MOSPD2: A novel therapeutic target for the treatment of inflammatory digestive diseases

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Disclosures

- All authors are employees and stock option holders of VBL Therapeutics.

Rationale of study

- Nonalcoholic fatty liver disease (NAFLD) is a major cause of liver-related morbidity and mortality worldwide, with no effective treatment currently available.
- Monocytes are important players in NAFLD progression.
- Peripheral monocytes are also involved in the pathogenesis of inflammatory bowel disease (IBD).
- Motile sperm domain-containing protein 2 (MOSPD2) is a membrane protein expressed by monocytes and regulates their migration in a chemokine-agnostic manner.

We tested the role of MOSPD2 in animal models of NASH and colitis, using MOSPD2-deficient mice and anti-MOSPD2 mAb.

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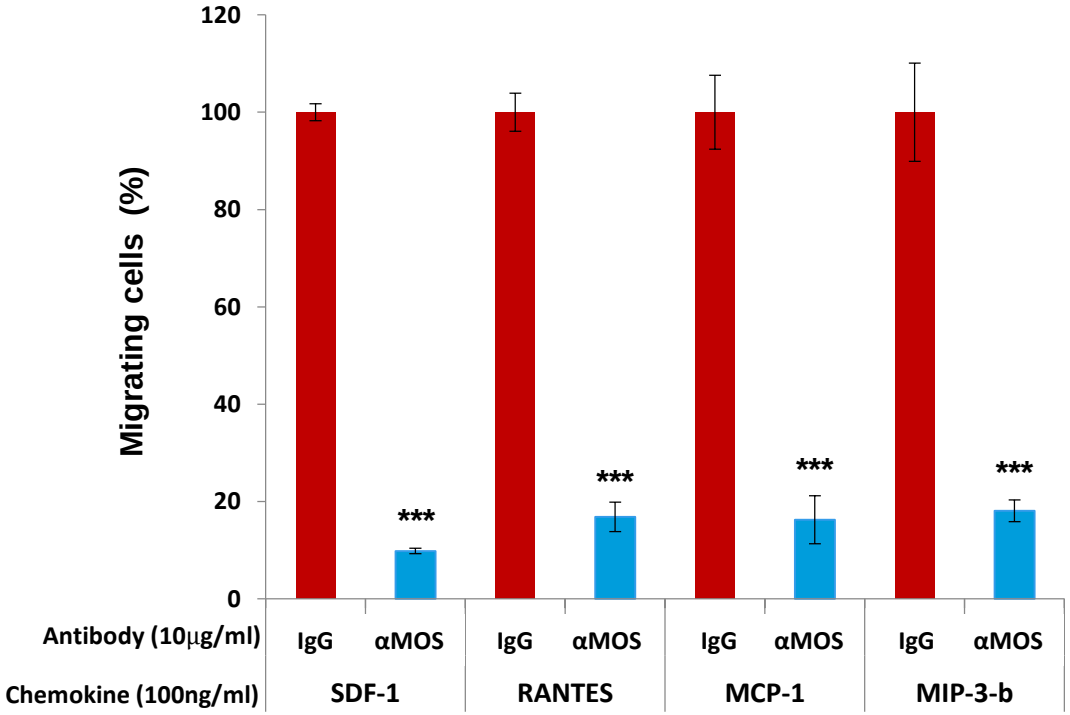
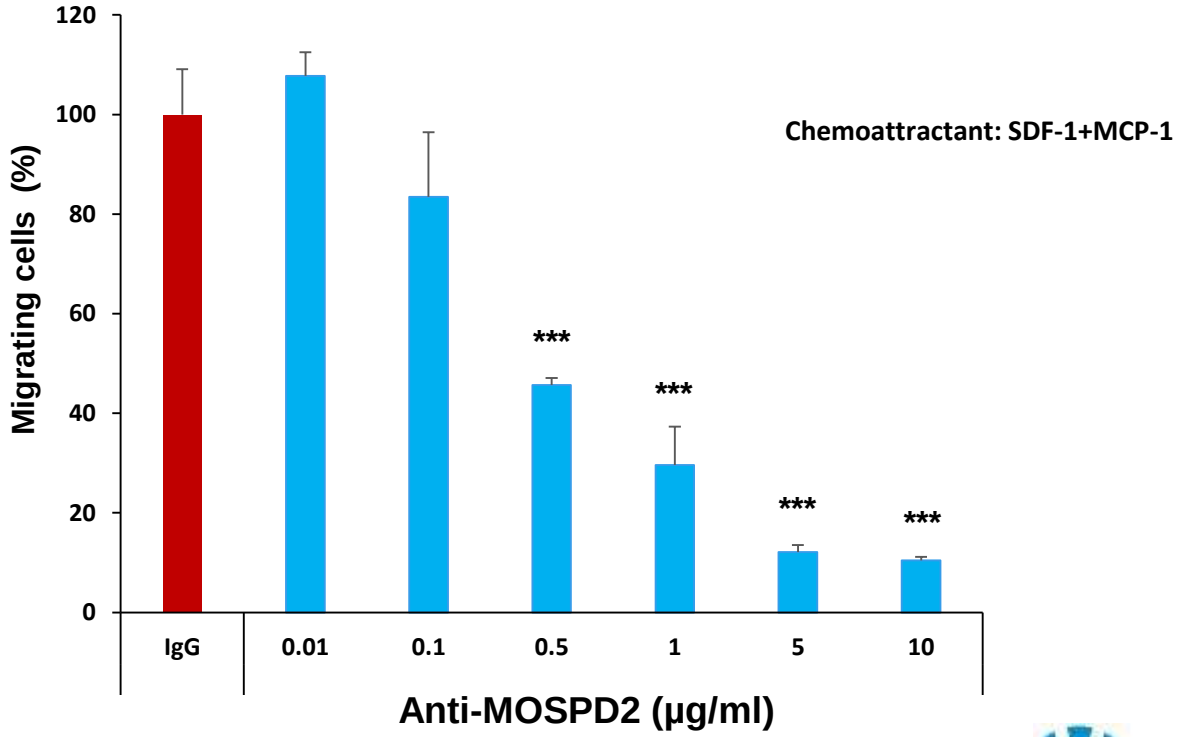
VBL's Anti-MOSPD2 Ab Leads to Inhibited Monocyte Migration in a Chemokine-Agnostic Manner

