

Predicting T-cell receptor specificity based on sequence similarity to previously characterized receptors

Presented by Raphael Trevizani

- MHC presenting an antigen to a T-Cell
- T-cell receptor:  $\alpha/\beta$  units
- Somatic recombination
- Each chain: 3 CDRs
- CDR3β
  - $\circ$  Most variable
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- How to find the most similar sequences?



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<sup>2023</sup> IEDB User Workshop

CDR3<sub>β</sub>

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Cinelli, Mattia. (2018). Analysis of murine CDR3β repertoires using machine learning techniques.

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TCR sequencing does not directly

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reveal the epitope recognized by a given CDR3β

Repertoire sequencing ...CASSIRSSYEQYF... ...CASSLEGYTEAFF... ...CASSSANYGYTF... ...CASSIRAAETQYF... ...CASSIRSSTEAFF... ...CASSSRSSYEQYF...

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TCR sequencing does not directly reveal the epitope recognized by a Problem: how do we know the epitope?

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MHC presenting an	IMMUNE EPIT AND ANALYSI	OPE DATA S Resour	BASE Home	Specialized Searches Analysis Res	Help More IEDB
	The IEDB has just launched its updated 3D viewers! Learn more via our help article <u>here</u> .				
T-cell receptor: $\alpha/\beta$ units	Welcome		START YOUR SEARCH HERE		Epitope Analysis Resource
Somatic recombination	The Immune Epitope Databa a freely available resource fund It catalogs experimental data or and T cell epitopes studied in h	ase (IEDB) is led by NIAID. n antibody umans, non-	Epitope (?)	Assay ()	T Cell Epitope Prediction (3) Scan an antigen sequence for amino acid
Each chain: 3 CDRs	human primates, and other anir in the context of infectious disea	mal species ase, allergy,		B Cell	MHC I Binding
CDR3β	also hosts tools to assist in and analysis of epitopes.	TCR	sequences wit	h known epito	DPES ocessing (Proteasome, TAP)
$\circ$ Most variable				, ,	munogenicity
<ul> <li>Directly interacts</li> <li>with epitope</li> </ul>	Upcoming Events &	6.40	(150,684 TCF	sequences)	B cell epitopes using:
Repertoire sequencing	AAI EXhibitor Booth M FOCIS Exhibitor Booth Ju <u>Virtual User Workshop</u> Oo * register <u>here</u>	ay 6-10 ine 21-24 ct 26-28	Ex: influenza, peanut	Class I Class II Non-classical	Antigen Sequence Properties Predict discontinuous B cell epitopes using antigen structure via:
Which epitope interacts	IEDB SARS-CoV-2 Epitope An Videos	alysis		O Ex: HLA-A*02:01	ElliPro
with this specific TCR?	Summary Metrics		Host (?)	Disease (?)	Epitope Analysis Tools (?)
TCRmatch: searches IEDB for a similar CDR3β	Peptidic Epitopes Non-Peptidic Epitopes T Cell Assays B Cell Assays	1,539,170 3,146 443,509 1,332,364	Any     Human     Mouse     Non-human primate     Ex: dog. camel     E Find	Any     Infectious     Allergic     Autoimmune     Ext asthma     Find	Analyze epitope sets of: Population Coverage Conservation Across Antigens Clusters with Similar Sequences
How to find the most similar sequences?	Epitope Source Organisms Restricting MHC Alleles References	4,631,827 4,234 970 23,297		Reset Search	

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TCR sequencing does not directly reveal the epitope recognized by a Solution: use the sequence of known TCRs to match the query,

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ASSIRSSYEQY

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Supported by a contract from the National Institute of Alergy and Infectious Diseases, a component of the National Institutes of Health in the Department of Health and Human Services

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CDR3β

Epitope



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Epitope

 $\mathsf{CSSIRSSYEQY} \longrightarrow \mathsf{not} \mathsf{found} \longrightarrow \mathsf{r}$ 

CDR3β

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Metric	Description	
Alignment Score	Alignment score divided by length of alignment	
Identity Alignment	Percent identity within length of alignment	
Identity Long	Percent identity within length of longer sequence	
Identity Short	Percent identity within length of shorter sequence	
Levenshtein distance	Minimum number of edits (substitutions, insertions, and deletions) necessary to transform one sequence into another	
TCRdist	Similarity-weighted mismatch distance between two sequences	
TCRMatch (MAIT Match)	Comprehensive comparison of all possible k-mers using BLOSUM62 observed frequency matrix	

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# ASSSANYGYT ASSIRAAETQY







ASSSANYGYT

ASSIRAAETQY





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ASSIRAAETQY





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# ASSSANYGYT ASSIRAAETQY





**AS**SIRAAETQY





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# ASSSANYGYT ASSIRAAETQY (...)

