Multipass membrane proteins are largely intractable as MAb targets due to their structures and high conservation. MPS Antibody Discovery platform is specifically tailored to work with membrane proteins, employing Lipoparticles, mRNA, chicken immunization, and hCAT direct humanization.

- High-concentration membrane proteins presented on virus-like particles (VLPs) in their native structure and orientation
- GPCRs, ion channels, transporters, and immuno-oncology targets displayed at concentrations ~50-200 pmol/mg

hCAT antibody humanization and affinity maturation
**Humanized Chicken Antibody Technology**

- Humanization of pools of MAbs prior to isolation
- CDR shuffling enables affinity maturation (pM)
- Single germline framework and synthetic/germline CDRs enhance developability
- Eliminates cost and time of downstream engineering

Antibody Discovery for Membrane Proteins

Lipoparticles present native antigen for immunization and panning.

- Small exposed regions
- Structurally complex antigens
- Protein structure dependent on lipid membrane
- Poor immunogenicity poorly expressed or toxic highly conserved

CCR8 Antibodies

- Panel of MAbs, nanomolar and subnanomolar EC50
- 99% human antibodies (excluding CDR regions)
- Reactivity with orthologs facilitating preclinical studies
- Exploring ADCC or ADC mechanisms

CCR8 MAb discovery yields diverse molecules

**Stage I**
- Target analysis of complex membrane proteins: small loops, poor expression
- Antigen production: mRNA + Lipoparticles, significant antigen engineering
- Immunization: 50 µl in 4/5 chickens

**Stage II**
- Lipoparticles-phage panning
- Screening: 3,200 clones
- Validated hits: 12 antigen molecules, 4 high CDR3 families

**Stage III**
- Subcloning
- Express/CHO expression
- Candidate panel: 6 high affinity MAbs

Key Features of CCR8 Validated MAbs

- Robust responses in chickens with mRNA immunization
- Depletion of Treg cells may sensitize tumors and provide strategy for therapy
- CCR8 is found in Treg cells in tumor microenvironment, but not in systemic lymphoid tissue

CCR8 and immune sensitization

**High affinity MAbs obtained from phage panning campaign**

- Preliminary data show ADCC-mediated cell killing

CCR8 MAbs show cross-species reactivity, including mouse

**Robust responses in chickens with mRNA immunization**

- mRNA enables robust immune responses for the most challenging targets

**Integral Molecular** is the industry leader in isolating MAbs against membrane protein targets and welcomes partnerships to discover lead therapeutic antibodies

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