Human primary monocytes

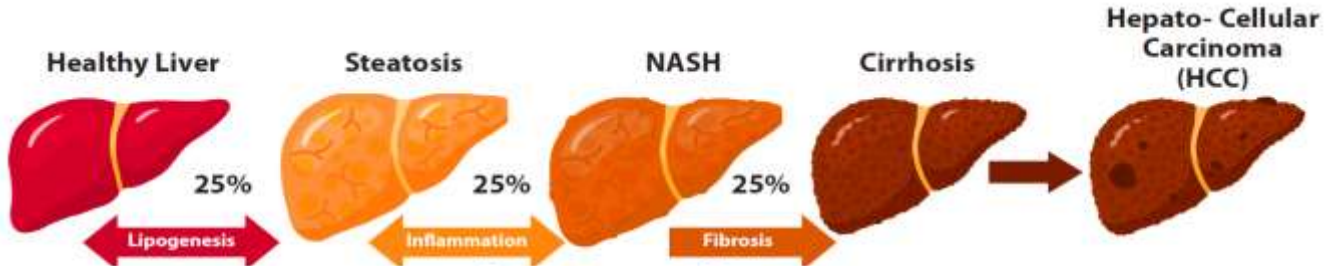
**p<0.01
***p<0.001
Compared to IgG control



