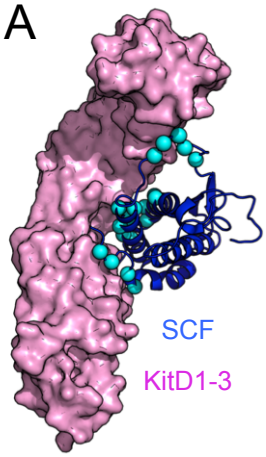
A

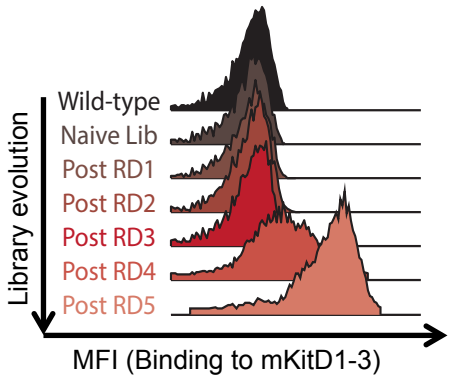


First-generation contact library:

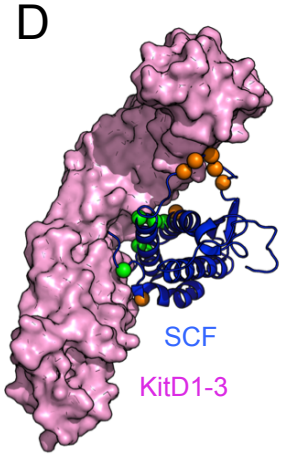
Theoretical diversity = 2.8×10^{13}

G5	S,T,A,G (RST)	K81	K,I,T,R (ANA)
N6	H,Q,N,K,D,E (VAW)	D84	H,Q,N,K,D,E (VAW)
T9	T,N,D,A (RMA)	D85	H,Q,N,K,D,E (VAW)
D10	H,Q,N,K,D,E (VAW)	V87	I,L,V,F (NTT)
I50	I,R,V,G (RKA)	L88	L,F,Y,H (YWT)
L54	I,L,V,F (NTT)	N97	H,Q,N,K,D,E (VAW)
T57	T,N,D,A (RMA)	I98	I,L,R,S (MKT)
L60	I,L,R,S (MKT)	K99	K,N,Q,H (MAW)
D61	H,Q,N,K,D,E (VAW)	E100	H,Q,N,K,D,E (VAW)
D77	H,Q,N,K,D,E (VAW)	R104	R,H,P,L (CNT)

B



D



Second-generation affinity maturation library:

Theoretical diversity = 4.4×10^{12}

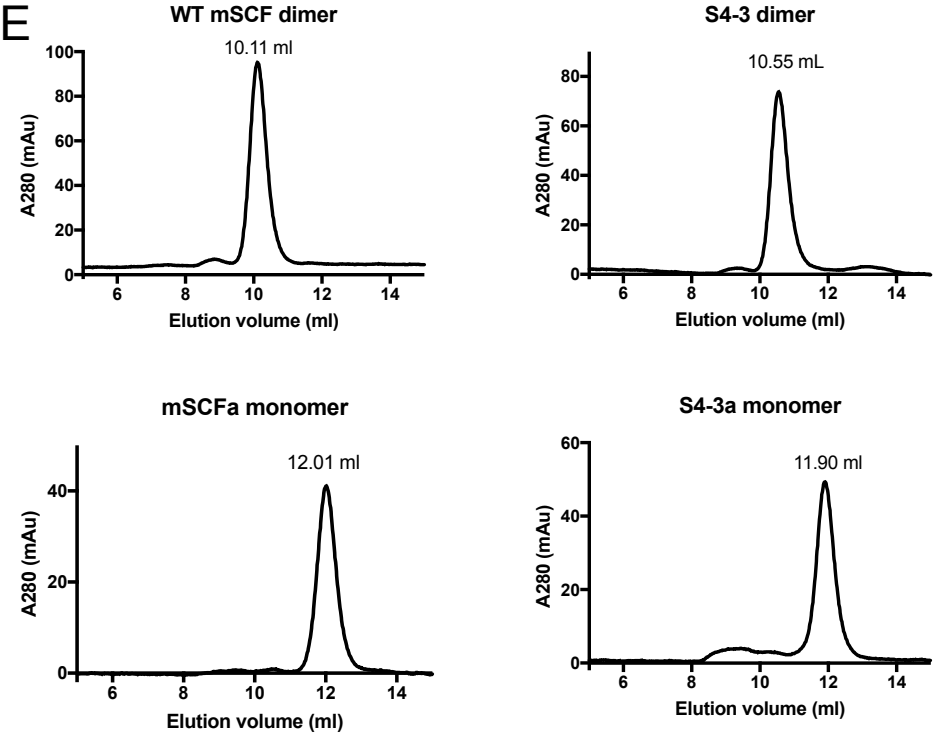
N6	D(GAT)	V87	F,I(WTT)
D10	Random(NNK)	L88	Y,F(TWT)
L54	Random(NNK)	N97	Random(NNK)
T57	E(GAA)	I98	Random(NNK)
D61	Random(NNK)	K99	Random(NNK)
D77	H(CAT)	E100	Random(NNK)
K81	I(ATT)	R104	Random(NNK)

C

First-generation sequence analysis

	WT	C5-1	C5-5	C5-7	Consensus
5	G		A		
6	N	D	D	D	D
10	D	E		E	
50	I	G			
54	L	V		F	
57	T	E	E	E	E
60	L		I		
61	D	N	E	E	
77	D	H	H	H	H
31	K	I	I	I	I
37	V	F	I	F	F/I
38	L	Y	Y	F	Y/F
97	N	E	E	Q	
98	I		L	L	
99	K	H		Q	
00	E	N	H	N	
04	R		L	L	

E



F

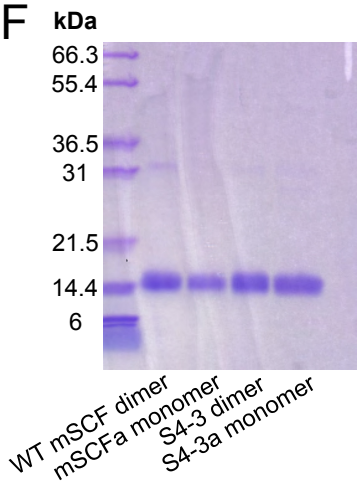


Figure S1