# Development of High Throughput Single-B Cell Antibody Discovery Platform

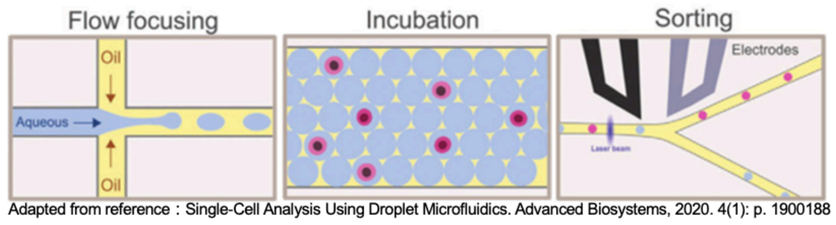
**Authors: Haisong Lu, Meng Yu, Shipin Lin, Su Liang, Liang Wang, Yan Yang**
BIOINTRON, Shanghai R&D/Production Center
www.biointron.com I info@biointron.com I Office: +1 (732) 515-4766

Connect with us on LinkedIn

## Abstract

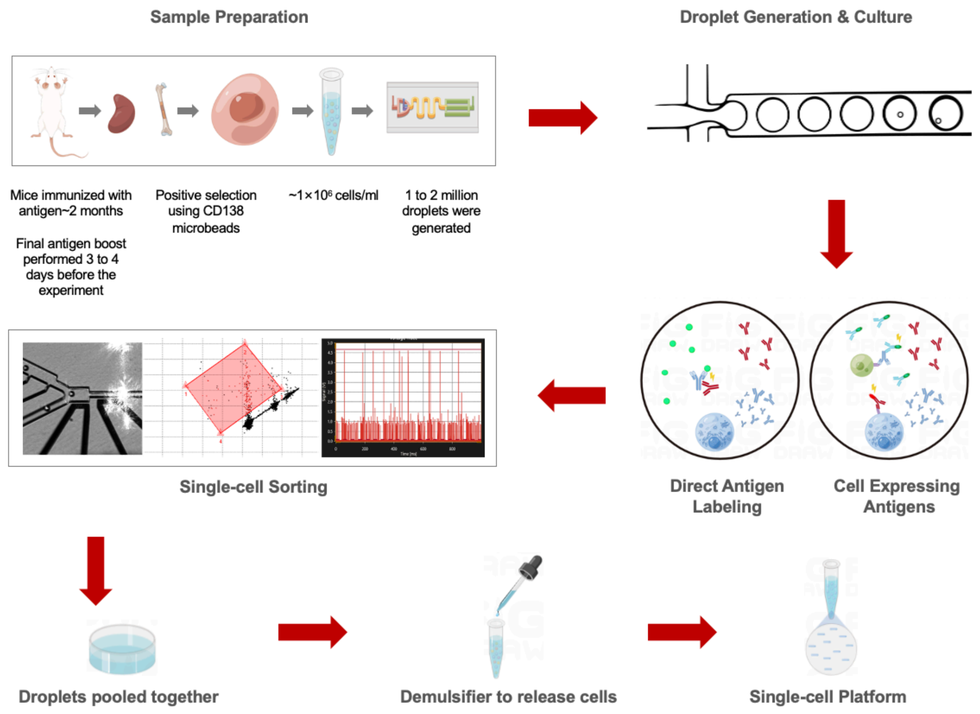
Single B cell technology is the up-to-date antibody discovery strategy that overcomes many bottlenecks encountered in traditional antibody discovery approaches. Biointron has established a microfluidic technology based, single B cell antibody discovery platform. Combined with our proprietary high throughput antibody expression capacity, it has been proven to be fast and efficient, as evidenced in many delivered projects.

| | Single B Cell Technology | Hybridoma Technology | Phage Display Technology |
|---|---|---|---|
| **Speed** | Rapid (days) | Slow (months) | Slow (1-2 months) |
| **Diversity** | High | Limited (by hybridoma making) | Limited (by library size) |
| **Antibody Maturation** | High (naturally paired and matured) | High (might requires optimization) | Moderate (needs further optimization |
| **Throughput** | High | Low | Moderate to high |



Adapted from reference：Single-Cell Analysis Using Droplet Microfluidics. Advanced Biosystems, 2020. 4(1): p. 1900188

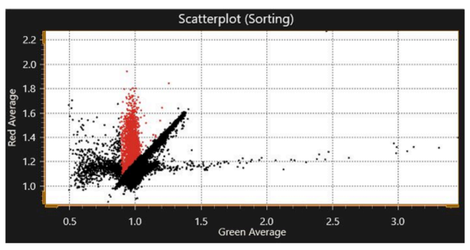
## Single B Cell Sorting Method




## Case Study 1: Tumor-Associated Antigen-Specific Antibody Screening

Project Objective: Obtain high affinity specific antibodies against tumor-associated antigens

