The HIV Immunology Database

IEDB User Workshop – 2023

Presenters:

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Jennifer Mamrosh
Jennifer Macke

Database PIs:

Jennifer Mamrosh (Immunology), Brian Foley (Sequence)

Additional database staff:

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Contract Office Representative: Anjali Singh, NIAID, NIH

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

LANL's HIV database complements IEDB:

- **WHOLE PATHOGEN Database**

Contains actively curated, comprehensive HIV data

- Also find limited Covid information.

And lists of immunogenic CD8+ (CTL) and CD4+ (HTL) T-cell epitopes

- Lists of all DB-annotated immunogenic HIV epitopes
- Best-defined HIV CTL epitopes

But has more than epitopes

- Linked to HIV SEQUENCE DATABASE
- Antibody annotations from literature
- Antibody neutralization data
- Patient information (for both Sequence and Immunology data)
- VARIANTS of T-cell epitopes (TCE)

Data Analysis Tools for defining epitopes, generating vaccines, identifying neutralizing antibodies and analyzing sequences

- Most can be used for any organism
- Covid CATNAP with neutralization data and analyses

Today's agenda:

Part I *(Elizabeth-Sharon Fung)*

T cell epitopes – entries and searches

Please feel free to follow along using our database online

Questions are welcome at any time!

hiv.lanl.gov

Part II *(Jennifer Mamrosh)*

Research example– T cell epitope search

Antibody searches

Tools for HIV antibodies

Part III *(Jennifer Macke)*

Antibodies and Neutralization Data

New! SARS-Cov-2 CATNAP

Tools for T cell epitope vaccine design

HIV DATABASES

https://www.hiv.lanl.gov

DATA TOOLS

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 ▸

CATNAP for SARS-CoV-2
Our colleagues at the COVID-19 Genome Analysis Pipeline have launched COV CATNAP (Compile, Analyze and Tally NAb Panels) for analysis of antibody neutralization data for SARS-CoV-2. *23 May 2023*

HIV Molecular Immunology 2022
HIV Molecular Immunology 2022 is now available online. The PDF version is hypertext enabled and features clickable table-of-contents, indexes, references and links to external web sites. *10 May 2023*

New features for curated alignments
Our curated HIV Alignments have 2 new download options. One option allows you to obtain a list of accessions, which can be used to obtain additional metadata for all the sequences in the alignment. A second option allows you to "pre-prune" the alignment to only include a select list of accessions. Instructions are provided in Alignment Help. *05 May 2023*

HIV Sequence Compendium 2021
HIV Sequence Compendium 2021 is now available online. The 2021 Compendium is available online in PDF format. *23 March 2023*

Keystone HIV Vaccines Conference 2023
LANL HIV Database staff will be presenting posters at the Keystone Conference on HIV Vaccines, Immunoprophylaxis and Drugs, June 6-10, 2023 in Keystone, Colorado. We will be giving training workshops and available to answer questions informally during the meeting. *14 March 2023*

HIV Sequence Compendium 2020
HIV Sequence Compendium 2020 is now available online. The 2020 Compendium is available online in PDF format. *02 March 2023*

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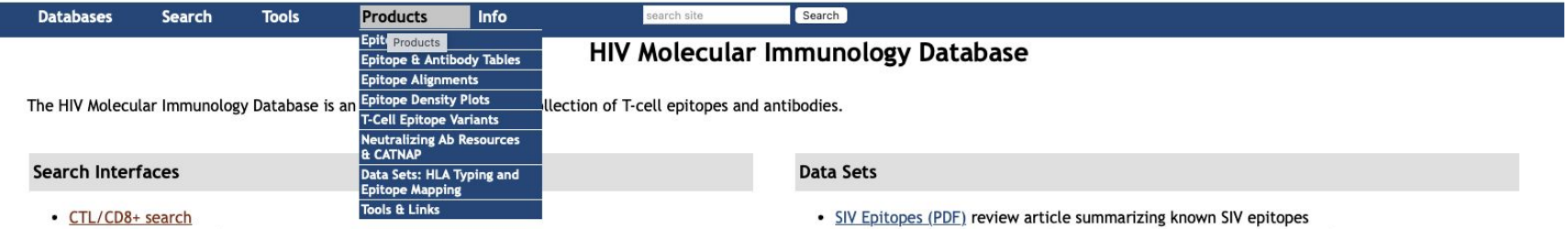

Multiple search options via drop-down menus or clickable links.

https://www.hiv.lanl.gov/content/immunology/index.html

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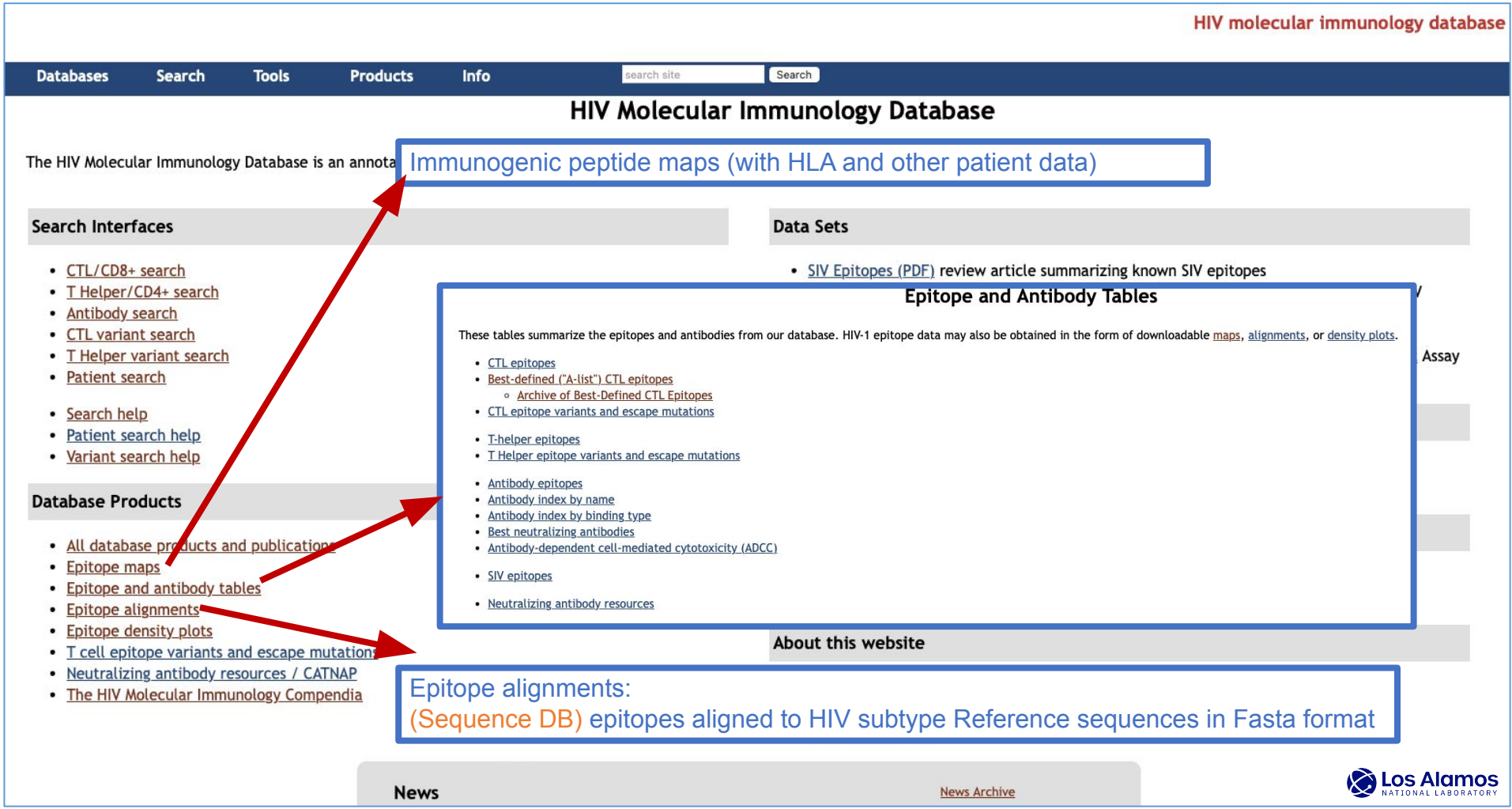
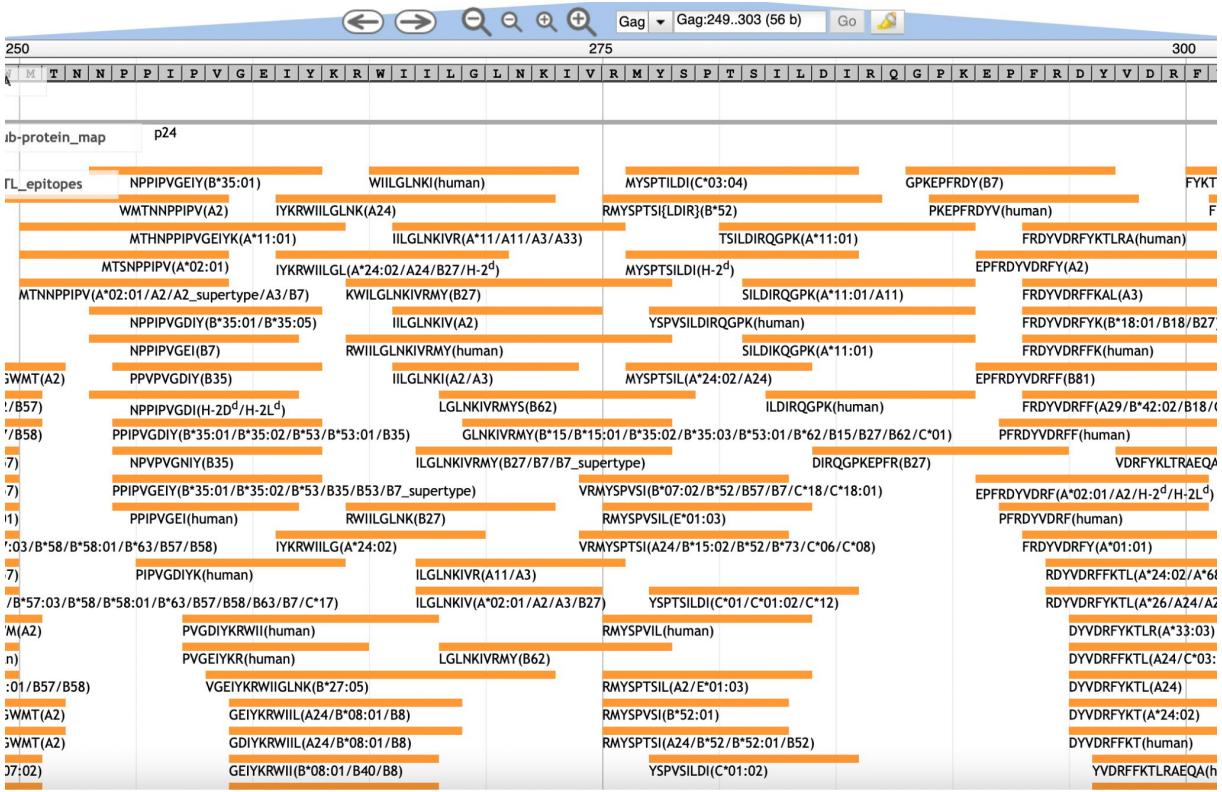
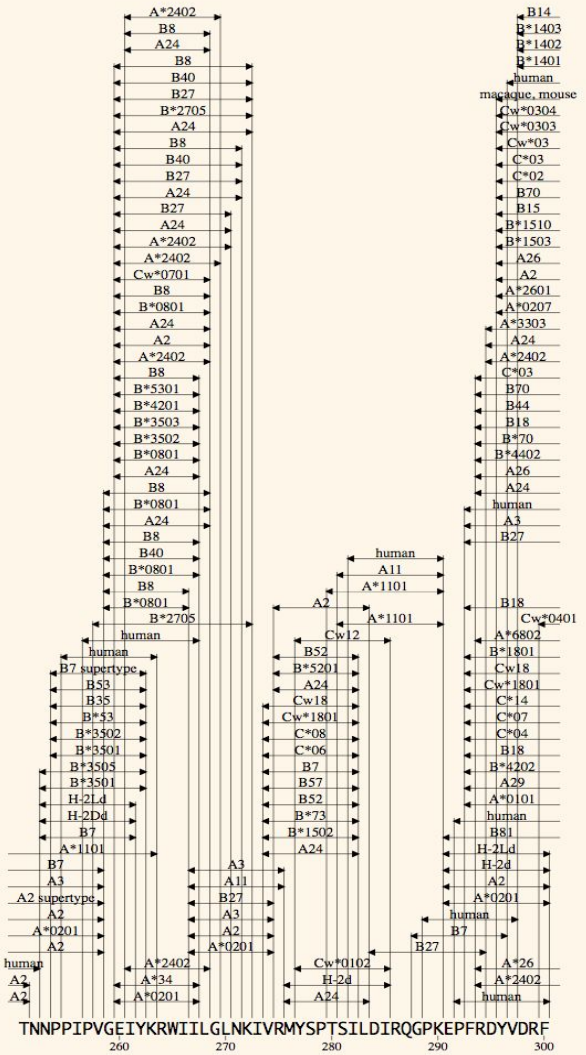

