NeoScreen®

Mapping the adaptive immune response to SARS-CoV2

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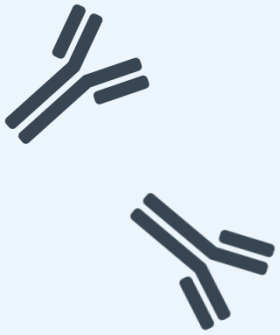
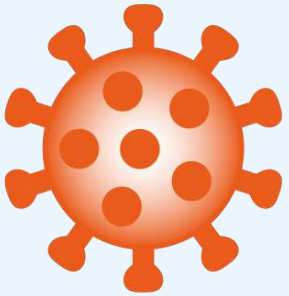
AGENDA



1. COVID19 Vaccine Development and Challenges
2. IMMUNITRACK BACKGROUND
3. OUR CONTRIBUTION TO THE ONGOING EFFORT IN VACCINE DEVELOPMENT



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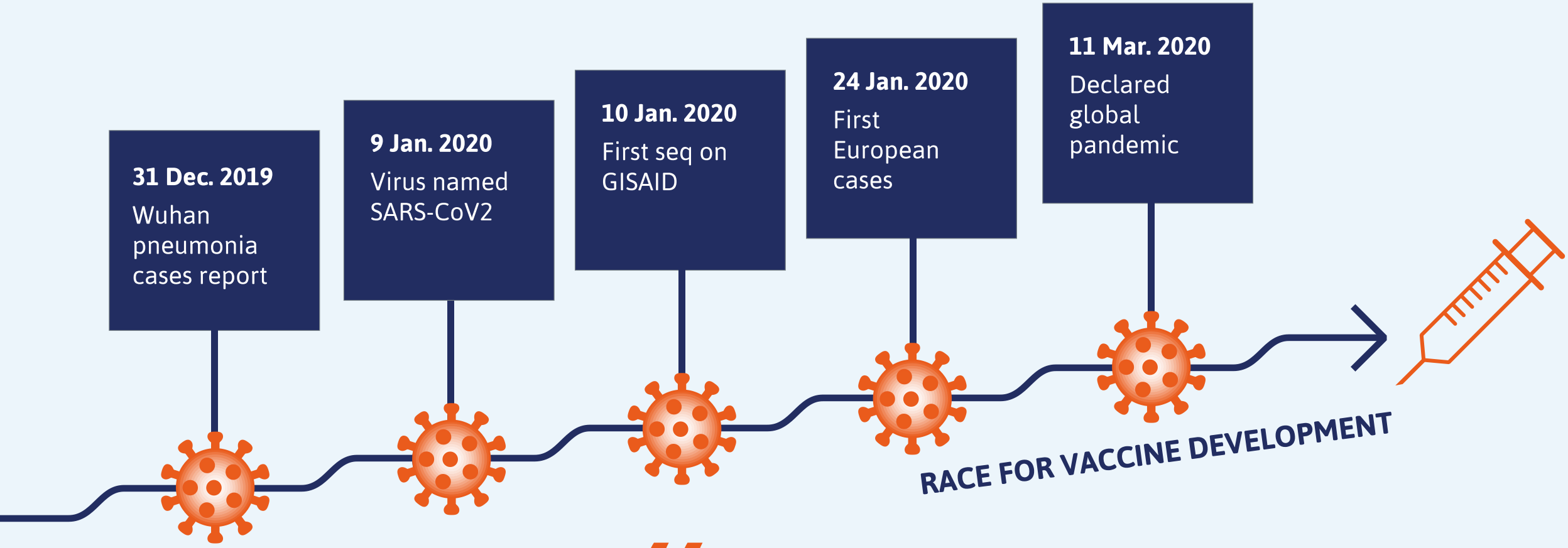

> Developing a vaccine is difficult at the best of times, but rarely have we been in a situation where basic knowledge about a virus has to be acquired so directly alongside the race to eradicate it.

Sheena Cruickshank · Professor in Biomedical Sciences, University of Manchester

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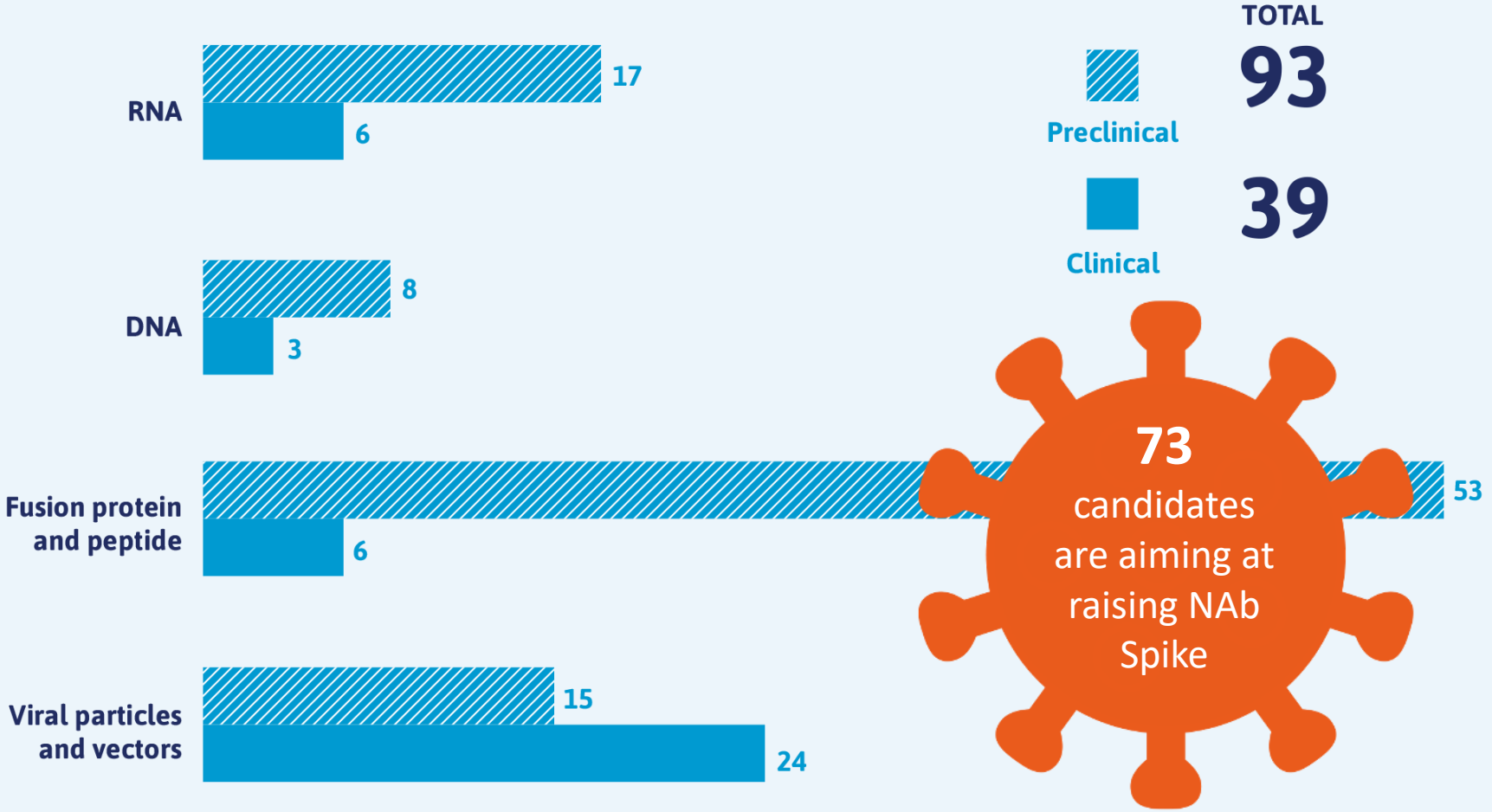
Vaccine Development Overview

There are more than 130 COVID-19-vaccine candidates in development globally.

