COVIDep platform for real-time reporting of vaccine target recommendations for SARS-CoV-2: Description and connections with COVID-19 immune responses and preclinical vaccine trials

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Abstract

We introduce COVIDep (https://COVIDep.ust.hk), a web-based platform that provides immune target recommendations for guiding SARS-CoV-2 vaccine development. COVIDep implements a protocol that pools together publicly-available genetic data for SARS-CoV-2 and epitope data for SARS-CoV to identify B cell and T cell epitopes that present potential immune targets for SARS-CoV-2. Correspondences between outputs of COVIDep and immune responses recorded in COVID-19 patients and preclinical vaccine trials are also indicated. The platform is user-friendly, flexible, and based on up-to-date data. It may help guide vaccine designs and associated experimental studies for SARS-CoV-2.

Description

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has brought much of the world to a virtual lockdown. As the virus continues to spread rapidly and the pandemic intensifies, the need for an effective vaccine is becoming increasingly apparent. A critical part of vaccine design is to identify targets, or epitopes, that can induce an effective immune response against SARS-CoV-2. This problem is challenged by our limited understanding of this novel coronavirus and of its interplay with the human immune system.

In response to this challenge, we have developed COVIDep (https://COVIDep.ust.hk), a first-of-its-kind web-based platform that pools genetic data for SARS-CoV-2 and immunological data for the 2003 SARS virus, SARS-CoV, to identify B cell and T cell epitopes to serve as vaccine target recommendations for SARS-CoV-2 (Figure 1). For T cell epitopes, it provides estimates of population coverage, globally and for specific regions. The COVIDep platform is updated periodically as data is deposited into public databases. This is important since SARS-CoV-2 sequences are being made available at an increasing rate through international data sharing efforts, and the identification of vaccine targets is influenced by newly observed genetic variation. COVIDep is flexible and user-friendly, comprising an intuitive graphical interface and interactive visualizations.

The vaccine targets recommended by COVIDep exploit the genetic similarities between SARS-CoV-2 and SARS-CoV, along with known immune targets for SARS-CoV that have been determined experimentally. The system implements a protocol that identifies from among the SARS epitopes that can induce a human immune response, those that are genetically similar in SARS-CoV-2. This idea, put forward in our preliminary study[1] based on limited early data, identified known SARS-CoV epitopes that had an identical genetic match in SARS-CoV-2. These epitopes presented initial vaccine target recommendations for potentially eliciting a protective, cross-reactive immune response against SARS-CoV-2. Similar ideas and results were reported subsequently in an independent study[2].

The use of SARS-CoV immunological data to inform vaccine targets for SARS-CoV-2 is being supported by experimental results. There is evidence of SARS-CoV-derived antibodies binding to genetically similar regions of SARS-CoV-2's spike protein[3], and also of cross-neutralization[4–6]. Conversely, studies have demonstrated that specific SARS-CoV-derived antibodies binding to the spike's receptor binding domain, which has significant genetic differences in SARS-CoV-2, have limited cross-reactivity[7]. Antibody and T cell responses against spike protein epitopes that are genetically similar in SARS-CoV and SARS-CoV-2 have also been reported in COVID-19 infected patients[8–10], and in preclinical vaccine trials[11,12]. Epitopes recommended by COVIDep have notable overlap with the findings in these experimental studies (Figures 2 and 3).

The recommendations provided by COVIDep may be used to guide vaccine designs and associated experimental studies, and may help to expedite the discovery of an effective vaccine for COVID-19.

Data availability

The SARS-CoV-2 full genome sequence data is periodically downloaded from the Global Initiative on Sharing Avian Influenza Database (GISAID; www.gisaid.org). The SARS-CoV epitope sequence data was downloaded from the Virus Pathogen Database and Analysis Resource (ViPR; www.viprbrc.org). The population coverage statistics of HLA alleles were obtained from the Immune Epitope Database and Analysis Resource (IEDB; www.iedb.org).

