

0888: TargetScan Platform Identifies Targets of CD8+ T cells in Ankylosing Spondylitis and Birdshot Uveitis

ACR Convergence 2025



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TScan is a fully integrated, clinical-stage, TCR-T cell therapy company

Proprietary discovery platform



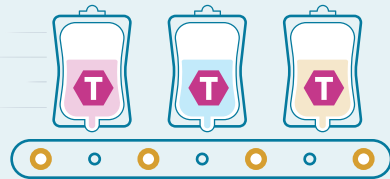
Rapid discovery of targets and TCRs

Clinical-phase oncology pipeline



Clinical-phase programs in heme and solid tumor malignancies

In-house GMP manufacturing



Transposon-based T cell engineering

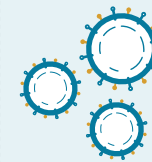
T-cell receptor
(TCR)



Broad therapeutic potential



Oncology

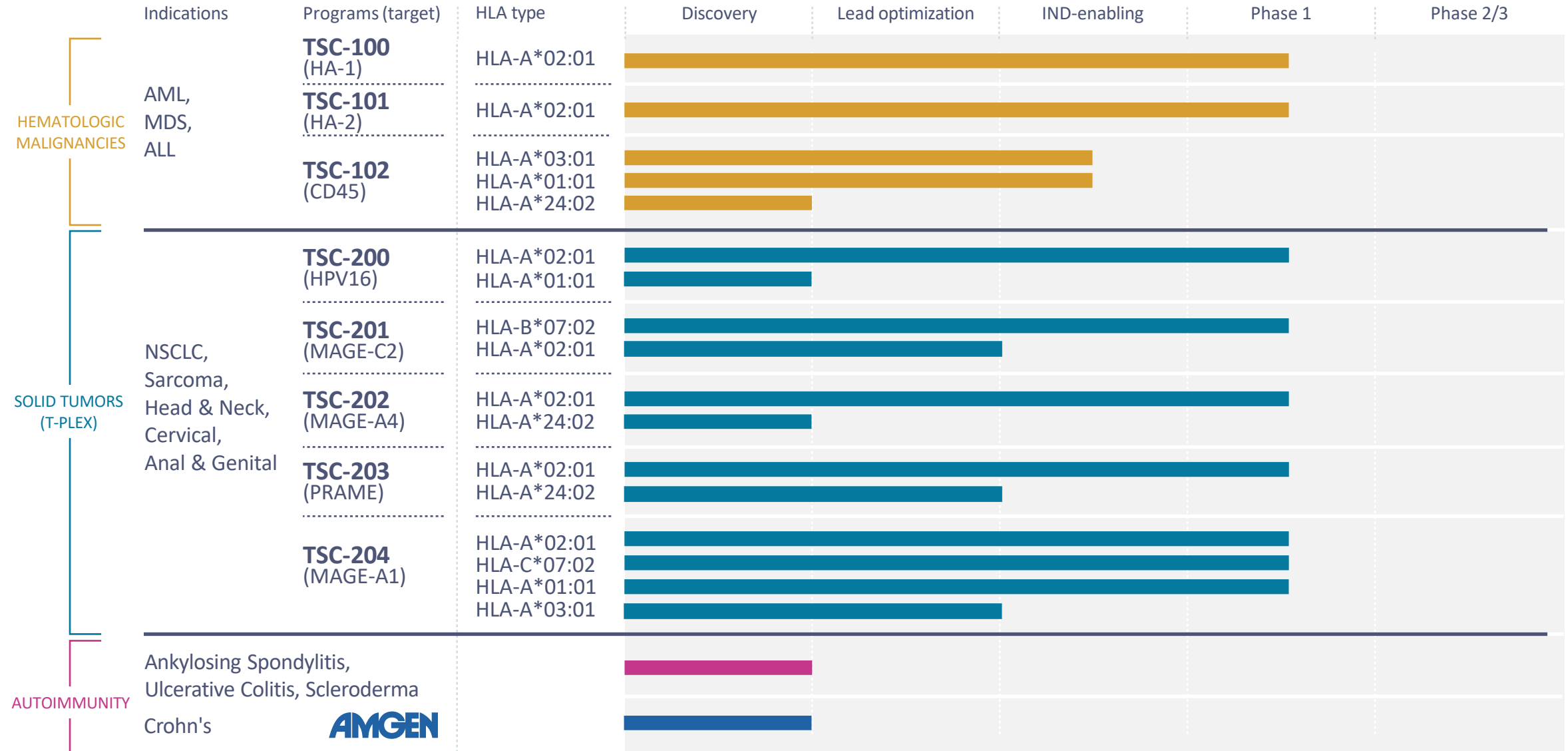


Infectious
disease

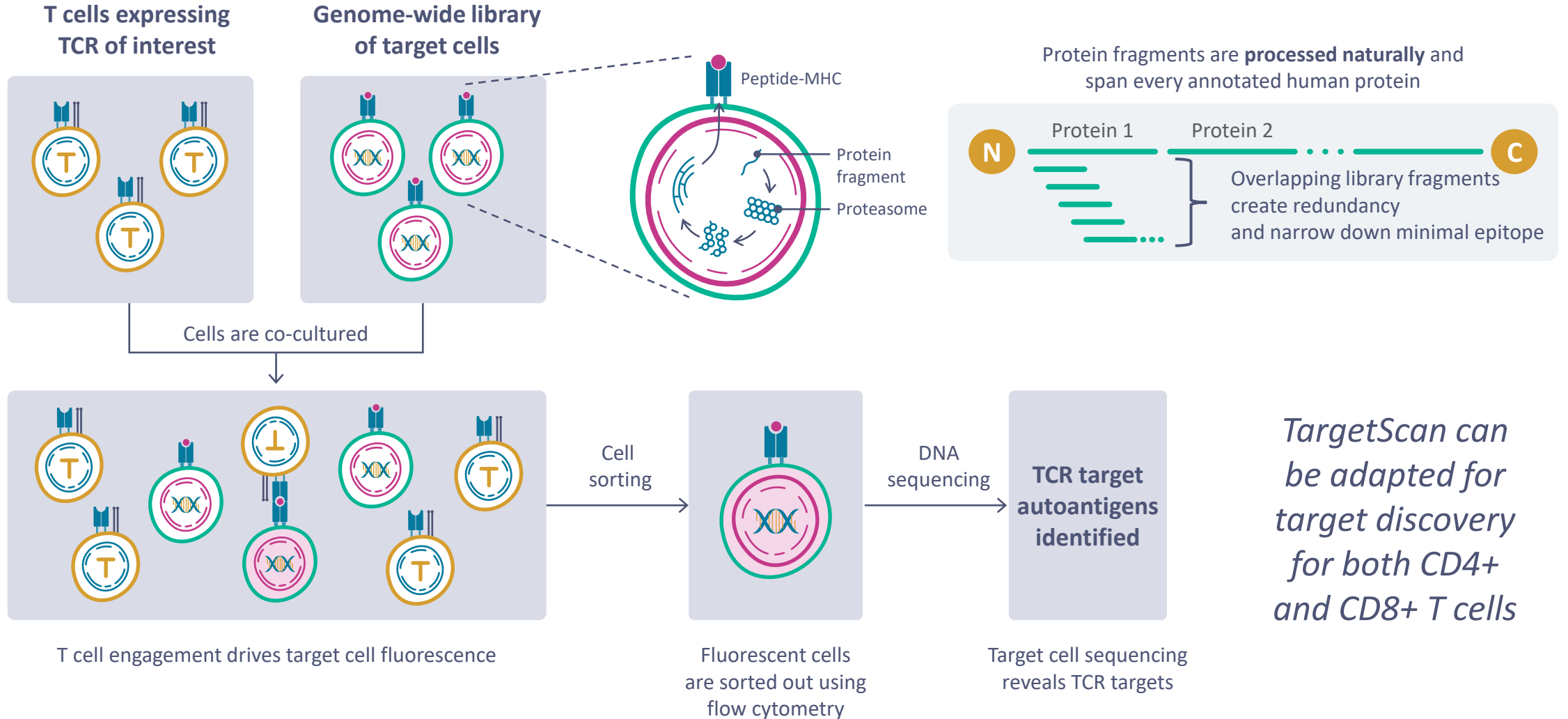


Autoimmune
disorders

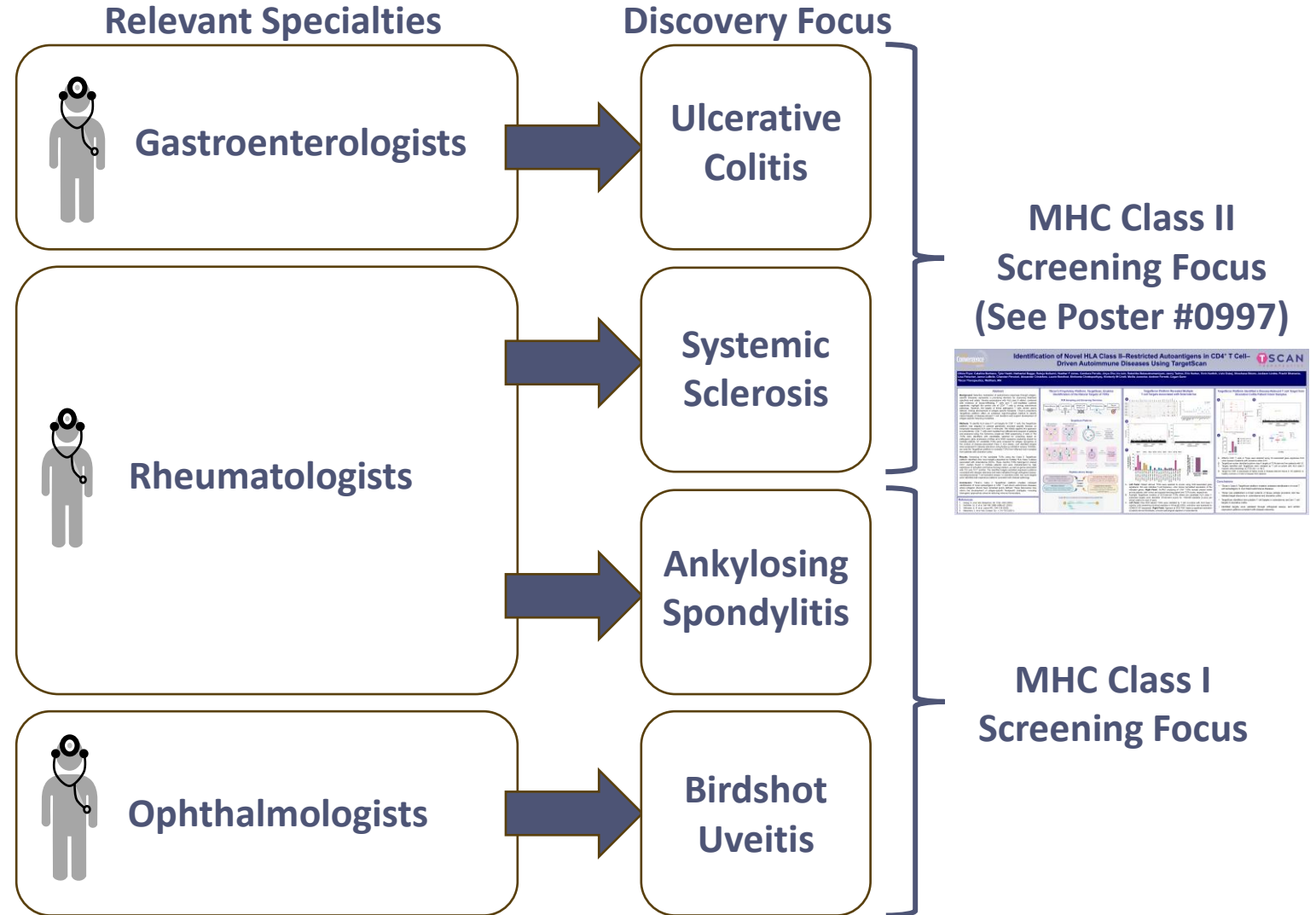
