NOVEL ANTI-CD3 HEAVY CHAIN-ONLY ANTIBODIES FOR USE IN T CELL-ENGAGING THERAPEUTICS

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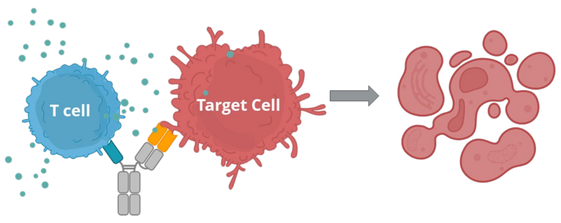
ADIMAB

INTRODUCTION TO T CELL ENGAGERS

T cell engagers (TCEs) are an increasingly validated class of multispecific antibodies. Through pairing an arm targeting CD3 with an arm targeting a tumor associated antigen, the TCE forces the T cell and tumor cell into close proximity, triggering T cell activation leading to tumor cell killing[1].

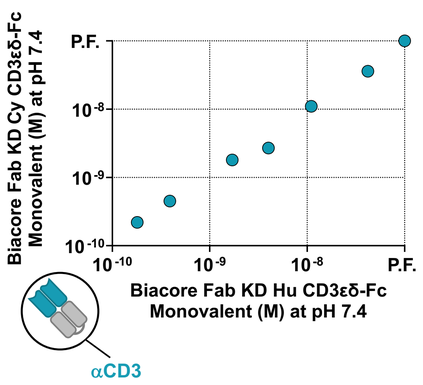
- Eleven TCEs are currently FDA approved
- TCEs can be engineered in multiple bi- and multispecific formats. Activation level can be influenced by format[1]

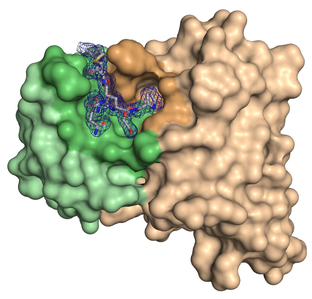
T cell engagers enable killing of target cells



ADIMAB a-CD3 CONVENTIONAL IgG LINEAGE: HUMAN x CYNO CROSS-REACTIVTY AND TUNABLE POTENCY

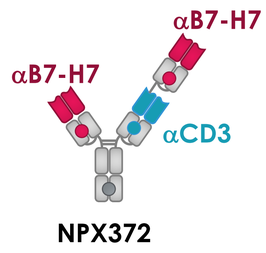
Adimab's aCD3 IgG/FAb/scFv panel spans a wide range of affinities and has hu-cyno cross-reactivity





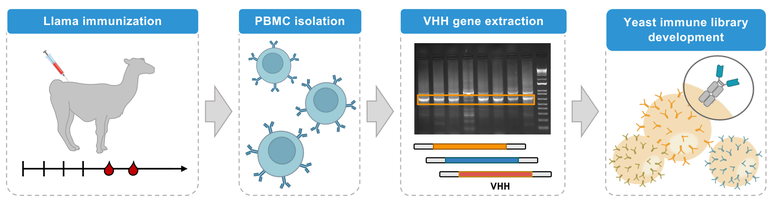
Adimab partner NextPoint progressing NPX372 into the clinic

