Hypercell® Single Cell Sorting Platform

For antibody discovery application

A Novel Macrophage Target

Bioelectronica

ABOUT HYPERCELL® & ABFINDER™

Hypercell® is a high-throughput cell analysis and sorting platform that enables researchers to identify and isolate cells that are secreting proteins of interest quickly and at an affordable price.

AbFinder™ is an advanced downstream solution for selecting promising antibody candidates generated by the Hypercell® single cell sorting platform.

By seamlessly integrating Hypercell® and AbFinder™, Bioelectronica provides an end-to-end solution for antibody discovery by leveraging the power of single-cell secretion sorting with next-generation sequencing (NGS).

INTRODUCTION

Monoclonal antibodies have become a function technology for groundbreaking therapeutic modalities, diagnostic methods, and scientific discovery. While many antibody screening technologies exist, there remains an unmet need to produce antibodies with high diversity, at high throughput, and low cost while retaining natural pairing of the heavy and light chains. In this study, we have demonstrated that the Hypercell® platform and the AbFinder™ bioinformatic tool can identify high affinity binders against a novel macrophage target which have a promising therapeutic potential.

RESULTS

Using the Hypercell® sorter, 500,000 plasma cells were screened within a single day. The sorted cells were subsequently processed with single cell sequencing and the AbFinder™ bioinformatic tool. From more than 1,000 paired antibody sequences identified, 23 antibodies were selected for downstream validation. 17 potent binders were confirmed in less than 4 weeks time, 88% with <1nM EC50 affinity, 100% <5nM affinity. Functional assay showed 24% of the binders with strong blocking function.
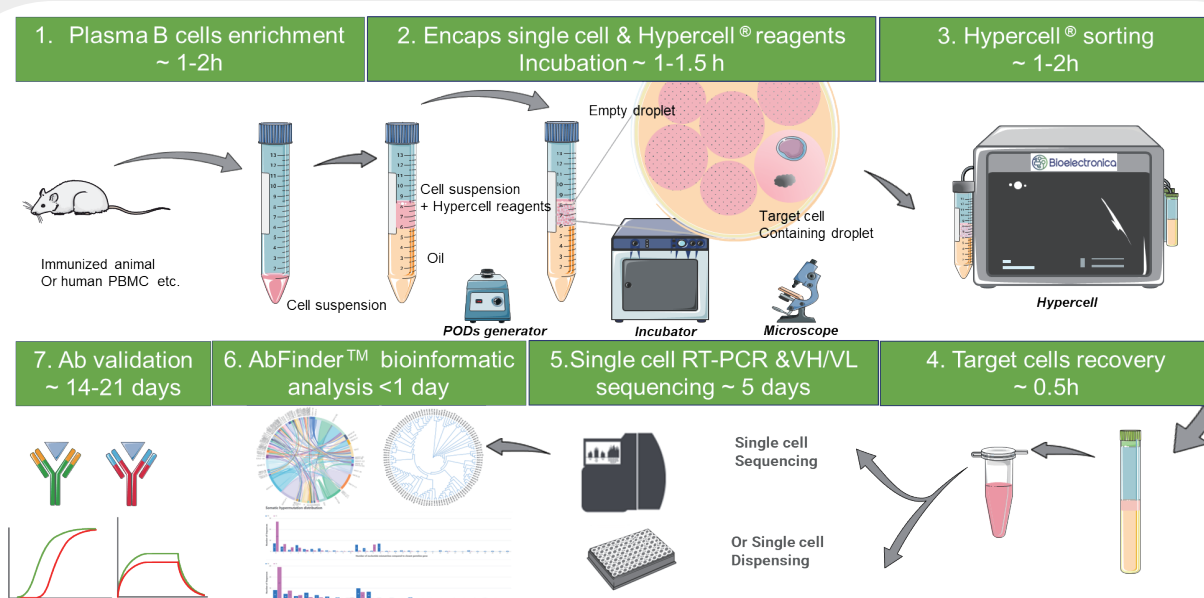

