



APPLICATION NOTE

Accelerating Antibody Discovery: The Powerful Synergy of Hypercell High-Throughput Single-Cell Sorting and Humanized Mice

Introduction: Breaking Through Traditional Limitations

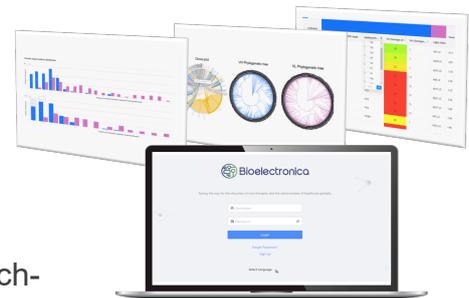
In today's competitive therapeutic landscape, **Pre-Clinical Candidate quality** and **speed to IND** determine market success. Leading biopharma companies and innovative biotech company are greatly interested in transformative approach that delivers:

- Human antibodies without time-consuming humanization engineering
- Months, not years from immunization to lead candidates
- Thousands, not hundreds of diverse antibodies to evaluate
- Superior candidates capturing rare, high-affinity clones traditional methods miss

Try out the strategic combination of humanized transgenic mice with Hypercell's breakthrough droplet microfluidics technology.



The Hypercell Platform
HT Single Cell Sorting



AbFinderAI Software
Antibody in Silico Analysis

Why This Combination Delivers Unprecedented Results

Comparison of methods in steps and time

Traditional Path ≥ 12 months



Synergistic Approach < 6 months

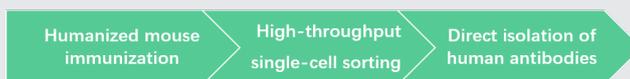


Figure 1: Upper: Comparison of traditional methods and combination methods in steps and time. Lower left: Transgenic mice adopt the original flavor replacement technology to integrate the human variable gene pool into the endogenous locus of BALB/c mice. Lower right: Schematic diagram of Hypercell single-cell sorting product.

Humanized mice eliminate downstream engineering:

- Human variable domains in a powerful mouse immune system
- No sequence liability issues from traditional humanization
- Maintains natural pairing and optimal binding properties

Hypercell-AbFinderAI's HT platform removes screening bottlenecks:

- Single-cell resolution prevents dominant clone bias
- Preserves natural heavy/light chain pairing

The Hypercell Solution: Redefining Antibody Pair Discovery

Our breakthrough platform combines Hypercell®'s high-throughput single B cell screening technology with AbFinderAI™'s rapid antibody identification and characterization capabilities, which dramatically shorten the timeline of therapeutic antibody discovery. By enabling direct isolation and analysis of functional antibodies from individual B cells, the integrated workflow delivers validated antibody candidates within just one day — streamlining early-stage research and accelerating the path to clinical development.

The Breakthrough Technology Platform



Figure 2: One day workflow of Hypercell

The Synergistic Approach Advantage

	Traditional Approach	Synergistic Approach	Your Advantage
		Hypercell + Humanized Mice	
Time to Lead Candidates	12-18 months	3-6 months	75% faster development cycle
Screening Capacity	Typically screens hundreds to thousands of clones	millions of B cells in a single experiment, identifying tens of thousands of antibody candidates	1000X greater coverage
Human Antibody Recovery	Requires extensive engineering	Direct isolation	No affinity loss from humanization
Rare Clone Discovery	Frequently missed	Routinely captured	Higher probability of best-in-class
Development Risk	High attrition in late stages	Reduced sequence liabilities	Lower development risk

Table 1: Performance comparison and key numbers

Case Study 1: Accelerating a Fast-Follow Strategy

The Challenge

A biotech company faced a critical timing challenge: develop a best-in-class therapeutic antibody against a metabolic disease target already being pursued by larger competitors. With limited resources and a tight timeline, they needed push for an aggressive timeline to candidate selection.

The Synergistic approach Solution

1. Strategic Immunization (~5 weeks)

Transgenic mice with human variable regions were utilized and followed a targeted immunization protocol, achieving robust 80,000 titers in just 5 weeks.

2. Streamlined Sample Processing (~60 minutes)

Our efficient workflow processed 1.2×10^8 spleen cells while preserving cellular integrity. Using advanced CD138+ enrichment, we isolated antibody-secreting cells to maximize screening efficiency.

3. Precision Single-Cell Encapsulation (~60 minutes)

We encapsulated 20,000 enriched B cells in proprietary Hypercell microfluidic droplets, creating thousands of miniaturized screening chambers. Our patented cluster detection system identified high-affinity binding events during controlled incubation, with real-time microscopy confirming positive signals throughout.

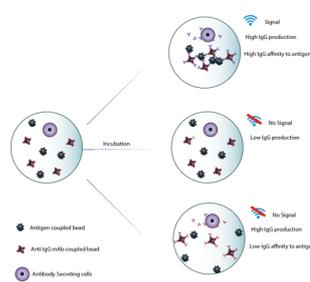
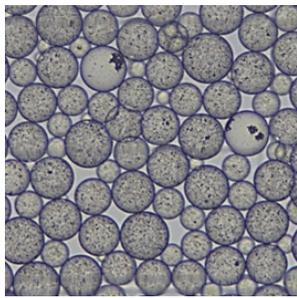


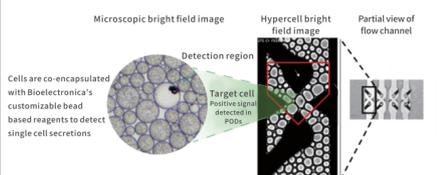
Figure 2: Hypercell Immuno-agglutination assay principle. Microscope (left) and schematic (right) images of cells and Hypercell reagents in droplets. Each single cell secretion assay takes place in a nanofluidic droplet called PODs (polydisperse oblate dispersion system).

