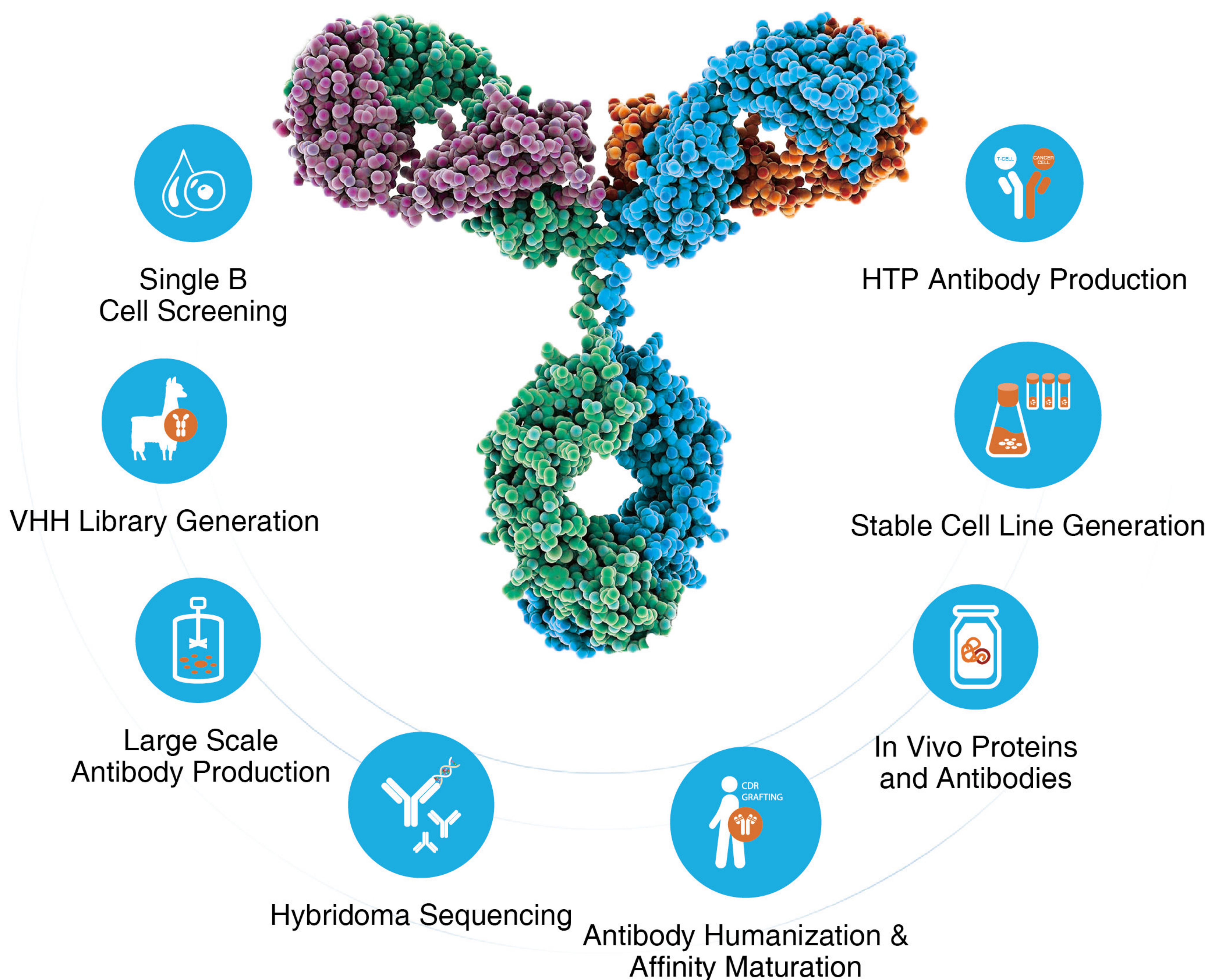


ACCELERATING YOUR ANTIBODY DISCOVERY



COMPANY PROFILE

About Biointron

Biointron is a CRO company for customized service provider and biological reagents manufacturer, specialized in early-stage antibody discovery. We have well-established platforms including high-throughput production in mammalian expression system, VHH library generation, single B cell screening, stable cell line generation, antibody humanization & affinity maturation, etc.

- Founded in 2012 in Taizhou, China
- Employee: 500+
- 14,600 m² lab
- ISO-9001:2015 certificate



CONTENTS

A SERVICE INTRODUCTION

High Throughput Antibody/Protein Expression.....01

Bispecific Antibodies (BsAbs) Production.....02

Large Scale Production.....03

Hybridoma Sequencing.....04

Antibody Humanization & Affinity Maturation.....05

VHH Library Generation.....06

Single B Cell Antibody Discovery.....07

Commercial License for CHO-K1.....08

Stable Cell Line Generation.....09

B CATALOG PRODUCT

Recombinant Anti-Mouse PD-110

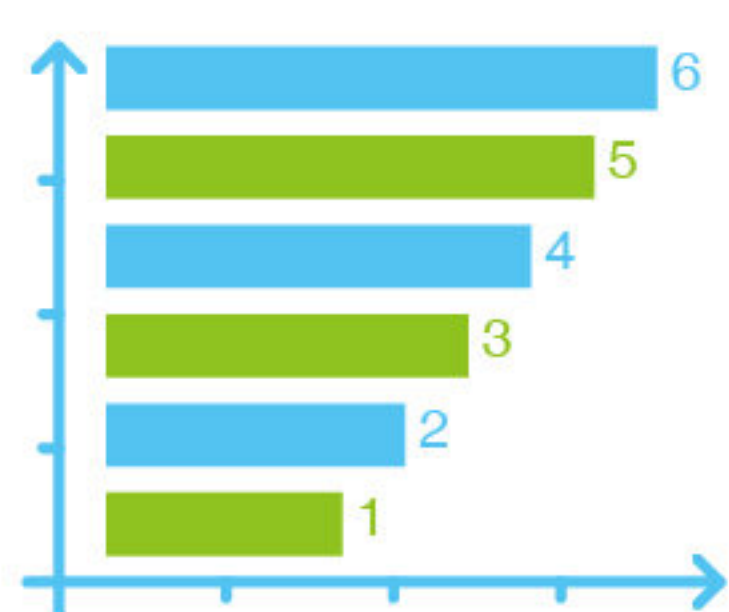
Biosimilar Antibodies (Positive Control)11

Isotype Control Antibodies (Negative Control)12

HIGH THROUGHPUT ANTIBODY/PROTEIN EXPRESSION

Biointron's high-throughput antibody production provides the most cost-effective option for recombinant antibodies, where you may choose to deliver either supernatant or purified antibodies (ug to gram level). From gene synthesis to purified antibodies (IgG, scFv, VHH, bispecific antibodies, etc.), it takes as short as 2 weeks. Any isotype, format or antibody fragments can be expressed, there is no number limitation.

FEATURES



High Throughput

1000+ mAb/batch



2-week

As short as 2 week for the production,
gene synthesis included.

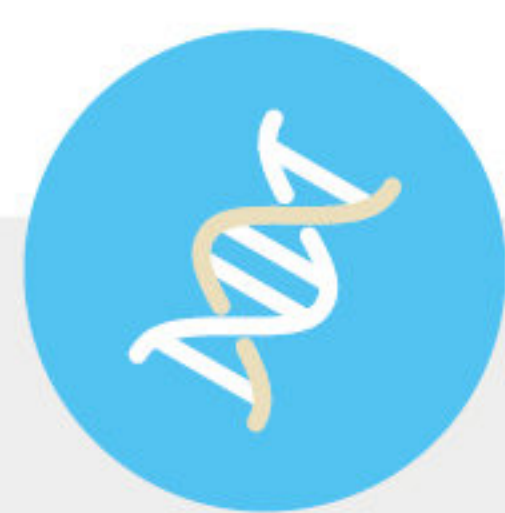


Expertise

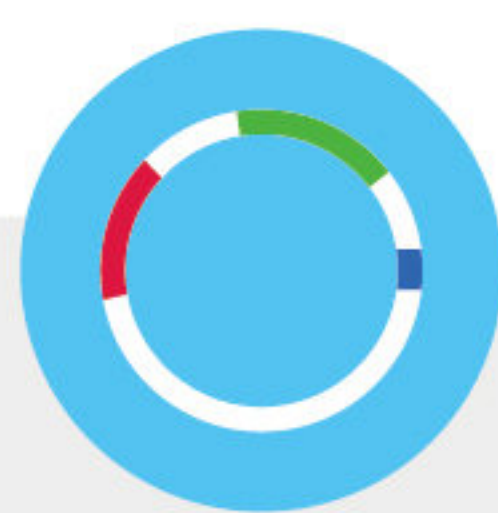
10+ years of experience
on antibody production

QC Standards: SDS-PAGE>95%, Endotoxin < 1 EU/mg, SEC-HPLC Detection

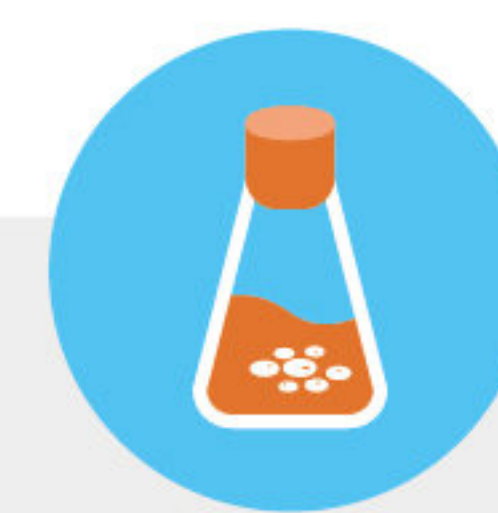
WORKFLOW



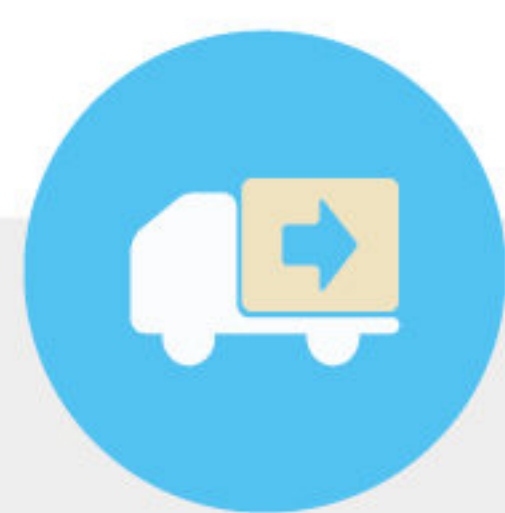
Sequence Design
and Synthesis



Plasmid Construction
and Preparation



Transient Expression



Delivery



Stringent Quality
Control



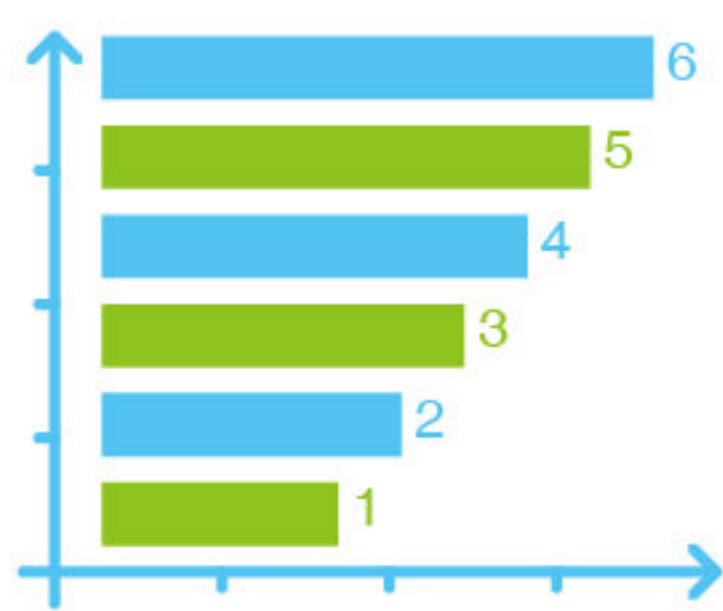
Affinity Purification

BISPECIFIC ANTIBODIES(BsAbs) PRODUCTION

Bispecific antibodies represent a key component of the next-generation of antibody therapy. Bispecific antibodies can target at least two different antigens at the same time, such as simultaneously binding tumor cell receptors and recruiting cytotoxic immune cells.

Biointron has expressed thousands of bispecific antibodies with extensive experience in bispecific antibody production. Any format can be expressed.

