

Antibody Drug Discovery & Development Services

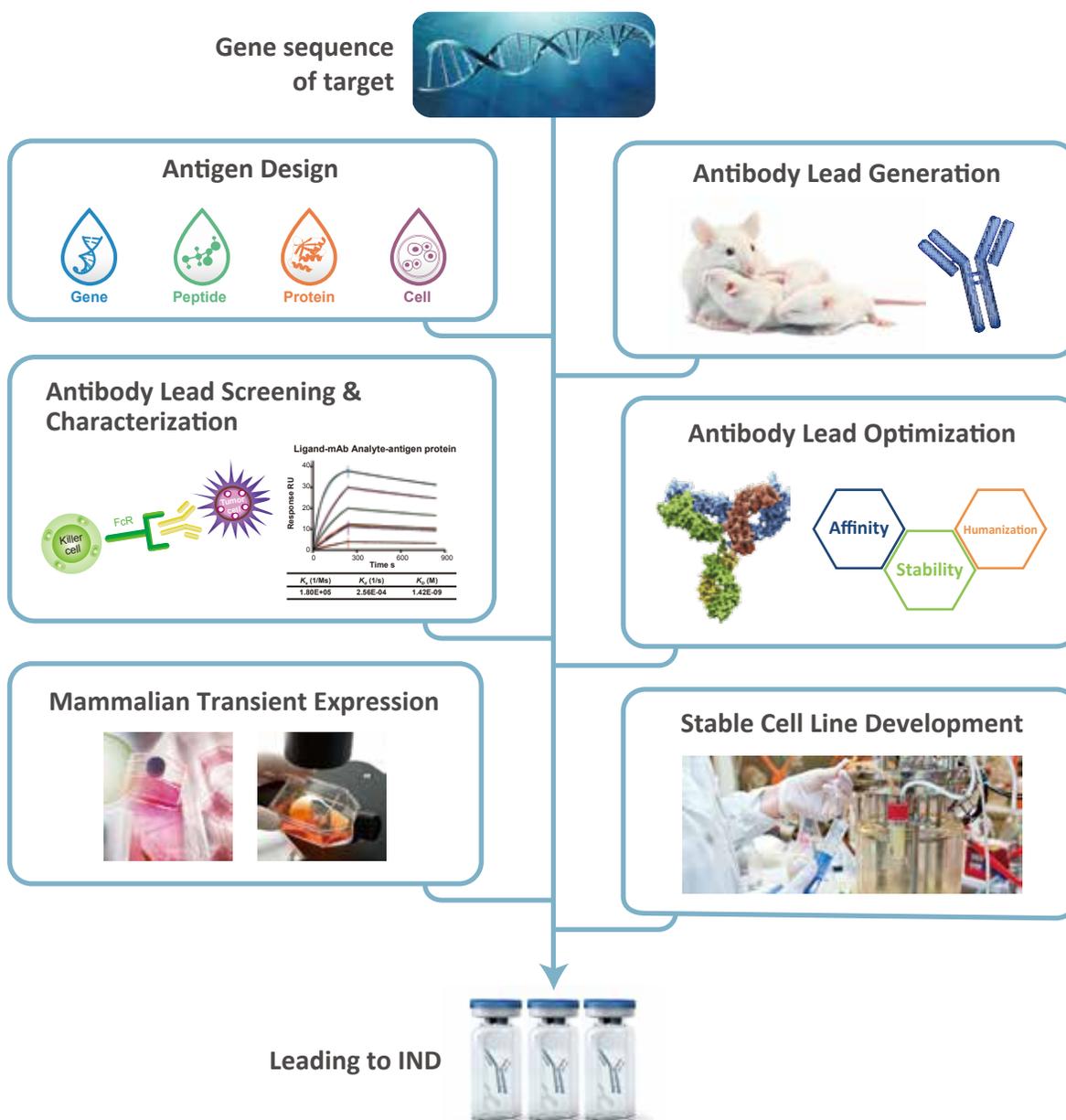
Identify your target, we'll do the rest



- Antibody Lead Generation
- Antibody Lead Screening & Characterization
- Antibody Lead Optimization
- Antibody Transient & Stable Expression

ACCELERATE YOUR ANTIBODY DRUG DISCOVERY & DEVELOPMENT

Since 2004, GenScript has been customizing antibodies for widespread applications. Our team has experience with over 150 antibody drug discovery projects. With extensive understanding and familiarity, we are proud to offer the critical services for antibody drug discovery & development. Select a single service as your needs require, or utilize our comprehensive offerings for a smooth and swift transition from lead generation, to optimization, all the way through production.