Common goal to most vaccines:
To stimulate production of neutralising antibodies.

Vaccine candidates by technology platform and development phase



Sources: https://www.biocentury.com/coronavirus
https://racetoacure.stanford.edu/development-leads

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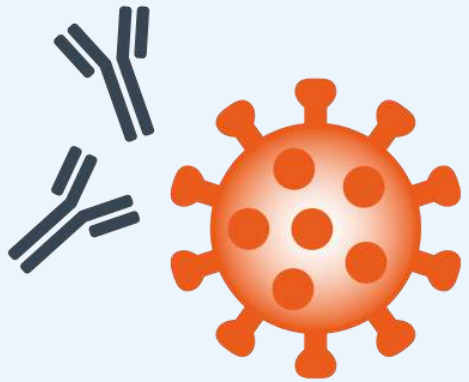
Vaccine development challenges

A NUMBER OF HURDLES REMAIN:

- Validation of unproven platform technologies
- Vaccine safety and protection against COVID-19 ?
- Most Approaches focus on raising NAb against SPIKE. Will it be sufficient for full Immunity?

13th of October Eli Lilly posed clinical trial of monoclonal antibody program due to safety concern.



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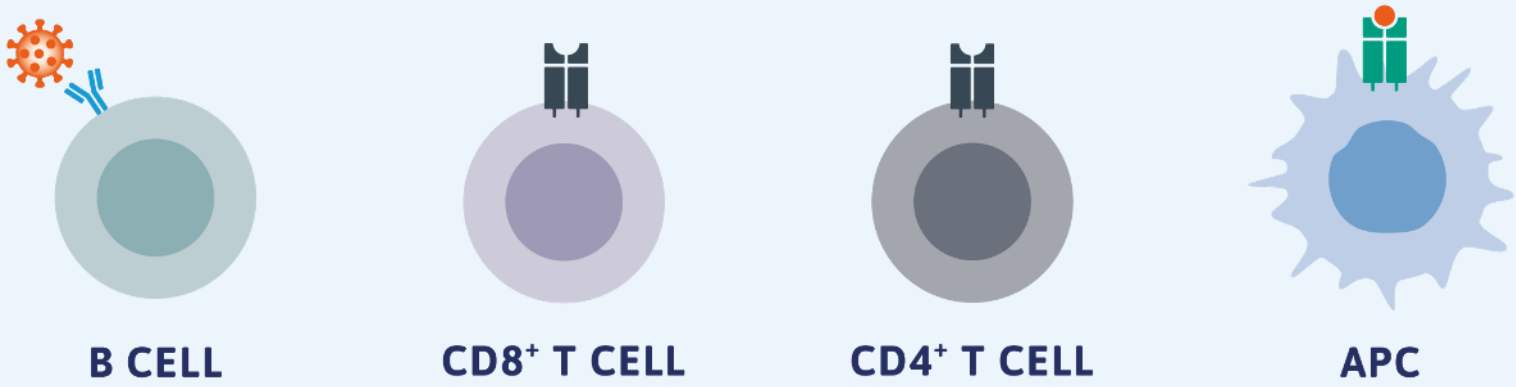
Full immunity requires proper B cell and T activation



T CELL RESPONSE IMPORTANT FOR FULL IMMUNITY FOR CORONAVIRUS

- For SARS-CoV1 anti-Spike Nab shown to lead to acute lung injury (cytokine rush) and linked to inadequate Th1 cell activity (CD4 T cells) (Liu et al., 2019).
- For SARS-CoV1 anti-Spike Ab response is short lived (Tang et al., 2011).
- Fast decline of antibody presence have been reported for SARS-CoV2 n (Seow et al., 2020; Vabret, 2020).
- For SARS-CoV2 multiple studies now show that T cell plays an important role in patients outcome following infection (Grifoni et al., 2020).

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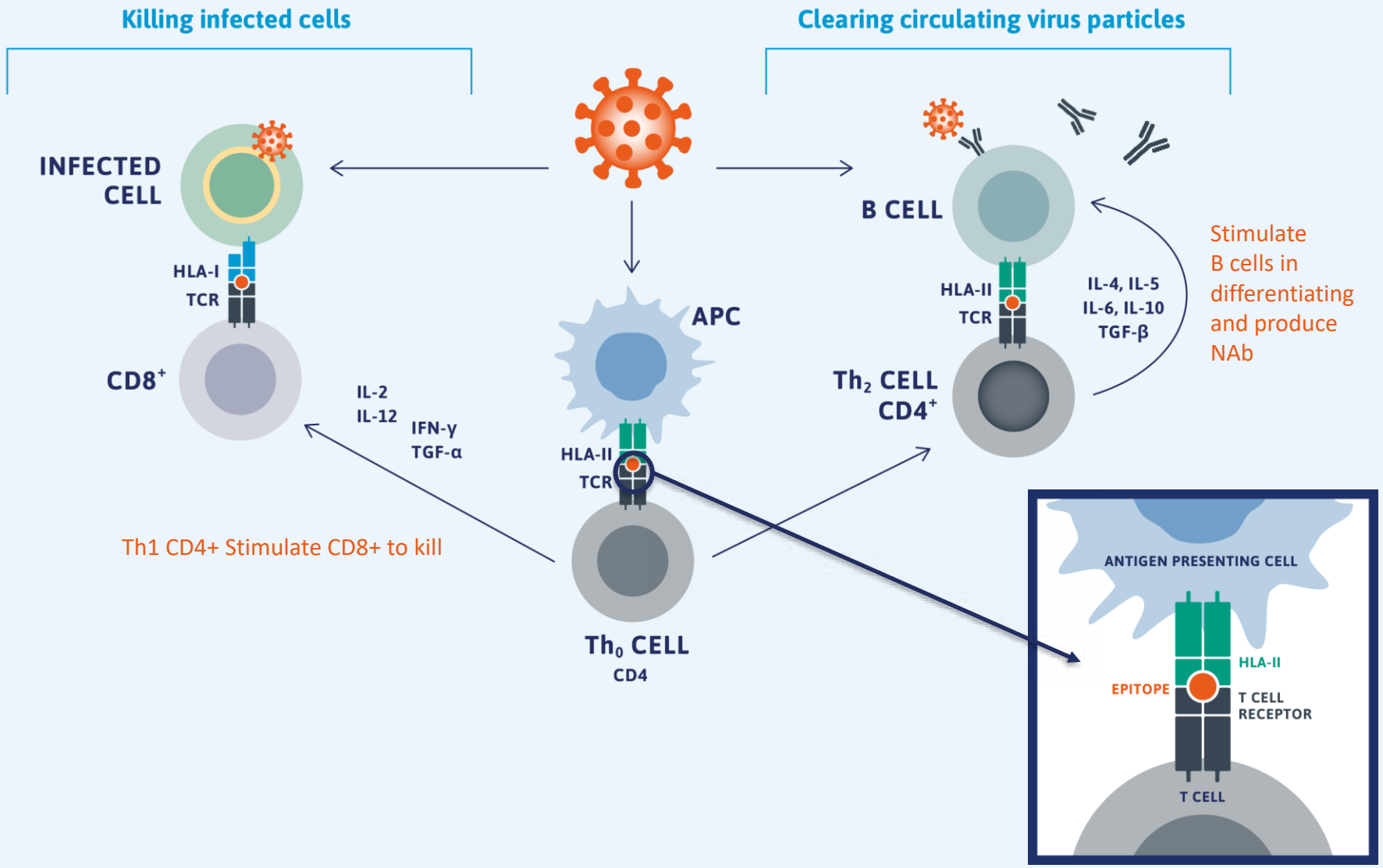
Epitope presentation by HLA receptors is central for viral clearance

Antigen (epitope) presentation by HLA on the surfaces of cells is the most decisive event in the activation or priming of the cellular immune response (T and B cells).