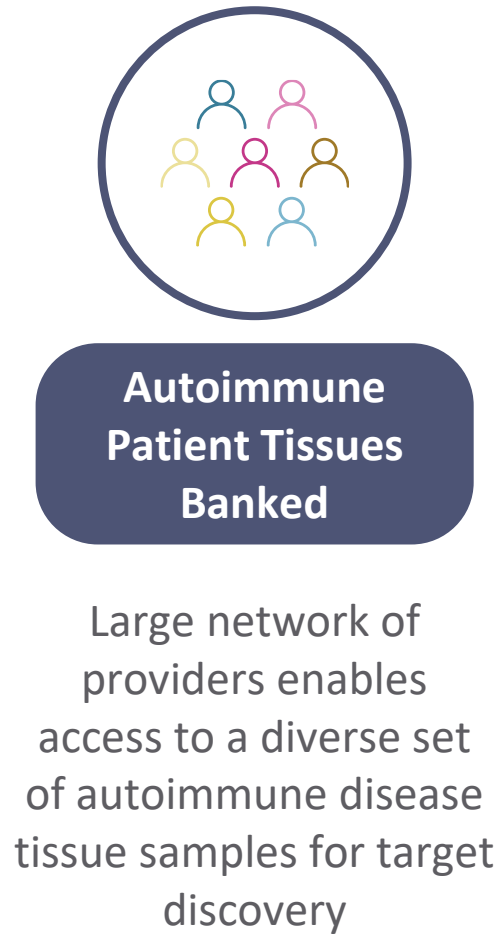
Nine TCR-T candidates in clinical development, with new TCR-Ts advancing



TargetScan enables the discovery of autoreactive T cell receptor targets



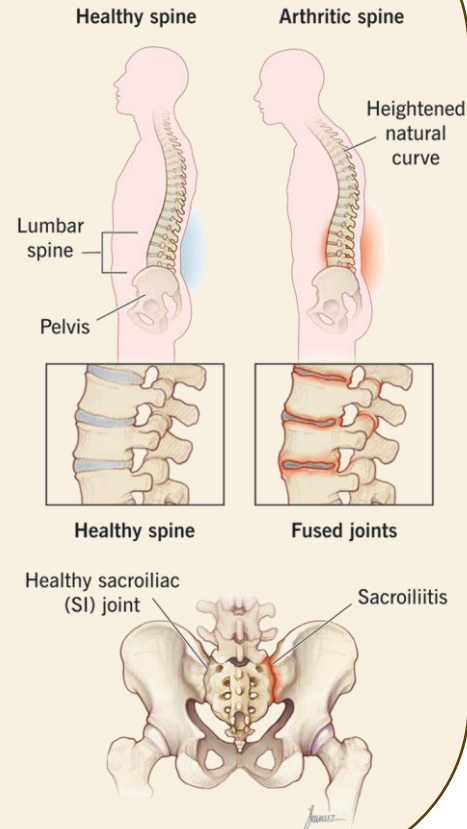
TScan has established a broad network of tissue sample providers for various autoimmune diseases and has initiated target discovery in focused indications



