important Ab and Virus details:
  - Ab binding region, links to PDB structure, links to the donor info
  - Clonal lineage and germline V/D/J designation, Ab sequences
  - Ab contacts, Env positions of interest related to neutralization sensitivity, etc.
  - Protein sequence variability by position
  - Virus subtype, country, patient health, infection stage
- Selects Ab and viruses in multiple ways:
  - Individual or all Ab and viruses, as well as by study
  - Antibodies by germline V/D/J genes and binding region
  - Viruses by tier, subtype, infection stage, 9 commonly used viral panels
  - User's list of viruses and antibodies
- Defines genetic neutralization signatures associated with sequences
- Custom INPUT: allows users to analyze and compare their own data with the stored CATNAP data

https://www.hiv.lanl.gov/components/sequence/HIV/neutralization/index.html

DATABASES SEARCH ALIGNMENTS TOOLS PUBLICATIONS GUIDES search site Search

CATNAP

Compile, Analyze and Tally NAb Panels

Purpose: To provide easy analysis of data associated with HIV-1 neutralizing antibodies, including neutralization panel data, sequences, and structures.

See also: Help | Other CATNAP tools | How to Cite

Can't find your antibodies or viruses? Find Names
Download CATNAP data

New! Click "Your list" to select antibodies and viruses from your own lists. Details...

Select by: Antibody and Virus | Study

Antibodies by: Names | Attributes | Your list

(# of Antibodies) Reset

Donor	Light V (IG)	Light J (IG)
127/C (2) 44 (1) BF520 (1) C38 (3)	KV1-1 (1) KV1-13*02 (1) KV1-17*01 (1) KV1-33*01 (11)	KJ1 (14) KJ1*01 (20) KJ2 (2) KJ2*01 (19)
Heavy V (IGHV)	**Heavy D (IGHD)**	**Heavy J (IGHJ)**
1-02*02 (9) 1-03*01 (1) 1-18*01 (2) 1-18*02 (8)	10 (2) 1-26 (1) 16 (4) 1-IR1 (1)	1 (2) 1*01 (9) 2 (9) 2*01 (4)

AB binding type

gp120 carbohydrates at glycosylation residues in...
gp120 CD4BS (99)
gp120-CD4 complex (2)
gp120 CD4i (3)

Display a record if

ALL selected conditions are true (intersection)
AT LEAST ONE selected condition is true (union)

Viruses by: Names | Attributes | Panels | Your list

# of Panels = 9

Select all	Name	Reference	# of viruses
☐	118 multi-clade	Seaman2010	118
☐	C clade 200	Rademeyer2016	200
☐	C clade magnitude-breadth 100	Hraber2017	100
☐	C clade magnitude-breadth 50	Hraber2017	50
☐	C clade serum screening panel	Hraber2017	12
☐	f61 fingerprinting	Doria-Rose2017	20
☐	Global	Decamp2014	12
☐	Most common 100		100
☐	Most common 200		200

Options

Retrieve: Antibody details | Virus details | Assay

Or

Analyze along with virus sequences: IC_{50} | IC_{80} | Both

Large sets of data run slowly. Limit the number of antibodies or viruses for quicker response.

☐ Exclude viruses having no sequence data

☐ Email results

Submit Reset

Select Antibodies and Viruses in Several Ways:

- Individual or all antibody and viruses
- Select by study
- Select antibodies by attributes (germline and binding region)
- Select viruses by attributes (Tier, Subtype, Infection stage)
- Select viruses by a virus panel

Example: 10E8 and PG9

Retrieve Antibody, Virus or Assay details

Analyze IC_{50}, IC_{80} or Both along with the viral sequences

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CATNAP: IC_{50} & IC_{80}/HIV-1 alignment

Collapse or expand details from individual studies

4 antibodies & 1007 viruses selected to search

More virus info in HIV Seq DB

*: Geometric means
(Expand to individual values)

●<0.1 ●<1 ●<10 ●≤50 ○>cutoff or 50 (μg/ml)

Virus name	Tier	10E8 IC50	10E8 IC80	PG9 IC50	PG9 IC80	PG
001428_2_42	2	1.48106*	6.44387*	0.01010*	0.01221*	0.0
0041_V3_C18	2	0.44000	3.70700	0.00100	0.00400	1.8
0077_V1_C16	2	1.45938*	9.19287*	0.09106*	0.35301*	UD:
00836_2_5	1B or 2	0.50193*	1.90470*	49.00000*	UD:>50*	31.
0260_V5_C36		9.80180*	30.00417*	1.57709*	13.80908*	0.0
0301_BM_A12		–	–	0.66000	–	–
0301_BM_A2		–	–	0.91000	–	–
0301_BM_A6		–	–	0.91000	–	–
0330_V4_C3	2	1.04674*	3.83465*	0.01468*	0.05294*	0.0
0404_BM_B9		–	–	0.08000	–	–
0404_BM_D4		–	–	6.87000	–	–
0404_BM_F3		–	–	0.04000	–	–
0404_BM_G3		–	–	0.58000	–	–
0404_BM_H4		–	–	0.01000	–	–
0439_V5_C1	2	1.16920*	4.69871*	UD:>50*	UD:>50*	UD:
0702_BM_B4		–	–	0.83000	–	–
0702_BM_B9		–	–	0.38000	–	–
0702_BM_D1		–	–	0.18000	–	–
0702_BM_H12		–	–	0.37000	–	–
0815_V3_C3	2	0.31354*	1.86820*	UD:>10, >25,...*	UD:>25, >50*	0.0
0907_V4_C12		–	–	–	–	–
Geometric mean of detected		0.35352	2.15327	0.18501	0.38293	0.0
Geometric mean of all (undetected set to 100)		0.46515	2.43935	0.92140	2.20904	0.9
% detected (detected/total)		95% (411/432)	97% (387/400)	74% (543/729)	69% (285/416)	64%

HXB2

```
MRVKE----KY-QHLW-RWG---WRWGTMLLG---MLMI---CSAT---
----.---------|--------.----|-------.-------|----
-------------10------------20-------------30----
```

```
MRVRGILR-NY-QQW--------WMWGVLGFW---MLMI---CNGV----
MRVRGILR-NW-QLW--------WTWGILGFW---MVMN---CNVR----
MRVMGSMR-NC-QRW--------WIWGILGFW---MLMT---CNME----
MRVRGIRR-NY-QHW--------WIWGILGFW---MLMI---CKGGR---
MRVMGIQR-NS-QCF--------LSWGMLVLG---IMMI---CSAV----
MRVRGMMR-NW-QQW--------WIWGILGFW---MLMI---CSVL----
MRVRGMMR-NW-QQW--------WIWGILGFW---MLMM---CSVL----
MRVRGMMR-NW-QQW--------WIWGILGFW---MLMM---CSVL----
MRVMGMQR-NS-RHL--------LLRWGIRILG--MIMI---CRTA----
MRVRGILR-NC-PQW--------WTWGILGFW---MLMI---CSVW----
MRVRGILR-NC-PQW--------WTWGILGFW---MLMI---CSVW----
MRVRGILR-NC-PQW--------WTWGILGFW---MLMI---CSVW----
MRVRGILR-NC-PQW--------WTWGILGFW---MLMI---CSVW----
MRVRGILR-NC-PQW--------WTWGILGFW---MLMI---YSVW----
MRVMGIQR-NC-QHL--------LRWGTLILG---LIII---CSTA----
MRVRGILR-NW-ELW--------WIWGILGFW---MFMI---CNML----
MRVRGILK-NW-KLW--------WIWGILGFW---MFMI---CNML----
MRVRGILR-NW-ELW--------WIWGILGFW---MFMI---CNML----
MRVRGILR-NW-KLW--------WIWGILGFW---IFMI---CNTL----
MRVMGIQM-NW-QQW--------WIWGILGFW---MLMV---CNGT----
MRAREMKR-NC-QNL--------WKWGIMLLG---ILMI---CSAA----
```

Potency and Breadth of neutralization over multiple studies

# of viruses found: 799
# of Abs found: 4
# of studies found:70

Download neutralization data with virus information

Download ● aa ○ na in Fasta

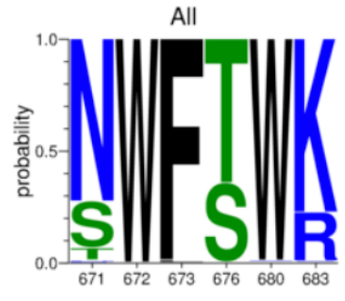
Go to antibody information section

Antibody context and feature position(s) (based on HXB2)

(See Spreadsheet of neutralizing antibody contexts and features (.xls) for more information)

- **10E8 contacts** (LogoByAll LogoBySubtype): N671 W672 F673 T676 W680 K683
- **PG9-like contacts** (LogoByAll LogoBySubtype): N156 N160 I165 G167 K168 V169 Q170 K171 Y173

Logo



Frequency by position

See full raw counts

	Percentage and raw count of non-gap
671	N: 72.14% (3947) S: 21.09% (1154) T: 5.63% (308) other: 1.13% (62)
672	W: 99.80% (5460) other: 0.20% (11)
673	F: 98.83% (5407) other: 1.17% (64)
676	T: 64.17% (3511) S: 35.48% (1941) other: 0.35% (19)
680	W: 98.92% (5412) other: 1.08% (59)
683	K: 77.82% (4257) R: 21.39% (1170) other: 0.79% (43)

Position analysis

Analyze HXB2 position 160 for Ab PG9

Pick Ab and click on contact position to analyze, or enter your own position

Run CombiNaber

Submit

# of viruses tested							
10E8 IC50: 432	10E8 IC80: 400	PG9 IC50: 729	PG9 IC80: 416	PGT121 IC50: 634	PGT121 IC80: 393	VRC01 IC50: 781	VRC01 IC80: 444

388 virus(es) tested against all antibodies retrieved will be submitted to CombiNaber.

Analysis at position 160 for Ab PG9

Amino Acid Counts

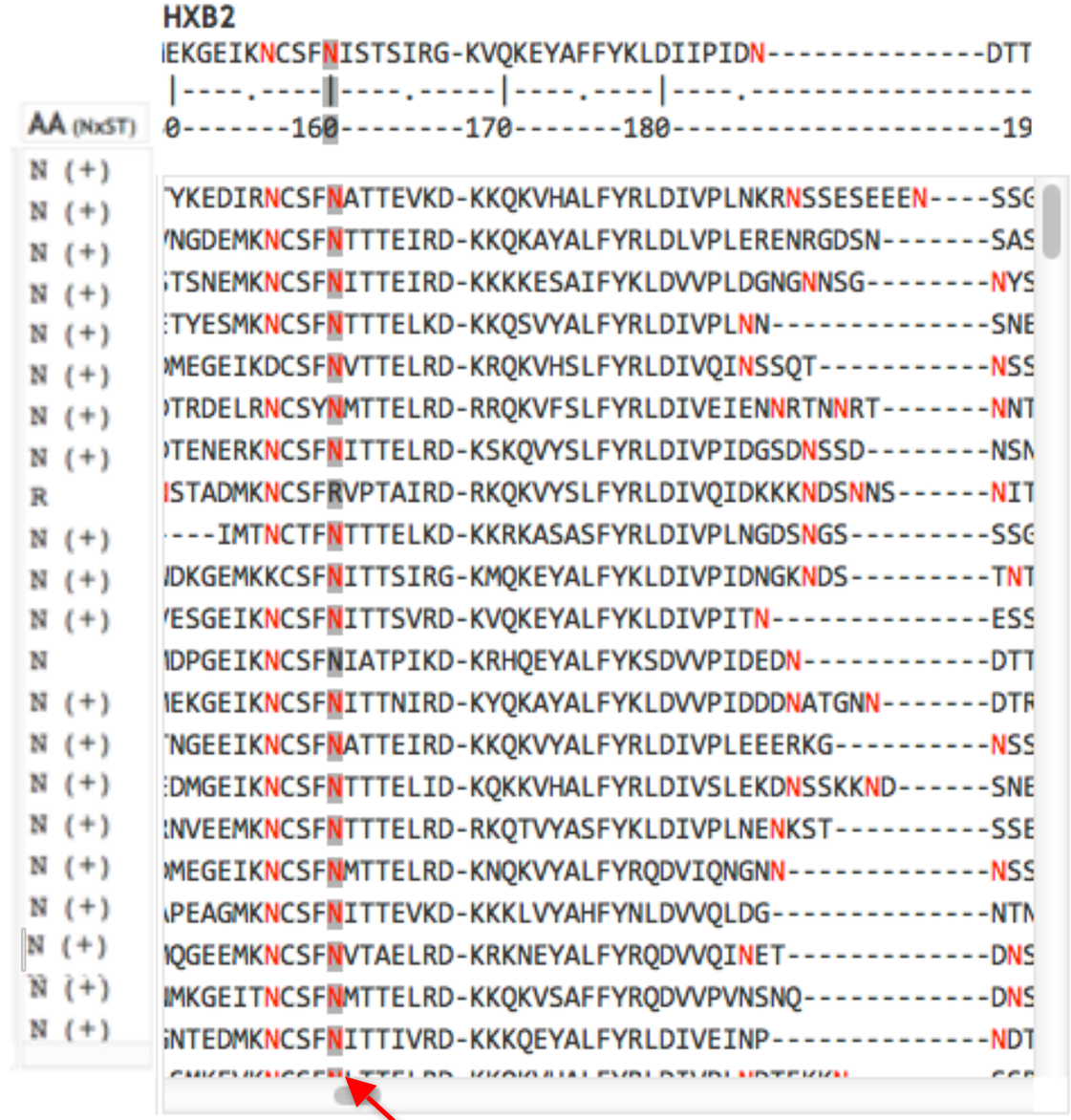
AA	Count	# for detected	# for undetected	Fisher test p-value	Odds ratio
N	544	425	119	< 2.2e-16	25.55874
D	10	0	10	1.37e-06	0
K	9	0	9	5.403e-06	0
S	5	1	4	0.01897	0.0884202
Y	5	1	4	0.01897	0.0884202
X	4	3	1	1	1.081824
R	3	0	3	0.01834	0
T	1	0	1	0.265	0
V	1	0	1	0.265	0
H	1	0	1	0.265	0
-	1	0	1	0.265	0
I	1	0	1	0.265	0
Total	585	430	155		
no seq	144				
Grand total	729				

N-linked Glycosylation Motif Counts

NxST	Count	# for detected	# for undetected	Fisher test p-value	Odds ratio
g+	531	424	107	< 2.2e-16	31.48806
g-	53	6	47	< 2.2e-16	0.03273309
-	1	0	1	0.265	0
Total	585	430	155		
no seq	144				
Grand total	729				

Note: phylogenetically corrected signatures **(via the Genetic Signature Tool)** have been pre-calculated

Odds ratio > 1: enriched for detected
Odds ratio < 1: enriched for undetected



Position highlighted

About this position

Position: Env 160 (193 in alignment above)
Entropy, M group: 0.401
Functional domain: gp120 (Kwong2000), V2 (Leonard1990)

Antibody features of this position

Mutation affects PG9-like Ab sensitivity: Loss of glycan confers resistance; PG9-like class includes PG16, PGT141, 145, CH01-CH04 (V1V2 glycan, Doria-RoseNA2012)
PG16 signature predictions: PG16: glycosylation at N160 is associated with increased susceptibility to neutralization; intermediate quality of support. (V1V2 glycan, West2013)
PG9-like contacts: PG9 glycan contact; PG9-like class includes PG16, PGT141, 145, CH01-CH04 (V1V2 glycan, McLellan2011)
PG9 signature predictions: PG9: N160 is associated with increased susceptibility to neutralization; intermediate quality of support. (V1V2 glycan, West2013)

(For more information, check Neutralizing Antibody Contexts & Features)

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One path through the database …

- Search database for a particular antibody record
- Examine comprehensive adaptive immune response data for the subject/patient of origin
  - Germline antibody sequences
  - Virus neutralization
- Cross-link to time-stamped viral sequence data
- Explore antibody-virus co-evolution to inform vaccine design

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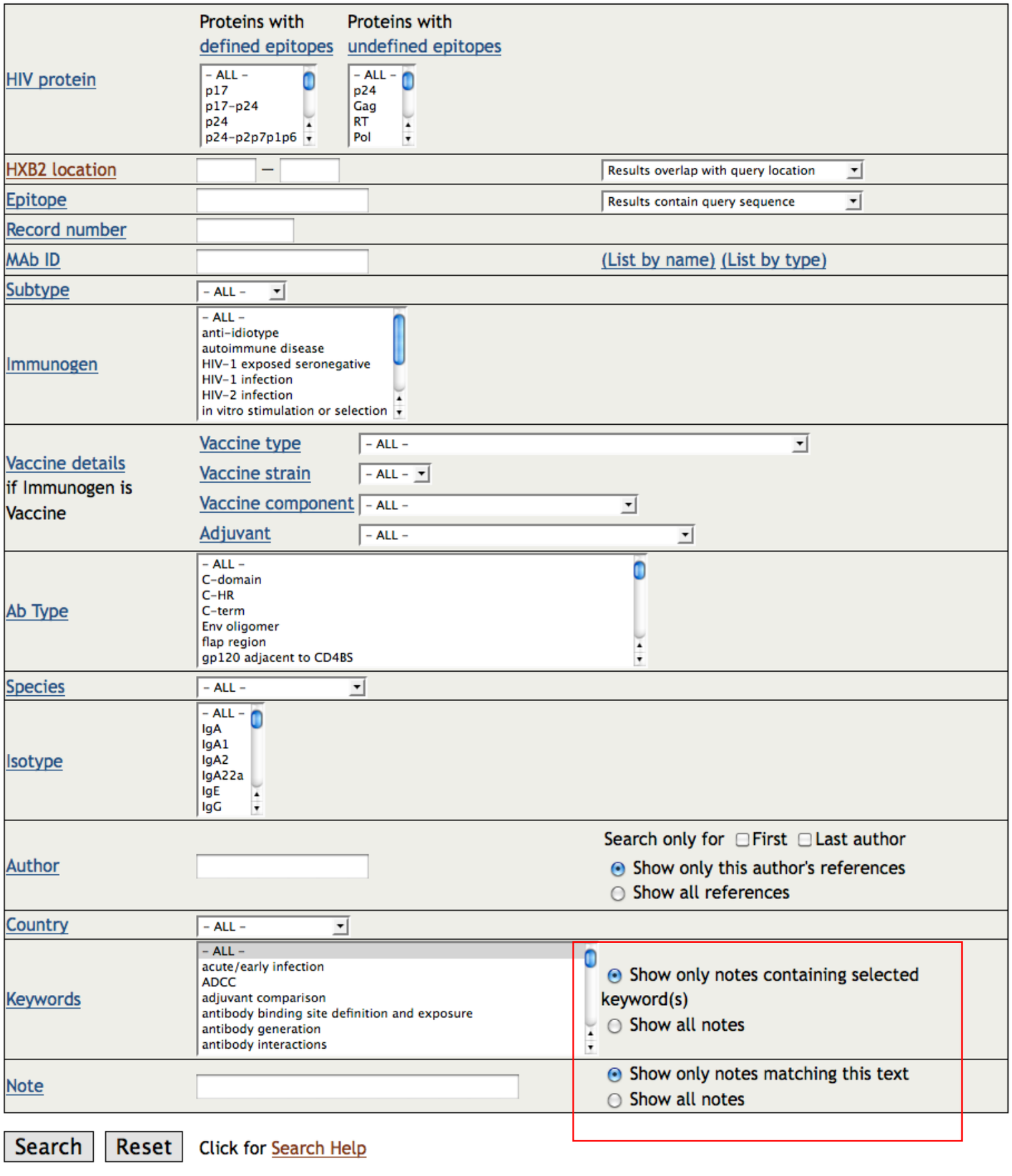
Antibody Search (https://www.hiv.lanl.gov/content/immunology/ab_search)



Search by

- HIV protein, Epitope Sequence, Subtype, Immunogen, Vaccine Details, Species, Author, Country, Keywords, Isotype
- MAb ID
  - List by Ab name
  - List by Ab type
    - By binding site, for example binding to similar region like V3 or near a common functional domain like CD4 binding site CD4Bs)
- Search examples:
  - 2F5 – 1 record with 815 references
  - Ab type: gp120 CD4BS – 438 records
  - Search for CH235.9

