## Understanding the T cell Repertoire in Autoimmune Diseases Using Highdimensional Single-cell Analysis of Antigen-specific CD4<sup>+</sup> and CD8<sup>+</sup> T cells

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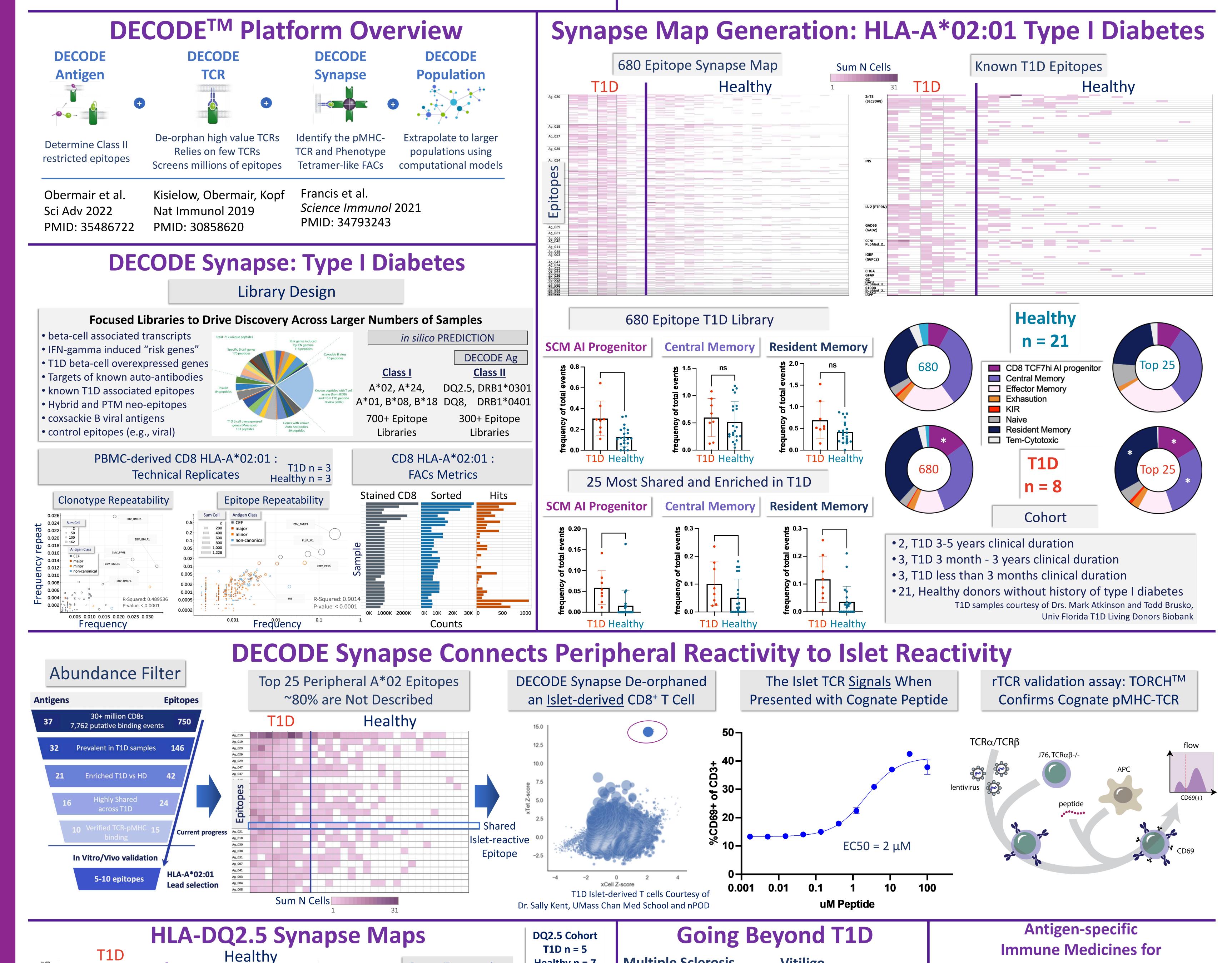
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## Introduction

- The DECODE<sup>TM</sup> platform integrates three technologies to discover disease-associated pMHC-TCR specificities and phenotypes
- DECODE Antigen experimentally determines peptides that are wellpresented by class II MHC in high-throughput
- DECODE TCR de-orphans or assesses the cross-reactivity of highvalue TCRs, such as tissue-derived TCRs, using thousands to millions of genetically encoded epitopes
- DECODE Synapse profiles reactivities and phenotypes of primary T cells using DNA barcoded multimers, FACs, and single-cell RNAseq

## Summary

- DECODE facilitates high-throughput pMHC-TCR identification across HLA Class I and II; when paired with phenotype, it yields "Synapse Maps"
- We developed Synapse Maps of HLA-A\*02:01 and class II risk alleles in Type 1 Diabetes, which include known and novel epitopes
- DECODE Synapse de-orphaned an A\*02-restricted islet-derived T cell and identified shared and enriched peripheral pMHC-TCR interactions
- DECODE is simultaneously being applied to Multiple Sclerosis and Vitiligo
- DECODE has the potential to identify the high impact antigens for generating antigen-specific immune therapies



**Multiple Sclerosis** 

Tx Naïve, New Onset RRMS

6 libraries, 3000+ Epitopes

Yale Univ

Dr. David Hafler

CSF and PBMC

Healthy n = 7

Th1-like

**Gene Expression** 

Thet

IFING

GATA3

IL13

IL13

IL13

IL13

IL13

BCL6

CXCR5

CD25

CD25

CD25

CXCR5

GZMH

GZMH

GZMH

GZMH

GZMH

GZMH

GZMH

GZMH

GZMH

GZNH

HAVCR2

STAT4

HAVCR2

ENTPD1

BATF

PDCD1

TIGIT

TIGIT

Clonotypes

**Vitiligo** 

**UMass Chan Med** 

Dr. John Harris

Skin and PBMC

7 libraries, 3000+ Epitopes

**New Onset** 

**Autoimmune Diseases** 

Target/APC

↓ Ag-specific Teff

↑ Ag-specific Treg

Ag-driven

Inflammatory-to-

**Tolerance Conversion**