- Incorporates Adimab aCD3
- B7-H7 binder from Adimab discovery platform

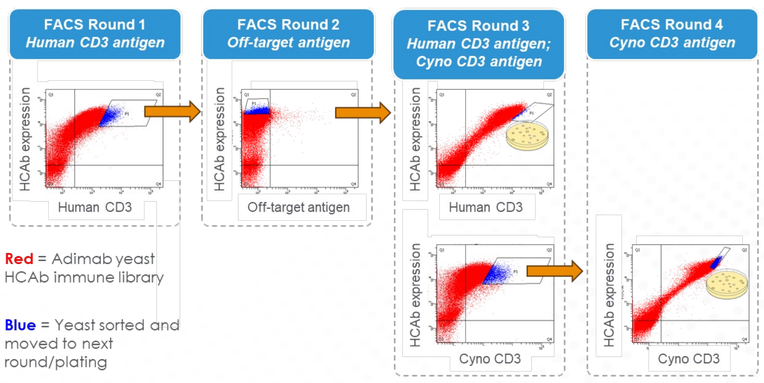


EXPANDING ADIMAB'S CD3 BINDERS: HCAB DISCOVERY

Libraries built from llamas immunized against CD3

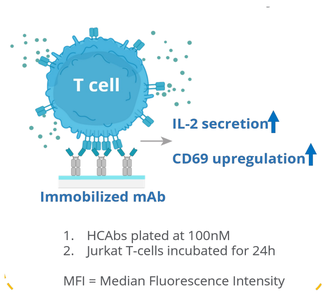


Rounds of selections performed on the Adimab yeast immune libraries to isolate aCD3 HCAbs with desirable properties



STIMULATING aCD3 HCABS DISCOVERED WITH FAVORABLE DEVELOPABILITY

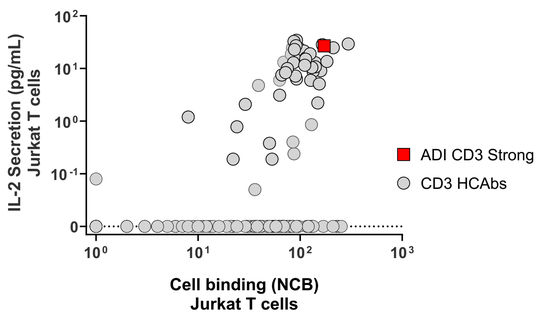
T cell stimulation assay



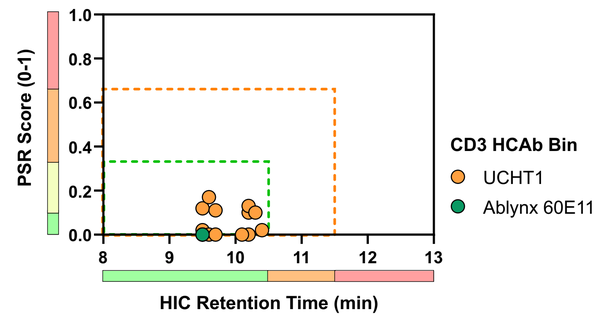
1. HCAbs plated at 100nM
2. Jurkat T-cells incubated for 24h

MFI = Median Fluorescence Intensity

~10% of discovered HCAbs stimulate T cells

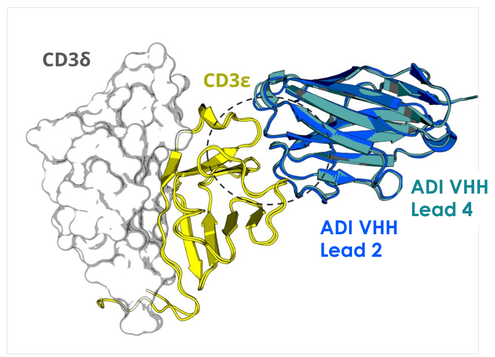


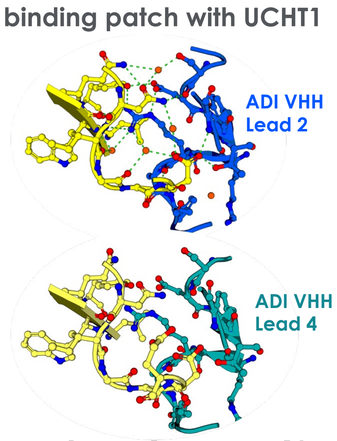
Stimulating HCAbs have favorable developability



