Mapping of the SARS-CoV-2 epitope-specific T-cell response using dCODE Dextramer® reagents

Schreibing, F. Hannani, M. *et al.* Dissecting CD8+ T-cell pathology of severe SARS-CoV-2 infection by single-cell epitope mapping. (2021) BioRxiv
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BACKGROUND

In this study, the CD8+ T-cell response in COVID-19 patients experiencing mild or severe disease was investigated using dCODE Dextramer® reagents by bulk and Single-Cell Analysis.

STUDY DESCRIPTION

Patient-derived T cells were initially screened for SARS-CoV-2-specificity using a panel of 38 different dCODE Dextramer® (HiT) reagents, including 4 positive and 4 negative controls. From the initial screening, a panel of 15 dCODE Dextramer® (10x compatible) reagents plus the 8 controls were selected for subsequent Single-Cell Analysis of the patient samples.

RESULTS

Screening of patient samples using dCODE Dextramer® (HiT) enabled identification of samples holding specifically enriched epitope-binding T-cell populations for subsequent Single-Cell Analysis with dCODE Dextramer® (10x compatible), (**Table 1**). By clustering epitope specificity based on dCODE Dextramer® (10x compatible) binding, researchers found unique recognition of four epitopes by T cells (**Fig. 1**) with the A*0101 epitope WTAGAAAYY being the most prevalent. In patients with severe COVID-19, Single-Cell Analysis of T cells binding dCODE Dextramer® (10x compatible) reagents revealed hyperactivation, T-cell exhaustion, and lack of long-lived memory T-cell features (**Fig. 2**).

HLA	Peptide	Target
A*0101	WTAGAAAYY	S Protein
A*0101	LTDEMIAQY	S Protein
A*0201	TLACFVLAAV	M Protein
A*0201	GMSRIGMEV	N Protein
A*0201	TLACFVLAAV	M Protein
A*0201	LLLDRLNQL	N Protein
A*0201	NLNESLIDL	S Protein
A*0201	ILLNKHIDA	N Protein
A*0201	FIAGLIAIV	M Protein
A*0301	TLKSFTVEK	S Protein
A*0301	QIYKTPPIK	S Protein
A*1101	LSYFIASFR	M Protein
A*1101	MTSCCSCLK	S Protein
A*1101	GYVFASTEK	S Protein
A*1101	TLKSFTVEK	S Protein

Table 1 Top 15 immunogenic epitopes selected in the dCODE Dextramer® (HiT) screening for single-cell immuno-profiling of patient-specific CD8+ T cells.

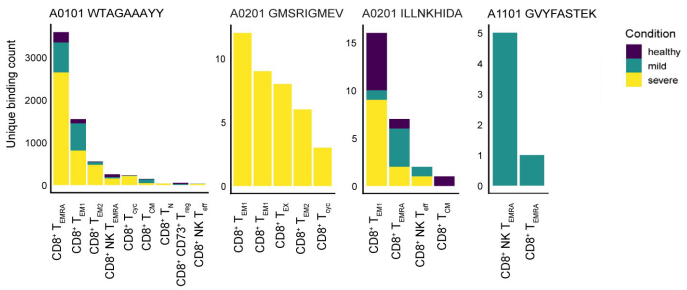

Fig. 1 The four uniquely recognized epitopes identified using dCODE Dextramer® (10x compatible) reagents are recognized by different T cell subsets.

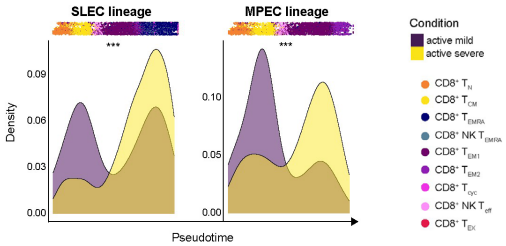

Fig. 2 Distribution of cell type frequency for active, mild, and severe COVID-19. SLEC = short-lived effector cells. MPEC = memory precursor effector cell.

CONCLUSIONS

- Relevant SARS-CoV-19 epitopes were identified in the initial screening using a panel of dCODE Dextramer® (HiT). Single-Cell Analysis of T cells binding dCODE Dextramer® (10x compatible) reagents identified the CD8+ T-cell epitope WTAGAAAYY.
- In patients with severe COVID-19, Single-Cell Analysis with dCODE Dextramer® (10x compatible) reagents revealed hyperactivation, T-cell exhaustion, and lack of long-lived memory T-cell characteristics.

CONTACT IMMUDEX
customer@immudex.com