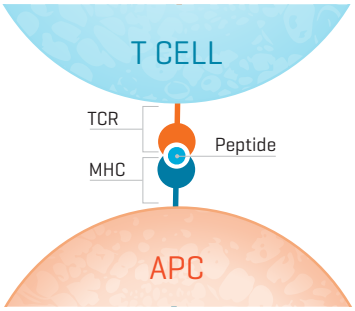
TCR-T Cell Therapy

IMMUDEX®
PRECISION IMMUNE MONITORING

Antigen-Specific Solutions for TCR-T Cell Therapy

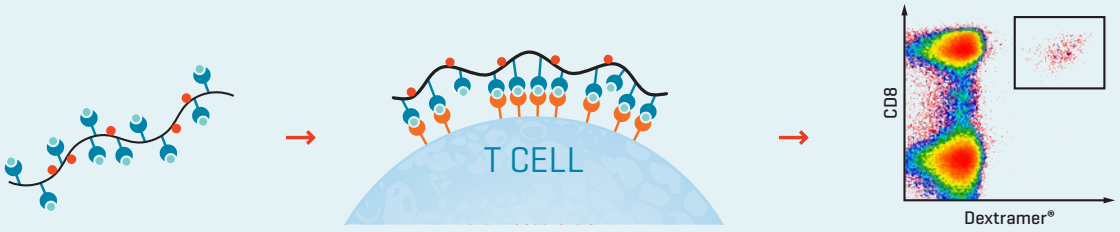
Antigen specific interaction is at the heart of TCR-T cell therapy. In order to develop an effective T cell-based therapeutic, it is necessary to discover not only the ideal TCR, but also the most suitable target epitope.

To understand the mechanism of action of the therapeutic, the antigen-specific interaction needs to be well characterized. A thorough analysis of antigen-specific responses in T cells is critical to demonstrate efficacy and investigate possible side effects.



Quality Control of TCR-T Cell Therapies

- Demonstrate that the infusion product meets defined lot release criteria:
- T Cell Number, Identity and Purity
- Clinical-Grade (GMP) Dextramer® reagents
- Analyze both the identity and purity of T cells in a single step



MHC Dextramer® reagent(s)

MHC Dextramer® binds to TCR on antigen-specific T cells

Assess % of target-specific Dextramer®-positive T cells by flow cytometry

TCR-T Cell Therapy: from Development to Manufacturing

Target Discovery

TCR Discovery and Specificity Profiling

- dCODE Dextramer®

Infusion Product Characterization and Validation

Biochemical Characterization and Biological Applications

- Soluble TCR Monomers
- TCR Dextramer®
- MHC Monomers
- MHC Dextramer®
- dCODE Dextramer®

Manufacturing and Release Testing for Clinical Trials

Assessment of T Cell Number, Identity and Purity

- Clinical-Grade Dextramer® (GMP)

Clinical Trials

Precision Immune Monitoring of Patient Response

- TCR Dextramer®
- MHC Dextramer®
- dCODE Dextramer®

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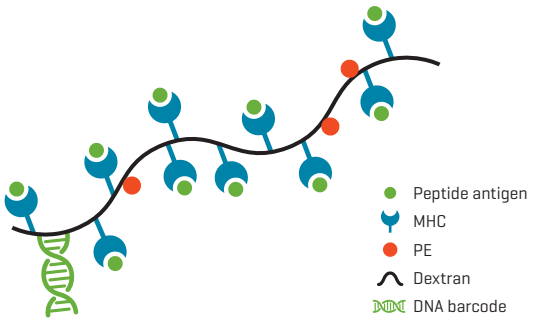
TCR Discovery

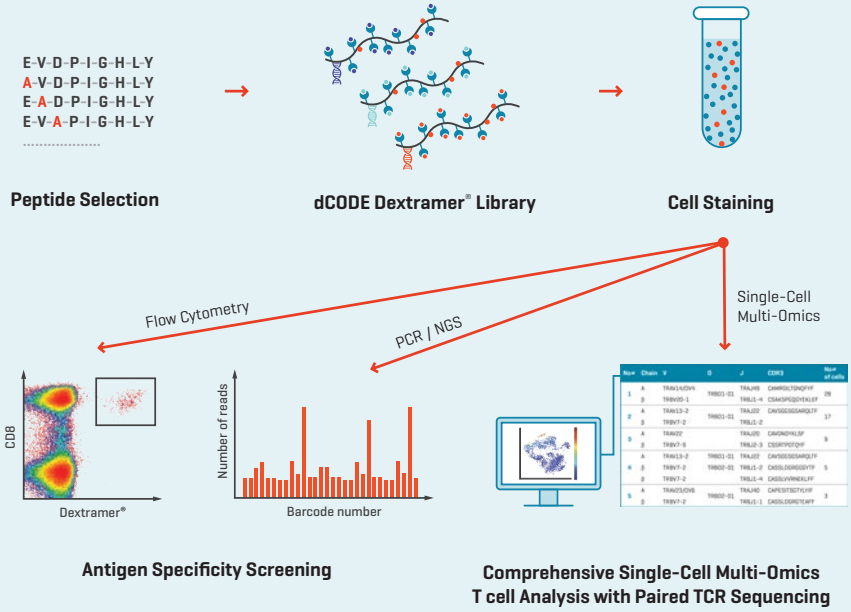
Perform single-cell V(D)J sequencing and TCR discovery at scale using dCODE Dextramer®libraries