5-11 9 1 С 4 2 S -1 3 3 Т -1 5 2 4 P 7 1 5 0 0 6 6 G 0 -1 -2 -3 -3 7 N -1 0 n -3 -2 6 8 -1 D 1 -4 -2 5 9 Е 0 2 0 -4 -3 -2 0 0 2 5 10 Q 0 -1 -2 -2 11 н -2 -2 1 -1 0 0 8 0 -3 -2 -2 12 -1 -2 -1 0 R -1 0 1 0 -3 13 -1 -2 2 5 K -1 -1 0 1 -1 14 M 0 -1 0 2 5 -1 15 -2 -1 -1 -4 -1 -2 -1 -2 -2 -2 -1 -4 2 2 16 L -4 -1 -2 -2 0 0 2 -2 -2 1 17 V -2 -2 -2 -4 -2 0 0 -1 6 18 F -1 0 -2 -2 -2 -2 7 19 Y 2 20 W W 14 15 16 17 18 19 20 10 11 12 13 2 з 8 9



# ASSIRAAETQY (...)

k = 1
ASSSANYGYT
ASSIRAAETQY
(...)



5-11 1 С 4 2 S 3 3 Т 2 P 4 7 1 5 Α 0 6 6 G 0 -1 -2 -3 7 -3 6 N -1 0 n -3 -2 6 8 -1 D 1 -4 -2 5 9 Е 0 2 0 -4 -3 -2 0 0 5 10 Q 0 2 -1 -2 -2 11 н -2 -2 1 -1 0 0 8 0 -3 -2 -2 12 -1 -2 -1 0 R -1 0 1 0 -3 13 -1 -2 2 5 K -1 -1 0 1 -1 14 M 0 -1 0 2 5 -1 15 -2 -1 -1 -4 -1 -2 -1 -4 -2 -2 -2 -1 -4 2 2 16 L -1 -2 -2 0 0 -2 -2 -2 1 17 V -2 -2 -2 -4 -2 -1 0 0 -1 6 18 F 0 -2 -2 -2 -2 7 19 Y 2 -1 2 20 W W 14 15 16 17 18 19 20 10 11 12 13 2 3 8 9



# ASSSANYGYT ASSIRAAETQY (...)





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ASSIRAAETQY

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# ASSSANYGYT ASSIRAAETQY











# ASSSANYGYT ASSIRAAETQY



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5 6 7 8 9

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4

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# ASSSANYGYT ASSIRAAETQY



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# ASSSANYGYT ASSIRAAETQY (...)





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## ASSSANYGYT ASSIRAAETQY



## ASSSANYGYT ASSIRAAETQY











TCRMatch output

- Original CDR3β query
- Matching CDR3β IEDB
- Matching epitope
- Receptor group
- TCRMatch score
- Antigen
- Organism