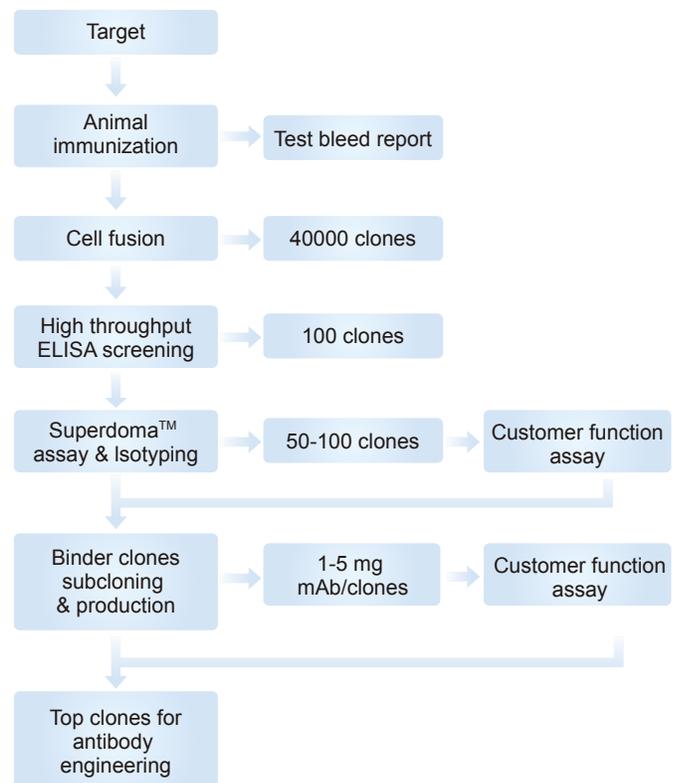


HYBRIDOMA ANTIBODY DRUG DISCOVERY

GenScript's **13 years** of custom antibody generation experience can deliver a panel of hybridomas under **4 months** with our standard protocol.

We Provide:

- **A full spectrum of immunization approaches:** protein, peptide, whole cells and DNA. OptimumAntigen™ Design Tool guarantee results*.
- **Optimized immunization:** transgenic mice generate high affinity antibodies. Proprietary adjuvant and immunogen modification breaks immunological tolerance for superior immune response.
- **Complete service:** from antigen production to hybridoma development and characterization.
- **High throughput:** high efficiency screening. Proprietary NativeSelect™ ELISA for soluble targets. HT March™, iQue HT Screener, and BD FACS Calibur with HT loader for membrane targets.
- **Comprehensive functional assays:** Validated functional assay platforms provide reliable *in vitro* screening.
- **Readily integrated with other drug discovery services:** Antibody sequencing, antibody humanization, recombinant antibody production and anti-idiotypic antibody generation.



Note:

1) We can customize your project based on your specific requirement.

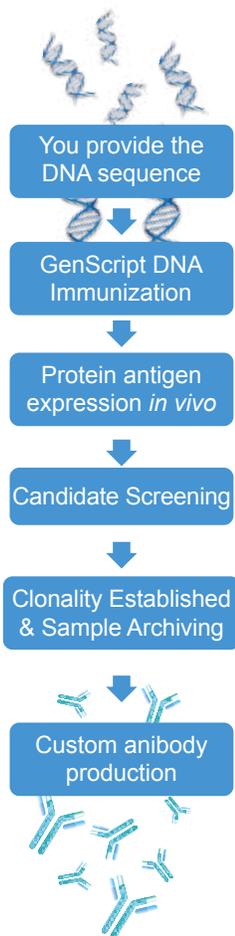
2) We provide free cell line storage service for 6 months from the date of cell freezing.