Databases
Search
Tools
Products
Info
search site
Search
HIV Molecular Immunology Database
The HIV Molecular Immunology Database is an annota
Immunogenic peptide maps (with HLA and other patient data)
Search Interfaces
CTL/CD8+ search
T Helper/CD4+ search
Antibody search
CTL variant search
T Helper variant search
Patient search
Search help
Patient search help
Variant search help
Database Products
All database products and publications
Epitope maps
Epitope and antibody tables
Epitope alignments
Epitope density plots
T cell epitope variants and escape mutations
Neutralizing antibody resources / CATNAP
The HIV Molecular Immunology Compendia
Data Sets
SIV Epitopes (PDF) review article summarizing known SIV epitopes
Epitope and Antibody Tables
These tables summarize the epitopes and antibodies from our database. HIV-1 epitope data may also be obtained in the form of downloadable maps, alignments, or density plots.
CTL epitopes
Best-defined ("A-list") CTL epitopes
Archive of Best-Defined CTL Epitopes
CTL epitope variants and escape mutations
T-helper epitopes
T Helper epitope variants and escape mutations
Antibody epitopes
Antibody index by name
Antibody index by binding type
Best neutralizing antibodies
Antibody-dependent cell-mediated cytotoxicity (ADCC)
SIV epitopes
Neutralizing antibody resources
Assay
About this website
Epitope alignments:
(Sequence DB) epitopes aligned to HIV subtype Reference sequences in Fasta format
News
News Archive

p17 CTL/CD8+ Genome Browser and Epitope Map



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



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

CTL/CD8+ Epitope Summary (B-list) ~ 2067 CTL epitopes

Epitope	Protein	HXB2 Location	Subtype	Species	HLA
MGARASVLSG	p17	1-10	CRF01_AE	human	
ASVLSGGEL	p17	5-13	B	human	
ASILRGGKLDK	p17	5-15	C	human	
SVLSGGQLDR	p17	6-15	B	human	A11
LSGGELDRWEK	p17	8-18		macaque	
GELDRWEKI	p17	11-19	B	human	B*4002, B40
GQLDRWEKI	p17	11-19	B	human	
GKLDSWEKIRLR	p17	11-22	A, CRF01_AE, CRF02_AG	human	

www.hiv.lanl.gov/content/immunology/tables/ctl_summary.html

Best-defined CTL Epitope Summary (A-list) ~ 280

- Experimentally validated optimal epitopes with known HLA presenting molecules
- Defined/curated by Christian Brander and colleagues

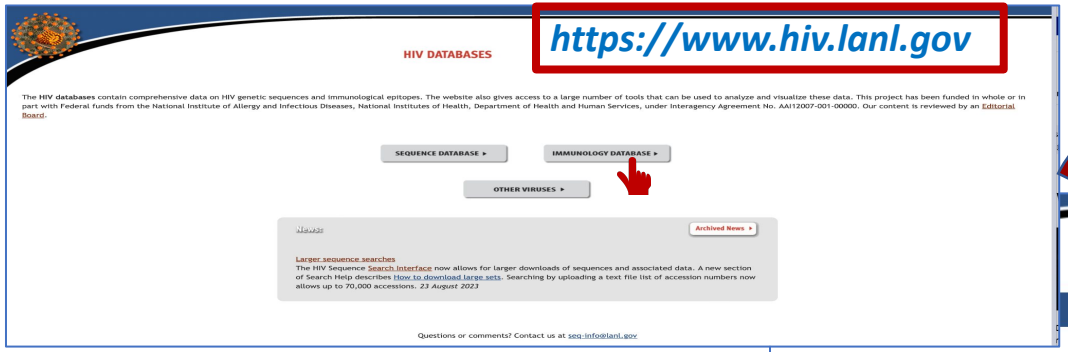
Epitope	Protein	HXB2 Location	Subtype	Species	HLA
GELDRWEKI	p17	11-19		human	B*4002
KIRLRPGGK	p17	18-26		human	A*0301
IRLRPGGKK	p17	19-27	B	human	B*2705
RLRPGGKKK	p17	20-28		human	A*0301
RLRPGGKKKY	p17	20-29	B	human	A*0301
GGKKKYKLK	p17	24-32	B	human	B*0801
KYKLKHIVW	p17	28-36	B	human	A*2402
HLVWASREL	p17	33-41		human	Cw*0804

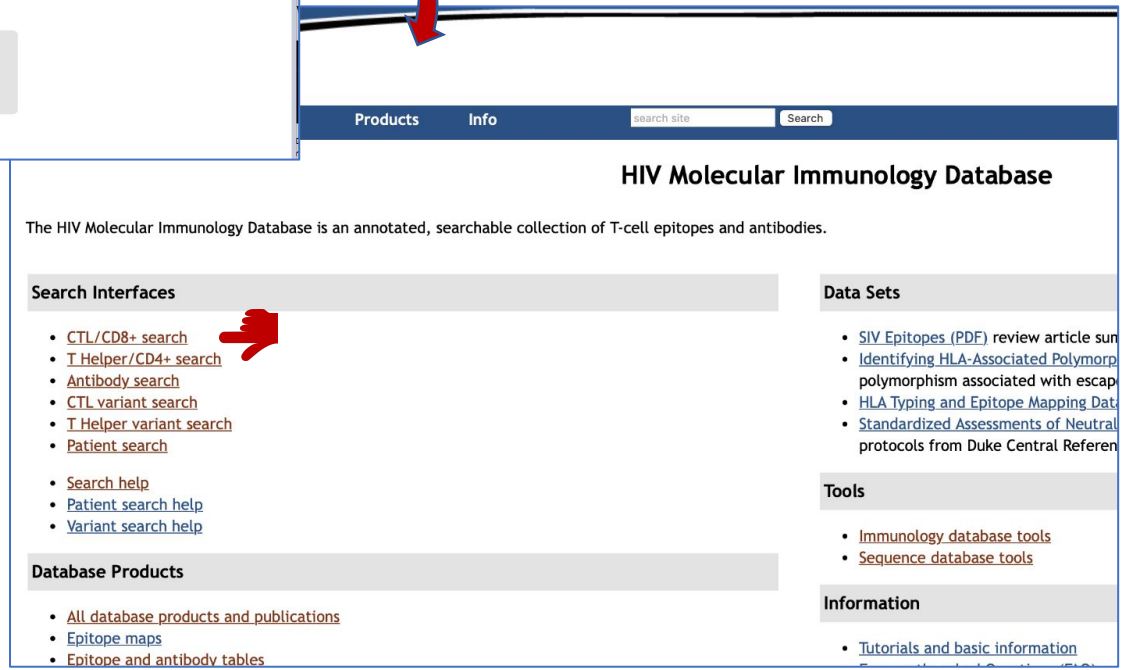
www.hiv.lanl.gov/content/immunology/tables/optimal_ctl_summary.html

Searchable epitope variants (~3500 CTL variants) from literature

www.hiv.lanl.gov/content/immunology/pdf/2010/escape_article_supplement.html

CTL epitope search:





