MOSPD2: A Novel Therapeutic Target for the Treatment of CNS Inflammation

Niva Yacov, Pinhas Kafri, Yaniv Salem, Oshrat Propheta-Meiran, Eyal Breitbart and Itzhak Mendel. VBL Therapeutics

Background

In multiple sclerosis (MS), blood-borne monocytes constitute a part of the central nervous system (CNS)-infiltrating cells and are paramount for disease pathogenesis. Therefore, inhibiting monocyte migration to the CNS of MS patients could have a therapeutic benefit. We previously identified MOSPD2 (Motile sperm domain–containing protein 2) as a protein which is predominantly expressed on the surface of human monocytes and is essential for their migration. In this study, we assessed the potential of MOSPD2 as a target for treating CNS inflammation, using experimental autoimmune encephalomyelitis (EAE) as a test model.

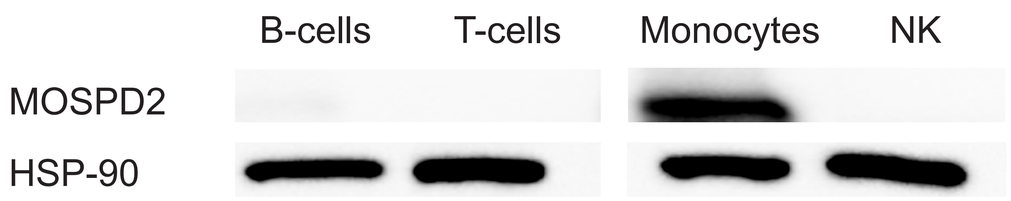
Methods

MOSPD2 knockout (KO) mice were generated by introducing the MOSPD2-targeting construct to embryonic stem cells via homologous recombination. Anti-MOSPD2 monoclonal antibodies (mAbs) were prepared by immunizing mice with the extracellular region of human MOSPD2 and isolating hybridoma producing antibodies. Antibodies were administered every 2-3 days. EAE was induced by immunizing mice with myelin oligodendrocyte glycoprotein (MOG) peptide 35-55 emulsified in complete Freund's adjuvant and pertussis toxin.

