IMMUNE EPITOPE DATABASE AND ANALYSIS RESOURCE

"How to use IEDB in your research"

Examples on Orthopox

Presented by: Alba Grifoni, PhD, Instructor/Research Faculty

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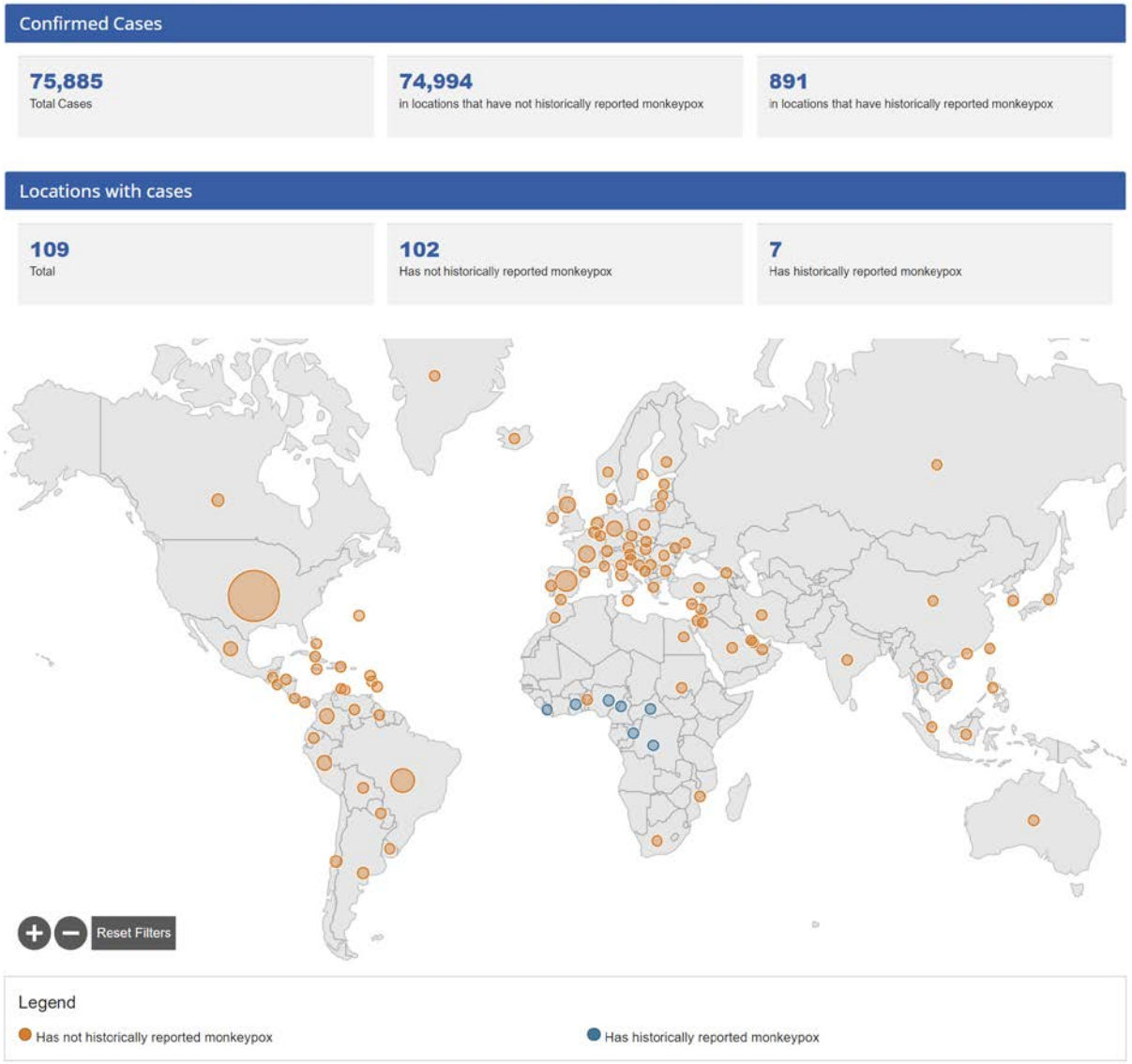
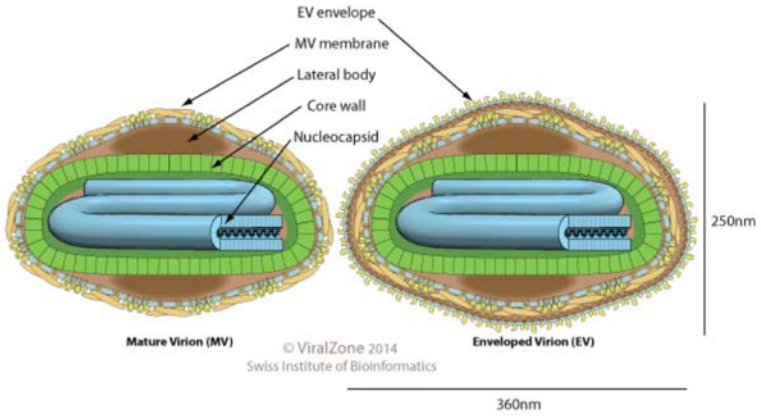
Monkeypox outbreak

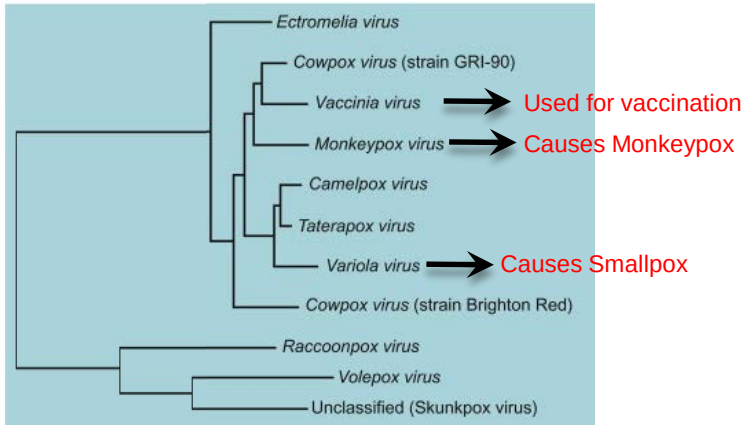


https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html

Orthopoxviruses



Orthopoxvirus

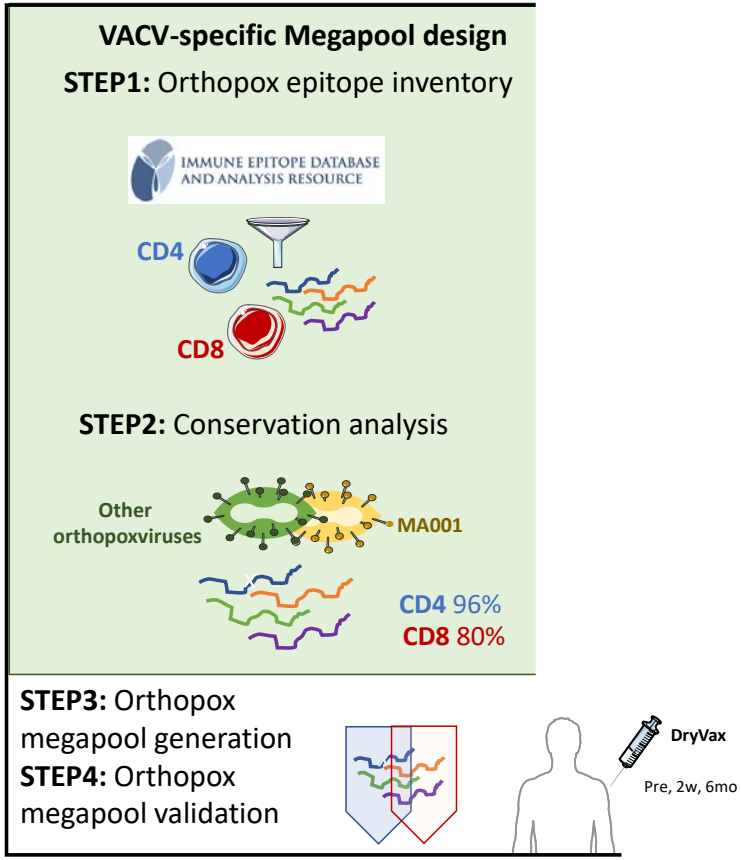


Virus Taxonomy, 2012 doi.org/10.1016/B978-0-12-384684-6.00028-8.

- All Orthopox viruses vaccines are based on **vaccinia virus**:
  - *Dryvax: live vaccine with combination of vaccinia strains discontinued in 1972.*
    High efficacy, Low safety profile ORFs≈ 240
  - *Acam2000: live vaccine, single vaccinia strains from Dryvax. Comparable to Dryvax.*
  - *MVA (Jyanneos): live vaccine non-replicating modified vaccinia Ankara*
    Efficacy tested only in animal models, High safety profile ORFs≈ 157

Acam2000 and MVA are both currently licensed for Monkeypox (ORFs ≈ 200)

Design peptide pools able to detect vaccine responses



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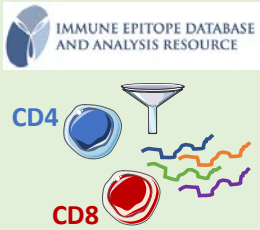
VACV-specific Megapool design

Table 1. IEDB inventory of orthopox virus CD4 and CD8 T cell epitopes

Type	Host	Orthopox virus					Total
		Cowpox	Ectromelia	Monkeypox	Vaccinia	Variola	
CD4	Humans	0	0	0	209	38	247
	Macaques	0	0	0	0	0	0
	Tg mice	0	0	0	0	0	0
	Mice	0	40	0	31	0	71
	Any	**0**	**40**	**0**	**240**	**38**	**318**
CD8	Humans	0	0	0	207	31	238
	Macaques	0	0	2	17	0	19
	Tg mice	0	0	0	182	0	182
	Mice	1	2	0	217	0	220
	Any	**1**	**2**	**2**	**623**	**31**	**659**

Tallies are non-redundant diminishing: macaques does not include those also recognized in humans, Tg mice does not include those recognized in humans or macaques, etc.