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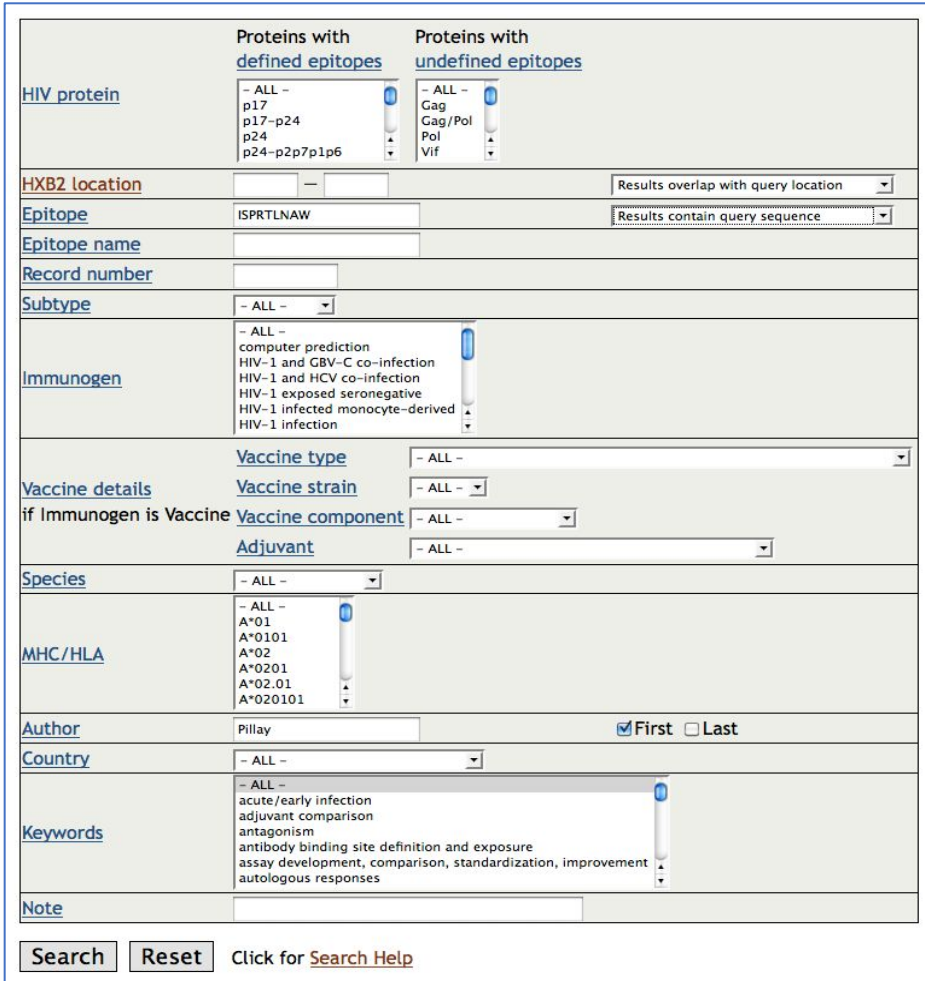
CTL/CD8+ Search



- Search by HIV protein, Epitope Sequence, Subtype, Immunogen, Vaccine Details, Species, presenting MHC/HLA, Author, Country, Keywords
- Search on epitope location and find fuzzy matches, overlaps and embedded epitopes
- Search examples:
  - *Example:*
    - SLYNTVATL – 319 entries
    - Narrow the search with keyword “escape” – 38 entries

Search for ISPRTLNAW with the first author Pillay

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Search CTL/CD8+ T-Cell Epitope Database

Found 1 matching record:

Displaying record number 53832

HXB2 Location	p24(15-23)
Author Location	Gag(147-155)
Epitope	ISPRTLNAW
Subtype	C
Species (MHC/HLA)	human(B57)
Immunogen	HIV-1 infection
Donor MHC/HLA	A*3001, A*66, B*4201, B*5802, Cw*0602, Cw*1701; A*66, A*68, B*57, B*5802, Cw*0602, Cw*0701
Country	South Africa
Experimental methods	CD8 T-cell Elispot - IFNy
Keywords	epitope processing, responses in children, mother-to-infant transmission, escape, acute/early infection

Link to Epitope Maps → p24 Epitope Map

Link to Epitope Alignment → Epitope Alignment

Variant details with annotator's notes → Show epitope variants

Notes

- HIV-specific CTLs in infants were shown to be able to select for viral escape variants early in life, despite a lack of escape with the same CTL specificity in the mother. Infant CTL responses may be compromised by transmission of escape variants that arose in the mother and also those that arose in the father, if the father was the source of the mother's infection.
- ISPRTLNAW is the C consensus form of the epitope and was the autologous form in the mother, and was transmitted to her infant. By 33 weeks a new dominant form of the epitope had emerged in the infant, mSPRTLNAW, and two additional variants had arisen, one with a substitution proximal to the epitope, plSPRTLNAW, and lSPRTLNAW.

References

Pillay2005 Thillagavathie Pillay, Hua-Tang Zhang, Jan W. Drijfhout, Nicola Robinson, Helen Brown, Munira Khan, Jagadesa Moodley, Miriam Adhikari, Katja Pfafferott, Margaret E. Feeney, Anne St. John, Edward C. Holmes, Hoosen M. Coovadia, Paul Klenerman, Philip J. R. Goulder, and Rodney E. Phillips. Unique Acquisition of Cytotoxic T-Lymphocyte Escape Mutants in Infant Human Immunodeficiency Virus Type 1 Infection. *J. Virol.*, 79(18):12100-12105, Sep 2005. PubMed ID: 16140787. Show all entries for this paper.

Immunological, virological, epidemiological contexts

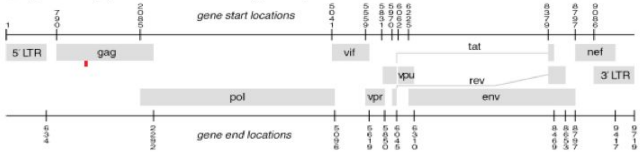
Epitope Alignment

Aligns epitope under study to latest premade HIV web alignment available through HIV Sequence database

www.hiv.lanl.gov/content/sequence/QUICK_ALIGNv2/QuickAlign.html

Genome map:

Query location(s) shown as colored bar(s) in map.



Summary & analysis:

Query: epitope

Query sequence	ISPRTLNAW
Query length	9
HXB2 Location	genome: 1228→1254, region: Gag 147→155
Alignment used	LANL HIV1 Gag Amino acid Filtered web

Summarize All | Summarize By Subtype (major subtype only) | Find Other Matches | Submit

Alignment slice:

Download alignment below in format fasta

"-" = identity to query sequence
"." = gap in sequence
"Red name" = perfect identity to query sequence

```
                                  epitope ISPRTLNAW
          B.FR.83.HXB2_LAI_IIIB_BRU.K03455 ---------
A1.CA.x.BCCFE_HOMER_HIV_GAG_3062.EU242119 L--------
            A1.CD.02.02CD_KTB035.AM000055 ---------
              A1.CD.97.97CD_KCC2.AM000053 L--------
              A1.CD.97.97CD_KTB13.AM000054 L--------
  A1.CH.03.HIV_CH_BID_V3538_2003.JQ403028 L--------
                  A1.CH.04.pBV23.KJ689262 L--------
                  A1.CH.05.pBV26.KJ689264 F--------
                  A1.CH.08.pBV20.KJ689259 L--------
                  A1.CH.09.pBV32.KJ689270 M--------
                  A1.CH.10.pBV17.KJ689256 M--------
                  A1.CH.11.pBV13.KJ689253 ---------
                  A1.CH.11.pBV22.KJ689261 L--------
                  A1.CH.11.pBV48.KJ689279 L--------
                  A1.CH.12.pBV58.KJ689285 L--------
                   A1.CM.06.BS02.JX244900 L--------
                  A1.CM.07.46_10.KP718918 L--------
                   A1.CM.07.BS10.JX244906 L--------
                 A1.CM.08.886_24.KP718928 L--------
               A1.CN.00.00CNLN14.EF122512 V--------
                  A1.CY.04.CY009.EU673416 L--------
                  A1.CY.05.CY012.EU673418 L--------
                  A1.CY.05.CY021.FJ388892 -A-KA-EG-
                  A1.CY.05.CY051.FJ388903 L--------
```

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Variant details

Displaying record number 53832

HXB2 Location	p24(15-23)	p24 Epitope Map
Epitope	ISPRTLNAW	Epitope Alignment
	mSPRTLNAW	escape documented in this paper
Variants	lSPRTLNAW	diminished response
	p|lSPRTLNAW	not determined
Species (MHC/HLA)	human(B57)	

Variant Details

Showing all 3 variants.

Variant ID.	1413
Epitope Seq.	ISPRTLNAW
Variant Seq.	mSPRTLNAW
Mutations	I/M
Epitope Location	I1M
HXB2 Location	I15M
Mutation Type	**E**: escape documented in this paper
Method	CD8 T-cell Elispot - IFNy, Sequence
Note	This is de novo variant seen in infant by week 33 of age. The index peptide was recognized, but not the variant.

Variant ID.	1414
Epitope Seq.	ISPRTLNAW
Variant Seq.	lSPRTLNAW
Mutations	I/L
Epitope Location	I1L
HXB2 Location	I15L
Mutation Type	**DR**: diminished response
Method	CD8 T-cell Elispot - IFNy, Sequence

Link back to epitope entry

Mutation type

Mutation type examples:

- E escape
- IE inferred escape
- DR diminished response
- SF susceptible form
- etc…

Note describing why the variant was designated as a particular mutation type

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Research Example- Mutations in the Gag protein in HIV long-term non-progressors:

- Consider the following research example: *(Ammaranond, Kelleher, et al., 2011; PMID: 21115730)*
  - 19 individuals were identified as long-term non-progressors and were not being treated with antiretrovirals
  - These individuals carried MHC Class I allele HLA-B*27, which is more frequently found in long-term non-progressors
  - Plasma viral load, CD4 count, and Gag sequencing were performed at study start & last follow-up (avg. 14 years)
  - During the course of the study, some of the individuals had their disease progress

Research Example- Mutations in the Gag protein in HIV long-term non-progressors:

- Certain mutations were identified in the Gag protein, some of which appeared over time:

individual #	Gag aa263-272 sequence, study start	Gag aa263-272 sequence, last follow-up
"WT" sequence	KRWIILGLNK	KRWIILGLNK
1	-----M----	-----M----
2	-----M----	-----M----
3	-----M----	-G--------
4	-K--VI----	-K--VI----
5	----------	-----M----
6	-Q---M----	-Q---M----
7	-----M----	-----M----
8	----------	----------
9	-----M----	-----M----
10		-----M----
11		----------
12	-----M----	-----M----
13	-G--------	-G--------
14		-K---M----
15	-----M----	-----M----
16		----------
17	-----M----	-----M----
18	----------	----------
19		-K---M----

- Do any of these mutations contribute to disease progression in certain individuals?

Research Example- Are there Gag R264 mutations in antibody or T cell epitopes?