FEATURES



High Throughput

500+ molecules/batch



Customized Service

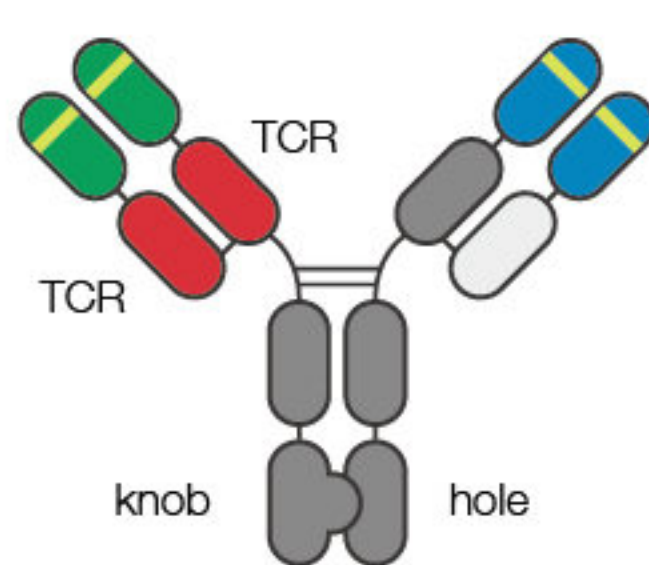
Any format can be produced



Fast Turnaround Time

As short as 3 weeks

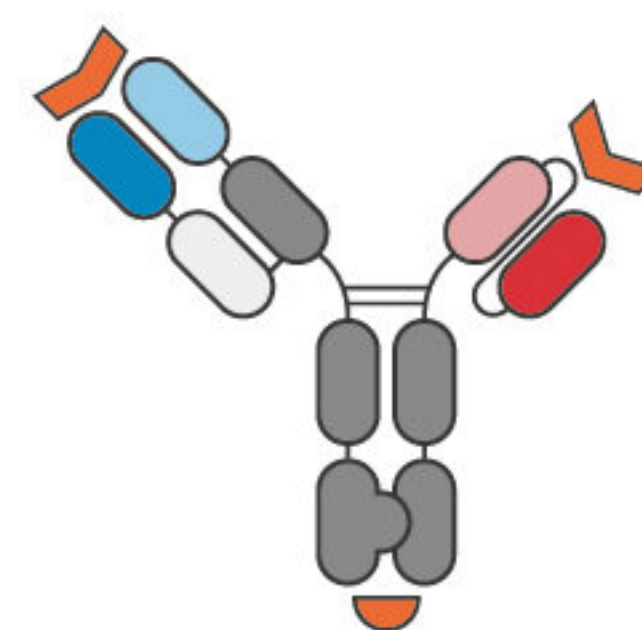
FORMAT EXAMPLES



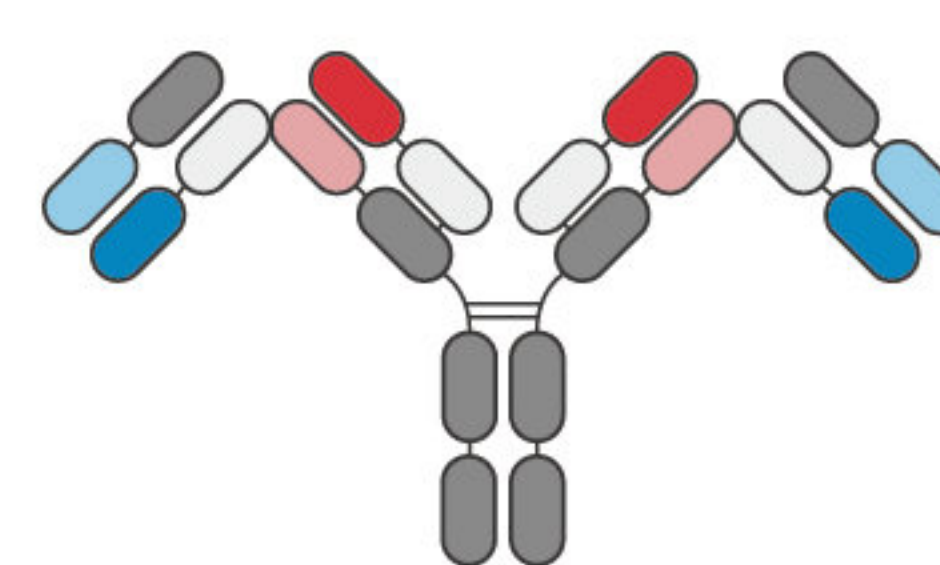
WuXi body



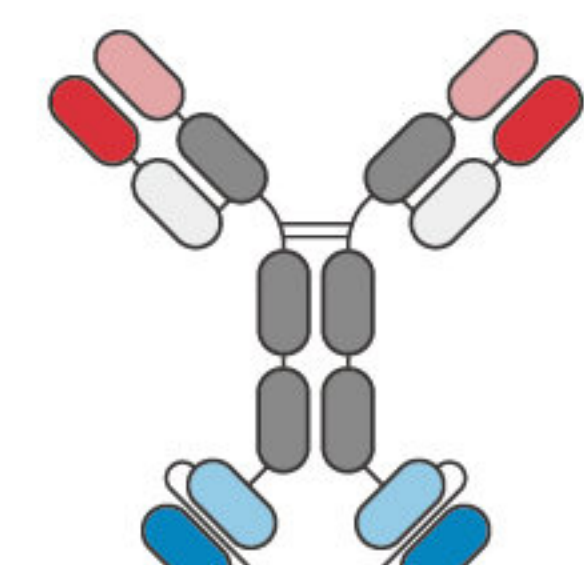
Knobs-into-holes



Y-body



FIT-Ig



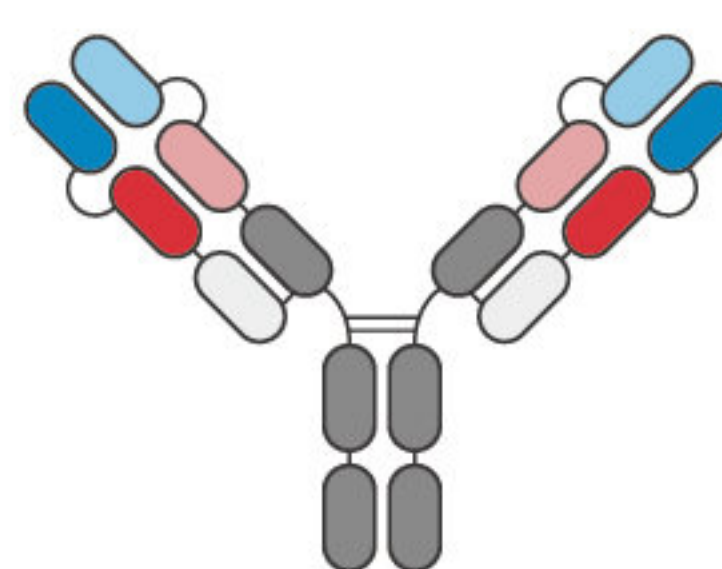
IgG-scFv



Cross MAB



Ortho-Fab IgG



DVD-Ig



bi-Nanobody



BiTE

CH CL V_AH V_AL V_BH V_BL

LARGE SCALE PRODUCTION

Manufacturing therapeutic antibody or protein in large quantities is required for many applications, including in vitro study, in vivo animal study or pre-clinical trials. Biointron large-scale manufacturing services offer scale-up production of recombinant antibodies/proteins from milligram to gram levels within weeks.

FEATURES



Consistency

One batch
SDS-PAGE > 95%, SEC-HPLC > 95%,
Endotoxin < 0.1 EU/mg



Fast Turnaround Time

As short as 3 weeks for
gram level production

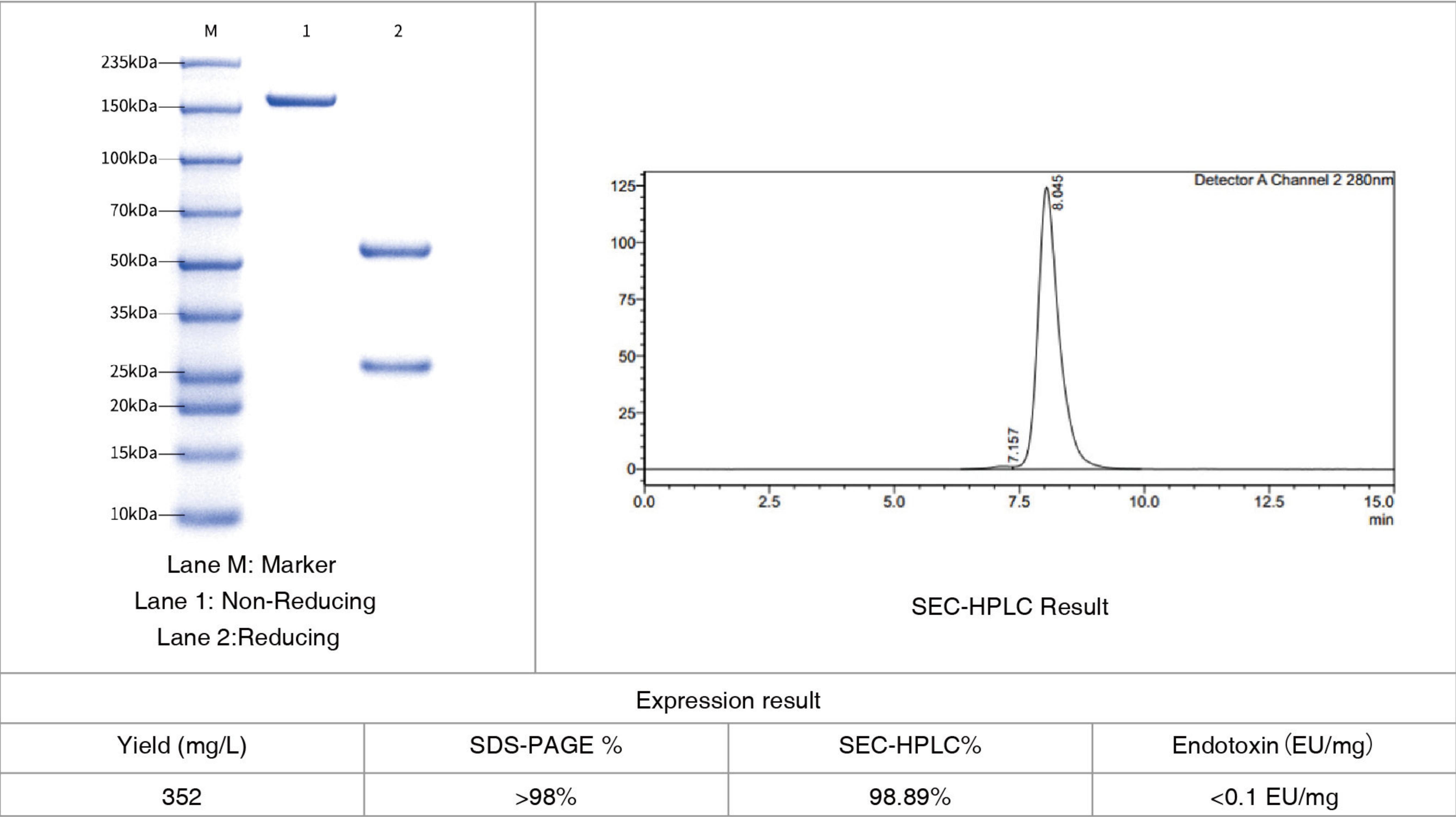


High Capacity

Up to hundreds of grams level

CASE STUDY

1000 mg recombinant mAb production in CHO cells



HYBRIDOMA SEQUENCING

The antibody sequence is crucial for patent application (distinguish your antibody from the others), recombinant antibody expression, antibody engineering (humanization & affinity maturation), etc.

Biointron offers a high-quality hybridoma sequencing service, for sequencing of the variable regions of monoclonal antibodies being produced from hybridoma cell lines. Once the sequences are confirmed, recombinant antibody can be expressed and purified in as soon as 2 weeks.

FEATURES



5' RACE

Simple and reliable



Fast Turnaround Time

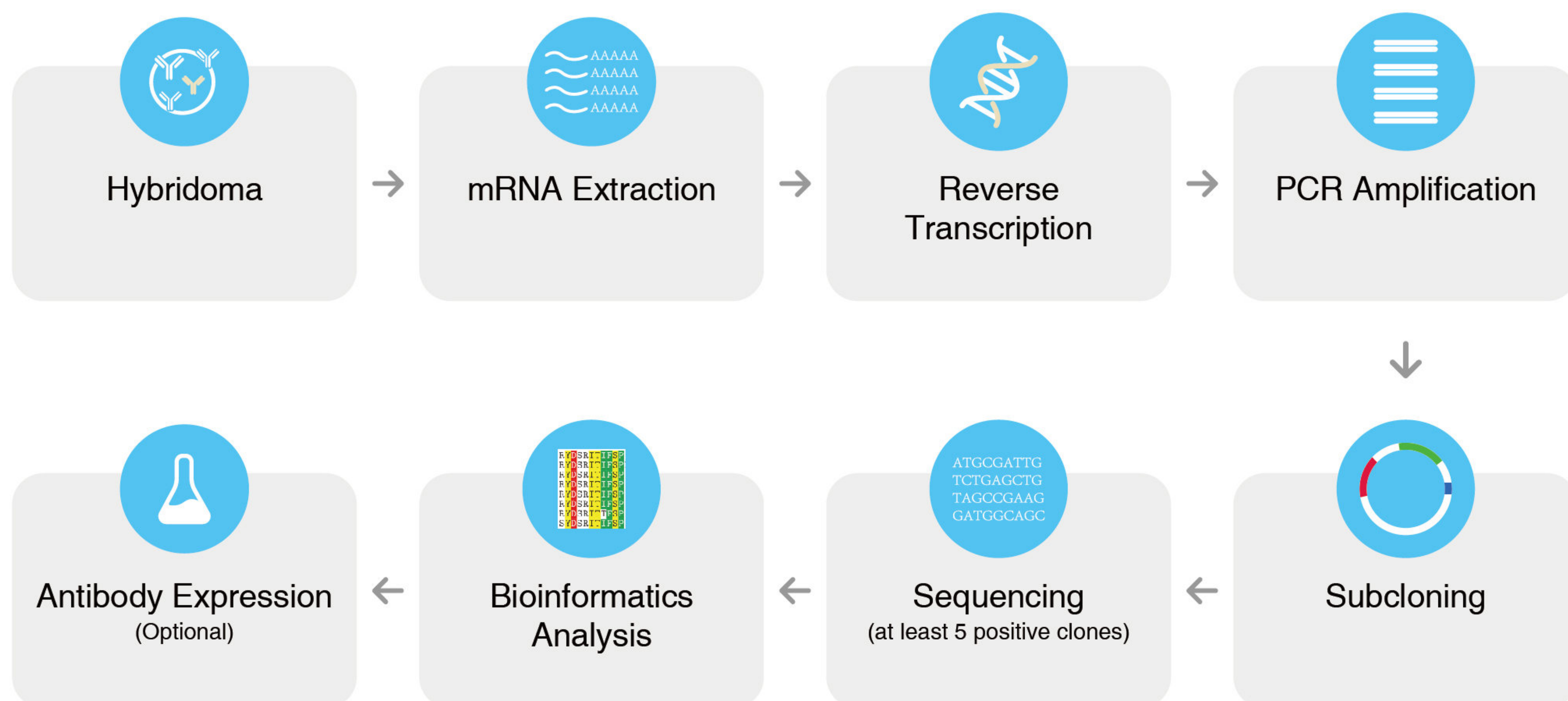
1 week



100% Accuracy

Cross verified with 5 independent clones

WORKFLOW



ANTIBODY HUMANIZATION & AFFINITY MATURATION

Recombinant antibody technologies are rapidly becoming available and showing considerable clinical success. However, murine monoclonal antibodies may induce immunogenic responses, potentially limiting their application for humans. Humanized antibodies can overcome these problems and are considered to be a promising alternative therapeutic agent.