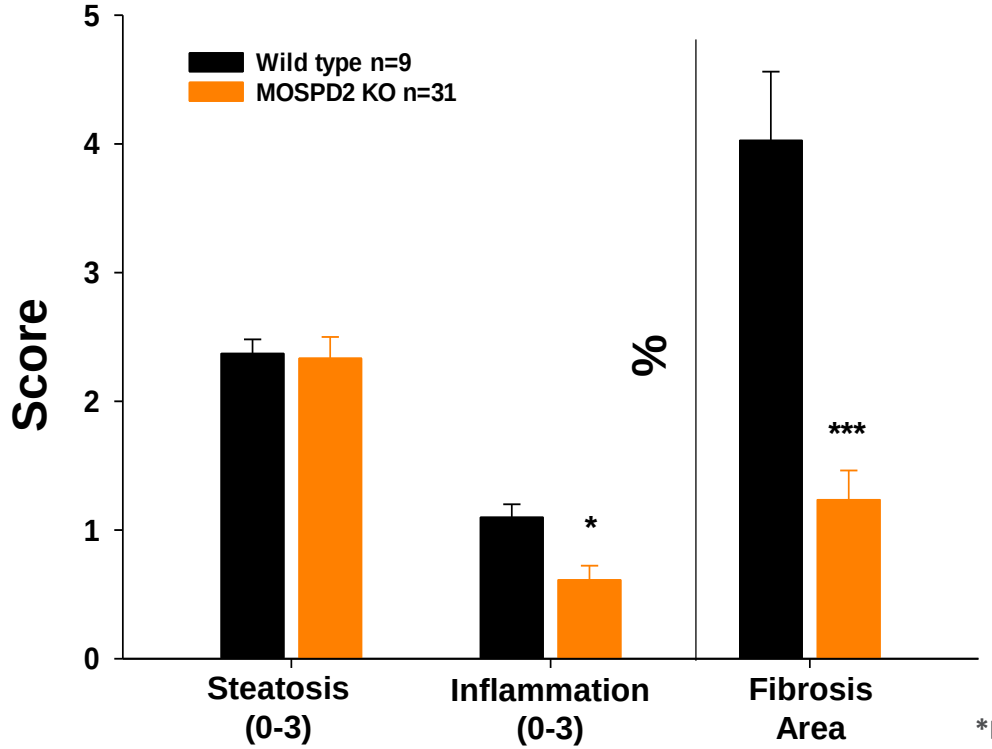


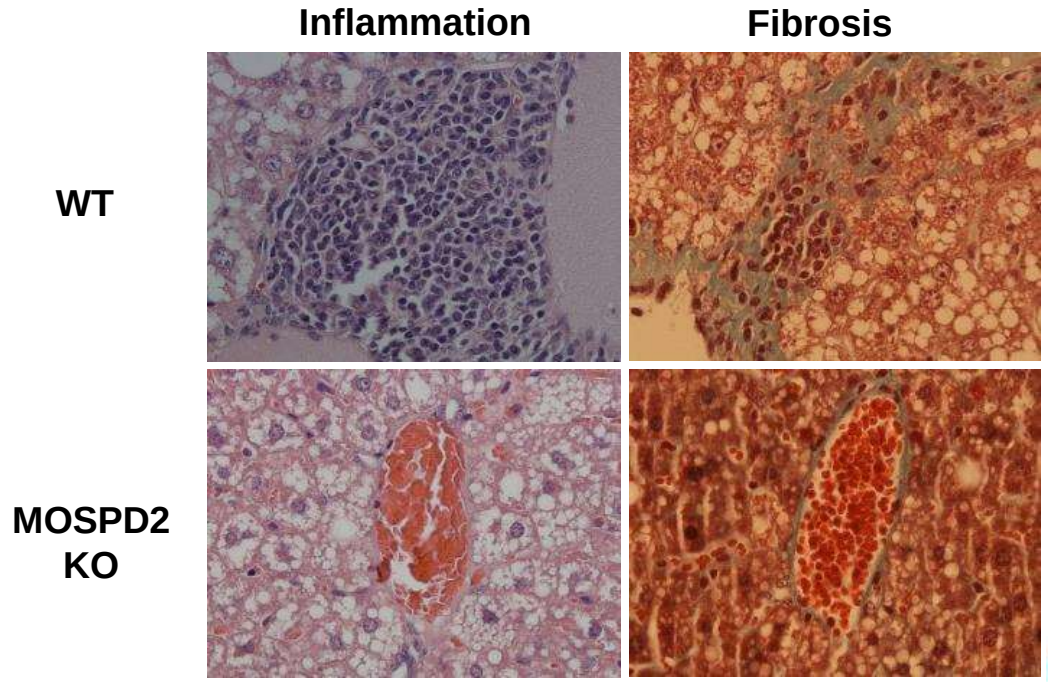
MOSPD2 KO Mice Show Reduced Inflammation and Fibrosis in HFHC* NASH Model

NASH Pathogenesis



*p<0.05
**p<0.01
***p<0.001





*High Fat High Carbohydrate diet combined with water enriched with fructose & sucrose for 18 weeks