Code availability

The source code for the developed platform is available at the COVIDep GitHub repository (https://github.com/COVIDep).

Acknowledgment

COVIDep is made possible by the open sharing of genome sequence data of SARS-CoV-2 sequences by research groups from around the world through the GISAID platform, and the open sharing of immunological data of experimentally-determined SARS-CoV epitopes through the ViPR database. We gratefully acknowledge the contributions of all the researchers, scientists and technical staff involved (a detailed acknowledgment is available at the Acknowledgments page of the COVIDep platform).

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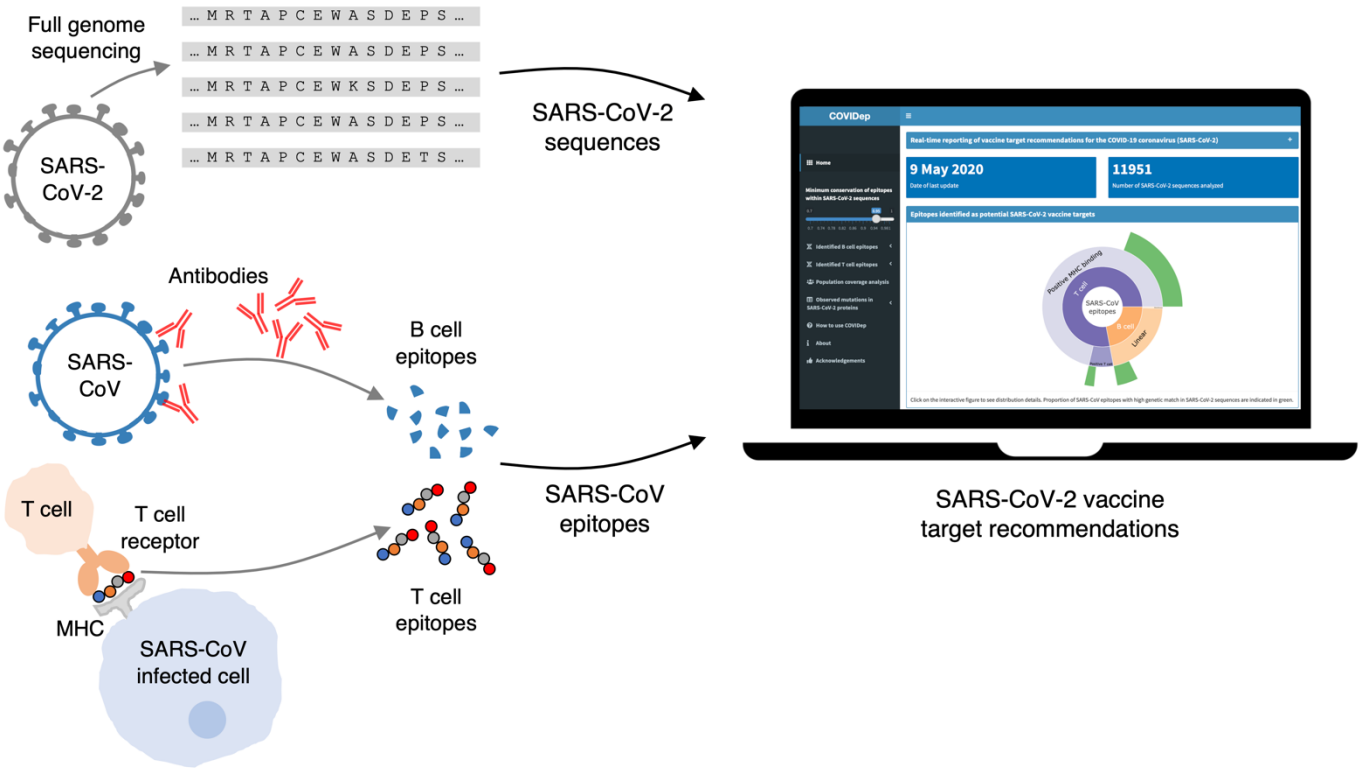

Figure 1. COVIDep provides sets of B cell and T cell epitopes that can serve as potential vaccine targets for SARS-CoV-2. The recommended epitopes are experimentally-derived from SARS-CoV and have a close genetic match with the available SARS-CoV-2 sequences (see Supplementary Figure 1 for a detailed protocol description).

