Harnessing the Adimab platform: Case studies exemplifying our path from de novo discovery to clinical advancement

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BACKGROUND

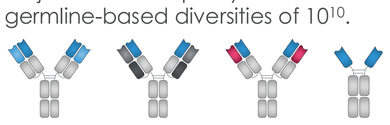
Adimab's discovery and optimization platform excels in identifying diverse, highly specific, and developable antibody panels. With over 15 years of expertise, Adimab's technology has been successfully leveraged on more than 600 therapeutic antibody campaigns with over 130 partners.

130+	600+	80+	5
Pharma/Biotech Partners	Therapeutic Programs	Clinical Advancements	*Commercial Products

ADIMAB'S DISCOVERY AND OPTIMIZATION PLATFORM

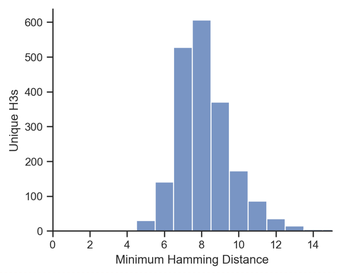
Adimab libraries:
Synthetic full-length IgG and HCAb libraries in highly engineered Adimab yeast strain

Projects use multiple synthetic **human** germline-based diversities of 10^{10}.



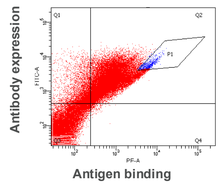
IgG-κ IgG-λ IgG-cLC HCAb

These libraries are highly **diverse** as shown by the Hamming distance from a random sampling of 2000 H3s from Adimab's IgG-based libraries.

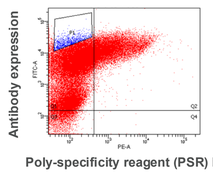


FACS selections:
FACS sorting is performed to obtain populations with desired therapeutic profiles.

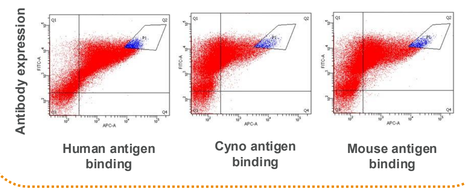
Affinity:



Developability:

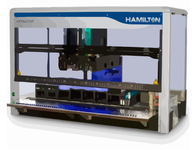


Species cross-reactivity:

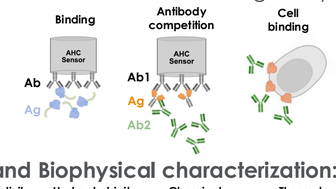


Sequencing, Production, and Characterization:
Adimab completes all aspects of the project from sequencing isolates to the production of all unique full length IgGs in the same production host. All biochemical and biophysical characterization data and purified protein is delivered to our partners.

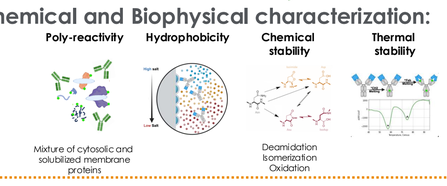
Production:
Thousands unique IgGs are produced in a week at scales from 20 ug to 1 mg



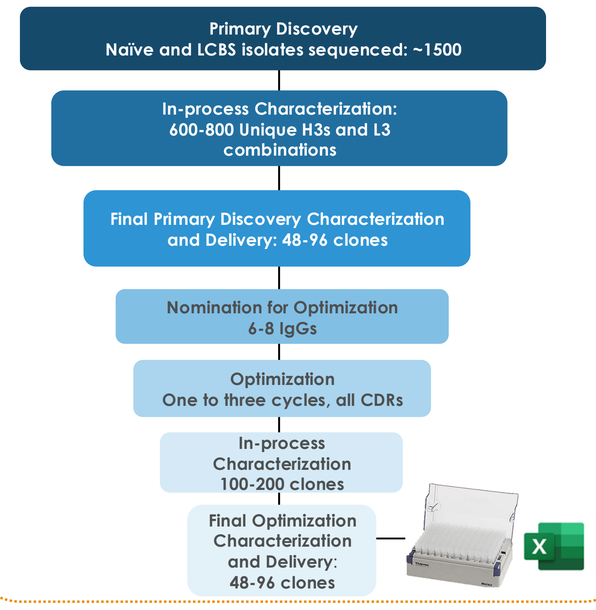
Specificity Assessments:
Multiple kinetics and cell-based binding assays