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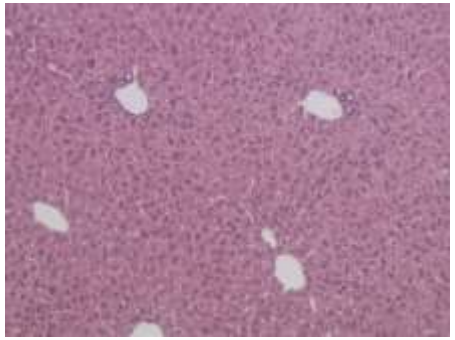
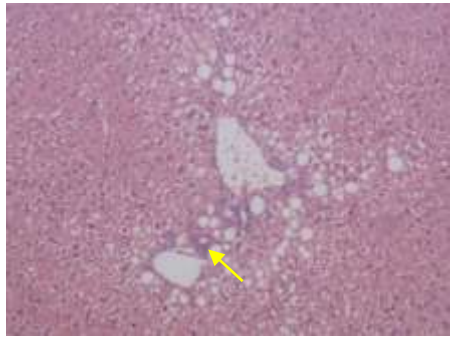
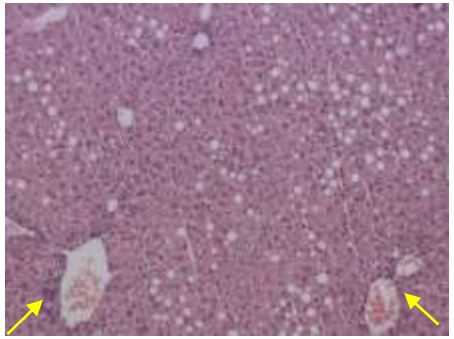
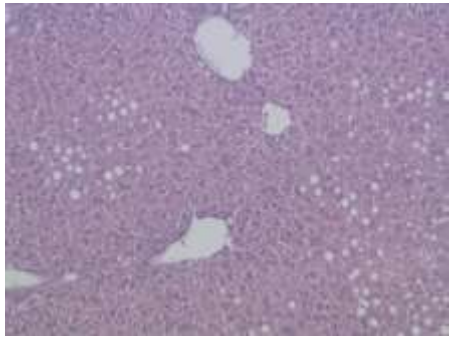
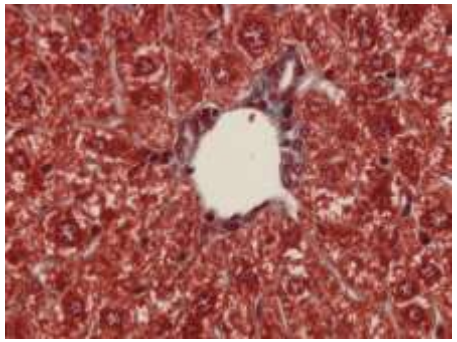
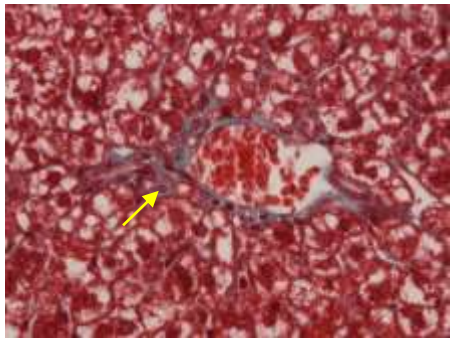
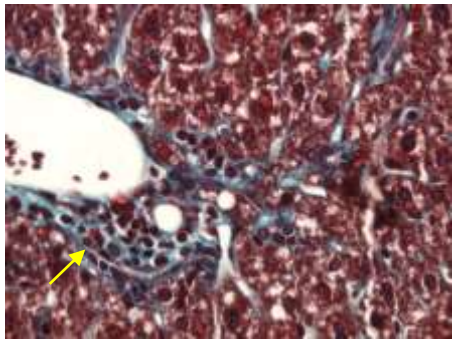
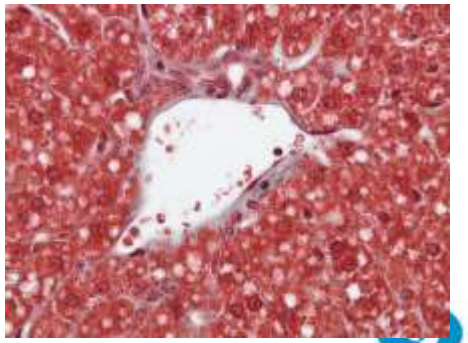
VBL's Anti-MOSPD2 mAb Reduces Inflammation and Fibrosis in HFHC NASH Mouse Model

