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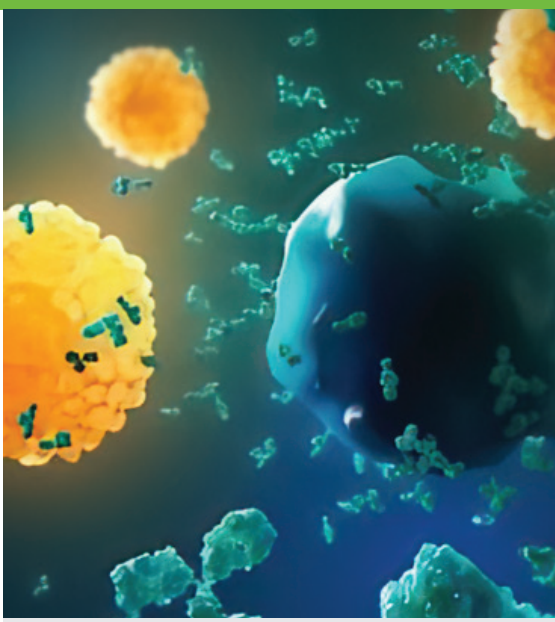
Overcoming the challenge of high-throughput single cell isolation



APPLICATION NOTE
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OVERVIEW

Therapeutic antibody discovery is a process of finding antibodies (specialized proteins) that can be used to treat diseases like cancer, autoimmune disorders, and infections. Proteins associated with the disease are identified, and antibodies are raised against these proteins. This process has evolved significantly since its inception, leveraging both traditional and cutting-edge technologies to develop targeted treatments for a wide range of diseases.

Antibodies can be generated through various methods, including animal (e.g., mice or transgenic models) immunizations, recovered human patients, or using display technologies such as phage display, which presents antibody fragments on the surface of bacteriophages.

A critical step in therapeutic antibody discovery is the screening of candidate antibodies for high specificity and affinity. Traditional methods such as enzyme-linked immunosorbent assay (ELISA) and flow cytometry (FACS) are commonly used to assess antibody-antigen interactions. ELISA enables detection of antibody binding to immobilized antigens, while FACS can evaluate binding to antigens expressed on the surface of cells. Both approaches are useful for assessing individual monoclonal antibodies (mAbs) but are limited when applied to polyclonal antibody mixtures, because they lack the ability to resolve the properties of individual antibodies or the B cells that produce them.

Single B cell screening offers a path to overcome this limitation, but conventional FACS-based methods rely on labeled, soluble antigens that must bind to membrane-bound antibodies on B cells. Although FACS provides single-cell resolution, it does not detect secreted proteins, making it less suitable for studying antibody-secreting cells such as plasma cells or hybridomas, where the functional output, namely, the secreted antibodies, is the key parameter of interest. In contrast, OmniAb, Inc.'s xPloration® is a single B cell screening platform that detects secreted antibodies, enabling functional screening across a broader range of targets and antibody formats. This approach provides single-cell resolution and expands the scope of antibody discovery beyond the constraints of traditional methods.

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Limitations of common methods highlight the need for more advanced screening technologies that can combine single-cell resolution with the ability to measure secreted proteins directly. Such innovations are crucial for improving the efficiency and precision of therapeutic antibody discovery.

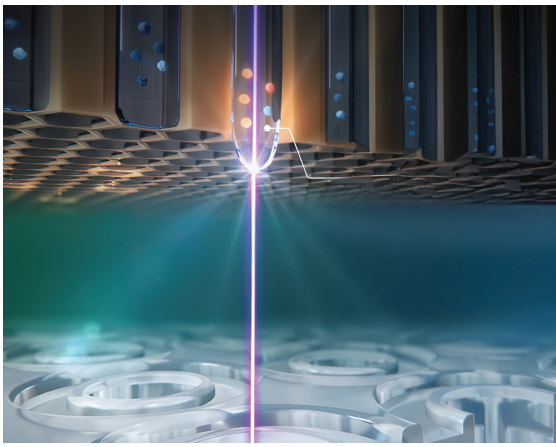
The Challenge

Therapeutic antibody discovery is a complex process involving the screening of millions of cells to isolate single B-cells of interest from immunized animals, which can take months to perform with traditional technologies.

The Solution

OmniAb utilizes xPloration, a high-throughput screening platform that harnesses machine learning and computer vision artificial intelligence (AI) to process millions of single B-cells in hours compared with weeks using traditional spatial separation techniques methods. The xPloration instrument employs the X-Cite XYLIS™ II from Excelitas® to identify the fluorescent B cell assay read out and a laser to isolate B cells of interest.

OmniAb leverages microcapillary array technology consisting of 1.5 million through-hole capillaries, each 40 µm in diameter. Cells suspended in solution are loaded into these capillaries, where they are held in place by surface tension. Because the capillaries are open at both ends, cells of interest, identified by their fluorescence using the XYLIS II, can be selectively ejected into a collection chamber using a laser pulse. This precise, high-throughput method enables the isolation of individual antibody-secreting cells based on functional output.



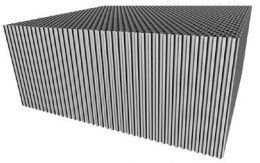
By combining single-cell resolution with the ability to directly measure secreted proteins, this platform overcomes key limitations of traditional screening methods like ELISA and FACS. As a result, OmniAb's technology significantly enhances the efficiency and accuracy of therapeutic antibody discovery.

Why use the X-Cite XYLIS II?

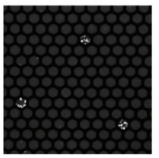
The broadband wavelength of the XYLIS II allows excitation of a range of fluorophores in the excitation region starting from 365 nm all the way to 750 nm. The XYLIS II is based on LED technology which allows for fast ON/OFF capabilities, prolonged LED lifetime, and protection for sensitive samples. The patented LaserLED Hybrid Drive® provides very high optical power between 500-600 nm. Through TTL, third-party software, or sending commands over USB in the case of xPloration, the unit can be controlled with ease. The high power of the XYLIS II allows high excitation efficiency of the fluorophore of interest, speeding up the process of locating and isolating cells of interest.

Summary

With the X-Cite XYLIS II as a key component, xPloration can rapidly screen millions of cells in less than two hours compared to traditional biochemical techniques that may take months.



Unique through-hole format



1.5 million,
40 µm diameter
microcapillaries

Images courtesy of OmniAb, Inc.