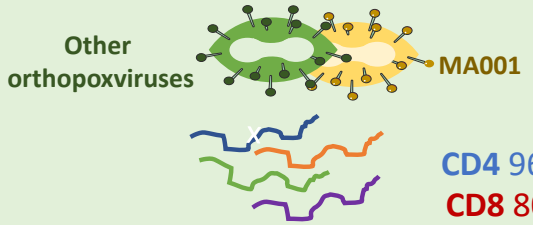
STEP1: Orthopox epitope inventory



OPXV CD4 MP: 318 epitopes identified in any host

OPXV CD8 MP: 238 epitopes identified only in Human

STEP2: Conservation analysis



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How to use IEDB to extract VACV epitopes

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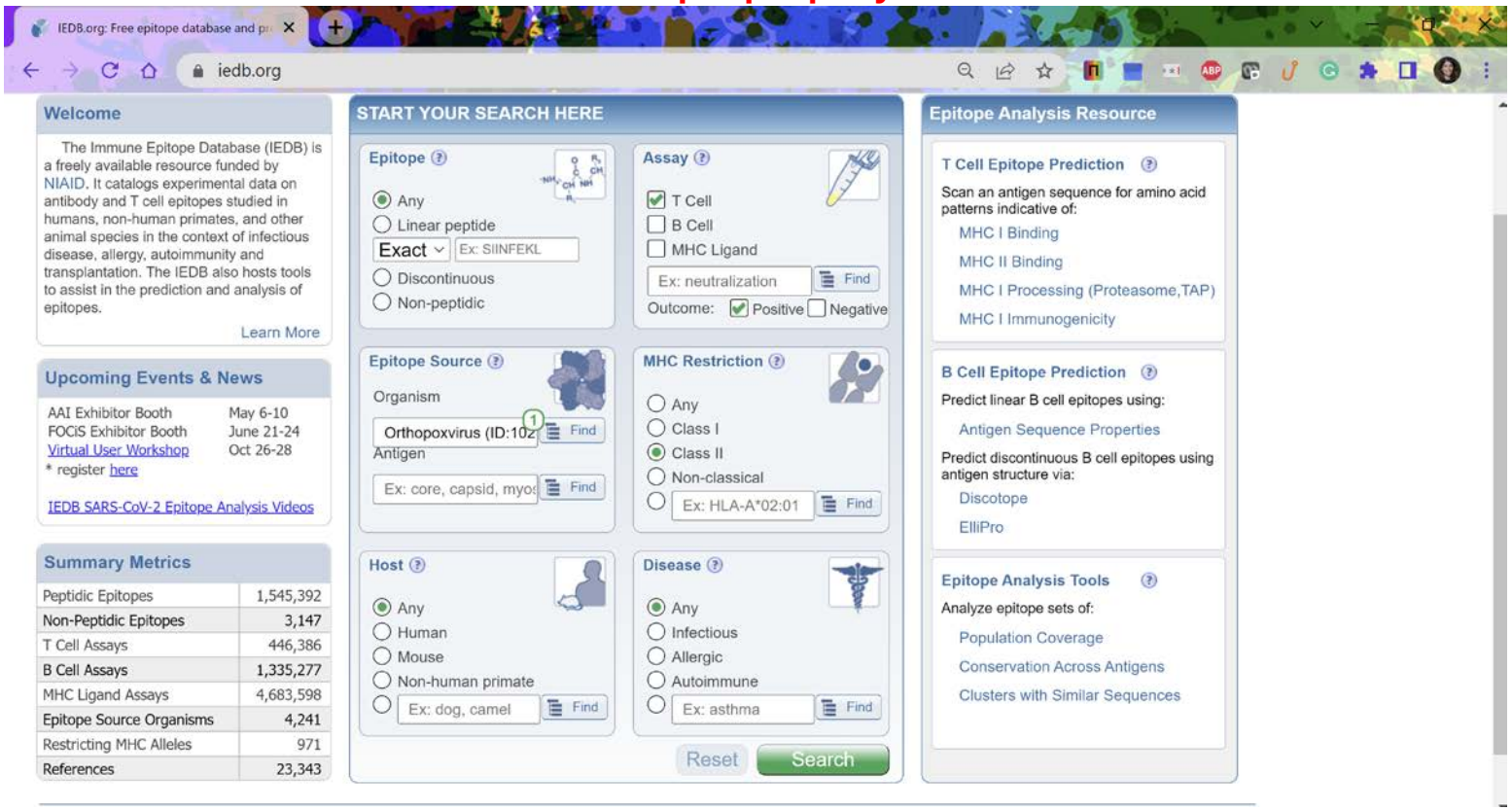
CD4 epitope query



How to use IEDB to extract VACV epitopes

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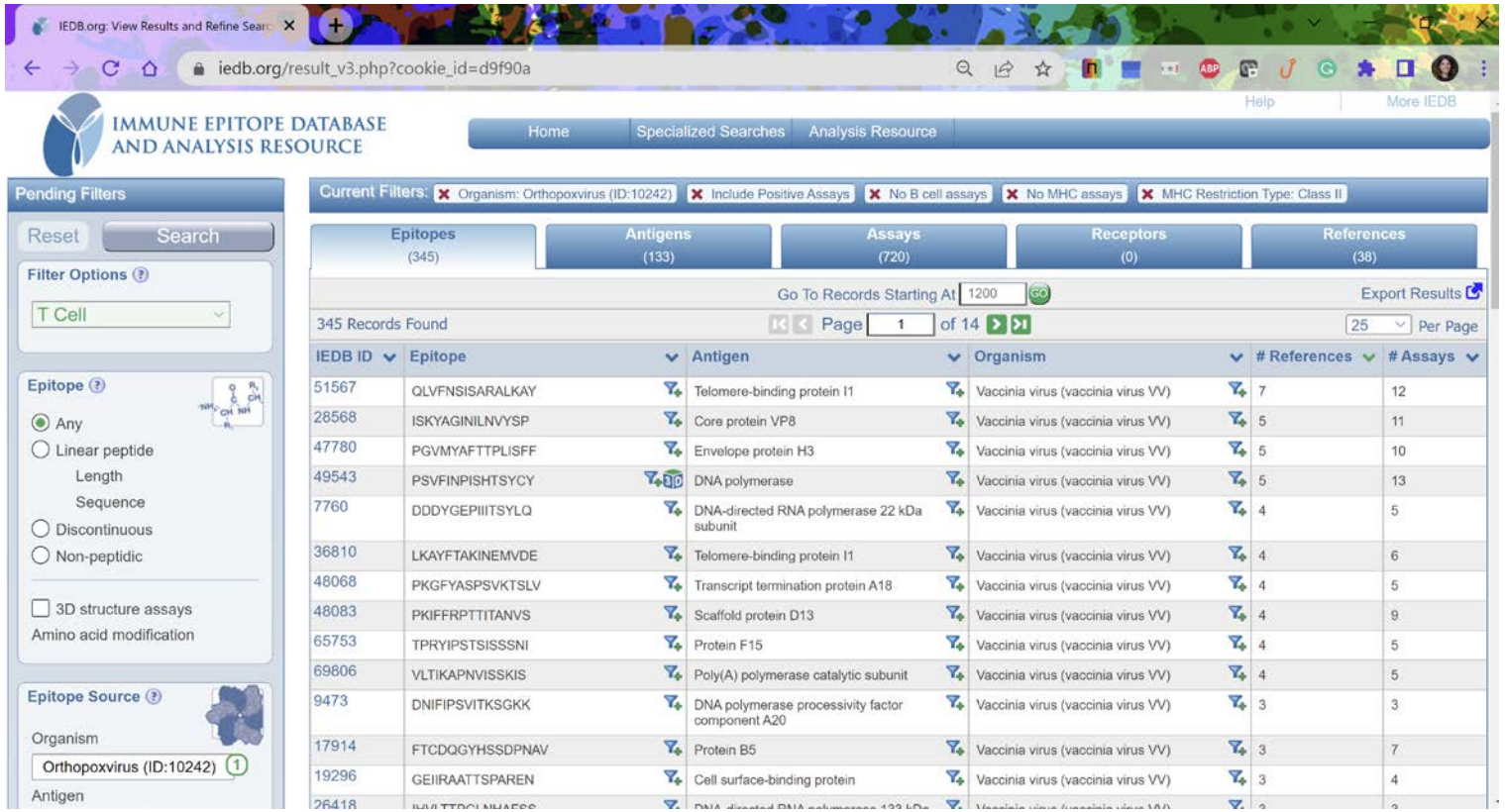
CD4 epitope results : Epitopes



IEDB ID	Epitope	Antigen	Organism	# References	# Assays
51567	QLVFNSISARALKAY	Telomere-binding protein I1	Vaccinia virus (vaccinia virus VV)	7	12
28568	ISKYAGINILNVYSP	Core protein VP8	Vaccinia virus (vaccinia virus VV)	5	11
47780	PGVMYAFTTPLISFF	Envelope protein H3	Vaccinia virus (vaccinia virus VV)	5	10
49543	PSVFINPISHTSYCY	DNA polymerase	Vaccinia virus (vaccinia virus VV)	5	13
7760	DDDYGEPIIITSYLQ	DNA-directed RNA polymerase 22 kDa subunit	Vaccinia virus (vaccinia virus VV)	4	5
36810	LKAYFTAKINEMVDE	Telomere-binding protein I1	Vaccinia virus (vaccinia virus VV)	4	6
48068	PKGFYASPSVKTSLV	Transcript termination protein A18	Vaccinia virus (vaccinia virus VV)	4	5
48083	PKIFFRPTTITANVS	Scaffold protein D13	Vaccinia virus (vaccinia virus VV)	4	9
65753	TPRYIPSTSISSSNI	Protein F15	Vaccinia virus (vaccinia virus VV)	4	5
69806	VLTIKAPNVISSKIS	Poly(A) polymerase catalytic subunit	Vaccinia virus (vaccinia virus VV)	4	5
9473	DNIFIPSVITKSGKK	DNA polymerase processivity factor component A20	Vaccinia virus (vaccinia virus VV)	3	3
17914	FTCDQGYHSSDPNAV	Protein B5	Vaccinia virus (vaccinia virus VV)	3	7
19296	GEIIRAATTSPAREN	Cell surface-binding protein	Vaccinia virus (vaccinia virus VV)	3	4

