CASE STUDY

UNLOCKING COMPLEX TARGETS WITH PAIRED ANTIBODY LIBRARIES

YUMAB

THE NEED

Antibody discovery for demanding targets

Antibodies derived from combinatorial libraries achieve high diversity by random pairing of heavy (VH) and light (VL) chains, enabling the identification of novel and high-affinity binders (Figure 1). This approach has proven effective across a broad range of targets.

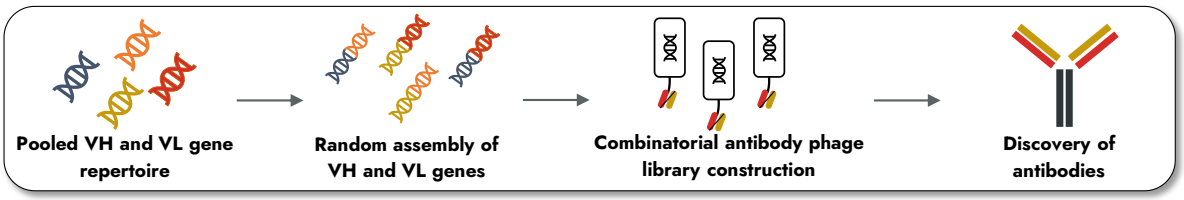

Figure 1: *Workflow for designing a combinatorial antibody library.*

However, for particularly challenging antigens – such as carbohydrates with complex or atypical binding patterns – highly specific structural recognition is essential. In such cases, a combinatorial antibody library may not be sufficiently precise.

THE SOLUTION

Paired libraries preserve natural pairing of VH and VL for better functionality

The immune system generates optimal antibodies through an efficient process of B cell maturation. Using this natural toolbox, paired libraries transfer the information from B cells after immunization into recombinant antibodies without disrupting the natural pairing of VH and VL. In a high throughput approach, several hundred thousand B cells are individually encapsulated and processed within the capsules to avoid cross-contamination (Figure 2).

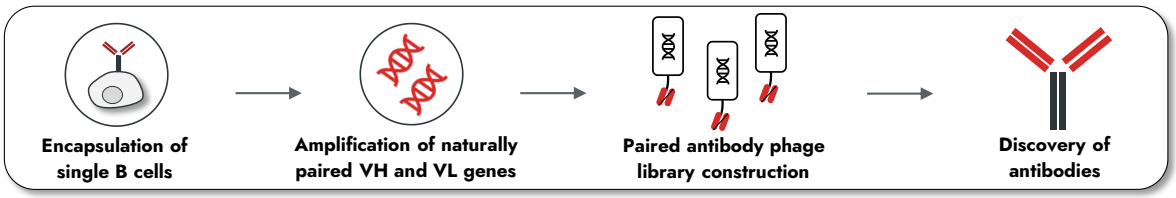

Figure 2. *Workflow for designing a paired antibody library.*

Extraction of the genetic material and cloning of recombinant antibodies occur inside the single droplets (Figure 2). In contrast to conventional B cell screening, this immortalized antibody repertoire allows an unlimited rescreening for multiple discovery campaigns.

THE IMPACT

More targets, higher affinities, unlimited re-screening

Paired antibody libraries enable the discovery of more functional antibodies with higher affinities, especially for complex or structurally demanding targets such as glycans. In this study, we have identified over 1,000 glycan-specific clones using paired libraries compared to just seven from a combinatorial library, demonstrating the power of preserving natural VH/VL pairing (Figure 3).

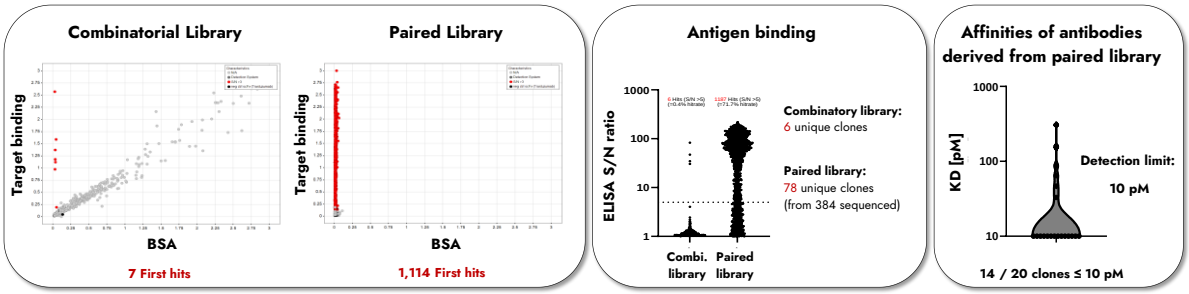

Figure 3. *Comparison of combinatorial and paired libraries in the generation of glycan-specific antibodies: The paired library generated more target-specific hits (left), stronger antigen-binding antibodies (middle) with high affinity (right).*

This approach ensures full coverage of the natural immune repertoire, supports unlimited re-screening, and allows in vitro selection for complex binding profiles. While conventional combinatorial libraries remain highly effective for a wide range of targets and offer significant diversity, paired libraries provide a valuable complement for cases requiring enhanced precision and functional performance.