

TECHNICAL NOTE:

RAPID ANTIBODY DISCOVERY THROUGH B CELL CLONING ON THE BEACON® PLATFORM

ADVANCE ANTIBODY DISCOVERY WITH SINGLE B CELL CLONING

Several methodologies have been developed for generating monoclonal antibodies. Hybridoma technology is the most widely used method for antibody generation. However, there are major disadvantages to this process, such as being time consuming, laborious and of low-efficiency. Phage display, another common method used for antibody discovery, can often provide limited and biased repertoires due to non-cognate VH/VL pairing. Both of these methods have notable limitations, despite being important and reliable antibody discovery engines.

TABLE 1. COMPARISON OF ANTIBODY GENERATION METHODS

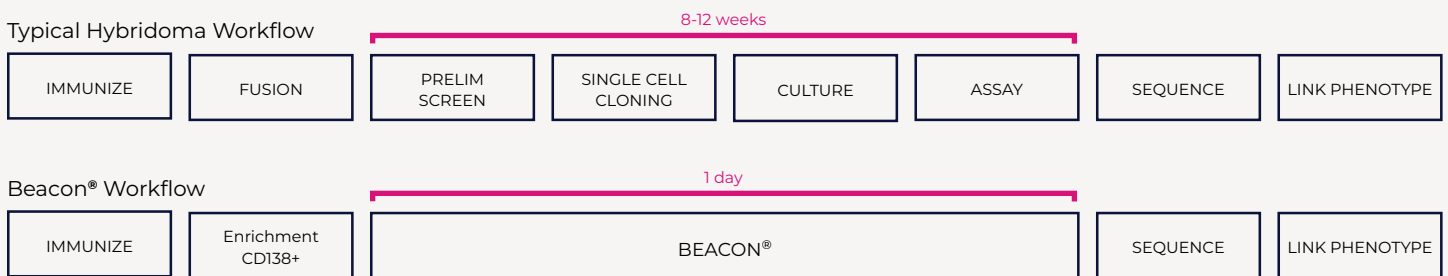
METHODS	ADVANTAGES	DISADVANTAGES
Hybridoma	<ul style="list-style-type: none"> Well-established processes Natural VH/VL pairing No need for special equipment Low R&D costs 	<ul style="list-style-type: none"> Low fusion efficacy; high cell number required Loss of clones due to chromosomal instability Loss of functional light chains due to genetic rearrangements Difficult to select and express low frequency positive clones from pools Long duration (> 4 months) Requires humanization of the Ab sequences Labor intensive to screen clones for desired binding and functional characteristics
Phage Display	<ul style="list-style-type: none"> Provides a direct linkage between phenotype and genotype of the antibody Avoids loss of sequence information in target-specific clones, unlike hybridoma and B cells Cell-free based approach allows for flexible and specific screening approaches 	<ul style="list-style-type: none"> Limited B cell repertoire depending upon library size Expression bias Efficacy on 500+ xenograft animal models Folding errors by unnatural pairings of VH/VL Restrictive post-translational modification due to prokaryotic expression Limited quantitative assays during panning process Labor intensive to screen clones for desired binding and functional characteristics
Single B Cell Cloning	<ul style="list-style-type: none"> Short antibody discovery timelines Function-first approach: Allows to screen antibody secreting plasma calls in multiple assays (binding, blocking, functional assays) within hours of isolation from the immunized animal Discovery of highly functional antibodies with high affinity and rich genetic diversity Natural VH/VL pairing Allows de novo antibody discovery from different species High-throughput and automation (Beacon platform) Requires low quantity of reagents and cell counts 	<ul style="list-style-type: none"> High screening efficiency can be achieved with fresh samples Strict operating regimen Reagents require fluorescent labeling while retaining functionality Requires humanization of antibody sequences or use of humanized animals