- Let's consider mutations at Gag amino acid R264, particularly R264K mutations:

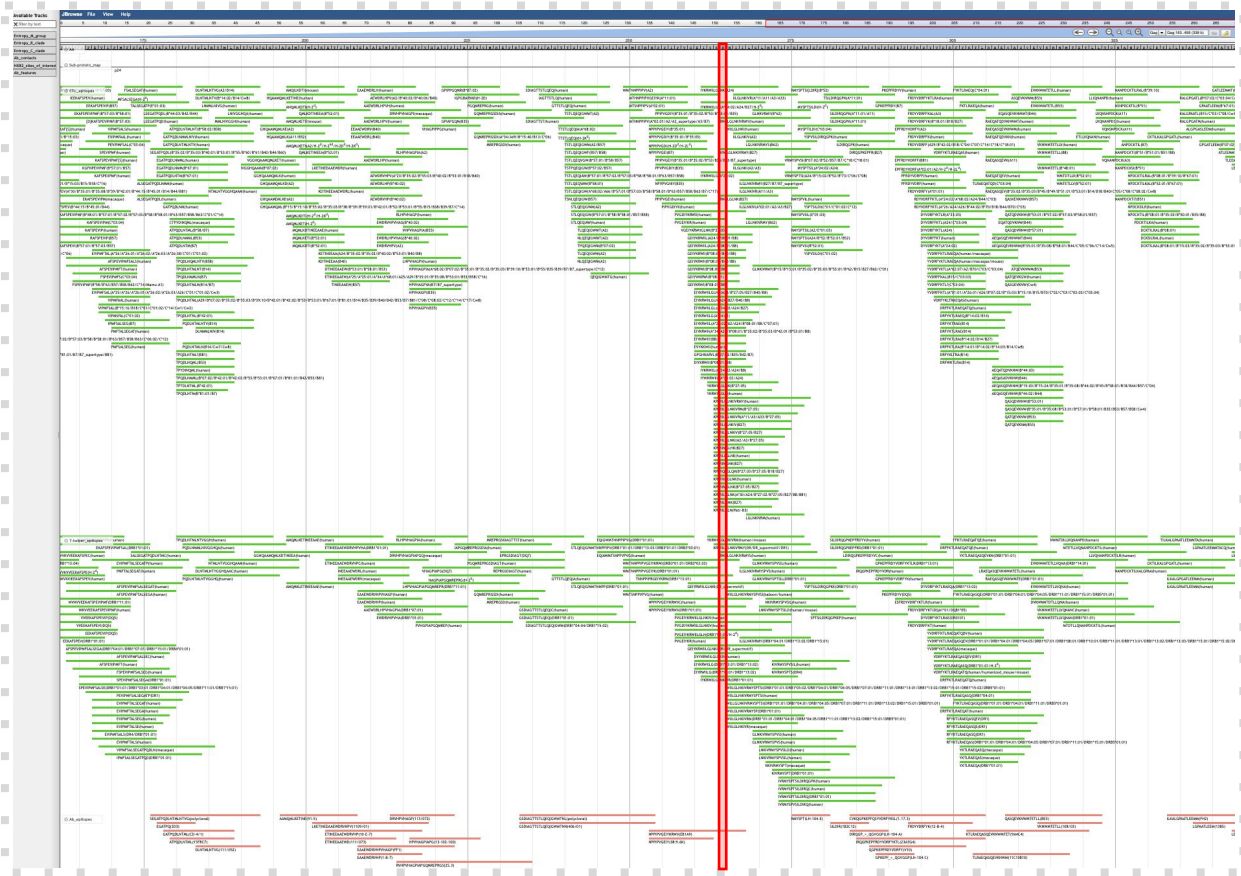
individual #	Gag aa263-272 sequence, study start
WT sequence	KRWIILGLNK

- How can we know which epitopes might contain this mutation?

- Our database offers a few options:
  - Visually look at epitopes on the HIV Genome Browser tool
  - Use the Epitope Location Finder tool
  - Search for specific sequences (antibody, CTL epitope, or T-helper epitope search interface)
  - Search for specific regions of Gag (antibody, CTL epitope, or T-helper epitope search interface)

Research Example- Are there Gag R264 mutations in antibody or T cell epitopes?

- We can look for antibody or T cell epitopes containing the WT sequence or R264 mutation in the HIV Genome Browser:



Research Example- Are there Gag R264 mutations in antibody or T cell epitopes?

- The Epitope Location Finder (ELF) tool suggests that our unmutated input sequence, KRWIILGLNK, is a CTL epitope:

Epitopes from our CTL database aligned to your query sequence

Bold **red** letters indicate residues that differ from the query sequence. The symbol ➤ means the HLA of the epitope matches one of your submitted HLAs. Click on the epitope to see full database entry. Click on "align" to align the epitope to the sequence database via QuickAlign.

Epitopes shown here are completely within the bounds of your query. Epitopes that overlap the ends of your query are included in the "View database records" links above.

Download this alignment in format table

KRWIILGLNK

KRWIILGLN Patr-B*03 align

KRWIILGLN align

RRWIQLGLQK B27 align

RRWIQLGLQK B*27:03 align

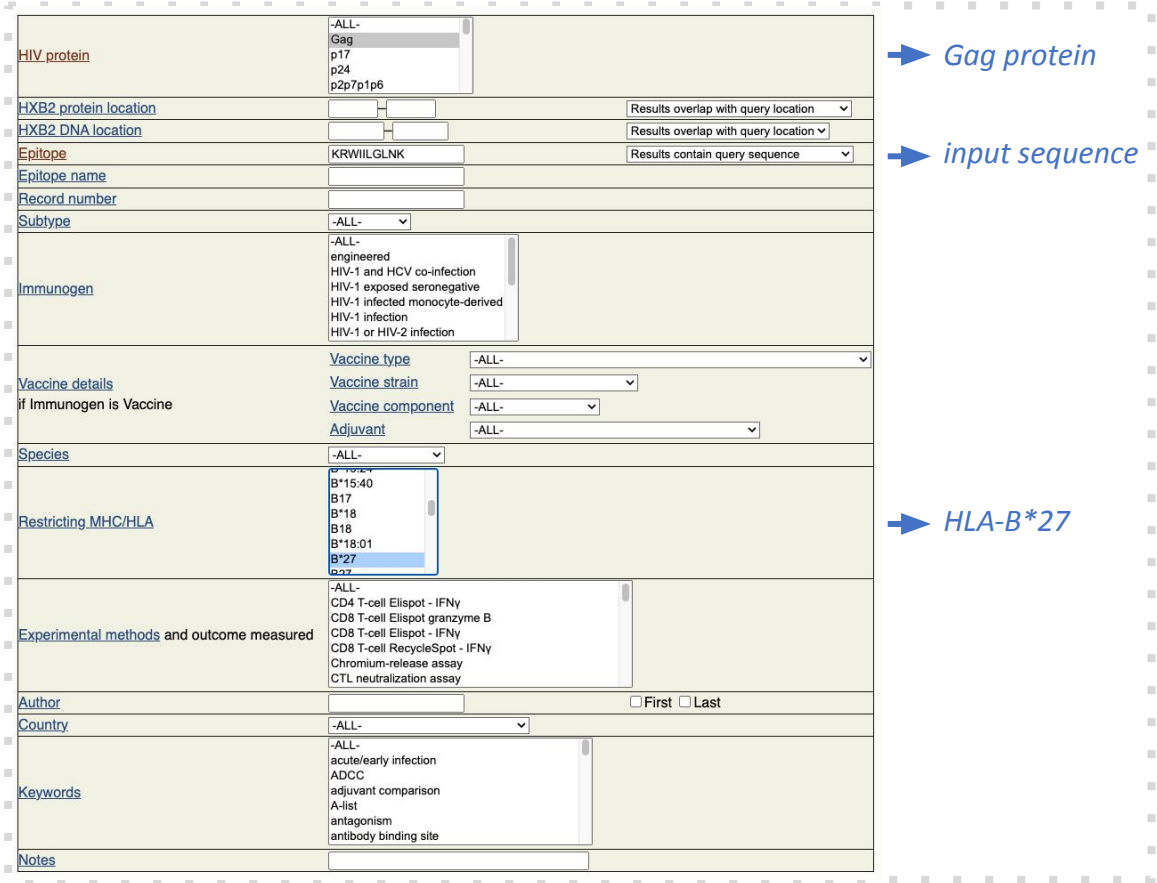
KRWIILGLNK B*27:05 align

KRWIILGLNK B27 align

KRWIILGLNK B*27 align ➤

Research Example- Is this CTL epitope immunogenic?

- Let's put our unmutated input sequence, KRWIILGLNK, into the CTL epitope search interface:



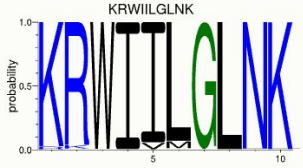
Research Example- Is this CTL epitope immunogenic?

- This epitope has been reported to be immunogenic in some individuals:

Displaying record number 57582

Download this epitope record as JSON. [Help]

HXB2 location	Gag(263–272) p24(131–140) DNA(1576..1605)	Gag Epitope Map
Author location	p24(131–140)	
Epitope	KRWIILGLNK	Epitope Alignment



Epitope name	KK10
Subtype	B
Species (Restricting MHC/HLA)	(B*27)
Immunogen	HIV-1 infection
Country	United States
Experimental methods	CD8 T-cell Elispot - IFNγ
Keywords	acute/early infection

Notes

- Responses to specific B57/58, B27, and B35-restricted epitopes were tested in a cohort of 45 subjects during primary infection. The presence of certain B57/58, B27, and B35-restricted T-cell responses during primary infection better defined disease progression than the HLA genotype alone, suggesting that it is the HIV-specific CD8+ T-cells and not the presence of a particular HLA allele, that determine disease progression.
- 5/7 B27-positive subjects responded to KRWIILGLNK and 67% of the patients' total response magnitude was derived from this specific response.
- This epitope was 87% conserved among M-group sequences and 82% conserved among B-subtype sequences.
- Epitope-specific HLA-B responses to KK10 and FY10 delayed declines in CD4+ T-cell counts more than 8 years in HLA-B27-positive subjects.

References

Dinges2010 Warren L. Dinges, Julia Richardt, David Friedrich, Emilie Jalbert, Yi Liu, Claire E. Stevens, Janine Maenza, Ann C. Collier, Daniel E. Geraghty, Jeremy Smith, Zoe Moodie, James I. Mullins, M. Juliana McElrath, and Helen Horton. Virus-Specific CD8+ T-Cell Responses Better Define HIV Disease Progression than HLA Genotype. *J. Virol.*, 84(9):4461-4468, May 2010. PubMed ID: 20147397. Show all entries for this paper.

- This is just one of 40 entries in our database for this sequence!

Research Example- Are CTL epitopes with R264 mutations no longer immunogenic?

- We can find some of this information in the CTL epitope search results
- However, our CTL epitope variant search is more specifically set up to address these kinds of questions
- Let's put our unmutated input sequence, KRWIILGLNK, into the CTL epitope variant search interface

Research Example- Are CTL epitopes with R264 mutations no longer immunogenic?

- Let's put our unmutated input sequence, KRWIILGLNK, into the CTL epitope variant search interface:

Displaying record number 57821

Download this epitope record as JSON. [Help]

HXB2 location	Gag(263–272) p24(131–140) DNA(1576..1605)	Gag Epitope Map View variants at this location
Epitope	KRWIILGLNK	Epitope Alignment

KRWIILGLNK

probability

Variants	KkWIILGLNK	escape documented in this paper, literature escape
	KkWIvLGLNK	escape documented in this paper, literature escape
	KqWIILGLNK	escape documented in this paper, inferred escape
	KqWIILGLNK	escape documented in this paper, literature escape
	KRWIImGLNK	susceptible form
Epitope name	KK10	
Species (Restricting MHC/HLA)	human(B*27)	

R264K

Variant Details

Showing all 5 variant(s).