• TRUST4

input_sequence	match_sequence	score	receptor_group	epitope	antigen	organism
AISEVGVGQPQH	ASSQDRDTQY	0.7716	4	17 VMAPRTLIL	glycoprotein	Human herpesvirus 5 (Human cytomegalovi
AISEVGVGQPQH	ASGDAGGGYEQY	0.7891	860	06 ASQKRPSQRSK	Myelin basic protein	Mus musculus (mouse)
AISEVGVGQPQH	ASGDAGGGYEQY	0.7891	1822	26 ASQKRPSQR	Myelin basic protein	Mus musculus (mouse)
AISEVGVGQPQH	ASTYHGTGY	0.7686	5	7 GELIGILNAAKVPAD,GELIGTLNA	triosephosphate isomerase 1	Homo sapiens (human)
AISEVGVGQPQH	ASSYLGNTGELF	0.7986	9	94 SLLMWITQC	Cancer/testis antigen 1	Homo sapiens (human)
AISEVGVGQPQH	ASGDASGAETLY	0.8028	124	13 ASQKRPSQR,ASQKRPSQR,ASC	Myelin basic protein,myelin bas	Mus musculus (mouse),Mus musculus (mou
AISEVGVGQPQH	ASGDASGGNTLY	0.7859	10	3 RGGASQYRPSQ		
AISEVGVGQPQH	ASGDFWGDTLY	0.7353	3469	95 GSLFLKTPKIVSSKD	L-lactate dehydrogenase A cha	Mus musculus (mouse)
AISEVGVGQPQH	ASGDFWGDTLY	0.7353	1854	18 WIYVYRPM		
AISEVGVGQPQH	ASRYRDDSYNEQF	0.7206	2996	59 FLRGRAYGL	nuclear antigen EBNA-3	Human herpesvirus 4 (Epstein Barr virus)
AISEVGVGQPQH	ASRYRDDSYNEQF	0.7206	10	9 EENLLDFVRF	Epstein-Barr nuclear antigen 6	Human herpesvirus 4 (Epstein Barr virus)
AISEVGVGQPQH	ASRYRDDSYNEQF	0.7206	2775	56 EENLLDFVRF	Epstein-Barr nuclear antigen 6	Human herpesvirus 4 (Epstein Barr virus)
AISEVGVGQPQH	ASRPGLAGGRPEQY	0.7822	5653	37 LLFGYPVYV	Protein Tax-1	Human T-cell leukemia virus type I (Human
AISEVGVGQPQH	ASRPGLMSAQPEQY	0.7903	2107	75 LLFGYPVYV	Protein Tax-1	Human T-cell leukemia virus type I (Human
AISEVGVGQPQH	ASGGGGTLY	0.754	2747	74 SIYRYYGL		
AISEVGVGQPQH	ASGGGGTLY	0.754	2118	38 AMKRHGLDNYREYSLGN		
AISEVGVGQPQH	ASPGLAGEYEQY	0.8053	11	16 LPEPLPQGQLTAY, LPEALPQGQ	BZLF1,Trans-activator protein	Human herpesvirus 4 (Epstein Barr virus),H
AISEVGVGQPQH	ASSYVGNTGELF	0.8131	18193	35 SLLMWITQV		
AISEVGVGQPQH	ASSYVGNTGELF	0.8131	17953	39 SLLMWITQC	Cancer/testis antigen 1	Homo sapiens (human)
AISEVGVGQPQH	ASSDWVSYEQY	0.774	192	ALWGFFPVL,FAPGFFPYL	chromosome 15 open reading f	Homo sapiens (human)
AISEVGVGQPQH	SARDLTSGANNEQF	0.7812	2684	7 ENPVVHFFKNIVTP,SLGNIHFFK	Myelin basic protein,polysacch	Homo sapiens (human),Sulfurovum sp. NB
AISEVGVGQPQH	SARDLTSGANNEQF	0.7812	18194	ENPVVHFFKNIVTPR,VHFFKNIV	Myelin basic protein,MBP,Myel	Homo sapiens (human),Homo sapiens (hur
AISEVGVGQPQH	AWSETGLGTGELF	0.8111	22	27 EAAGIGILTV,ELAGIGILTV,AAGIG	Melanoma antigen recognized 🖡	Homo sapiens (human),Homo sapiens (hur
AISEVGVGQPQH	ASSWDRAGNTLY	0.7675	2113	0 AHHPIWARMDA, AMKRHGLDNY	Chain A, Hen Egg White Lysoz	Gallus gallus (chicken)
AISEVGVGQPQH	ASSWDRAGNTLY	0.7675	23	37 AMKRHGLDNYRGYSLGN,GAMK	Chain A, Hen Egg White Lysoz	Gallus gallus (chicken)
AISEVGVGQPQH	ASSARSGELF	0.8034	2561	17 HPVGEADYFEY	EBNA-1	Human herpesvirus 4 (Epstein Barr virus)
AISEVGVGQPQH	ASSARSGELF	0.8034	25	1 HPVGEADYFEY, HPVAEADYFE	BBNA-1,EBNA-1,Epstein-Barr	Human herpesvirus 4 (Epstein Barr virus),H
AISEVGVGQPQH	SARDGTGNGYT	0.7825	17664	18 GLCTLVAML	Transcriptional regulator IE63 h	Human herpesvirus 4 (Epstein Barr virus)
AISEVGVGQPQH	SARDGTGNGYT	0.7825	19044	14 GLCTLVAML	Transcriptional regulator IE63 h	Human herpesvirus 4 (Epstein Barr virus)
AISEVGVGQPQH	SARGGSYNSPLH	0.782	195	53 FSWGAEGQRPGFG	MBP protein	Homo sapiens (human)
AISEVGVGQPQH	ATSALGDTQY	0.8338	191	19 ENPVVHFFKNIVTPR	Myelin basic protein	Homo sapiens (human)
AISEVGVGQPQH	ASSLNNANSDYT	0.7588	125	51 ADLIAYLKQATK	Cytochrome c	Manduca sexta (Carolina sphinx)
AISEVGVGQPQH	ASSLNWSQDTQY	0.7699	193	2 ANERADLIAYLKQATK	Cytochrome c	Manduca sexta (Carolina sphinx)
AISEVGVGQPQH	ASGQGNFDIQY	0.789	32	23 FLRGRAYGL	nuclear antigen EBNA-3	Human herpesvirus 4 (Epstein Barr virus)
AISEVGVGQPQH	ASSYVSQNNEQF	0.7935	32	24 CLGGLLTMV,ALGGLLTMV.CLAG	Latent membrane protein 2	Human herpesvirus 4 (Epstein Barr virus)