Biointron's antibody humanization service is based on the CDR grafting and back mutation with PTM analysis. For affinity maturation service, it is applied to increase the antibody's affinity.

ANTIBODY HUMANIZATION

FEATURES



Affinity Guaranteed
No less than 3 times

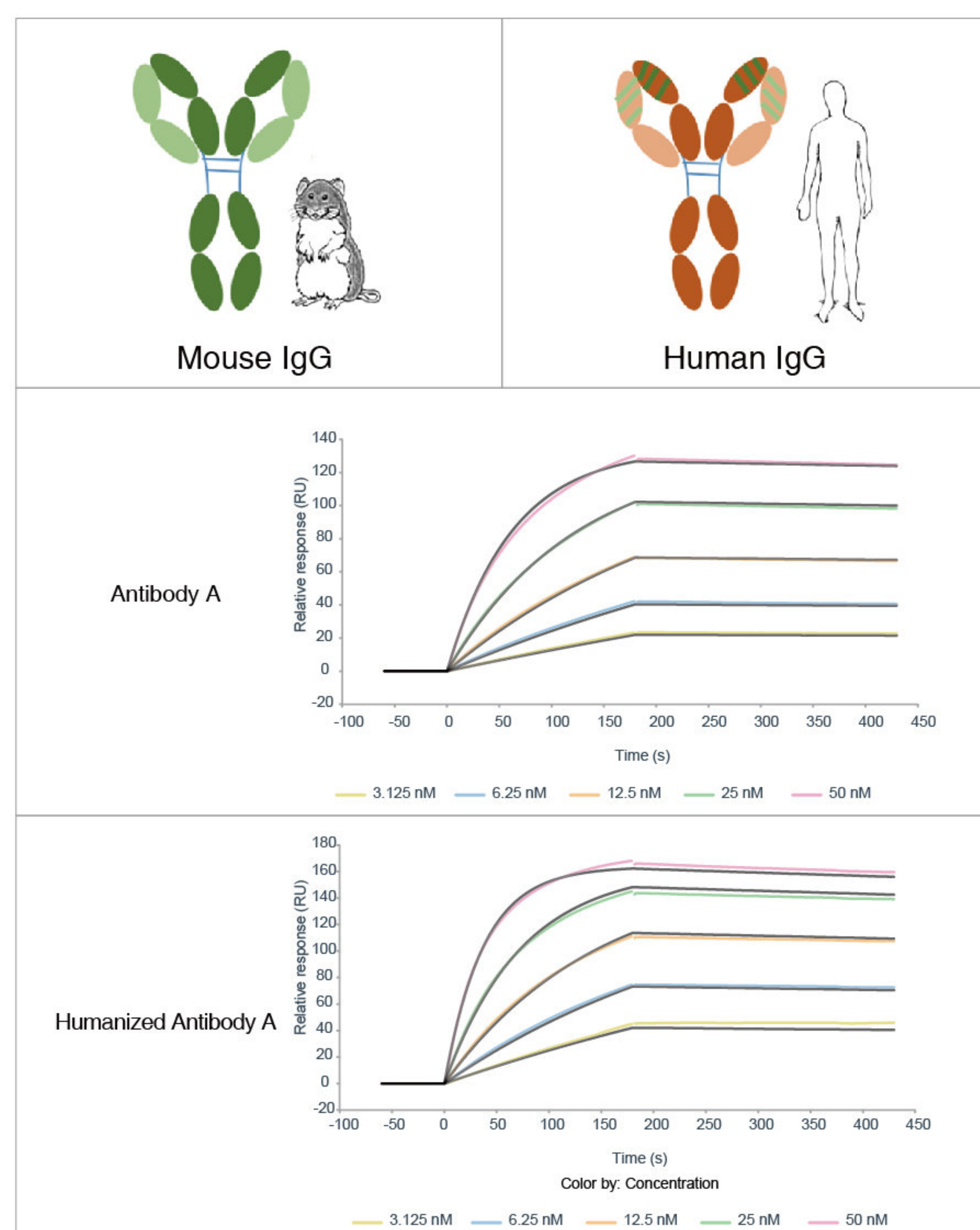


Fast Turnaround Time
As short as 3 weeks



Expertise
10+ years in humanized antibody design / produce 20,000 antibodies

CASE STUDY

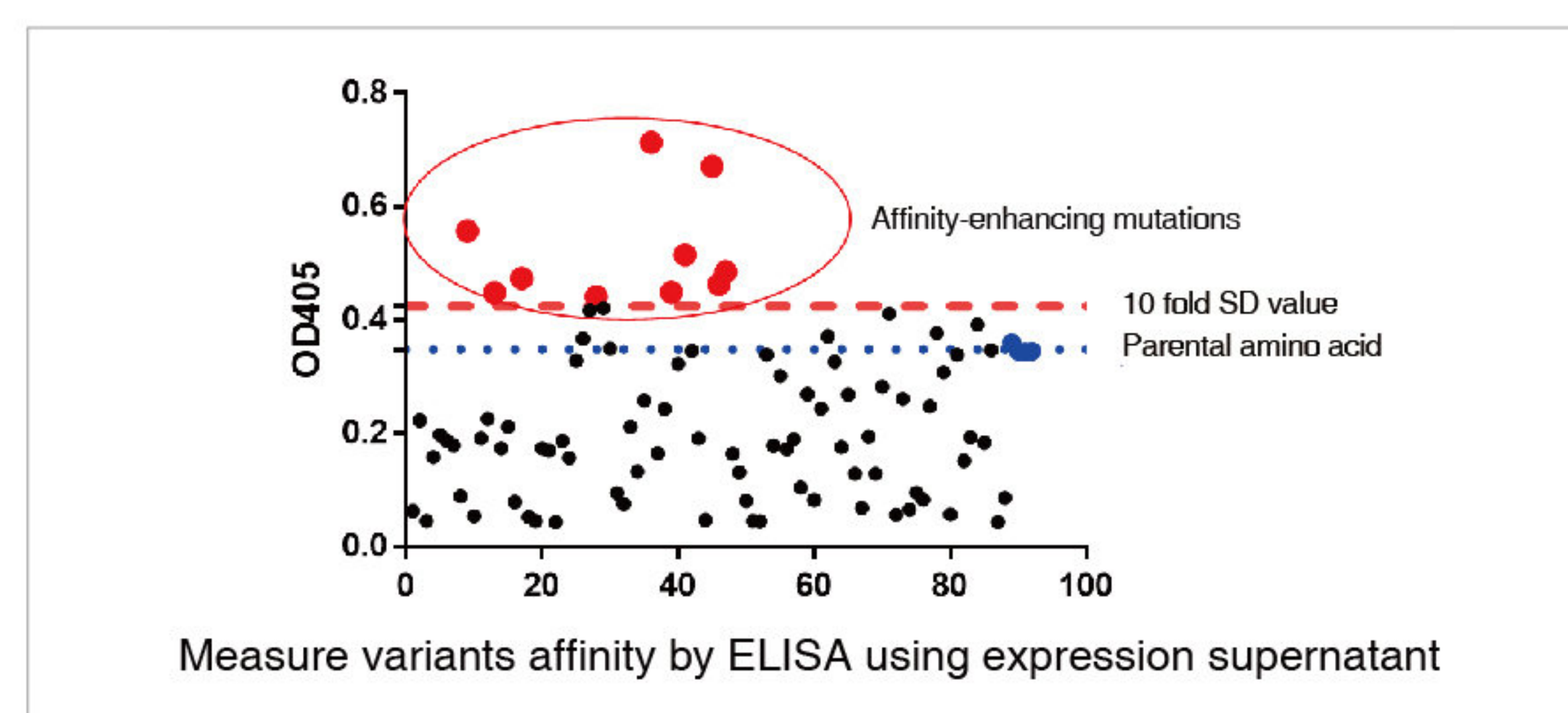
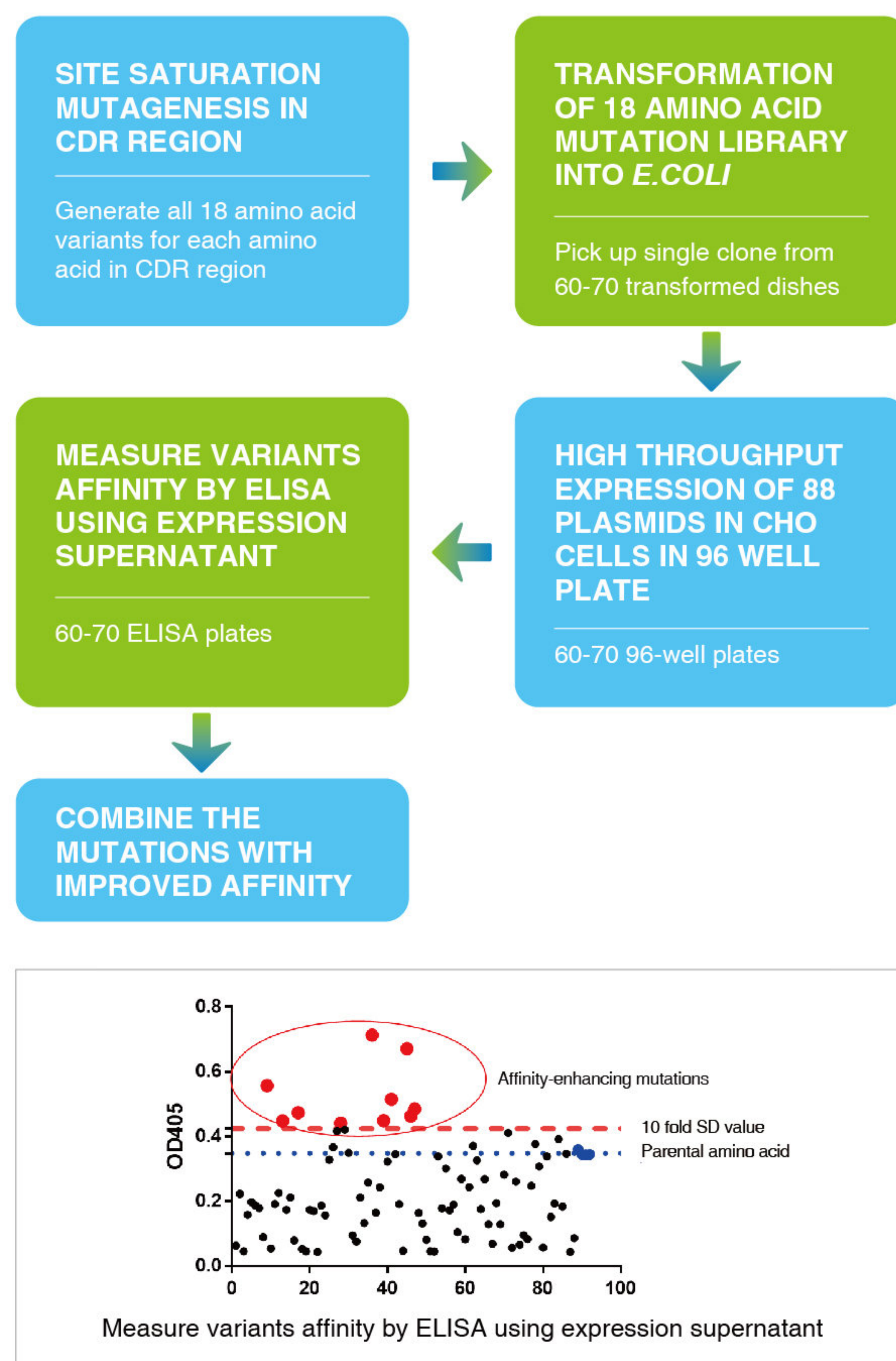


AFFINITY MATURATION

FEATURES

- Guarantee at least 5 fold affinity improvement
- Site Saturation Mutagenesis in CDR Region

WORKFLOW



VHH LIBRARY GENERATION

SdAb or VHH is a promising next-generation therapeutic antibody technology for cancer immunotherapy and other applications.

Biointron is a well-recognized leader in the field of single domain antibody discovery. Based on our advanced phage display technology and high-throughput antibody expression platform, our scientists are specialized in the production and discovery of specific single domain antibodies.