Details of the identified B cell epitopes in the S protein

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Search:

IEDB	Epitope	Length	Start	End	Conservation
30987	KGIYQTSN	8	310	317	0.9646
70719	VRFPNITNLCPFGEVFN	17	327	343	0.9948
15972	FGEVFNAT	8	338	345	0.9976
52020	QQFGRD	6	563	568	0.9999
18594	GAGICASY	8	667	674	0.9993
22321	GSFCTQLN	8	757	764	0.9996
16183	FIEDLLFNKVTLADAGF	17	817	833	0.9952
18515	GAALQIPFAMQMAYRFN	17	891	907	0.9989
47479	PFAMQMAYRFNGIGVTQ	17	897	913	0.9993
3176	AMQMAYRF	8	899	906	0.9994
41177	MAYRFNGIGVTQNVLYE	17	902	918	0.9995
10778	DVVNQNAQALNTLVKQL	17	950	966	0.9988
50311	QALNTLVKQLSSNFGAI	17	957	973	0.999
2092	AISSVLNDILSRLDKVE	17	972	988	0.9994
27357	ILSRLDKVEAEVQIDRL	17	980	996	0.9997
11038	EAEVQIDRLITGRLQSL	17	988	1004	0.9997
54599	RLITGRLQSLQTYVTQQ	17	995	1011	0.9997
59425	SLQTYVTQQLIRAAEIR	17	1003	1019	0.9995
51379	QLIRAAEIRASANLAAT	17	1011	1027	0.9979
53202	RASANLAATKMSECVLG	17	1019	1035	0.998
462	AATKMSECVLGQSKRVD	17	1025	1041	0.9989
67220	TVYDPLQPELDSFKEEL	17	1136	1152	0.9696
32508	KNHTSPDVDLGDISGIN	17	1157	1173	0.9974
9094	DLGDISGINASVVNIQK	17	1165	1181	0.9981
12426	EIDRLNEVAKNLNESLIDLQELGKYEQY	28	1182	1209	0.9974
558417	EIDRLNEVAKNLNESLIDLQELGKYEQY	28	1182	1209	0.9974
14626	EVAKNLNESLIDLQELG	17	1188	1204	0.9979
6476	CKFDEDDSEPVLKGVKLHYT	20	1254	1273	0.9911
7868	DDSEPVLKGVKLHYT	15	1259	1273	0.9914

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Figure 2. B cell linear epitopes in the spike protein of SARS-CoV-2 identified by COVIDep (as of 21 May 2020) and their overlap with emerging experimental results. The majority of the identified epitopes (24/29; shown in a shaded box) are located in the S2 functional subunit of the spike protein, reported to be a main region targeted by cross-reactive[3] and cross-neutralizing[4] antibodies. The epitopes with IEDB IDs 70719 and 15972 overlap with regions in the S1 functional subunit of the spike protein reported to be targeted by cross-neutralizing antibodies[5,6]. The specific overlapping residues are underlined. The epitopes with IEDB IDs 9094, 12426, and 558417 overlap with an epitope (located at positions 1178-1189) reported to be targeted by neutralizing antibodies in a preclinical trial of a SARS-CoV-2 vaccine candidate[11]. Interestingly, the partial overlaps of the (consecutive) epitopes 9094 and 12426/558417 cover the experimentally-reported epitope[11] completely. Note that epitopes 12426 and 558417 share the same sequence; they have different IDs due to differences in the associated experimental procedures. The epitopes with IEDB IDs 52020 and 16183 overlap with the regions reported to be recognized by neutralizing antibodies in the sera of recovered COVID-19 patients[8].

