curia

Antibody discovery & engineering services

Overview of antibody discovery & development at Curia

The Curia Antibody Center offers comprehensive antibody discovery and engineering services, including identification, optimization, and characterization of new leads.

DISCOVERY	ENGINEERING	DEVELOPMENT	MANUFACTURING
• Hybridoma platform for *in vivo* discovery • *In vitro* phage and yeast display platforms • Antibody functional characterization • Epitope binning and mapping	• Humanization • Affinity maturation and measurement • Sequence liability identification • Therapeutic developability assessment	• Downstream antibody transient and stable production, process development, and GMP manufacturing services are offered by other Curia sites.	

The Antibody Center's goal is to help researchers discover potent and functional antibodies.

To achieve this goal, the Antibody Center offers a variety of high-performance hybridoma- and display-based technologies. The specific discovery approach depends on project-intrinsic parameters, which include goals, timelines, and scientific considerations.

In vivo hybridoma approach to identify novel therapeutic-grade antibodies

The Curia hybridoma platform offers multiple immunization approaches to achieve maximum plasma titers. Curia has developed a robust hybridoma-based workflow for the discovery of diverse high-quality monoclonal antibodies with desired functional and specificity attributes.

CHAIN OF DISCOVERY℠ PACKAGE INCLUDES:

- Strategy design
- Multiple immunization approaches
- 384-well plate-based hybridoma screening
  - » Target binding via ELISA or FACS
  - » Cyno and/or mouse cross-reactivity
  - » Counterscreens for specificity
  - » Kinetics and epitope binning using Octet® system or Carterra® LSA® platform
  - » Ligand blocking
  - » Cell assays
- Hybridoma subcloning and variable region sequencing
- Purified mAbs from hybridoma for EC_{50}, KD analysis, etc.

The package is fully customizable.

HYBRIDOMA CAMPAIGNS BY THE NUMBERS

95+
completed discovery campaigns

97%
hit identification success rate

45+
clients served

Curia's due diligence

To increase the probability of campaign success, Curia conducts rigorous target analysis utilizing bioinformatics, literature, and patent data to identify target-specific considerations that could impact discovery effort. Throughout the campaign, clients will receive data updates, enabling Chain of Discovery tracking from immunizations to mAb sequences.

Campaign customization options

RODENTS
Wildtype and fully human antibody-producing transgenic mouse strains are available.

BINDING AND FUNCTIONAL ASSAYS
Curia can customize epitope binning, blocking, internalization, cell assays, and more.

IMMUNOGEN OPTIONS
Curia can custom design and prepare antigens based on client needs.

IMMUNIZATIONS
A variety of immunizations are available to suit each client's project goals and timelines.

- Tolerance-breaking approaches can achieve titer against mouse targets and increase epitope diversity.
- Proprietary DNA immunogen and UberCell℠ approaches can lead to high titers against challenging transmembrane targets such as GPCRs.
- Rapid protein-based approaches such as HT-HOCK℠ can achieve high titer within a short time frame.

Curia's PentaMice® platform

A proprietary set of wildtype mice designed to achieve maximum plasma titers in hybridoma campaigns

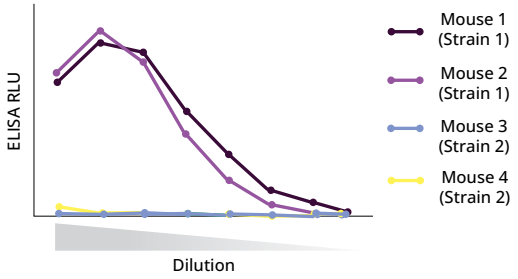
Conventional immunization approaches utilized in hybridoma-based antibody discovery campaigns typically use one or two common wildtype (WT) mouse strains (e.g. Balb/c or C57Bl/6). This approach likely limits the identification of high-quality antibodies to just those target antigens that are efficiently processed and presented by a restricted major histocompatibility complex (MHC) repertoire.

Curia's PentaMice platform is a royalty-free set of mice comprising 5 WT strains that cover 9 distinct MHC haplotypes. A total of 10 mice (2 mice of each strain) are included in each set to achieve maximum plasma titers, thus boosting the opportunity to generate high-quality antibodies *in vivo*.