*) We recommend GenScript provides immunogen for highest quality .

DNA IMMUNIZATION

Leverage *In Vivo* Antigen Expression:

Problematic immunizations involving antigens that are difficult to synthesize, unstable, insoluble, or hard to purify, can be resolved with DNA immunization. As the immune response generated via DNA immunization is against **native protein structure**, loss of recognition due to lack of maturation or manipulation is prevented. Additionally, compared to traditional immunization regimens, DNA immunization results in smaller amounts of protein expressed, ultimately yielding higher affinity antibodies. There is also an opportunity for codon optimization and design of appropriate plasmid vectors that can promote transfection efficiency. Further still, engineering specialized adjuvant and immune mediators can enhance immune response. Beyond these advantages, little differs between traditional regimens and DNA immunization as outlined below.



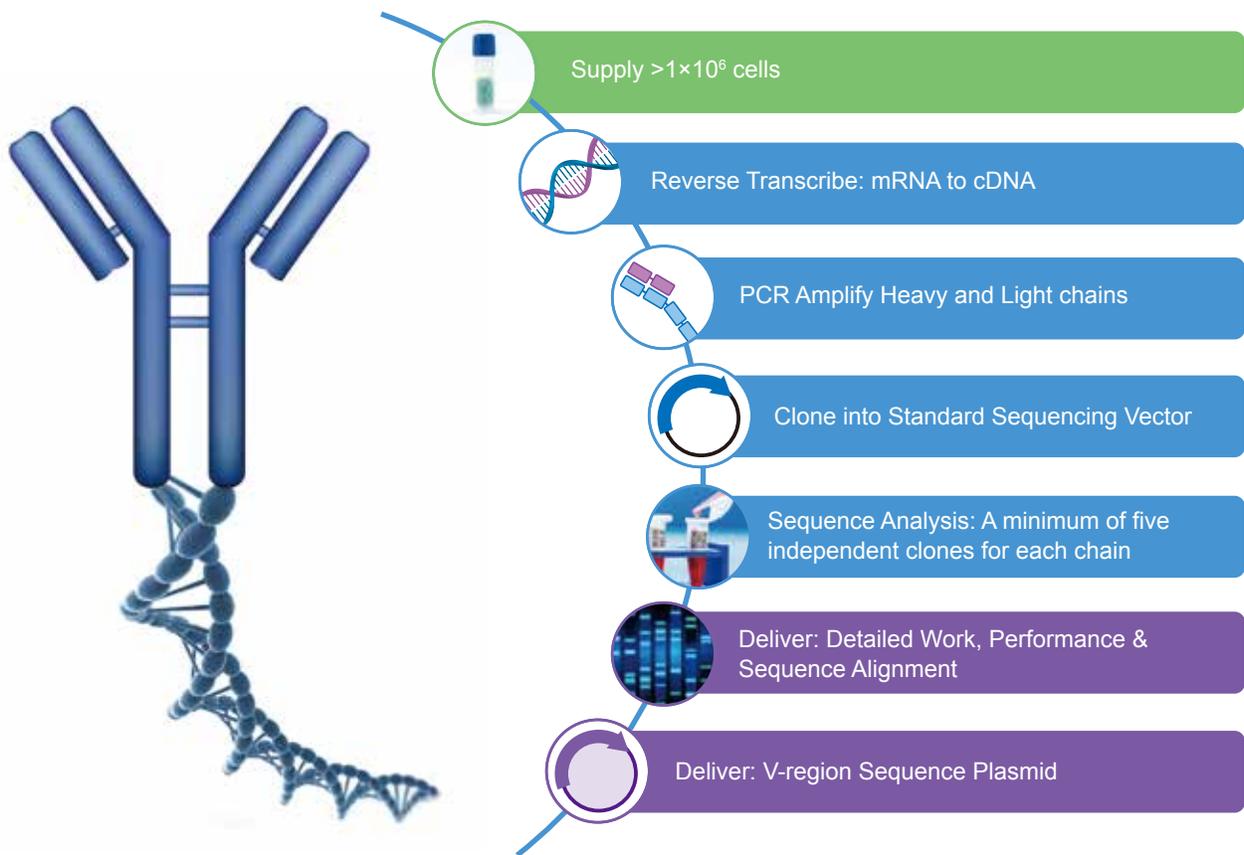
Protocol	Timeline
<ul style="list-style-type: none"> Codon optimization Gene synthesis & plasmid preparation <i>In vitro</i> cell transfection for expression validation 	2-3 weeks
<ul style="list-style-type: none"> DNA immunization via gold particle bombardment with gene gun Test bleed by ELISA and/or FACS 	6-10 weeks
<ul style="list-style-type: none"> Animals selected for fusion based on titer Primary screening by whole cell based ELISA or HT FACS Customer can evaluate hybridoma supernatants and select the top clones for their application Additional screening options available 	4-6 weeks
<ul style="list-style-type: none"> Hybridomas are subcloned by limiting dilution according to the customer's valuation result, then expanded & frozen 	
<ul style="list-style-type: none"> Production of mAbs for each cell line with roller bottle culture or ascites Purification ELISA, FACS and other characterization results 	Project Based

