damage model *in vivo* and (b) reduce biliary damage and improve hepatocyte function in a chronic liver damage model *in vivo*.

In one aspect, there is provided use of a Notch2-specific antagonist in the manufacture of a medicament for treating liver fibrosis in a patient having liver fibrosis, wherein the Notch2-specific antagonist is an anti-Notch2 antagonist antibody.

In one aspect, there is provided a method of inducing hepatic differentiation, the method comprising the step of contacting an oval cell *in vitro* with an effective amount of a Notch2-specific antagonist, thereby inducing hepatic differentiation of the oval cell, wherein the Notch2-specific antagonist is an anti-Notch2 antagonist antibody.

In one aspect, there is provided use of a Notch2-specific antagonist in the manufacture of a medicament for inducing hepatic differentiation, wherein the medicament is to be contacted with an oval cell *in vivo* to thereby induce hepatic differentiation of the oval cell, and wherein the Notch2-specific antagonist is an anti-Notch2 antagonist antibody.

In one aspect, there is provided use of a Notch2-specific antagonist in the manufacture of a medicament for reducing aberrant bile duct proliferation in a patient with liver fibrosis, wherein the Notch2-specific antagonist is an anti-Notch2 antagonist antibody.

In one embodiment, a method of treating a liver condition characterized by liver damage is provided, the method comprising administering to a patient having such condition an effective amount of a Notch2-specific antagonist. In certain embodiments, the liver condition is chronic liver disease. In certain embodiments, the liver condition is liver fibrosis.

In any of the above embodiments, the Notch2-specific antagonist may be an anti-Notch2 antagonist antibody. In certain embodiments, the anti-Notch2 antagonist antibody is an anti-Notch2 NRR antibody. In one such embodiment, the anti-Notch2 NRR antibody binds to the LNR-A and HD-C domains of Notch2 NRR. In another such embodiment, the anti-Notch2 NRR antibody is Antibody D, Antibody D-1, Antibody D-2, or Antibody D-3. In another such embodiment, the anti-Notch2 NRR antibody comprises the heavy and light chain variable region CDRs of Antibody D, Antibody D-1, Antibody D-2, or Antibody D-3. In certain embodiments, the anti-Notch2 antagonist antibody is an anti-Notch2 antibody that binds to one or more EGF-like repeats of Notch2.

The above and further aspects and embodiments of the disclosure are provided herein.

BRIEF DESCRIPTION OF THE FIGURES

Figures 1A-G show transcriptional profiling of hepatic progenitor cells and Identification of active Notch signaling in hepatic progenitors *in vivo*.

WHAT IS CLAIMED IS:

1. Use of a Notch2-specific antagonist in the manufacture of a medicament for treating liver fibrosis in a patient having liver fibrosis, wherein the Notch2-specific antagonist is an anti-Notch2 antagonist antibody.

2. The use of claim 1, wherein the anti-Notch2 antagonist antibody is an anti-Notch2 NRR antibody.

3. The use of claim 2, wherein the anti-Notch2 NRR antibody binds to the LNR-A and HD-C domains of Notch2 NRR.

4. The use of claim 2, wherein the anti-Notch2 NRR antibody is selected from the group consisting of:

a) an antibody comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 1, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 4, an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 5, an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 6, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 15;

b) an antibody comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 2, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 4, an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 5, an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 7, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 16;

c) an antibody comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 2, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 4, an HVR-H3

comprising the amino acid sequence of SEQ ID NO: 5, an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 8, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 12, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 17; and

d) an antibody comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 2, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 4, an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 5, an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 9, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 18.

5. The use of claim 2, wherein the anti-Notch2 NRR antibody is selected from the group consisting of:

a) an antibody comprising a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 20 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 22;

b) an antibody comprising a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 21 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 23;

c) an antibody comprising a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 21 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 24; and

d) an antibody comprising a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 21 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 25.

6. The use of claim 1, wherein the anti-Notch2 antagonist antibody is an anti-Notch2 antibody that binds to one or more EGF-like repeats of Notch2.

7. The use of claim 1, wherein the Notch2-specific antagonist is to be administered by intramuscular, intraperitoneal, intracerobrospinal, subcutaneous, intra-articular, intrasynovial, intrathecal, oral, topical, or inhalation route.

8. A method of inducing hepatic differentiation, the method comprising the step of contacting an oval cell *in vitro* with an effective amount of a Notch2-specific antagonist, thereby inducing hepatic differentiation of the oval cell, wherein the Notch2-specific antagonist is an anti-Notch2 antagonist antibody.

9. Use of a Notch2-specific antagonist in the manufacture of a medicament for inducing hepatic differentiation, wherein the medicament is to be contacted with an oval cell *in vivo* to thereby induce hepatic differentiation of the oval cell, and wherein the Notch2-specific antagonist is an anti-Notch2 antagonist antibody.

10. Use of a Notch2-specific antagonist in the manufacture of a medicament for reducing aberrant bile duct proliferation in a patient with liver fibrosis, wherein the Notch2-specific antagonist is an anti-Notch2 antagonist antibody.