FEATURES



Self-owned Alpaca Breeding Base

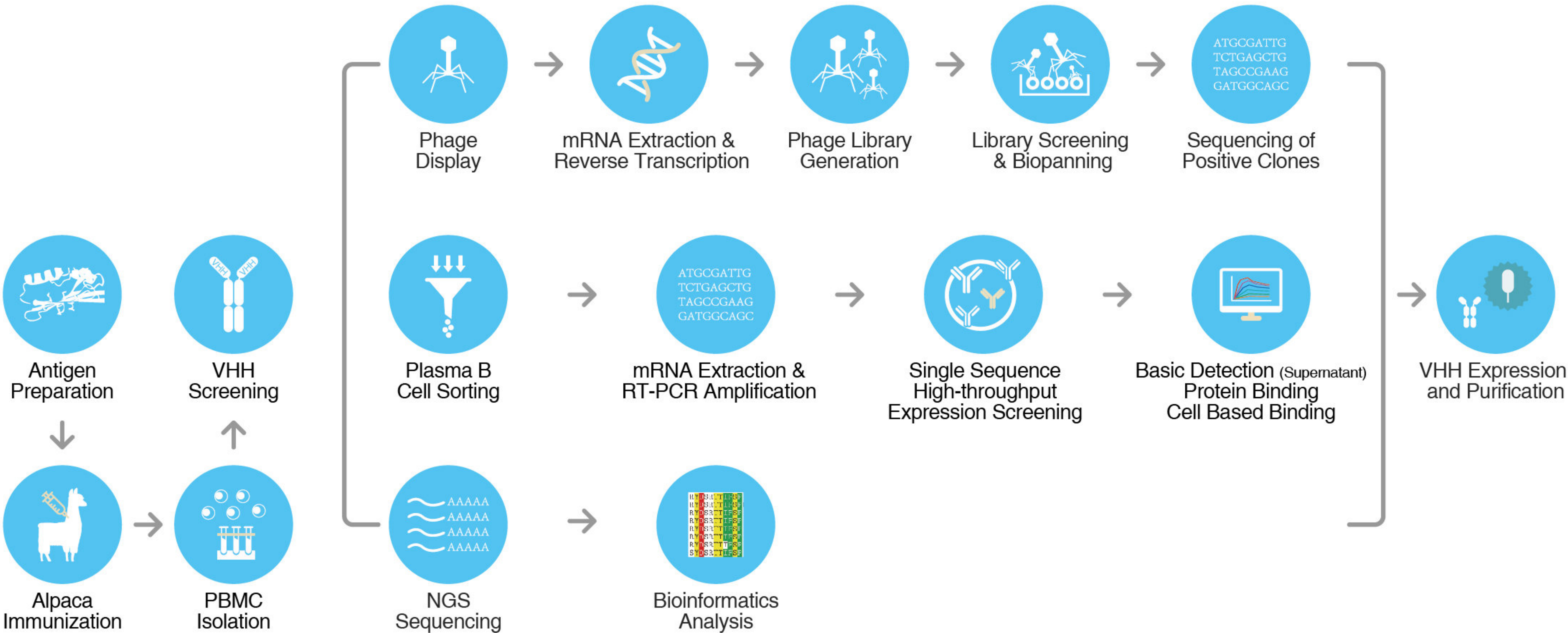


Guaranteed 20+ Unique Binders



High Diversity & Large Capacity

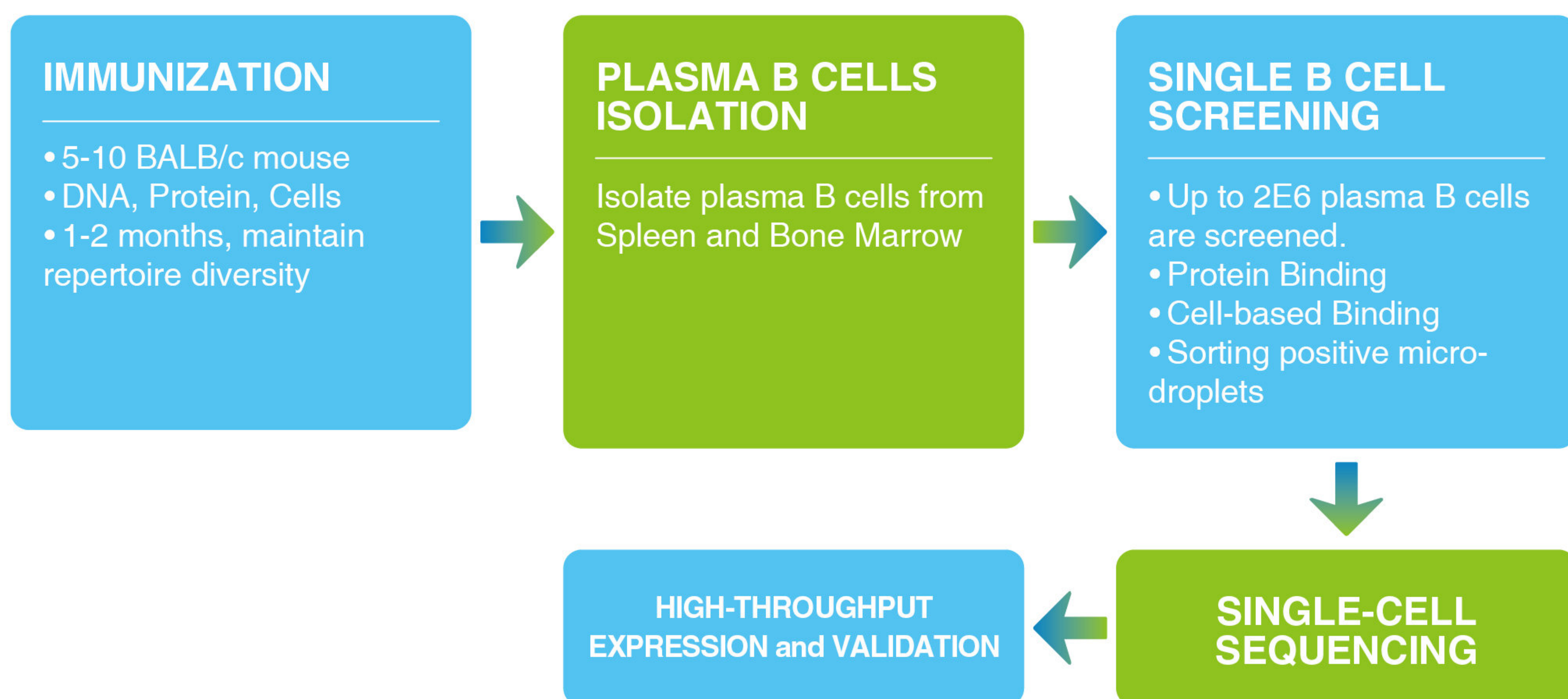
WORKFLOW



SINGLE B CELL ANTIBODY DISCOVERY

Biointron offers a high-throughput, full integrated platform for accelerating antibody discovery. Biointron's high-throughput single B cell screening platform can screen 2×10^6 plasma B-cells from immunized animals. Antigen specific antibody-secreting cells can be isolated. It allows detection of those very rare antibodies or potential drugs with unique properties that are exceptionally hard to find.

ABOUT 2 MONTHS: FROM TARGET TO ANTIBODY SEQUENCE DISCOVERY



FEATURES



COMMERCIAL LICENSE FOR CHO-K1

Biointron’s CHOK1BN cell line, licensed from ECACC (CHO-K1), is suspension-adapted in basic CD media. The cell line can be sublicensed for commercial use, it meets the requirements for registration in both China and US.

FEATURES

Worldwide Sublicense

One-time Sublicense For Multiple Products

Perpetual & Irrevocable

Meet the requirements for registration in both China and US

FEATURES OF CHOK1BN

Suspension-adapted in basic CD medium and can apply to various medium

High stability and productivity (> 10 g/L)

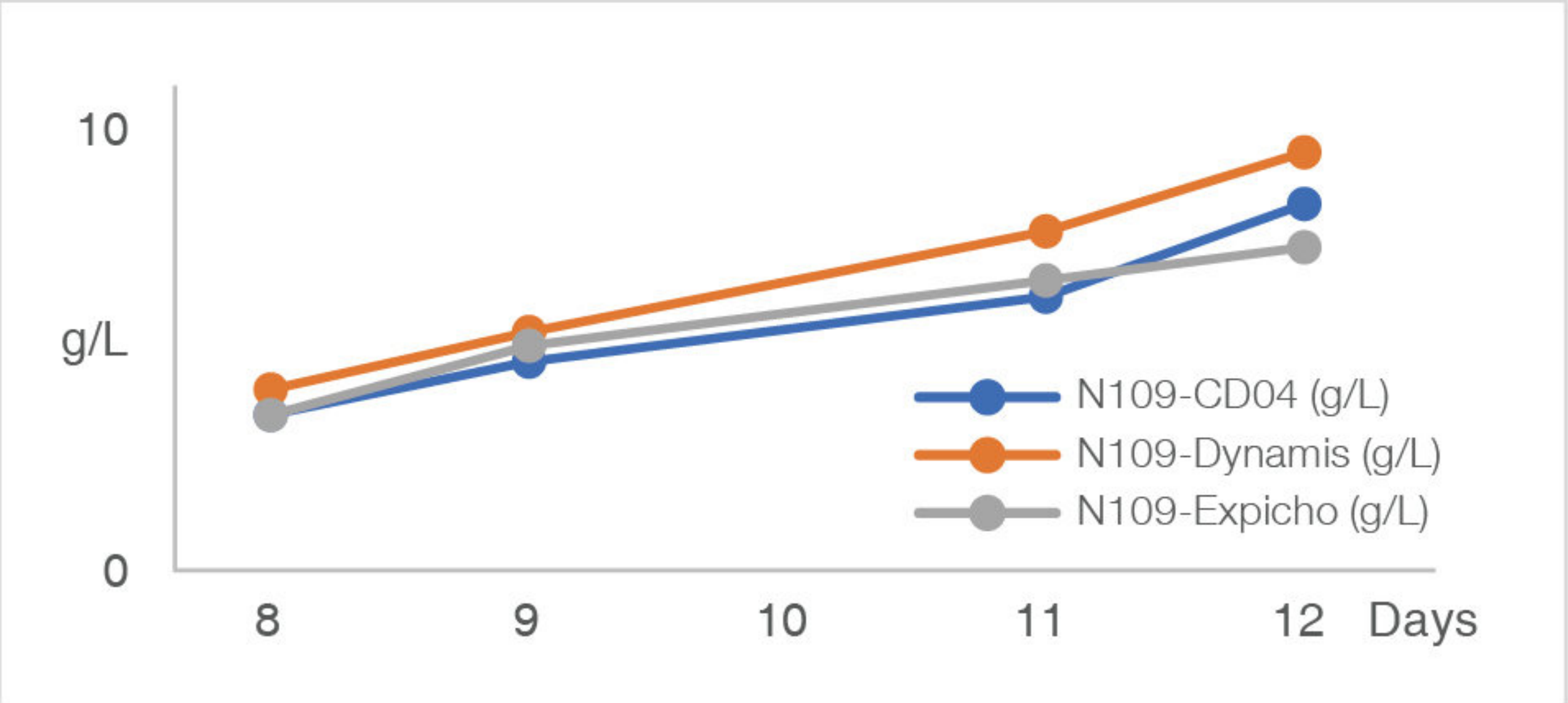
Suitable for monoclonal antibody, bispecific antibody, factors, etc

Adaption of CHOK1BN

Thawed CHOK1 cell line from ECACC

Culture the adherent CHOK1 cell line

Suspended adaption of CHOK1 cell line by CD serum-free medium to get CHOK1BN cell line

