mAbs
ANTIBODIES
FOR MEDICINE

GET YOUR PURIFIED RECOMBINANT MAB HITS AGAINST DIFFICULT TARGETS IN LESS THAN 5 MONTHS USING BEACON® SINGLE CELL TECHNOLOGY

Despite demonstrated efficiency in antibody generation, classical immunization strategies and subsequent hybridoma generation often face strong limitations when it comes to complex targets like GPCRs or tetraspanins. We have developed innovative approaches combining mRNA immunization and Bruker single cell screening platform to provide unique opportunities to dramatically speed up antibody discovery against such challenging targets.

Typical Beacon Workflow

Immunization

Rec-protein Transfectant mRNA

BALB/c model KO model in C57Bl/6

Wistar model

ATX-Gx humanized mice (Alloy-tx)

ATX-Gx Certified Service Provider

Beacon screen, export and sequencing

BRUKER

Beacon system and OptoSelect™ chip

Clone 10,000s of single B cells into NanoPen™ chambers

Characterize function within minutes using multiple assays

Bioinformatic hit selection step

MOE modelling
- Sequence analysis
- Analysis of CDR liabilities
- Analysis of CDR patches

Beacon steps (14-20 days)

On chip single cell screening, amplification, sequencing, in silico analysis, selection of hits to produce

Up to 100 Hits

From Bioinfo selection

Cloning

Human Cκ

Human IgG

VL

VH

Production/purification

EC50 /affinity/functional

Ab4 Ab3 Ab2 Ab1

Selected hits

Robotized production of hits 100 µg level (up to 100 hits), or mg level if lower numbers (<50 hits): 40 to 60 days

Get your purified recombinant mAb hits against difficult targets in less than 5 months using Beacon® Single Cell technology

Key advantages of the technology

Increased depth of screening, and diversity for difficult antigens, without the need for recombinant soluble antigen

- 40,000 plasmocytes from either spleen or bone marrow screened per Beacon® campaign
- mRNA immunization followed with bone marrow plasmocyte selection
- Compatible with the use of human IgG expressing mice (e.g. Alloy Therapeutics)

Rapid functional on-chip screening at single cell level with recombinant antigen or transfectant expressing antigen

- A choice of selection criteria as recognition of antigen, preliminary functional (blocking) or crossreactivity properties
- Obtention of the sequences within a week of all the screened hits allowing *in silico* pre-selection to avoid antibodies with obvious liabilities
- Production of the selected hits based on binding or functional criteria and *in silico* pre-selection

Decreased turnaround time from hit identification to recombinant production and evaluation

- Recovery and production of your hits without the need for cell culture or gene synthesis
- Delivery of up to 100 hits at 100µg scale (i.e. purified antibody) within 8 weeks after initial screening.

What we require and what we deliver

What do we need?

- 1 mg of recombinant antigen, or mRNA coding for your antigen or a cell line expressing your antigen for immunization
- A cell line expressing the antigen or recombinant protein for screening

What do you get within 5 months?

- A collection of up to 100 recombinant mAbs, at 100 µg scale level, with EC_{50} characteristics

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Track record

- We have run more than 10 successful Beacon® campaigns with standard recombinant antigen, or peptide with 50-200 high affinity mAbs recovered in each run.
- We have obtained collections of antibodies against difficult antigens where no recombinant protein antigen was available :
  - **50 antibodies against a GPCR with minimum extracellular domain**
  - **12 antibodies against an ion channel where no antibodies were available worldwide.**

Conclusion

Using innovative approaches like mRNA immunization and single B cell screening, MImAbs has developed the know-how to tackle the challenge of antibody generation against difficult targets like GPRCs, ion channels or other complex proteins with multiple transmembrane domains. Combined with multiple functional assays upon candidate selection and possible use of ATX-Gx™ humanized mice, the delivery time of therapeutic candidates can now be significantly shortened.

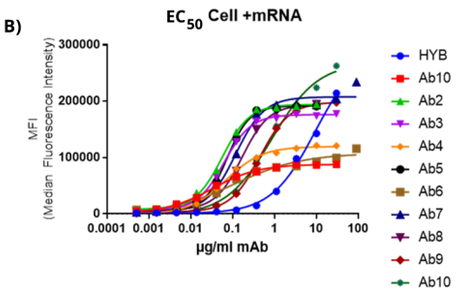
GPCR Campaign Example (comparison with hybridoma)

Table A summarizes data from all campaigns performed on the targeted GPCR (* mice remaining from hybridoma campaign). Figures B and C illustrate comparative EC_{50} on human-target expressing cells for antibodies generated from different immunization strategies and figure D highlights cross-reactive clones against cynomolgus monkey ortholog.

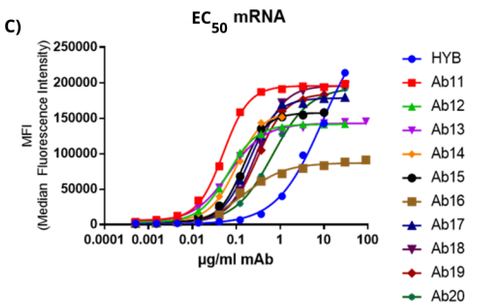
A)

Mice Immunization (nb of mice)	Nb of campaigns	Screened colonies/clones	Positive clones
Cells only (>10)	4 (hybridoma, historical data)	> 5,000	0
mRNA only (6)	1 (hybridoma)	2,963	0
Cells + mRNA (6)	1 (hybridoma)	2,266	1
mRNA only or cells + mRNA *	**1 (Beacon®)**	**> 35,000**	**26 unique mAbs**

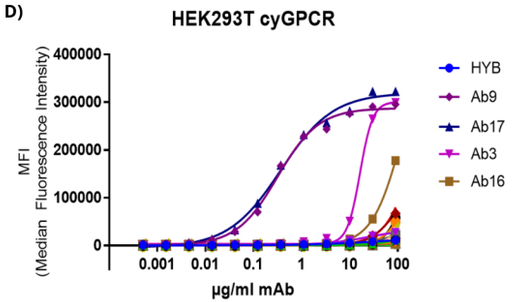
B)



C)



D)



ANTIBODY DISCOVERY WAS STRIKINGLY IMPROVED USING THE COMBINATION OF mRNA IMMUNIZATION AND SINGLE B CELL SCREENING. NO DIFFERENCE IN AFFINITY COULD BE OBSERVED BETWEEN CLONES RESULTING FROM MIXED IMMUNIZATION OR mRNA ONLY AND 1 CROSS-REACTIVE CLONE WAS OBTAINED FROM EACH GROUP.

Contact

Wish to get more information about our Single B cell platform to speed up your antibody development ?

Contact our business team at contact@mimabs.com or +33 675177351
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