The concept behind the PentaMice platform

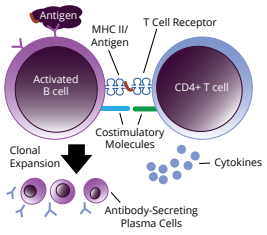
1

Plasma titers are highly predictive of antibody discovery success. Based on Curia's experience, there is often a strong strain-dependent difference in plasma titers for most targets.



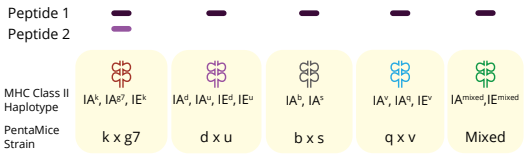
2

High plasma titers require T cell help, and one of the requirements for effective T cell activation is recognition of cognate antigens presented by the MHC. Only certain peptides are effectively presented by certain MHC.



3

MHCs are highly polymorphic. Curia's scientists hypothesize that this polymorphism drives strain-dependent differences in plasma titers. Hence, the PentaMice platform is designed to cover a wide range of MHC haplotypes to enable effective T cell help.



Two different peptide binding profiles are shown as examples. Peptide 1 is effeciently presented by most MHC II. Peptide 2 is only efficiently presented by IA^{g7}.

The five wildtype strains in the PentaMice platform


b x s


d x u


k x g7


q x v


Mixed

In vitro display approach for antibody discovery and development

Curia offers various display platforms for *de novo* antibody discovery and engineering.

COMPREHENSIVE SERVICE INCLUDES:

- Strategy design
- Custom library construction and screening using naïve, semi-synthetic, or immune libraries of scFvs, Fabs or llama VHH
- Primary and secondary functional screens (multiple hits)
- Lead antibody characterizations:
  - » Kinetics and epitope binning using Octet® system or Carterra® LSA® platform
  - » Ligand blocking
  - » ELISA
  - » Cell assays

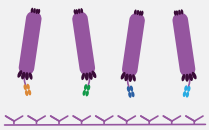
ENGINEERING PROJECTS BY THE NUMBERS

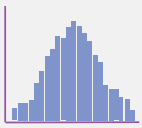
105+
completed projects

88%
lead identification success rate

25+
clients served







STRATEGY DESIGN	LIBRARY CONSTRUCTION	SCREENING AND SELECTION	1° OR 2° FUNCTIONAL SCREENS	LEAD ANTIBODY CHARACTERIZATION
• Flexible workflow • Parallel campaigns	• Large & diverse • Different antibody scaffolds	• Immobilized, cell, or soluble antigens • ELISA/FACS binding • Preliminary kinetics using Carterra LSA platform	• Cell based assays • Reporter assays • Neutralization assays	• IgG reformatting • Kinetics & epitope binning • Ligand blocking

Curia Library collections for phage and yeast display

CURIA CUSTOM IMMUNE LIBRARY

Antibody Formats
scFv/Fab/VHH via phage
scFv via yeast

Turnaround Time
5 months

Licensing Terms
None

Curia's custom immunization-based libraries are very versatile as they can be applicable to multiple species, antibody formats, and transgenic models. Utilizing patients' or animals' natural immune response coupled with the advantages of phage/yeast display platforms enables discovery of high affinity and specificity antibodies. In many cases, there is no additional need for affinity maturation.

Risk Mitigation
Early developability assessment of hits, *in silico* immunogenicity prediction, and humanization are recommended.

Applications
- Antibody discovery for therapeutics, diagnostics, and reagents purposes
- Suitable for diverse targets and antigen formats as well as CAR T generation

XOMA HUMAN Fab AND scFv LIBRARY

Antibody Formats
scFv/Fab via phage

Turnaround Time
3 months

Licensing Terms
Pre-negotiated, reduced terms

Curia has partnered with XOMA to provide XOMA040 scFv and XOMA031 Fab human naïve phage libraries. Both libraries have large diversity (>10^{11}), fully human and natural repertoire, and originate from 30 healthy donors. A wide range of high affinity antibodies can be generated without affinity maturation.

Multiple antibodies generated from XOMA libraries are in clinical trials.

Risk Mitigation
Early developability assessment of hits are recommended.

Applications
- Antibody discovery for therapeutics purposes
- Bispecifics, scFv library is suitable for CAR T generation
- Suitable for diverse targets including toxins and pathogens

Antibody engineering

Curia offers a wide portfolio of antibody engineering and optimization services.