How to use IEDB to extract VACV epitopes

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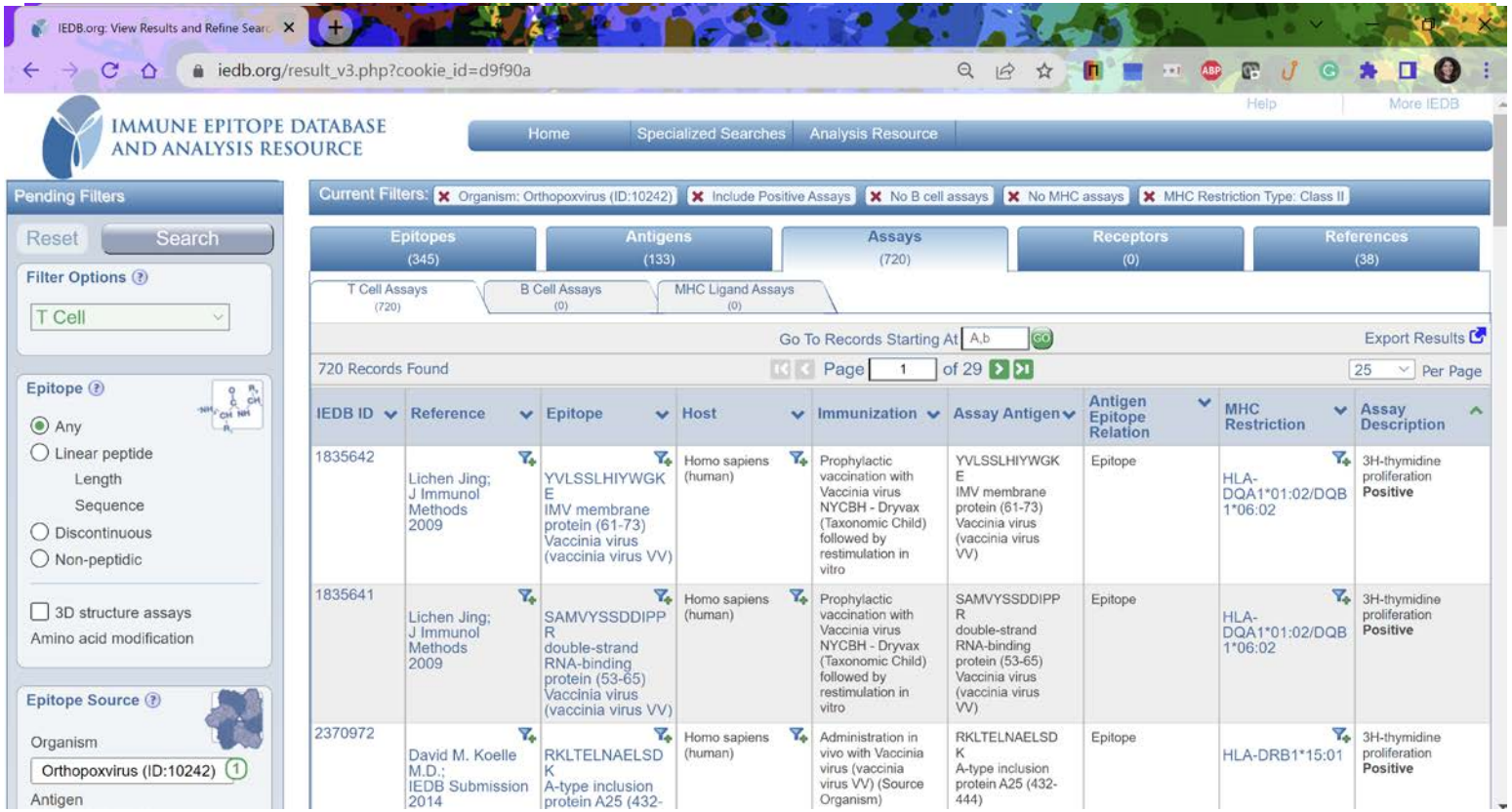
CD4 epitope results : Assays



How to use IEDB to extract VACV epitopes

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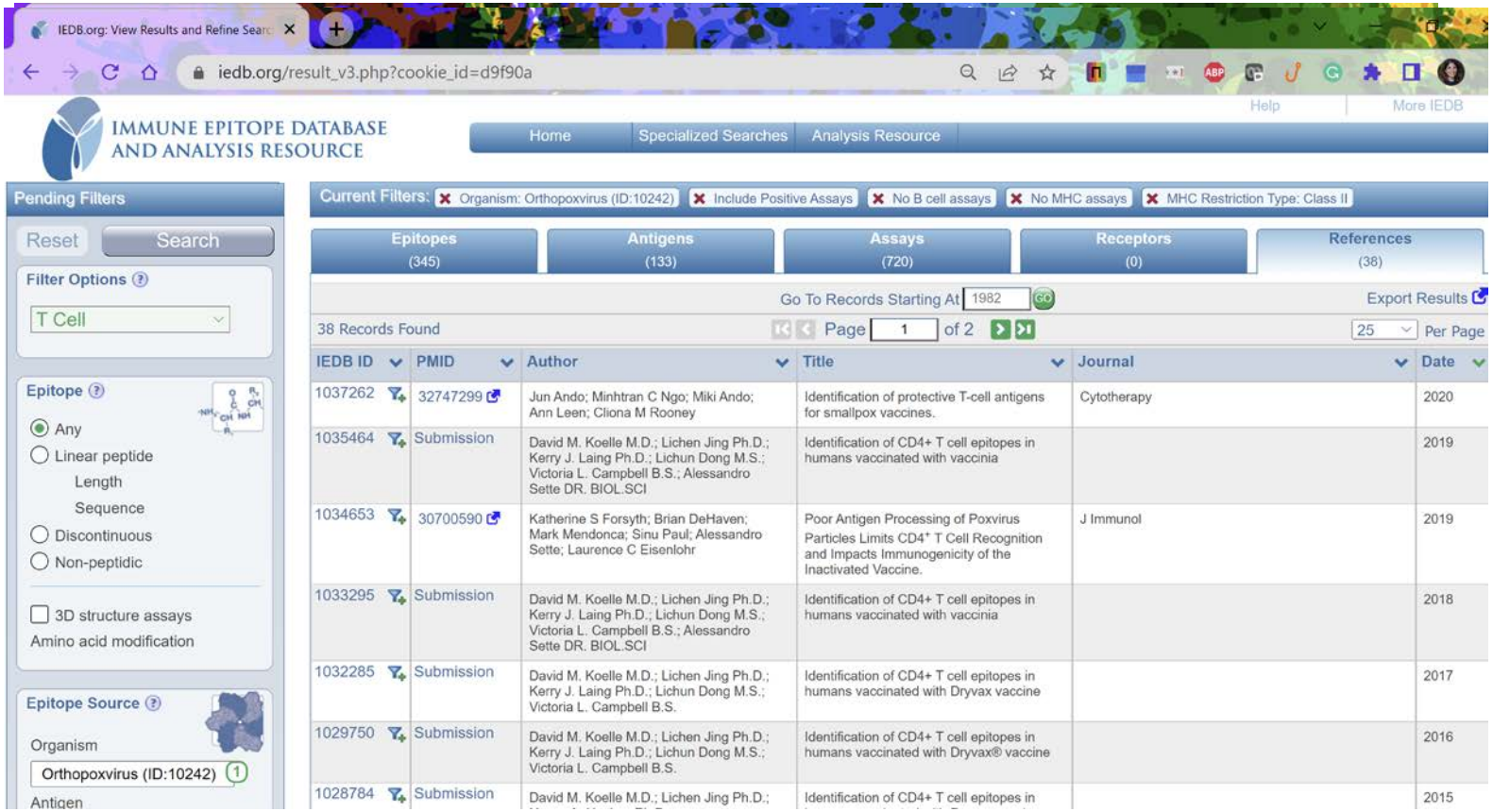
CD4 epitope results : References



IEDB ID	PMID	Author	Title	Journal	Date
1037262	32747299	Jun Ando; Minhtran C Ngo; Miki Ando; Ann Leen; Cliona M Rooney	Identification of protective T-cell antigens for smallpox vaccines.	Cytotherapy	2020
1035464	Submission	David M. Koelle M.D.; Lichen Jing Ph.D.; Kerry J. Laing Ph.D.; Lichun Dong M.S.; Victoria L. Campbell B.S.; Alessandro Sette DR. BIOL.SCI	Identification of CD4+ T cell epitopes in humans vaccinated with vaccinia		2019
1034653	30700590	Katherine S Forsyth; Brian DeHaven; Mark Mendonca; Sinu Paul; Alessandro Sette; Laurence C Eisenlohr	Poor Antigen Processing of Poxvirus Particles Limits CD4+ T Cell Recognition and Impacts Immunogenicity of the Inactivated Vaccine.	J Immunol	2019
1033295	Submission	David M. Koelle M.D.; Lichen Jing Ph.D.; Kerry J. Laing Ph.D.; Lichun Dong M.S.; Victoria L. Campbell B.S.; Alessandro Sette DR. BIOL.SCI	Identification of CD4+ T cell epitopes in humans vaccinated with vaccinia		2018
1032285	Submission	David M. Koelle M.D.; Lichen Jing Ph.D.; Kerry J. Laing Ph.D.; Lichun Dong M.S.; Victoria L. Campbell B.S.	Identification of CD4+ T cell epitopes in humans vaccinated with Dryvax vaccine		2017
1029750	Submission	David M. Koelle M.D.; Lichen Jing Ph.D.; Kerry J. Laing Ph.D.; Lichun Dong M.S.; Victoria L. Campbell B.S.	Identification of CD4+ T cell epitopes in humans vaccinated with Dryvax® vaccine		2016
1028784	Submission	David M. Koelle M.D.; Lichen Jing Ph.D.;	Identification of CD4+ T cell epitopes in		2015