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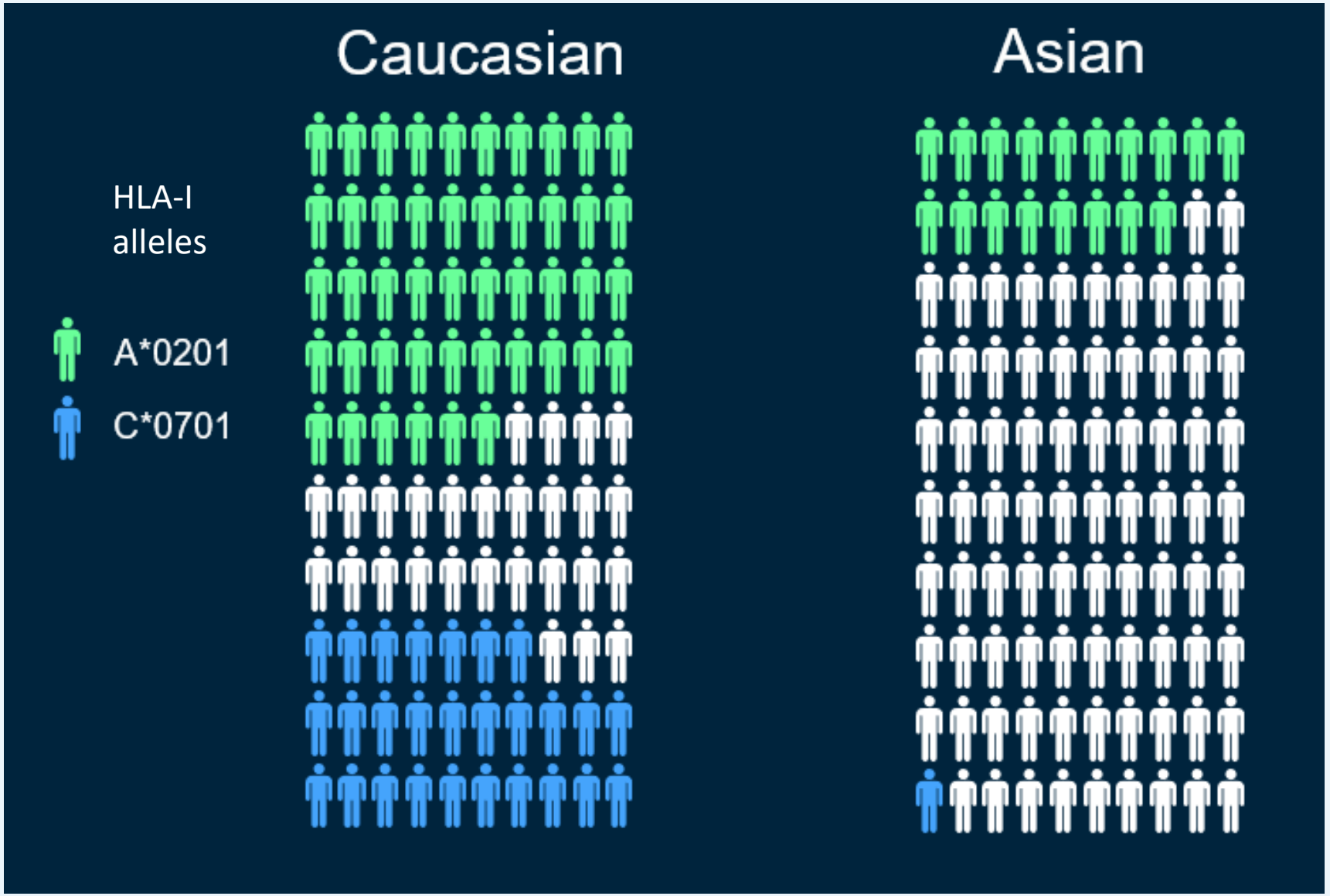
HLA composition varies across populations



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HLA composition varies across populations

Various Combinations Need to Be Studied for Population Coverage

Allele	White	Allele	Black	Allele	Hispanic	Allele	Asian or Pacific Islander
A*02:01	45.6%	C*04:01	29.0%	A*02:01	37.1%	A*11:01	38.4%
C*07:01	27.7%	C*07:01	25.4%	C*04:01	25.4%	A*24:02	33.7%
A*01:01	27.4%	C*06:02	23.0%	A*24:02	24.9%	C*07:02	33.3%
A*03:01	23.8%	A*02:01	22.3%	C*07:02	24.2%	C*01:02	27.7%
C*07:02	21.5%	A*23:01	20.7%	C*07:01	20.8%	A*33:03	23.3%
C*04:01	21.2%	C*02:02	19.0%	C*03:04	14.4%	C*08:01	21.6%
B*44:02	20.2%	A*03:01	18.7%	A*03:01	14.3%	C*03:04	19.9%
B*07:02	18.1%	C*07:02	18.1%	B*07:02	13.2%	A*02:01	18.1%
B*08:01	18.1%	B*53:01	18.1%	B*35:01	12.8%	B*40:01	15.2%
C*05:01	17.2%	B*07:02	15.8%	C*06:02	12.3%	C*04:01	14.0%
C*03:04	16.8%	C*16:01	15.7%	C*05:01	11.9%	B*58:01	13.3%
C*06:02	15.7%	B*15:03	13.9%	A*01:01	11.4%	B*46:01	12.7%
A*11:01	15.3%	B*58:01	13.5%	A*11:01	11.0%	B*51:01	12.4%
B*40:01	13.6%	A*68:02	12.7%	B*51:01	10.8%	C*03:02	12.0%
A*24:02	12.1%	C*17:01	11.7%	C*16:01	10.6%	B*38:02	11.4%
B*35:01	10.7%	B*45:01	10.8%	B*44:03	9.9%	A*02:07	11.0%
C*03:03	10.6%	B*42:01	10.5%	C*01:02	9.7%	B*15:01	9.4%
B*51:01	10.4%	A*30:01	10.4%	A*29:02	9.7%	A*02:06	9.3%
C*12:03	9.9%	B*35:01	10.1%	C*08:02	9.3%	C*03:03	9.2%
B*15:01	9.6%	A*01:01	10.0%	B*18:01	9.1%	B*15:02	9.1%
A*29:02	8.9%	C*03:04	9.3%	A*31:01	8.9%	A*02:03	8.8%

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IMMUNITRACK – Background

Biotech company with a unique knowhow in mapping CD4 and CD8 T cell epitopes.

STRONG SCIENTIFIC FOUNDATION

- CSO, Sune Justesen PhD

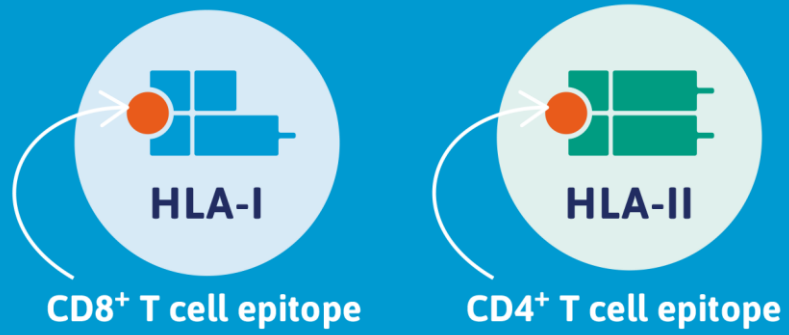
At the University of Copenhagen ran the largest HLA recombinant platform.