N=10-11	CHOW diet	HFHC diet Baseline (9 weeks)	HFHC diet Control Ab (18 weeks)	HFHC diet Anti-MOSPD2 (18 weeks)
H&E X100				
	Normal histology	Fatty liver +inflammation	Fatty liver +inflammation	Fatty liver, no inflammation
Masson trichome x400				
	Normal histology	Mild fibrosis	Severe fibrosis	No fibrosis

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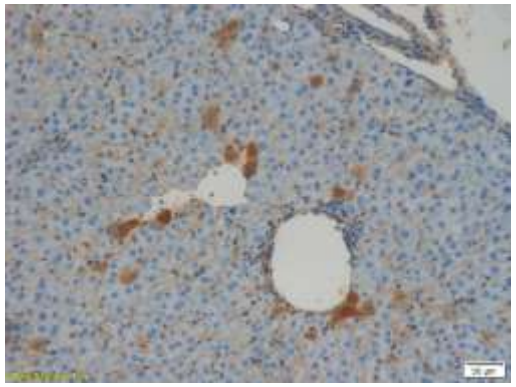
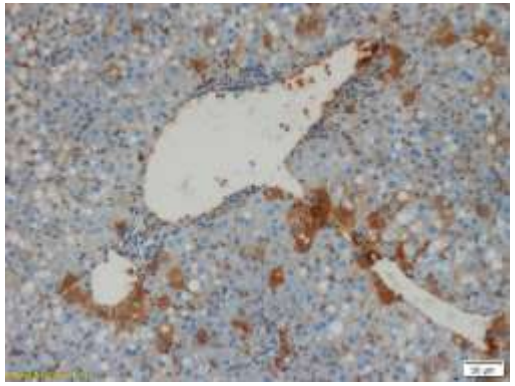
VBL's Anti-MOSPD2 mAb Reduces Monocyte Accumulation and Fibrosis in HFHC NASH Mouse Model