How to use IEDB to extract VACV epitopes

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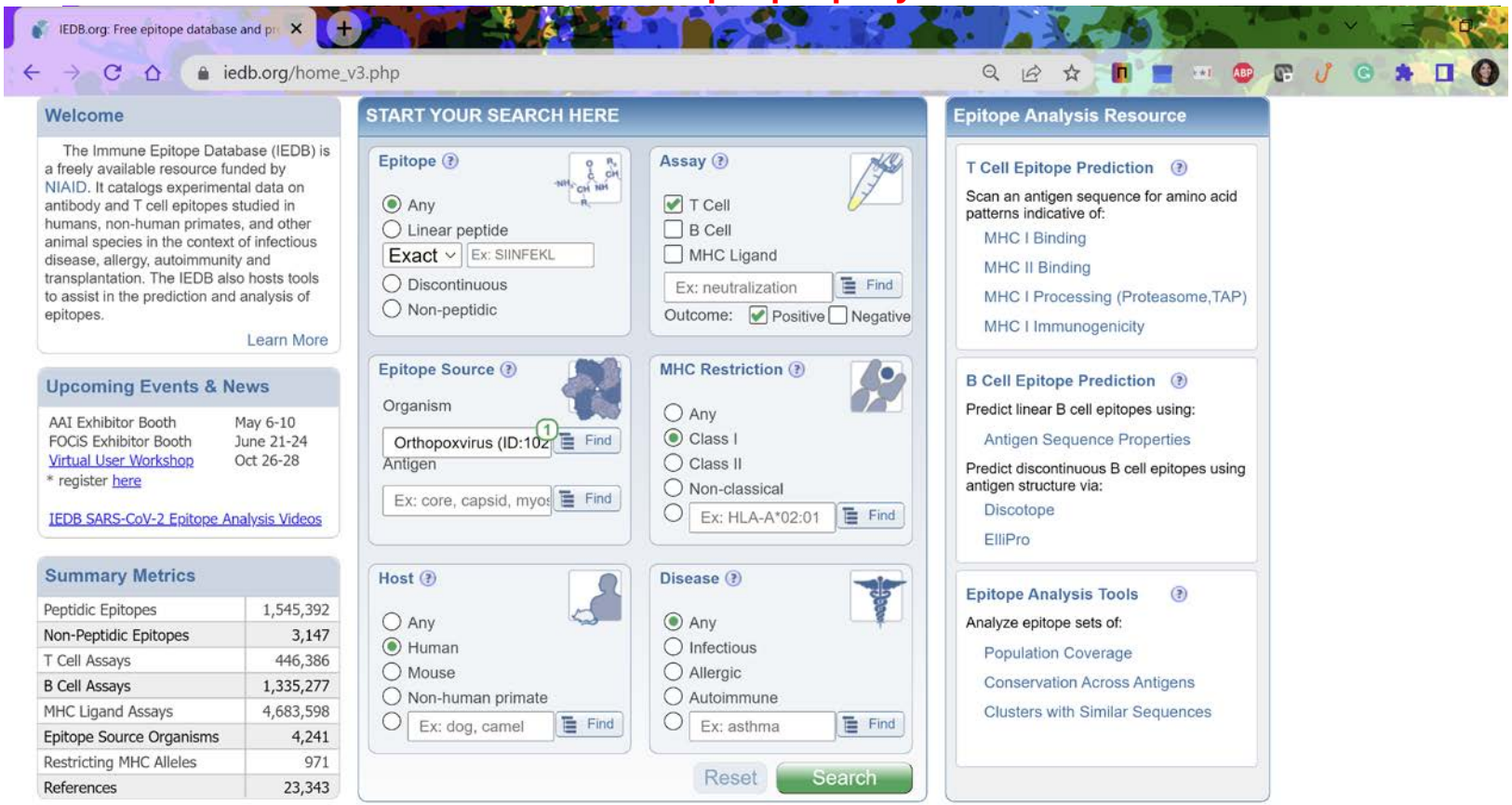
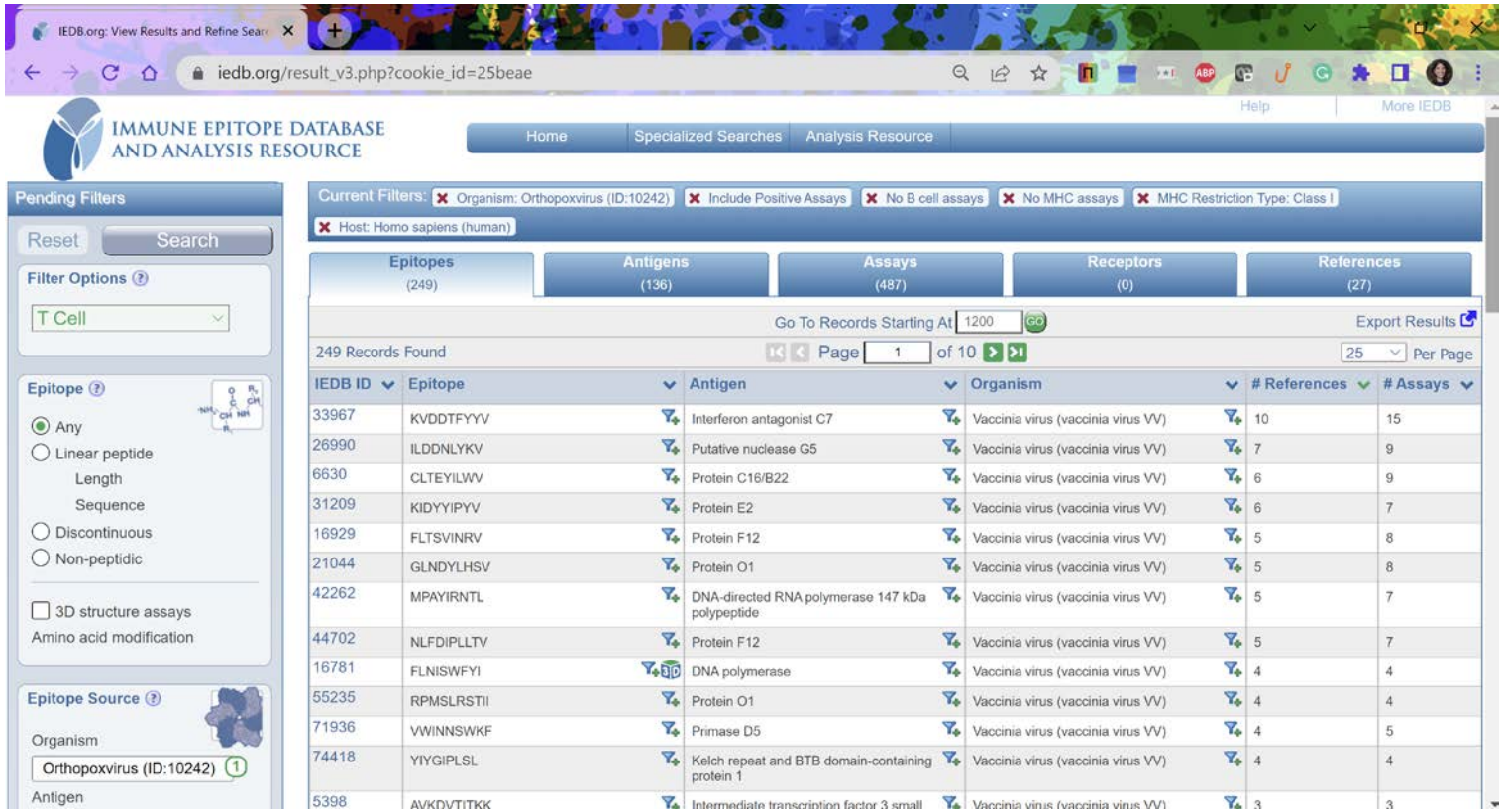
CD8 epitope query



How to use IEDB to extract VACV epitopes

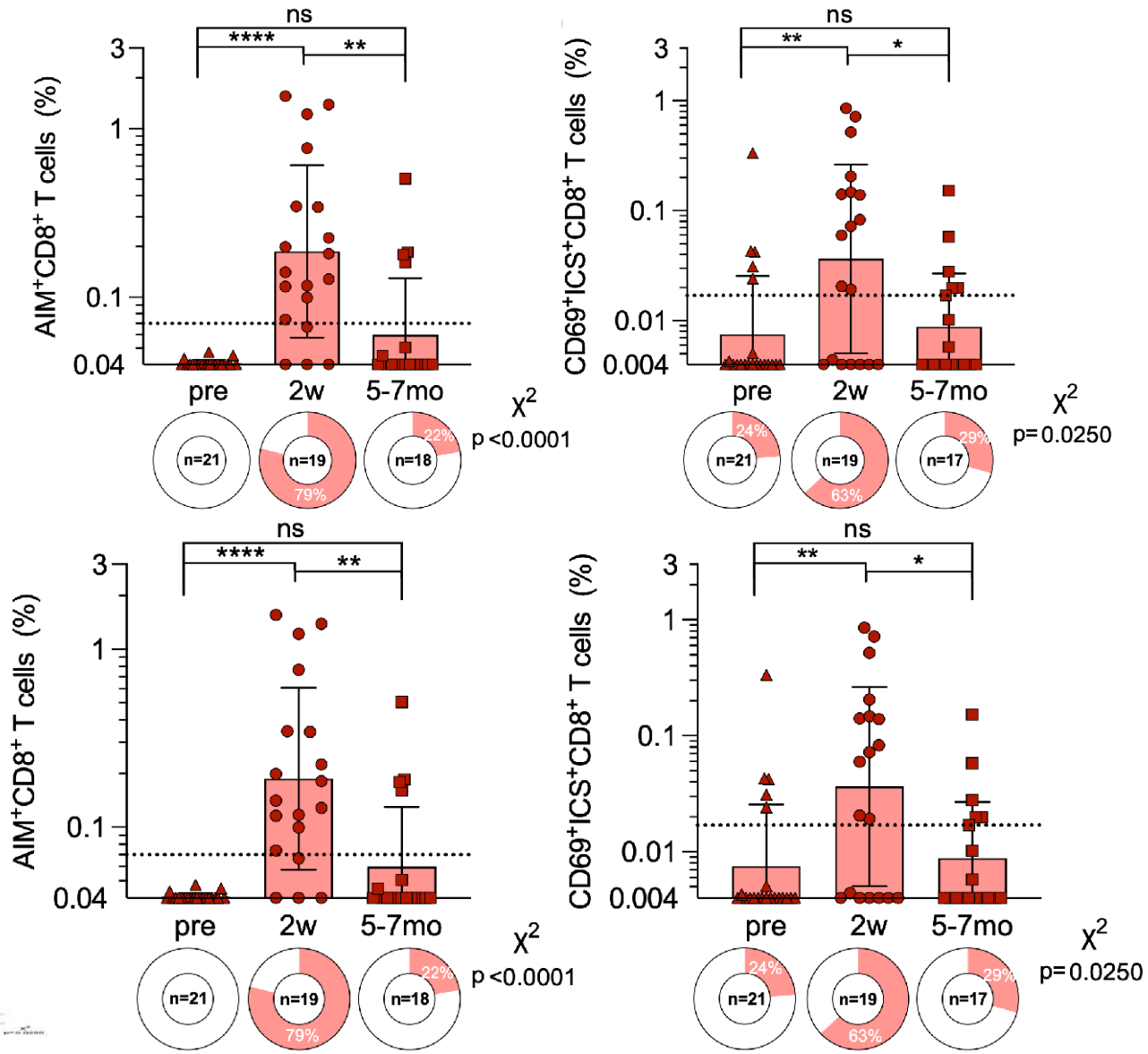
IMMUNE EPITOPE DATABASE AND ANALYSIS RESOURCE

CD8 epitope results : Epitopes



IEDB ID	Epitope	Antigen	Organism	# References	# Assays
33967	KVDDTFYYV	Interferon antagonist C7	Vaccinia virus (vaccinia virus VV)	10	15
26990	ILDDNLYKV	Putative nuclease G5	Vaccinia virus (vaccinia virus VV)	7	9
6630	CLTEYILWV	Protein C16/B22	Vaccinia virus (vaccinia virus VV)	6	9
31209	KIDYYIPYV	Protein E2	Vaccinia virus (vaccinia virus VV)	6	7
16929	FLTSVINRV	Protein F12	Vaccinia virus (vaccinia virus VV)	5	8
21044	GLNDYLHSV	Protein O1	Vaccinia virus (vaccinia virus VV)	5	8
42262	MPAYIRNTL	DNA-directed RNA polymerase 147 kDa polypeptide	Vaccinia virus (vaccinia virus VV)	5	7
44702	NLFDIPLLTV	Protein F12	Vaccinia virus (vaccinia virus VV)	5	7
16781	FLNISWFYI	DNA polymerase	Vaccinia virus (vaccinia virus VV)	4	4
55235	RPMSLRSTII	Protein O1	Vaccinia virus (vaccinia virus VV)	4	4
71936	VWINNSWKF	Primase D5	Vaccinia virus (vaccinia virus VV)	4	5
74418	YIYGIPLSL	Kelch repeat and BTB domain-containing protein 1	Vaccinia virus (vaccinia virus VV)	4	4
5398	AVKDVTITKK	Intermediate transcription factor 3 small	Vaccinia virus (vaccinia virus VV)	3	3