Variant record number	2642
Epitope sequence	KRWIILGLNK
Variant sequence	KkWIILGLNK
Mutations	R/K
Epitope mutation location	R2K
HXB2 mutation location	R264K
Mutation type	**E**: escape documented in this paper **LE**: literature escape
Epitope subtype	B
Variant subtype	B
Variant method	CD8 T-cell Elispot - IFNγ, Sequence
Note	Previously-documented escape mutant documented in B*27-positive patients. No response in B*27 individuals was seen in this study.

Variant record number	2643

Research Example- Summary

- There is ample evidence from multiple publications that R264 mutations can confer immune escape in individuals with HLA-B*27

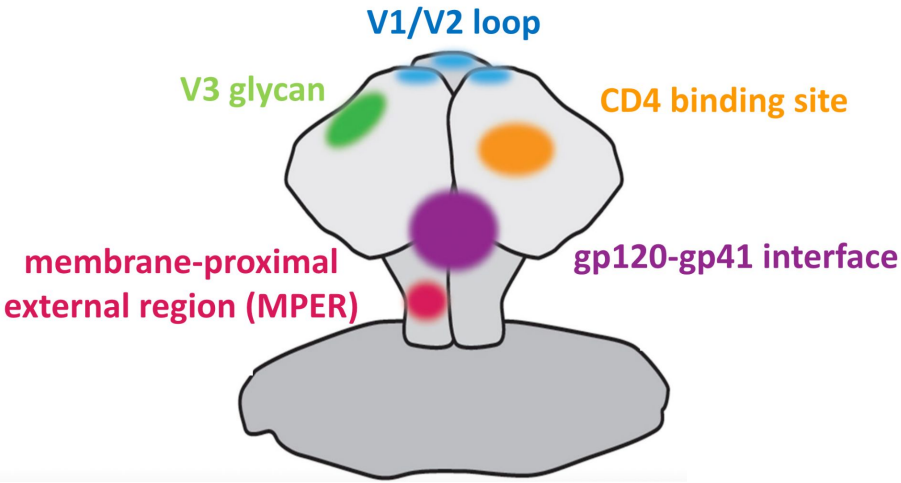
- Our database can be used to obtain annotated publication data for HIV immunogenic epitopes, even when the epitope location in a sequence is unknown

LANL's HIV Immunology Database also offers antibody searches:

- Antibody epitopes can be more complex than CTL epitopes:
  - They often depend upon protein folding/can be discontinuous
  - They can be unknown

- Our database allows you to search for antibodies or antibody epitopes meeting specific criteria

- Antibodies with HIV neutralizing activity are typically against the Env protein; several regions are of particular interest:



adapted from Hsu et al. 2021 | PMID: 34322136

Antibody search input page

HIV protein: -ALL- / Gag / p17 / p24 / p2p7p1p6

HXB2 protein location: [ ] – [ ] Results overlap with query location

HXB2 DNA location: [ ] – [ ] Results overlap with query location

Epitope: [ ] Results contain query sequence

Epitope name: [ ]

MAb name: [ ] Exact Match (List by name) (List by type)

Record number: [ ]

Subtype: -ALL-

Immunogen: -ALL- / anti-idiotype / autoimmune disease / engineered / HIV-1 exposed seronegative / HIV-1 infection / HIV-2 infection

Vaccine details if Immunogen is Vaccine: Vaccine type -ALL- / Vaccine strain -ALL- / Vaccine component -ALL- / Adjuvant -ALL-

Ab type: -ALL- / Antisense protein (ASP) / C-domain / C-HR / C-term / flap region / fusion peptide // near gp41-gp120 interface

Species: -ALL-

Isotype: -ALL-

Author: [ ] Search only for ☐ First ☐ Last ◉ Show only this author's references ○ Show all references

Country: -ALL-

Keywords: -ALL- / acute/early infection / adjuvant comparison / antibody binding site / antibody generation / antibody gene transfer / antibody interactions ◉ Show only notes containing selected keyword(s) ○ Show all notes

Notes: [ ] ◉ Show only notes matching this text ○ Show all notes

Search Reset

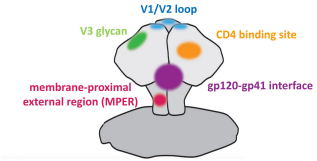
← protein

← epitope

← antibody name

← to limit search to antibodies from vaccines

← antibody binding type (region of Env or other proteins)



← keywords

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Antibody search example output page

Displaying record number 2777

Download this epitope record as JSON. [Help]

MAb name	10-1074 (10.1074) ← *Antibody name*
HXB2 location	Env
Author location	Env
Epitope	
Subtype	A
Ab type	gp120 V3 // V3 glycan (V3g)
Neutralizing	P (tier 2)
Contacts and Features	View contacts and features ← *Link to more info on antibody binding*
Species (Isotype)	human(IgG)
Immunogen	HIV-1 infection
Patient MHC/HLA	Donor 17:
Keywords	antibody binding site, antibody generation, antibody interactions, anti-idiotype, assay or method development, autologous responses, complement, co-receptor, effector function, elite controllers, enhancing activity, glycosylation, immunoprophylaxis, mutation acquisition, neutralization, SIV, therapeutic vaccine, vaccine antigen design, variant cross-reactivity, vaccine-induced immune responses, computational prediction, acute/early infection, escape, binding affinity, immunotherapy, early treatment, HAART, ART, supervised treatment interruptions (STI), review, subtype comparisons, antibody sequence, structure, antibody lineage, antibody polyreactivity, bispecific/trispecific, broad neutralizer, chronic infection, contact residues, HIV reservoir/latency/provirus, polyclonal antibodies ← *Keywords*

Env Epitope Map

Data on antibody neutralizing activity → View neutralization details

Notes

Showing 74 of 74 notes. ← *Multiple notes (representing publications) are possible per antibody*

- 10-1074: Several antibodies including 10-1074 were isolated from B-cell clone encoding PGT121, from a clade A-infected African donor using YU-2 gp140 trimers as bait. These antibodies were segregated into PGT121-like (PGT121-123 and 9 members) and 10-1074-like (20 members) groups distinguished by sequence, binding affinity, carbohydrate recognition, neutralizing activity, the V3 loop binding and the role of glycans in epitope formation. The epitopes for both groups contain a potential N-linked glycosylation site (PNGS) at Asn332gp120 and the base of the V3 loop of the gp120 subunit of the HIV spike. However, the 10-1074–like Abs required an intact PNGS at Asn332gp120 for their neutralizing activity, whereas PGT121-like antibodies were able to neutralize some viral strains lacking the Asn332gp120 PNGS. All PGT121 variant antibodies neutralized 9 pseudoviruses and didn't neutralize the r1166.cl control lacking PNGS at gp120 position 332. Group 10-1074 exhibited remarkable potency and breadth, but no detectable binding to protein-free glycans. Crystal structures of unliganded PGT121 and 10-1074 were compared and revealed differential carbohydrate recognition maps to a cleft between (CDR)H2 and CDRH3, occupied by a complex-type N-glycan. Detail information on the binding and neutralization assays are described in the figures S2-S11. *Mouquet2012a* (**antibody generation**, **neutralization**, **glycosylation**, **binding affinity**, **structure**, **broad neutralizer**)
- 10-1074: HIV therapy by combinations of 5 bNAbs was tested in YU2-infected humanized mice. Penta-mix (PG16, 45-46W, 3BC176, PGT128 and 10-1074) was the most effective in controlling viraemia compared to tri-mix (PG16, 45-46, 3BC176) and monotherapy (Fig S9). Viral escape with 10-1074 monotherapy was associated with mutations at residues 332 or 334, both of which abrogate the same potential N-linked glycosylation site in V1/V2 loop. *Klein2012a* (**escape**, **immunotherapy**)

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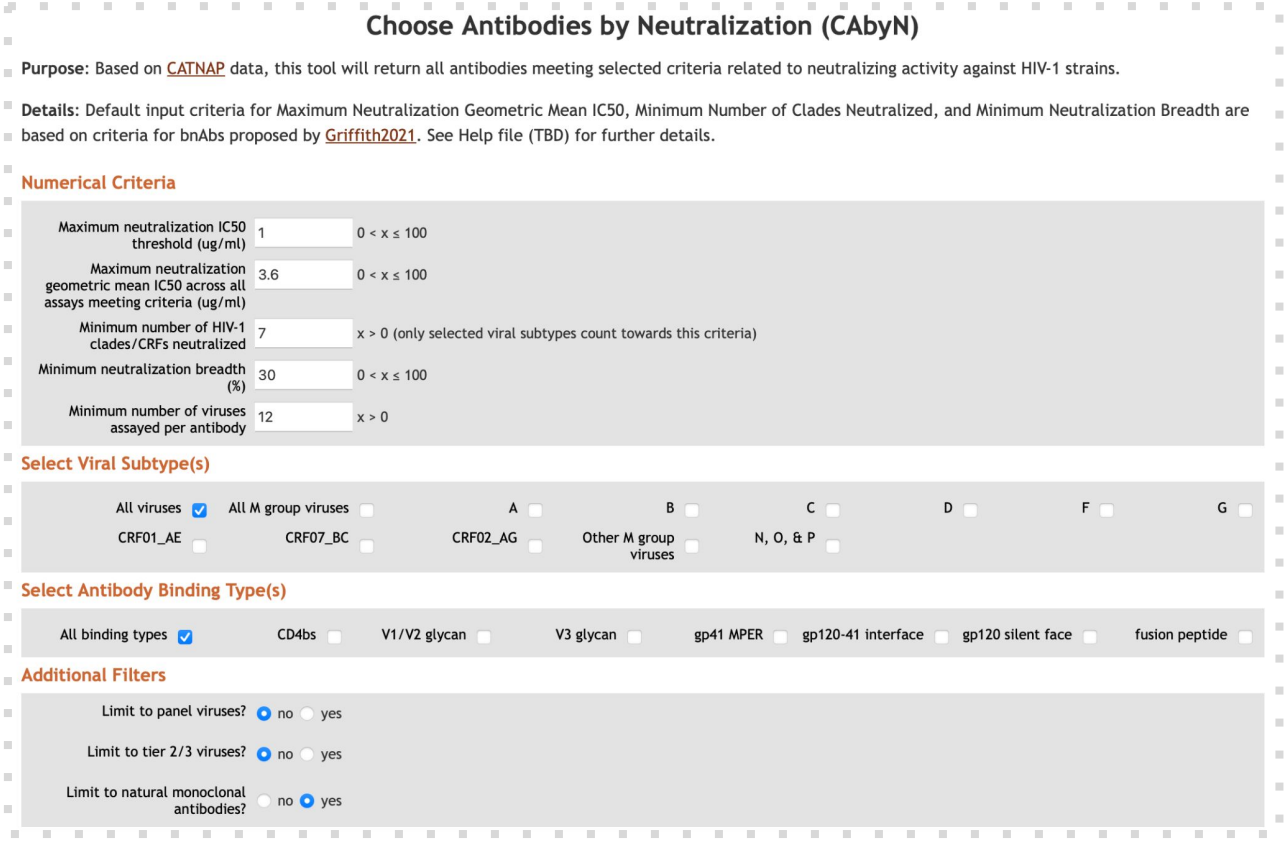
Additional tools for HIV antibodies

- We will soon make our CAByN (Choosing Antibodies by Neutralization) tool available, which allows users to search for antibodies based on their neutralizing properties:



Choose Antibodies by Neutralization (CAbyN)

Purpose: Based on CATNAP data, this tool will return all antibodies meeting selected criteria related to neutralizing activity against HIV-1 strains.