- Collaborate and assist leading research in vaccine and immuno-oncology **Uni Liverpool**, **Johns Hopkins**, **Dana Farber**, **MD Anderson** as well **as 170 Pharma and Biotech companies**

WHAT WE DO

NeoScreen® platform

- We perform *in vitro* binding assays to assess the likelihood of epitopes being presented by HLA-I and HLA-II receptors
- Produce HLA/epitope reagents for CD4 and CD8 T cell studies.



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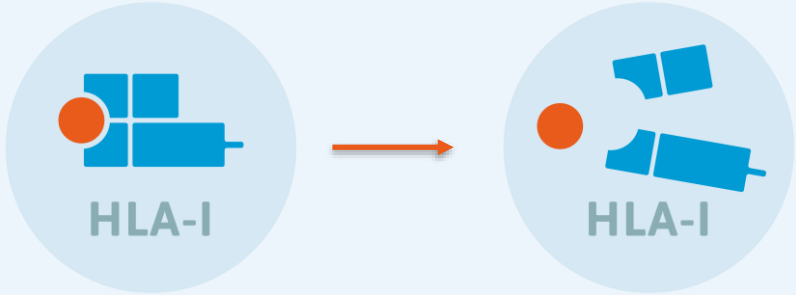
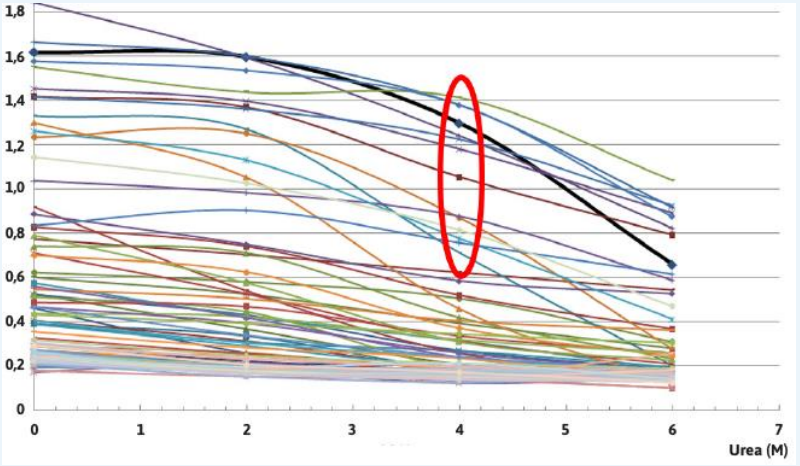
Our solution

A unique in vitro platform assessing any epitope's likelihood of being presented by HLA class I and class II and stimulate a T cell response

Stability Assessment



Stability of HLA/epitope complexes assessed using urea, pH or temperature



KEY FEATURES

- High throughput platform (thousands of HLA/epitope assessments/week)
- Broad HLA portfolio (70 HLA class I and 15 HLA class II covering all ethnicities)
- Data is clear and simple to interpret and outperforms all prediction tools.
- Strong correlation of data with confirmed T cell epitopes

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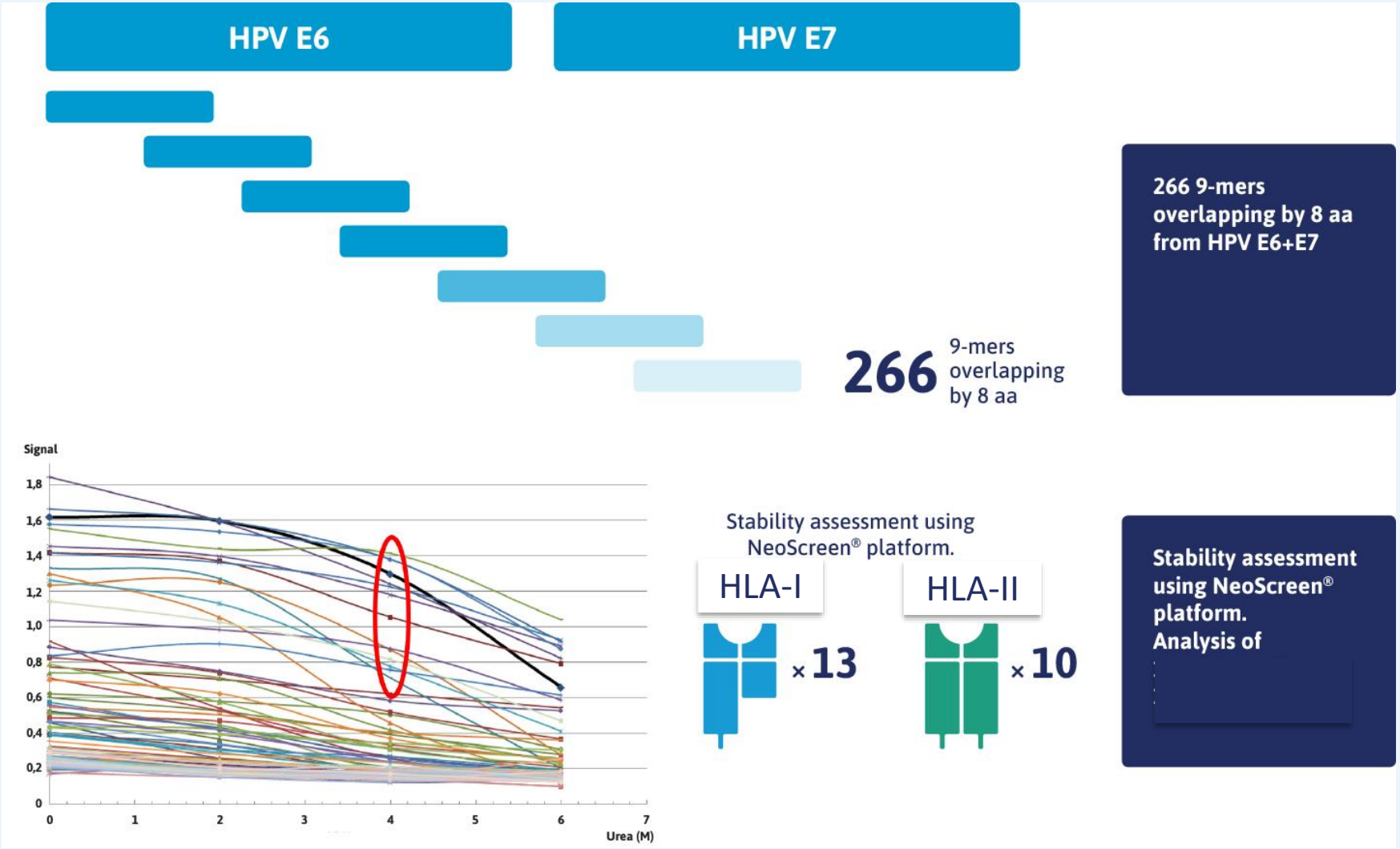