BEACON® PLATFORM FOR SINGLE B CELL TECHNOLOGY FOR ANTIBODY DISCOVERY

Recently, a nanofluidic optoelectronic antibody screening technique, the Berkeley Lights, Inc. Beacon® platform, was introduced that integrates individual cell trafficking, imaging and culturing on a chip that is smaller than a business card. This screening platform is designed with the concept of putting “function first”. The distinguishing feature of the discovery workflow is that it enables the user to directly screen single antibody-secreting plasma cells against multiple assays within hours of isolation from an immunized animal (or person). Standard assays include screening for antigen specificity, cross-reactivity, and functional activity. By using the Beacon® for antibody discovery, the probability of identifying higher numbers of quality antibody leads against difficult targets is significantly improved.

Through our partnership with Berkeley Lights, ChemPartner offers services using the innovative Optofluidic based Beacon® platform at our South San Francisco research facility. The nanochip technology of the Beacon® platform enables us to analyze binding and functional characteristics of antibodies secreted from tens of thousands of single plasma B cells. Our Beacon® antibody service offers an accelerated antibody discovery workflow for obtaining high affinity and diverse antibodies compared to standard methods such as hybridoma technology and phage display.

FIGURE 1. AN ACCELERATED ANTIBODY DISCOVERY WORKFLOW BY THE BEACON® PLATFORM



ADVANTAGES OF USING BEACON® VERSUS OTHER PLATFORMS

Although a number of single-cell cloning approaches based on different technologies have been utilized for antibody discovery, the Beacon® offers many advantages over other platforms:

- Speed: Identify functional leads in a single day by multi-parameter phenotyping with high-throughput features
- Function First: Workflow enables streamlined selection of lead candidates through on-chip assays for antibody specificity, cross-reactivity, and functionality
- Diversity: Direct screening of plasma B cells representing a greater proportion of the immune repertoire
- Automation: Fully automated workflow including cell loading, single-cell penning, cell and/or protein-based assays, and exporting for sequencing
- Low risk: Reduced loss of positive clones for antibody sequencing
- Superior quality: Antibody leads with superior cross-reactivity, affinity and functionality

WHY WORK WITH CHEMPARTNER FOR ANTIBODY DISCOVERY WITH BEACON®?

At ChemPartner, as the first CRO adopter of the Beacon® Optofluidic System, we take immense pride in providing faster and unparalleled single-cell cloning solutions through this revolutionary technology. Our commitment to excellence and our dedication to optimizing the antibody discovery and antibody generation process sets us apart in the industry.

The Beacon® system has revolutionized single-cell cloning, but its success hinges on the expertise of the team operating it. Our highly experienced and skilled scientists form the backbone of our success because the intricacies of the single-cell antibody discovery process demand meticulous attention to detail. Without optimized reagents, assays, and processes, the final run risks failure. This is why our team invests significant effort upfront to maximize success rates. We understand that precision and accuracy are paramount to delivering top-notch results to our clients.

WE OFFER:

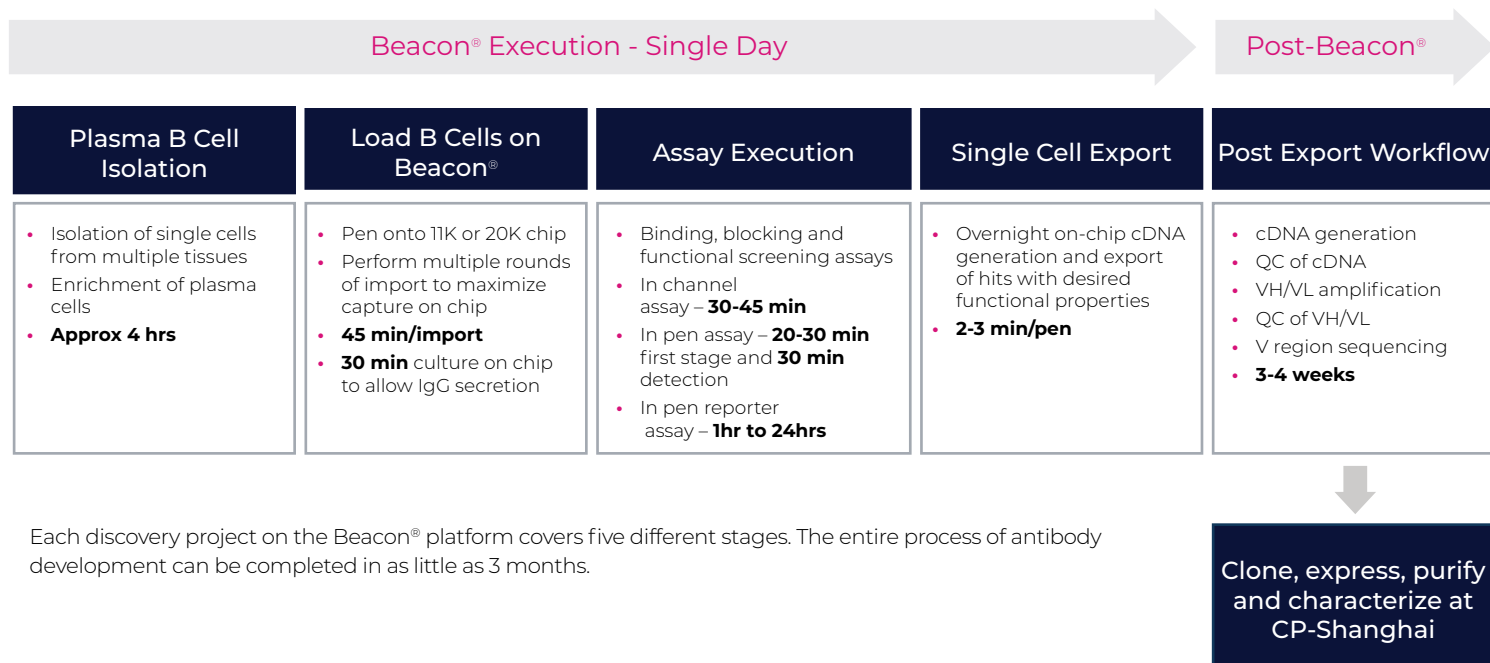
- Extensive experience with Beacon screening strategy design
- Strong support for Biologics discovery and development from CRO/CDMO teams
- Collaborative Bay Area partnership with Berkeley Lights (Beacon platform) and our South San Francisco research team
- Established workflows that enable antibody generation from multiple animal species
- Exploring single-cell cloning approach in various applications and therapeutic areas

Let us be your Beacon® to success. Our expert team is ready to show you the impact of precision and efficiency in your research.