Details: Default input criteria for Maximum Neutralization Geometric Mean IC50, Minimum Number of Clades Neutralized, and Minimum Neutralization Breadth are based on criteria for bnAbs proposed by Griffith2021. See Help file (TBD) for further details.

Numerical Criteria

Maximum neutralization IC50 threshold (ug/ml)	1	0 < x ≤ 100
Maximum neutralization geometric mean IC50 across all assays meeting criteria (ug/ml)	3.6	0 < x ≤ 100
Minimum number of HIV-1 clades/CRFs neutralized	7	x > 0 (only selected viral subtypes count towards this criteria)
Minimum neutralization breadth (%)	30	0 < x ≤ 100
Minimum number of viruses assayed per antibody	12	x > 0

Select Viral Subtype(s)

All viruses ☑ | All M group viruses ☐ | A ☐ | B ☐ | C ☐ | D ☐ | F ☐ | G ☐

CRF01_AE ☐ | CRF07_BC ☐ | CRF02_AG ☐ | Other M group viruses ☐ | N, O, & P ☐

Select Antibody Binding Type(s)

All binding types ☑ | CD4bs ☐ | V1/V2 glycan ☐ | V3 glycan ☐ | gp41 MPER ☐ | gp120-41 interface ☐ | gp120 silent face ☐ | fusion peptide ☐

Additional Filters

Limit to panel viruses? ◉ no ○ yes

Limit to tier 2/3 viruses? ◉ no ○ yes

Limit to natural monoclonal antibodies? ○ no ◉ yes

Neutralization criteria *(breadth, potency, etc.)*

Limit results to certain viral subtypes

Limit results to certain antibody binding types

Additional tools for HIV antibodies

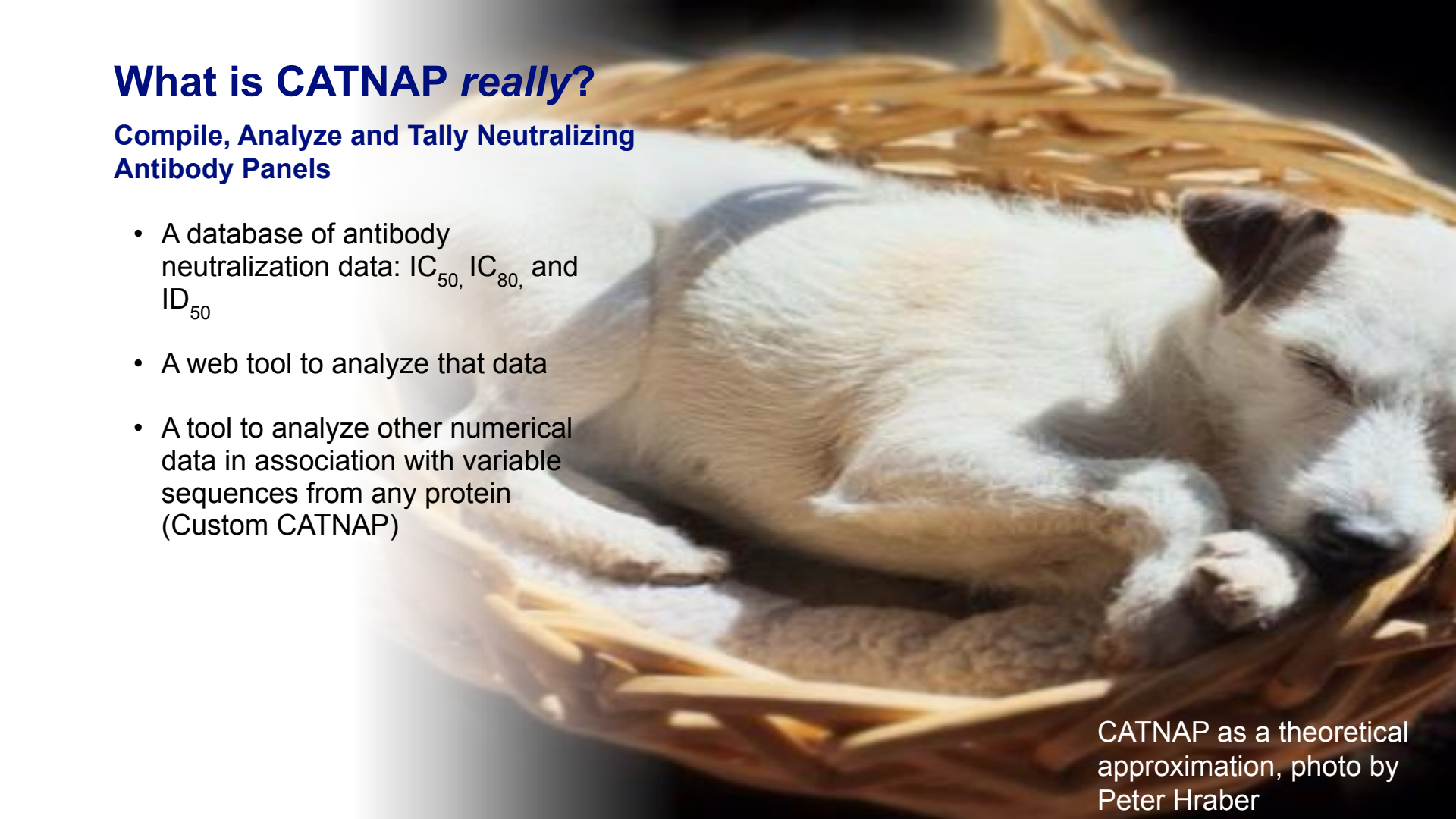
- **Immunogen Database**

  We are in the process of developing a database & associated tools for antibodies elicited by certain types of vaccines (“Env immunogens”), to help users investigate what makes a successful vaccine immunogen.

What is CATNAP *really*?

Compile, Analyze and Tally Neutralizing Antibody Panels

- A database of antibody neutralization data: $IC_{50,}$ $IC_{80,}$ and ID_{50}
- A web tool to analyze that data
- A tool to analyze other numerical data in association with variable sequences from any protein (Custom CATNAP)



CATNAP as a theoretical approximation, photo by Peter Hraber

https://hiv.lanl.gov/catnap

CATNAP

Compile, Analyze and Tally NAb Panels

The CATNAP family of tools has been designed to facilitate the analysis of neutralizing antibodies (NAbs) through the identification of potential genetic signatures resulting from a NAb's interaction with a protein. While interactions between NAbs and HIV-1 Env are the emphasis, the Custom Input version can accommodate many other types of data, including other proteins and organisms.

CATNAP

Purpose: Analyze our database of IC_{50}, IC_{80}, and ID_{50} neutralization data from publicly-available sources, in conjunction with HIV Env sequences. Or download these data for your own analyses.

- CATNAP Help
- CATNAP download: download all CATNAP neutralization data, Env alignment, antibody sequences, and germline genes
- Find Names: convert your mAb and virus names to CATNAP standard names

Download and analyze built-in HIV antibody IC50/80 data

Full DB downloads available

CATNAP: Custom Input

Purpose: Find potential genetic signatures based on your own data in association with protein sequences. In addition to neutralization data, this tool can accommodate almost any numerical data in conjunction with almost any protein sequence.

- Custom CATNAP Help

Analysis of **your data** for any organism: numerical data linked to aligned sequences

CATNAP: Hybrid

Purpose: Compare and analyze your HIV-1 IC_{50} and IC_{80} neutralization data with published data. This tool will display your data side-by-side with data from our database of published HIV-1 neutralization data.

- Hybrid CATNAP Help

Analysis of built-in IC50/80 data together with your own HIV antibody IC50/80 data