CHOW diet



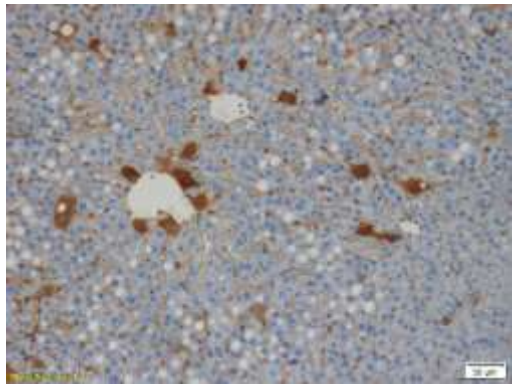
HFHC diet

Isotype control

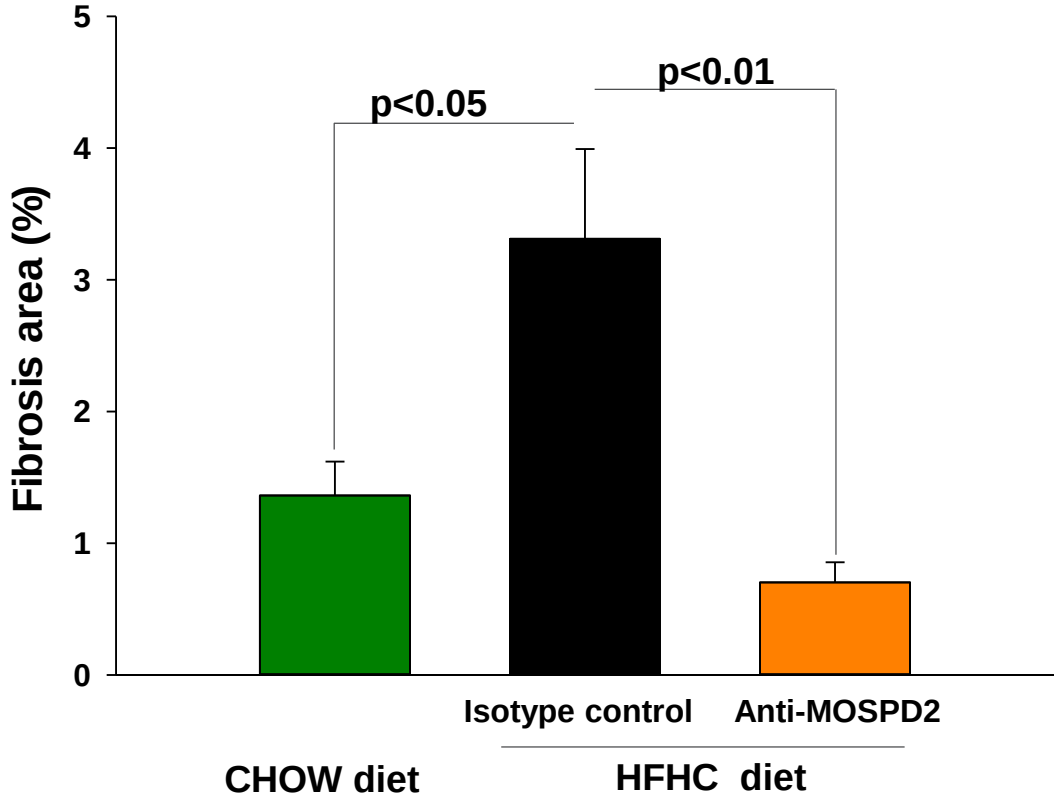


Increased accumulation of CD68+ cells

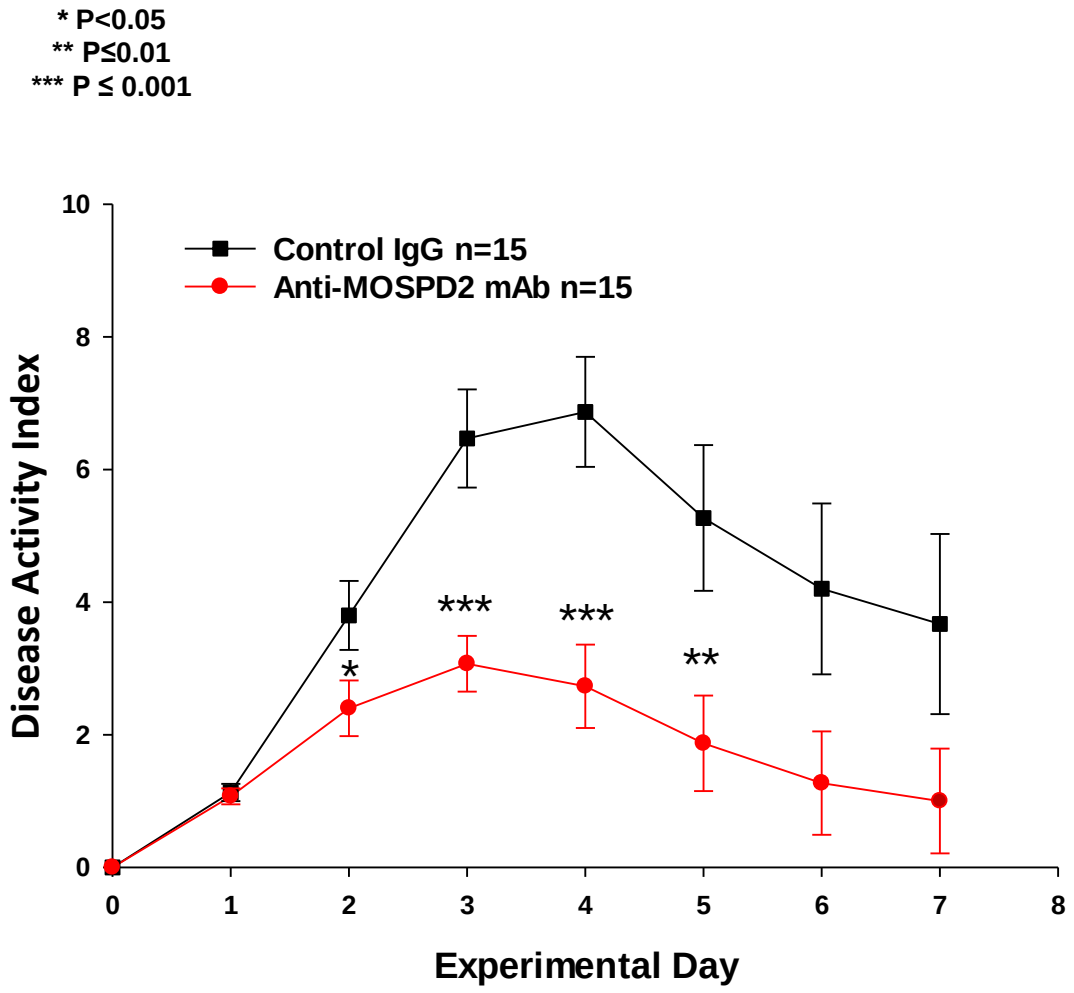
Anti-MOSPD2

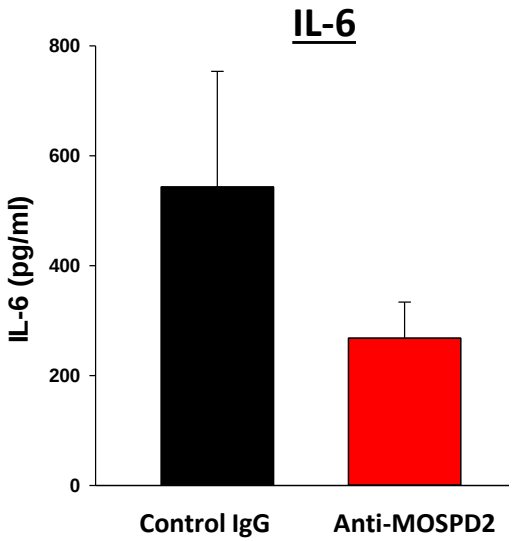


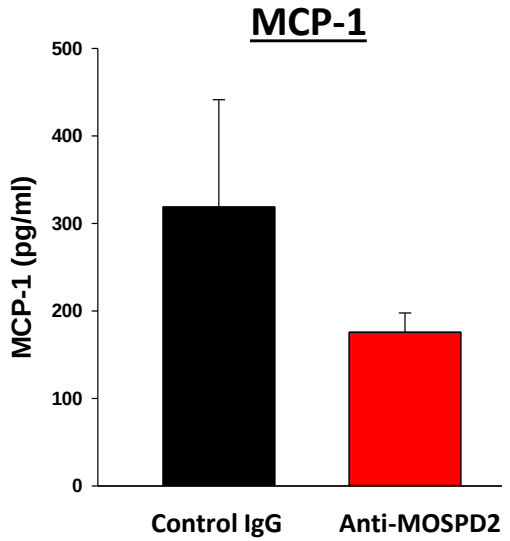
Reduced number of CD68+ cells

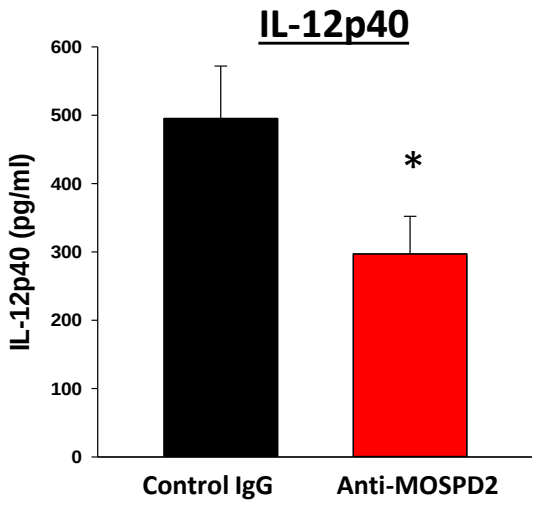


VBL's Anti-MOSPD2 mAb Treatment Significantly Ameliorates Disease Activity in TNBS-Induced Colitis Mouse Model









Conclusions

- VBL has identified MOSPD2 is a key regulator of monocyte migration, that functions in a chemokine-agnostic manner. Use of anti-MOSPD2 antibodies opens up a way to overcome the redundancy of multiple chemoattractant and their receptors.
- MOSPD2 plays an important role in regulating inflammation and fibrosis in NASH:
  - MOSPD2-deficient mice, and mice with established disease that were treated with anti-MOSPD2 mAb, display significantly reduced inflammation and fibrosis.
- VBL's anti-MOSPD2 mAb suppresses colitis, as evident by reduced disease score and cytokine levels

Targeting MOSPD2 using mAbs may hold promise as a treatment for NASH, liver fibrosis and colitis through inhibition of monocytes accumulation in the affected tissues.

VBL is advancing proprietary lead candidate antibody VB-601 towards first-in-human study.

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