Initial target discovery is focused on ankylosing spondylitis and birdshot uveitis because of strong associations with HLA

Ankylosing Spondylitis (AS)

- Chronic inflammatory disease-causing back pain and spinal stiffness
- **90% of patients carry HLA-B*27:05**, suggesting shared antigenic targets
- CD8⁺ T cell involvement: Pathogenic **TCR motifs and TRBV9⁺ CD8⁺ T cell expansions** identified
- Current treatments: **anti-TNF, anti-IL-17, or JAK inhibitors**

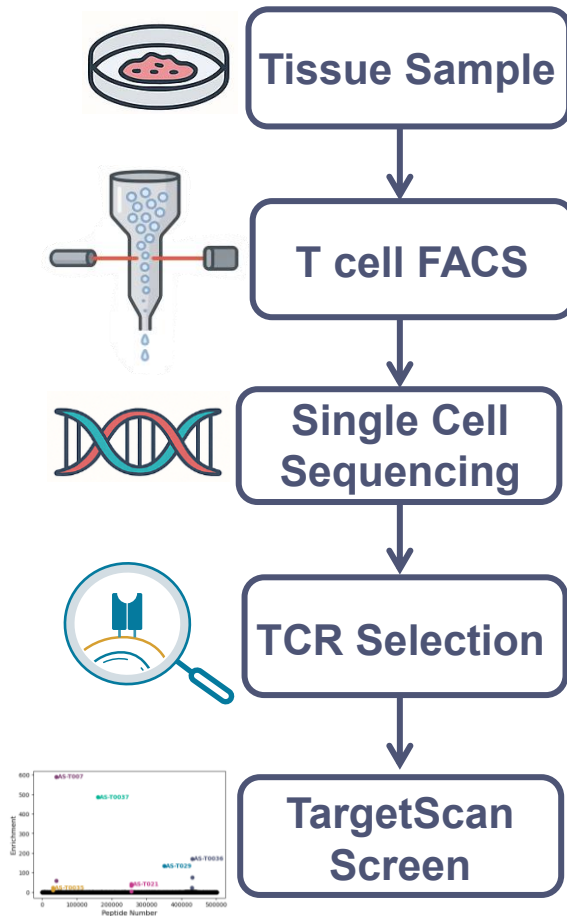


Birdshot Uveitis (BU)

- Loss of peripheral vision in advanced cases, floaters, blurred vision
- **85%–95%** of affected patients carry the **HLA-A*29:02** haplotype
- Strongly implicates **CD8⁺ T-cell** activation. **Th1-like** profile drives inflammation
- Current treatments: anti-TNF, anti-IL-6, corticosteroids and immunosuppressants



TCRs were sourced containing a well-characterized TCR sequence motif associated with AS pathology



TCR Selection

- Clonally expanded CD8⁺ T cells carrying the TRBV9⁺ gene segment are enriched in blood, joints and eyes of AS patients^{1,2,3}