As with all GenScript services, we can tailor any protocol to custom fit your research.

ANTIBODY SEQUENCING

Our experienced hands, Your unique sequence

GenScript takes the greatest care to insure a 100% accurate sequence. Each chain is cross verified amongst 5 independent clones. No mutations are introduced with both 5' and 3'-RACE Full Length sequencing of the variable region from FR1.



Value and Speed:

In as little as 6 days, GenScript delivers the data needed to protect your intellectual property. Sequencing of antibody binding regions also opens further development such as humanization and recombinant antibody production.

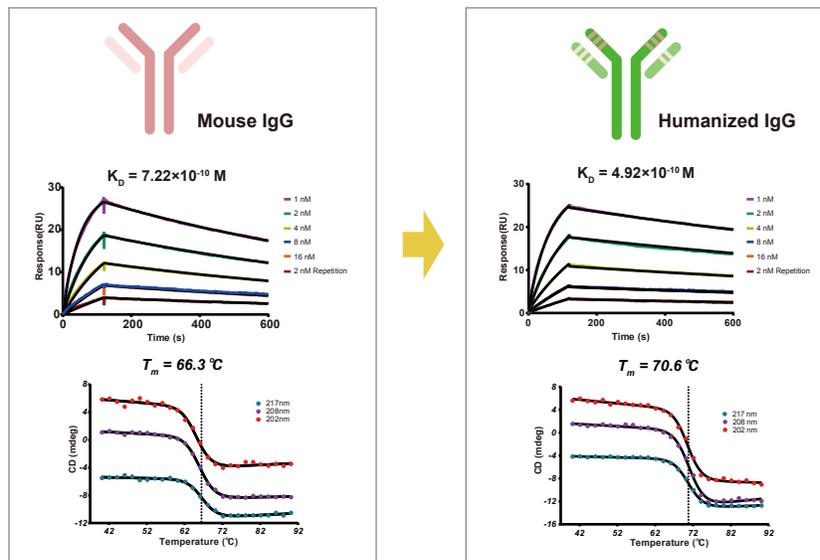
ANTIBODY HUMANIZATION

Lose the immunogenicity, keep the accuracy.

Replacing everything but the complementarity determining region (CDR) reduces the degree to which an antibody drug can itself act as an immunogen. Immunization against an antibody drug lowers efficacy through reduction in circulating half-life and/or neutralization.

Our Strategy:

- **CDR-grafting**
- **Patented** library based “framework assembly”
- **FASEBA**: FASEB Screening for Expression level, Biophysical properties, and Affinities



The engineering and screening procedures are integrated, allowing for simultaneous antibody humanization and stabilization. We even guarantee the affinity of the humanized antibody will be equal to or higher than the affinity of your parental antibody.