TCRMatch output

- Original CDR3β query
- Matching CDR3β IEDB
- Matching epitope
- Receptor group
- TCRMatch score
- Antigen
- Organism
- TRUST4

#### nature methods

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#### Brief Communication Published: 13 May 2021

TRUST4: immune repertoire reconstruction from bulk and single-cell RNA-seq data

"...for reconstructing the clonal architecture of TCR repertoires from high-throughput sequencing data"

We introduce the TRUST4 open-source algorithm for reconstruction of immune receptor repertoires in  $\alpha\beta/\gamma\delta$  T cells and B cells from RNA-sequencing (RNA-seq) data. Compared with competing methods, TRUST4 supports both FASTQ and BAM format and is faster and more sensitive in assembling longer–even full-length– receptor repertoires. TRUST4 can also call repertoire sequences from single-cell RNA-seq (scRNA-seq) data without V(D)J enrichment, and is compatible with both SMART-seq and 5' 10x Genomics platforms.

./run-trust4 -f human\_IMGT+C.fa --ref human\_IMGT+C.fa -1 example/example\_1.fq -2 example/example\_2.fq -o TRU

#### TCRMatch output

- Original CDR3β query
- Matching CDR3β IEDB
- Matching epitope
- Receptor group
- TCRMatch score
- Antigen
- Organism
- TRUST4

epoch ~/prog/TRUST4 master ?27 → ./run-trust4 -f hg38\_bcrtcr.fa --ref human\_IMGT+C.fa -1 example/example\_1.fq -2 example/example\_2.fq -o TRUST\_example |

→ ls TRUST\_example\_\*
TRUST\_example\_airr\_align.tsv
TRUST\_example\_airr.tsv
TRUST\_example\_annot.fa
TRUST\_example\_assembled\_reads.fa
TRUST\_example\_cdr3.out
TRUST\_example\_final.out
TRUST\_example\_raw.out
TRUST\_example\_report.tsv
TRUST\_example\_toassemble\_1.fq
TRUST\_example\_toassemble\_2.fq