- Multiplex up to 1000 different specificities
- Simultaneously identify the TCR sequences as well as the epitopes with which the TCRs interact
- Detect even low affinity TCRs reliably so you don't miss out on important TCR candidates



Specificity Profiling

- Perform large scale epitope recognition profiling using dCODE Dextramer®libraries
- Discover epitopes for which epitope-reactive TCR clonotypes with the desired phenotypic characteristics can be identified
- Investigate TCR cross-reactivity with potential off-target antigens

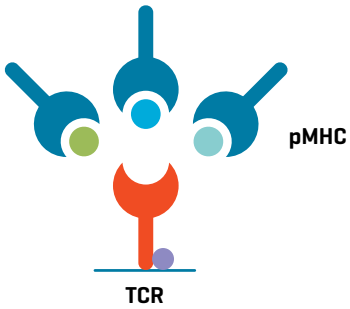


Assess pMHC Binding Affinity

Create plates coated withPeptide-Receptive MHC Monomers

- pMHC binding affinity influences the accumulation of epitope on the cell surface
- Assess the binding affinity between MHC and different target peptides

Biochemical Characterization of the TCR:pMHC Interaction

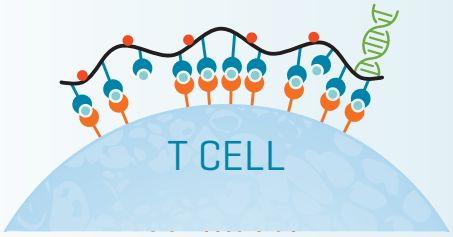


- Develop *ex vivo* assays using immobilized Soluble TCR Monomers and libraries of pMHC Monomers
- Screen for TCR Cross-Reactivity against potential off-target antigens to mitigate the risk of toxicity
- Assess TCR:pMHC binding strength using cell-free plate or bead-based binding strength and duration assays

TCR Validation

- Demonstrate TCR interaction with the target pMHC
- Assess TCR surface expression level
- Investigate TCR:pMHC complex affinity
- Characterize pMHC-reactive T cell clonotypes

MHC Dextramer® or dCODE Dextramer® bind to TCR on antigen-specific T cells enabling analysis by flow cytometry or single-cell multi-omics

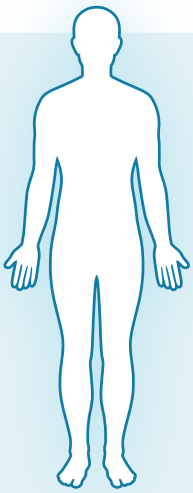


T Cell Isolation, Enrichment and Expansion

Use MHC Dextramer® to

- Isolate and enrich antigen-specific T cells for further *in vitro* characterization
- Stimulate T cells so that they expand more rapidly

Precision Immune Monitoring of the Patient Response



Use MHC Dextramer® or dCODE Dextramer® in flow cytometry or single-cell multi-omics:

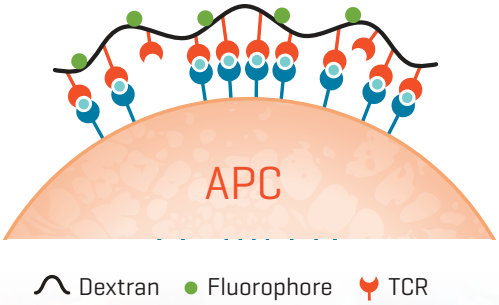
- Monitor kinetics and persistence of the infused T cells in patient blood samples
- Thoroughly investigate antigen-specific T-cell response to therapy
- Analyze T cell clones and their functional phenotypes
- Discover biomarkers predictive of response
- Investigate epitope spreading