Milestones	Deliverables	Timeline
Humanized Fab Library design and construction	<ul style="list-style-type: none"> • Sequence, DNA and 1 mg of purified protein of humanized antibody with affinity matching its parental non-human antibody • Report 	19 weeks
Phage display and FASEBA screening		
Humanized antibody production and characterization		

TRANSIENT EXPRESSION

Scale-up Production

GenScript manufactures recombinant antibodies (rAbs) from microgram to gram quantities in our Mammalian Transient Expression System. We use Chinese Hamster Ovary (CHO) and Human Embryonic Kidney (HEK) 293 cells as our primary cell lines for transient expression. They are easy to handle, have robust growth rates, excellent transfectability and high yield recombinant protein-generation capacity. After the client provides the antibody sequence, transfection through antibody production can be accomplished in as little as three weeks.

Standardized Expression Packages	When to use this service	Features*	Timeline
High Throughput Gene to Antibody	<ul style="list-style-type: none"> For rAb production of samples 24 and up, up to mg. 	<ul style="list-style-type: none"> Starts with either codon optimization and gene synthesis or using customer-supplied DNA Deliverables include affinity purified rAb, report & QC data 	As soon as 3 weeks
MamPower™ mammalian rAb expression	<ul style="list-style-type: none"> For rAb production up to 500mg at ≥95% purity. 	<ul style="list-style-type: none"> Starts with codon optimization & gene synthesis Guaranteed service Deliverables include synthetic genes, optimized gene sequence report, rAb, QC data 	As soon as 5 weeks
Large scale rAb production	<ul style="list-style-type: none"> For large scale rAb production up to 5g at ≥99% purity. 	<ul style="list-style-type: none"> Starts with codon optimization & gene synthesis Guaranteed service Deliverables include purified rAb, report, QC data 	9-12 weeks



* Required for the guaranteed packages but optional for Custom services

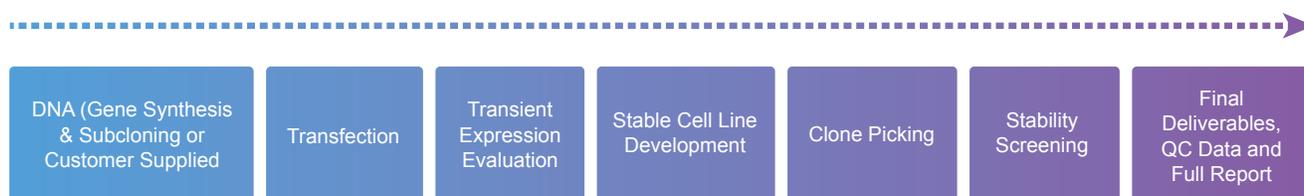
QC data: SDS-PAGE and/or HPLC will be performed to determine protein and rAb purity. BCA or Bradford assay will be used to measure protein concentration and A280 will be used to measure rAb concentration. LC-MS/MS peptide mapping will be used to determine protein identity if necessary. GenScript uses The Endosafe®-PTS™ endotoxin testing system from Charles River Laboratories, for rapid endotoxin detection.

“Guarantee” indicates that deliverables will meet or exceed requirements listed for the respective service. If deliverables do not meet guarantee, there is no charge to customer.

STABLE EXPRESSION CELL LINES

GenScript offers comprehensive stable cell line development capabilities that either begin with client provided DNA or seamlessly integrate with our fast, high efficiency gene synthesis service. Regardless of source, the result is delivery of high quality, stable clones of your design. Long term, consistent, reliable antibody production can be achieved from one of our stable cell line options below.

		Guaranteed Gram Level (SC1709)	Stable Bioproduction (SC1503)	Advanced Bioproduction (SC1557)
Features	Selection system	GS	GS or DHFR	GS or DHFR
Steps	Guaranteed yield	✓	✓	✓
	1. Gene synthesis & subcloning (optional)	✓	✓	✓
	2. Transient expression evaluation	✓	✓	✓
	3. Stable cell line development	✓	✓	✓
	4. Process development	optional	optional	✓
	5. Production service	optional	optional	optional
Deliverables	Target gene(s) in pUC57 & vector map	✓	✓	✓
	Expression Report	✓	✓	✓
	Top 3 stable clones (5 clones for SC1557)	✓	✓	✓
	Comprehensive report	–	–	✓
Time (weeks)		14-17	26-29	36-39



