Empowering the Efficient Discovery of Ultralong CDRH3 Antibodies with High-Throughput xPloration® Workflows

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Abstract

The discovery of ultralong CDRH3 antibodies presents a promising frontier in therapeutic development, offering access to cryptic epitopes beyond the reach of conventional antibodies. OmniUltra™, a transgenic chicken platform engineered to express bovine-like ultralong CDRH3 antibodies in a human scaffold, combines the evolutionary advantages of avian immunology with the structural uniqueness of the stalk-knob architecture. To accelerate discovery, OmniAb® leverages xPloration®, an AI-powered, high-throughput single B-cell screening platform capable of analyzing millions of antibody-secreting cells and recovering thousands of unique sequences within hours. xPloration features a fluidics-free microcapillary system and precision laser recovery, enabling rapid capture of rare, high-value antibodies.

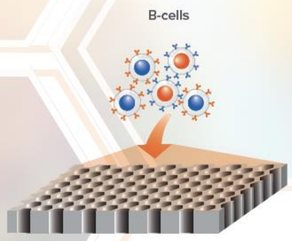
xPloration®: Simplifying Antibody Screening

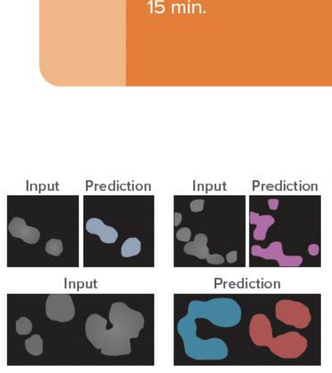
xPloration®

How it works

1 Load

Millions of B-cells and assay reagents such as target cells or beads are easily and quickly loaded onto xPloration's microcapillary array in less than 15 min.



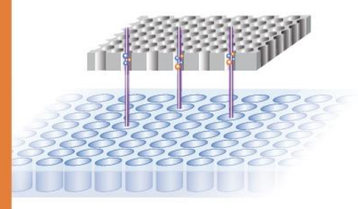


2 Analyze

xPloration instrument scans the array using AI-based image analysis to analyze every cell and identify thousands of positive hits based on your desired binding profile in real time.

3 Recover

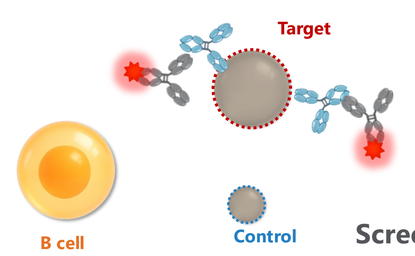
A proprietary, precision laser recovery method gently and rapidly extracts your chosen live cells into a proprietary 96-well recovery plate, ready for immediate sequencing.



High-throughput Discovery Workflow

Case Study: PSMA is a protein highly expressed on prostate cancer cells, making it a key target for diagnosis and advanced treatments such as radioligand therapy and antibody-drug conjugates.

xPloration Screening

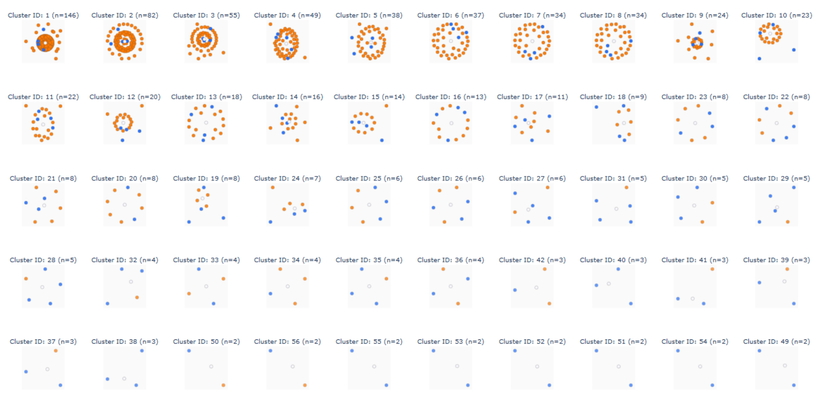


Bird	# Cells Screened	# Hits
1	14.4 M	790
2	7.2 M	1000
3	4.8 M	916
Total	**26.4 M**	**2,706**

Screening Method:

- Each bird was screened with a multiplex, protein-based, bead assay
- Hits were recovered in a pooled manner, recovering hits into 1 well

Sequence Selection



Ultralong clustering method:

All sequences will have

- Same Cysteine pattern
- ≤ 3aa edit distance in knob (complete linkage)

- Selected 196 sequences
  - Covered 81 clusters

Hit Validation

From xPloration to EC50 Validation

77%

Recovery

Unique Antibodies

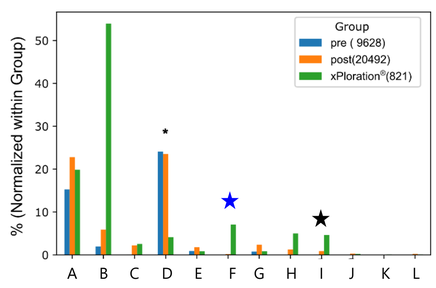
178

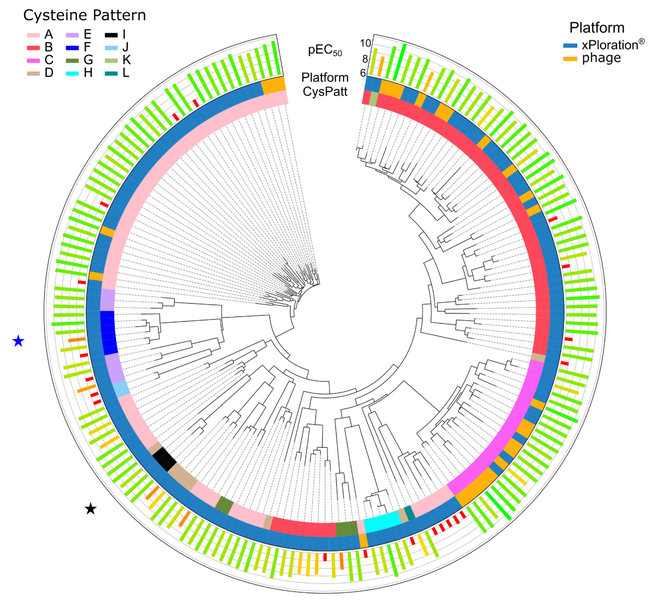
Expressed

Lineages

81

Tested





- Large range of hits from xPloration exceed phage panning
- OmniUltra™ can generate cysteine patterns distinct from germline with relevant activities against target

Conclusions

- Screening millions of cells yielded a pooled set of thousands of hits. From this repertoire, we tested and validated hundreds of candidates across more than 80 lineages.
- The combined power of xPloration® high-throughput screening and sorting, NGS, and OmniUltra™ enables large-scale discovery of antibodies with ultralong CDRH3s—and the scaffolded peptides they support.

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