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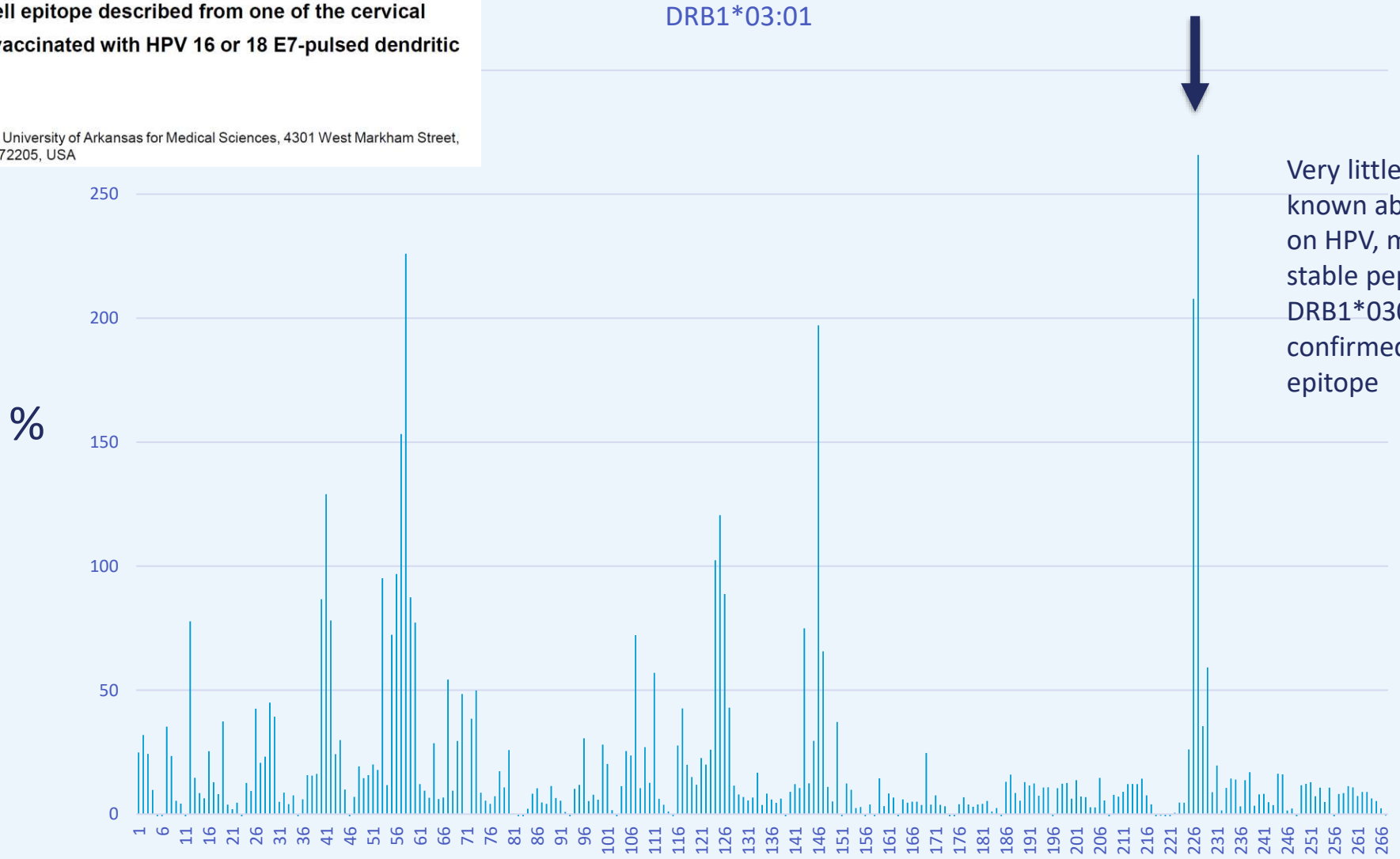
HPV E6/7 screening result for HLA-II (DRB1*0301)

A novel CD4 T-cell epitope described from one of the cervical cancer patients vaccinated with HPV 16 or 18 E7-pulsed dendritic cells

Xuelian Wang,
Department of Pathology, University of Arkansas for Medical Sciences, 4301 West Markham Street, Slot 824, Little Rock, AR 72205, USA



Very little is known about CD4 on HPV, most stable peptide on DRB1*0301 was confirmed epitope

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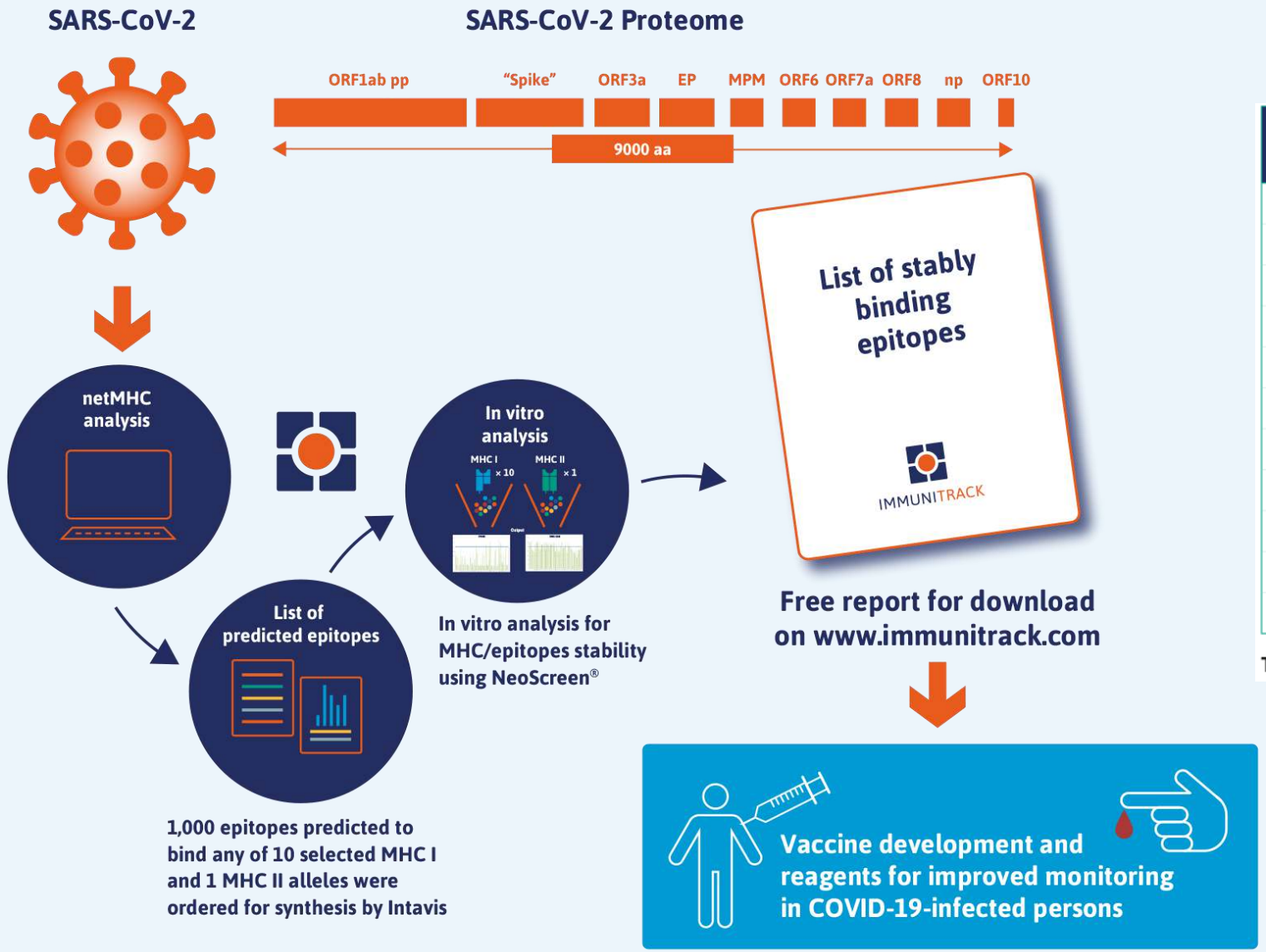
Our initial work on SARS-CoV-2



Allele	Number of predicted epitopes with min. 60 % stability
A*0101	14
A*0201	15
A*0301	41
A*1101	49
A*2402	30
B*4001	30
C*0102	3
C*0401	1
C*0701	3
C*0702	3
DRB1*0401	22

Table 1. SARS-CoV-2 Epitopes

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Outcome

More than 900 individuals downloaded the report.