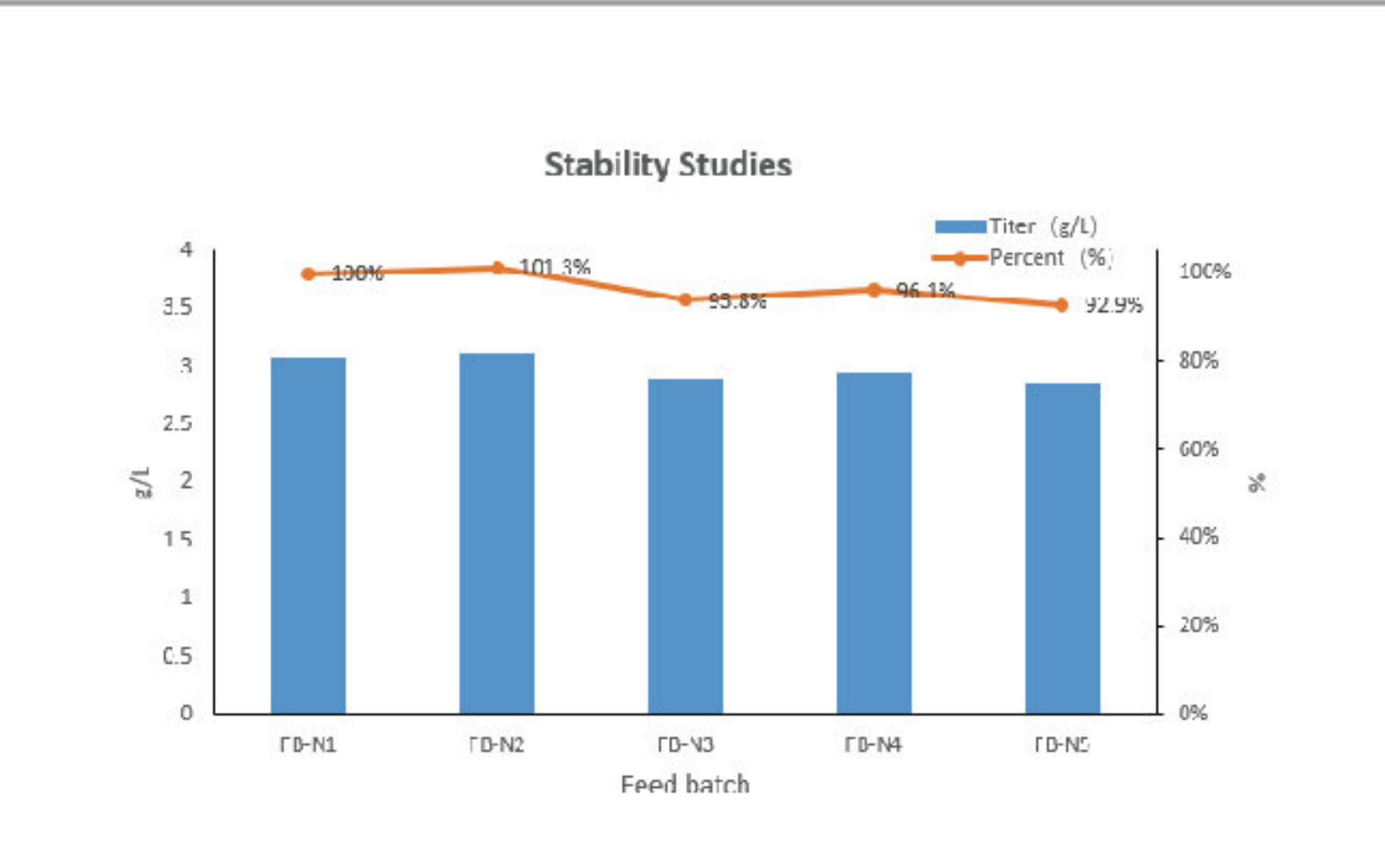
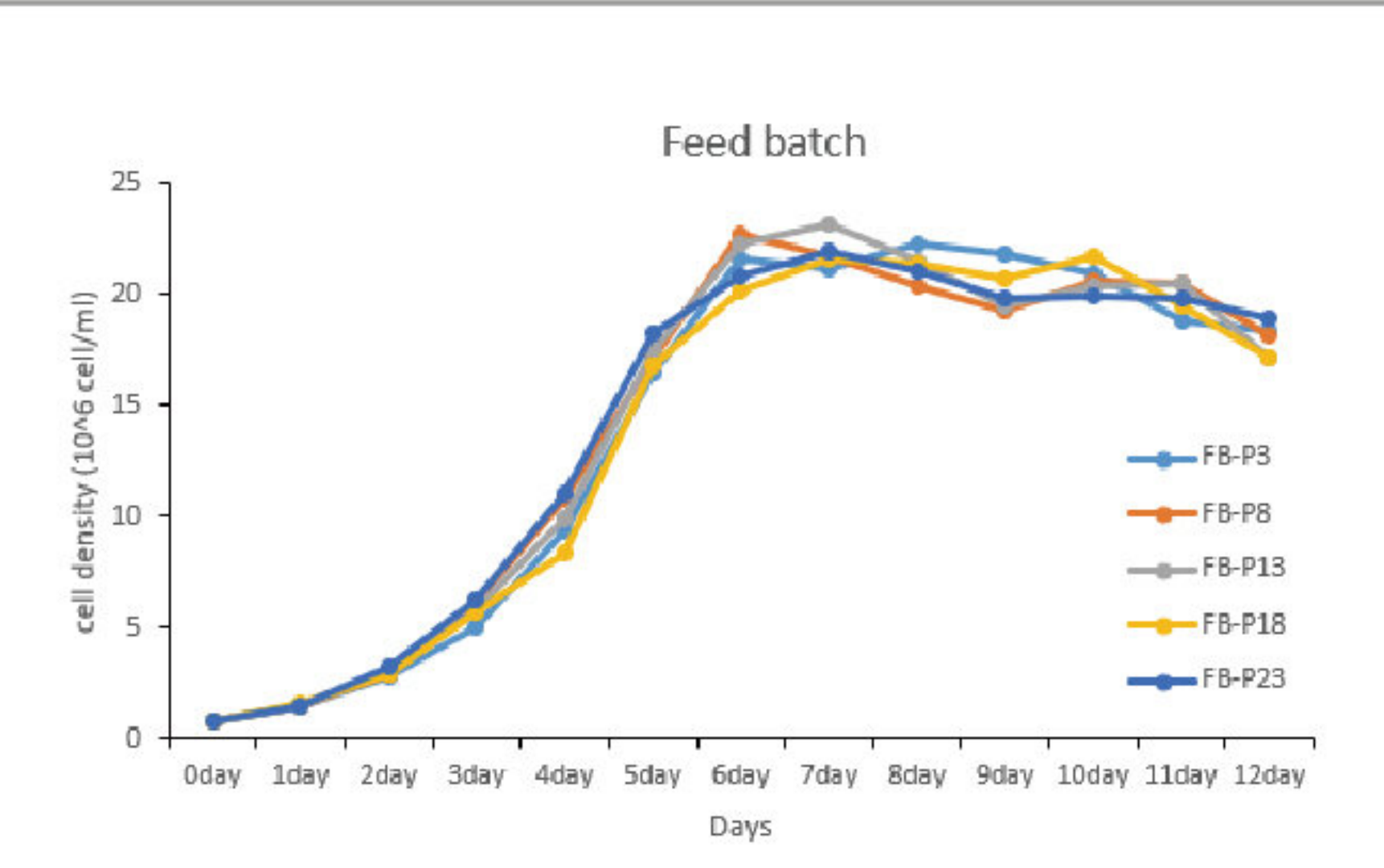
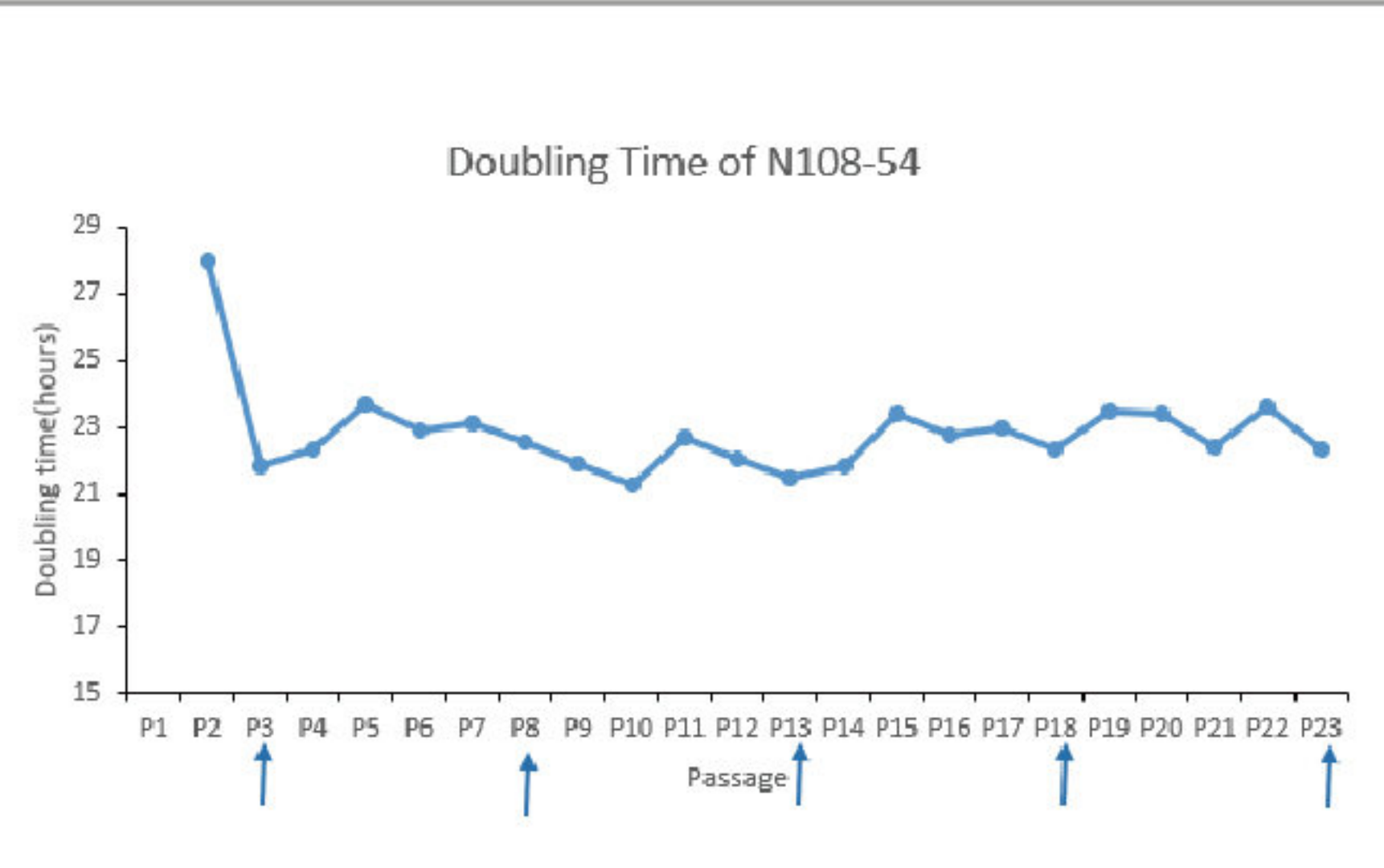


Suitable for various medium with high monoclonal antibody yield

FOR RECOMBINANT PROTEINS: STABILITY TEST FOR OVER 2 MONTHS

The doubling time of the cells is 22±1 hours. During the plateau period of feed batch, the cell density is 20-25*10^6 cell/ml,making it easier for scale up production.

Excellent batch difference, the titer variation is just <10%



STABLE CELL LINE GENERATION

Biointron can provide stable cell line development service for bioproduction purpose. Our stable cell line service, based on ECACC licensed CHO-K1 cell, aims to provide high-yield guaranteed and speedy timeline to meet your downstream application.

FEATURES



High-yield

>10 gram/L for antibody



Expertise

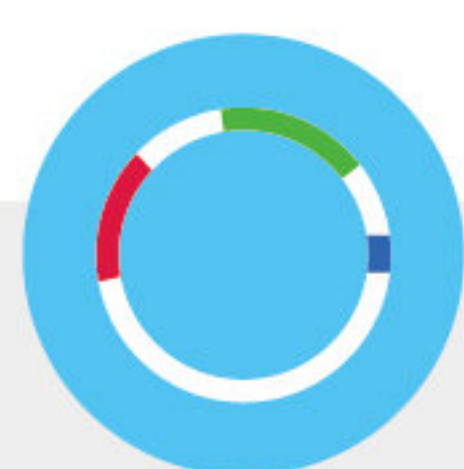
10+ years of experience,
100+ cell lines delivered



One-time Sublicense

For multiple products

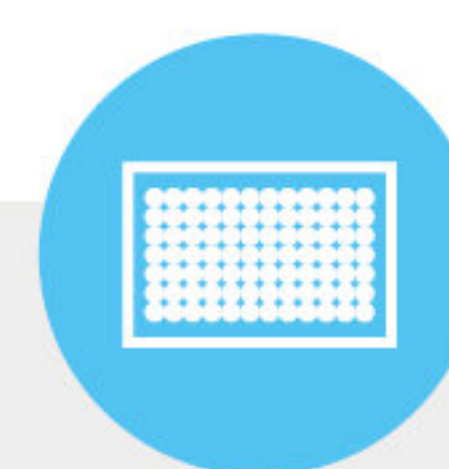
WORKFLOW



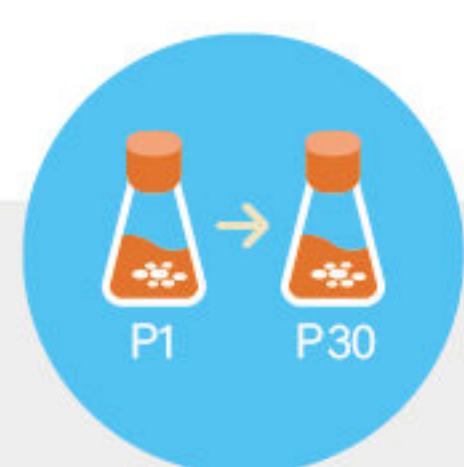
Gene Synthesis and
Expression Vector
Construction