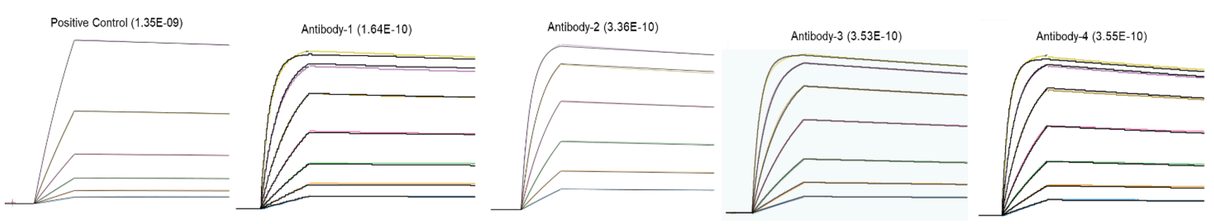
**a**




**b**

| Detection | Binding ELISA | SPR |
|---|---|---|
| Positive Clone | 62 | >$10^{-8}$ M, 17 antibody<br>>$10^{-9}$ M, 14 antibody<br>>$10^{-10}$ M, 4 antibody<br>40 undetected |

**c**




**a**. Single cells are encapsulated in droplets, and after culturing, secreted antibodies bind to the fluorescently labeled antigens in the droplets. Using fluorescent-labeled secondary antibody after excitation by FRET, the droplets which contain antigen-specific plasma B cells are selected by the emitting fluorescent signals at 620nm.

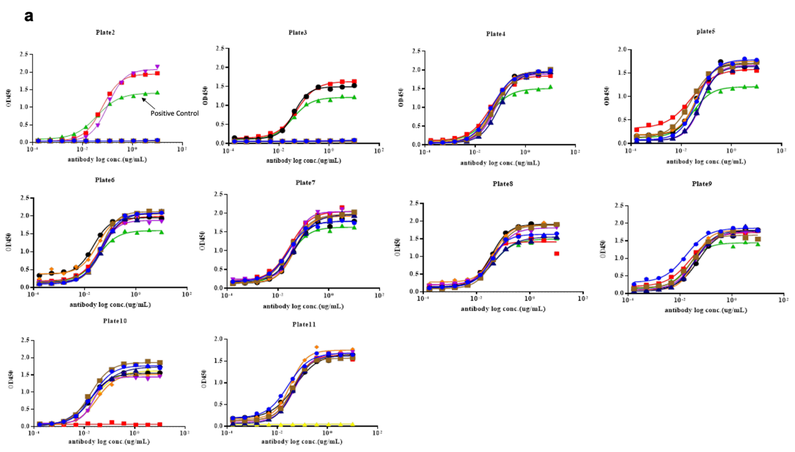
**b**. After preliminary ELISA screening, we obtained 62 antibodies that bind to the antigen, 22 of which were selected by the customer for affinity measurement by SPR. The affinity of SPR-measured antibodies ranges from 0.1-1 nM.

**c**. Some antibodies generated from the platform exhibited faster binding rates and lower KD compared to a positive control.

## Case Study 2: PD-1-Specific Antibody Screening

Project Objective: Obtain specific antibodies against PD-1 at different epitopes

**a**

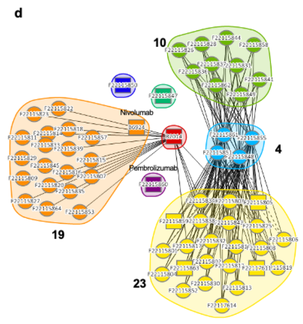



**b**

| Detection | Binding ELISA | SPR |
|---|---|---|
| Positive Clone | 59 | ~$10^{-9}$ M, positive control<br>>$10^{-10}$ M, 20 antibody<br>>$10^{-9}$ M, 58 antibody<br>>$10^{-8}$ M, 59 antibody |

**c**

**d**




**a.** 59 antibodies specifically binding to PD-1 were screened by our platform.

**b.** We ranked the affinity of 59 antibodies by SPR, and the affinity of nearly all antibodies ranged from 0.1-1 nM. BMK was the positive control (nivolumab biosimilar).

**c.** We analyzed the diversity of CDR sequences of the light and heavy chains of the 59 antibodies, which demonstrated good diversity.

**d.** We performed epitope binning for all antibodies and found that the hits could be divided into 4 epitope groups. B6924 (nivolumab biosimilar) and B2014 (pembrolizumab biosimilar) were our positive controls in this section. The result showed that we successfully identified many antibodies binding to distinct epitopes on PD-1 compared to controls.

## Conclusion and Future Prospects

- In summary, we developed a stable, high-throughput single B cell antibody discovery platform capable of generating diverse, high-affinity antibodies against various epitopes within 2~3 months.
- The platform effectively screened antibodies against soluble antigens, and a detection scheme for transmembrane proteins, particularly GPCRs, is currently underway.
- This versatile platform has the potential to accelerate therapeutic development for a broad range of targets, including challenging transmembrane proteins.