VHH CRYSTAL STRUCTURES DEMONSTRATE BINDING TO CD3δε

Humanized ADI VHH Leads have overlapping binding patch with UCHT1

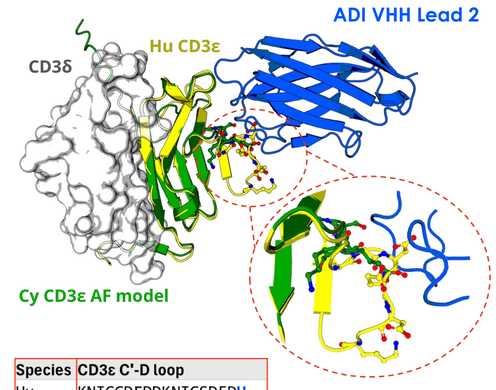




mAbs	B-C	C	C'			C'-D							D		F	F-G					
UCHT1	E35	L37			N44	I45	G46	G47	D48	E49		K52	S56	D57	Y78	R80	G81	S82	K83	P84	E85
ADI Lead 4	E35	L37		K43	N44			G47	D48	E49	D50		S56		Y78	R80	G81	S82	K83	P84	
ADI Lead 2	E35	L37	Q39		N44			G47	D48	E49	D50		S56		Y78		G81	S82	K83	P84	