Details of the identified T cell epitopes in the S protein

Show 25 entries

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Search: HLA-A*02:01

IEDB	Epitope	Length	Start	End	MHC allele class	MHC allele names	Conservation
36724	LITGRLQSL	9	996	1004	I	HLA-A2/HLA-A*02:01	0.9998
54507	RLDKVEAEV	9	983	991	I	HLA-A*02:01/HLA-A*02:02/HLA-A*02:06/HLA-A*02:03/HLA-A*68:02	0.9998
54725	RLQSLQTYV	9	1000	1008	I	HLA-A*02:01/HLA-A*02:02/HLA-A*02:03/HLA-A*02:06/HLA-A*68:02	0.9998
37544	LLLQYGSFC	9	752	760	I	HLA-A*02:01	0.9997
37724	LLQYGSFCT	9	753	761	I	HLA-A*02:01	0.9997
69657	VLNDILSRL	9	976	984	I	HLA-A*02:01	0.9997
71663	VVFLHVTYV	9	1060	1068	I	HLA-A*02:01/HLA-A*02:02/HLA-A*02:03/HLA-A*02:06/HLA-A*68:02	0.9995
2801	ALNTLVKQL	9	958	966	I	HLA-A*02:01	0.9994
44814	NLNESLIDL	9	1192	1200	I	HLA-A*02:01	0.9993
26710	IITTDNTFV	9	1114	1122	I	HLA-A*02:01	0.9992
54680	RLNEVAKNL	9	1185	1193	I	HLA-A*02:01	0.9992
16156	FIAGLIAIV	9	1220	1228	I	HLA-A*02:01/HLA-A*02:02/HLA-A*02:03/HLA-A*02:06/HLA-A*68:02/HLA-A2	0.9991
20907	GLIAIVMVTI	10	1223	1232	I	HLA-A*02:02/HLA-A*02:03/HLA-A*02:01/HLA-A*02:06/HLA-A*68:02	0.9985
37289	LLFNKVTLA	9	821	829	I	HLA-A*02:01/HLA-A*02:02/HLA-A*02:03/HLA-A*02:06/HLA-A*68:02	0.9976

Showing 1 to 14 of 14 entries (filtered from 75 total entries)