TCRMatch output

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	<pre>#count frequency</pre>	CDR3nt	CDR3aa
	8 0.0833333	TGTGCGAGAGGGCAGGACGGTGACTACGTGGGCGAGCCCGGGGAGTCTACTACTACTACATGGACGTCTGG	out_of_frame
	6 0.0625	TGTGCGAGGGGGGCGAACGATAATATTGTAGTAGTACCAGCTGCTATCTTCCATTTGCTTTTGATATCTGG	out_of_frame
	5 0.0520833	TGTGCGAGAGATGGTACCCCGGATGTAGTAGTACCAGCTGCTATGTTTCTTAAACCGGTTGTCTGACTACTGG	out_of_frame
	4 0.0416667	GGGGTATTACGATTTTTGGAGTGGTTATAAAAGCGGGGGTACTACTACTACGGTATGGACGTCTGG	GVLRFLEWL_KRGYYYYGMDVW
	3 0.03125	TGTGCAAGAGATGTAGGAGGGGTATTTCCATTGTAGTGGTGGTAGCTGCTATGCTGGTTCGACCCCTGG	CARDVGGVFPL_WW_LLCWFDPW
	3 0.03125	TGTGCGAGACCCTATAGCAGCAGCTGGTACGAAAGTTTACTACTACTACTACGGTATGGACGTCTGG	out_of_frame
	3 0.03125	TGTGCGAAGGAGGTTGGGTGGTGGTGGTGGCAGGGAAACTACTACTGCGGTGGACGTCTGG	out_of_frame
	3 0.03125	TGTGCGAGAGACCCTCCCCGGAGCAGTGGCTGGGCGTCCCCTCTTCGTTTTTGACTACTGG	out_of_frame
	3 0.03125	TGTGCGAGAAAACCGACCCGGAAACGGATATTGTAGTGGTGGTAGCTGCTACTCGCGGTACCCCTCTACACTTGGTTCGACCCCTGG	out_of_frame
	3 0.03125	TGTGCGAAAGATCTAGGAAAGGTAGTCGCCGTATAGCAGCTCGTCCGGAGGGGATTTCTTCCTACTACTACTACTACGGTATGGACGTCTGG	out_of_frame
•	3 0.03125	TGTGCGAGCGCAGCACGGGATATTGTAGTGGTGGTAGCTGCTACGGTTCATTTATGACTACTGG	out_of_frame
8 - querv	3 0.03125	TGTGCGAGAAATGGGAGTTCGGATTTTGATCCAATCTCCTCGGGGGATTGTAGTAGTACCAGCTGCCTACTACTACTACATGGACGTCTGG	out_of_frame
	3 0.03125	TGTGCGAGACAAGTGGGAGCGACCCTCATGATGCTTTTGATATCTGG	out_of_frame
	2 0.0208333	TGTGCGAGAGATAGGGAGTTGTAGTAGTACCAGCTGCTGCTGCCACGGGACTACTACTACTACTACATGGACGTCTGG	CARDRELYQLLSRDYYYYYMDVW
	2 0.0208333	TGTTATTGTAGTAGTACCAGCTGCTATTACTACTACGGTATGGACGTCTGG	CYCSSTSCYYYYYGMDVW
38 - IEDB	2 0.0208333	TGTGCGAGAGGCGATACCCGGTATTACGATTTTTGGAGTGGTTATTATCCGCAAAGAGGACCAGGGCAGTCCTACTACTACTACGGTATGGACGTCTGG	CARGDTRYYDFWSGYYPQRGPGQSYYYYGMDVW
-р . <u></u> _	2 0.0208333	TGTGGGGTTCGGGGAGTTAACATCGATAAGAAGTAATACTACTACTACTACGGTATGGACGTCTGG	CGVRGVNIDKK_YYYYGMDVW
	2 0.0208333	TGTGCAAGAGACCTAAGACATACCAGCTGCTATACTTTGACTACTGG	out_of_frame
	2 0.0208333	TGTGCGAGAGAGGGATAGCAGTGGCTTGGGTACTACTACTACTACATGGACGTCTGG	CAREG_QWLGYYYYMDVW
pe	2 0.0208333	TGTGCGAGAGATATTGTTGTAGTGGTGGTAGCTGCTACTCCCAGGGCCCAAATTTACTGG	CARDIVVVVAATPRAQIYW
1	2 0.0208333	TGTGCGAAAGACGTTGCAAGCACCAGGGCACTGCCGAAACCCCCAGTTGTAGTAGTAGTACCAGCTGCTATCCCCTTTGACTACTGG	CAKDVASTRALPKPPVVVVPAAIPFDYW
	2 0.0208333	TGTGCGAGAGTGCAAGTGACCTAATAGCAGTGGCTGGTACGATTCCATACTTTGACTACTGG	out_of_frame
	2 0.0208333	TGTAGTGGTGGTAGCTGCTATAGTAAGTACTACTTTGACGACTGG	CSGGSCYSKYYFDDW
)	2 0.0208333	TGTGCGGCTTTACTATGGTTCAGCCCGGGGTGCTTTTGATATCTGG	out_of_frame
	2 0.0208333	TGTGCGAGCAACGCTGGATTGTACTGGTGGTGTATGCTAAACAATGGATTTAGATCGAGGGGAAGAAGTTACTACTACTACTACATGGACGTCTGG	CASNAGLYWWCMLNNGFRSRGRSYYYYYMDVW
	2 0.0208333	TGTGCACGGCACCCGGGTCTGTGCCTAGTATTACTATGGTTCAGGGATACTACTACATGGACGTCTGG	out_of_frame
	2 0.0208333	TGTGTGTCCCTCAGAATTACTATGGTTCAGATTCGAACTCGAAGAACTACTACTACTACTACATGGACGTCTGG	out_of_frame
re	2 0.0208333	TGTGCGATGGGTGGGTCGGTCCTCGGGCAGTACAACTGGTTCGACCCCTGG	out_of_frame
	2 0.0208333	TGTGCGAGGGTACCCCGCGATGATAGTAGTGGTTAAACAACCCTTTGACTACTGG	out_of_frame
	1 0.0104167	TGTGCGAGAGACCTCGGCCGTAGGTATAGCAGTGGCTGGTTCTGTTTCGACCCCTGG	CARDLGRRYSSGWFCFDPW
	1 0.0104167	TGTGCGAGAGCTGTAACTTATATTGTAGTAGTACCAGCTGCGGGCTGACAGTTTACTACTACTACTACGGTATGGACGTCTGG	out of frame