ESTABLISHED BEACON® WORKFLOW AND PROJECT TIMELINE FOR ANTIBODY DISCOVERY AT CHEMPARTNER

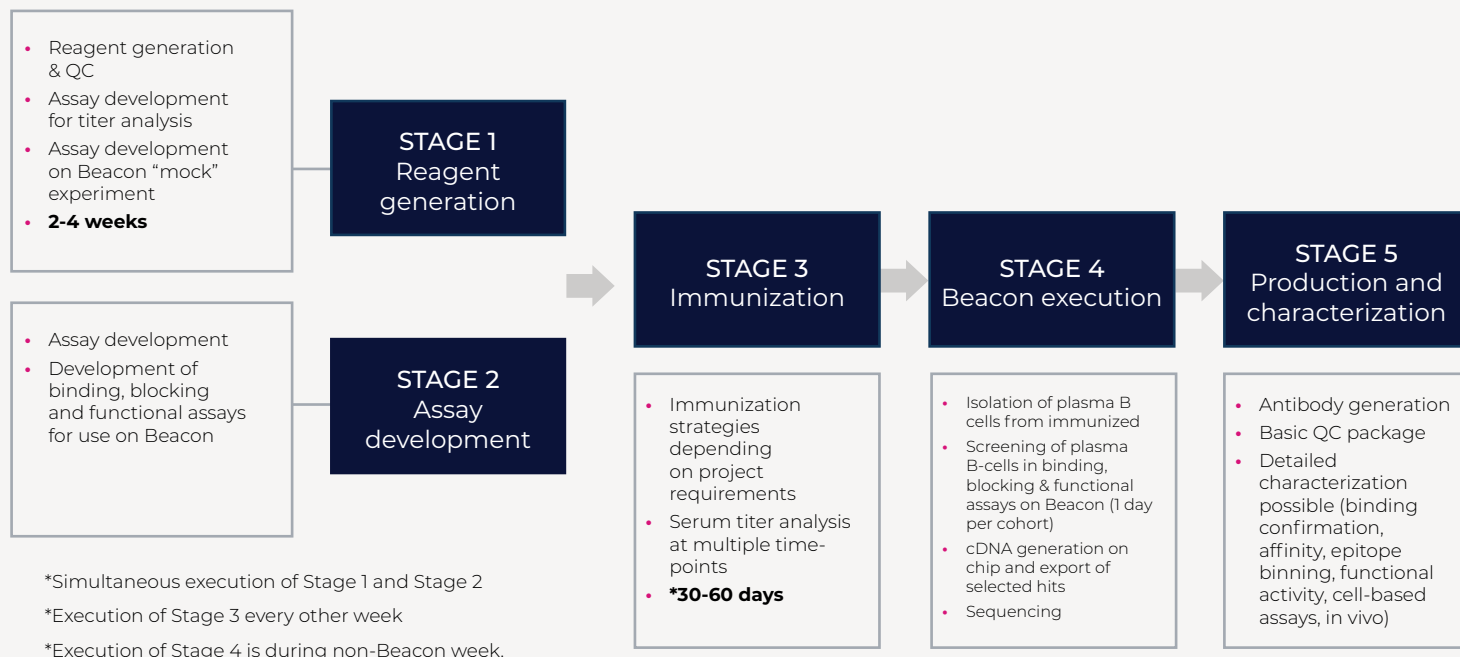
By working with us on the Beacon® platform, positive functional hits of your antibody candidates can be identified in a single day. Antibody sequencing and production can also be completed with the integrated and streamlined services offered at ChemPartner.

FIGURE 2. THE WORKFLOW OF PLASMA CELL SCREENING BY BEACON®



Each discovery project on the Beacon® platform covers five different stages. The entire process of antibody development can be completed in as little as 3 months.

FIGURE 3. OVERVIEW OF DIFFERENT PHASES OF BEACON® PROJECTS FOR ANTIBODY DISCOVERY



SINGLE B CELL APPROACH FOR ANTIBODY GENERATION AND MORE

In addition to our established capabilities for screening mouse, rabbit and human antibodies, ChemPartner’s Beacon® plasma B-cell workflow will soon be available for antibody discover services for additional species, including rat, alpaca/llama, and chicken. Recently, Beacon® technology has also been used for single cell phenotypic and genotypic characterization, identification of CRISPR-Cas9 edited primary T cells and analysis of T cell receptor repertoires. With a growing demand for T cell therapeutics, ChemPartner will soon be offering our T cell cloning services to enable clients to screen desired individual T cell phenotypes within heterogeneous T cell clones.

TABLE 2. BEACON® APPLICATIONS FOR MORE CLONING PLATFORMS

A. Antibody discovery: Various species available for plasma B cell workflow

SPECIES	AVAILABILITY	ASSAYS FOR
Mouse	Now	Specificity, cross-reactivity, blocking, functional activity
Rat		
Human		
Rabbit		
Alpaca/Llama		
Chicken		

LEARN MORE AT [CHEMPARTNER.COM/ANTIBODY-GENERATION-BEACON-OPTOFLUIDIC/](https://chempartner.com/antibody-generation-beacon-optofluidic/)