contact residues

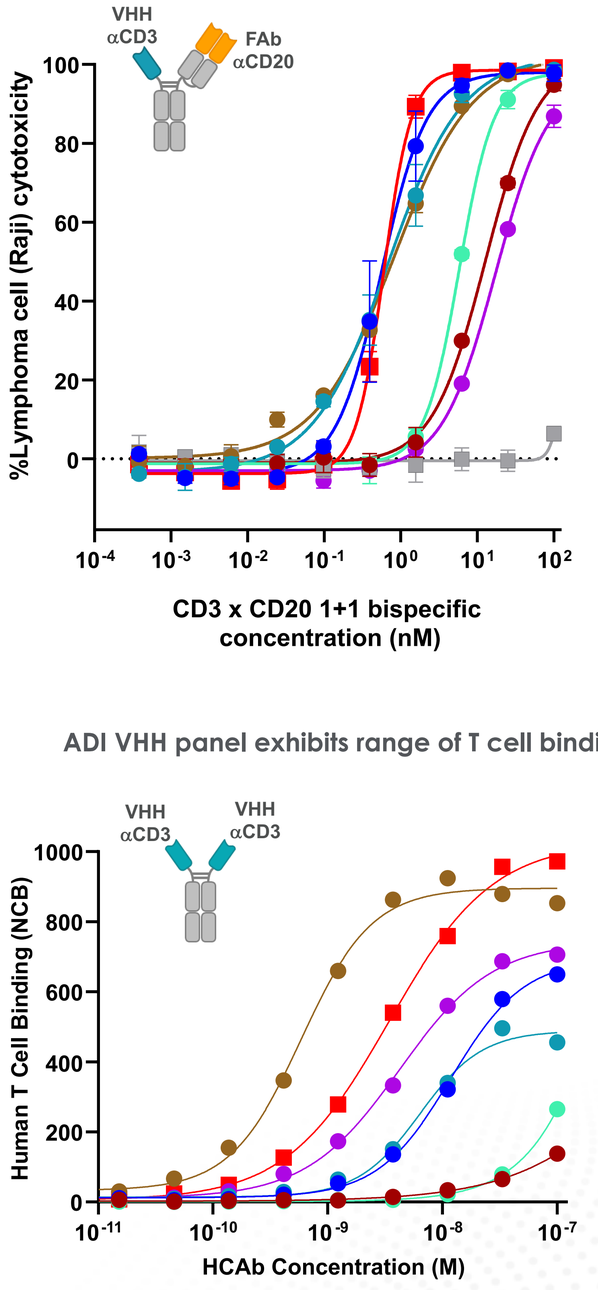
ADI VHH Leads are specific to Hu CD3ε



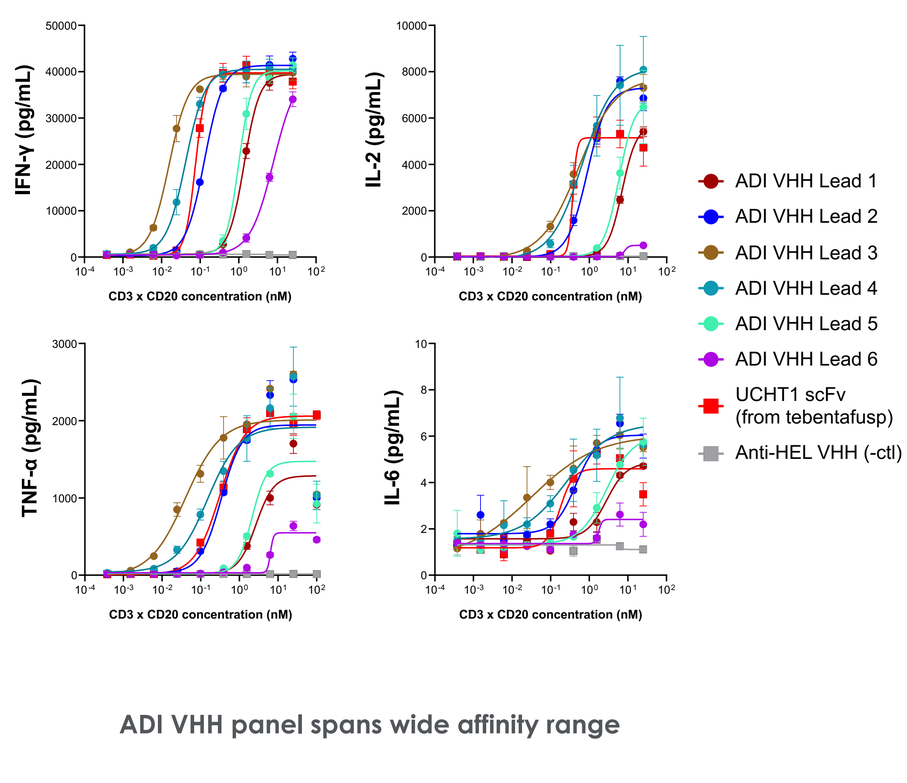
Species	CD3ε C'-D loop
Hu	KNIGGDEDDKNIGSDEDH
Cy	KN---KEDSG------DR
Rh	KN---KEDSG------DR

aCD3 T CELL ENGAGERS SHOW FUNCTIONAL ACTIVITY IN MULTIPLE FORMATS

CD3 VHH x CD20 bispecific TCEs elicit killing

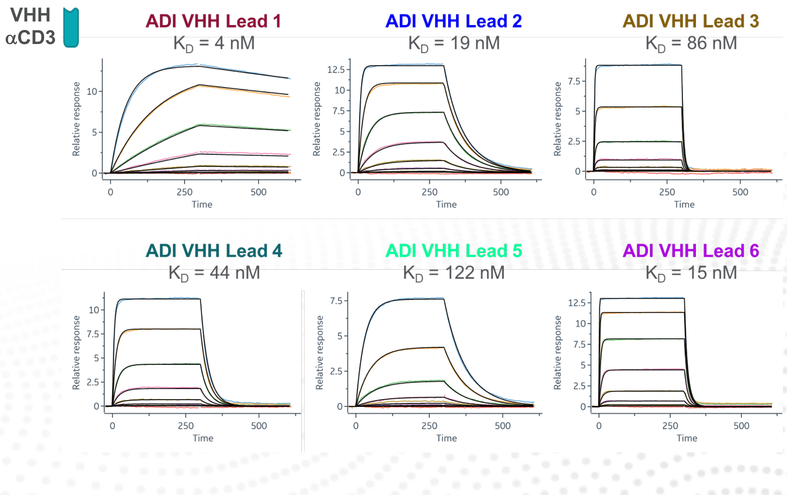


Cytokine secretion correlates with killing potency



ADI VHH panel exhibits range of T cell binding

ADI VHH panel spans wide affinity range



SUMMARY

- CD3 VHHs reduce the manufacturing complexity of TCEs
- Adimab's VHHs have functional activity comparable to clinically validated TCEs in both IgG bispecific and TCR fusion formats
- Crystal structures obtained for two of the leads show over an overlapping binding patch with UCHT1
- CD3 VHHs are accessible as part of Adimab's non-exclusive TCE offering

PARTNER AND DISCLOSURE

Please reach out to our Business Development department at bd@adimab.com.

The QR code on the right links to Adimab posters and other resources.

The presenting author has no conflicts of Interest to declare.