TCRMatch output

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	#count frequency CDR3aa	V	D J	С	cid o	cid_full_	length	
	80.0833333 out_of_frame	IGHV1-3*01	IGHD1-26*0 IGHJ6*	0≄.	assemble1		0	
	6 0.0625out_of_frame	IGHV4-61*01	IGHD2-2*01 IGHJ3*	0≯.	assemble2		Θ	
	50.0520833out_of_frame	IGHV4-61*01	IGHD2-2*01 IGHJ4*	9≯IGHM	assemble2⊧		Θ	
	40.0416667GVLRFLEWL_KRGYYYYGMDVW	IGHV3-48*04	IGHD3-3*01 IGHJ6*	0≯IGHM	assemble1⊧		0	
	3 0.03125 CARDVGGVFPL_WW_LLCWFDPW	IGHV3-74*01	IGHD2-15*0 IGHJ5*	0≯IGHM	assemble2⊧		0	
	3 0.03125out_of_frame	IGHV1-3*01	IGHD6-13*0 IGHJ6*	0≯IGHM	assemble3⊧		0	
	3 0.03125out_of_frame	IGHV3-NL1*0⊧	IGHD2-21*0 IGHJ6*	0≯.	assemble3		0	
	3 0.03125out_of_frame	IGHV3-11*01	IGHD6-19*0 IGHJ4*	0≯IGHM	assemble5		0	
	3 0.03125 out_of_frame	IGHV3-69-1*⊧	IGHD2-15*0 IGHJ5*	0≯.	assemble1⊧		Θ	
8 - auerv	3 0.03125out_of_frame	IGHV3-NL1*0⊧	IGHD6-6*01 IGHJ6*	0≯.	assemble3⊧		Θ	
	3 0.03125 out_of_frame	IGHV3-11*04	IGHD2-15*0 IGHJ4*	0≯IGHM	assemble2⊧		Θ	
	3 0.03125out_of_frame	IGHV1-18*01	IGHD2-15*0 IGHJ6*	0¢IGHM	assemble1⊧		Θ	
36 - IFDB	3 0.03125out_of_frame	IGHV5-51*01	IGHD1-26*0 IGHJ3*	0≯IGHM	assemble1⊧		0	
5p 1200	20.0208333 CARDRELYQLLSRDYYYYYMDVW	IGHV3-11*04	IGHD2-2*01 IGHJ6*	0¢IGHM	assemble3⊧		0	
	20.0208333 CYCSSTSCYYYYYGMDVW	IGHV3-13*01	IGHD2-2*01 IGHJ6*	0≯.	assemble1⊧		0	
ne	20.0208333 CARGDTRYYDFWSGYYPQRGPGQSYYYYGMDVW	IGHV3-11*04	IGHD3-3*01 IGHJ6*	9≯IGHM	assemble4⊧		Θ	
pe	20.0208333CGVRGVNIDKK_YYYYYGMDVW	IGHV3-49*02	IGHD3-10*0 IGHJ6*	9≯IGHM	assemble6⊧		0	
	20.0208333out_of_frame	IGHV3-47*01	IGHD2-2*02 IGHJ4*	0≯IGHM	assemble1⊧		0	
<b>`</b>	20.0208333 CAREG_QWLGYYYYMDVW	IGHV5-51*01	IGHD6-19*0 IGHJ6*	0≯.	assemble4⊧		0	