Transfection and
Stable Pool Devel-
opment



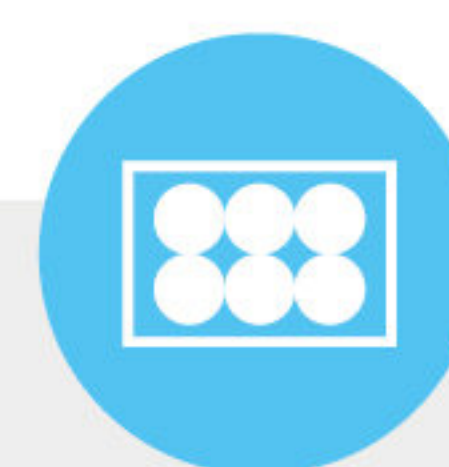
Single Cell Clone
Screening



Stability Test for
PCB



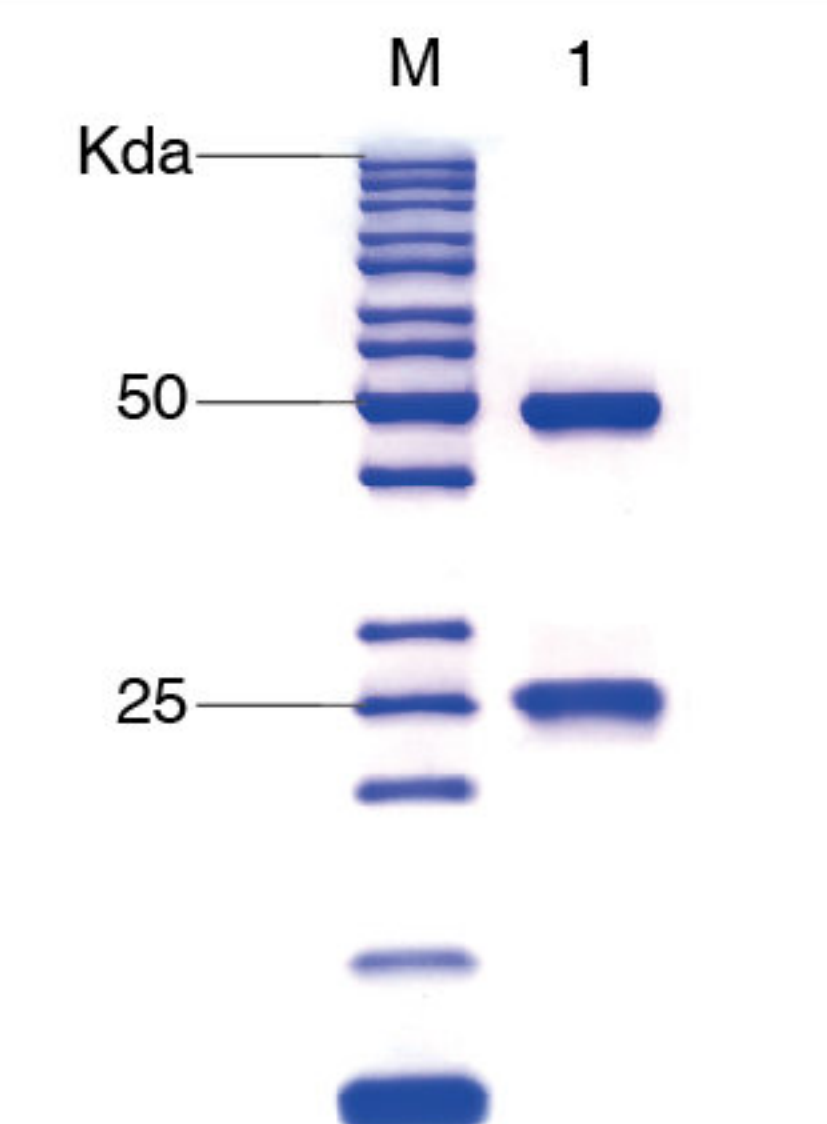
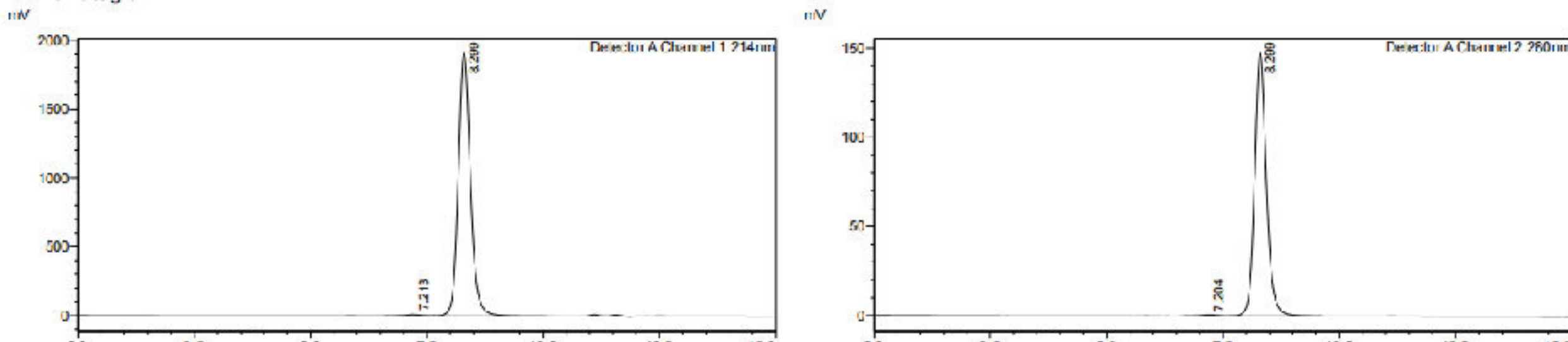
PCB Establishment

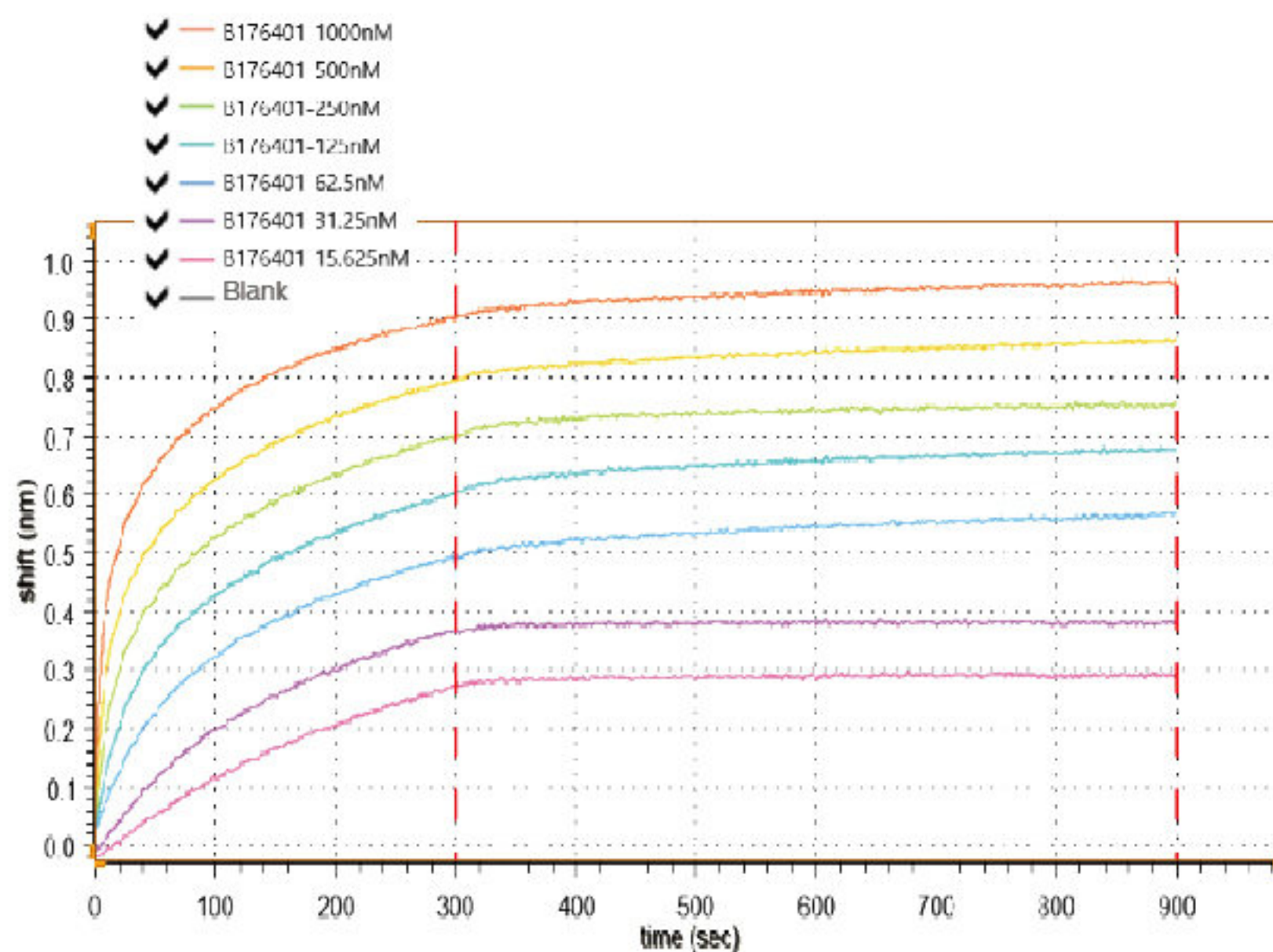
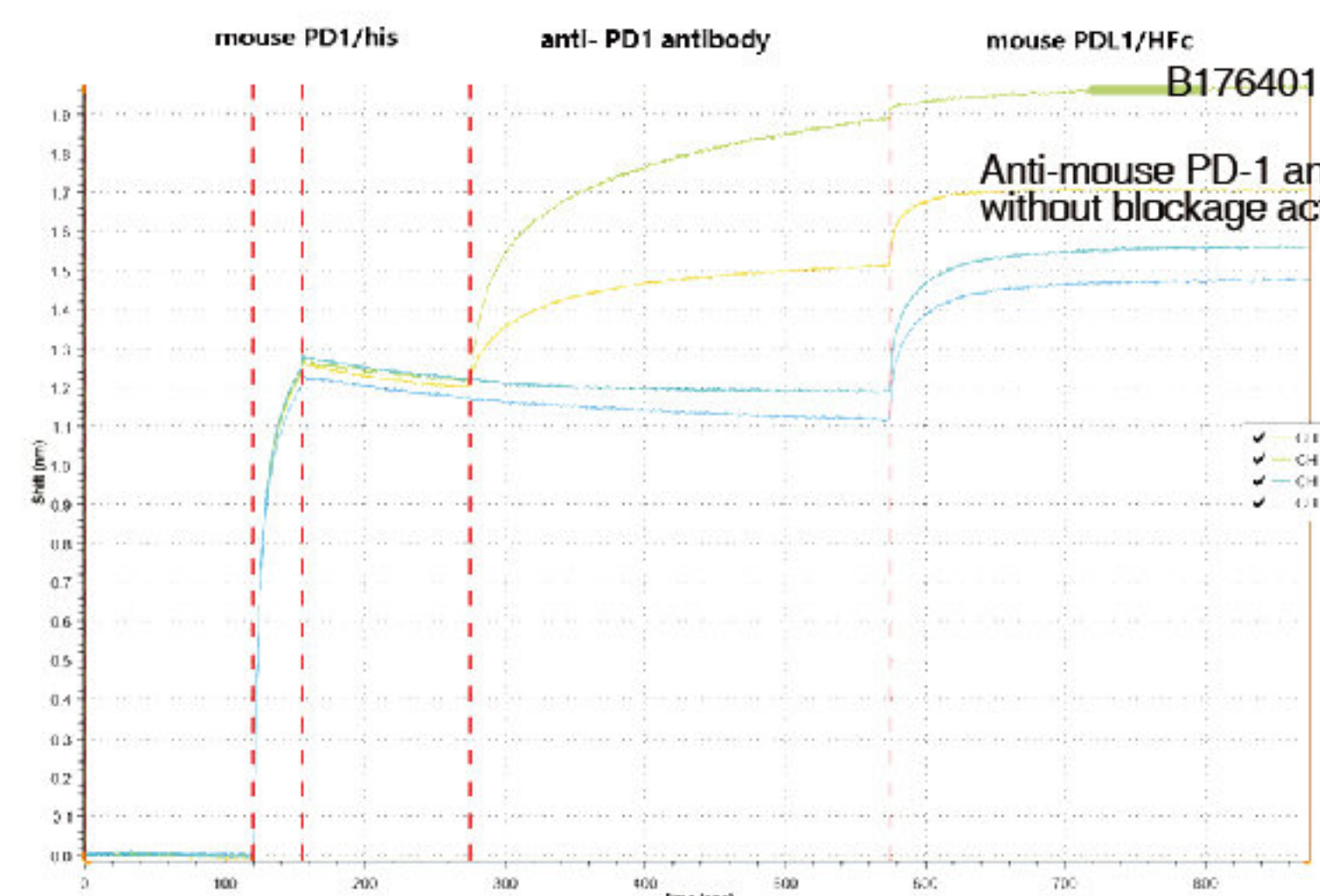
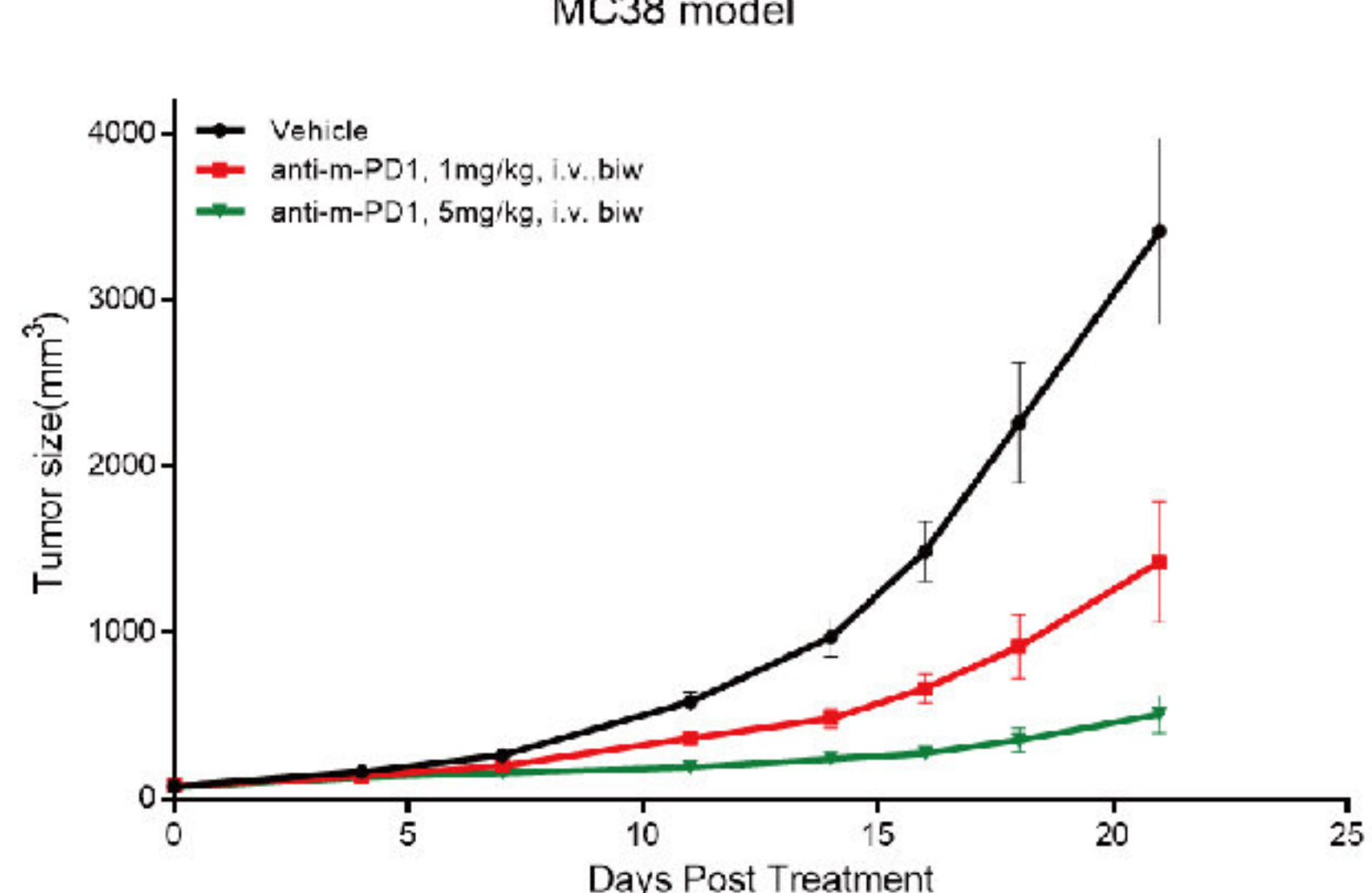


