integral molecular

Case Study:
Discovery of antagonist MAbs against the GPCR CB1 for treating NASH

THE NEED

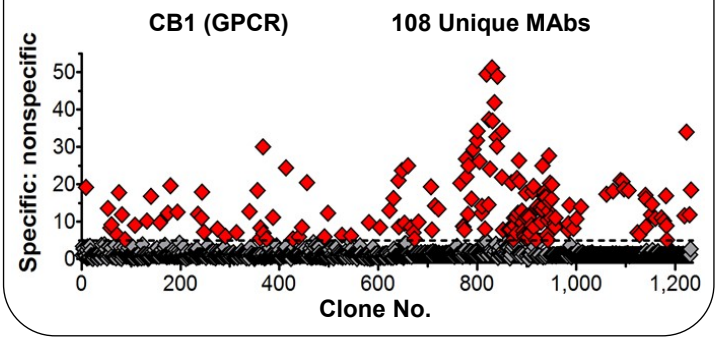
Cannabinoid receptor type 1 (CB1) is a therapeutic GPCR target for nonalcoholic steatohepatitis (NASH). Antagonist drugs are needed that inhibit CB1 in liver without altering CB1 in brain. MAbs offer a promising solution because they cannot cross the blood-brain barrier. However, CB1 is very difficult to target with MAbs because it is toxic, poorly expressed, highly conserved (93% identical to mouse), and has a large, complex, and membrane-dependent structure (7 TMs with small extracellular loops).

THE SOLUTION

MPS Antibody Discovery

Integral Molecular used its MPS Antibody Discovery platform to isolate a large, diverse panel of antibodies that bind native CB1 on the cell, including antibodies that bind with high affinity and inhibit cellular signaling of CB1.

Antibody discovery strategies included antigen optimization to increase expression and reduce toxicity, DNA + Lipoparticle immunization of divergent species to obtain a robust immune response, and functional screening to identify potent antagonists.



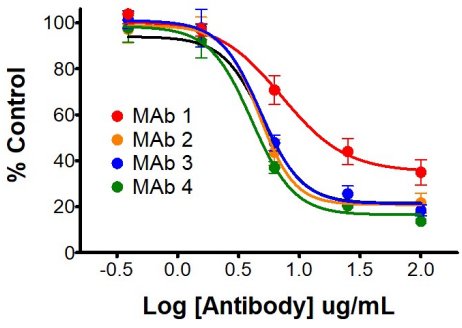
THE IMPACT

Lead Candidate MAbs

Lead candidate CB1 MAbs discovered with the MPS platform are among the most potent antibody antagonists described for CB1, and are being advanced for the treatment of NASH.

Clinical Implications

Although an important target for NASH, CB1 in liver has been undruggable by small molecules due to CNS side effects. Integral Molecular's CB1 antagonist MAbs enable a new modality of inhibiting liver CB1 without crossing the blood-brain barrier.



Contact us to discuss MPS Antibody Discovery partnerships

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