Testing VACV pools on a Dryvax vaccinated cohort



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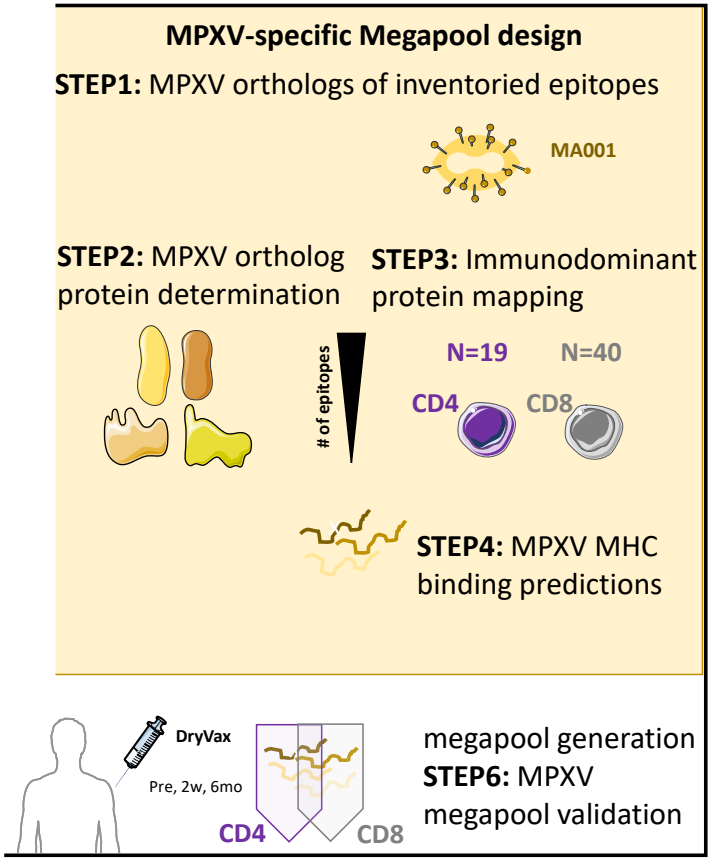
Design peptide pools able to detect MPXV responses



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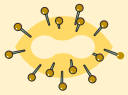
MPXV-specific Megapool design

STEP1: MPXV orthologs of inventoried epitopes



MA001

STEP2: MPXV ortholog protein determination

STEP3: Immunodominant protein mapping

N=19 N=40

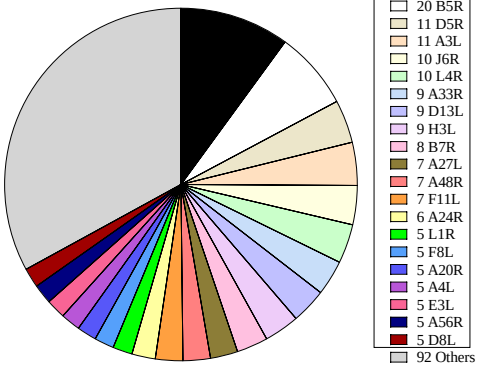
CD4 CD8

STEP4: MPXV MHC binding predictions

Selected proteins with 5 or more epitopes

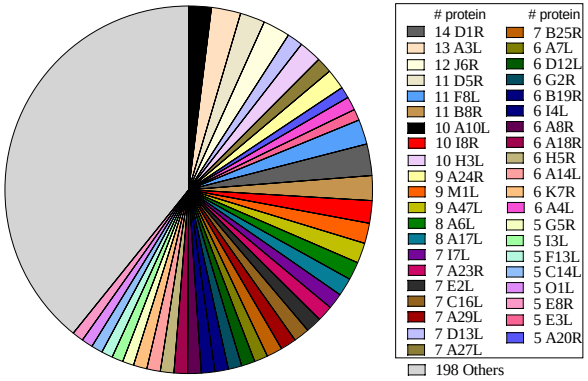
CD4

67%



CD8

61%



MPXV CD4 MP: 276

MPXV CD8 MP P1-P5: 1647- divided in 5 pools

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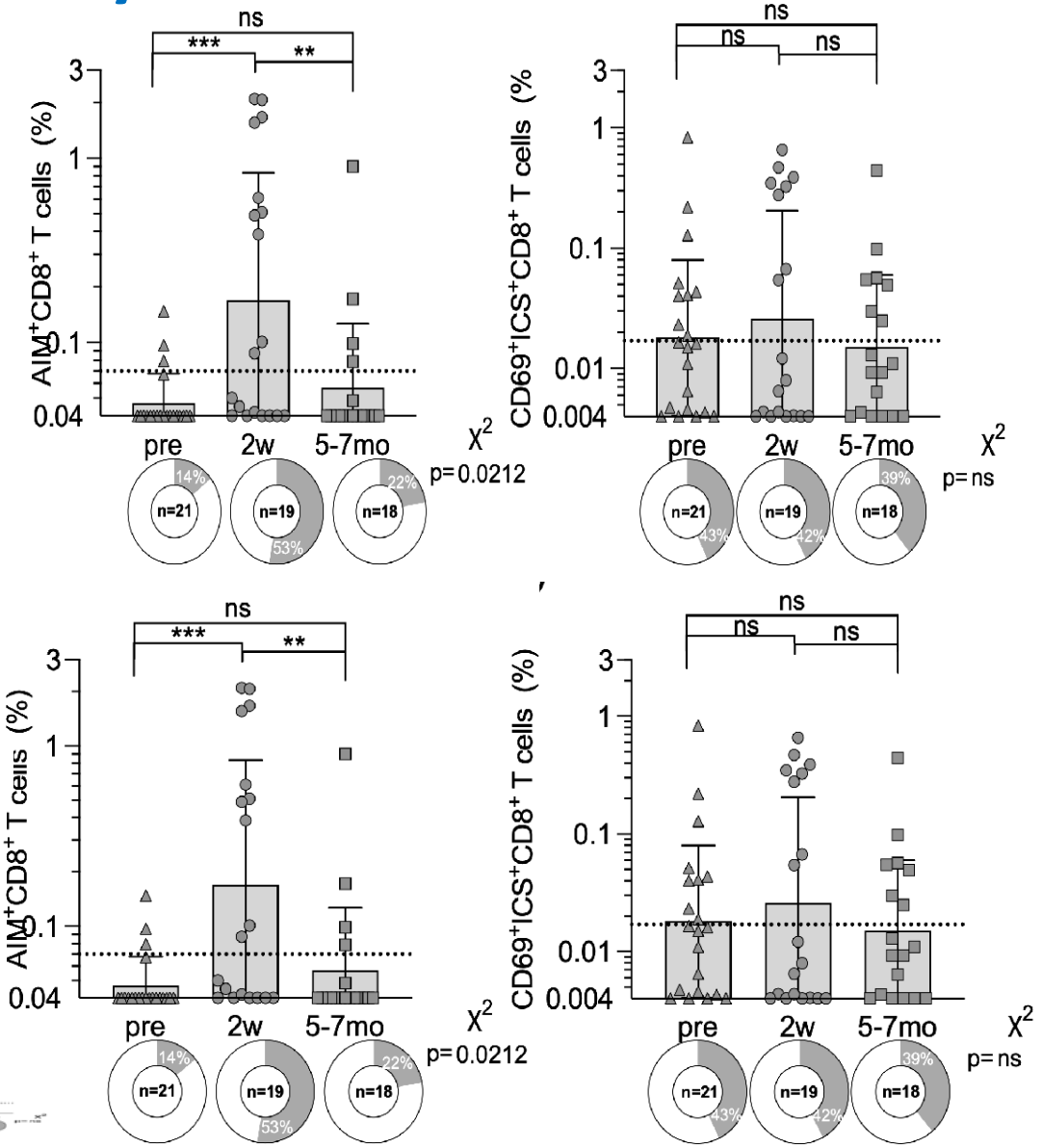
Testing MPXV pools to assess T cell cross-reactivity on a Dryvax vaccinated cohort



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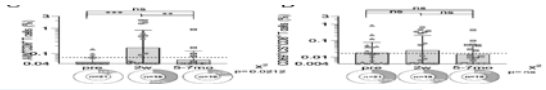
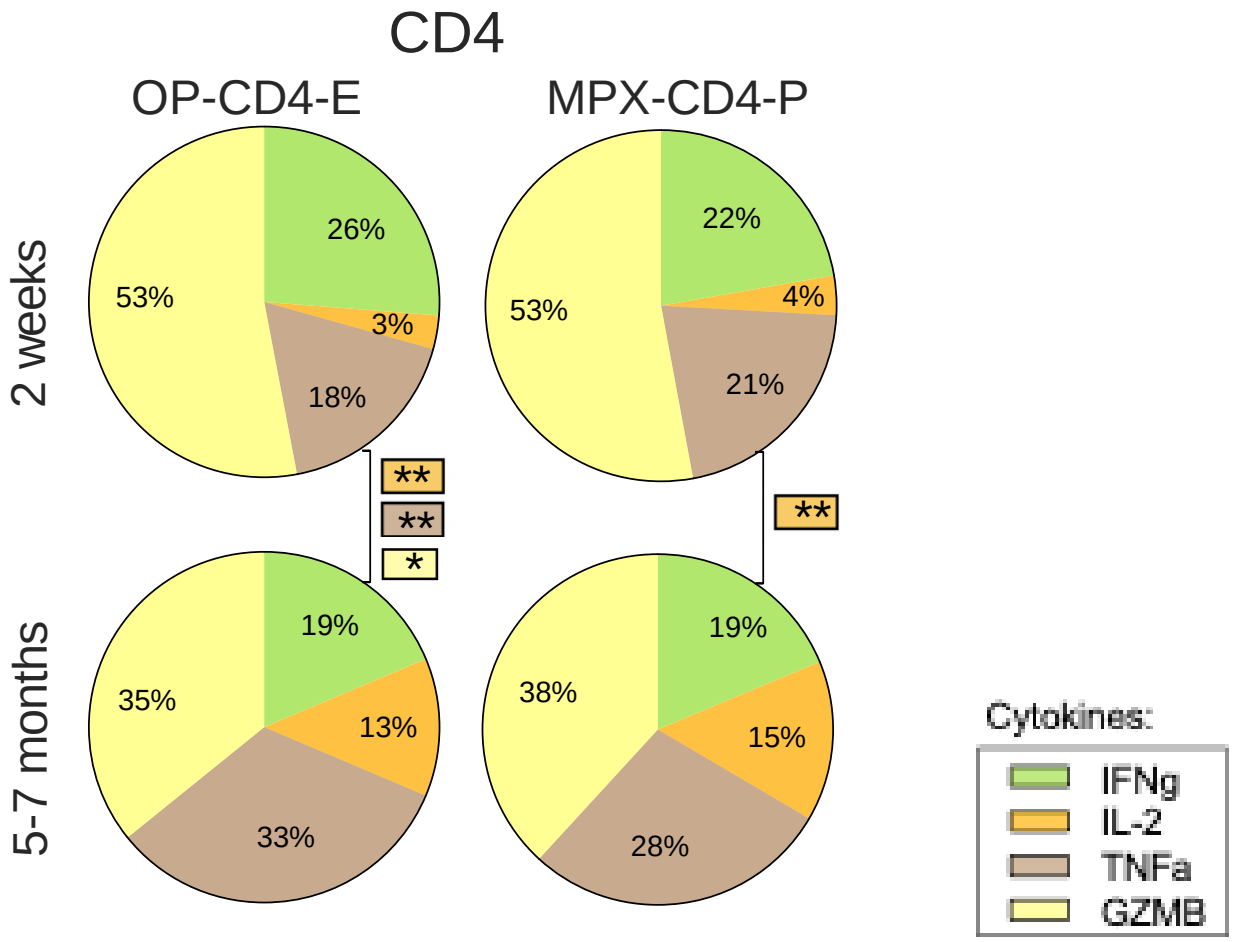


