

# Case Study: Discovering antibodies against GLUT4, a complex 12-TM transporter

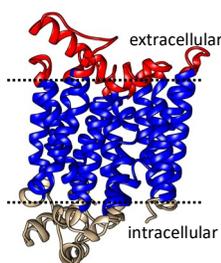
## THE NEED

GLUT4 is an important transporter that regulates glucose uptake in response to insulin. Antibodies against native GLUT4 are needed to study its function but are very challenging to obtain. GLUT4 is highly conserved (95%) between human and mouse, has 12 TM domains with very small loops, and must be in a membrane to be in its proper conformation. For these reasons, conventional technologies have been unable to isolate antibodies against native GLUT4.

## THE SOLUTION

### MPS Antibody Discovery

The MPS platform was used to generate a diverse panel of MAb that bind native GLUT4 epitopes. These antibodies have long CDR3 regions (up to 26 aa) that can efficiently penetrate the target structure.



To obtain a robust immune response, GLUT4 was incorporated into Lipoparticles and used to immunize chickens. This strategy overcame immune tolerance and elicited MAbs with long CDR3 regions. A large, diverse panel of antibodies recognizing native epitopes was isolated using Lipoparticle phage display.

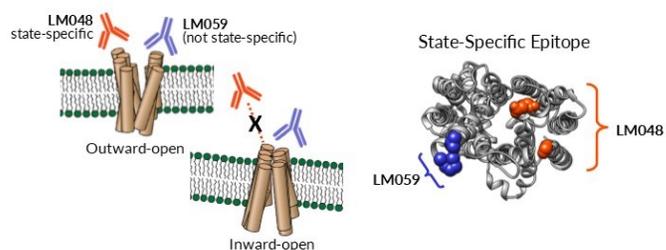
### Epitope Mapping

Shotgun Mutagenesis Epitope Mapping was used to map GLUT4 MAbs. The epitope data allowed the characterization of state-specific MAbs that bound epitopes on inward-open or outward-open conformations of the transporter.

## THE IMPACT

### State-Specific Antibodies

The GLUT4 antibodies generated by the MPS Antibody Discovery platform are valuable reagents to study glucose uptake in response to insulin. These antibodies can be used to directly measure the trafficking of GLUT4 on the surface of cells to enable drug discovery.



The state-specific, long-CDR3 GLUT4 antibodies are unique reagents for probing the conformational states of GLUT4. These reagents can provide information on the mechanisms of action of GLUT4 and drugs targeting the transporter.

### Publication

Data featured in Tucker, et al., 2018, *PNAS*.

Looking for more information? Contact us below:

info@integralmolecular.com | 215.966.6061 | www.integralmolecular.com