Can show only notes and references containing selected keywords or user's text

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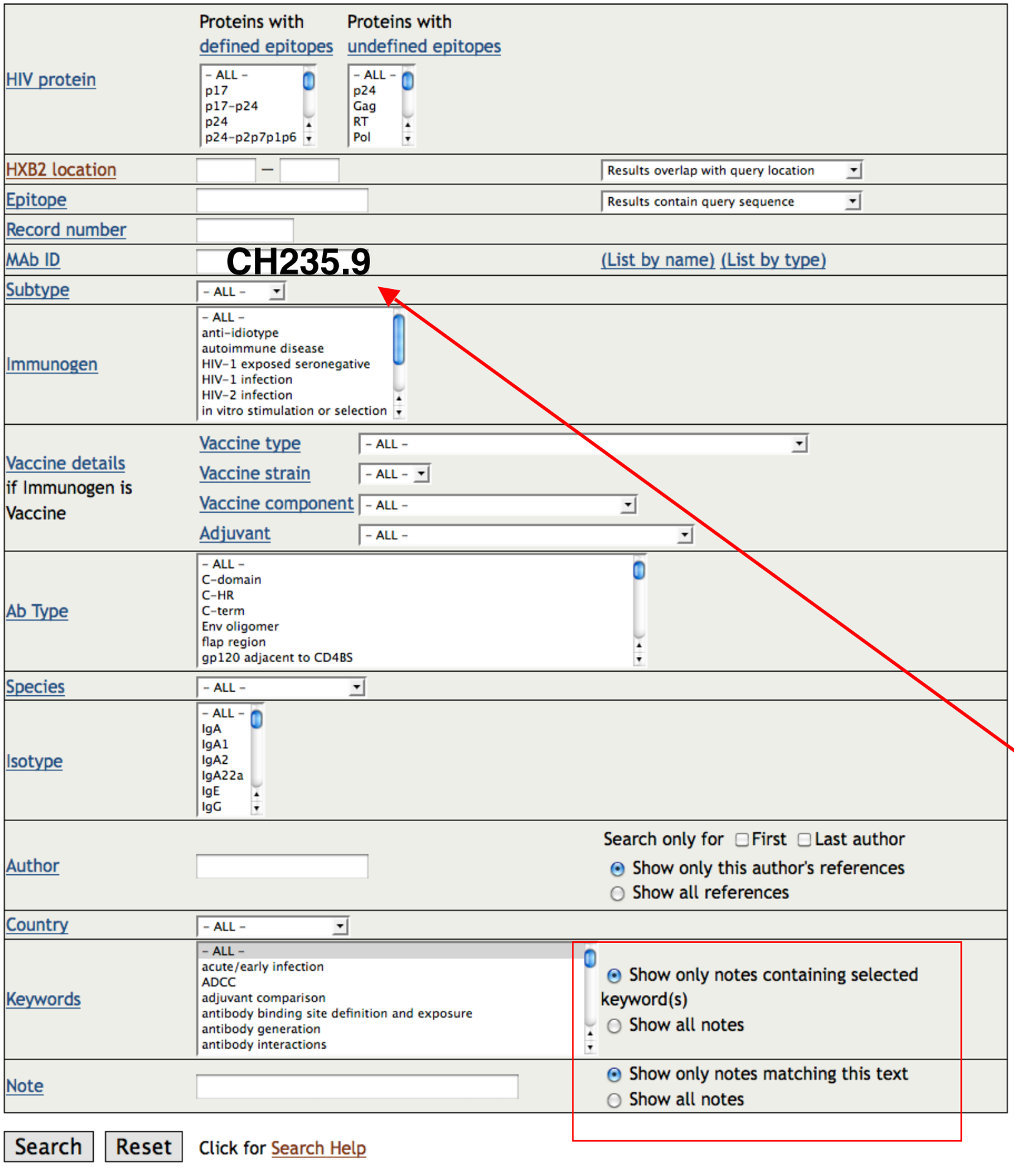
Antibody Search (https://www.hiv.lanl.gov/content/immunology/ab_search)



Search by

- HIV protein, Epitope Sequence, Subtype, Immunogen, Vaccine Details, Species, Author, Country, Keywords, Isotype
- MAb ID
  - List by Ab name
  - List by Ab type
    - By binding site, for example binding to similar region like V3 or near a common functional domain like CD4 binding site CD4Bs)
- Search examples:
  - 2F5 – 1 record with 815 references
  - Ab type: gp120 CD4BS – 438 records
  - Search for CH235.9

Can show only notes and references containing selected keywords or user's text

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Antibody search example: CH235.9

Search Antibody Database

Found 1 matching record:

Displaying record number 3291

MAb ID	CH235.9 (CH493)
HXB2 Location	Env
Author Location	Env
Epitope	
Subtype	C
Ab Type	gp120 CD4BS
Neutralizing	P (tier 2) View neutralization details
Contacts and Features	View contacts and features
Species (Isotype)	human
Patient	Donor CH505
Immunogen	HIV-1 infection
Keywords	antibody generation, antibody lineage, antibody sequence, binding affinity, escape, mutation acquisition, neutralization, review

Env Epitope Map

Notes

Showing 3 of 3 notes.

- CH235.9: This review discussed antibody-virus coevolution and lineage development as a path to elicit broadly neutralizing Abs. CD4bs mAbs from donor CH505 (lineages CH103 and CH235) were used as main examples. *Bonsignori2017a* (**review**, **antibody lineage**)
- This patent application states that CH493 is also referred to as CH235.9. *Lam2017*
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Author Location	Env
Epitope	
Subtype	C
Ab Type	gp120 CD4BS
Neutralizing	P (tier 2) View neutralization details
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Species (Isotype)	human
Patient	Donor CH505
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References

Showing 3 of 3 references.

Antibody search example: subject CH505

Patient Detail

Patient Code	Donor CH505 (703010505)
Patient Sex	Male
Risk Factor	Heterosexual (SH)
Infection Country	MW
Infection City	
Infection Year	2008
HLA Type	A*30, A*30, B*4202, B*570301, Cw*17, Cw*18
Patient Ethnicity	African
Progression	
Species	human
Patient Note	African donor enrolled approximately 4 weeks after infection and followed for over 6 years. During this time viral load ranged from 14,460 to 847,279 copies/ml (median = 173,667 copies/ml), and CD4 counts ranged from 69 to 431 cells/mm3 (median = 294 cells/mm3). A single founder virus is estimated to have established HIV-1 clade C with development of autologous neutralizing antibodies at 14 weeks; Abs CH103,CH104,CH105,CH106 isolated 136 weeks post-infection. Antibody CH235 was isolated from the patient's week 41-peripheral blood memory B cells in culture.
CTL CD8+ Records	59059, 59060
T-Helper CD4+ Records	
Antibody Records	CH103 (2861), CH104 (2862), CH105 (2863), CH106 (2864), IA1 (3176), IA2 (3177), IA3 (3178), IA4 (3179), IA5 (3180), IA6 (3181), IA7 (3182), IA8 (3183), CH103 UCA (3184), CH235 (3185), CH236 (3186), CH239 (3187), CH240 (3188), CH241 (3189), CH186 (3190), CH187 (3191), CH188 (3192), CH200 (3193), DH151 (3234), DH228 (3235), CH235.9 (3291), CH235.12 (3292), CH243 (3374), CH244 (3375), CH245 (3376), CH247 (3377), CH248 (3378), 1AH92U (3380), CH235.7 (3381), CH235.10 (3382), CH235.11 (3383), CH235.13 (3384)
Sequence Database Patient ID Record	56552

Antibody search example: subject CH505

Patient Detail

Patient Code	Donor CH505 (703010505)
Patient Sex	Male
Risk Factor	Heterosexual (SH)
Infection Country	MW
Infection City	
Infection Year	2008
HLA Type	A*30, A*30, B*4202, B*570301, Cw*17, Cw*18
Patient Ethnicity	African
Progression	
Species	human
Patient Note	African donor enrolled approximately 4 weeks after infection and followed for over 6 years. During this time viral load ranged from 14,460 to 847,279 copies/ml (median = 173,667 copies/ml), and CD4 counts ranged from 69 to 431 cells/mm3 (median = 294 cells/mm3). A single founder virus is estimated to have established HIV-1 clade C with development of autologous neutralizing antibodies at 14 weeks; Abs CH103,CH104,CH105,CH106 isolated 136 weeks post-infection. Antibody CH235 was isolated from the patient's week 41-peripheral blood memory B cells in culture.
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Sequence Database Patient ID Record	56552 **Access to all available HIV sequences from this subject**

Antibody search/HIV sequence links: patient CH505

Record for patient 703010505

Retrieve all sequences for this patient

Retrieve all sequences for this patient; include time point information

Patient Code	703010505
Patient Sex	M
Risk Factor	Heterosexual
Infection Country	
Infection City	
Infection Year	2008
HLA type	A*3001/24 A*3002/33 B*4202 B*570301 C*1701/02/03 C*1801/02
Patient ethnicity	
Project	CHAVI
Progression	
Patient comment	
# of patient seqs	624
# of patient timepoints	24
Species	
Cluster Name	
Accession(s)	KC247375 KC247376 KC247377 KC247378 KC247379 KC247380 KC247381 KC247382 KC247383 KC247384 KC247385 KC247386 KC247387 KC247388 KC247389 KC247390 KC247391 KC247392 KC247393 KC247394 KC247395 KC247396 KC247397 KC247398 KC247399 KC247400 KC247401 KC247402 KC247403 KC247404 KC247405 KC247406 KC247407 KC247408 KC247409 KC247410 KC247411 KC247412 KC247413 KC247414 KC247415 KC247416 KC247417 KC247418 KC247419

Antibody search/HIV sequence links: patient CH505

Record for patient 703010505

Retrieve all sequences for this patient

Retrieve all sequences for this patient; include time point information

Patient Code	703010505
Patient Sex	M
Risk Factor	Heterosexual
Infection Country	
Infection City	
Infection Year	2008
HLA type	A*3001/24 A*3002/33 B*4202 B*570301 C*1701/02/03 C*1801/02
Patient ethnicity	
Project	CHAVI
Progression	
Patient comment	
# of patient seqs	624
# of patient timepoints	24
Species	
Cluster Name	
Accession(s)	KC247375 KC247376 KC247377 KC247378 KC247379 KC247380 KC247381 KC247382 KC247383 KC247384 KC247385 KC247386 KC247387 KC247388 KC247389 KC247390 KC247391 KC247392 KC247393 KC247394 KC247395 KC247396 KC247397 KC247398 KC247399 KC247400 KC247401 KC247402 KC247403 KC247404 KC247405 KC247406 KC247407 KC247408 KC247409 KC247410 KC247411 KC247412 KC247413 KC247414 KC247415 KC247416 KC247417 KC247418 KC247419

Antibody search/HIV sequence links: patient CH505

HIV sequence database

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Displaying **1 - 100** of **623** sequences found:

Note: 1 problematic sequences were removed from this result.

Select all | Unselect all | Invert selection | Show all Select record to List 100 records per page

Click on field name to sort in ascending or descending order

#	Select	Patient Code (id)	Accession	Name	Subtype	Country	Sampling Year	Days from first Sample	Fiebig Stage	Days from treatment end	Days from treatment start	Days from Infection	Days from Seroconversion	Genomic Region	Sequence Length	Organism
1	☐	Blast 703010505(56552)	KC247608	703010505_w4_61	C	MALAWI	2008		4			28	0		2541	HIV-1
2	☐	Blast 703010505(56552)	KC247606	703010505_w4_56	C	MALAWI	2008		4			28	0		2541	HIV-1
3	☐	Blast 703010505(56552)	KC247604	703010505_w4_54	C	MALAWI	2008		4			28	0		2541	HIV-1
4	☐	Blast 703010505(56552)	KC247602	703010505_w4_51	C	MALAWI	2008		4			28	0		2541	HIV-1
5	☐	Blast 703010505(56552)	KC247600	703010505_w4_49	C	MALAWI	2008		4			28	0		2541	HIV-1
6	☐	Blast 703010505(56552)	KC247598	703010505_w4_47	C	MALAWI	2008		4			28	0		2541	HIV-1
7	☐	Blast 703010505(56552)	KC247596	703010505_w4_45	C	MALAWI	2008		4			28	0		2541	HIV-1
8	☐	Blast 703010505(56552)	KC247594	703010505_w4_43	C	MALAWI	2008		4			28	0		2541	HIV-1
9	☐	Blast 703010505(56552)	KC247592	703010505_w4_41	C	MALAWI	2008		4			28	0		2541	HIV-1
10	☐	Blast 703010505(56552)	KC247590	703010505_w4_39	C	MALAWI	2008		4			28	0		2541	HIV-1
11	☐	Blast 703010505(56552)	KC247588	703010505_w4_37	C	MALAWI	2008		4			28	0		2541	HIV-1
12	☐	Blast 703010505(56552)	KC247586	703010505_w4_34	C	MALAWI	2008		4			28	0		2541	HIV-1
13	☐	Blast 703010505(56552)	KC247584	703010505_w4_32	C	MALAWI	2008		4			28	0		2541	HIV-1
14	☐	Blast 703010505(56552)	KC247582	703010505_w4_29	C	MALAWI	2008		4			28	0		2541	HIV-1
15	☐	Blast 703010505(56552)	KC247580	703010505_w4_27	C	MALAWI	2008		4			28	0		2523	HIV-1
16	☐	Blast 703010505(56552)	KC247578	703010505_w4_25	C	MALAWI	2008		4			28	0		2541	HIV-1
17	☐	Blast 703010505(56552)	KC247576	703010505_w4_23	C	MALAWI	2008		4			28	0		2541	HIV-1
18	☐	Blast 703010505(56552)	KC247574	703010505_w4_21	C	MALAWI	2008		4			28	0		2541	HIV-1
19	☐	Blast 703010505(56552)	KC247572	703010505_w4_19	C	MALAWI	2008		4			28	0		2541	HIV-1

... 623 sequences in total ...

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Antibody search/HIV sequence links: patient CH505

HIV sequence database

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4	☐	Blast 703010505(56552)	KC247602	703010505_w4_51	C	MALAWI	2008		4			28	0		2541	HIV-1
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6	☐	Blast 703010505(56552)	KC247598	703010505_w4_47	C	MALAWI	2008		4			28	0		2541	HIV-1
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2	☐	Blast 703010505(56552)	MF353069	703010505_w323_8	C	MALAWI	2014					2264	2236		2568	HIV-1
3	☐	Blast 703010505(56552)	MF353068	703010505_w323_7	C	MALAWI	2014					2264	2236		2568	HIV-1
4	☐	Blast 703010505(56552)	MF353067	703010505_w323_6	C	MALAWI	2014					2264	2236		2565	HIV-1
5	☐	Blast 703010505(56552)	MF353066	703010505_w323_5	C	MALAWI	2014					2264	2236		2574	HIV-1
6	☐	Blast 703010505(56552)	MF353064	703010505_w323_30	C	MALAWI	2014					2264	2236		2568	HIV-1
7	☐	Blast 703010505(56552)	MF353063	703010505_w323_3	C	MALAWI	2014					2264	2236		2595	HIV-1
8	☐	Blast 703010505(56552)	MF353062	703010505_w323_29	C	MALAWI	2014					2264	2236		2565	HIV-1
9	☐	Blast 703010505(56552)	MF353061	703010505_w323_28	C	MALAWI	2014					2264	2236		2568	HIV-1
10	☐	Blast 703010505(56552)	MF353060	703010505_w323_27	C	MALAWI	2014					2264	2236		2253	HIV-1
11	☐	Blast 703010505(56552)	MF353059	703010505_w323_26	C	MALAWI	2014					2264	2236		2568	HIV-1
12	☐	Blast 703010505(56552)	MF353058	703010505_w323_25	C	MALAWI	2014					2264	2236		2568	HIV-1
13	☐	Blast 703010505(56552)	MF353057	703010505_w323_24	C	MALAWI	2014					2264	2236		2568	HIV-1
14	☐	Blast 703010505(56552)	MF353056	703010505_w323_23	C	MALAWI	2014					2264	2236		2565	HIV-1
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16	☐	Blast 703010505(56552)	MF353054	703010505_w323_21	C	MALAWI	2014					2264	2236		2574	HIV-1
17	☐	Blast 703010505(56552)	MF353053	703010505_w323_2	C	MALAWI	2014					2264	2236		2568	HIV-1
18	☐	Blast 703010505(56552)	MF353052	703010505_w323_18	C	MALAWI	2014					2264	2236		2565	HIV-1
19	☐	Blast 703010505(56552)	MF353051	703010505_w323_16	C	MALAWI	2014					2264	2236		2568	HIV-1

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Antibody search example: CH235.9

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References

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Displaying record number 3291

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Author Location	Env
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Ab Type	gp120 CD4BS
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- CH235.9: This review discussed antibody-virus coevolution and lineage development as a path to elicit broadly neutralizing Abs. CD4bs mAbs from donor CH505 (lineages CH103 and CH235) were used as main examples. *Bonsignori2017a* (**review**, **antibody lineage**)
- This patent application states that CH493 is also referred to as CH235.9. *Lam2017*
- CH235.9: In 5 years additional members of the CH235 clonal lineage were isolated based on deep sequencing of donor CH505's V_L and V_H chains at 17 timepoints in the donor's infection. Two of these had greater neutralization potency, CH235.9 and CH235.12. Study of crystal structures indicated a site of vulnerability near the Env CD4 binding site. The lineages of CH103 and CH235, both derived from Donor CH505 were compared - CH103 lineage K_d increased an order of magnitude each step of maturation but maintained a fast association rate; CH235 lineage however, had slower K_ds and K_as over maturation. This mAb was autoreactive, at the cytoplasmic level. CH235.9 CDRL3 interacts with HIV-1 N280 in gp120, forming 3 H-bonds which are proposed to be disrupted due to autologous virus escape mutations in patient CH505, N280S and N280T. CH235.9 was produced as a recombinant mAb of V_H and V_L sequences found at week 152. CH235.9 neutralized 44% of a 75-autologous virus panel, 77% of a 202-multiclade Env-psuedovirus panel and 58% of an 113-patient CH505-derived autologous pseudoviral panel as part of CH235 lineages, all at potencies of <50 µg/ml. It also acquired the ability to neutralize all loop D mutants that were resistant to early members of the CH235 lineage. *Bonsignori2016* (**antibody generation**, **mutation acquisition**, **neutralization**, **escape**, **binding affinity**, **antibody sequence**, **antibody lineage**)

References

Showing 3 of 3 references.

Neutralization Data: CH235.9

DATABASES SEARCH ALIGNMENTS TOOLS PUBLICATIONS GUIDES search site Search

Go to CATNAP main page

Antibody information

Number of antibodies: 1

Download heavy and light aa na sequences in Fasta

Download table below

Expand table below to show heavy and light chain sequences and sources for germline data

Antibody	Antibody binding type	Structure	Donor	Clonal lineage	Isolation paper	Neutralizing antibody feature	Heavy V (IGHV)	Heavy D (IGHD)	Heavy J (IGHJ)	Light V (IGKV or IGLV)	Light J (IGKJ or IGLJ)	Light chain type	GenSig analysis	Aliases	LANL comments
CH235.9	gp120 CD4BS	EMD-8080 EMD-8081 5F9O	Donor CH505	CH235	Bonsignori2016	○ Antibody-driven selection in donor CH505 ○ Electrostatic interactions with D368	1-46*01	3-10*01	4*02	3-15*01	1*01	K	IC_{50}	CH493	

Assay

Analyze assay data in CATNAP Submit

Number of data: 199

Download table below with additional virus info

Expand table below to show virus infomation

Antibody	Virus	Reference	IC50	Mean IC50	IC80	Mean IC80	ID50	Mean ID50
CH235.9	0013095_2_11	Bonsignori et al. Cell 165:449 (2016)	>50	UD				
CH235.9	001428_2_42	Bonsignori et al. Cell 165:449 (2016)	0.417	0.417				
CH235.9	0077_V1_C16	Bonsignori et al. Cell 165:449 (2016)	41.7	41.7				
CH235.9	00836_2_5	Bonsignori et al. Cell 165:449 (2016)	>50	UD				
CH235.9	0260_V5_C36	Bonsignori et al. Cell 165:449 (2016)	10.5	10.5				
CH235.9	0330_V4_C3	Bonsignori et al. Cell 165:449 (2016)	1.88	1.88				

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Neutralization Data: CH235.9

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Assay

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CH235.9	0330_V4_C3	Bonsignori et al. Cell 165:449 (2016)	1.88	1.88				

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Neutralization Data: CH235.9

- Antibodies with neutralization data are linked to CATNAP
  - Detailed antibody information including Ab sequences and germlines
  - Inhibition assay results against virus panels
  - Genetic signatures associated with antibody sensitivity or resistance

Antibody information

Number of antibodies: 1

Download heavy and light aa na sequences in Fasta

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Collapse

Antibody	Antibody binding type	Structure	Donor	Clonal lineage	Isolation paper	Neutralizing antibody feature	Germline paper	Germline software & DB	Heavy V (IGHV)	Heavy D (IGHD)	Heavy J (IGHJ)	Heavy CDR3 length	Heavy CDR3 seq	Light V (IGKV or IGLV)	Light J (IGKJ or IGLJ)	Light CDR3 length	Light CDR3 seq	Light chain type	Heavy chain	Light chain	GenSig analysis	Aliases	LANL comments
CH235.9	gp120 CD4BS	EMD-8080 EMD-8081 5F9O	Donor CH505	CH235	Bonsignori2016	○ Antibody-driven selection in donor CH505 ○ Electrostatic interactions with D368	Bonsignori2016	Cloanalyst	1-46*01	3-10*01	4*02	15	CVRNVGTAGSLLHYDHW	3-15*01	1*01	8		K	CH235.9 immunoglobulin heavy chain QVRLLQYGGGVKRPGASMTISCVASGYNFNDYYIHWVRQAPGQGLELMGW IDPSGGRTDYAGAFGDRVSMYRDKSMNTLYMDLRSLRSGDTAMYYCVRNV GTAGSLLHYDHWGLGVMVTVSS KU570037 CAGGTGCGACTACTACAATATGGGGGTGGAGTGAAGAGGCCTGGGGCCTC AATGACGATTTCCTGCGTGGCGTCTGGATACAACTTCAACGACTACTATA TACACTGGGTGCGACAGGCCCCTGGACAAGGCCTCGAATTGATGGGATGG ATCGACCCTAGTGGTGGTCGCACAGATTACGCAGGGGCGTTTGGGGACAG AGTGTCCATGTACAGGGACAAGTCCATGAACACACTCTACATGGACCTGA GGAGCCTGAGATCTGGCGACACGGCCATGTATTATTGTGTTAGAAATGTG GGAACGGCTGGCAGCTTGCTCCACTATGACCACTGGGGCCTGGGAGTTAT GGTCACCGTCTCCTCA		IC50	CH493	