Pox-specific T cells produce multiple cytokines



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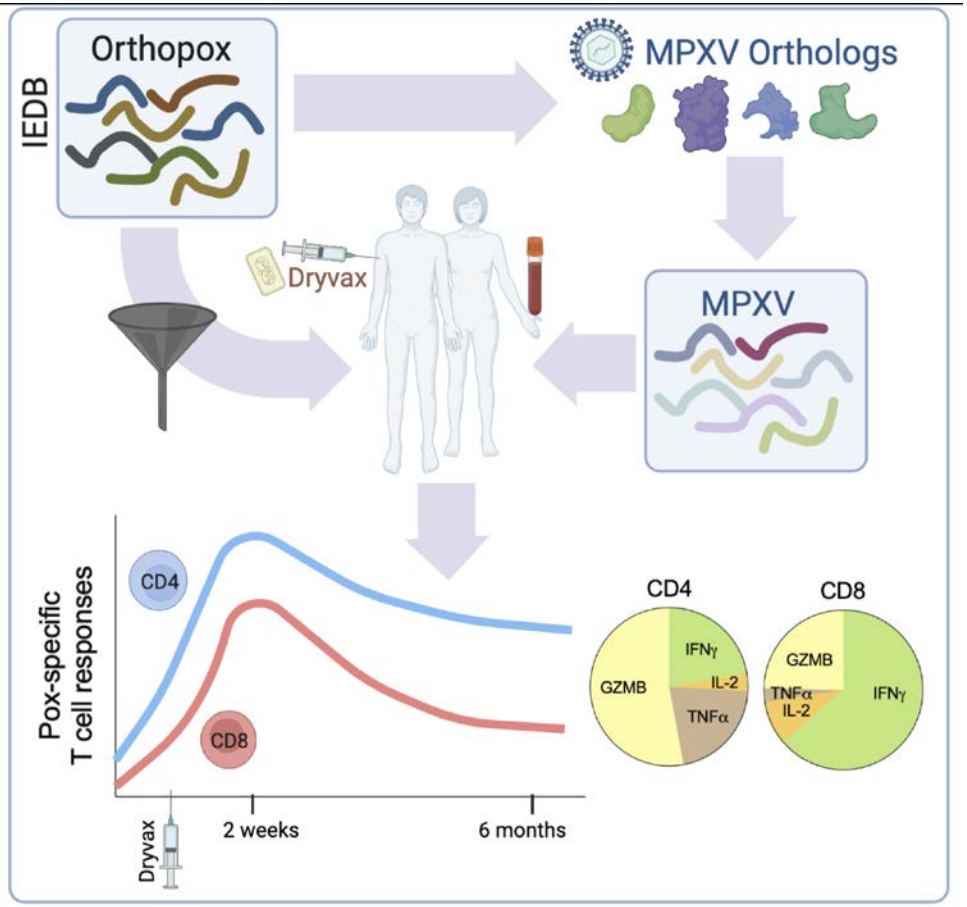
Conclusions



- We defined dominant cross-reactive ORFs to generate peptide MPs to measure T cell responses
- Wide breadth of both CD4+ and CD8+ T cell immune responses
- T cell epitopes are largely conserved between VACV and MPXV
- CD4 responses are more durable over time than CD8
- There is a large population of Pox-specific Granzyme B+ CD40L+ CD4 T cells

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Examples on SARS-CoV-2

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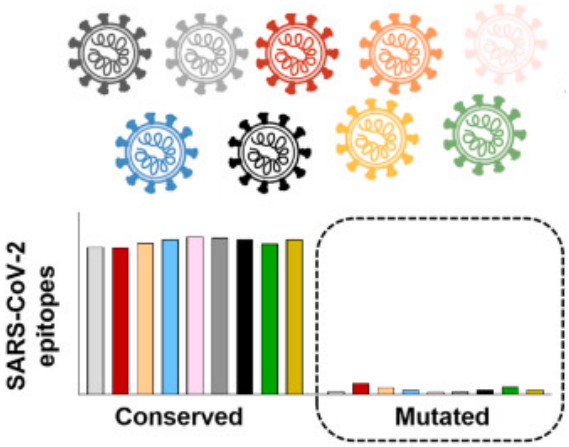
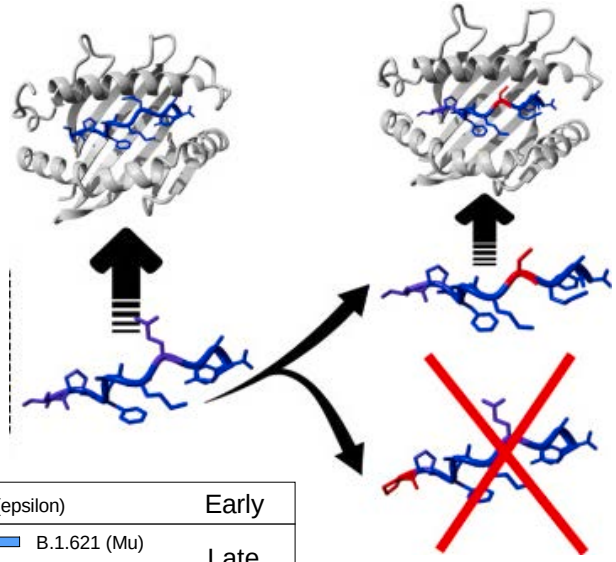
Predicted impact of mutated epitopes

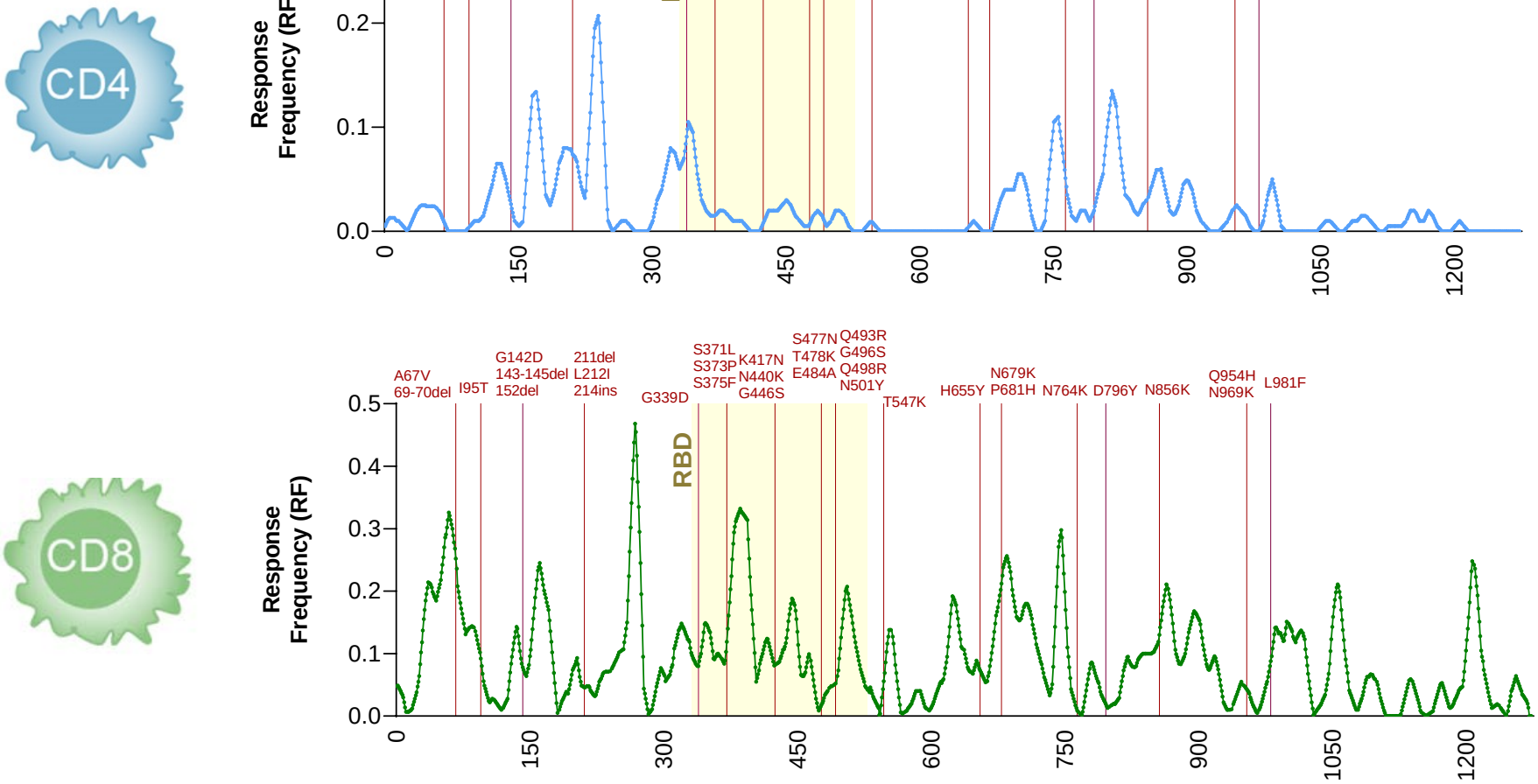




B.1.1.7 (alpha)	B.1.351 (beta)	P.1. (gamma)	B.1.427/429 (epsilon)		Early
B.1.1.519	B.1.525 (eta)	B.1.526 (iota)	B.1.526.1	B.1.621 (Mu)	Late
B.1.617.1 (kappa)	B.1.617.2 (delta)	C37 (lambda)	R1		
B.1.1529 (Omicron)					Ongoing