AS-associated TCR Motif²

TCRalpha CDR3

AV21	CAVSLGTGAGSYQLF	-AJ28
AV21	CAVSSPQGGSEKLVE	-AJ57
AV21	CAVLSPVQETSGSRLTF	-AJ18
AV21	CAVSNFNKFYF	-AJ21

TCRbeta CDR3

BV9	CASSVGL	YSTDTQ	BJ2-3
BV9	CASSVGL	YSTDTQ	BJ2-3
BV9	CASSVGL	FSTDTQ	BJ2-3
BV9	CASSVAT	YSTDTQ	BJ2-3

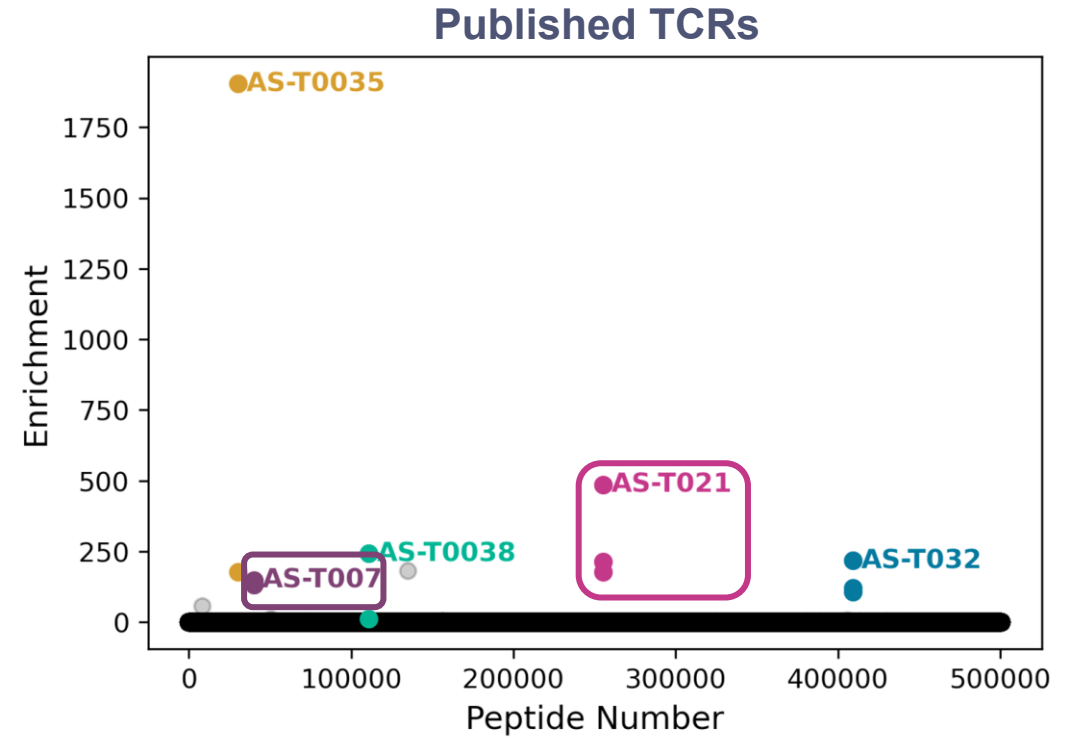
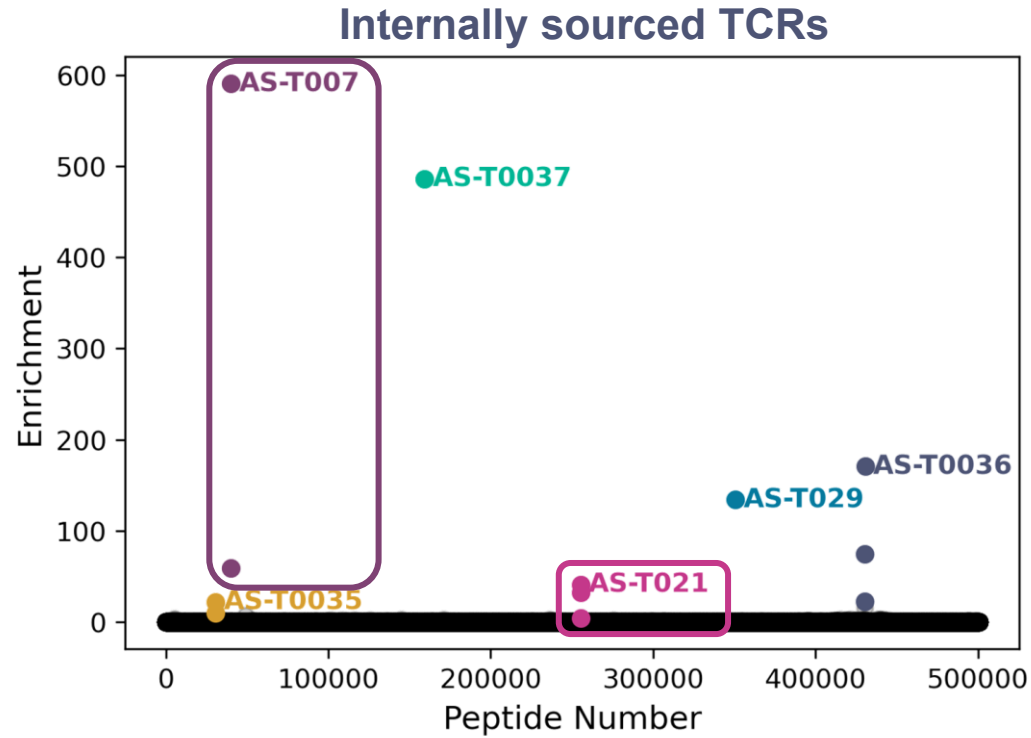
- Targeted depletion of T cells with this motif is a proposed therapy for AS³
- TScan has identified TCRs with this motif from internally acquired samples, and has screened TCRs carrying this motif from published sources

¹Faham, M. *et al. Arthritis Rheumatol.* **69**, 774–784 (2017).

²Yang, X. *et al. Nature* **612**, 771–777 (2022).

³Britanova, O. *et al. Nat Med* **29**, 2731–2736 (2023).

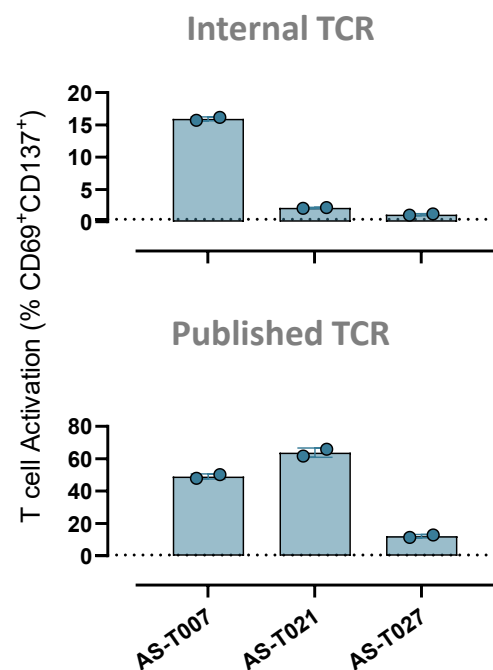
TargetScan identified novel targets recognized by TCRs with AS-associated sequence motif