,	20.0208333 CARDIVVVVAATPRAQIYW	IGHV3-66*01	IGHD2-15*0 IGHJ4*	9≯IGHM	assemble3⊧		Θ	
	20.0208333 CAKDVASTRALPKPPVVVVPAAIPFDYW	IGHV3-23*01	IGHD2-2*01 IGHJ4*	0≯IGHM	assemble3⊧		0	
~	20.0208333out_of_frame	IGHV1-46*01	IGHD6-19*0 IGHJ4*	9≯IGHM	assemble6⊧		0	
C	20.0208333CSGGSCYSKYYFDDW	IGHV3-23*01	IGHD2-15*0 IGHJ4*	9≯IGHM	assemble4⊧		Θ	
	20.0208333 out_of_frame	IGHV3-41*02	IGHD3-10*0 IGHJ3*	0≯IGHM	assemble3⊧		Θ	
	20.0208333 CASNAGLYWWCMLNNGFRSRGRSYYYYYMDVW	IGHV1-69*01	IGHD2-8*02 IGHJ6*	0¢IGHM	assemble9		0	
	20.0208333 out_of_frame	IGHV2-70*01	IGHD3-10*0 IGHJ6*	0¢IGHM	assemble4⊧		Θ	
	20.0208333out_of_frame	IGHV1-NL1*0⊧	IGHD3-10*0 IGHJ6*	0¢IGHM	assemble2⊧		0	
	20.0208333out_of_frame	IGHV1-3*01	IGHD1-1*01 IGHJ5*	0≯.	assemble3⊧		0	
	20.0208333out_of_frame	IGHV4-38-2*⊧	IGHD3-22*0 IGHJ4*	0≯IGHM	assemble2⊧		Θ	
	10.0104167 CARDLGRRYSSGWFCFDPW	IGHV3-71*01	IGHD6-19*0 IGHJ5*	0≯.	assemble1⊧		0	
	10.0104167out_of_frame	IGHV1-3*01	IGHD2-2*01 IGHJ6*	0≯IGHM	assemble5⊧		Θ	
	10.0104167out_of_frame	IGHV1-46*01	IGHD6-19*0 IGHJ4*	0≯.	assemble7⊧		0	
	10.0104167out_of_frame	IGHV3-52*01	IGHD4-23*0 IGHJ6*	0¢IGHM	assemble6⊧		0	
	10.0104167out_of_frame	IGHV4-61*01	IGHD3-22*0 IGHJ5*	0≯.	assemble7⊧		Θ	
	10.0104167 CARDGSGVLRFLEWFFRPYYYYMDVW	IGHV3-11*04	IGHD3-3*01 IGHJ6*	0¢IGHM	assemble6⊧		Θ	
	10.0104167out_of_frame	IGHV3-NL1*0⊧	IGHD5-12*0 IGHJ4*	0≯.	assemble5⊧		0	
	10.0104167CARDEITIF_LVII_PSWF_VP_NPPNLRNYW	IGHV1-3*01	IGHD3-9*01 IGHJ4*	0≯.	assemble5⊧		Θ	

#### Acknowledgments

**Bioern Peters** Alessandro Sette Nina Blazeska Jason Greenbaum Austin Crinklaw Swapnil Mahajan Randi Vita Zeynep Kosaloglu-Yalcin Will Chronister Zhen Yan Leon Jessen (DTU) Morten Nielsen (DTU) Scott Christley (UTSW) Lindsay Cowell (UTSW)