Tarke……. Grifoni and Sette Cell 2022
Grifoni and Sette CRI 2022

Impact of spike Omicron mutations on T cell epitopes



Tarke Grifoni and Sette Front. Bioinf. 2022

How to use ImmunomeBrowser to define spike T cell immunodominant regions

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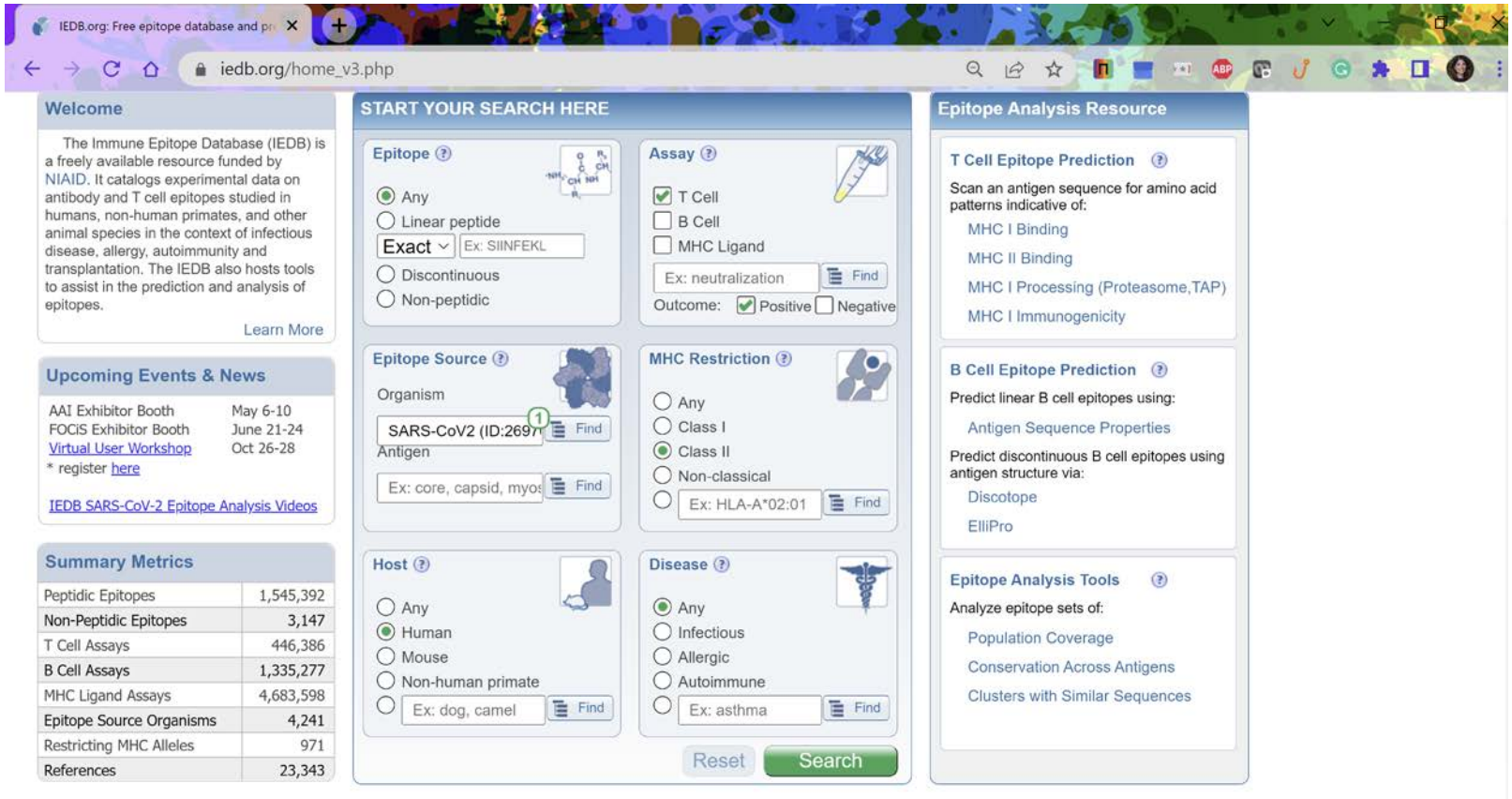
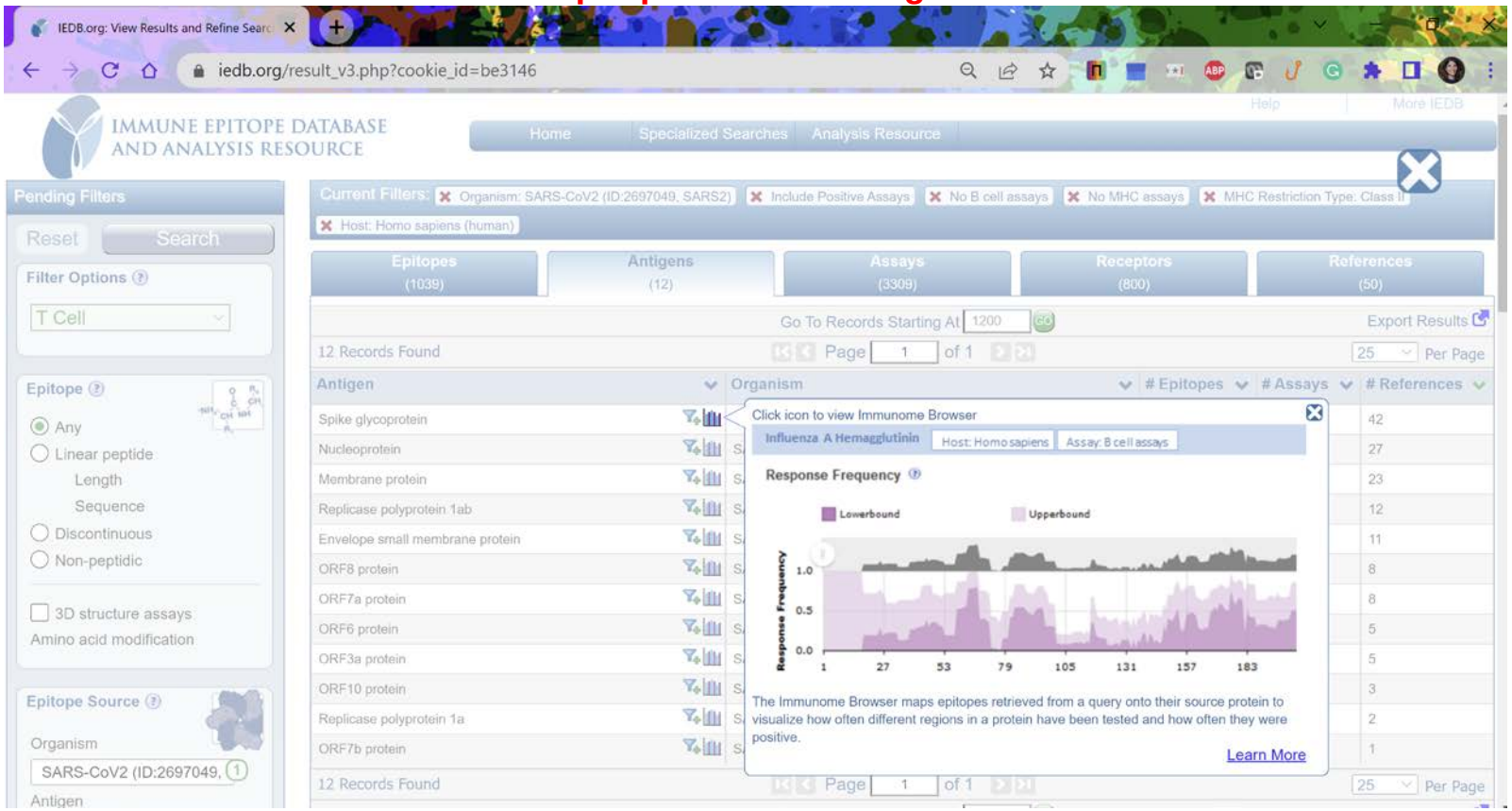
CD4 epitope query