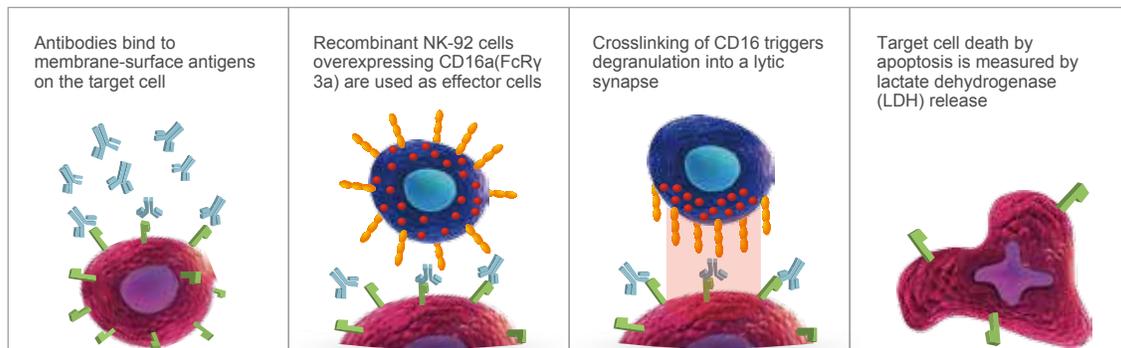
ADCC & CDC ASSAYS

Antibody therapy has been proven to be highly powerful for cancer treatment. Two important mechanisms used by antibody drugs to kill targeted tumor cells are Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC), and Complement Dependent Cytotoxicity (CDC). GenScript is pleased to present to you both a PBMC-based ADCC assay and natural kill cell-based ADCC assay. The readout is endpoint-driven (target cell lysis). The CDC assay uses normal human serum as the source of complement. By implementing strict QC standards, GenScript can provide the assurance of the efficacy and potency profiles of your therapeutic antibodies.

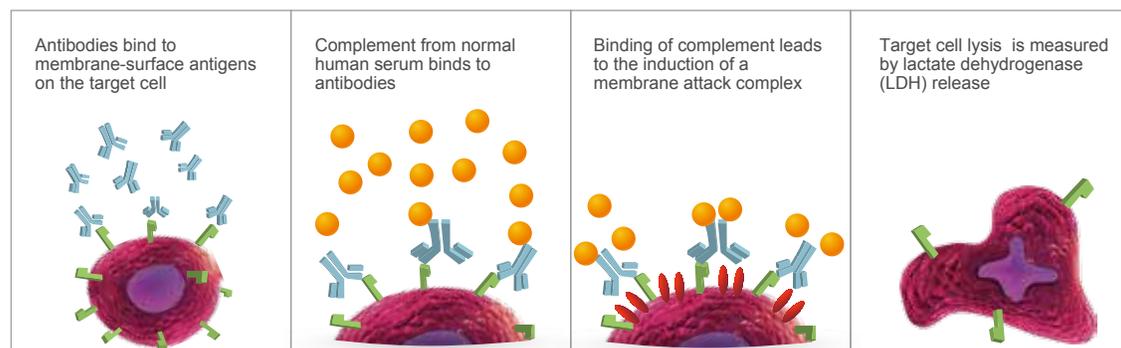
Key Features

- Data readout is driven by the target cell lysis endpoint
- Over 240 target tumor cell lines across 22 cancer types free of charge to be used in ADCC assays
- Ready-to-go ADCC assay format for at least 4 targets: HER2/ErbB2, CD20, EGFR, and TNF α
- Ready-to-go CDC assay format for at least 2 targets: CD20 and TNF α
- High throughput assay service for bulk antibody drug screening

Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)



Complement-Dependent Cytotoxicity (CDC)



HUMAN TUMOR CELL LINE PROFILING

Oncology drug discovery requires knowing the pharmacological mechanism, and efficacy of drug molecules on human tumor cell lines. GenScript's human tumor cell line profiling packages, OncoProfiler and XenoProfiler, provide you with a combined panel of over 240 human tumor cell lines as well as a range of high throughput screening (HTS) options. Together, they can not only provide efficacy data in human tumor cell lines, but also ensure translation of efficacy from *in vitro* to *in vivo* models.