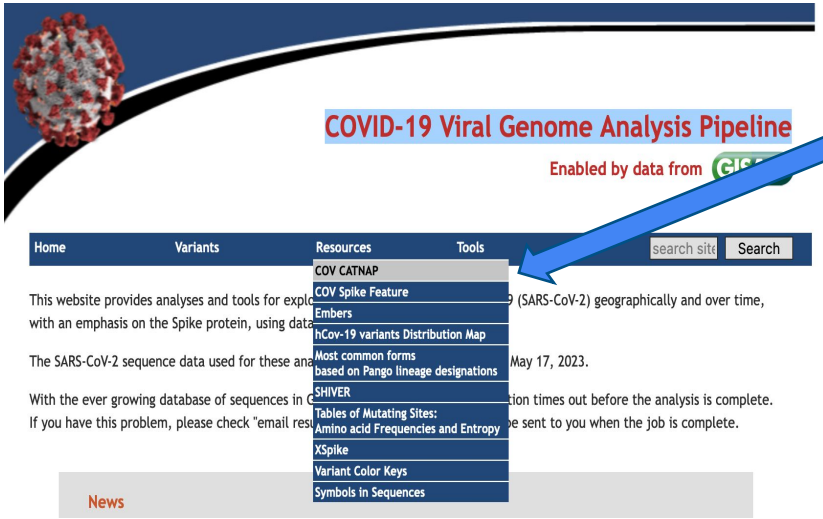
COV CATNAP

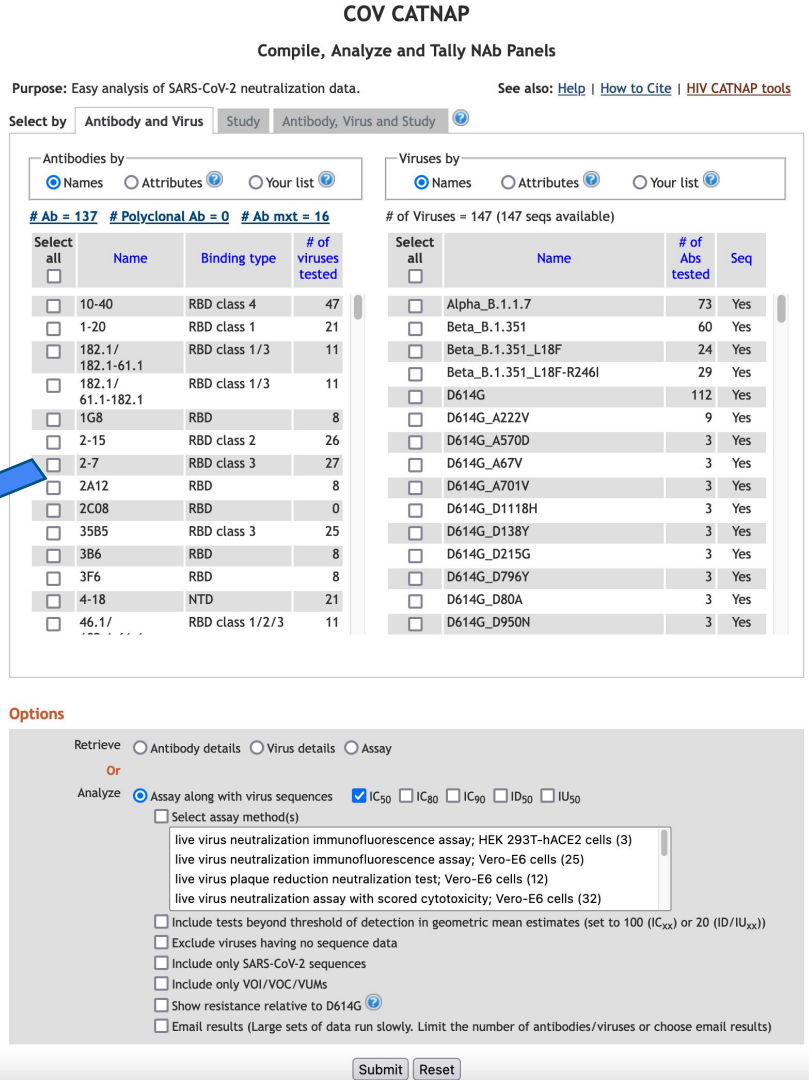
Purpose: Analyze our database of $IC_{50}$and IC_{80} neutralization data from anti-SARS-CoV-2 antibodies, in conjunction with COV Spike sequences.

COV CATNAP

COVID-19 Viral Genome Analysis Pipeline

https://cov.lanl.gov





Show resistance relative to D614G
Analyze IC_{50}

*: Geometric means
Expand to individual vals

IC_{xx}: ●<0.01 ●<0.1 ●<1 ●≤5 O>cutoff or 5 (μg/ml)

Virus name	LY-CoV1404:IC50	LY-CoV1404:IC50 Resis. rel. to D614G	S309:IC50	S309:IC50 Resis. rel. to D614G
Omicron_XBB_alt	UD	UD	0.170900	–
Pango_B.1	0.004	–	0.119	–
Pango_R.1	–	–	0.03	2.727273
SARS-CoV-1_BJ01	–	–	0.02	–
SARS-CoV-1_D28	–	–	0.042478*	–
SARS-CoV-1_GZ50	–	–	0.028	–
SARS-CoV-1_HKU-39849	UD	UD	0.03162*	0.422402
Sarbecovirus_BtKY72_K493Y-T498W	–	–	13	–
Sarbecovirus_LYRa11	–	–	0.011*	–
Sarbecovirus_Pang17	–	–	0.39833*	–
Sarbecovirus_Pangolin-GD	0.00863	11.552878	0.057966*	–
Sarbecovirus_RaTG13	UD	UD	UD	UD
Sarbecovirus_Rs4084	–	–	UD	UD
Sarbecovirus_Rs4231	–	–	0.141*	–
Sarbecovirus_Rs7327	–	–	UD	UD
Sarbecovirus_SHC014	–	–	UD	UD
Sarbecovirus_WIV1	–	–	0.069882*	–
WT	0.0030047*	1.666667	0.042492*	–
WT_S247R	0.001	–	0.072111*	–
XBC.1.6	–	–	0.276	13.800000
Merbecovirus_MERS	–	–	UD	UD
Geometric mean of detected	0.0027226		0.24468	
Geometric mean of detected & undetected**	0.010806		0.33268	
% detected (detected/total)	87% (106/122)		95% (130/137)	

```
NC_045512
M----FVFLVLLPLVSS----QCVNLTTRTQLPPAYTNSFTRGVYYPDK
--------.----|--------.----|----.----|----.----|-
----------10----------20--------30--------40--
M----FVFLVLLPLVSS----QCVNLITRTQ---SYTNSFTRGVYYPDK
M----FVFLVLLPLVSS----QCVNLRTRTQLPPAYTNSFTRGVYYPDK
M----FVFLVLLPLVSS----QCVNLTTRTQLPPAYTNSFTRGVYYPDK
M----FIFLLFLTLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYYPDE
M----FIFLLFLTLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYYPDE
M----FIFLLFLTLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYYPDE
M----FIFLLFLTLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYYPDE
MKF--FILLSLLSFTTA--QEGCGILSNKSNPALTQYFSSRRGFYYFDD
MFLTCFILSFSLFCVSGDSIDTCETFDDVSPPQQNLVSSSKRGVYYPDD
M----FVFLFVLPLVSS----QCVNLTTRTGIPPGYTNSSTRGVYYPDK
M-L--FFFFLHFALVNS----QCVNLTGRAAIQPSFTNSSQRGVYYPDT
M----FVFLVLLPLVSS----QCVNLTTRTQLPPAYTNSSTRGVYYPDK
MK---LLVLVFATLVSSYTIEKCLDFDDRTPPANTQFLSSHRGVYYPDD
M----FIFLFFLTLTSGSDLESCTTFDDVQAPNYPQHSSSRRGVYYPDE
MK---LLVLVFATLVSSYTIEKCLDFDDRTPPANTQFLSSHRGVYYPDD
MK---LLVLVFATLVSSYTIEKCLDFDDRTPPANTQFLSSHRGVYYPDD
MK---LLVLVFATLVSSYTIEKCLDFDDRTPPANTQFLSSHRGVYYPDD
M----FVFLVLLPLVSS----QCVNLTTRTQLPPAYTNSFTRGVYYPDK
M----FVFLVLLPLVSS----QCVNLTTRTQLPPAYTNSFTRGVYYPDK
M----FVFLVLLPLVSS----QCVNLITRTQLSPAYTNSFTRGVYYPDK
```

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

# of antibodies or mixtures found: 2
# of viruses found: 146
# of studies found: 29 Trim

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

Download alignment Fasta

Cao2022a Cao2023_GitHub Chen2022 Dijokaite-Guraliuc2022 Dijokaite-Guraliuc2023 Duerr2023 Fang2022 Guenthoer2023 Guo2023 He2023 Huang2023 Huo2023 Liu2022a Liu2023a Luo2023 Misasi2022 Nutalai2022 Sheward2022a Tuekprakhon2022 Wang2022 Wang2022f Wang2022g Wang2023 Wang2023c Wang2023d Westendorf2022 Yisimayi2023_GitHub Yuan2022 Zhou2022a

Go to antibody information section

Antibody contact and feature position(s) (based on NC_045512)

- **LY-CoV1404 binding** (Annotation Logo) : R346 R408 L441 K444 V445 G446 G447 N448 N450 P499 E516
- **LY-CoV1404 contacts** (Annotation Logo) : T345 R346 N439 N440 L441 S443 K444 V445 G446 G447 N448 Y449 N450 Q498 P499 T500 N501 G502 V503 Q506 R509
- **LY-CoV1404 neutralization** (Annotation Logo) : K444 V445 G446
- **S309 binding** (Annotation Logo) : C336 P337 E340 A344 T345 K356 I358 C361 N440 V445 H519
- **S309 contacts** (Annotation Logo) : I332 T333 N334 L335 P337 G339 E340 V341 @343 A344 T345 R346 N354 K356 R357 I358 S359 N360 C361 N440 L441 K444

Position analysis

Antibody contact and feature position(s) (based on NC_045512)

- **LY-CoV1404 binding** (Annotation Logo) : R346 R408 L441 K444 V445 G446 G447 N448 N450 P499 E516
- **LY-CoV1404 contacts** (Annotation Logo) : T345 R346 N439 N440 L441 S443 K444 V445 G446 G447 N448 Y449 N450 Q498 P499 T500 N501 G502 V503 Q506 R509
- **LY-CoV1404 neutralization** (Annotation Logo) : K444 V445 G446
- **S309 binding** (Annotation Logo) : C336 P337 E340 A344 T345 K356 I358 C361 N440 V445 H519
- **S309 contacts** (Annotation Logo) : I332 T333 N334 L335 P337 G339 E340 V341 @343 A344 T345 R346 N354 K356 R357 I358 S359 N360 C361 N440 L441 K444

Position analysis

Analyze | NC_045512 position | 498 | LY-CoV1404:IC50

Analysis at position 498 for Ab LY-CoV1404:ic50

Amino Acid Counts

AA	Count	# for detected	# for undetected	Fisher test p-value	Odds ratio
R	79	65	14	0.05017	0.2286941
Q	40	40	0	0.001279	Inf
Y	2	0	2	0.01626	0
H	1	1	0	1	Inf
Total	122	106	16		

N-linked Glycosylation Motif Counts

NxST	Count	# for detected	# for undetected	Fisher test p-value	Odds ratio
g+	0	0	0	1	0
g-	122	106	16	1	0
-	0	0	0	1	0
Total	122	106	16		

Odds ratios <1 indicate that R498 and Y498 are associated* with resistant viruses

Odds ratios >1 indicate that Q498 and H498 are associated* with neutralized viruses

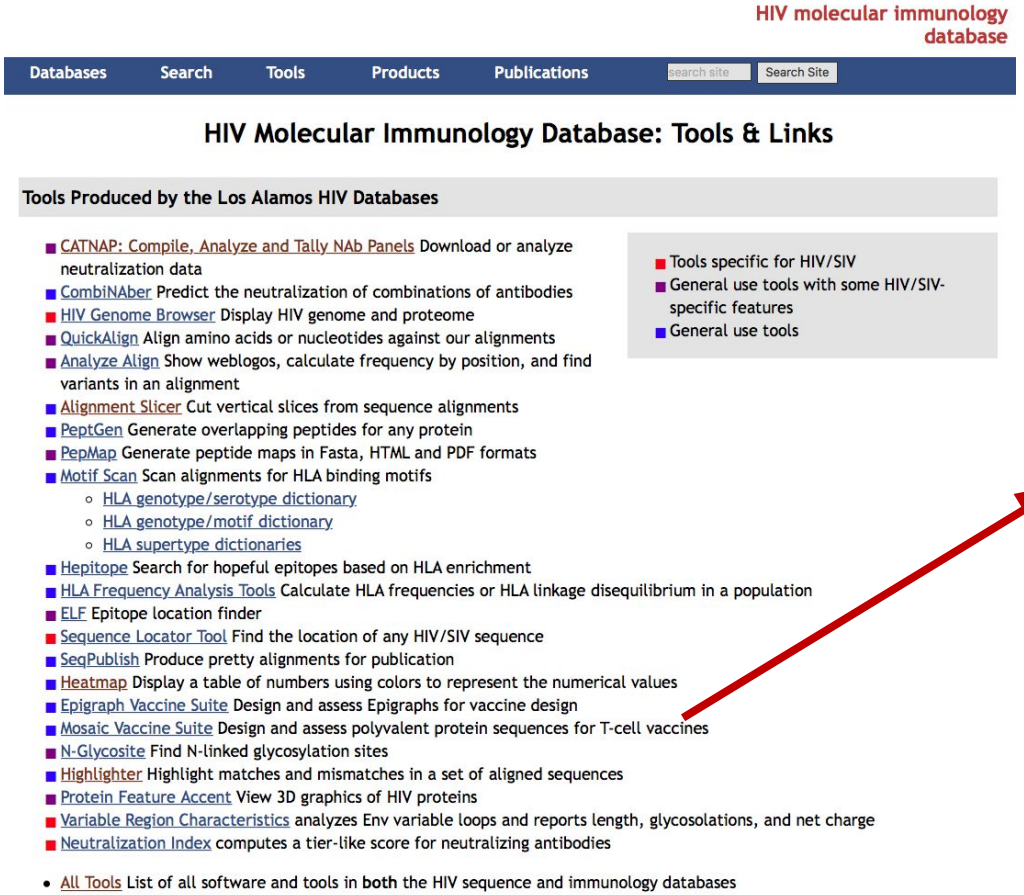
* these associations are purely statistical, and not phylogenetically corrected

---

Who is CATNAP'ing and why?