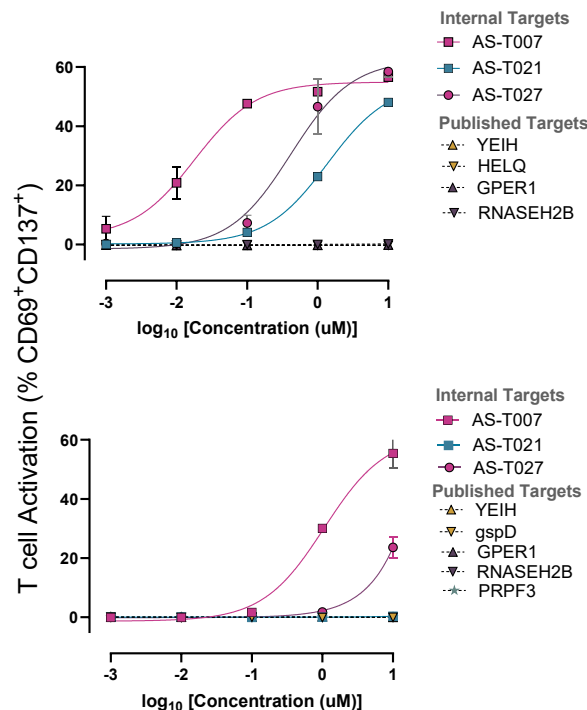
TargetScan screens identified 38 targets that were not previously described

Identified targets are shared across patients and have biologic links to AS pathology