Chronister 2021, Front. Immunol. DOI: 10.3389/fimmu.2021.640725

## ...there's one more thing we'd like to show you...



# **BCRMatch**

A webserver to predict antibodies binding to a common epitope

Presented by Mahita Jarjapu

# **BCRMatch**



## A webserver to predict antibodies binding to a common epitope

IMMUN AND AN	E EPITOPE DATABASE Alysis resource	
Ripeline Map 🗗	1	
	BCRMatch	(a) (b) (c). (F) Docs API Download Cite
	Input Sequence(s)	
	Ex: Soq_Name CDRL1 CDRL 1 NNIGSKS DDS WDS 2 SQDISNY YTS DFT 3 ASCNIHN YYT HFY 4 SESVDNYGISF AAS 5 ASQDISN YFT QYS	2 CDRL3 CDRH1 CDRH2 CDRH3 SSDHA GFTFDDY SWNTGT RSYVVAAEYYFH LPF GYTFTHY YPGNGD GGSYRYDGGFD YSTPR GFSLTGY WGDGN RDYRLD SKEVPL GYTFTSS HPNSGN RYGSPYYFD TVPW GYDFTHY NTYTGE PYYYGTSHWYFD
	Prediction Parameters	•
	Prediction Model(s)	O RF GNB ANN
	Training Data	e iedb Abligity
		Reset
Terrane		Results will load once step is run
dia		

**i.** User provides sequences of CDR loops of antibodies with and without known epitope (referred to as antibody of interest)

ii. User has the option to select machine learning models (five ML models are provided) and training dataset for making predictions.

# **BCRMatch**



### A webserver to predict antibodies binding to a common epitope

line Map 📴	Training Data	O IEDB Abligity	
			Reset
	Peptide fable		
			(4) Save Table State
	Show 50 V rows	1 to 50 of 1,265 rows	Previous 1 2 3 4 5 26 Next
	Show 50 V rows	1 to 50 of 1,265 rows RF prediction	Previous 1 2 3 4 5 26 Next
	Show 50 V rows antibody pair 1,1	1 to 50 of 1,265 rows # prediction 1	Previous 1 2 3 4 5 26 Next
	Show 50 V rows antibody pair 3.1 3.2	1 to 50 of 1,265 rows	Previous 1 2 3 4 5 26 Next
	Show 50 v rows setilody pair 3.1 3.2 1.3	1 to 50 of 1,265 rows	Previous         1         2         3         4         5          26         Next           all
	Show 50 v rows antibody pair 3,1 3,2 3,3 3,4	1 to 50 of 1,265 rows	Offer Previous         1         2         3         4         5          26         Next           08         Prediction         1 <td< td=""></td<>
	Show 50 v rows antiboly pair 3.1 3.2 3.3 3.4 3.5	1 to 50 of 1,265 rows	Previous         1         2         3         4         5          26         Next           0
	Show 50 v rows actiony pair 3.1 3.2 3.3 3.4 3.5 2.1 2.1	1 to 50 of 1,265 rows	Previous         1         2         3         4         5          26         Next           OB         Prediction         -
	Show 50 v rows antibody pair 3.1 3.2 3.3 3.4 3.5 3.4 3.5 3.4 3.5 3.2 3.2 3.3 3.4 3.5 3.2 3.2 3.3 3.4 3.5 3.2 3.2 3.3 3.4 3.5 3.5 3.5 3.5 3.5 3.5 3.5 3.5	1 to 50 of 1,265 rows	Previous         1         2         3         4         5          26         Next           0         -
	Show 50 v rows setiboly pair 3.1 3.2 3.4 3.4 3.5 2.1 2.2 2.2 2.3	1 to 50 of 1,265 rows	Previous         1         2         3         4         5          26         Next           28         Prediction         1
	Show 50 v rows setiody pair 3.1 3.2 1.3 3.4 3.5 2.1 2.3 2.3 2.3 2.4 3.5 3.4 3.5 3.5 3.1 3.5 3.5 3.1 3.5 3.5 3.1 3.5 3.5 3.5 3.5 3.5 3.5 3.5 3.5	1 to 50 of 1,265 rows	Previous         1         2         3         4         5          26         Next           am         -

iii. Webserver uses the selected pre-trained models to predict what antibodies share the same epitope with the antibody of interest

**iv.** Results of each prediction is listed in a table. We recommend using a consensus of the predictions of all five machine learning models to guide the final result.