integral molecular

Novel immuno-modulatory targets

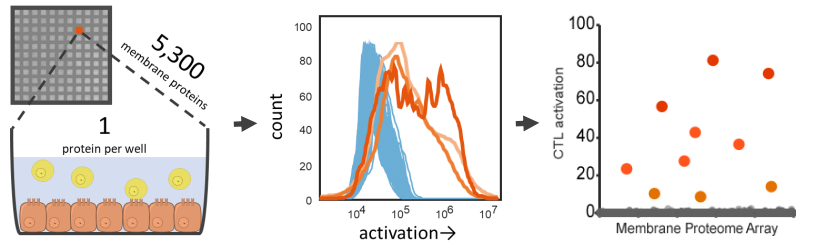
Phenotypic target discovery using the Membrane Proteome Array

Membrane Proteome Array

The Membrane Proteome Array™ contains 5,300 different human membrane proteins, each **expressed in live human cells**. Each protein in the array can be individually screened for binding by antibodies, proteins and other ligands. Proteins in the array can also be screened for biological function to discover new therapeutic targets.

The Membrane Proteome Array is the largest library of its kind, comprising **95% of the human membrane proteome**, with all protein classes represented — including GPCRs, transporters and IgV-set proteins.

Approach



Co-culture of Membrane Proteome Array and cytotoxic T-cells

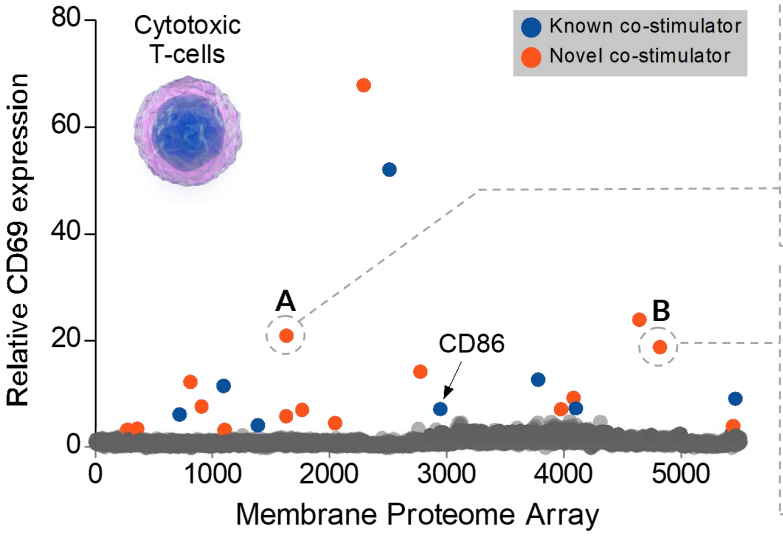
High-throughput flow cytometry using standard T-cell activation markers

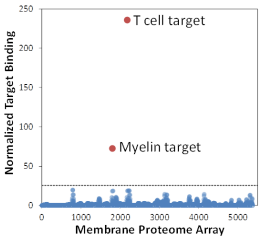
Profile of T-cell activation across by 5,300 membrane proteins

Phenotypic T-cell signaling assay assessing **co-stimulatory activity across 5,300 membrane proteins**

Identification of new cell-surface proteins that modulate cytotoxic T-cell activation

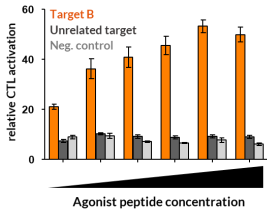
Modulation of immune cell subsets has proven a successful therapeutic approach for treating cancers — e.g. PD-(L)1 inhibitors. However, current attempts to identify new immunomodulatory proteins rely on homology-based approaches. In contrast, the Membrane Proteome Array is ideally suited to the discovery of new therapeutic targets as each protein is expressed in its native form on the surface of live human cells, enabling signaling assays to detect functional interactions. Using this platform, we were able to discover **dozens of new immuno-modulatory proteins** in a hypothesis free manner — generating a list of **novel druggable targets along multiple therapeutic axes**.





Target A: Defining new signaling networks

A soluble form of Target A was probed on the Membrane Proteome Array to find its tissue-specific binding partner. Two physiologically-distinct binding partners were identified. This approach is capable of identifying large signaling networks and increases the number of potential druggable targets within a therapeutic axis.



Target B: Novel targets are druggable

A peptide agonist to Target B was tested for its ability to stimulate t-cell activation. Target B has previously been implicated in breast and hepatic cancers — our data suggests that Target B activity could modify the tumor micro-environment.

Other Applications

Phenotypic screening
- Glucose sensitization
- Neuro-inflammation

Specificity profiling of biologics
- Off-target screening
- Antibody/ligand de-orphaning

More information

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www.integralmolecular.com/membrane-proteome-array