Single Clone
Selection

RECOMBINANT ANTI-MOUSE PD-1

| | | | |
|------------------|--|---------------------|---|
| Product Name | Recombinant Anti-Mouse PD-1 | Target | Murine programmed cell death 1 (mPD-1) |
| Catalog Number | B176401 | Isotype | Mouse IgG1-Kappa |
| Host Cells | CHO cells | Formulation | PBS, PH7.4, contains no stabilizers or preservatives |
| Endotoxin Level | <1EU/mg(<0.001EU/ug) Determined by LAL assay | Purity | >98% Determined by SDS-PAGE; Aggregates <2% Determined by SEC-HPLC |
| Sterility | 0.2 μm filtered | Purification Method | Affinity chromatography with protein A |
| Molecular Weight | 150Kda | Size | 1mg / 5mg / 25mg / 50mg / 100mg |
| Storage | Product is shipped at -70°C Dry Ice 12 months, -20°C under sterile conditions Avoid repeated freeze and thaw cycles 2 weeks, 2°C to 8°C under sterile conditions 24 months, -70°C under sterile conditions | | |

| SDS-PAGE | SEC-HPLC | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|--|-------------|-------------|-----------|-----------------|---------------|---------|-----------------|---------|----------------|--------------|-------|------|------------------|-------|---------------|------------------|----------------|------------------|---|-------|-----------|------|--------|-------|---|-------|--------|------|-------|---|-------|----------|---------|--------|-------|--|----------|---------|--|-------|-----------|------|--------|-------|---|-------|-------|-----|-------|---|-------|---------|--------|--------|-------|--|---------|--------|--|
|  <p>Lane M: Marker Lane 1: B176401 Reducing</p> | <div><p><Sample Information></p><table><tr><td>Sample Name</td><td>SEC-B176401</td></tr><tr><td>Sample ID</td><td>SEC-B176401.tcd</td></tr><tr><td>Data Filename</td><td>SEC.kim</td></tr><tr><td>Method Filename</td><td>SEC.kim</td></tr><tr><td>Batch Filename</td><td>20070724.kim</td></tr><tr><td>Val 1</td><td>1.27</td></tr><tr><td>Injection Volume</td><td>20 uL</td></tr><tr><td>Date Acquired</td><td>2007/25 09:05:05</td></tr><tr><td>Date Processed</td><td>2007/25 08:58:28</td></tr></table><p>Sample Type: Unknown Acquired by: System Administrator Processed by: System Administrator</p><p><Chromatogram></p></div> | Sample Name | SEC-B176401 | Sample ID | SEC-B176401.tcd | Data Filename | SEC.kim | Method Filename | SEC.kim | Batch Filename | 20070724.kim | Val 1 | 1.27 | Injection Volume | 20 uL | Date Acquired | 2007/25 09:05:05 | Date Processed | 2007/25 08:58:28 | <div><p>Detector A Channel 1 214nm</p><table><tr><th>Peak#</th><th>Ret. Time</th><th>Area</th><th>Height</th><th>Conc.</th></tr><tr><td>1</td><td>7.213</td><td>234217</td><td>9738</td><td>0.669</td></tr><tr><td>2</td><td>8.299</td><td>34776239</td><td>1908474</td><td>99.331</td></tr><tr><td>Total</td><td></td><td>35010455</td><td>1918212</td><td></td></tr></table><p>Detector A Channel 2 280nm</p><table><tr><th>Peak#</th><th>Ret. Time</th><th>Area</th><th>Height</th><th>Conc.</th></tr><tr><td>1</td><td>7.204</td><td>15349</td><td>678</td><td>0.584</td></tr><tr><td>2</td><td>8.299</td><td>2610743</td><td>147517</td><td>99.416</td></tr><tr><td>Total</td><td></td><td>2626092</td><td>148195</td><td></td></tr></table></div> | Peak# | Ret. Time | Area | Height | Conc. | 1 | 7.213 | 234217 | 9738 | 0.669 | 2 | 8.299 | 34776239 | 1908474 | 99.331 | Total | | 35010455 | 1918212 | | Peak# | Ret. Time | Area | Height | Conc. | 1 | 7.204 | 15349 | 678 | 0.584 | 2 | 8.299 | 2610743 | 147517 | 99.416 | Total | | 2626092 | 148195 | |
| Sample Name | SEC-B176401 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Sample ID | SEC-B176401.tcd | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Data Filename | SEC.kim | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Method Filename | SEC.kim | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Batch Filename | 20070724.kim | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Val 1 | 1.27 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Injection Volume | 20 uL | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Date Acquired | 2007/25 09:05:05 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Date Processed | 2007/25 08:58:28 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peak# | Ret. Time | Area | Height | Conc. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 | 7.213 | 234217 | 9738 | 0.669 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2 | 8.299 | 34776239 | 1908474 | 99.331 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Total | | 35010455 | 1918212 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peak# | Ret. Time | Area | Height | Conc. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 | 7.204 | 15349 | 678 | 0.584 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2 | 8.299 | 2610743 | 147517 | 99.416 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Total | | 2626092 | 148195 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

| | | |
|--|---|--|
| <p>Binding test of B176401 with mouse PD-1</p>  | <p>B176401 inhibits the interaction of mPD-1 with mPD-L1</p>  | <p>B176401 have anti-tumor activity in Syngeneic model</p> <p>MC38 model</p>  |
|--|---|--|

BIOSIMILAR ANTIBODIES (POSITIVE CONTROL)

- ✓ To benchmark novel biotherapeutics (biologics) for pre-clinical lead identification.
- ✓ For the development of potency assays.

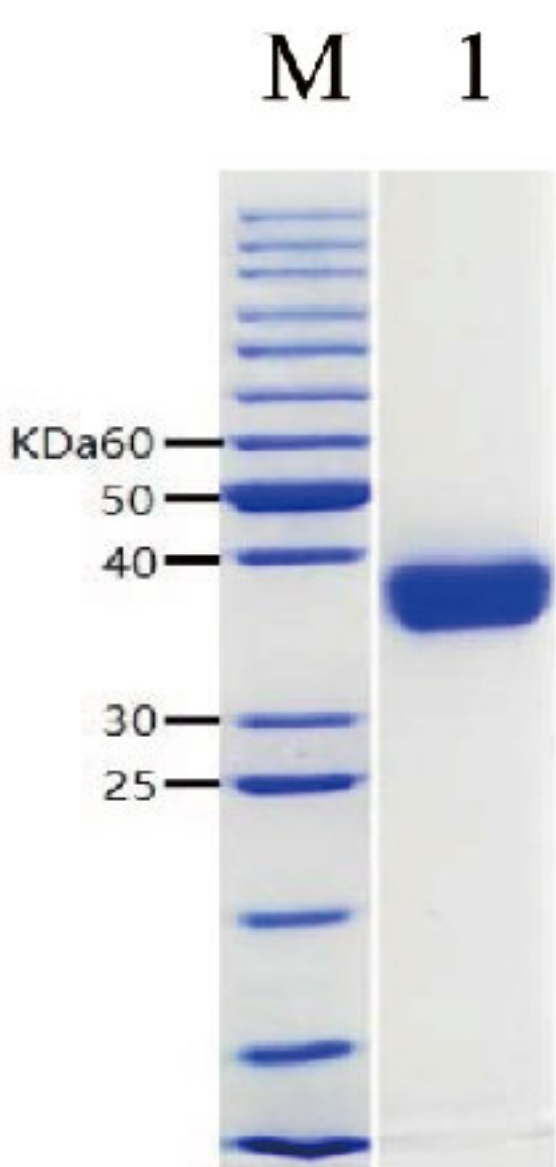
Our research grade biosimilars can be used as positive controls FOR RESEARCH USE ONLY.

SPECIFICATIONS

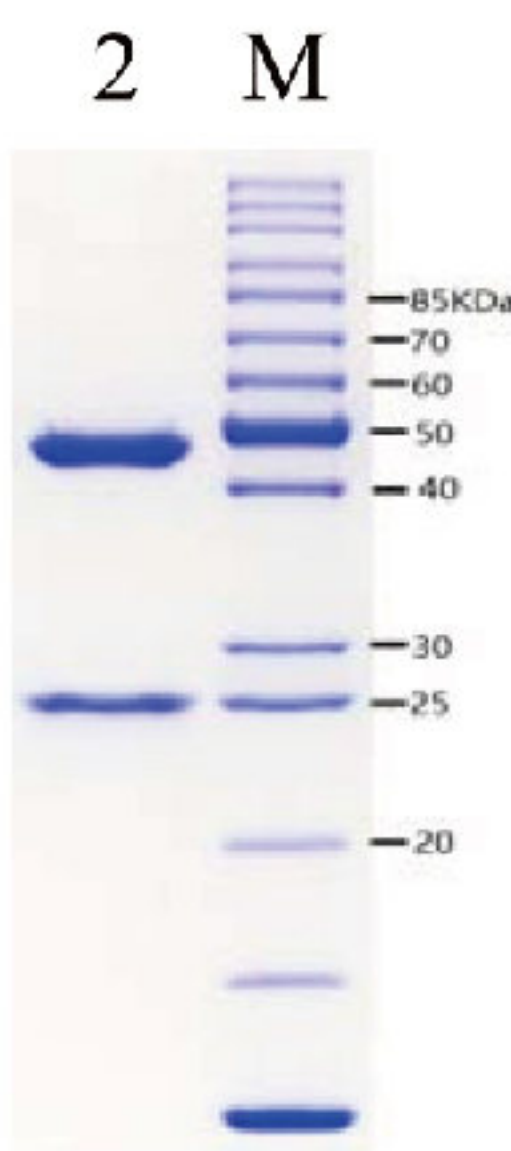
Endotoxin < 1.0 EU/mg determined by the LAL method

Purity > 95% determined by SEC-HPLC

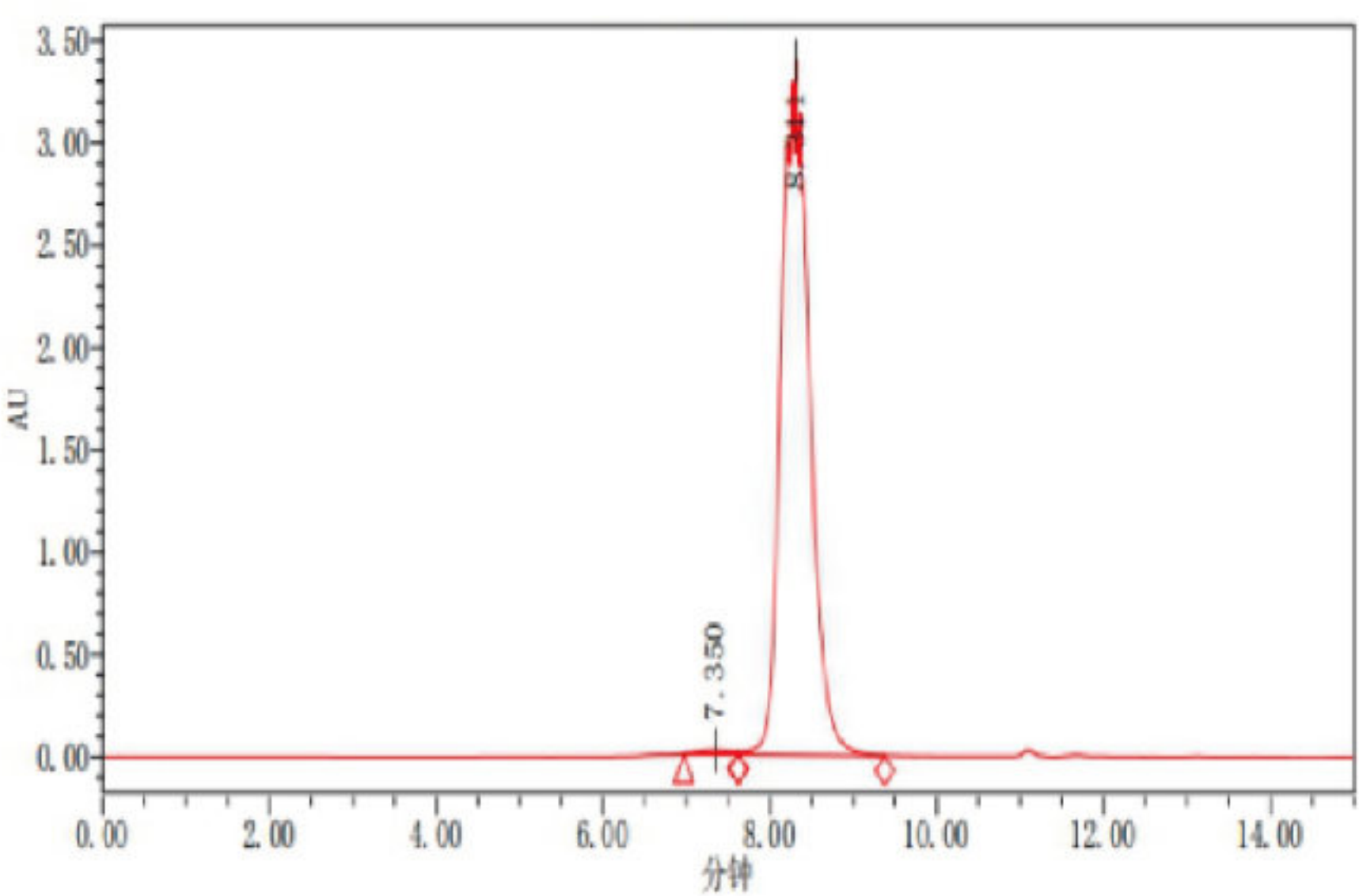
SDS-PAGE Image of Human PDL1/His Protein