Assay

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Number of data: 199

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Antibody	Virus	Subtype	Tier	Infection stage	Coreceptor	Country	Year	Accession	Alias	Reference	IC50	Mean IC50	IC80	Mean IC80	ID50	Mean ID50
CH235.9	0013095_2_11	C	2	intermediate	CCR5	INDIA	2000	EF117267	0013095, 0013095-2.11, 0013095.2.11, HIV_0013095_2_11, HIV-0013095-2.11	Bonsignori et al. Cell 165:449 (2016)	>50	UD				
CH235.9	001428_2_42	C	2	intermediate	CCR5	INDIA	2000	EF117266	001428, 001428-2.42, HIV_001428_2_42, HIV-001428-2.42	Bonsignori et al. Cell 165:449 (2016)	0.417	0.417				
CH235.9	0077_V1_C16	C	2	early		TANZANIA	2003	HM215254	0077, 0077_V1.C16, 0077.V1.C16	Bonsignori et al. Cell 165:449	41.7	41.7				

Neutralization Data: CH235.9

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  - Inhibition assay results against virus panels
  - Genetic signatures associated with antibody sensitivity or resistance

Antibody information

Number of antibodies: 1

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Collapse

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Assay

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Number of data: 199

Download table below with additional virus info

Collapse

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Neutralization Data: CH235.9

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Antibody information

Number of antibodies: 1

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Collapse

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Assay

Analyze assay data in CATNAP Submit

Number of data: 199

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Collapse

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Neutralization Data: CH235.9

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CATNAP

Search for 1 Ab(s)
Analyze IC_{50},IC_{80},ID_{50}

More virus info in HIV Seq DB

$IC_{50/80}$: ●<0.1 ●<1 ●<10 ●≤50 ○>cutoff or 50 (μg/ml)
ID_{50}: ●≥1000 ●≥500 ●≥200 ●≥50 ○<cutoff or 50 (μg/ml)

Virus name	Tier	CH235.9:IC50
0013095_2_11	2	UD
001428_2_42	2	0.417
0077_V1_C16	2	41.7
00836_2_5	1B or 2	UD
0260_V5_C36		10.5
0330_V4_C3	2	1.88
0439_V5_C1	2	3.49
0815_V3_C3	2	0.549
0921_V2_C14	2	1.76
16055_2_3	2	0.768
16845_2_22	2	28
16936_2_21	2	1.85
231965_C1	2	UD
235_47	2	2.25
242_14	1B or 2	UD
247_23	2	3.32
25710_2_43	1B or 2	0.983
25711_2_4	1B or 2	4.57
25925_2_22	1B or 2	2.51
26191_2_48	2	1.65
263_8	2	2.93
269_12	2	UD
Geometric mean of detected		2.7782
Geometric mean of detected & undetected*		6.24706
% detected (detected/total)		77% (154/199)

HXB2
MRVKE---KYQHLWRWG-WRWGT---MLLG-MLMI--CSAT--EKLWVT
----.-------|-----.-------|-----.------|------.--
----------10----------20----------30---------
MRVKGILRNYQQW-----WIWSI---LGFW-MLMN--CNVG--GNLWVT
MRVRGILRNYQQW-----WMWGV---LGFW-MLMI--CNGV--ENLWVT
MRVMGSMRNCQRW-----WIWGI---LGFW-MLMT--CNME--EDLWVT
MRVRGIRRNYQHW-----WIWGI---LGFW-MLMI--CKGGR-EDLWVT
MRVMGIQRNSQCF-----LSWGM---LVLG-IMMI--CSAV--GNLWVT
MRVMGMQRNSRHLL----LRWGI---RILG-MIMI--CRTA--GQLWVT
MRVMGIQRNCQHL-----LRWGT---LILG-LIII--CSTA--DKLWVT
MRVMGIQMNWQQW-----WIWGI---LGFW-MLMV--CNGT--GK-WVT
MRVRGILRNYPQW-----WIWGI---LGFW-MI----CNVV--GNLWVT
MRVRGILRNYQQW-----WIWGI---LGFW-VLMI--CN----GNLWVT
MRVRGMLRNYQQW-----WIWGV---LGFW-MLMN--CNVG--GNLWVT
MRVRGILRNYRQW-----WIWGV---LGFW-IMS---CNVV--GNLWVT
MRVREIQRNYQYL-----WRWGT---MLLG-MLMT--YSVA--EQFWVT
MRVMGIQKNYPLL-----WRWGV---IIFW-IMII--CNA---ERLWVT
MKVMGIQKNYPSF-----WRWGM---ILFW-IMMI--CNA---TNLWVT
MRVRGIKRNYPHL-----WIWGT---MLLG-MLLM-SYSAA--NNLWVT
MRVRGTLRNYQQW-----WIWGV---LGFW-MLMI--CNVG--GNLWVT
MRVKGTRKSYQQW-----WIWAV---LGFW-MLMI--CNVG--GNLWVT
MRVRGTLRNYQQW-----WIWGV---LGFW-MLMV--CNVV--GNLWVT
MRVRETQRNYLQW-----WIWGV---LGFW-MLMN--CNVG--GNLWVT
MRVKGTQMNWPSL-----WRWGT---LILG-LVTI--CSAS--DKLWVT
MRVKETORNCOLL-----WKWGI---LILG-LVIV--CSA---SNLWVT

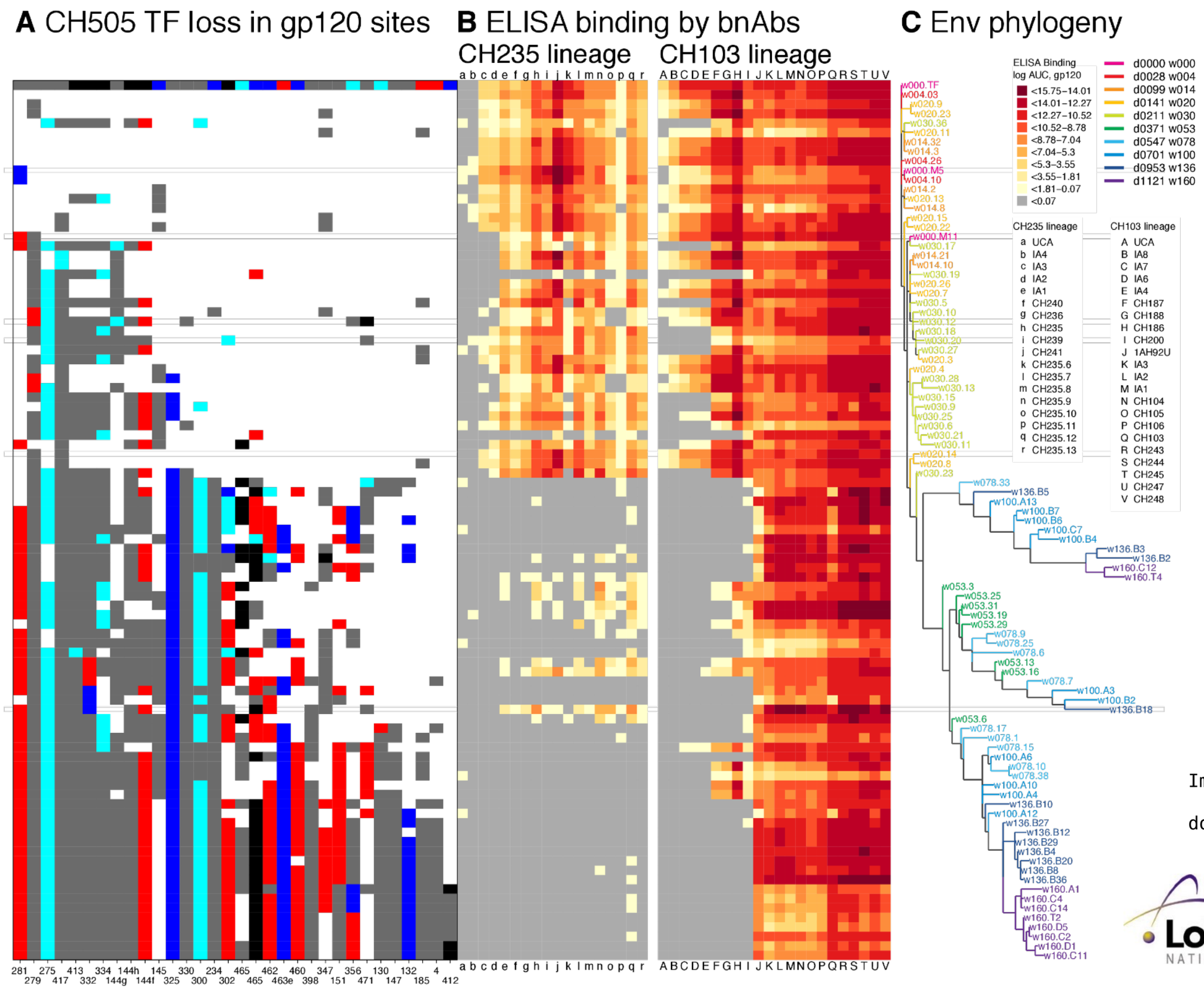
* *Values are considered as undetected, if ($IC_{50/80}$)>cutoff or >100, ($ID_{50/80}$)<cutoff or <20. For the purpose of calculating means, each undetected sets to 100($IC_{50/80}$) or 20($ID_{50/80}$).*

# of antibodies or mixtures found: 1
# of viruses found: 199
# of studies found: 1
Bonsignori2016

Download neutralization data
include ☑ virus info ☐ slice of alignment from position analysis

Download alignment ◉ aa ○ na Fasta

Immune pressure drives HIV Env evolution



Korber et al. 2017
Immunological Reviews
275:230–244
doi:10.1111/imr.12516

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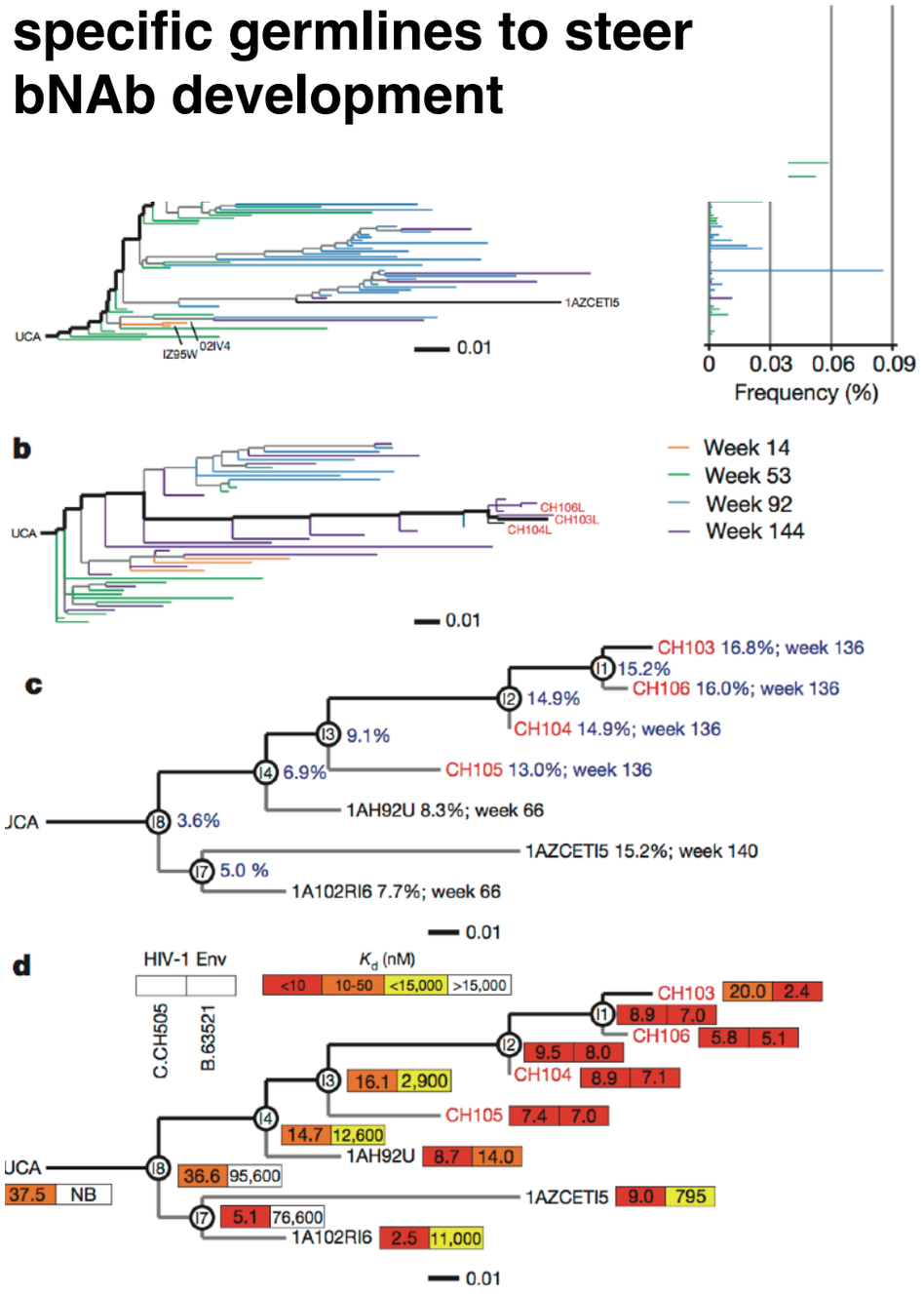
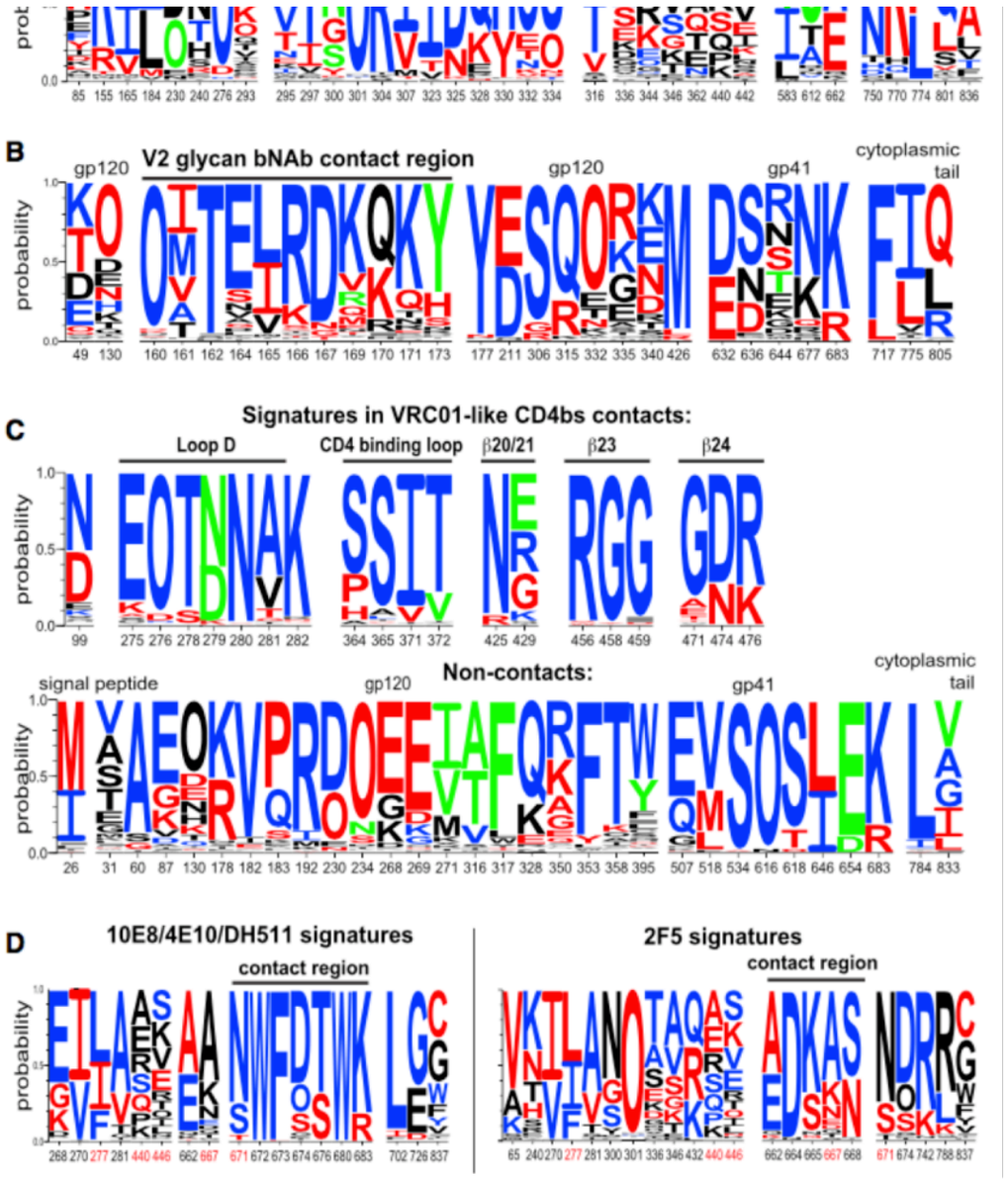
Natural infection as a guide to vaccine design: 2 examples

Immunogens that bind specific germlines to steer bNAb development

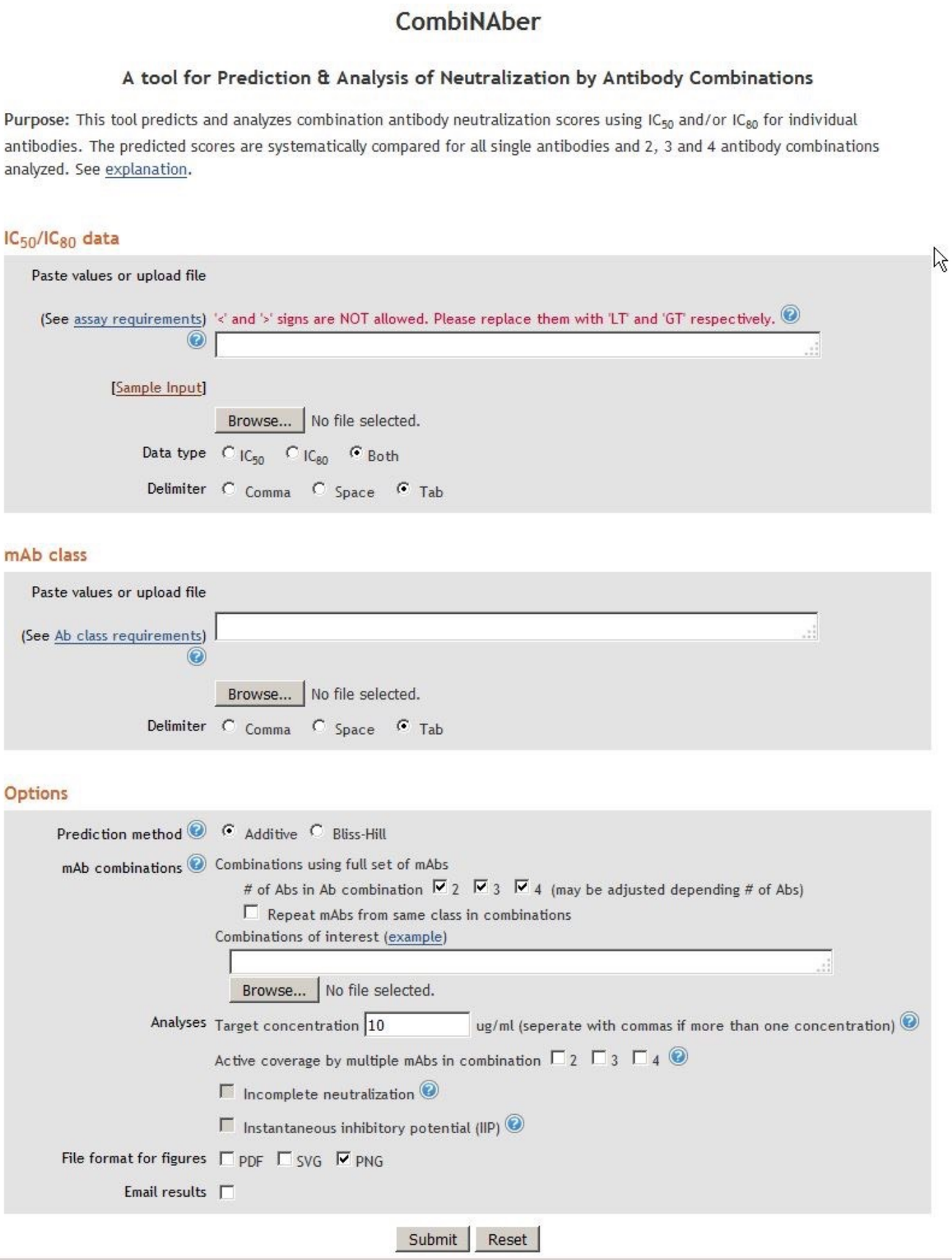


Liao et al. (2013) Co-evolution of a broadly neutralizing HIV-1 antibody and founder virus. DOI:10.1038/nature12053

