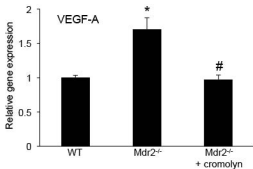
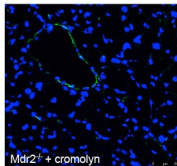
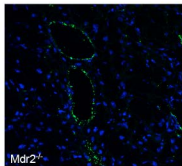
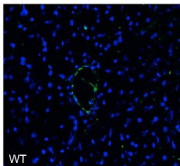


Supplemental Figure 1 Immunofluorescence for Factor VIII reveals that there is an upregulation of vascular cell positivity in Mdr2^{-/-} mice compared to WT and treatment with cromolyn decreases the cellular positivity of Factor VIII (Supplemental Figure 2). Further, VEGF-A gene expression was increased in Mdr2^{-/-} mice compared to WT and decreased in Mdr2^{-/-} mice treated with cromolyn sodium (Supplemental Figure 2). Data are expressed as mean ± SEM of at least 3 experiments for immunofluorescence and 6 experiments for real-time PCR. *p<0.05 versus WT; #p<0.05 versus Mdr2^{-/-} mice. Images are 40x magnification.

Supplemental Figure 2 Schematic diagram of the interplay of different cell types during hepatic fibrosis, including mast cells, cholangiocytes and myofibroblasts/hepatic stellate cells. In normal liver, cholangiocytes and HSCs are quiescent and mast cell numbers are low. Following liver damage, there is biliary proliferation and mast cell infiltration that induces an increase in inflammatory factors like histamine. This event then activates HSCs and potentially portal myofibroblasts, which then induce collagen deposition and hepatic fibrosis. Mast cells can act on both cholangiocytes and hepatic stellate cells to promote fibrosis. Cromolyn sodium (blocking mast cell-derived histamine) reverses these events and contributes to the regression of hepatic fibrosis.

Supplemental Figure 1

Vwf



Supplemental Figure 2

Normal Liver



FVB/NJ



Dormant
Cholangiocyte



Quiescent
Stellate Cells



Mast Cell Infiltration
and Activation

Hepatic Injury



Mdr^{-/-}



Cholangiocyte
Proliferation

Growth Factors
Cytokines
TGF β
 \uparrow Histamine



Mast Cell Infiltration
and Activation

Fibrogenesis



Mdr^{-/-}



Collagen Deposition



Activated
Stellate Cells



Portal Myofibroblasts

Resolution



Mdr^{-/-} + Cromolyn



Collagen Degradation

\downarrow IBDM/Proliferation
 \downarrow HSC Activation
 \downarrow Fibrosis
 \downarrow Histamine



Mast Cell Infiltration
and Activation