The circles with dark edges of various sizes are PODS

4. High-Resolution Single-Cell Sorting (~90 minutes)

Hypercell Proprietary sorting algorithms analyzed droplet binding patterns, precisely identifying high-affinity antibody-producing cells. Multi-parameter analysis distinguished true positives from background, while gentle recovery preserved cell viability. The entire sorting process completed in less than 2 hours—capturing all valuable B cells efficiently.

Computer Vision utilize reliable visual recognition algorithms to identify PODs with Aggregates and Secretor Cell of interest.



PODs of interest change size via Electrical Shock and are sorted based on droplet size.

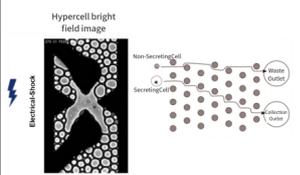


Figure 3: Hypercell Detection and sorting principle. Left: Encapsulation discretizes clustering chemistry in many small partitions. The cluster features, like size, darkness, grayscale contrast etc. correlates with antibody's affinity & quantity. Right: Electromerge triggered by cluster features followed with microfluidic isolation.

5. Next-Generation Sequencing & AI-Guided Analysis (<7 days)

Using 10X Chromium technology and 5' V(D)J sequencing, we preserved critical heavy/light chain pairing while capturing the complete antibody repertoire. Our AbFinder AI platform identified 465 unique antibody candidates and grouped related sequences to ensure optimal diversity for final selection.

6. Expression & Validation (<21days)

23 diverse candidates were selected for expression based on structural and sequence analysis. After rapid production and purification, binding assessments revealed exceptional results: 17 antibodies (73.9%) showed positive binding, yielding numerous high-affinity antibodies with high potential.

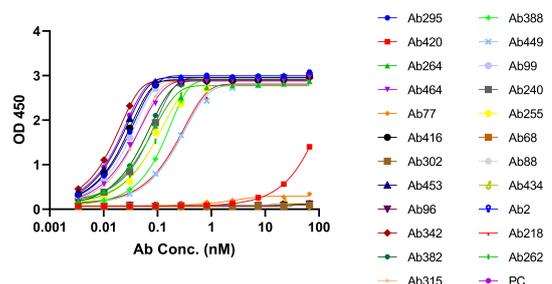


Figure 4: EC50 measurement with ELISA

Case Study 2: Development of Antibodies Against A Competitive I/O Target

Experimental Process

A humanized mouse platform for immunization was adopted, combined with high-throughput single-cell Hypercell sorting platform for selection, and utilized an AI-powered Abfinder bioinformatics platform to analyze and recommend all candidate antibodies.

Results

This combined approach achieved exceptional outcomes with minimal resource investment:

- Identification of 2,230 unique sequences within just 7 days
- 96 antibodies were selected for expression as the first batch of test samples. In ELISA validation experiments, 52 antibodies (54.2%) were tested positive, with 43 antibodies (44.8%) showing OD450 >1.

Ab ID	OD450	Ab ID	OD450
Ab31	2.781599998	Ab481	3.062299967
Ab61	2.995800018	Ab505	2.926599979
Ab63	2.861399889	Ab518	2.792999983
Ab81	1.050999999	Ab594	2.881700039
Ab112	1.453199983	Ab613	2.317800045
Ab120	2.771399975	Ab634	3.111000061
Ab121	2.424200058	Ab661	2.724200001
Ab136	2.980000019	Ab662	2.917599916
Ab148	2.117199898	Ab741	2.821300003
Ab149	2.787600004	Ab759	2.8125
Ab158	2.801100016	Ab793	2.074700117
Ab167	3.083300114	Ab1050	2.682100058
Ab200	3.009799957	Ab1063	2.841900111
Ab230	2.889100075	Ab1097	2.411799908
Ab253	2.90019989	Ab1098	3.077800035
Ab261	2.609299898	Ab1172	2.674799919
Ab325	2.830300093	Ab1229	3.016999996
Ab328	2.702600002	Ab1238	2.315900087
Ab344	2.657000065	Ab1262	2.823499918
Ab474	3.077500105	Ab1300	2.954900026
Ab480	2.498199994	Ab1362	2.727799892
		Ab1422	1.447600007

Figure 5: ELISA binding results

Transform Your Antibody Discovery

The synergy between high-throughput single-cell sorting and humanized mice isn't just incremental improvement—it's 1+1>2 accelerator in therapeutic antibody discovery.

Superior Economics

- Reduce development costs
- Get to key decision points faster
- Minimize late-stage attrition risks
- Maximize resource efficiency

Competitive Advantage

- Identify best-in-class candidates others miss
- Move quickly in crowded therapeutic areas
- Bring better therapeutics to patients faster

Technical Excellence

- Access unprecedented antibody diversity
- Discover rare clones with exceptional properties
- Obtain fully human antibodies without engineering
- Capture complete heavy/light chain pairing information

Start Your Discovery Revolution

Whether you're developing therapeutic antibodies, diagnostic reagents, or research tools, our platform delivers:

- Faster time-to-candidate
- Superior antibody quality
- Greater diversity and epitope coverage
- Reduced development risk

Your next breakthrough antibody is waiting to be discovered.

Ready to accelerate your antibody program?

Contact our scientific team for a confidential consultation.

Contact us

Bioelectronica Holdings Inc.
www.bioelectronica.com
Email: hello@bioelectronica.com



www.bioelectronica.com



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