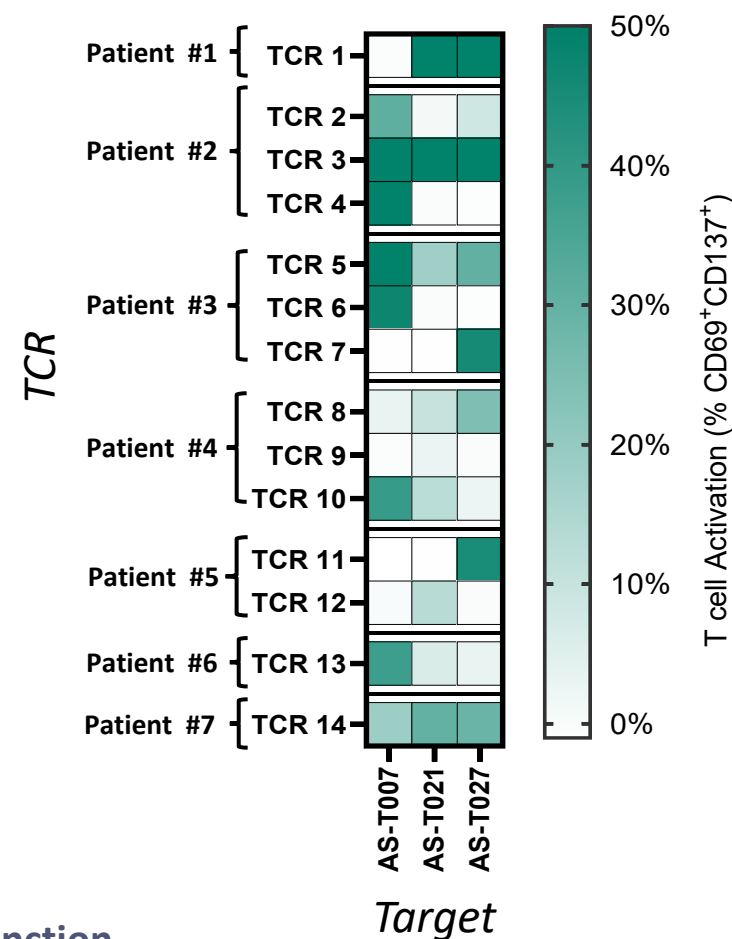
Reactivity to full-length protein



Reactivity to minimal epitopes

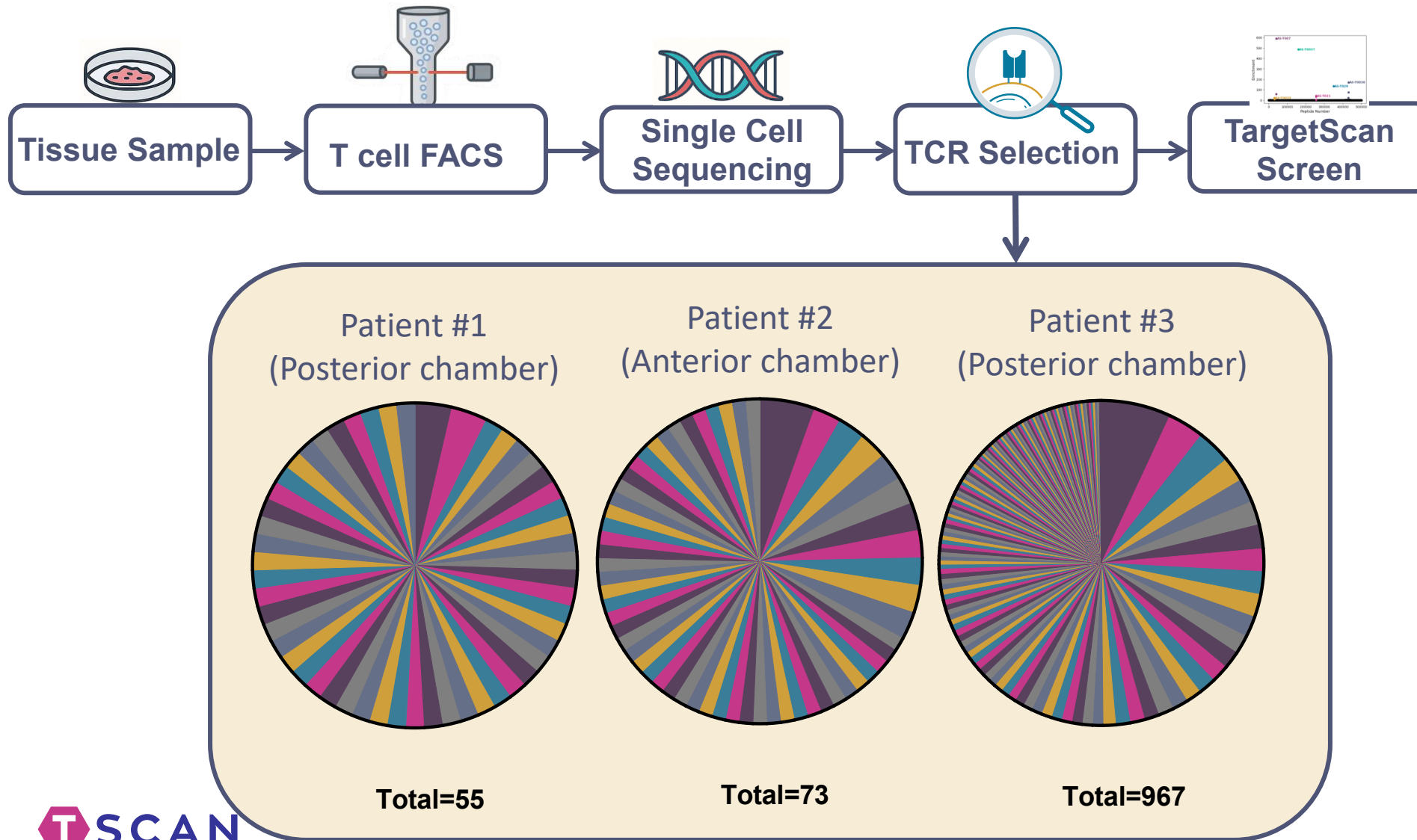


Reactivity across patients



- **AS-T027 epitope shares 100% homology** with a protein from the AS-associated commensal bacteria *Klebsiella pneumoniae*
- **AS-T007 and AS-T021** shape the extracellular matrix and are expressed in chondrocytes with known **association to axial skeletal and connective tissue function**