Biochemical and Biophysical characterization:



Primary Discovery and Optimization Workflow:
Adimab's process is rich in data with a primary delivery of ~100 diverse IgGs after 3.5 months. 6-8 nominees can be selected for optimization after functional testing for further affinity maturation and specificity optimization.

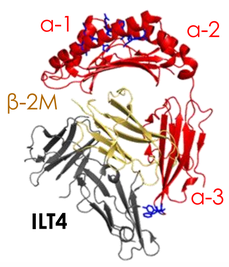


***Commercial products:** Sintilimab (Tyvyt) // Pemivibart (Pemgarda) // Tafolecimab (Sintbilo) // Equecabtagene autoleucel (Fucaso) // Cosibelimab (Unloxcyt)

DISCOVERY AND OPTIMIZATION OF CLINICAL MOLECULE TTX-080

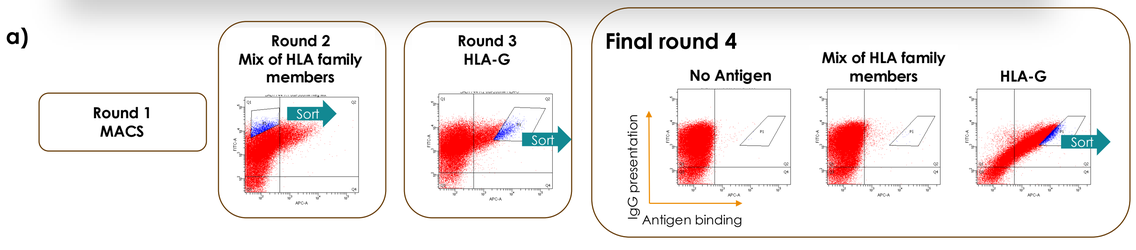
Tizona Therapeutics' TTX-080 molecule is highly specific for HLA-G, blocks ILT2 and ILT4, and does not bind other class I MHC molecules. **ILT4** binding residues differ from other class I MHC molecules by only **two** residues

TIZONA THERAPEUTICS



	193	194	195	196	197	198
HLA-G	P	V	**F**	D	**Y**	E
HLA-A1	P	I	S	D	H	E
HLA-A2	A	V	S	D	H	E
HLA-B7	P	I	S	D	H	E
HLA-B35	P	V	S	D	H	E
HLA-CW7	P	L	S	D	H	E

Adimab's discovery and optimization process for TTX-080



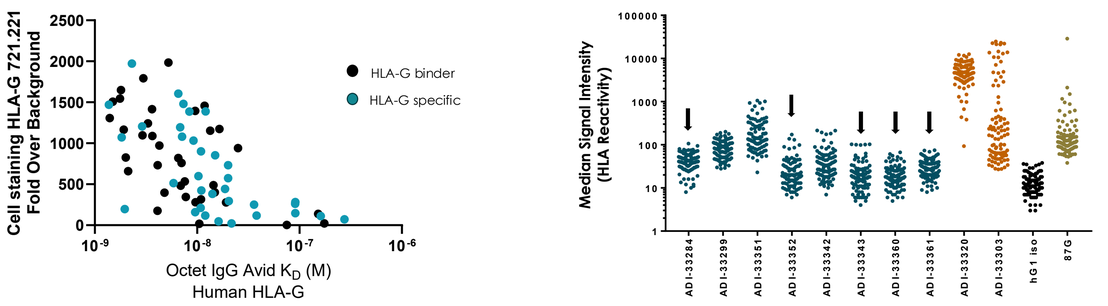


Figure 1: a) Enrichment of specific HLA-G binding population with minimal binding to a mix of HLA family members led of a delivery of 70 HLA-G binding IgGs, all exhibiting good developability. **b)** 34 delivered IgGs were HLA-G specific (teal). **c)** 8 passed the LabScreen specificity test against 94 off-target HLAs, from which 5 IgGs were nominated for optimization (black arrows).