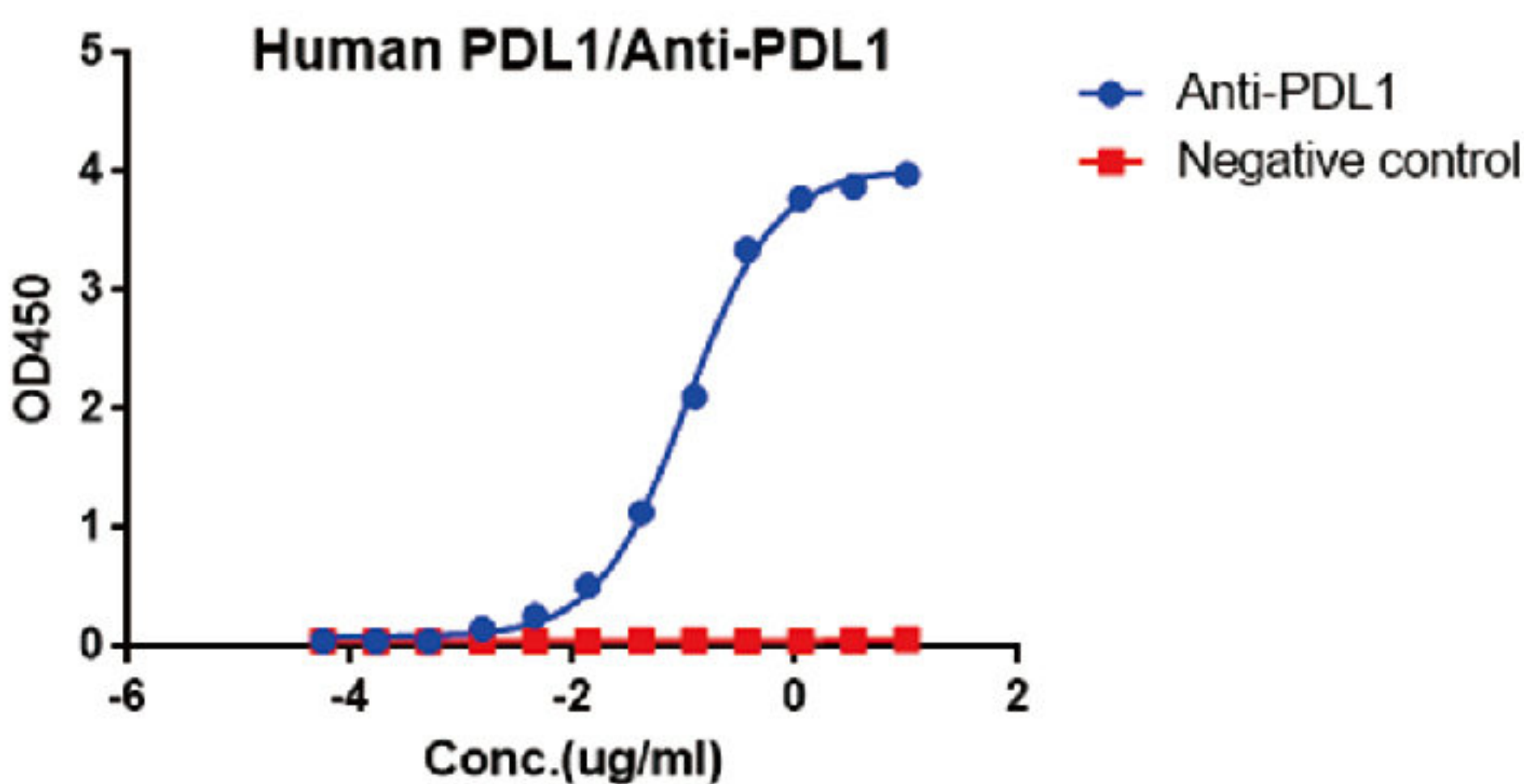
SDS-PAGE Image of Anti-PDL1 [Atezolimumab]



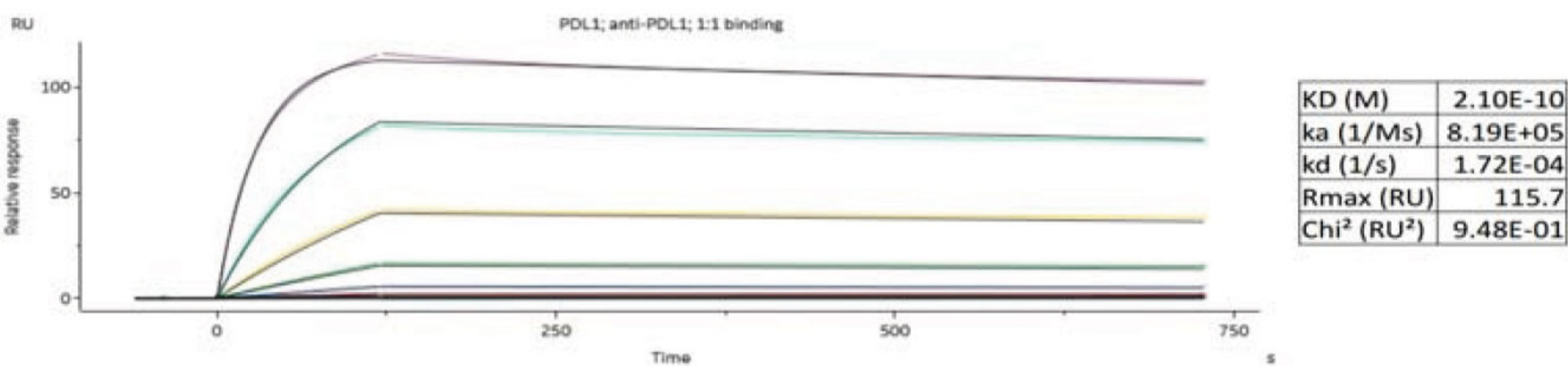
The purity was more than 99% as determined by SEC-HPLC



Human PD-L1 Protein, His Tag (Cat. No. H-PDL1-1) can bind Research Grade Biosimilar Anti-PDL1 Antibody [Atezo]



Kinetics analysis for PDL1(Cat: H-PDL1-1) binding to Research Grade Biosimilar Anti-PDL1 Antibody [Atezolimumab](Cat: B2016)(Top dose 40nM, 3-fold dilution)



Observations:
Close KD values were obtained for PDL1 binding to anti-PDL1 antibody compared with historical data(0.4 nM).

ISOTYPE CONTROL ANTIBODY

Choosing the correct isotype control antibody is an important part of most antibody-based experiments. Isotype control antibodies have no relevant specificity, they enable the researcher to distinguish non-specific "background" binding from antigen-specific antibody binding. Our isotype controls are specific anti-HEL(Hen Egg Lysozyme) and without any known cross-reactive to human.

| Number | Product Name | Number | Product Name |
|---------|----------------------------|---------|-----------------------------------|
| B118301 | anti-HEL- Mouse IgG1 | B109801 | anti-HEL-Human IgG1 (N297A) |
| B115101 | anti-HEL- Mouse IgG2A | B107803 | anti-HEL-Human IgG2 |
| B192301 | anti-HEL- Mouse IgG2A LALA | B109803 | anti-HEL-Human IgG3 |
| B117901 | anti-HEL-Human IgG1 | B109805 | anti-HEL-Human IgG4 (S228P L235E) |
| B109802 | anti-HEL-Human IgG1 LALA | B107804 | anti-HEL-Human IgG4 (S228P) |

* FOR MORE PRODUCTS AND RELATED DETAILS, PLEASE CONTACT US. WWW.BIOINTRON.COM

SDS-PAGE Image of Human IgG1 Isotype Control mAb

The purity was more than 98% as determined by SEC-HPLC.

No cross-reactivity (e.g. A549 cells, FACS)

| Sample Name | Geom | Mean |
|-------------------------|------|------|
| anti-HEL_aphymlgG2a_006 | 11.3 | 12.7 |
| anti-HEL_mlgG2a_005 | 11.5 | 14.0 |
| mlgG1_iso_004 | 11.2 | 12.8 |
| anti-mlgG-PE_only_002 | 11.1 | 12.7 |
| Cetuximab_007 | 223 | 268 |
| anti-hlgG-PE_only_003 | 10.7 | 12.0 |
| Blank_001 | 11.1 | 12.7 |

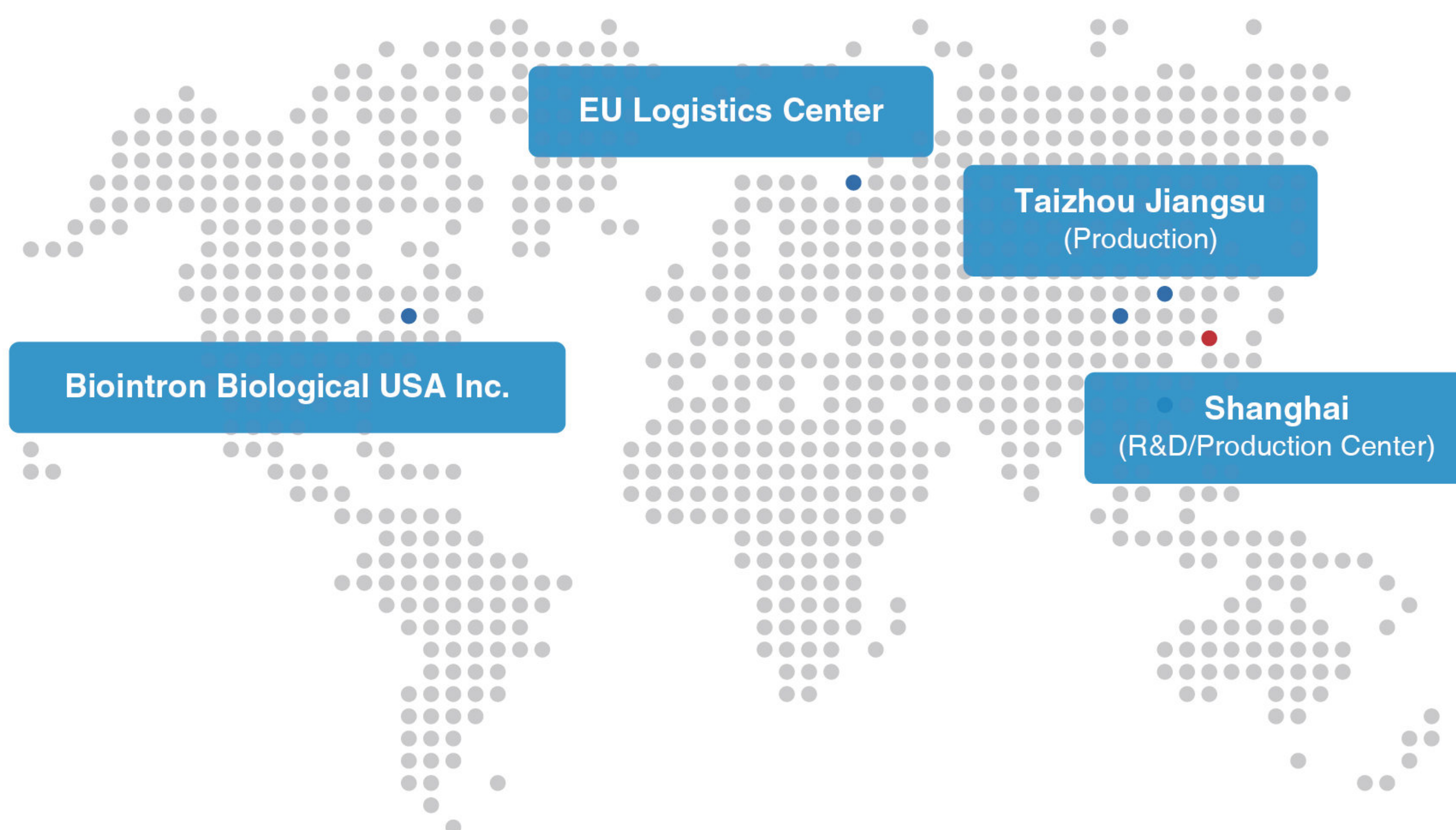
Specific binding to HEL (ELISA)

Body Weight Changes of Mice (BALB/c nude)


Hep3B Human Liver Carcinoma Xenograft Model (BALB/c nude)





- Founded in 2012 in Taizhou, China
- Employee: 500+
- 14,600 m² lab
- ISO-9001:2015 certificate



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