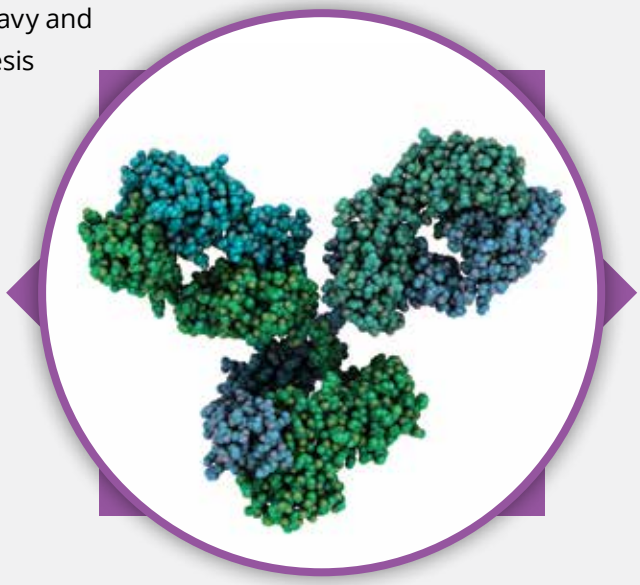
AFFINITY MATURATION
Increase target binding affinity via light chain shuffling or heavy and light chain CDR mutagenesis

ANTIBODY HUMANIZATION
Modify lead antibodies to be more human-like

- Humanization analysis via Curia's validated platform — the T20 score analyzer

BISPECIFIC ANTIBODY GENERATION & CHARACTERIZATION

- Binding and functional assays
- Expression and development



EPITOPE BINNING
Group antibodies with similar profiles into bins specific to the same or overlapping epitopes using array SPR-based Carterra® LSA® platform or BLI-based Octet® HTX system

ANTIBODY REFORMATTING
Reformat different antibody scaffolds into IgGs of multiple isotypes or species

SEQUENCE LIABILITY IDENTIFICATION
Assess candidate quality by identifying sequences that can present potential liabilities to product quality

Carterra® LSA® platform

Octet® HTX system

HuMAT℠ approach

Save time and costs with Curia's proprietary one-step antibody humanization and affinity maturation approach.

Developability assessment

Evaluating developability of antibodies early on can help circumvent potential development issues in downstream processes.

DISCOVERY → ENGINEERING → OPTIMIZATION → PRECLINICAL → IND

Run developability assays earlier to circumvent development issues later

CURIA OFFERS A SERIES OF FAST, SMALL-SCALE TESTS AND PREDICTIVE TOOLS TO ASSESS DEVELOPABILITY

In silico Developability Check
- DNA codon preference
- Protein sequence liability analysis
- Immunogenicity analysis

Activity Check
- Affinity assays including SPR (Biacore® system, Carterra® LSA® platform) or BLI (Octet® system)
- Epitope binning with Carterra® LSA® platform or Octet® HTX system
- Cell-based functional assays

PK Readiness Check
- Polyspecificity ELISA
- Surface hydrophobicity assay

Productivity Readiness Check
- Small-scale transient production in CHO system

Biophysical Profile Check
- Intact mass/peptide mapping by mass spectrometry
- Thermostability assessment by DSF or DSC
- Aggregation and purity analysis by SEC-UPLC and CE-SDS
- Biophysical profiling over various stress conditions

LabChip® GXII Touch™

Nano DSC

UNcle®

Carterra® LSA®

Q-TOF Mass Spec

Three developability packages to suit your needs

RAPID AND SMALL-SCALE ASSESSMENT OF DRUG CANDIDATES

DEVELOPABILITY PACKAGE 1

- *In silico* Sequence Liability analysis
- *In silico* Immunogenicity analysis
- Turnaround time: 1 week

DEVELOPABILITY PACKAGE 2

- Polyspecificity Assessment
- Integrity and Stability Assessment
  - » Aggregation
  - » Purity
  - » Charge Variant
  - » Thermostability
  - » Post-translational modifications
- Turnaround time: 2–3 weeks

FORMULATION AND STABILITY STUDY

DEVELOPABILITY PACKAGE 3

- Buffer Exchange
  - » Curia standard panel formulations
  - » Client may opt to choose their buffers
- Forced Degradation
  - » Thermal stress
  - » Freeze thaw
- Available optional stress services
  - » Agitation
  - » Oxidation
  - » Photostability (Light)
  - » pH acid/base

Curia's integrated solutions for antibody discovery through development and manufacturing