Figure 1. Plasma B Cell Antibody Discovery Workflow. Schematic representation of the Hypercell® sorting process (steps 1-4), which is completed within one day. The subsequent steps include single-cell RT-PCR and VH/VL sequencing (step 5), bioinformatic analysis (step 6), and antibody validation (step 7), all of which can be completed in less than one month. In this study, we employed single-cell V(D)J sequencing for high-throughput recovery. As an alternative downstream workflow for low- to mid-throughput, a single-cell dispensing solution in a well plate format can also be used.
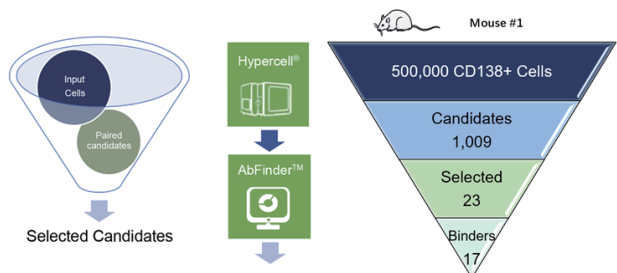
Figure 2. Key numbers in the Hypercell® and AbFinder™ workflow. A magnetic bead-based CD138+ positive selection kit (Stemcell) was used to enrich plasma B cells from the spleen of the immunized mouse. 500,000 plasma cells were screened on the Hypercell for sorting. All sorted cells were encapsulated with DNA-barcoded gel beads using a 10x Chromium controller and processed using the B cell single cell V(D)J solution according to manufacturer's instructions. After library construction and sequencing (NovaSeq 6000), 1,009 non-redundant antibodies were obtained. With AbFinder™, we selected 23 candidates for downstream synthesis, expression and binding validation, of which, 17 binders were confirmed (with binding ratio of 73.91%).

Cells #	VH families #	VL families #	Clonotypes #
1,009	90	76	577
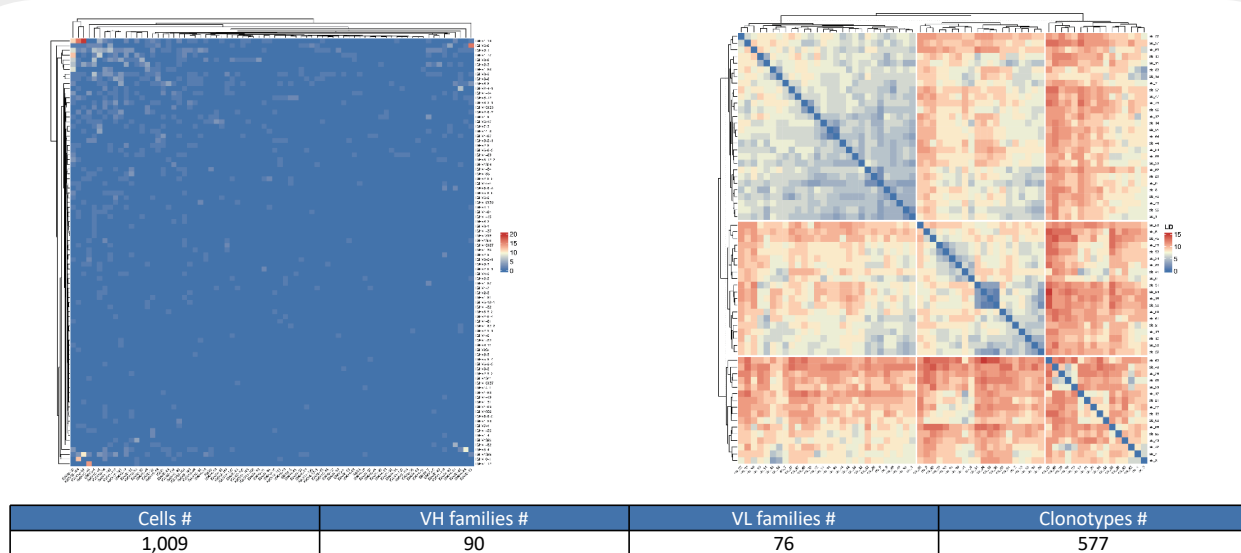
Figure 3. Heatmaps presenting diverse V gene families and clonotypes of 1,009 of sorted antibodies. Left panel: V-gene family diversity; Right panel: clonotype diversity. A high diversity of IgGs covering multiple V-gene families were observed with the sorted population. We've identified 90 VH families and 76 VL families. The clonotype diversity is reflected by the Levenshtein distance (LD) which is used to measure of the similarity between clonotypes. It takes into account the number of insertions, deletions and substitutions operations needed to transform one string into the other. In this figure, only clonotype size>2 is presented.
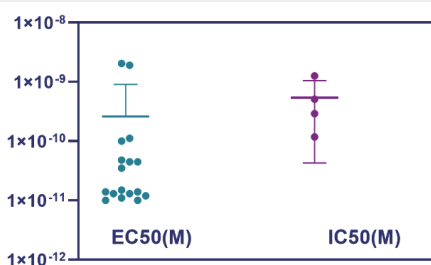
Figure 4. AbFinder™ helps users to narrow down the number of candidates to be tested while maintaining high diversity. From 17 confirmed binders, 15 antibodies (88%) with <1nM EC50 affinity, 100% <5nM affinity. Blocking assay showed 4 desired candidates (24%) with strong blocking effect.

SUMMARY

Hypercell®'s plasma B cell workflow, in combination with AbFinder™ software, provides users an end-to-end solution for antibody discovery, which delivers quality antibody candidates efficiently with significant time and cost reduction.

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