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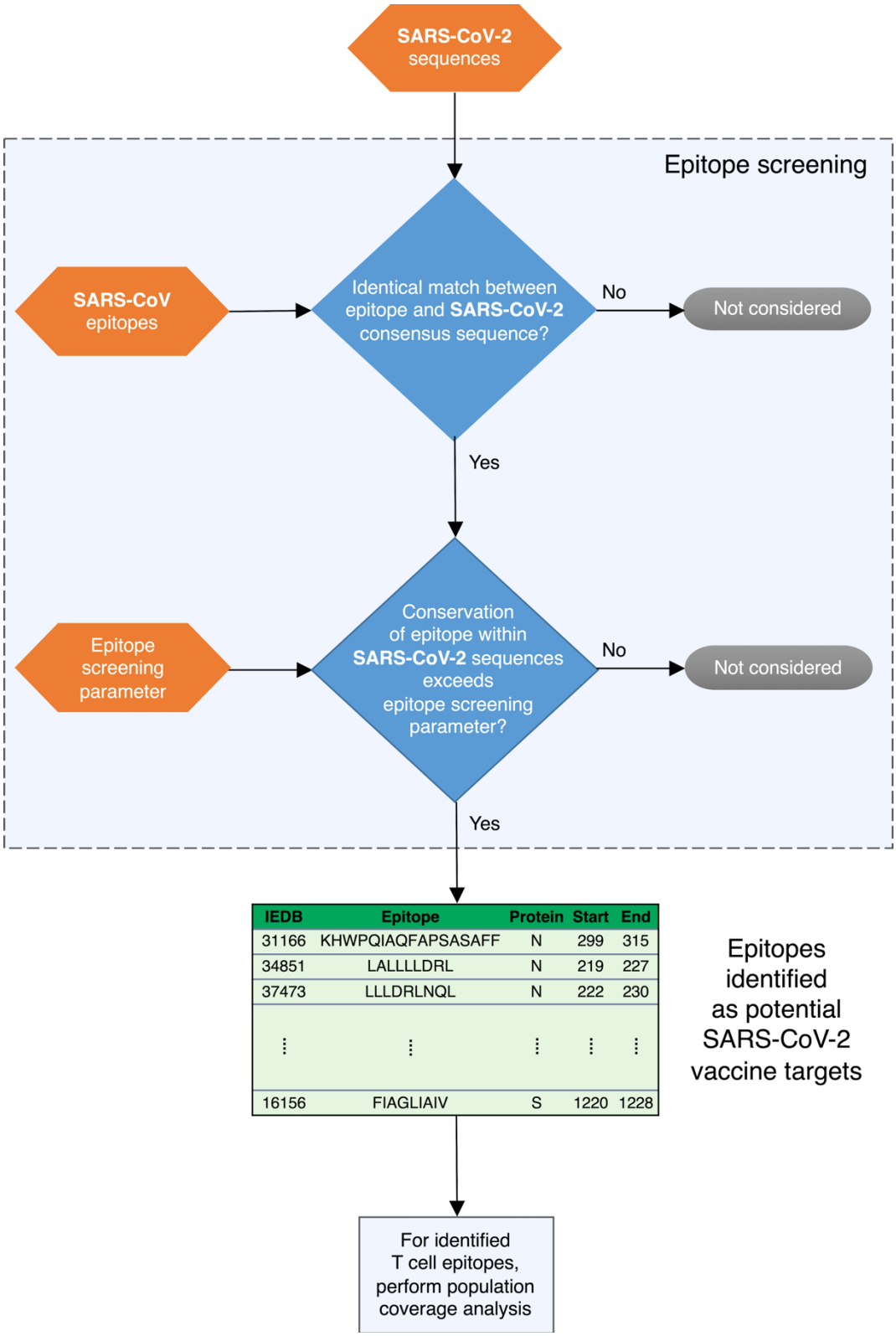
Figure 3. T cell epitopes in the spike protein of SARS-CoV-2 identified by COVIDep (as of 21 May 2020) and their overlap with emerging experimental results. Of the 14 HLA-A*02:01-restricted spike protein epitopes identified by COVIDep, nine epitopes (IEDB IDs 36724, 54507, 54725, 69657, 71663, 2801, 54680, 16156, and 37289) overlap, completely or significantly, with epitopes against which cytotoxic CD8+ T cell responses have been observed in peripheral blood mononuclear cells isolated from COVID-19 patients[9,10]. In a preclinical vaccine trial[12], T cell responses have also been recorded against a protein region comprising the identified epitope with IEDB ID 71663. The specific overlapping residues are underlined, with double-underline reflecting that a response was observed in two studies. A more prominent underline is used to distinguish the epitope with IEDB ID 54725, since a response against this epitope was observed in ten COVID-19 patients (of fourteen studied)[10]. Therefore, this epitope appears to be particularly immunogenic. The epitopes with IEDB IDs 36724, 69657, 71663, 2801, 54680, and 16156 were originally reported based on positive T cell assays for SARS-CoV, while those with IEDB IDs 54507, 54725, and 37289 were reported based on positive MHC binding assays.



Supplementary Figure 1. Epitope screening protocol used by COVIDep for providing vaccine target recommendations for SARS-CoV-2. COVIDep periodically pools SARS-CoV-2 sequence data and compares with experimentally-determined B cell and T cell epitopes of SARS-CoV. The system outputs those epitopes that are genetically similar in SARS-CoV-2, based on an epitope screening parameter. This user-defined parameter allows the user to select epitopes based on their conservation in the SARS-CoV-2 sequence data, where conservation is defined as the fraction of SARS-CoV-2 sequences with the exact epitope sequence. For the identified T cell epitopes, population coverage analysis is performed to estimate the percentage of a specified population that can elicit a response against them.