Step 1 >

ANTIBODY DISCOVERY & ENGINEERING

- Hybridoma platform for *in vivo* discovery
- Phage and yeast display for *in vitro* discovery
- Affinity maturation, humanization, and more

Step 2 >

ANTIBODY SEQUENCING

Cloning and sequencing services are available for:

- Hybridoma IgG regions from multiple species including mice, rats, rabbits, and hamsters
- Primate B cell IgG and IgM
- *De novo* sequencing of antibodies

Step 3 >

MOLECULAR CONSTRUCTION

Synthesis of antibody variable region, plasmid design and construction services:

- Multiple species and isotypes are available, with the option of synthesizing a custom constant region

Step 4 >

TRANSIENT PRODUCTION

CHO Transient Antibody Production

CHO cells are preferred since antibodies will maintain similar PTM profile to stable CHO cells. Curia's proprietary TunaCHO℠ platform offers:

- Productivity as high as 1.5 g/L

High-Throughput 96-Block Antibody Production

A fast and cost-effective way to produce large quantity of antibodies for fast antigen binding assays and productivity screening.

- 96 antibodies can be constructed, produced, purified, and delivered in 5–7 weeks

Step 5 >

STABLE PRODUCTION

Streamlined service includes stable cell line development using Curia's proprietary CHO-GSN℠ platform for research/master cell bank generation.

Step 6 >

PROCESS DEVELOPMENT

- Upstream, downstream, and analytical process development
- Assay development

Step 7 >

GMP PRODUCTION

GMP process design & development:

- Proof of concept
- Small-scale models
- Seamless tech transfer
- Reliable scale-up processes
- Engineering and GMP runs for DS and DP
- Release testing of DS and DP
- Stability studies for DS and DP
- Biorepository for GMP materials

Curia's integrated solutions for discovery through development and manufacturing of analyte-specific reagents

Analyte-specific reagents (ASRs) such as monoclonal antibodies against idiotypes, proteins, or haptens are used for identification and quantification of substances in biological specimens. Curia offers integrated solutions for ASR discovery, development, and GMP manufacturing, with all services performed in the Bay Area.

CURIA INTEGRATED SOLUTIONS

ANTIBODY DISCOVERY

- Fast, on-demand antibody discovery against any targets
- Multiple formats available (IgG, Fab, scFv, VHH)

DEVELOPMENT

- Transient protein production using Curia's TunaCHO platform
- Stable cell line development using Curia's CHO-GSN platform
- Streamlined process development for parameter setting before GMP manufacturing

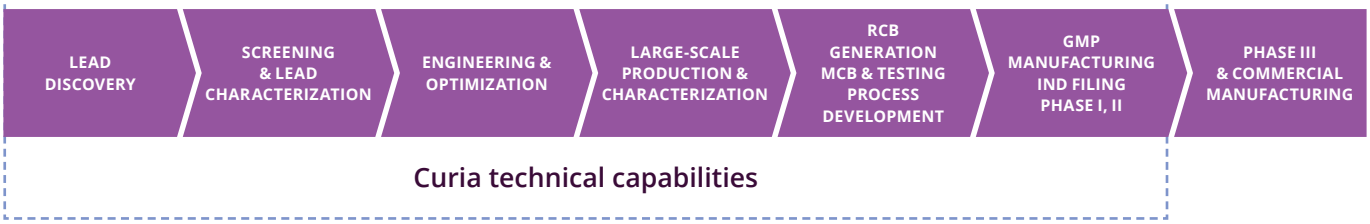
GMP MANUFACTURING

- Various customization options available including concentrations, release criteria, and quantity

WORKING WITH CURIA

- Complete technology platform
- Technical consultation with experts specialized in antibody discovery and development
- Curia's online client portal — the Data & Process Management System — allows 24/7 access to project information (timelines, data, team communications)
- Strong project management with regular project updates

Curia provides integrated solutions for biologics development



ABOUT CURIA

Curia is a Contract Development and Manufacturing Organization with over 30 years of experience, an integrated network of 29 global sites and over 3,500 employees partnering with customers to make treatments broadly accessible to patients. Our biologics and small molecule offering spans discovery through commercialization, with integrated regulatory and analytical capabilities. Our scientific and process experts and state-of-the-art facilities deliver best-in-class experience across drug substance and drug product manufacturing. From curiosity to cure, we deliver every step to accelerate and sustain life-changing therapeutics. ***Learn more at curiaglobal.com***

Solutions developed by Curia

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