Immunogens with signatures of bNAb sensitivity elicit greater neutralization breadth



Bricault et al. (2019) HIV-1 Neutralizing Antibody Signatures and Application to Epitope-Targeted Vaccine Design. DOI:10.1016/j.chom.2018.12.001



CombiNAber

- Background
  - Kong *et al*, 2015, *J Virol*
  - Wagh *et al*, 2016, *PLOS Pathogens*
  - Questions: Kshitij Wagh, kshitij@lanl.gov
- Purpose: predict neutralization by antibody combinations (to optimize immunotherapy options)
- Input:
  - Neutralization data (IC50 and / or IC80) with antibody and virus names
  - Antibody type (i.e. binding region)

www.hiv.lanl.gov/content/sequence/COMBINABER/combinaber.html

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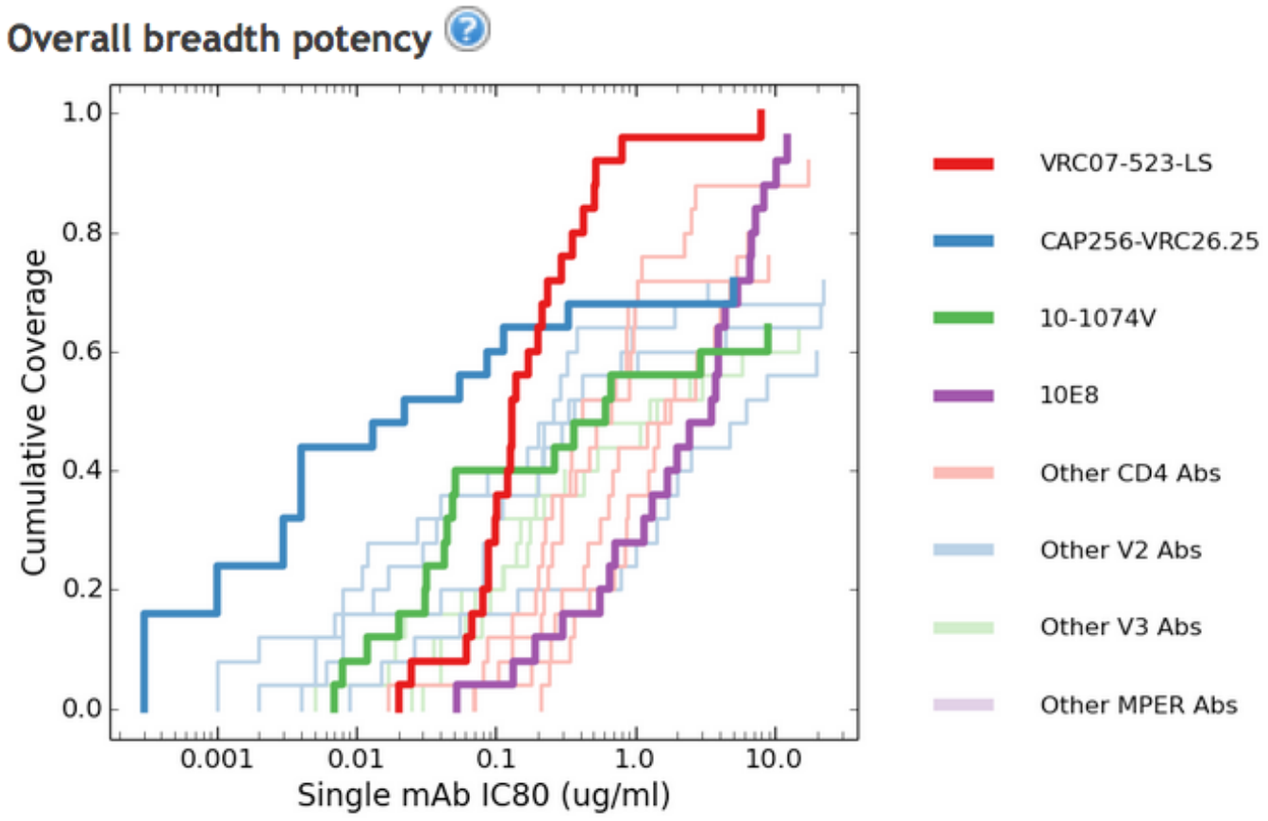
CombiNAber



Single mAbs

https://www.hiv.lanl.gov/content/sequence/COMBINABER/combinaber.html

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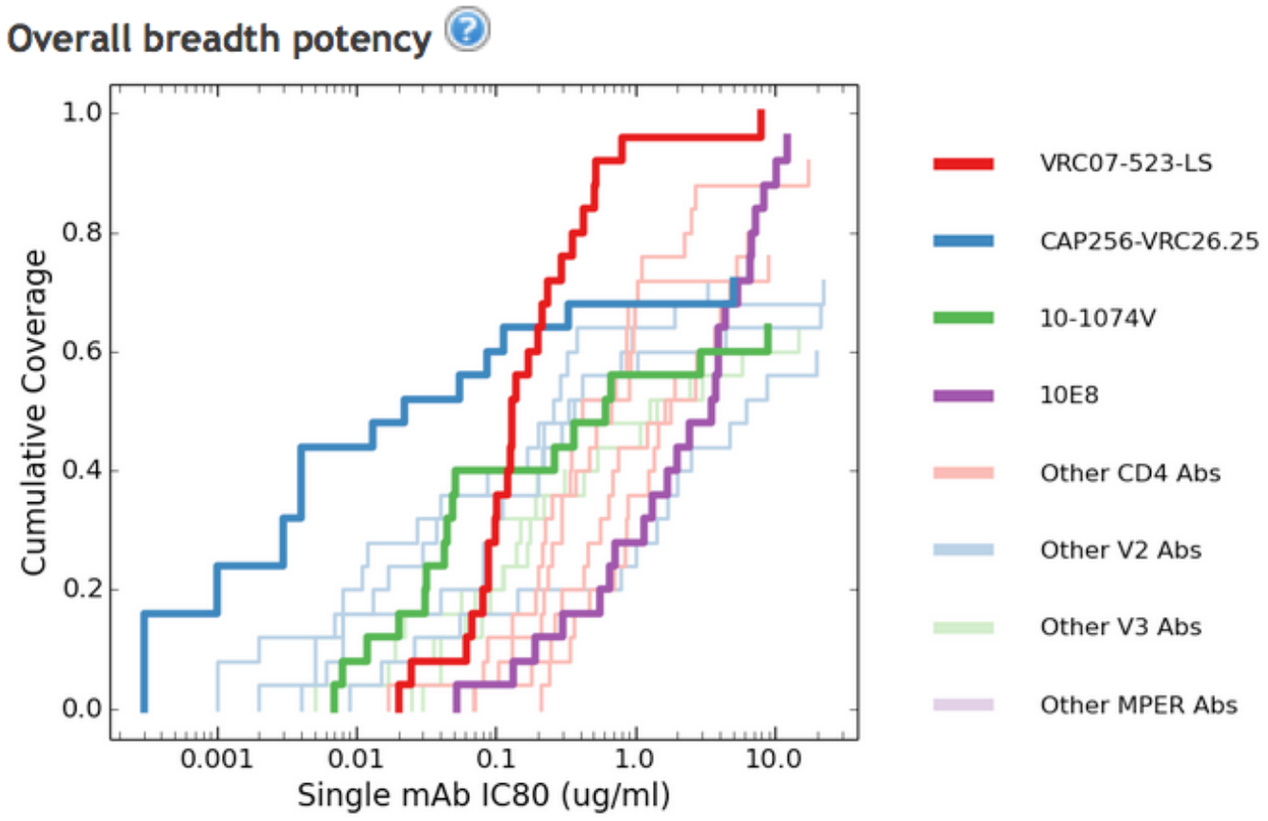
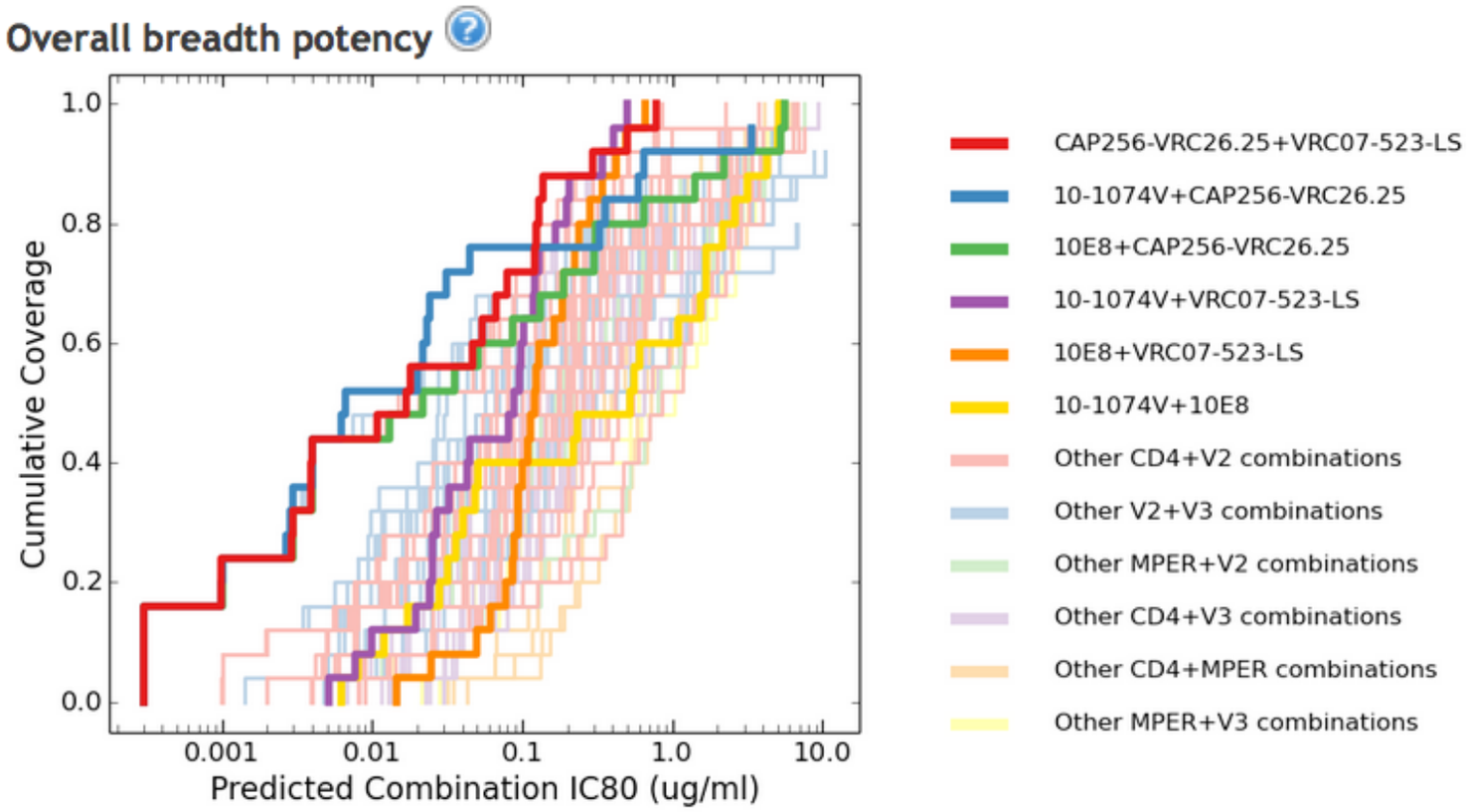
CombiNAber



Single mAbs



2-mAb combinations

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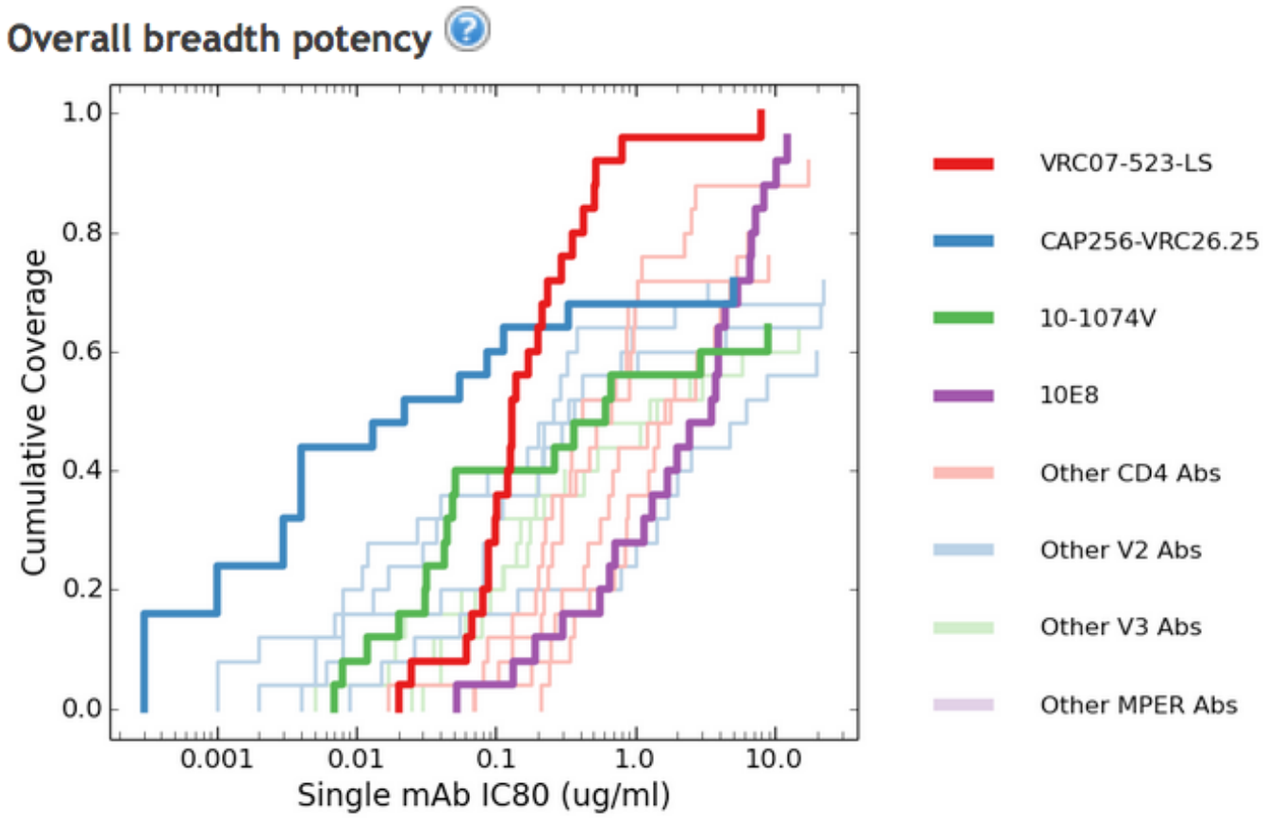
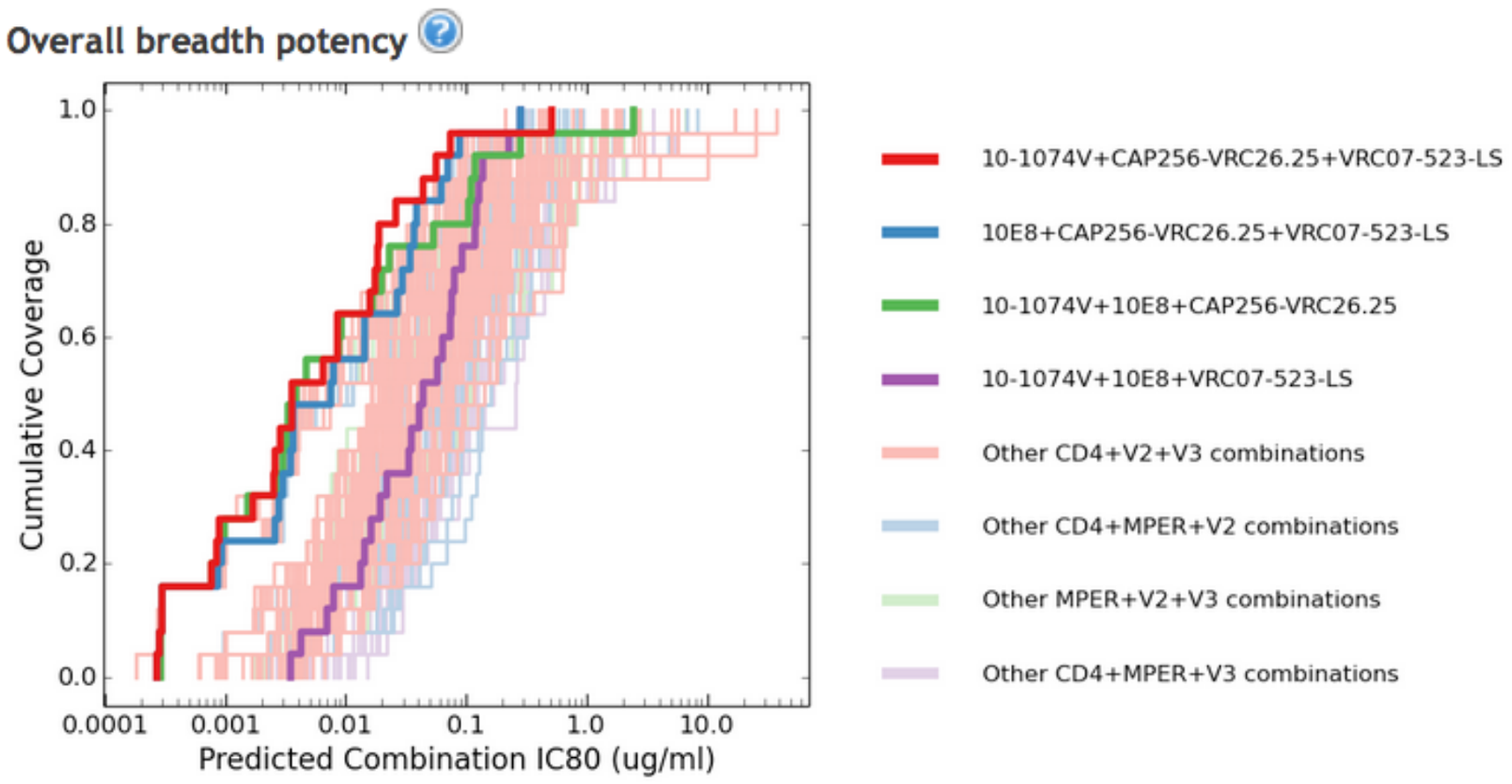
CombiNAber