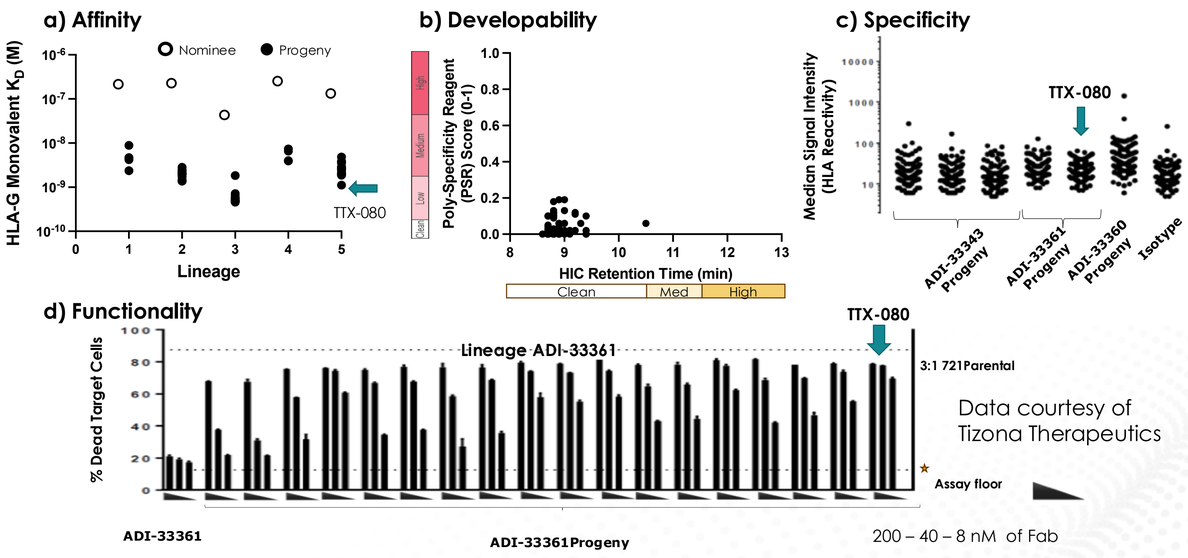


Figure 2: Optimization libraries for 5 nominated clones were diversified across all CDRs. Selections were performed for specificity (negative selection against HLA mix) and affinity for HLA-G. Progeny showed improved **a)** affinity, **b)** good developability, and **c)** specificity in LabScreen test against 94 HLAs. **d)** ILT2 HLA interaction leads to cell killing suppression with progeny exhibiting improved blocking of the cell killing suppression.

DISCOVERY AND OPTIMIZATION OF CLINICAL MOLECULE SOLNERSTOTUG

Sensei's solnerstotug molecule is a pH-dependent binder for VISTA with strong binding at pH6 and no binding at pH7.4. Solnerstotug blocks PSGL-1 interaction the key receptor regulating VISTA's immunosuppressive activity.