Multiple studies of T cell response on COVID-19 patient ongoing.

1 we are involved in where 100 patients who recovered from COVID will be analysed

1 study on healthcare workers to be initiated

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Report being referred to in publishes articles

SARS-CoV-2 infected cells present HLA-I peptides from canonical and out-of-frame ORFs

Shira Weingarten-Gabbay[1,2*§], Susan Klaeger[1*§], Siranush Sarkizova[1*], Leah R. Pearlman[1], Da-Yuan Chen[3,4], Matthew R. Bauer[1,5], Hannah B. Taylor[1], Hasahn L. Conway[3,4], Christopher H. Tomkins-Tinch[1,2], Yaara Finkel[6], Aharon Nachshon[6], Matteo Gentili[1], Keith D. Rivera[1], Derin B. Keskin[1,7,8,9], Charles M. Rice[10], Karl R. Clauser[1], Nir Hacohen[1,11†], Steven A. Carr[1†], Jennifer G. Abelin[1†], Mohsan Saeed[3,4†§], Pardis C. Sabeti[1,2,12,13,14†]

[1]Broad Institute of MIT and Harvard, Cambridge, MA 02142, USA.
[2]Department of Organismic and Evolutionary Biology, Harvard University, Cambridge, MA 02138, USA.

synthetic peptides validated the viral peptides that we observed in infected cells (Table 1). FASEAARVV from nsp2, IRQEEVQEL from ORF7a, KRVDWTIEY from nsp14, and YLNSTNVTI from nsp3 were also independently confirmed in previously generated biochemical binding assays (Covid19 Intavis_Immunitrack stability dataset 1, https://www.immunitrack.com/free-coronavirus-report-for-download/). One peptide, HADQLTPTW, was also detected in non-infected A549 cells and thus, we removed it from all subsequent analyses.

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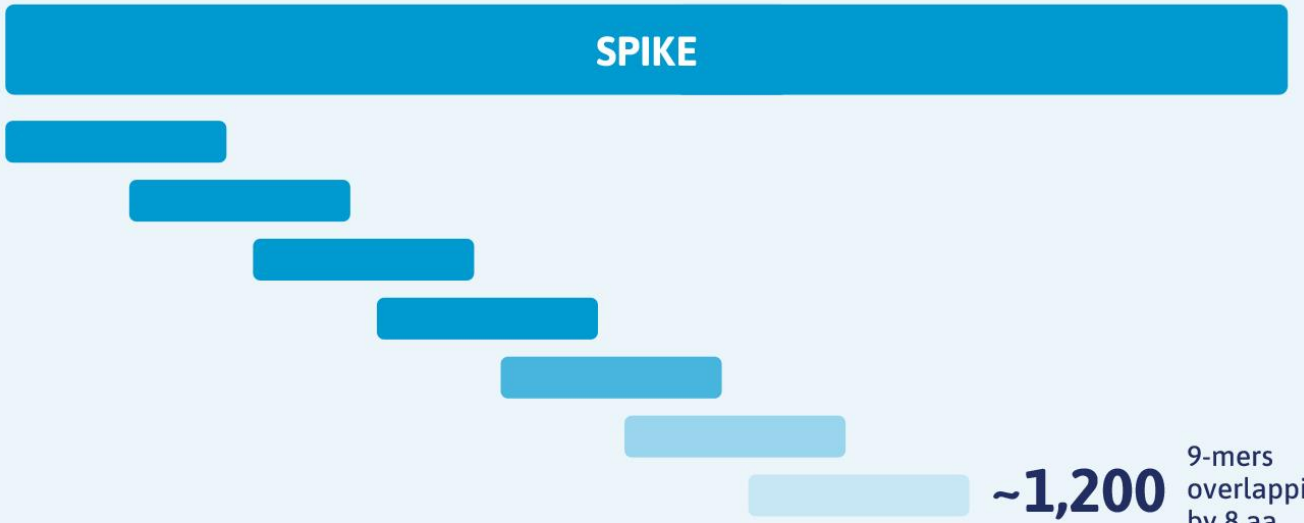
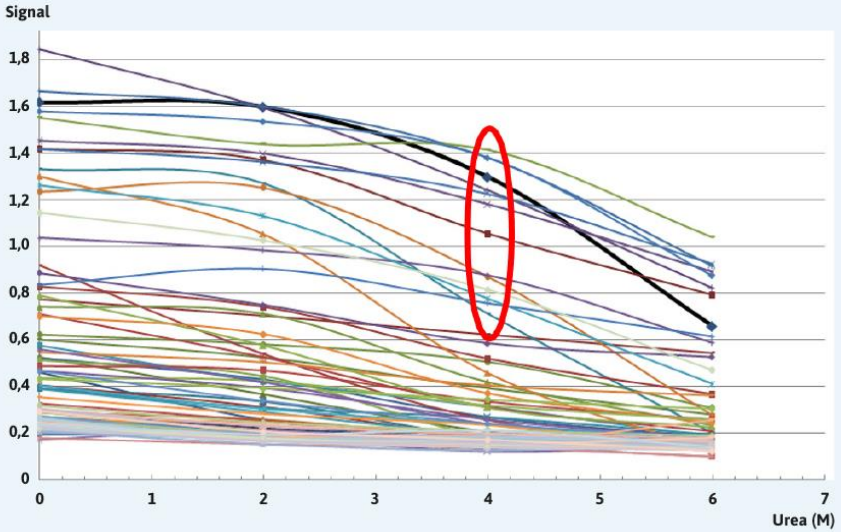
Mapping T cell epitopes in Spike



~1,200 9-mers overlapping by 8 aa from Spike



HLA-I	HLA-II
A*01:01	DRB1*01:01
A*02:01	DRB1*03:01
A*03:01	DRB1*04:01
A*11:01	DRB1*08:01
A*24:02	DRB1*11:01
B*07:02	DRB1*13:01
B*08:01	DRB3*02:02
C*04:01	DRB4*01:01
C*07:02	DRB5*01:01
	DPA1*0103/DPB1*0401

Stability assessment using NeoScreen® platform. Analysis of 9 HLA-I and 10 HLA-II alleles

