integral molecular
membrane protein solutions

Epitope Mapping
using Shotgun Mutagenesis technology

Value of Epitope Mapping for MAbs

Intellectual Property

Epitope data provides support for MAb patent requirements

- Novelty: epitope data can differentiate novel MAbs from 'prior art'
- Non-obviousness: MAbs with conformational epitopes are challenging to elicit and more patentable
- Written description: detailed epitopes demonstrate that the inventor is 'in possession' of the invention, and support broad patent claims

Mechanism of Action

- Epitope mapping identifies functional region targeted by MAb
- Epitopes differentiate candidate MAbs

95% Success Rate

Integral Molecular's proprietary Shotgun Mutagenesis technology is the only high-throughput technique that can reliably map conformational epitopes at single amino acid resolution. We have mapped 500+ epitopes to date with >95% success, including highly complex epitopes such as:

- Epitopes on GPCRs, transporters and viral structural proteins
- Conformational epitopes
- Epitopes on multi-subunit proteins
- Receptor state-dependent epitopes

500+ Epitopes Mapped

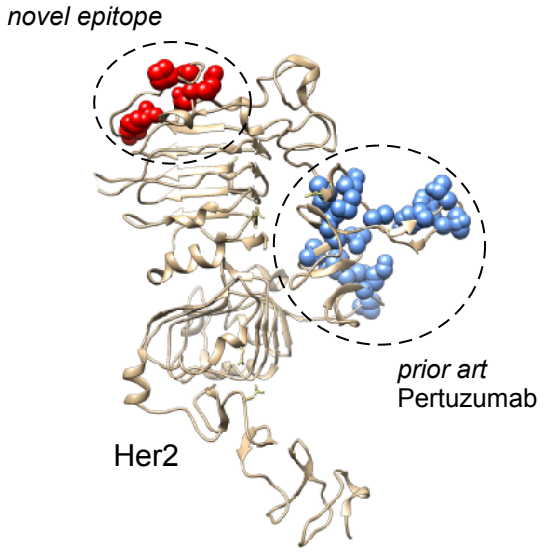
Epitopes mapped by Shotgun Mutagenesis have been featured in 30+ publications in journals such as Cell, Nature and PNAS. The success of this approach is based upon:

- 15+ years experience in membrane protein expression
- Comprehensive Ala-scan mutagenesis technology
- High-throughput MAb binding on native proteins expressed in human cells
- Ability to identify residues that are energetically critical for binding

Epitope Mapping Services

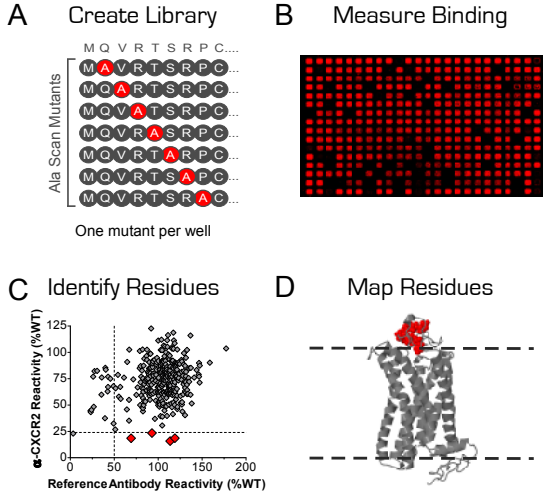
Shotgun Mutagenesis epitope mapping services are provided to customers on a fee-for-service basis. This includes comprehensive mutagenesis of user-specified proteins, data collection, and mapping onto protein structures.

Epitope Mapping for MAb Patents



Shotgun Mutagenesis was used to map the epitope of a novel MAb against oncology target Her2. The novel MAb was shown to bind to a site that is clearly distinct from the 'prior art', FDA approved MAb Pertuzumab, providing increased value for patentability and freedom-to-operate.

Shotgun Mutagenesis Technology



Overview of Shotgun Mutagenesis Epitope Mapping
A. Each well of a Shotgun Mutagenesis array contains a plasmid clone with a sequenced alanine mutation. **B.** Each mutant is tested for antibody binding. **C.** Data is analyzed to identify residues that are critical for antibody interactions. **D.** Residues of interest are mapped onto protein structures.

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