Single mAbs



3-mAb combinations

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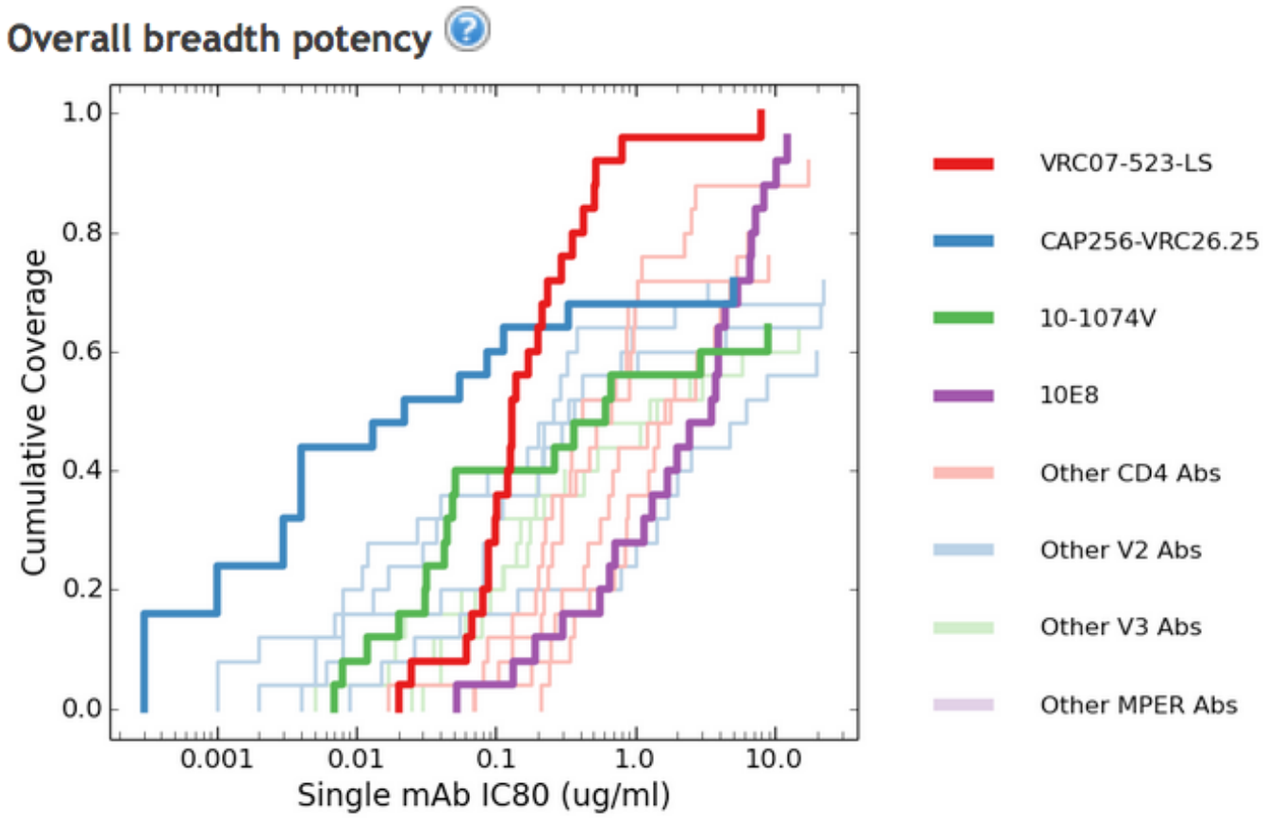
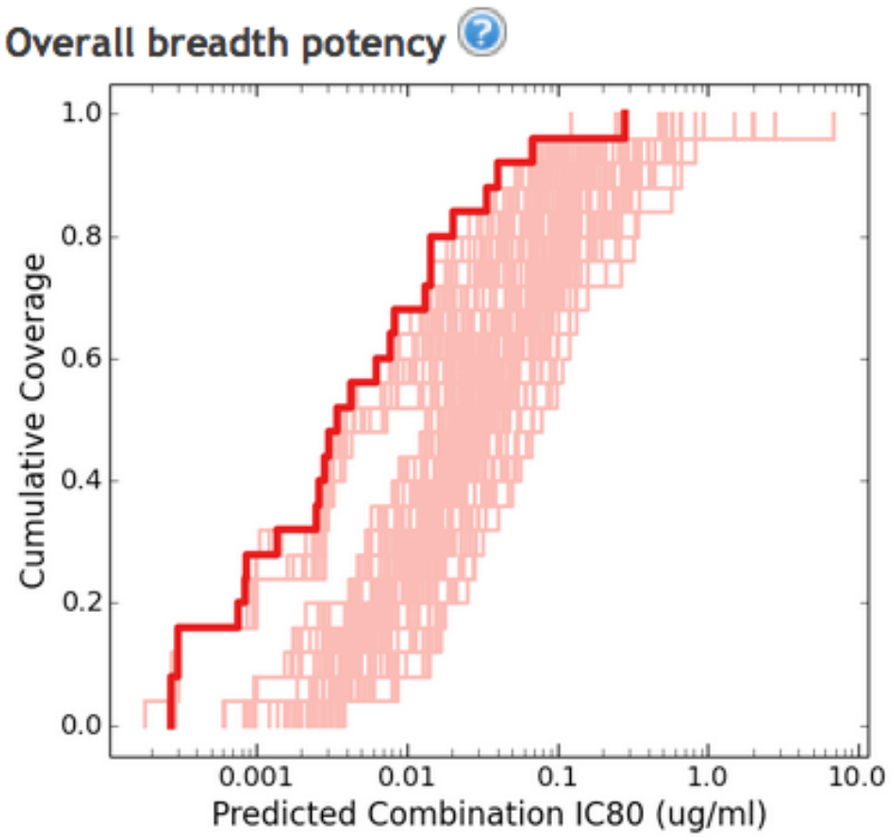


Single mAbs



4-mAb combinations

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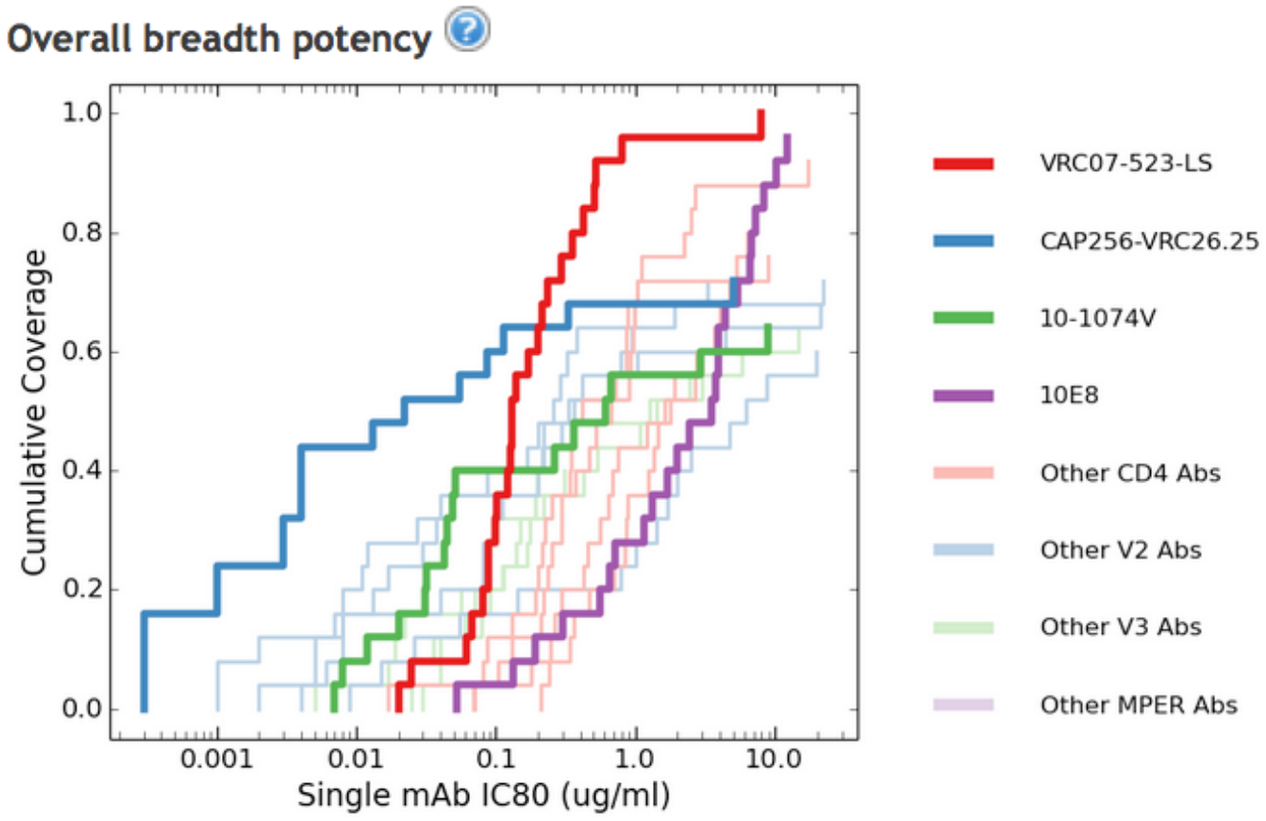
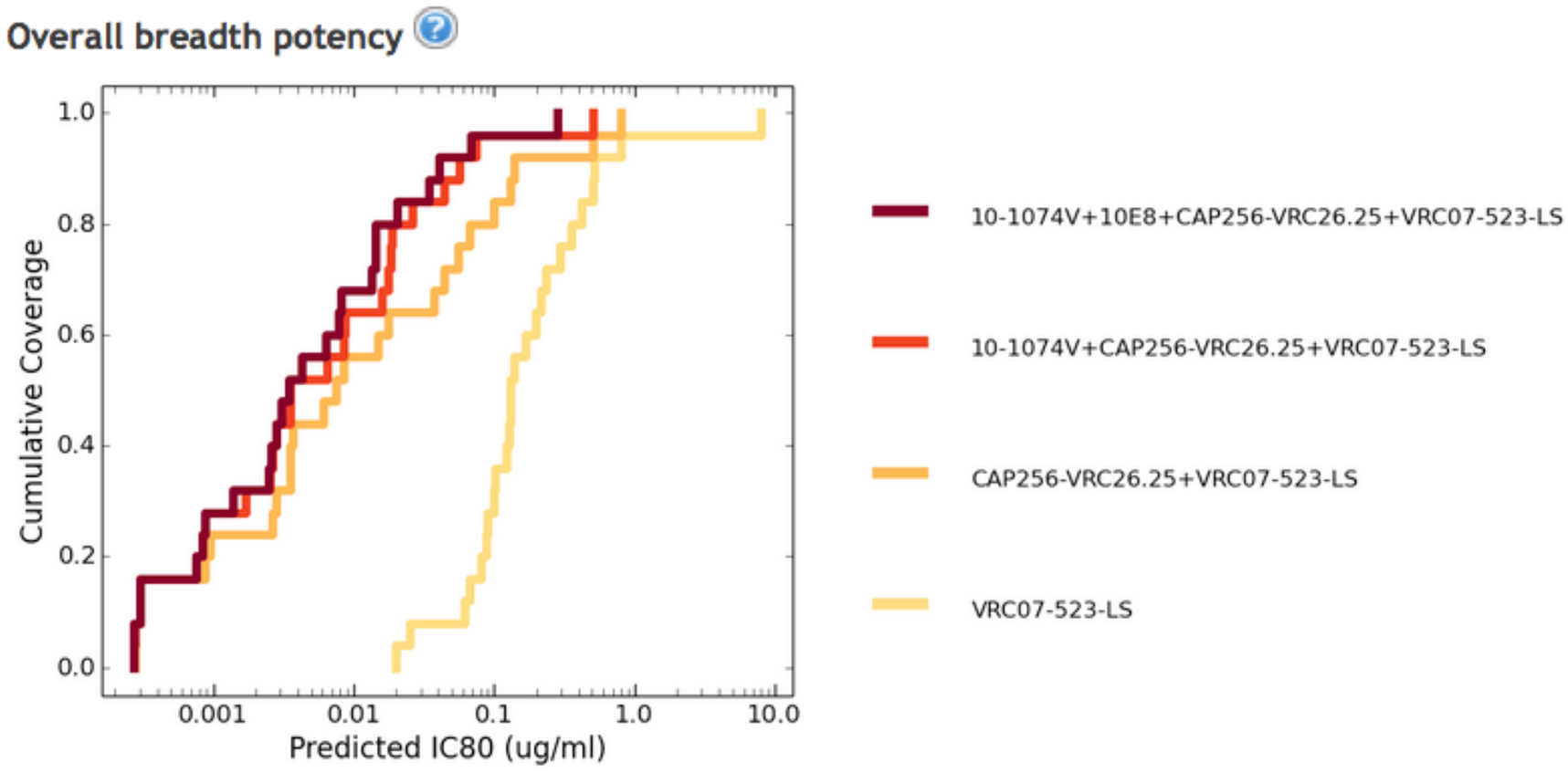
CombiNAber



Single mAbs



Best 4, 3, 2, 1 Combinations

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Glycan Shield Mapping

We developed a sequence- and structure-based method to predict the glycan shield for a given Env sequence.

- Maps potential N-linked glycosylation sites (PNGS) for a given Env sequence onto a reference trimer structure.
- Assumes each PNGS is occupied and shields 10Å around Asn C-alpha.
- Compares the given Env's glycan shield against M-group conserved glycan shields to find rare glycan holes.

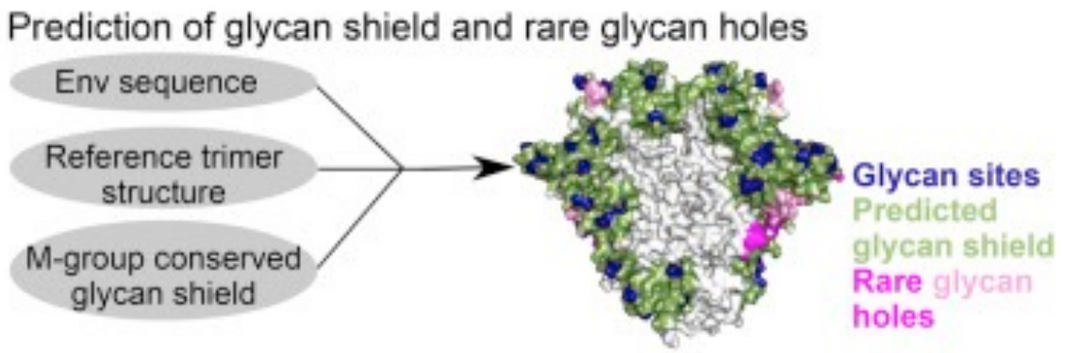
Wagh et al. used this method to show that the more complete the transmitted-founder virus' glycan shield, the higher the neutralization breadth developed in HIV-1 infections.

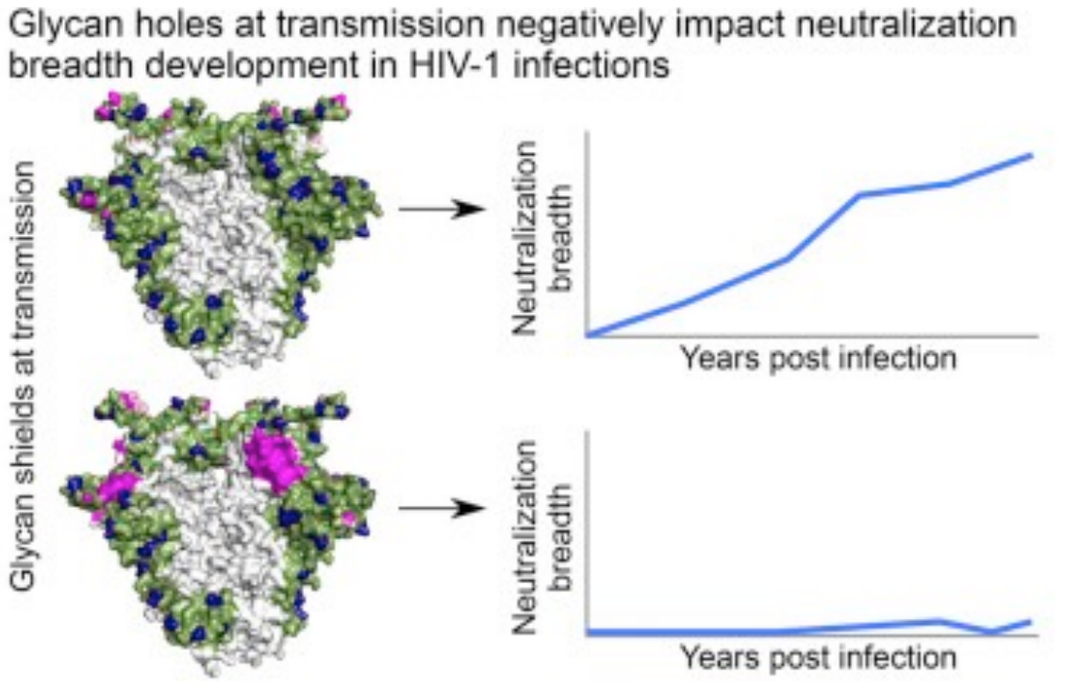
Cell Reports
Volume 25, Issue 4, 23 October 2018, Pages 893-908.e7
open access

Article

Completeness of HIV-1 Envelope Glycan Shield at Transmission Determines Neutralization Breadth

Kshitij Wagh [1, 9], Edward F. Kreider [2, 9], Yingying Li [2], Hannah J. Barbian [2], Gerald H. Learn [2], Elena Giorgi [1], Peter T. Hraber [1], Timothy G. Decker [2], Andrew G. Smith [2], Marcos V. Gondim [2], Lindsey Gillis [3], Jamie Wandzilak [3], Gwo-Yu Chuang [4], Reda Rawi [4], Fangping Cai [5], Pierre Pellegrino [6], Ian Williams [6], Julie Overbaugh [7], Feng Gao [5], Peter D. Kwong [4], Barton F. Haynes [5], George M. Shaw [2], Persephone Borrow [8], Michael S. Seaman [3], Beatrice H. Hahn [2, 10], Bette Korber [1, 10, 11]



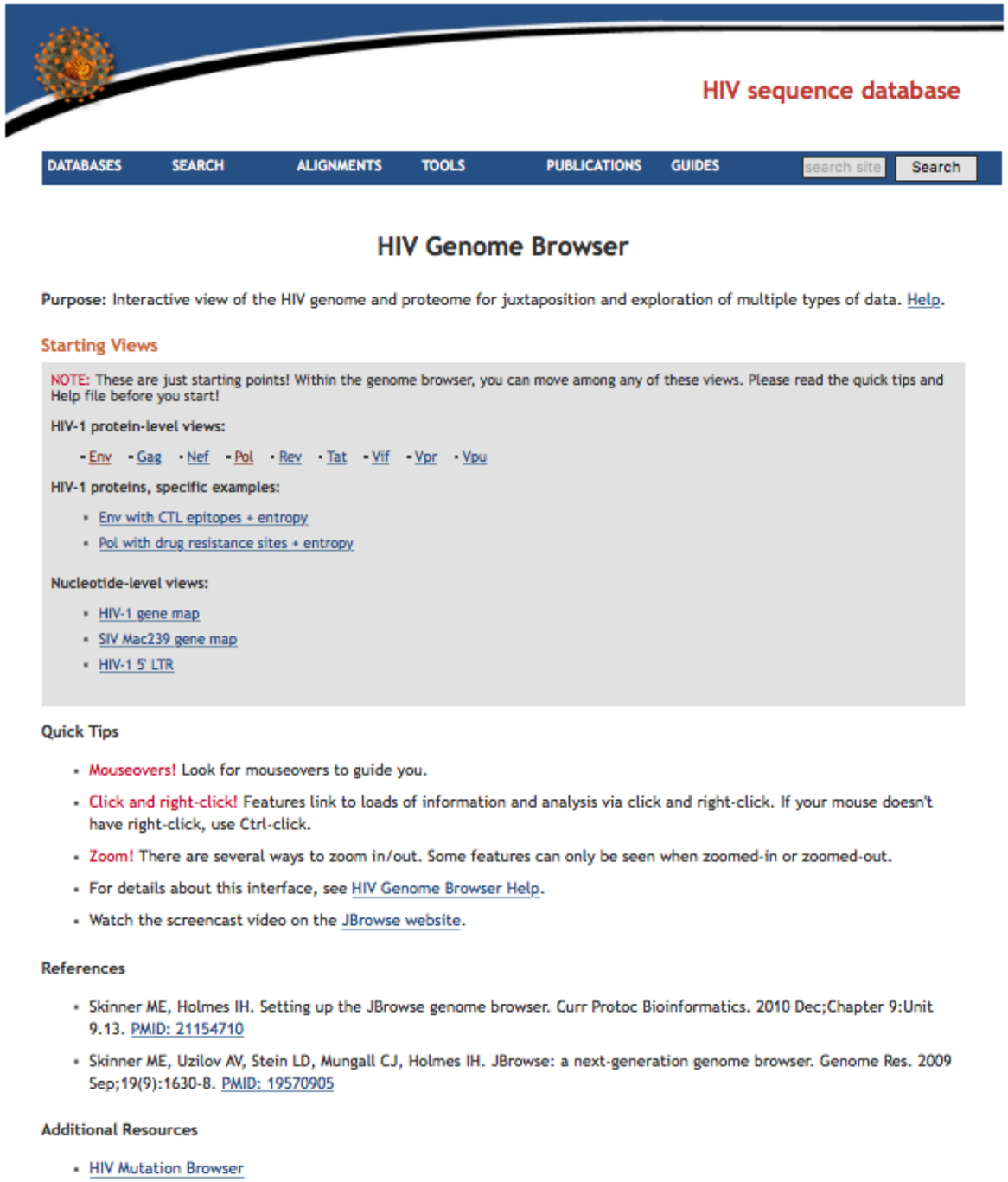


https://www.hiv.lanl.gov/content/sequence/GLYCOSITE/glycosite.html

Genome Browser

A tool at the interface between the sequence and immunology database

- Provides a multi-level scalable view of the HIV genome/ proteome
- Includes antibody and CTL epitopes, protein features, selected mutation sites, entropy ...



HIV sequence database

DATABASES SEARCH ALIGNMENTS TOOLS PUBLICATIONS GUIDES search site Search

HIV Genome Browser

Purpose: Interactive view of the HIV genome and proteome for juxtaposition and exploration of multiple types of data. Help.

Starting Views

NOTE: These are just starting points! Within the genome browser, you can move among any of these views. Please read the quick tips and Help file before you start!