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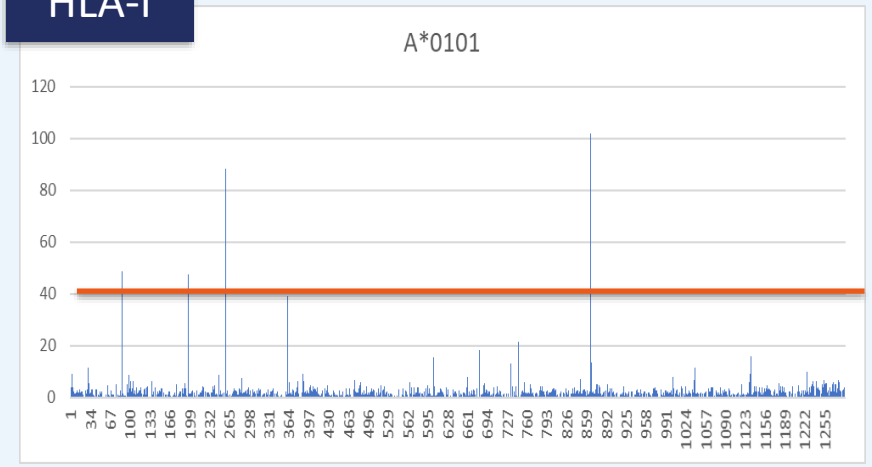
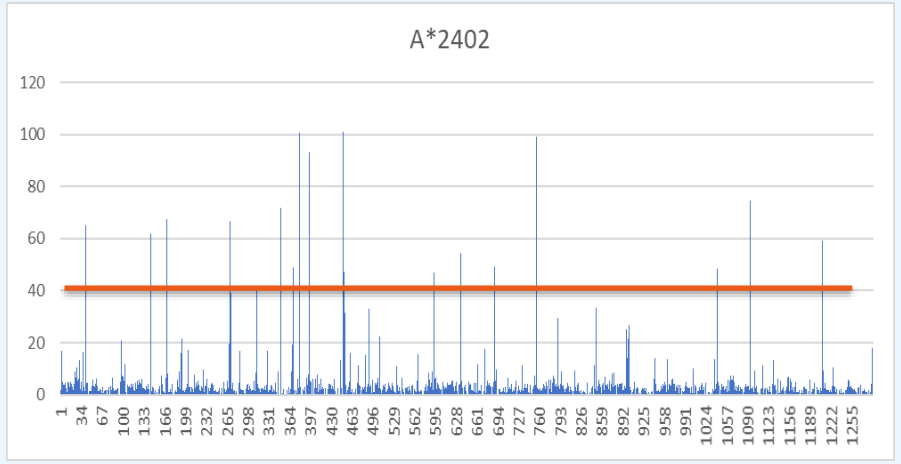
T cell epitopes identified by stability

In total, approx. 100 CD8 and 100 CD4 T cell epitopes were identified and HLA restricted.

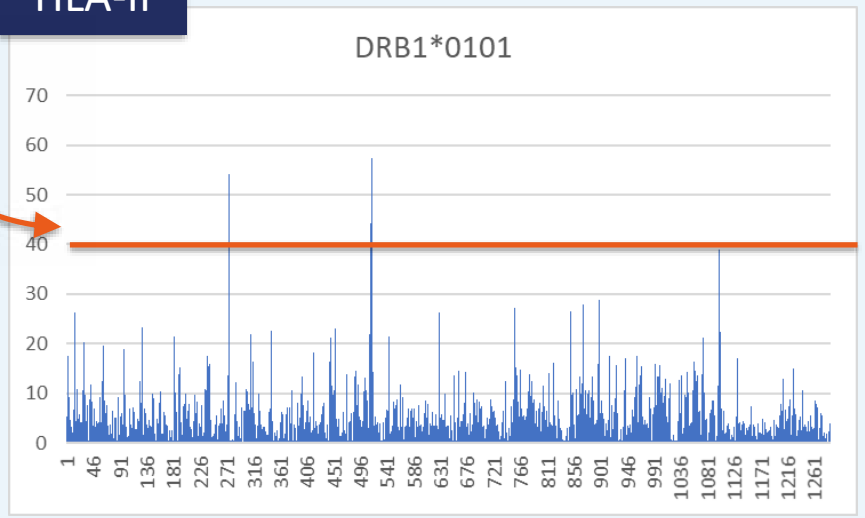
> 40
Likely T cell epitope

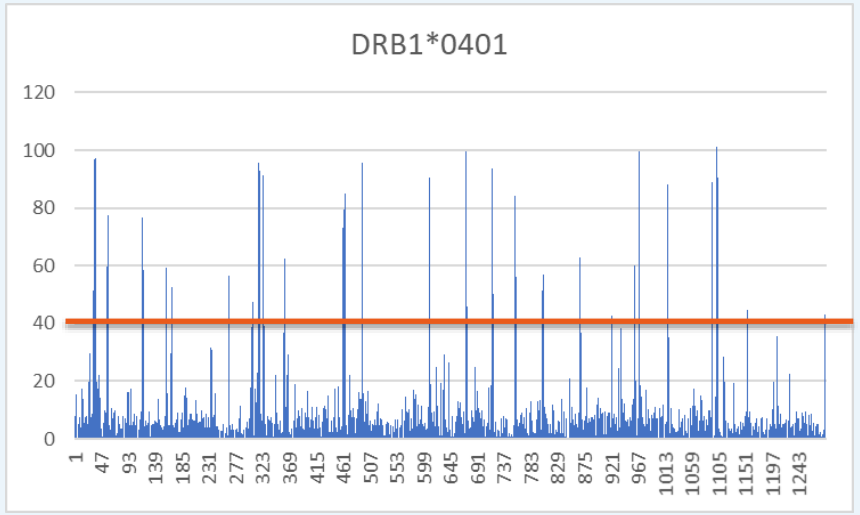
HLA-I





HLA-II





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Resulting T cell epitopes

Most T cell epitopes are found and HLA-restricted in our study.

Interestingly, several epitopes bind multiple HLA-I and HLA-II.

nature immunology

ARTICLES

https://doi.org/10.1038/s41590-020-0782-6

Broad and strong memory CD4+ and CD8+ T cells induced by SARS-CoV-2 in UK convalescent individuals following COVID-19

Protein	Peptide	Position	amino acid sequence	CD4/CD8	Individuals	HLA I	HLA II
Spike	S-34a	166–180	CTFEYVSQPFLMDLE	4	10	2	2
Spike	S-39	191–205	EFVFKNIDGYFKIYS	NA	1	1	
Spike	S-42	206–230	KHTPINLVRDLPQGF	NA	1	1	1
Spike	S-43	211–225	NLVRDLPQGFSALEP	NA	1	1	
Spike	S-71	351–365	YAWNRKRISNCVADY	4	1		4
Spike	S-77	381–395	GVSPTKLNDLCFTNV	4	1	1	
Spike	S-90	446–460	GGNYNYLYRLFRKSN	NA	1	2	3
Spike	S-91	451–465	YLYRLFRKSNLKPFE	NA	1	4	2
Spike	S-103	506–520	VVLSFELLHAPATVC	4	1	2	1
Spike	S-106	526–540	GPKKSTNLVKNKCVN	8	1	3	
Spike	S-145	721–735	SVTTEILPVSMTKTS	NA	1	1	
Spike	S-150	746–760	STECSNLLLQYGSFC	NA	1		1
Spike	S-151a	751–765	NLLLQYGSFCTQLNR	4	8	3	3
Spike	S-161	801–815	NFSQILPDPSKPSKR	4	2		3
Spike	S-174a	866–880	TDEMIAQYTSALLAG	4	6	2	2
Spike	S-235	1,171–1,185	GINASVVNIQKEIDR	NA	1		1
Spike	S-240	1,196–1,210	LIDLQELGKYEQYI	NA	1		
Spike	S-242	1,206–1,220	YEQYIKWPWYIWLGF	NA	1	2	1

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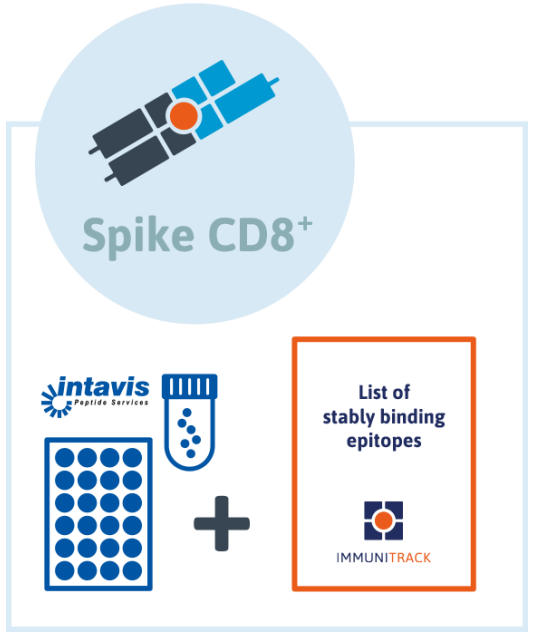
Product release

Stability data and ranking of most likely T cell epitopes derived from Spike.

