integral molecular

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

THE NEED

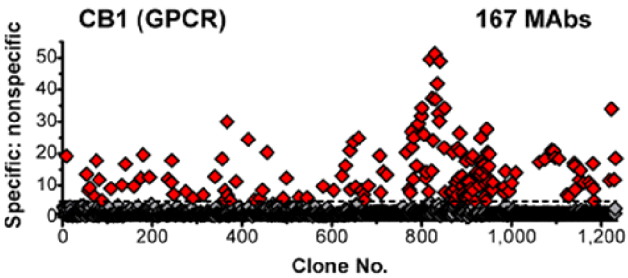
The GPCR CB1 is a therapeutic target for non-alcholic steatohepatitis (NASH). Antagonist drugs are needed that inhibit CB1 in the liver without affecting CB1 in the brain. CB1 is a very difficult antibody target as it is toxic, poorly expressed, highly conserved (93% identical to mouse), has 7 transmembrane domains with small loops, and has a membrane dependent structure.

THE SOLUTION

MPS Antibody Discovery

Integral Molecular's antibody platform was used to isolate a large, diverse panel of antibodies that bind native conformation CB1 on the surface of cells. Lead candidates bind CB1 with high affinity and inhibit cellular signaling of CB1.

MPS strategies included antigen optimization to increase expression and reduce toxicity, DNA+Lipoparticle immunization in divergent species to obtain a robust immune response and screening in functional assays to identify potent CB1 antagonists.



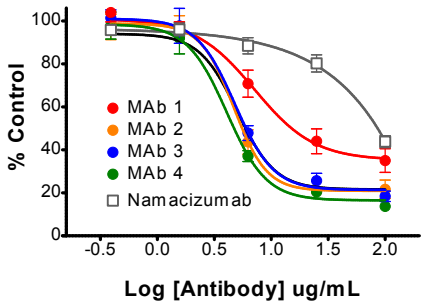
THE IMPACT

Lead Candidate MAbs

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

Clinical Implications

Liver CB1 is an important clinically validated target for NASH but has been undruggable with small molecules due to inhibitory effects on CB1 in the brain. The CB1 antagonist antibodies discovered by Integral Molecular enable a new modality of inhibiting liver CB1 without undesirable side effects.



Looking for more information? Contact us below:

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