HIV-1 protein-level views:

- Env - Gag - Nef - Pol - Rev - Tat - Vif - Vpr - Vpu

HIV-1 proteins, specific examples:

- Env with CTL epitopes + entropy
- Pol with drug resistance sites + entropy

Nucleotide-level views:

- HIV-1 gene map
- SIV Mac239 gene map
- HIV-1 5' LTR

Quick Tips

- Mouseovers! Look for mouseovers to guide you.
- Click and right-click! Features link to loads of information and analysis via click and right-click. If your mouse doesn't have right-click, use Ctrl-click.
- Zoom! There are several ways to zoom in/out. Some features can only be seen when zoomed-in or zoomed-out.
- For details about this interface, see HIV Genome Browser Help.
- Watch the screencast video on the JBrowse website.

References

- Skinner ME, Holmes IH. Setting up the JBrowse genome browser. Curr Protoc Bioinformatics. 2010 Dec;Chapter 9:Unit 9.13. PMID: 21154710
- Skinner ME, Uzilov AV, Stein LD, Mungall CJ, Holmes IH. JBrowse: a next-generation genome browser. Genome Res. 2009 Sep;19(9):1630-8. PMID: 19570905

Additional Resources

- HIV Mutation Browser

https://www.hiv.lanl.gov/content/sequence/genome_browser/browser.html

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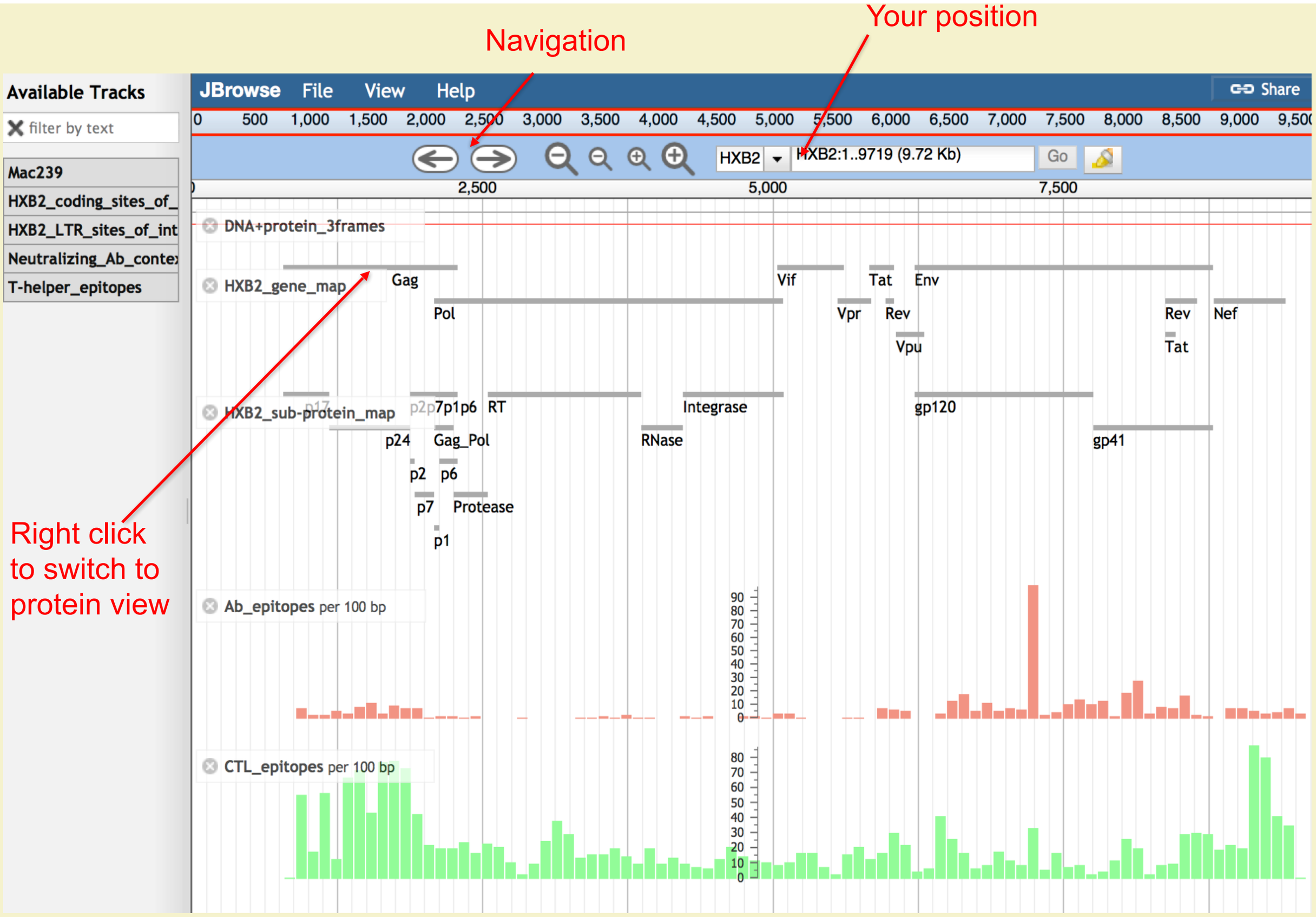
HIV Genome Browser: Nucleotide view



Available Tracks

filter by text

Sub-protein_map
T-helper_epitopes
Ab_epitopes
Entropy_C_clade
Entropy_B_clade

JBrowse File View Help Share

0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600 620 640 660 680 700 720 740 760 780 800 820 840

Env Env:154..230 (78 b) Go

175 200 225

AA

Entropy_M_group

CTL_epitopes

IRDKVQKEY (B27)
YSENSSEYY (A*01)
SVITQACPK (A*11
IPIHYCAPA (B*0702
KNCSFNMTT (human)
NCSFNISTSI (Cw8)
YRLINCNTSV (A2)
CPKVSFEPI (B*0702
HYCAPAGFAIL (human)
TLTSCNTSV (A*0201
KMSFEPIPIH (A29)
ILRSCNTSV (A2)
VSFEPIPPHYCA (A2)
KLTSCNTSV (A2)
VSFEPIPIHY (A29)
RLISCNTSV (A2)
YCAPAGFAIL (Cw*01
CTPAGYAILKC (human)
CAPAGFAIL (Cw1)

Search immunology database entries
Highlight this region
Quickalign: epitope aligned to database seqs
Switch to nucleotide view

Right-click: Links

Neutralizing_Ab_contexts

Env156: PG9-like contacts
Env160: PG9-like contacts
Env160: Mutation affects PG9-like Ab sensitivity
Env160: PG9 signature predictions
Env160: PG16 signature predictions
Env165: PG9-like contacts
Env167: PG9-like contacts
Env168: PG9-like contacts
Env169: PG9-like contacts
Env169: Mutation associated with RV144 vaccine efficacy
Env169: Mutation affects PG9-like Ab sensitivity
Env167: Mutation affects sensitivity
Env170: PG9-like contacts
Env173: PG9-like contacts
Env173: Mutation affects PG9-like Ab sensitivity
Env171: Mutation affects PG9-like Ab sensitivity
Env171: PG16 signature predictions
Env171: PG9-like contacts
Env171: PG9 signature predictions
Env181: Mutation associated with RV144 vaccine efficacy
Env180: Mutation affects sensitivity
Env184: PGT121 signature predictions
Env185: IGg1b12 signature predictions
Env196: CD4 contacts
Env197: Mutation affects sensitivity
Env198: CD4 contacts
Env199: Mutation affects PGV04, b12, VRC01, CD4-IgG
Env197: CD4 independence, intrinsic reactivity

Left-click: Details

Env160: PG16 signature predictions

Protein Location: 160..160
Protein: HXB2
DNA_pos: 6702..6704
Annotation: PG16: glycosylation at N160 is associated with increased susceptibility to neutralization; intermediate quality of support.

HXB2_sites_of_interest

glycosite160
Coreceptor-specific(R5/X4)site
LDI/LDVtripeptidebindsintegrin
Coreceptor-specific(R5/X4)site
CoreceptorbindingsiteoutsideV3
glycosite156
V2hypervariableregion
Cys196:linkedtoCys126
Cys205:linkedtoCys119
Cys218:linkedtoCys247
V2loop
Coreceptor-specific(R5/X4)site
Cys157linkedtoCys131toformV1loop
glycosite186
CD4contactresidue,side-chain-onlycontact
glycosite197
Coreceptor-specific(R5/X4)site
Coreceptor-specific(R5/X4)site

More tools for Immunologists

Most tools are applicable to any organism and some to any numerical data

- **CATNAP**: Compile, Analyze and Tally published and your own NAb Panels
- **CombiNAber**: Predict and analyze neutralization by antibody combinations
- **Sequence Locator:** Find epitope location on the reference genome
- **PepMap:** Map an input set of peptides on the reference sequence (Fasta, PDF and HTML)
- **PeptGen:** Generate sets of overlapping peptides for epitope mapping.
- **QuickAlign** and **AnalyzeAlign:** Align query sequences or discontinuous positions to an alignment, create WebLogos, calculate frequency by position, tally variants in an alignment
- **ELF:** Epitope Location Finder. Search query sequence for
  - Known epitopes from our HIV immunology databases
  - HLA binding motifs
  - Epitopes predicted by the IEDB binding algorithm.
- **N-Glycosite:** Find potential N-linked glycosylation sites in an alignment
- **Mosaic** and **Epigraph:** Generate candidate vaccine protein cocktails with optimized potential epitope coverage, calculate and visualize coverage
- **Heatmap:** Display and organize neutralization or other quantitative data.
- And more …

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HIV/SIV Sequence Locator Tool

- Calculates DNA or protein fragment location relative to a reference strain
  - Available for HIV-1, SIV, HCV, and similar tools exit in HFV database
  - Such numbers, often included in the literature, are frequently incorrect

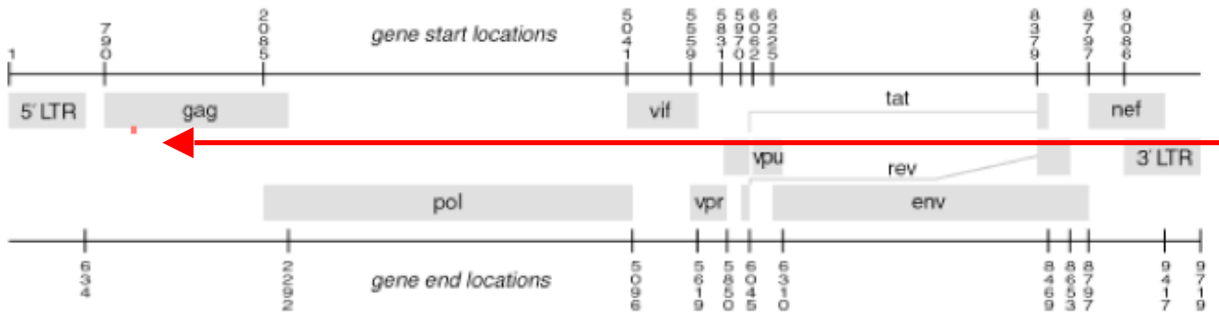
Find the location of a sequence

Sequence type ◉ Let program decide ○ HIV ○ SIV

Paste your input here [Sample Input]

SLYNTVATL

Paste or type a DNA or protein sequence here.



Location in genome mapped in red.

Table of protein regions touched by query sequence. AA = amino acid, NA = nucleic acid.					
CDS	**AA** position relative to protein start in HXB2	**AA** position relative to query sequence start	**AA** position relative to polyprotein start in HXB2	**NA** position relative to CDS start in HXB2	**NA** position relative to HXB2 genome start
Gag	77 → 85	1 → 9	NA	229 → 255	1018 → 1044
p17	77 → 85	1 → 9	NA	229 → 255	1018 → 1044

Alignment of the query sequence to HXB2 (Similarity 100.0%):

```
Query SLYNTVATL  9
      :::::::::
 HXB2 SLYNTVATL
```

http://www.hiv.lanl.gov/content/sequence/LOCATE/locate.html

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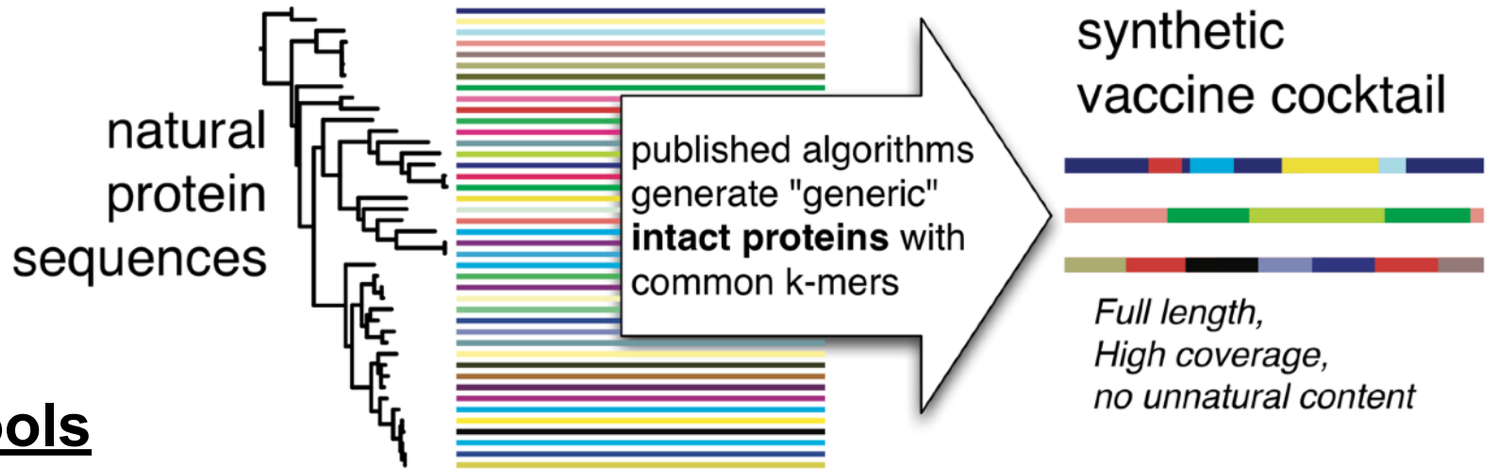
Vaccine Design Tools (Mosaic/Epigraph)



Design Tools

Generate candidate vaccine protein cocktails that optimize coverage of potential T-cell epitopes (as linear *k*-mers) based on frequencies in sets of natural pathogen sequences — "all-natural" throughout, including breakpoints

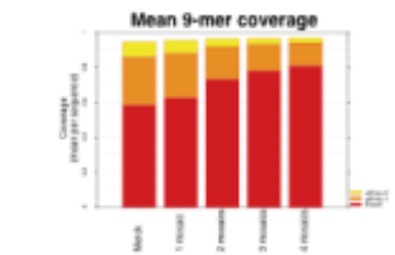
Mosaic Vaccine Designer — genetic algorithm (Fischer et al. 2007)

https://www.hiv.lanl.gov/content/sequence/MOSAIC/makeVaccine.html

Epigraph — graph theoretic approach (Theiler et al. 2016)

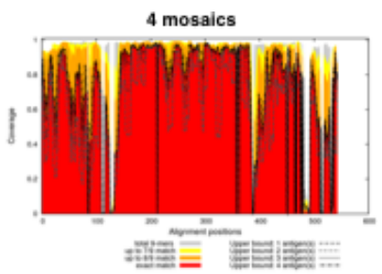
https://www.hiv.lanl.gov/content/sequence/EPIGRAPH/epigraph.html

Evaluation tools



Epitope Coverage Assessment (EPICOVER)

Alignment-independent "k-mer" coverage by vaccines or peptides.



Positional Epitope Coverage Assessment (POSICOVER)

Alignment-based coverage by vaccines or peptides.

https://www.hiv.lanl.gov/content/sequence/MOSAIC/

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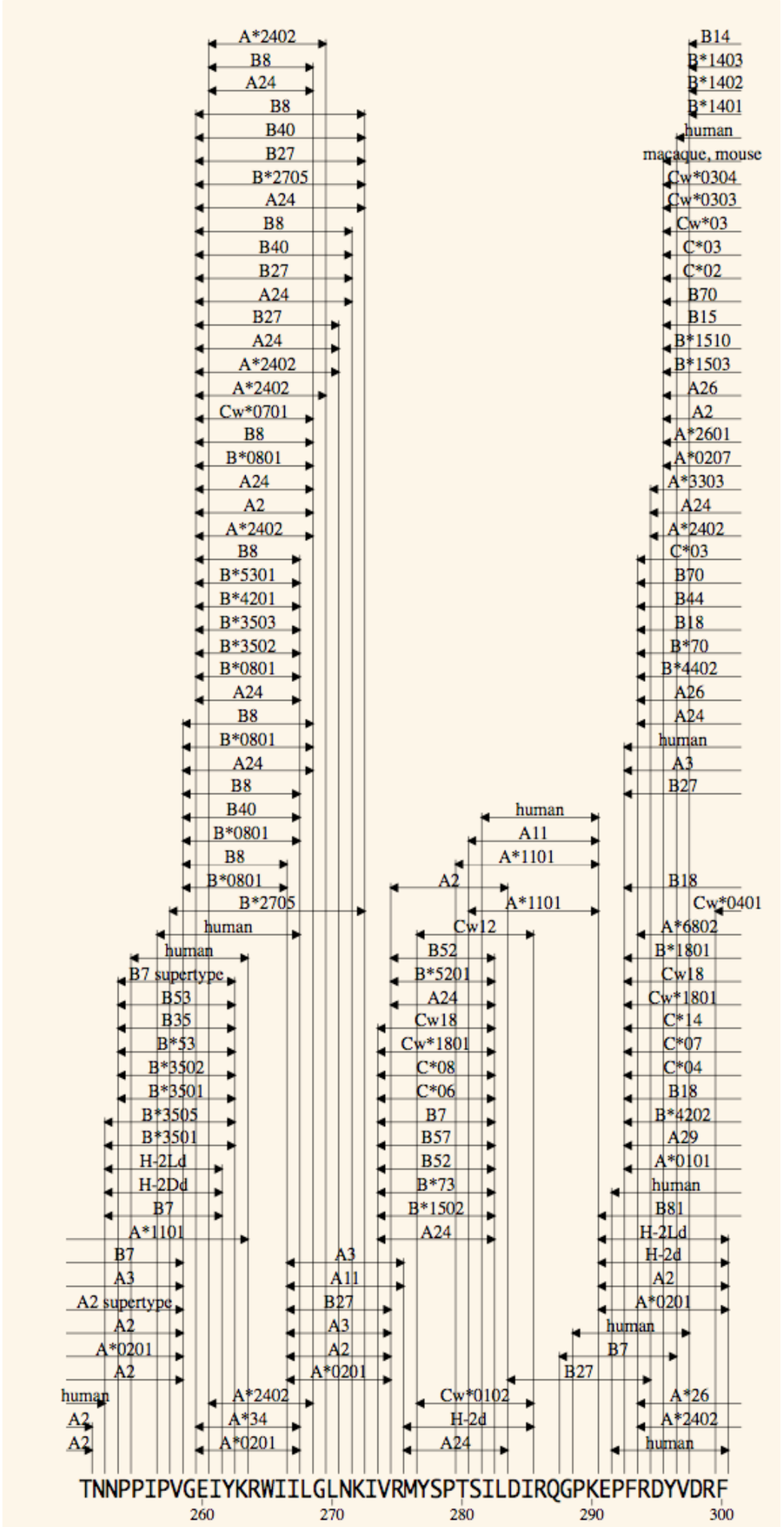
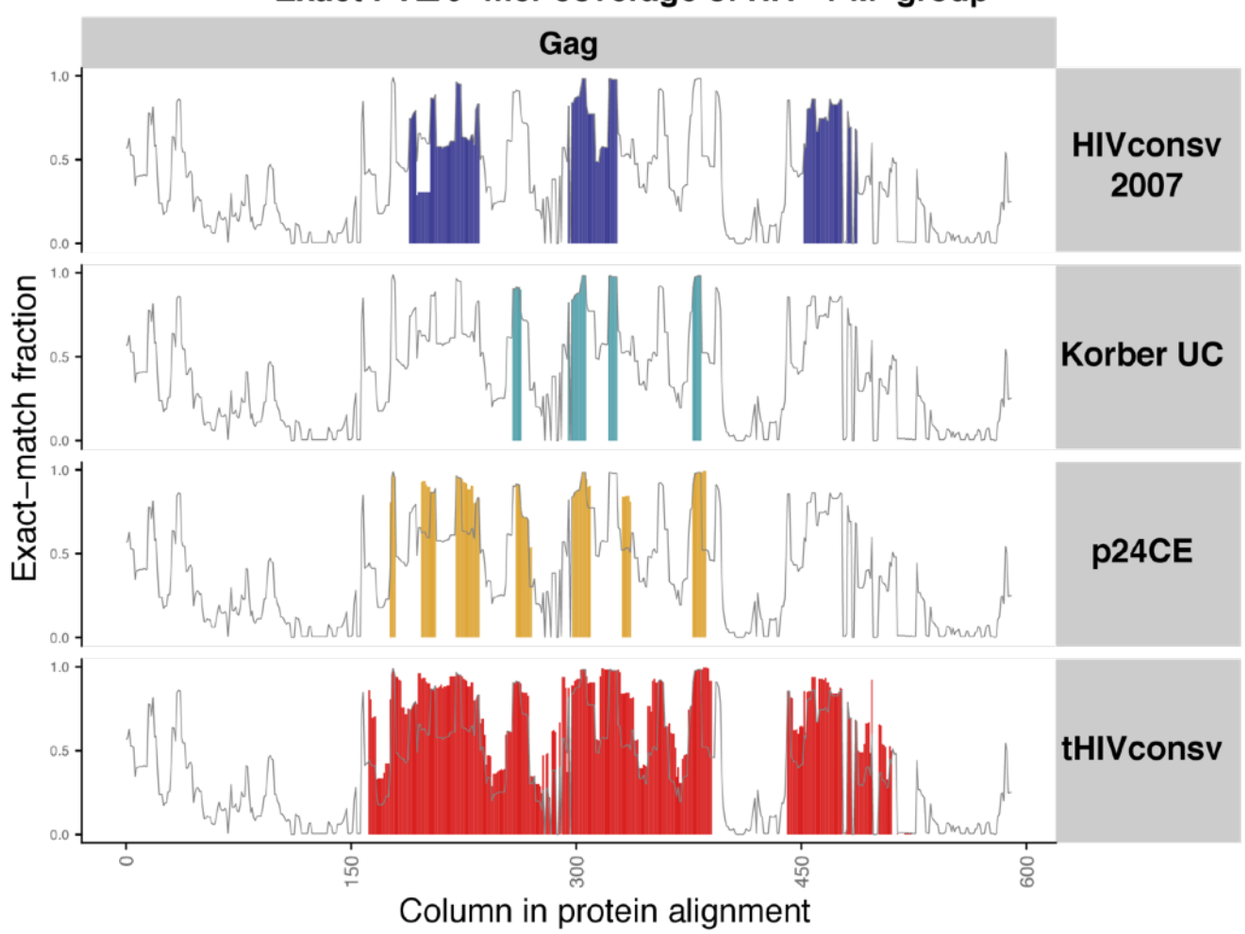
HIV epitopes are densely packed at the population level

