ChemPartner
Dedicated to LifeScience

PHAGE DISPLAY

Royalty Free, Fully Human Therapeutic Antibody Discovery from our Proprietary Naive Phage Display

- Proprietarily constructed scFv naïve library with diversity ~10^11
- Built with predefined V-gene composition to match the human immune repertoire
- All V-gene families are individually cloned and assembled to maximize library diversity and reduce gene bias due to PCR cloning
- Customized library selection and screening for special targets and epitopes, including cell-based panning
- Rapid ranking of library selection outputs with high throughput robotics

Antibody Discovery from Naive Library

Solid and liquid-phase panning

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ELISA test >2000 clones crude scFv preperation

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100-300 top positive binders Blocking, FACS, Biacore

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30-50 IgGs produced Binding and Bioassays

↓

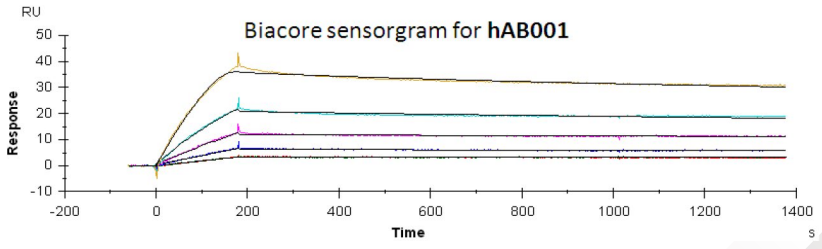
2-3 best candidates (optional optimization step)

Case Study

Top clones showed double-digit pM binding affinity after converting to full-length IgG (determined by Biacore)

Antibody Code	k_a (1/Ms)	k_a (1/s)	K_D (M)	Cell Proliferation Assay IC_{50} (nM)
hAB001*	1.726E+7	2.495E-4	1.446E-11	0.04
hAB002	7.565E+7	2.366E-3	3.128E-11	0.08
hAB003	4.694E+7	1.015E-3	2.162E-11	0.14
hAB004	1.297E+8	1.647E-3	1.270E-11	0.05
hAB005	5.350E+7	1.196E-3	2.235E-11	0.25
hAB006	4.815E+7	2.193E-3	4.556E-11	3.51
hAB007	3.204E+6	8.959E-5	2.796E-11	1.15

*Top candidate hAB001 has been chosen by the client for preclinical animal studies



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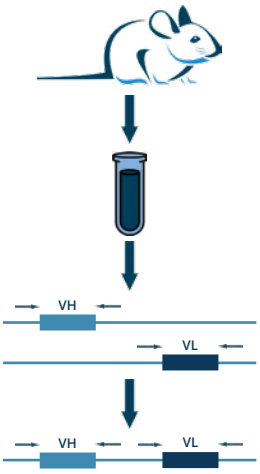
Phage Display

Phage Library Construction from Immunized Repertoires



Potential advantages of immune library strategy vs. hybridoma

- High throughput: up to 10^8~9 library size
- Non-rodent animal mAb discovery
- Sequences immediately obtained
- Enrichment of desired hits by negative selection/panning
- Randomization of VH and VL pairs: more diversity

Case Study of Antibody Discovery from Immune Library

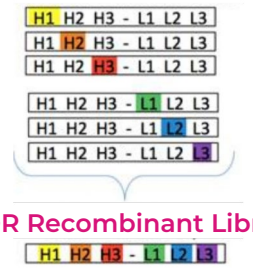
- Heterodimer receptor hXaYb antibody discovery project from a big pharma
- Construction of library with size > 10^8 from protein, cell, and gene immunization
- 3 rounds of cell based panning using hXaYb recombinant cell line, > 6000 fold enrichment of output against parental cell panning
- > 90% output FACS+; 48 unique clones identified by screening of ~600 clones
- Representative 19 clones with different binding specificity/preference to XY family members converted to IgGs
- 2 clone showed very specific binding to hXaYb, with very low binding to other family members

Affinity Maturation

Antibody Affinity Maturation

- Biotinylation of antigen
- scFv affinity libraries construction by CDR targeted mutagenesis, with a focus on H3 and L3
- Other CDR libraries optional, and can combine later
- Library selection process can be performed by reducing the antigen or with more stringent wash condition
- Initial screening with ELISA & off-rate ForteBio ranking
- Characterization of best clones in hIgG format by Biacore and bioassays

Individual CDR Mutation Libs



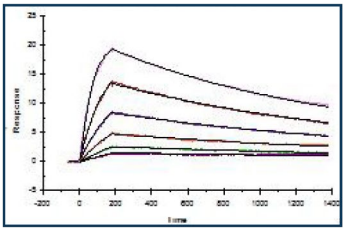
Case Study

Affinity Maturation of Anti-IL1β by CDR Mutagenesis

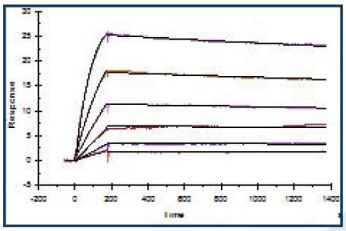
AB ID	CDR-H2	CDR-L1	k_a (1/MS)	K_D (1/S)	K_D (M)
Parental	Wild Type	Wild Type	2.215E+05	7.284E-04	3.288E-09
#1	-A-I-	Wild Type	3.967E+05	9.469E-05	2.387E-10
#2	Wild Type	-RTV-	3.328E+05	1.520E-04	4.567E-10
#3	Wild Type	-SVV-	4.093E+05	1.320E-04	3.226E-10
#4	-A-I-	-RTV-	4.887E+05	3.040E-05	6.159E-11
#5	-A-I-	-SVV-	5.063E+05	2.439E-05	4.817E-11

Combination of mutations from two DCRs yield ~70 fold improvements in full-length IgG KD measured by Biacore

Parental Ab



#5: ~70X Improvement



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