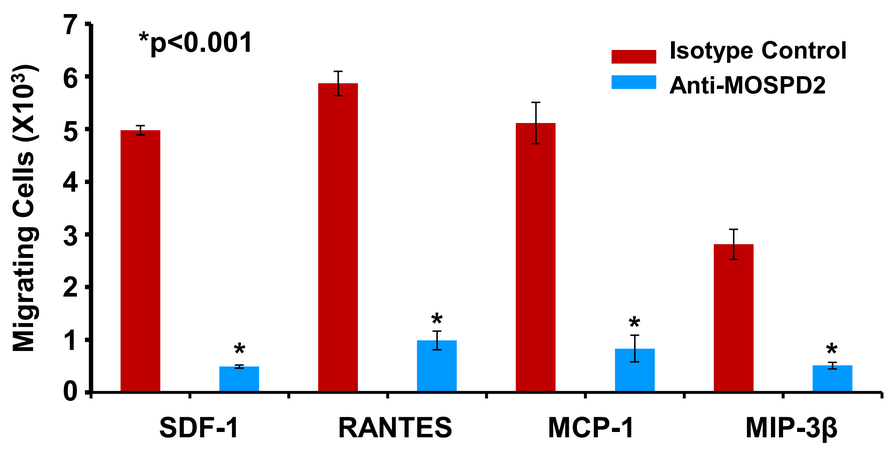
Results

MOSPD2 Promotes Monocytes Migration

MOSPD2 is Expressed on Monocytes

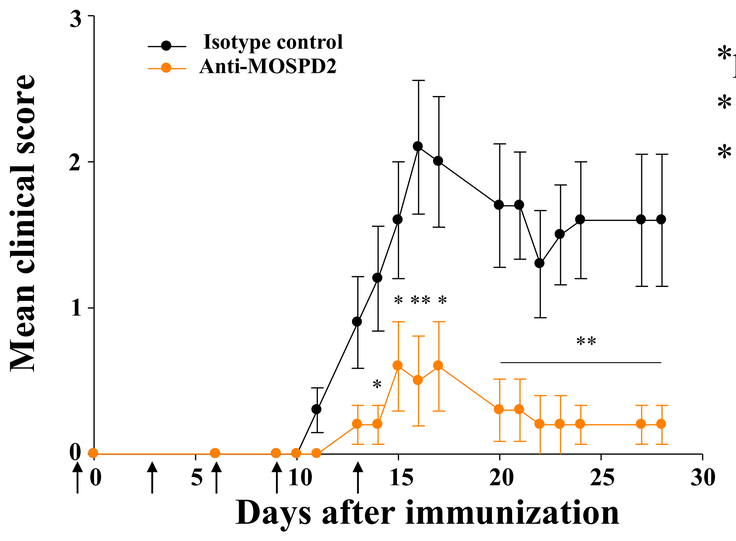


Migration Inhibition of CD14+ Human Primary Monocytes

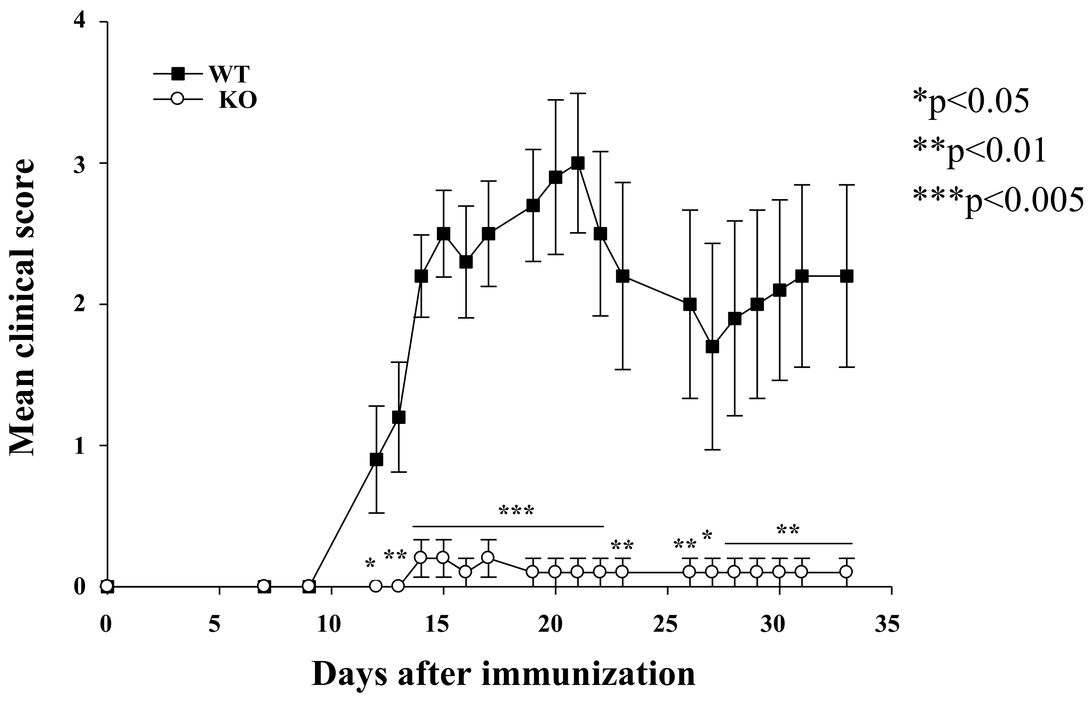


Anti-MOSPD2 mAb Inhibits EAE Pathogenesis

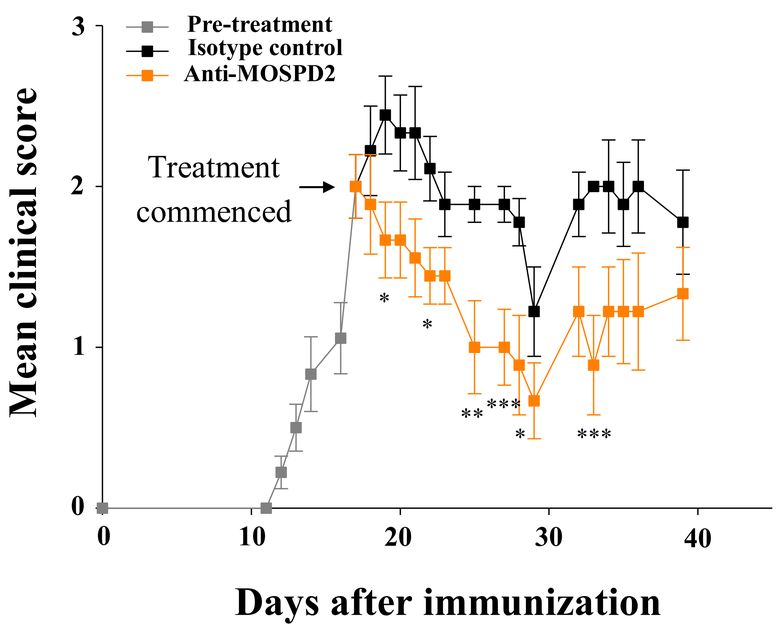
Prevention

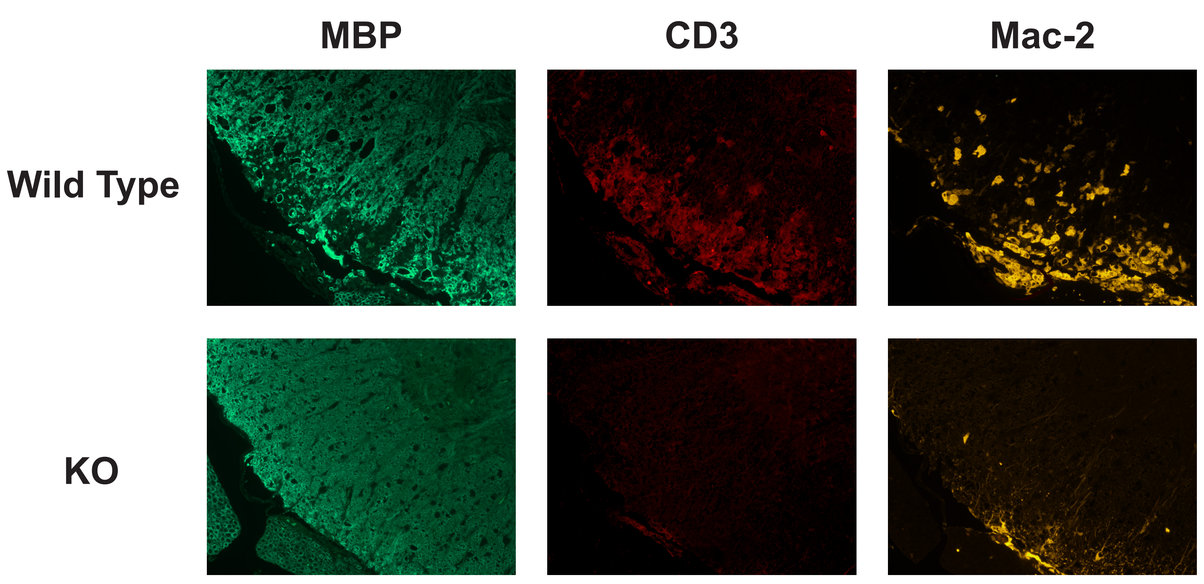


EAE is Suppressed in MOSPD2 KO mice



Treatment





Conclusions

- MOSPD2 is expressed on monocytes and required for their migration
- Using KO mice and mAb, we demonstrate that MOSPD2 is essential for EAE pathogenesis
- MOSPD2 is a novel potential target for the treatment of CNS inflammation
- **VBL is developing its VB-600 platform of biologics targeting MOSPD2 for inflammatory and oncology indications**