How to use ImmunomeBrowser to define spike T cell immunodominant regions

IMMUNE EPITOPE DATABASE AND ANALYSIS RESOURCE

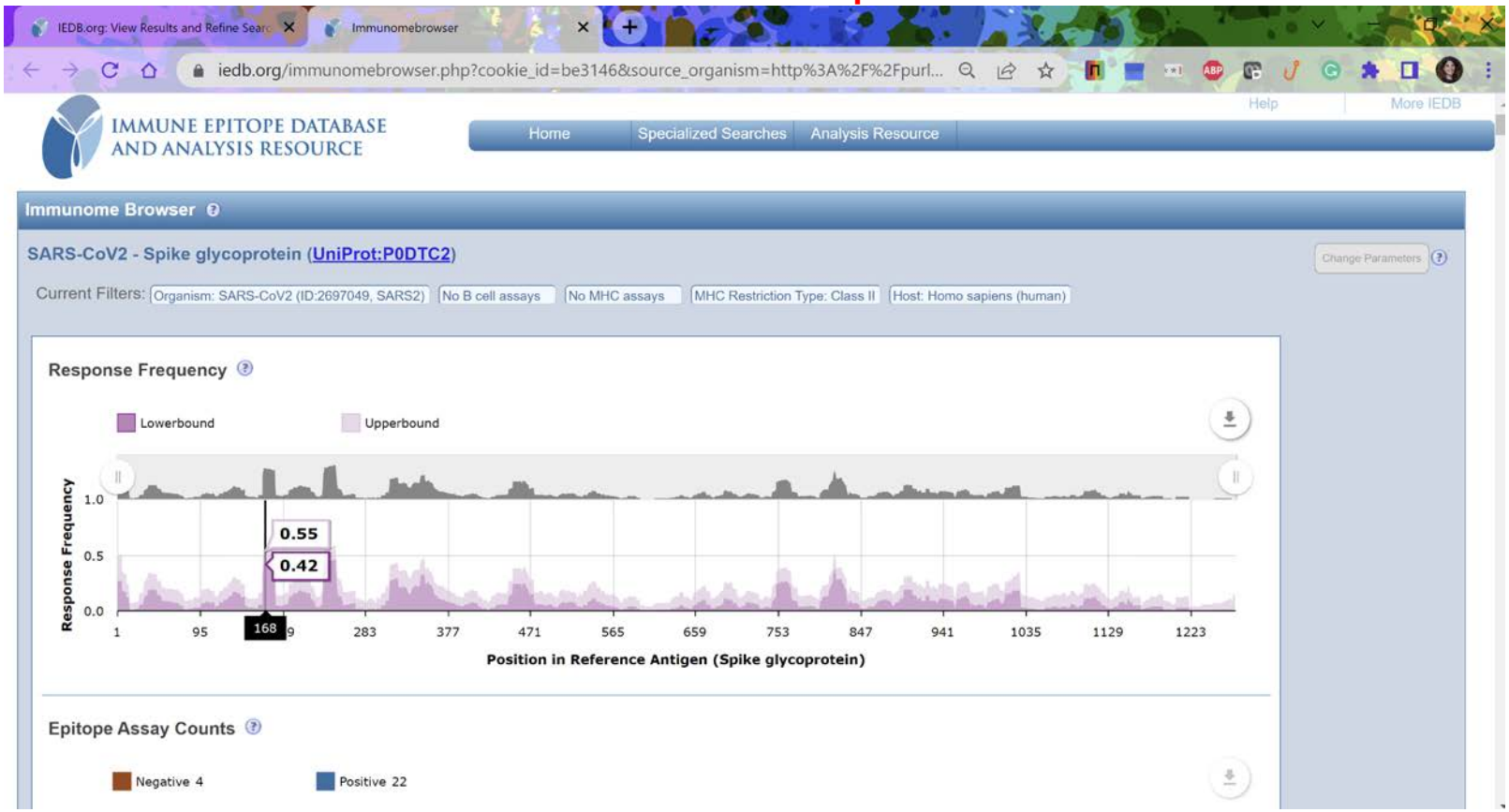
CD4 epitope results : Antigen



How to use ImmunomeBrowser to define spike T cell immunodominant regions

IMMUNE EPITOPE DATABASE AND ANALYSIS RESOURCE

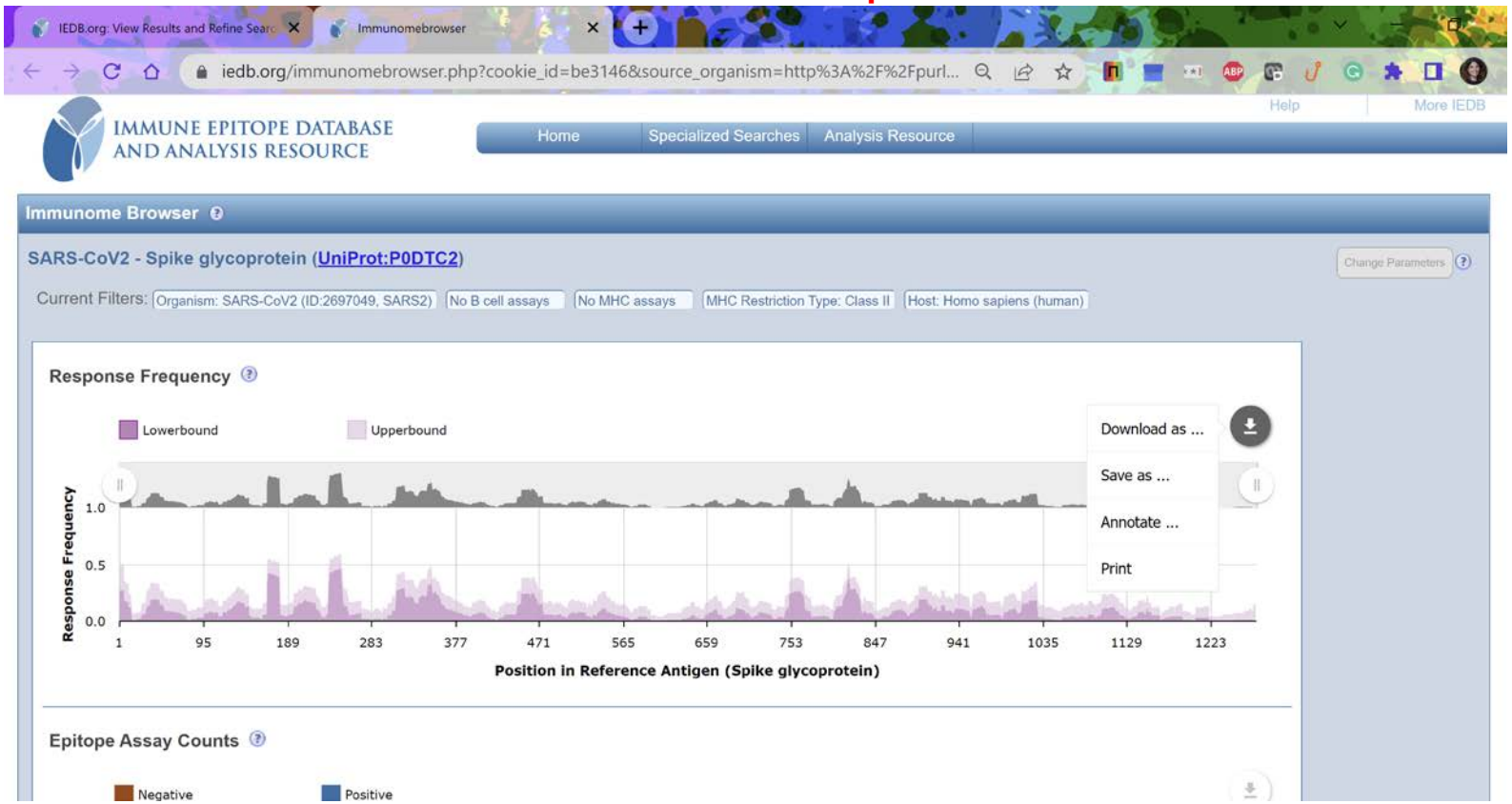
CD4 Immunobrowser: Spike



How to use ImmunomeBrowser to define spike T cell immunodominant regions

IMMUNE EPITOPE DATABASE AND ANALYSIS RESOURCE

CD4 Immunobrowser: Spike



How to use ImmunomeBrowser to define spike T cell immunodominant regions

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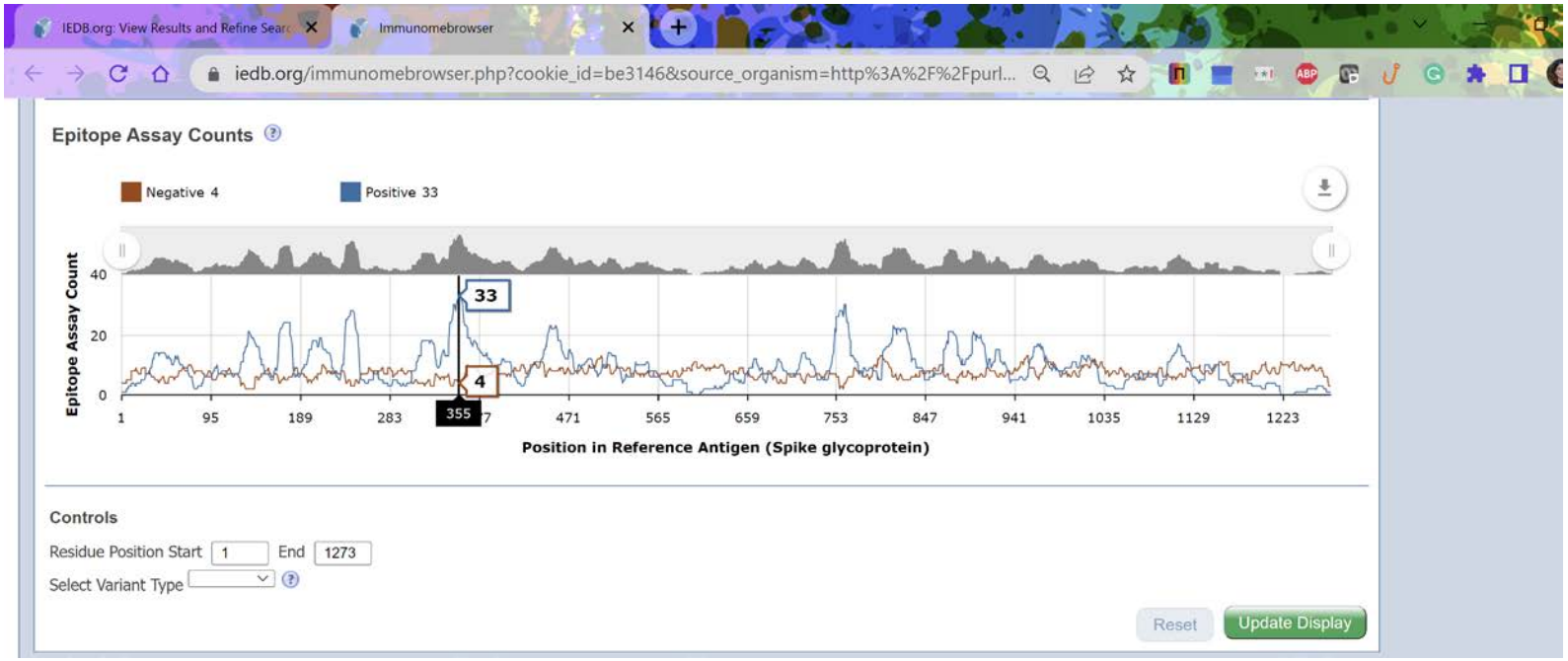
CD4 Immunobrowser: Spike



How to use ImmunomeBrowser to define spike T cell immunodominant regions

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CD4 Immunobrowser: Spike

How to use ImmunomeBrowser to define spike T cell immunodominant regions

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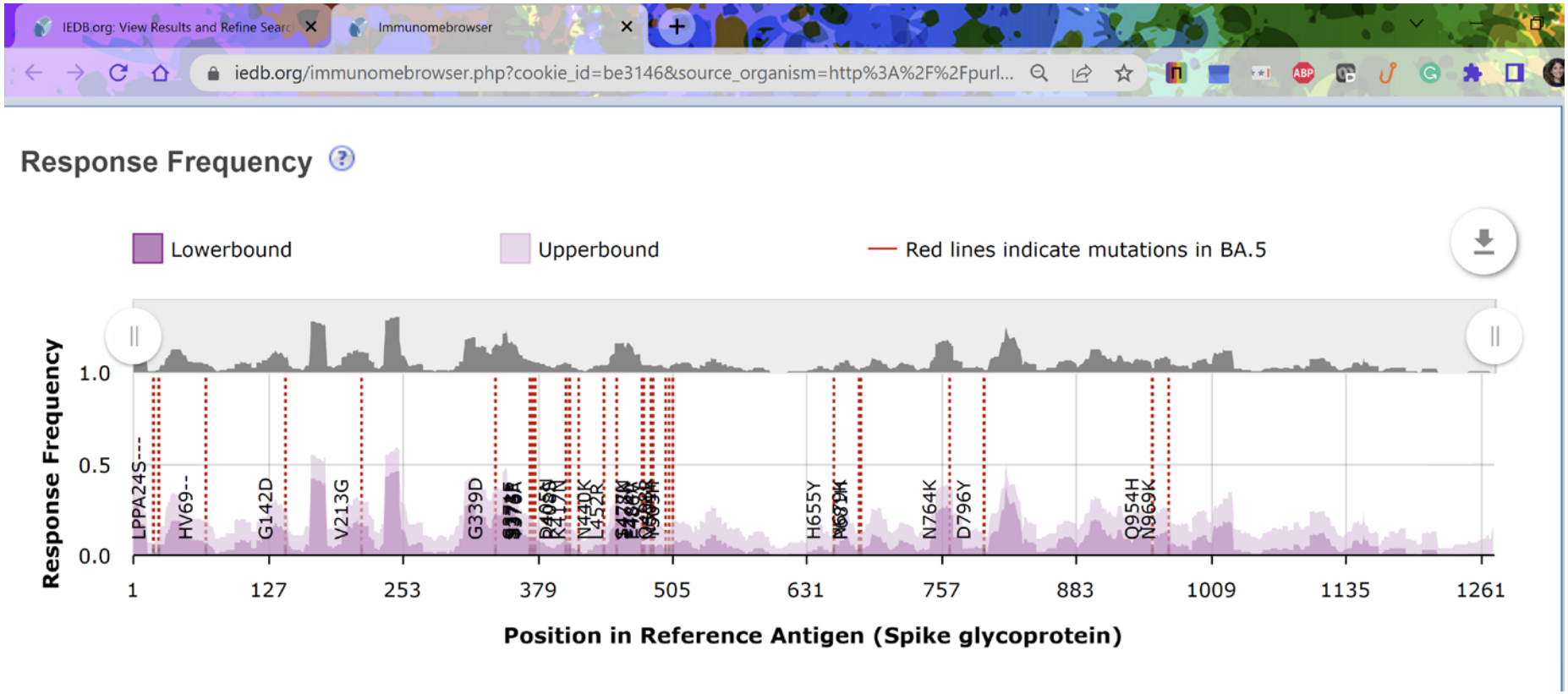
CD4 Immunobrowser: Spike



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