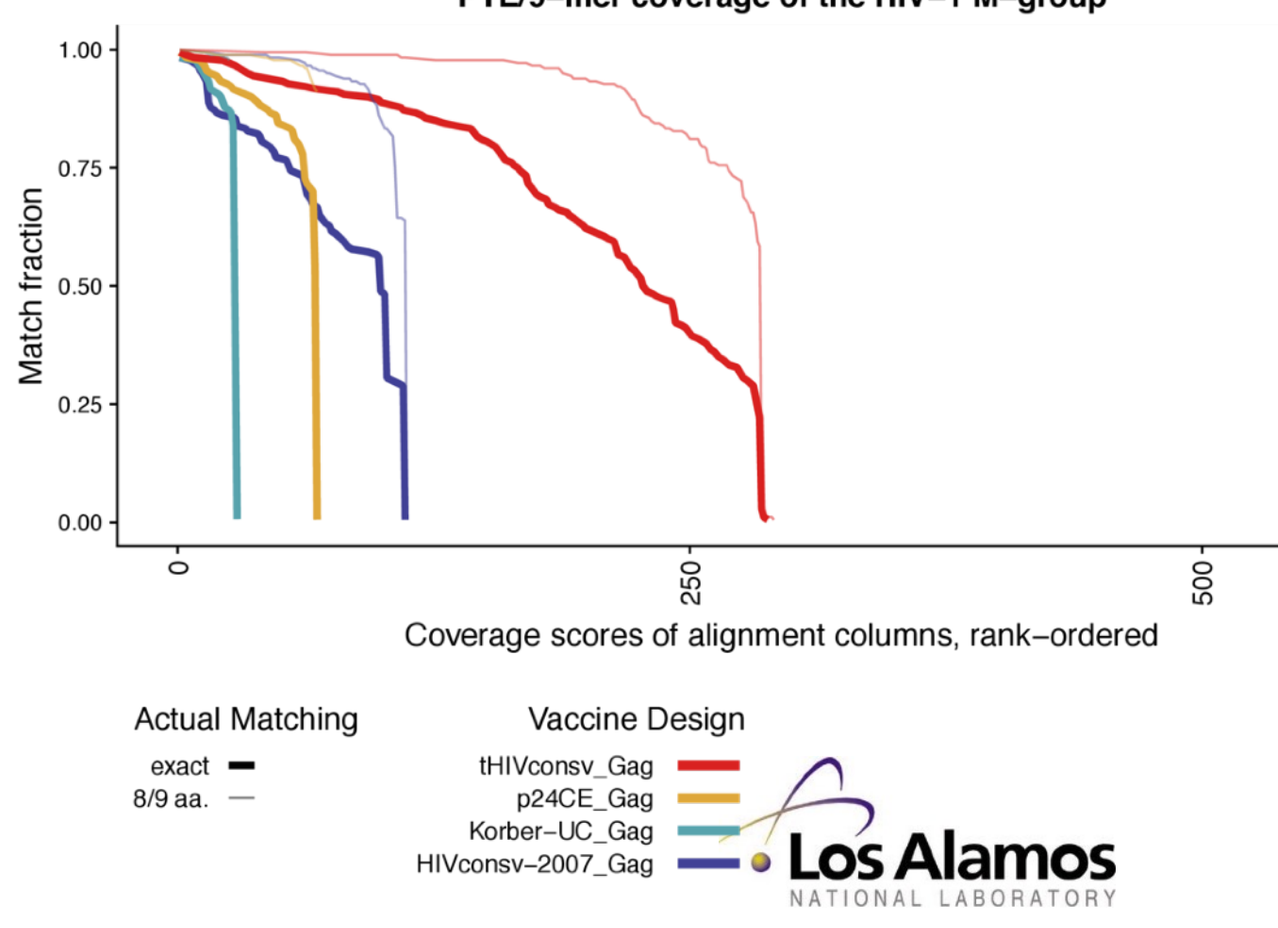
- Vaccinating a diverse population with individual epitopes is infeasible
- Escape forms for one HLA are frequently sensitive for a different HLA
- It may not be necessary to ***predict*** epitopes — but only to ***deliver*** them
- Optimized immunogen cocktails could deliver most epitopes likely to be present in infecting virus



New tool for comparing HIV vaccine antigens: VACC_COVER

- Plots vaccine proteome coverage
- Shows 9-mer coverage of known pathogen variants
- Computes numbers of reported epitope regions and associated MHC alleles





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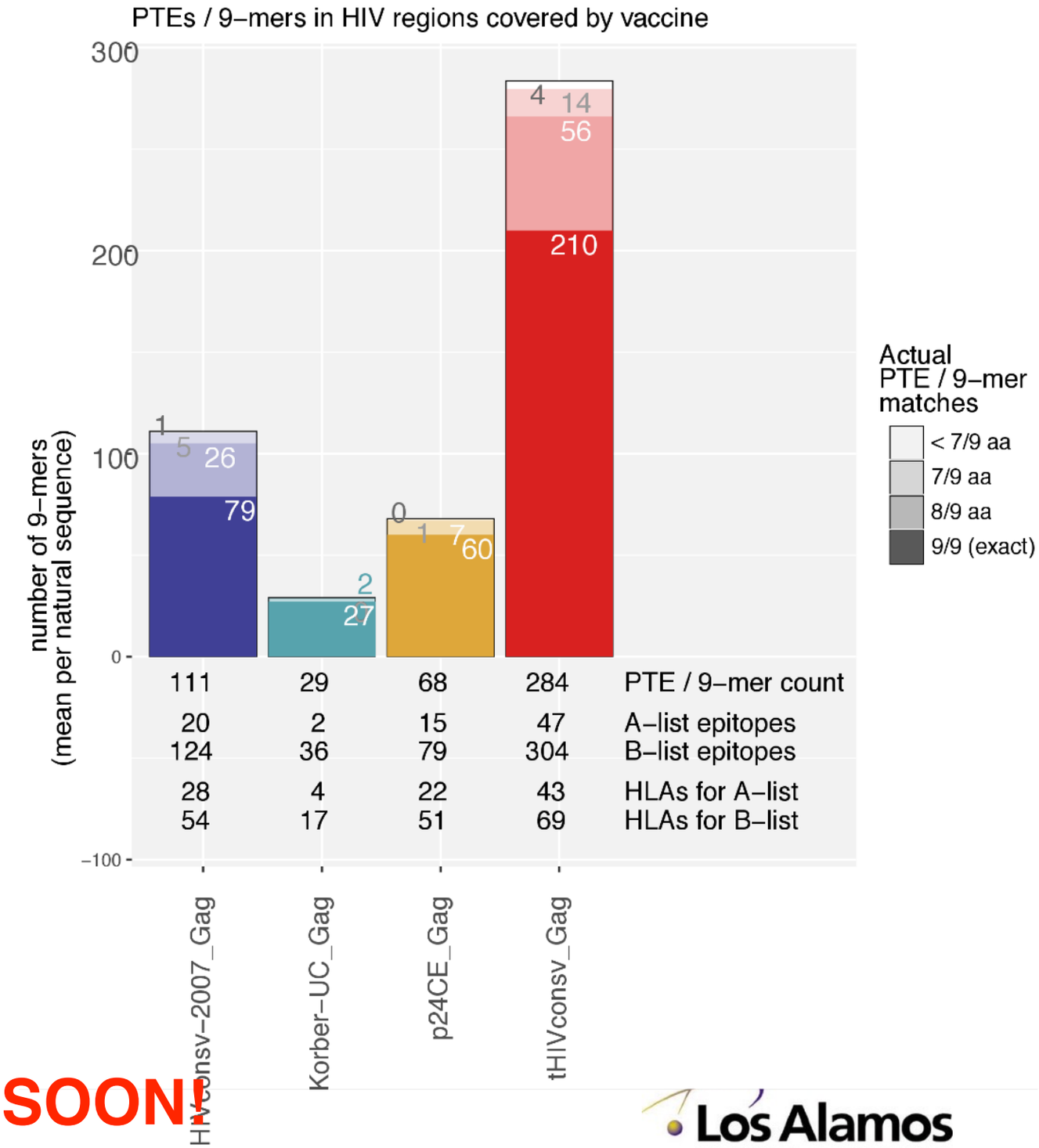
New tool for comparing vaccine antigens: VACC_COVER

- Counts epitopes (and their MHC alleles) in the regions included in the vaccine
- Reports the proportions of 9-mers (potential epitopes) that match pathogen populations
- Allows comparisons between candidate vaccines to consider epidemiological and immunological context
- DOI:10.1080/21645515.2019.1666957



In development: AVAILABLE SOON!

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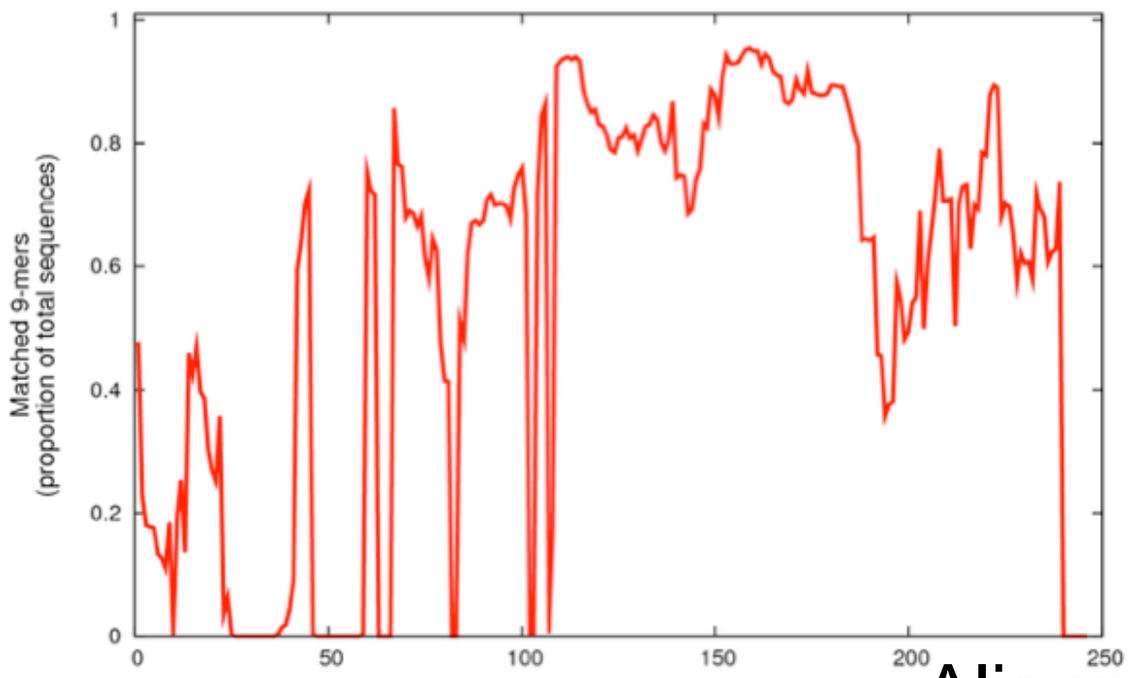
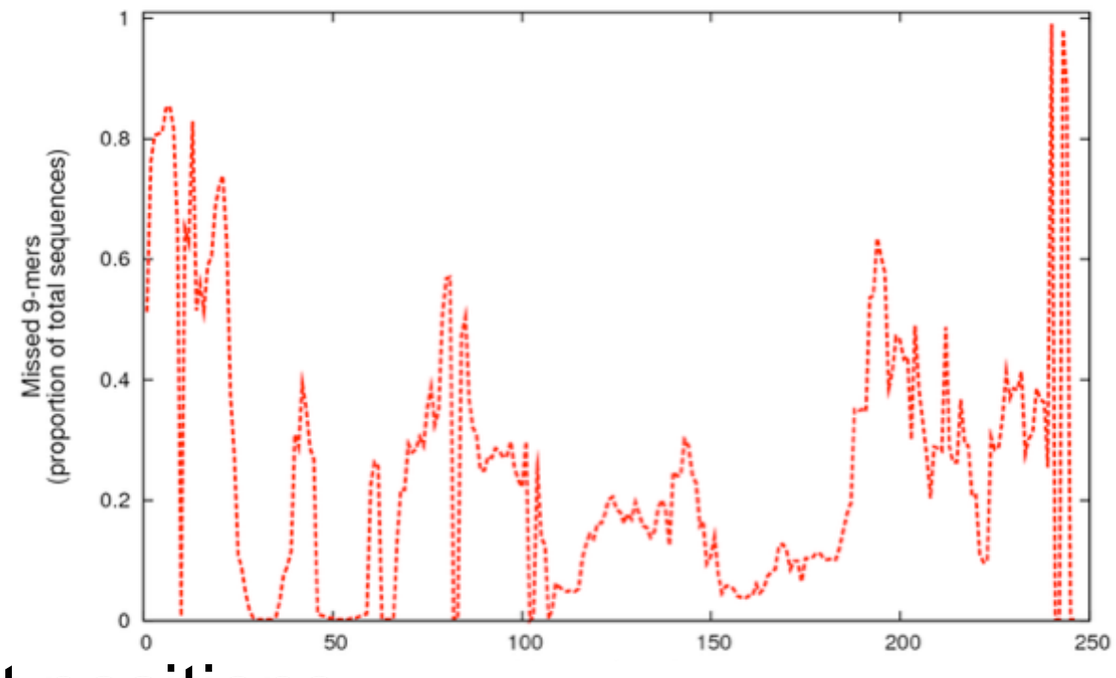
Posicover output (1-dimensional summaries)