- **Training data & meta-analysis**
  - "Extrapolating missing antibody-virus measurements across serological studies"
    - Einav & Cleary, Cells Systems 2022
  - "Prediction of HIV sensitivity... using amino acid sequences and deep learning"
    - Dănăilă & Buiu, Bioinformatics. 2022
  - "Potential neutralizing antibodies discovered for novel coronavirus using machine learning"
    - Magar et al., Sci Rep 2021
  - "Super LeArner Prediction of NAb Panels (SLAPNAP)"
    - Williamson et al., 2021, Bioinformatics 2021
  - "Optimizing clinical dosing of combination broadly neutralizing antibodies for HIV prevention"
    - Mayer, et al., PLoS Comput Biol. 2022
  - "Probabilities of HIV-1 bNAb development in healthy and chronically infected individuals"
    - Kreer, et al., bioRxiv, 2023
- **A suite of tools built to visualize the data**
  - U of Minnesota, Herschhorn lab: https://hiresist.umn.edu

Our database has additional tools, many of which are not HIV-specific:



HIV molecular immunology database

Databases | Search | Tools | Products | Publications | search site | Search Site

HIV Molecular Immunology Database: Tools & Links

Tools Produced by the Los Alamos HIV Databases

- Tools specific for HIV/SIV
- General use tools with some HIV/SIV-specific features
- General use tools

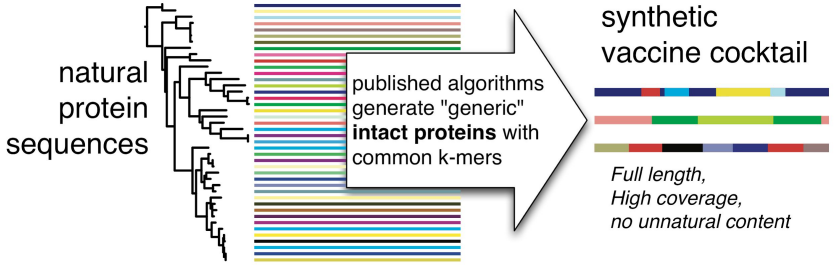
- CATNAP: Compile, Analyze and Tally NAb Panels Download or analyze neutralization data
- CombiNAber Predict the neutralization of combinations of antibodies
- HIV Genome Browser Display HIV genome and proteome
- QuickAlign Align amino acids or nucleotides against our alignments
- Analyze Align Show weblogos, calculate frequency by position, and find variants in an alignment
- Alignment Slicer Cut vertical slices from sequence alignments
- PeptGen Generate overlapping peptides for any protein
- PepMap Generate peptide maps in Fasta, HTML and PDF formats
- Motif Scan Scan alignments for HLA binding motifs
  - HLA genotype/serotype dictionary
  - HLA genotype/motif dictionary
  - HLA supertype dictionaries
- Hepitope Search for hopeful epitopes based on HLA enrichment
- HLA Frequency Analysis Tools Calculate HLA frequencies or HLA linkage disequilibrium in a population
- ELF Epitope location finder
- Sequence Locator Tool Find the location of any HIV/SIV sequence
- SeqPublish Produce pretty alignments for publication
- Heatmap Display a table of numbers using colors to represent the numerical values
- Epigraph Vaccine Suite Design and assess Epigraphs for vaccine design
- Mosaic Vaccine Suite Design and assess polyvalent protein sequences for T-cell vaccines
- N-Glycosite Find N-linked glycosylation sites
- Highlighter Highlight matches and mismatches in a set of aligned sequences
- Protein Feature Accent View 3D graphics of HIV proteins
- Variable Region Characteristics analyzes Env variable loops and reports length, glycosolations, and net charge
- Neutralization Index computes a tier-like score for neutralizing antibodies

- All Tools List of all software and tools in **both** the HIV sequence and immunology databases

- **Mosaic Vaccine Suite** and **Epigraph Vaccine Suite** (using T-cell epitopes):

  Generate candidate vaccine protein cocktails with optimized potential epitope coverage, calculate and visualize coverage

Vaccine Design Tools: Mosaic and Epigraph



Generate candidate T-cell vaccine protein cocktails that optimize coverage of potential T-cell epitopes based on frequencies in sets of natural pathogen sequences.

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

Epigraph — graph-theory approach (Theiler et al. 2016)

Vaccine Design Tools: Mosaic/Epigraph

Mosaic/Epigraph vaccine designs have been applied to *many* pathogens.

Influenza (Kingstad-Bakke et al. Vaccine, 2019 37:5051 (PMID: 31300285); Florik *et al.*, PLoS One, 2017 Aug 3;12(8):e0181738; and Kamlangdee *et al*, J Virol. 2016 Jul 11;90(15):6771-6783 and J Virol. 2014 Nov;88(22):13300-9, PMID:25210173)

Dengue (Hou et al. Front Immunol. 2019 Jun 20;10:1429, PMID: 31281322)

Rabies (Stading *et al.*, Plos Negl Trop Dis, 2017, PMID: 28976983)

Pan-filoviruses (Theiler *et al.*, Sci Rep. 2016, PMID: 27703185, Rahim et al., PLoS Pathog. 2019 Feb 28;15(2):e1007564 PMID: 30817809)

Chlamydia trachomatis (Badamchi-Zadeh *et al.*, Front Immunol, 2016, PMID: 27199987)

Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) (Cui *et al.*, PLoS One. 2019 Jan 31;14(1) PMID: 30794703)

Dengue Fever (Hou *et al.*, Front Immunol. 2019 Jun 20;10:1429. PMID: 31281322)

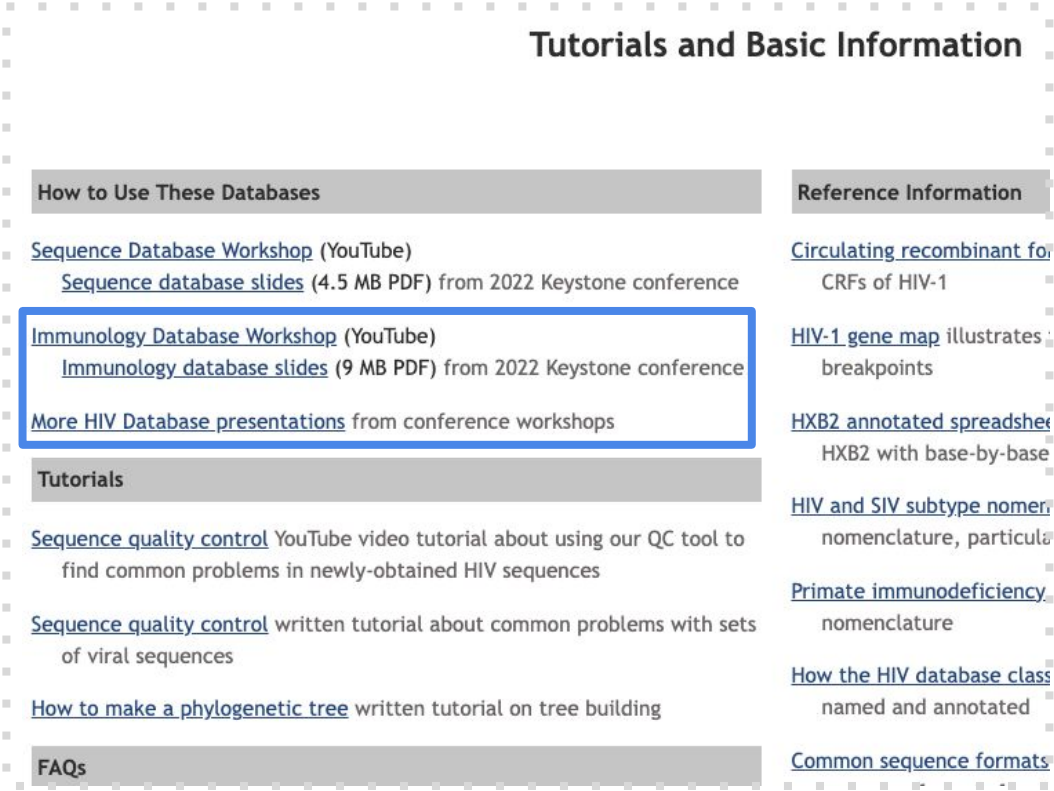
Hepatitis B (Bruening E, Douglas J, Yusim K, *et al.*, being experimentally tested)

Hepatitis C (Yusim *et al.*, Clin Vaccine Immunol, 2013, PMID: 23221002)

Lassa Virus (Alex Bukreyev, https://apps.dtic.mil/sti/citations/AD1116972)

Additional tutorials available on our website

hiv.lanl.gov/content/sequence/TUTORIALS/Tutorials.html



Tutorials and Basic Information

How to Use These Databases

Sequence Database Workshop (YouTube)
Sequence database slides (4.5 MB PDF) from 2022 Keystone conference

Immunology Database Workshop (YouTube)
Immunology database slides (9 MB PDF) from 2022 Keystone conference

More HIV Database presentations from conference workshops

Tutorials

Sequence quality control YouTube video tutorial about using our QC tool to find common problems in newly-obtained HIV sequences

Sequence quality control written tutorial about common problems with sets of viral sequences

How to make a phylogenetic tree written tutorial on tree building

FAQs

Reference Information

Circulating recombinant fo
CRFs of HIV-1

HIV-1 gene map illustrates
breakpoints

HXB2 annotated spreadshe
HXB2 with base-by-base

HIV and SIV subtype nomer
nomenclature, particul

Primate immunodeficiency
nomenclature

How the HIV database class
named and annotated

Common sequence formats

Our database depends upon users like you!

We are an NIH-funded resource. Please contact us with questions, problems, or suggestions.

immuno@lanl.gov