This is the most comprehensive epitope/HLA restriction analysis to date.

- **CD8+ Research Kit:**

Microscale peptides and HLA/epitope binding report for CD8+



- **CD4+ Research Kit:**

Microscale peptides and HLA/epitope binding report for CD4+

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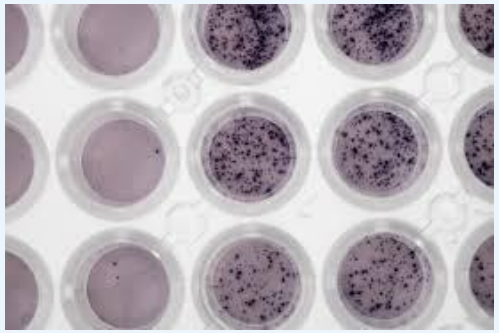
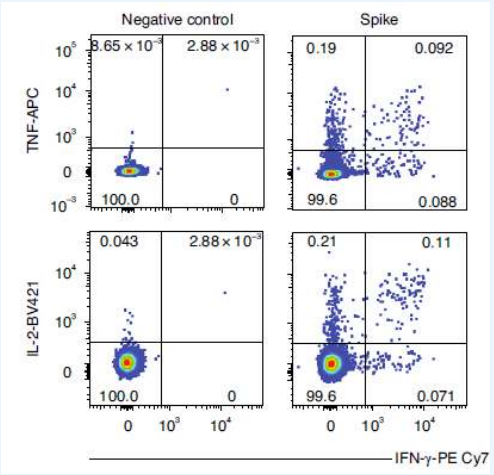
Application of data

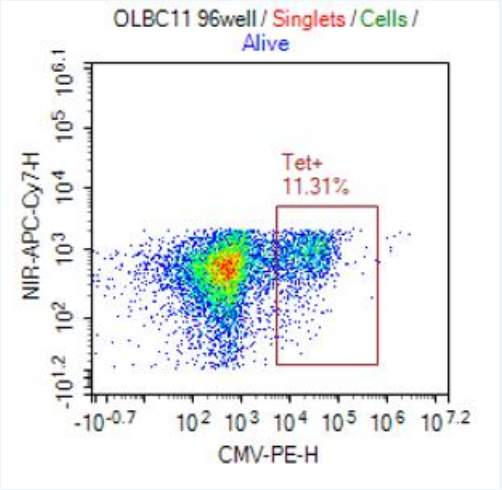
Deeper understanding of patients' adaptive immune response to SARS-CoV-2 infection and to vaccines

Selection of immunodominant epitopes for novel vaccine development.





ELISpot assays intracellular cytokine staining (**ICS**) **assays.**



Select HLA/epitope tetramers for in depth studies of CD4+ and CD8+ T cells.

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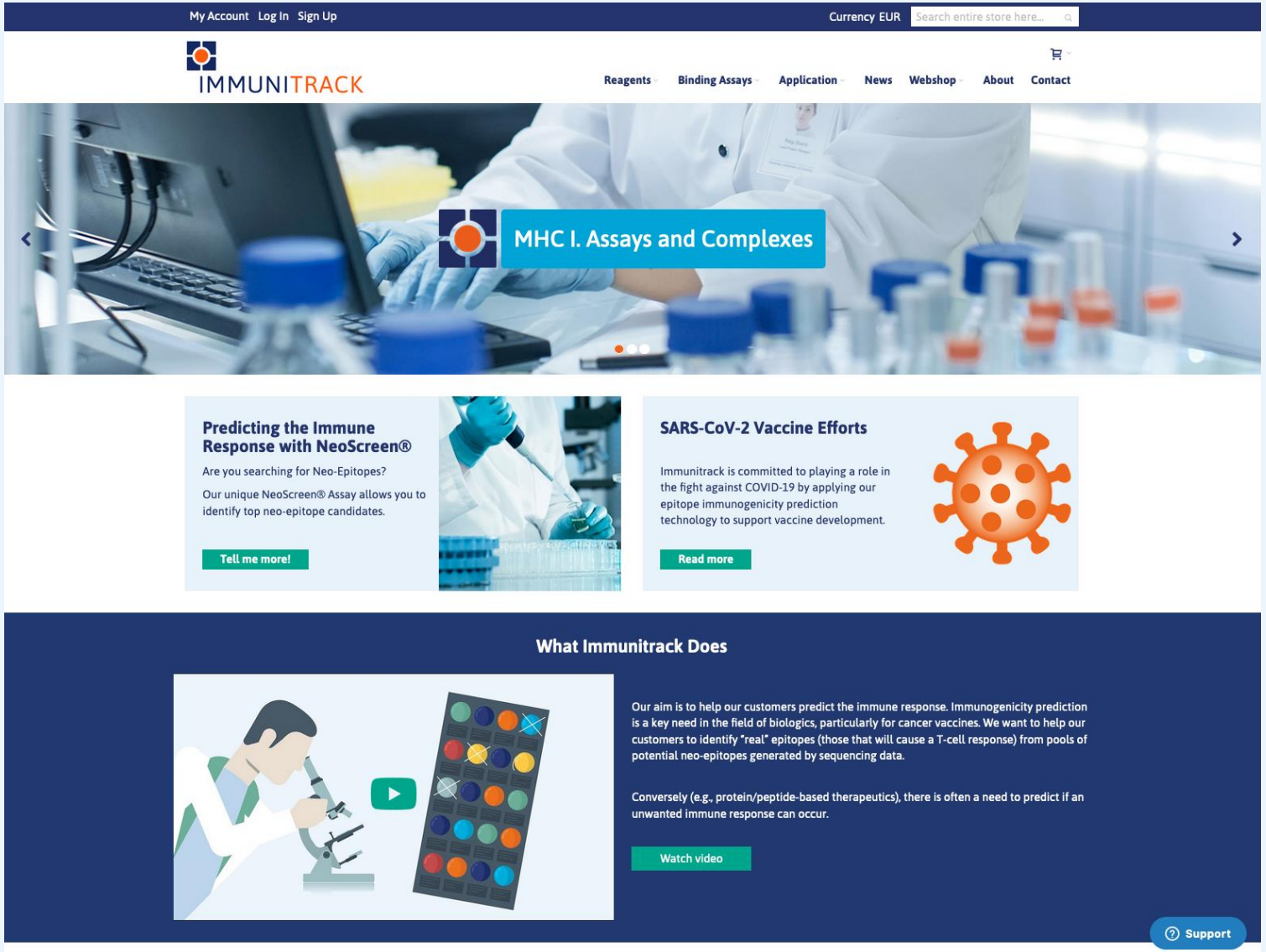
Thank you!

www.immunitrack.com

EMAIL:
sthor@immunitrack.com



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THANK YOU!