integral molecular

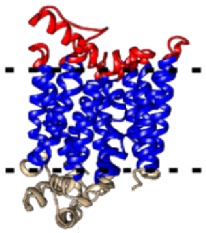
Case Study:
Discovering antibodies against GLUT4, a complex 12-TM transporter

THE NEED

GLUT4 is a transporter that regulates glucose uptake in response to insulin. Antibodies against natively folded GLUT4 are needed to study its function. GLUT4 is a very challenging antibody target because it is highly conserved (95% to mouse), has 12 transmembrane domains with very small loops, and its correct conformation depends on GLUT4 being maintained in a membrane. Previous efforts using conventional technologies were unable to isolate antibodies that bind native GLUT4.

THE SOLUTION

MPS Antibody Discovery



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

To obtain a robust immune response, GLUT4 was incorporated into Lipoparticles and used to immunize chickens. This strategy was able to overcome immune tolerance and elicit 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. This led to the characterization of state-specific MAbs that bound epitopes on inward-open or outward-open conformations of the transporter.

THE IMPACT

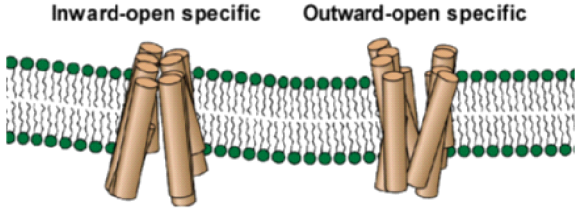
State-Specific Antibodies

The GLUT4 antibodies generated by MPS represent 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 that can probe GLUT4 conformational states. This can elucidate the mechanism-of-action of GLUT4 and drugs that target it.

Publication

Data submitted for publication. Tucker et al. 2017.



Looking for more information? Contact us below:

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