sensei BIO

Adimab's discovery and optimization process of Solnerstotug

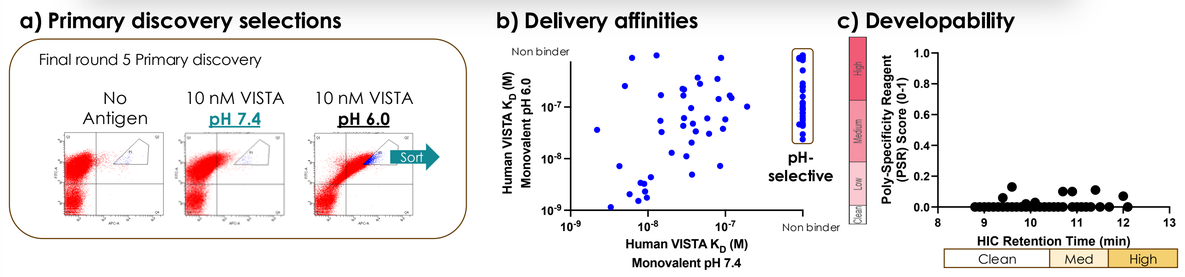


Figure 3: a) Adimab libraries were interrogated for binding to human VISTA applying pH pressure to isolate pH selective IgGs with better binding at pH 6.0 versus 7.4. **b)** 81 IgGs were delivered with 36 exhibiting pH selectivity. **c)** All IgGs had good developability. Sensei nominated 8 clones based on PSGL-1 blocking on activated CD4 T cells.

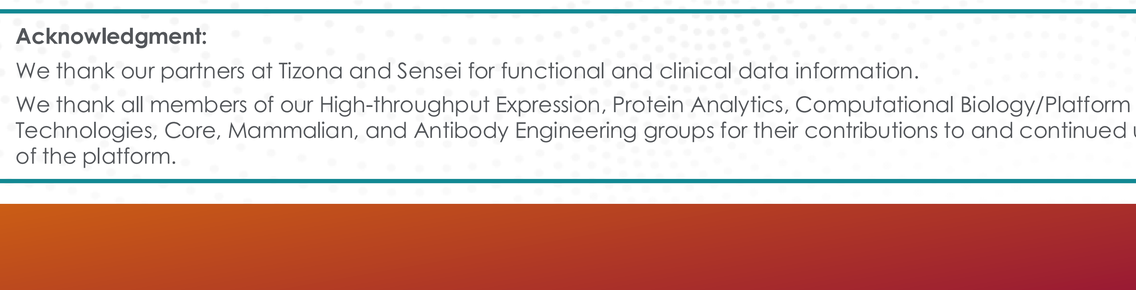
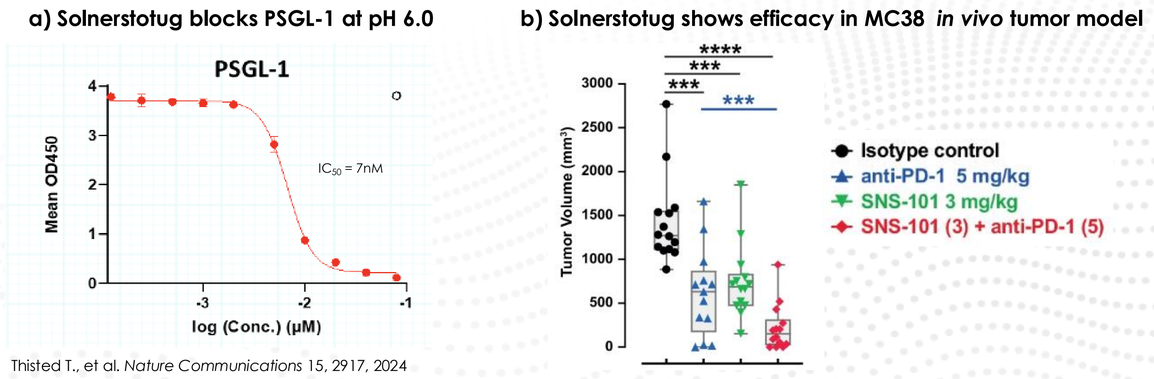


Figure 4: Optimization for affinity and pH dependency for multiple lineages lead to, **a)** improved affinity and pH selectivity for three lineages (Open circles nominated parents, closed circles progeny). **b)** One progeny from ADI-55873 lineage became solnerstotug and exhibited the desired pH dependency.



Thisted T., et al. *Nature Communications* 15, 2917, 2024

Figure 5: a) Solnerstotug blocks PSGL-1 binding to VISTA at pH6, **b)** has high efficacy in in vivo tumor models. Solnerstotug is currently in Ph I/II clinical trials.

Acknowledgment:

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