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 a liver condition characterized by liver damage in a patient having such condition, wherein the liver condition is chronic liver disease or an acute liver condition.

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.

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.

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 in need thereof.

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 ~~invention~~ 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 a liver condition characterized by liver damage in a patient having such condition.

2. The use of claim 1, wherein the liver condition is chronic liver disease.

3. The use of claim 2, wherein the chronic liver disease is liver fibrosis.

4. The use of claim 2 wherein the chronic liver disease is liver cirrhosis.

5. The use of claim 1, wherein the liver condition is an acute liver condition.

6. The use of claim 5, wherein the acute liver condition is acetaminophen toxicity.

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

8. The use of claim 7, wherein the anti-Notch2 antagonist antibody is an anti-Notch2 NRR antibody.

9. The use of claim 8, wherein the anti-Notch2 NRR antibody binds to the LNR-A and HD-C domains of Notch2 NRR.

10. The use of claim 8, wherein the anti-Notch2 NRR antibody is Antibody D, Antibody D-1, Antibody D-2, or Antibody D-3.

11. The use of claim 8, wherein 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.

12. The use of claim 7, wherein the anti-Notch2 antagonist antibody is an anti-Notch2 antibody that binds to one or more EGF-like repeats of Notch2.

13. 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.

14. 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.

15. 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.

16. Use of a Notch2-specific antagonist in the manufacture of a medicament for reducing aberrant bile duct proliferation in a patient in need thereof.

WHAT IS CLAIMED IS:

1. Use of a Notch2-specific antagonist in the manufacture of a medicament for treating a liver condition characterized by liver damage in a patient having such condition, wherein the liver condition is chronic liver disease or an acute liver condition.

2. The use of claim 1, wherein the chronic liver disease is liver fibrosis.

3. The use of claim 1, wherein the chronic liver disease is liver cirrhosis.

4. The use of claim 1, wherein the acute liver condition is acetaminophen toxicity.

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

6. The use of claim 5, wherein the anti-Notch2 antagonist antibody is an anti-Notch2 NRR antibody.

7. The use of claim 6, wherein the anti-Notch2 NRR antibody binds to the LNR-A and HD-C domains of Notch2 NRR.

8. The use of claim 6, 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.

9. The use of claim 6, 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.

10. The use of claim 5, wherein the anti-Notch2 antagonist antibody is an anti-Notch2 antibody that binds to one or more EGF-like repeats of Notch2.

11. 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.

12. 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.

13. 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.

14. Use of a Notch2-specific antagonist in the manufacture of a medicament for reducing aberrant bile duct proliferation in a patient in need thereof.