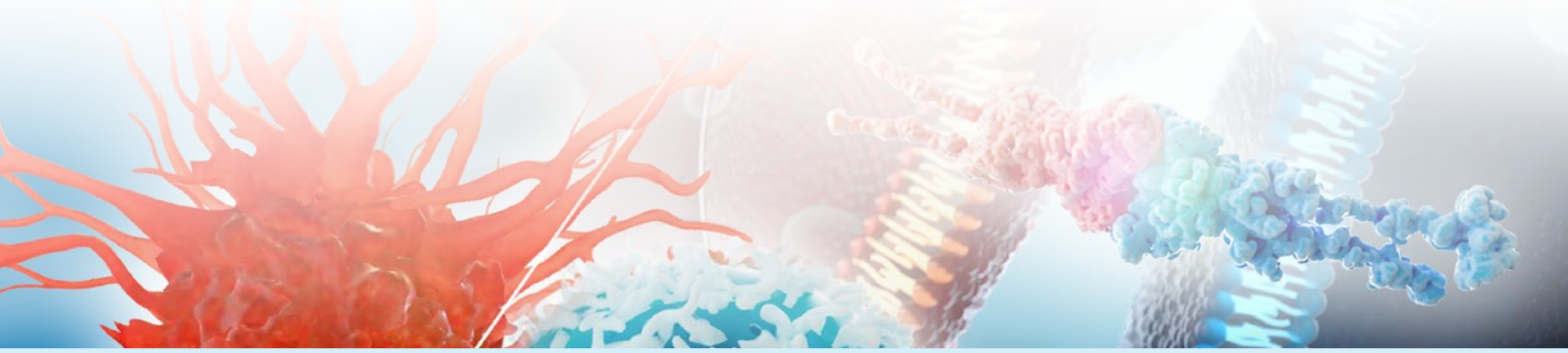
APC Detection

The detection and quantification of Antigen-Presenting Cells (APCs) is important to:

- Stratify and select patients with demonstrated expression of the target antigen
- Confirm if the target antigen is present predominantly in the target tissue, and thus avoid potential toxicity
- Monitor the presence of the target antigen and possible tumor escape

TCR Dextramer® binds to pMHC on antigen-presenting cells





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Further Reading

Read more about how Dextramer® technology is being applied in the development of T cell-based therapeutics.

Detection and quantification of T cells:
Rapoport *et al.* Nat Med (2015) 21(8):914-921.
doi: 10.1038/nm.3910

Walseng *et al.* Sci Rep (2017) 7(1):10713.
doi: 10.1038/s41598-017-11126-y

Proics *et al.* Gene Ther (2022)
doi: 10.1038/s41434-022-00358-x

Foy *et al.* Nature (2022) Nov 10;1-10.
doi: 10.1038/s41586-022-05531-1

Stevens *et al.* Authorea (2022).
doi: 10.22541/au.165727810.00978327/v1

Kinetics and persistence of infused cells:
Hong *et al.* Nat Med (2023) 29, 104–114.
https://doi.org/10.1038/s41591-022-02128-z

Detection of APCs with TCR multimers:
Zhu *et al.* J Immunol (2006) 176(5):3223-32.
doi: 10.4049/jimmunol.176.5.3223

TCR discovery:
Zhang *et al.* Sci Adv (2021) 7(20).
doi: 10.1126/sciadv.abf5835

TCR validation:
Silva *et al.* Front Immunol (2022) 13:896242.
doi: 10.3389/fimmu.2022.896242

Vazquez-Lombardi *et al.*
Immunity (2022) 55(10):1953-1966.e10.
doi: 10.1016/j.immuni.2022.09.004

Validation of specificity:
Bunse *et al.* Nat Commun 12, 240 (2021).
https://doi.org/10.1038/s41467-020-20488-3
Ma *et al.* Cytotherapy (2016) 18(8):985-994.
doi: 10.1016/j.jcyt.2016.05.001

Cross-reactivity screening:
Bentzen *et al.* Nat Biotechnol. (2018).
doi: 10.1038/nbt.4303

Yamarkovich *et al.* Nature (2021) 599(7885):477-484.
doi: 10.1038/s41586-021-04061-6

Resources

Cell Therapy

Explore how Dextramer® reagents support the development and manufacturing of effective cell therapies.

Learn more:*immudex.com/cell-therapy*

TCR Discovery

Explore how TCR discovery can advance the development of novel T-cell therapies.

Learn more: *immudex.com/tcr-discovery*

Case Studies and Application Notes

Immerse yourself in educational content exploring the applications of Dextramer® technology.

Learn more: *immudex.com/education*

TCR Solutions

- Soluble TCR Monomers
- TCR Dextramer®

Learn more: *immudex.com/tcr-solutions*

MHC Dextramer®

- Sensitive and reliable detection of antigen-specific T cells

Learn more: *immudex.com/dextramer*

Clinical-Grade (GMP) Dextramer®

- Extended battery of QC checks
- Established shelf-life

Learn more: *immudex.com/dextramer-gmp*

dCODE Dextramer®

- Analysis of antigen-specific T cells by NGS or single-cell multi-omics

Learn more: *immudex.com/dCODE*

MHC Monomers

- Ready-to-Use Monomers
- Peptide-Receptive Solutions

Learn more: *immudex.com/monomers*

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