single cell TECHNOLOGY AND CASE STUDY CINEMAS PRESENT

MISSION:POSSIBLE

MEMBRANE-BOUND TARGETS DON'T STAND A CHANCE.

single cell TECHNOLOGY

Mission: Possible

SurfScreen for membrane-bound targets

The Problem

AbTheneum efficiently screens antibody binding profiles with recombinant proteins, yet some membrane targets require screening with cells due to their structure.

The Solution

SurfScreen is a new module for AbTheneum for screening antibodies against membrane targets.

Wild-type mice were immunized with TIGIT protein. Antibody-secreting cells were isolated using CD138 positive selection. The CD138+ cells were deposited onto a picowell device and aligned with a second device loaded with both TIGIT-expressing cells and Parental cells expressing GFP. The two devices were pressed together aligning all picowells, allowing antibodies from CD138+ cells to interact with TIGIT and Parental cells (Fig. 1).

The two devices were separated, the TIGIT cells were stained with fluorescent secondary antibody to detect cell-binding antibodies. Two antibody arrays were captured from the CD138+ cells and stained with recombinant human and cynomolgus TIGIT protein (Fig. 1, gray rectangles)

All CD138 cells were lysed antibodies captured for sequencing using AbTheneum sequence capture protocols. Clonotypic antibodies show similar protein and cell binding profiles as expected (Fig. 2).

Twelve (12) diverse mAbs were selected from the output—2 non-cell binders and 10 cell-binders—and validated by Flow against TIGIT and Parental cells (Fig. 3). All 12 mAbs were negative against Parental cells (not shown), and all 10 cell-binders showed high affinity against TIGIT cells, EC50 between 13 pM to 1 nM. The 2 non-cell binding antibodies showed no binding to TIGIT cells, confirming the predictive power of the assay.

SurfScreen is also being used for multipass membrane targets like GPCRs and using virus-like particles in the AbTheneum workflow.

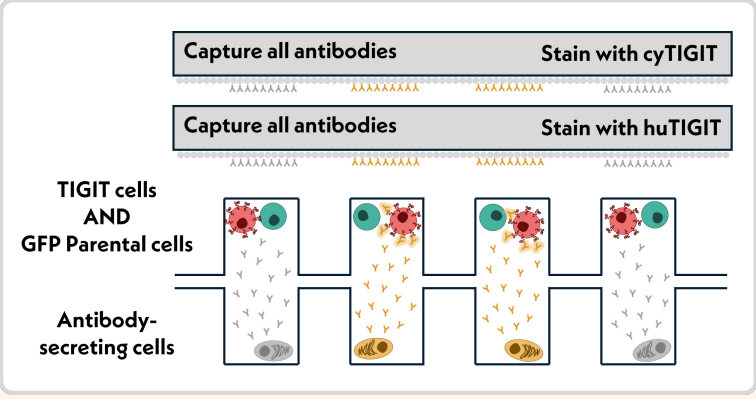

Figure 1. Schematic of SurfScreen project, screening secreted antibodies against TIGIT-expressing cells, Parental cells, recombinant human TIGIT protein, and recombinant cyno TIGIT protein.

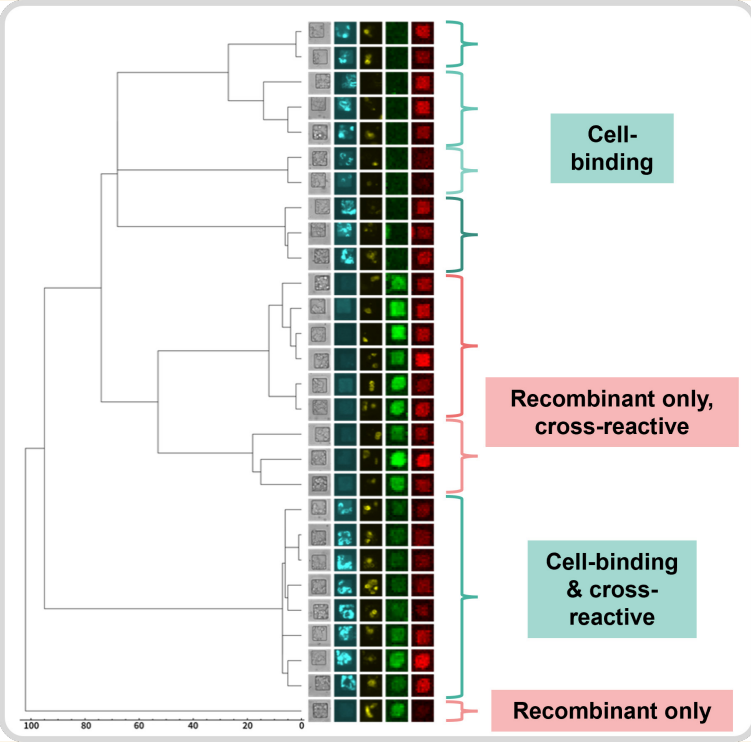

Figure 2. Antibody sequences from a SurfScreen campaign on TIGIT, showing sequence similarity on a dendrogram and images from the screen: Brightfield, Cell-binding signal (cyan), Parental cell signal (yellow), Recombinant hTIGIT (green), Recombinant cyTIGIT (red). Related antibody clonotypes show similar phenotypes.

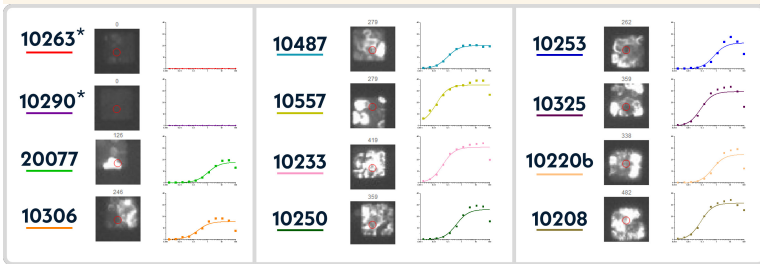

Figure 3. Twelve antibodies expressed, 2 non-cell binding* and 10 cell-binding. Each mAb presented with cell-binding signal captured via SurfScreen and Flow cytometry plot against TIGIT cells.

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