Key Features

- OncoProfiler – Choose from over 200 cancer cell lines to profile for apoptosis and growth
- Xenoprofiler – Choose from over 40 cancer cell lines validated in *in vivo* xenograft models
- High quality assay criteria and short turnaround time
- High throughput screening (HTS) options available

As a fully custom service, we offer a wide range of assays to use for proliferation and apoptosis profiles. Additionally, we offer biomarker, cytokine induction and combinatorial drug effect screening

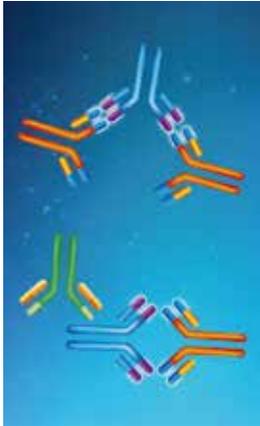
Profile	Assay Description	Throughput
Proliferation	Luminescent cell viability assay	384-well
	MTT/MTS assay	96-well
	LDH assay	96-well
	SRB assay	96-well
Apoptosis	Caspase assay	384-well
	Annexin V/PI assay	96-well
	Other FACS analysis	96-well
Biomarker	Genotyping of cell line	48-well
	Sequencing	
	mRNA expression level	96-well
Cytokine induction	Cell viability assay with optimized incubation time	96-well
Combinatorial drug effect	Using any of the above assays	
Custom	Customer defines assay type for any of the profiles	

Tumor/cancer cell lines represented in OncoProfiler and XenoProfiler

Custom	Gastric	Oral	Rabdomyo Sarcoma
Bone	Kidney	Ovarian	Skin
Brain	Leukemia	Pancreatic	Spleen Macrophage
Breast	Liver	Prostate	Synovial
Cervical	Lung	Rectal	Uterine
Colon	Lymphoma		

ANTI-IDIOTYPE ANTIBODY

Detect the Targeting Moiety



Pharmacokinetics (**PK**), Pharmacodynamics (**PD**), and **Immunogenicity** studies of antibody drugs rely on measuring circulating concentrations. Adding an artificial tag or label to a antibody drug could introduce confounding results. To avoid this risk, GenScript generates **antibodies against the complementarity determining region** (CDR), the unique sequence intrinsic to the antibody drug. Such anti-idiotype (anti-ID) antibodies have their own CDRs specific to the variable region of the antibody drugs. Anti-ID antibodies can directly detect antibody drug levels in **PK/PD studies** or can be used as positive control in **Immunogenicity** studies. Since the CDR is such a small portion relative to the whole IgG, typical immunizations generate a very small percentage of antibodies against this region. It is therefore very difficult to recover any anti-ID antibody. Despite this, GenScript has a **100% success rate** in generation of anti-ID antibodies thanks to proprietary antibody affinity and specificity development technologies.

Services	Anti-idiotype monoclonal antibody	Anti-idiotype polyclonal antibody
Starting material	Target antibody drug 2-3mg	Target antibody drug 20 mg or more
Work flow	<ul style="list-style-type: none"> Immunize mouse/rat/rabbit using target Ab drug ↓ Cell fusions to create 10,000-20,000 clones ↓ Positive screening with target Ab drug to identify >100 binders ↓ Specificity screening with control antibody ↓ Select clones for subcloning, collect supernatant, and deliver 	<ul style="list-style-type: none"> Collect pre-immune sera ↓ Immunize rabbit using target Ab drug ↓ 1st boost ↓ Test bleed and ELISA ↓ 2nd boost (&3rd boost when necessary) ↓ Terminate and final bleed ↓ Purify anti-ID Ab using target Ab drug ↓ Cross absorption using control IgG
QC	Cross-reactivity with control IgG <10%	Cross-reactivity with control IgG <10%
Deliverables	Hybridoma cell lines, supernatants and purified anti-ID antibody (optional)	0.5-3mg purified anti-ID antibody/rabbit

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