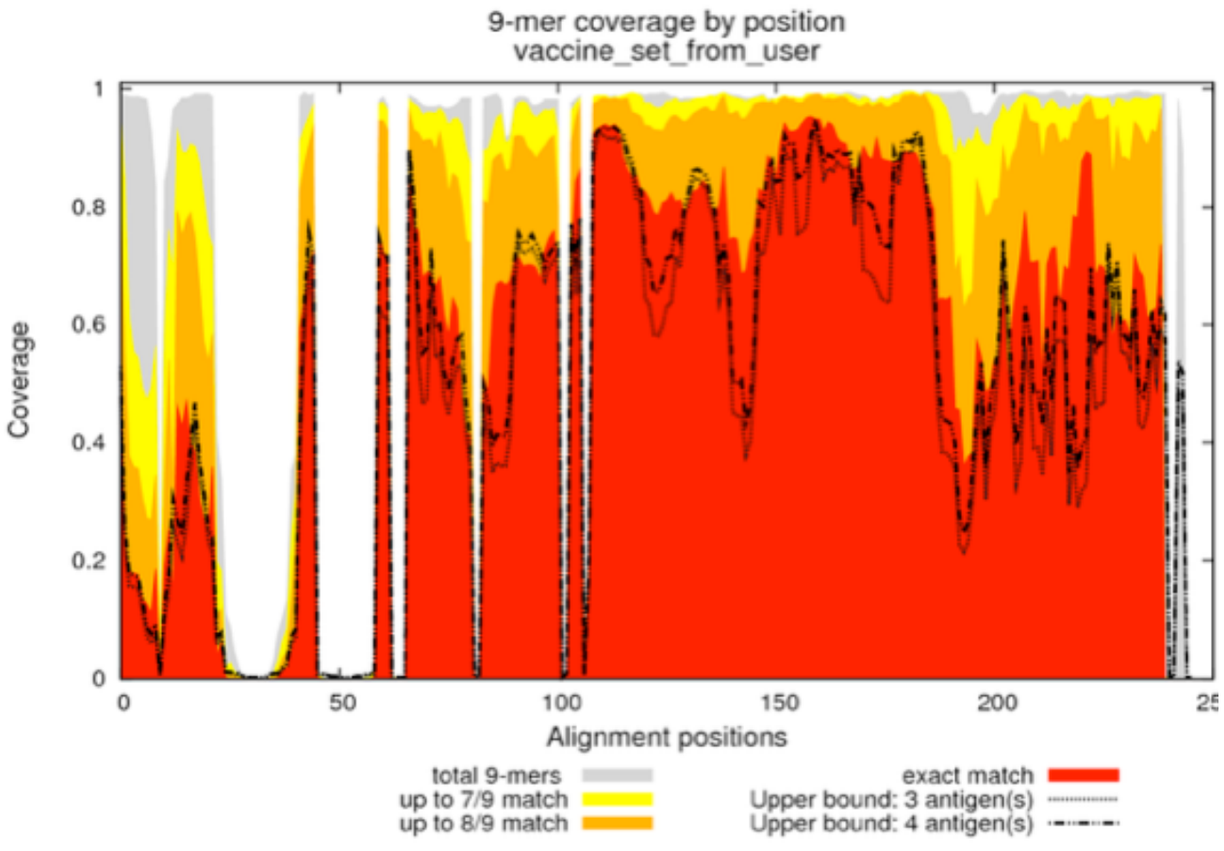
Matched 9-mers

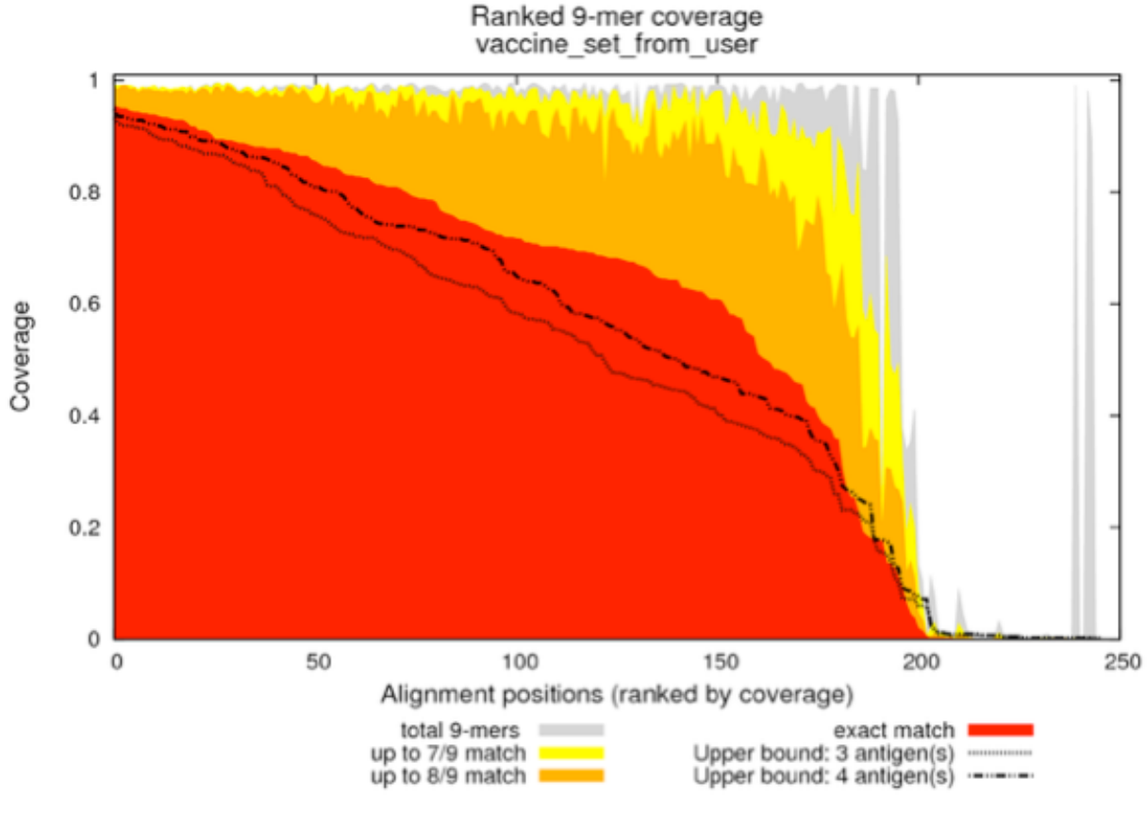


Missed 9-mers

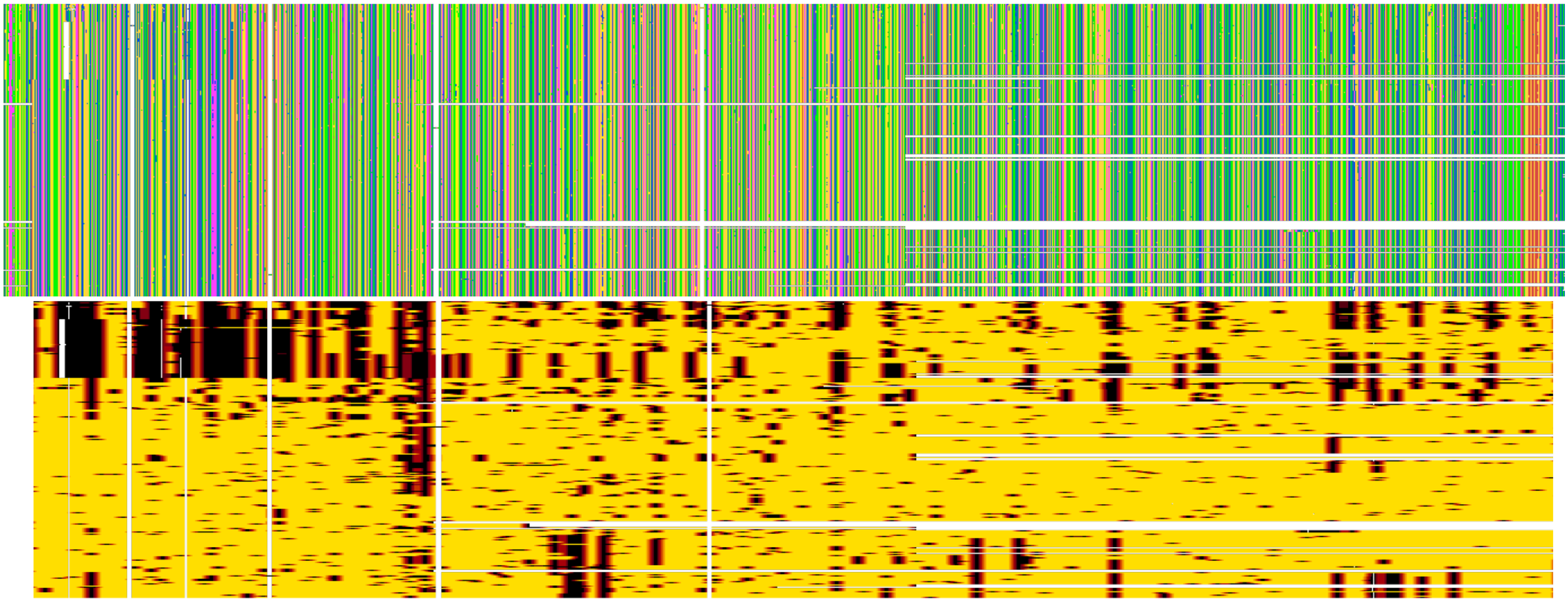


Alignment positions



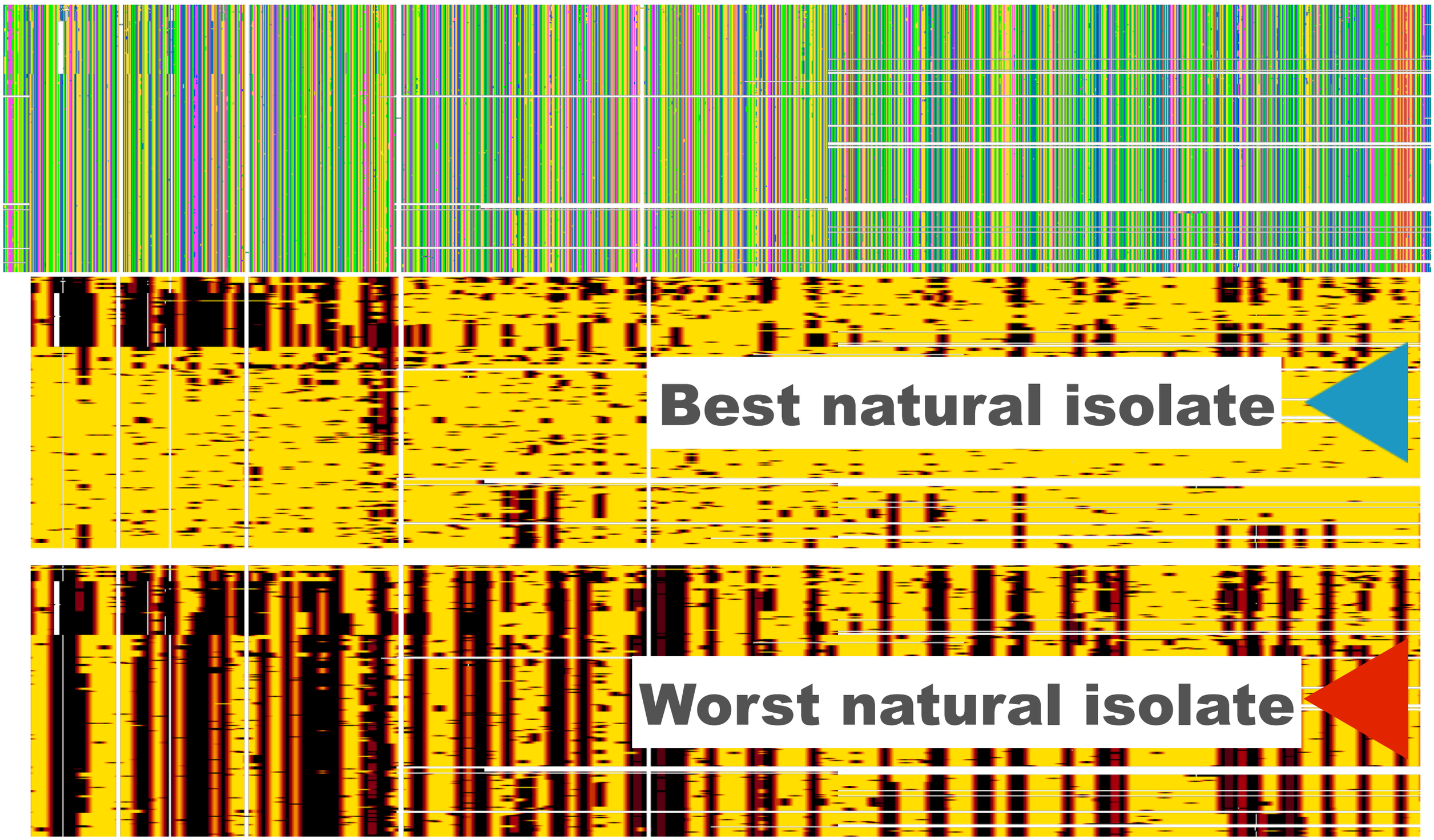


Posicover output (2 dimensional)



Posicover *k*-mer coverage (yellow-black gradient shows how many of each residue's *k*-mers appear in vaccine)

Posicover output (2 dimensional)



Variable Region Characteristics

Purpose: Variable Region Characteristics analyzes protein sequences for V1, V2, V3, V4, V5 and reports length, glycosylation sites, and net charge.

Details: The tool accepts a set of aligned protein sequences in Fasta, IG, table, and other formats, along with an optional reference sequence.

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Variable Region Characteristics

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Details: The tool accepts a set of aligned protein sequences in Fasta, IG, table, and other formats, along with an optional reference sequence.

- Allows comparison of unalignable regions w.r.t. properties relevant to antibody binding
- For HIV, pulls out defined variable regions from alignment,
- Computes lengths, charge, and number of PNG sites

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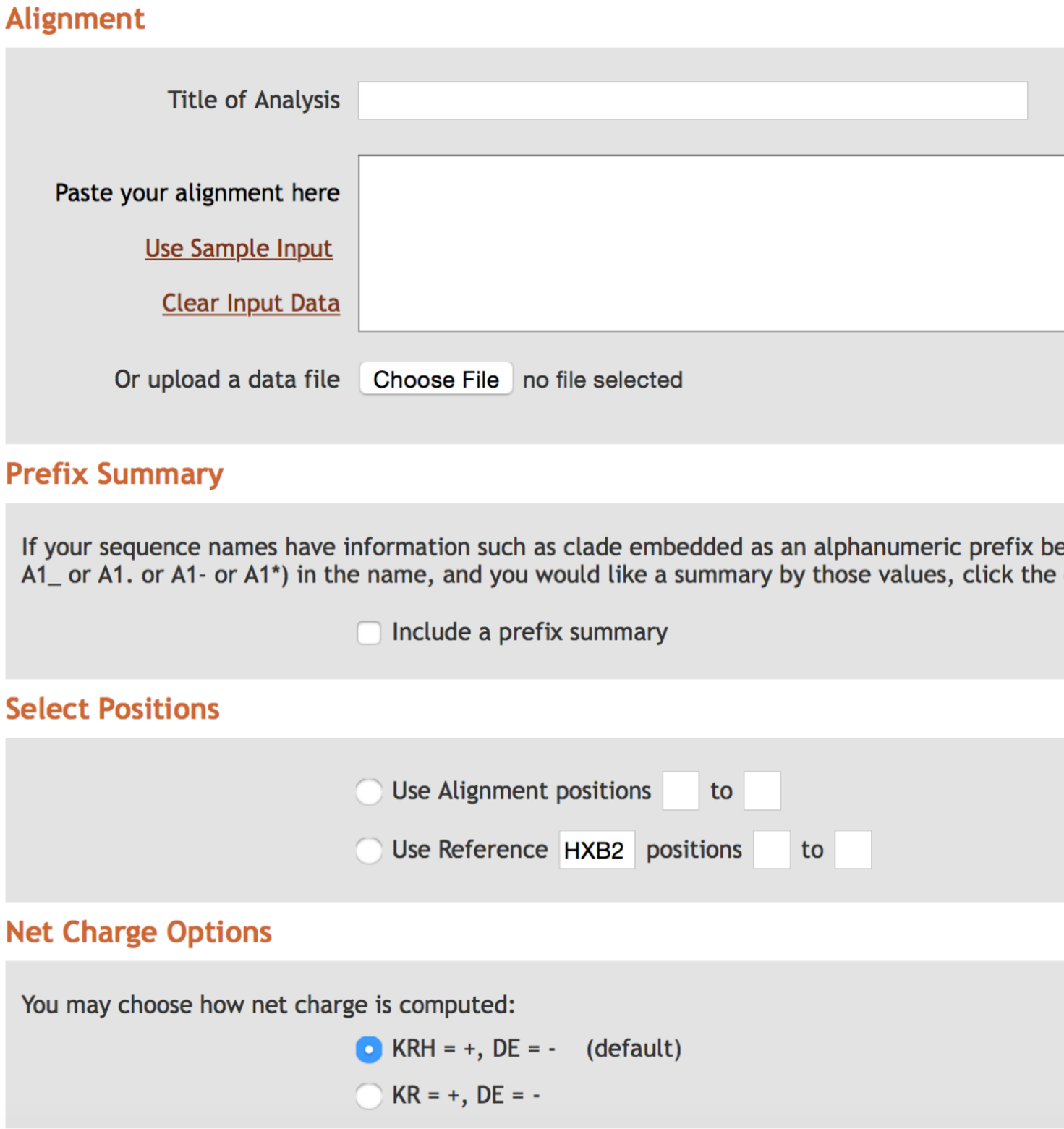

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- Allows comparison of unalignable regions w.r.t. properties relevant to antibody binding
- For HIV, pulls out defined variable regions from alignment,
- Computes lengths, charge, and number of PNG sites

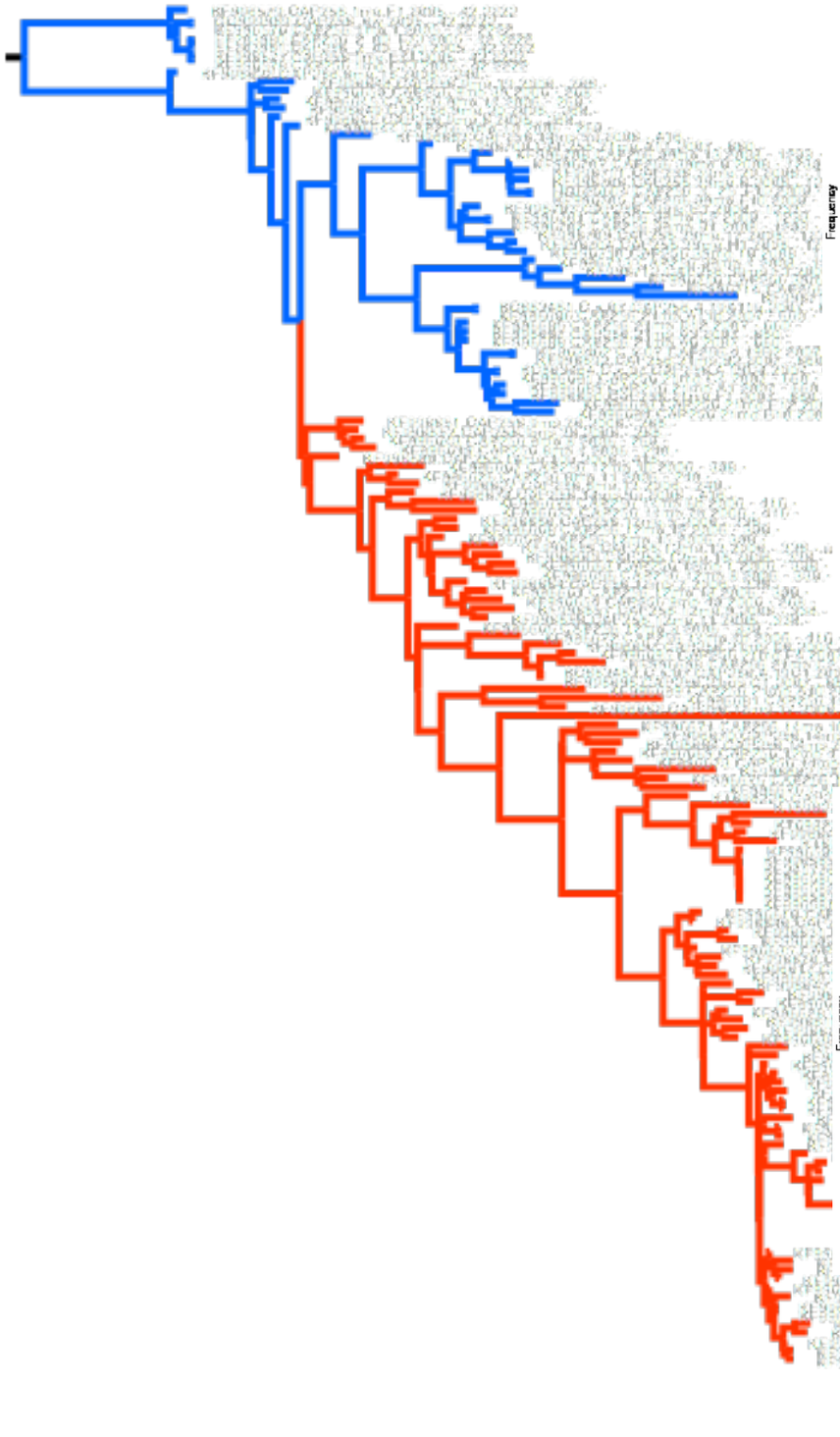
Select Regions

If you input an HIV alignment that includes HXB2, check the regions you wish to have characterized.

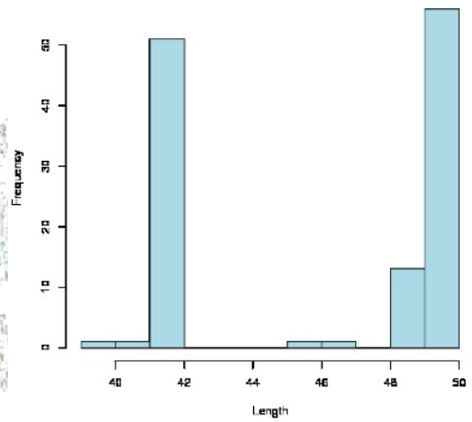
Make sure you understand the explanation before using these options.

V1:	☐ Full loop (131-157)	☐ Hypervariable region
V2:	☐ Full loop (158-196)	☐ Hypervariable region
V1+V2:	☐ Full loop 131-157 + 158-196)	☐ Hypervariable region
V3:	☐ Full loop (296-331)	(loop not hypervariable)
V4:	☐ Full loop (385-418)	☐ Hypervariable region
V5:	☐ Full loop (460-469)	☐ Hypervariable region

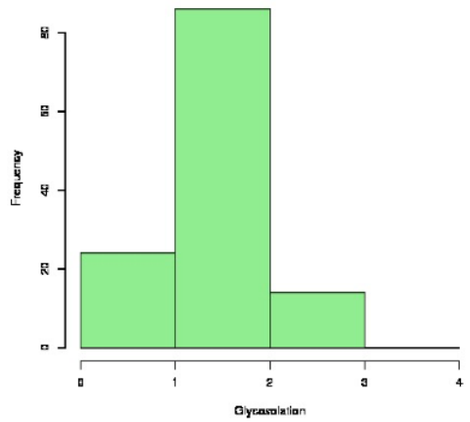
Variable Region Characteristics



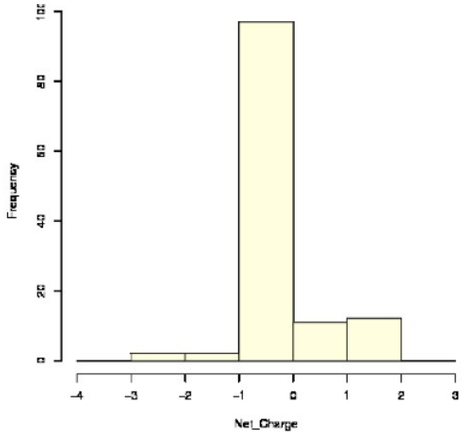
Length



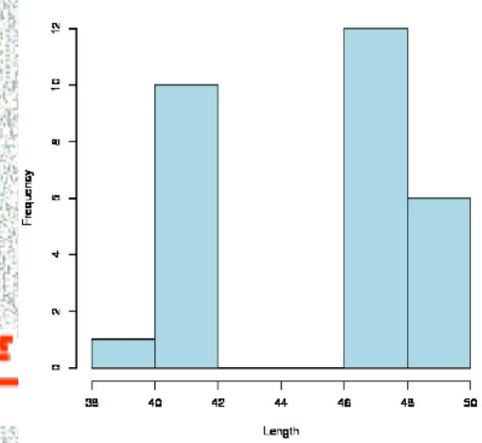
Glycosylation sites



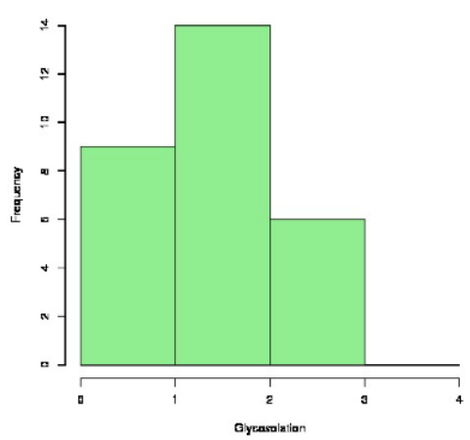
Charge



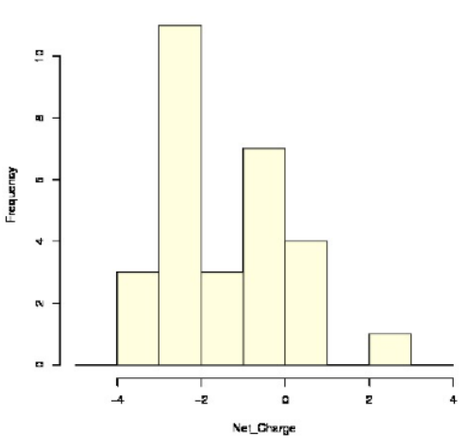
Length



Glycosylation sites



Charge



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Thank you for attending!

Please send us comments, questions, and suggestions!

Your comments will help us provide future training and better tools.

Slides available at https://tinyurl.com/HIVDB-2019-IEDB

Contact us: seq-info@lanl.gov or immuno@lanl.gov

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