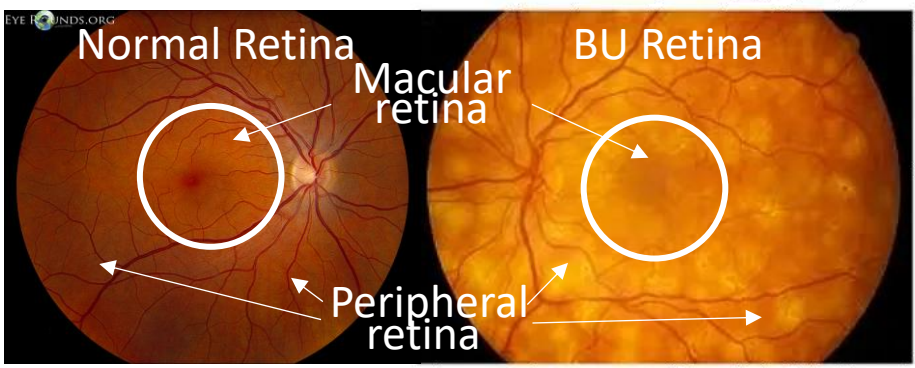
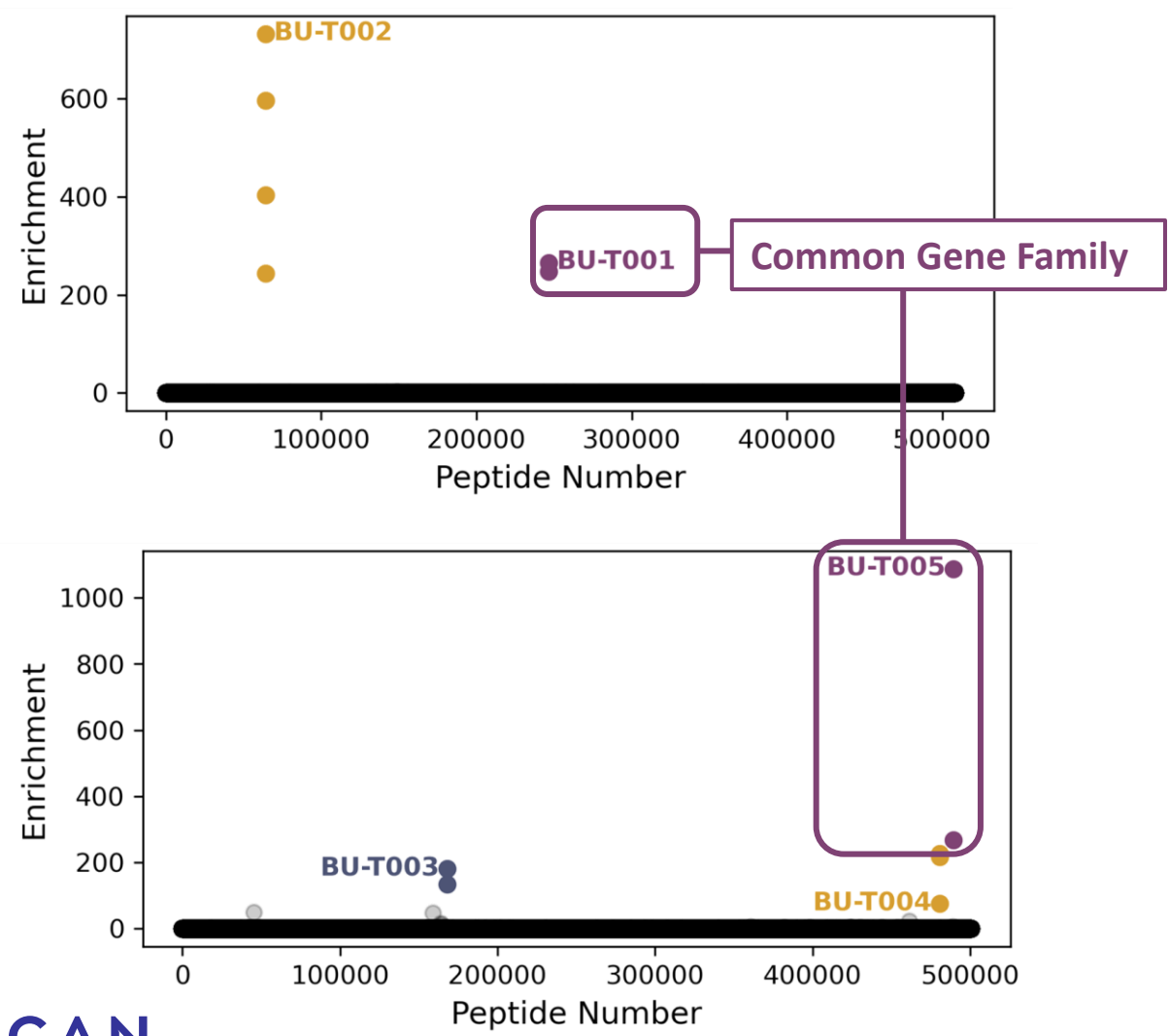
TCRs from BU inflamed eye samples were screened using TargetScan



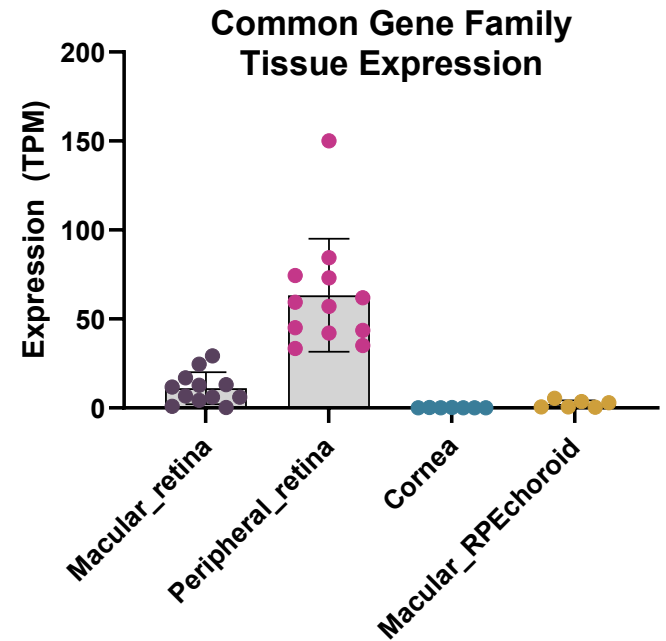
Few TCR clones are obtained from eye fluid samples

TCRs are prioritized using abundance in the sample

TargetScan identified a family of genes recognized by TCRs from inflamed BU eye tissue



Peripheral retina adjacent to vasculature are more commonly affected in BU



Conclusions

- TScan's proprietary platform, TargetScan, enables the unbiased identification of novel T cell autoantigens for both MHC Class I and Class II presented T cell antigens
- TScan has established a broad network of tissue sample providers for various autoimmune diseases, and has initiated target discovery in ankylosing spondylitis and birdshot uveitis, class I associated autoimmune diseases
- Identified targets in AS are shared across patients and have biologic links to AS pathology
- Many identified targets in BU belong to the same gene family, a family expressed in relevant eye tissue

Acknowledgements

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Tissue sample providers

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