more transcription factors selected from the group consisting of PROX1, NR5A2, NR0B2, MTF1, SREBP1, EP300, and POM121C.

In one aspect, the present disclosure refers to use of a composition in the manufacture of a medicament for treating liver disease in a subject in need thereof, wherein the composition comprises one or more expression vectors comprising one or more nucleic acids encoding one or more transcription factors selected from the group consisting of NR5A2, NR0B2, MTF1, SREBP1, EP300, and POM121C and a nucleic acid that encodes HNF4α isoform 2 (P1), wherein said composition is to be used to increase an amount or function of one or more transcription factors selected from the group consisting of NR5A2, NR0B2, MTF1, SREBP1, EP300, and POM121C in a hepatocyte.

In some examples, the composition is a vector, and wherein the vector comprises one or more nucleic acids that encode the one or more of PROX1, NR5A2, NR0B2, MTF1, SREBP1, EP300, and POM121C. In some examples, the vector comprises one or more nucleic acids that encode the PROX1 and/or SREBP1. The one or more nucleic acids can be a DNA or a mRNA.

In some examples, disclosed herein is a method of treating a liver disease in a subject in need thereof comprising administering to the subject a composition, wherein the composition decreases an amount or suppresses a function of one or more transcription factors selected from the group consisting of DNAJB1/HSP40, ATF6, ATF4, and PERK.

In some examples, disclosed herein is a use of a composition for the preparation of a medicament for treatment a liver disease in a subject in need thereof comprising administering to the subject the composition, wherein the composition decreases an amount or function of one or more transcription factors selected from the group consisting of DNAJB1/HSP40, ATF6, ATF4, and PERK.

In some examples, the administration of the composition increases an amount of HNF4α in a nucleus of a hepatocyte in the subject. In some examples, the administration of the composition does not increase a total amount of HNF4α in the hepatocyte. In some examples, the administration of the composition increases a total amount of HNF4α in the hepatocyte.

In some examples, the vector further comprises a nucleic acid that encodes HNF4α. In some examples, the method further comprises administering to the subject a vector that comprises a nucleic acid that encodes HNF4α. In one example, the nucleic acid encodes HNF4α isoform 2.

In some examples, disclosed herein is a composition comprising a vector, wherein the vector comprises one or more nucleic acids that encode one or more transcription factors selected from the group consisting of PROX1, NR5A2, NR0B2, MTF1, SREBP1, EP300, and POM121C, and functional fragments thereof.

In one aspect, the present disclosure refers to a composition comprising a vector, wherein the vector comprises one or more nucleic acids that encode HNF4α isoform 2 (P1) and one or more transcription factors selected from the group consisting of NR5A2, NR0B2, MTF1, SREBP1, EP300, and POM121C.

In some examples, disclosed herein is a method of treating a liver disease in a subject in need thereof comprising administering to the subject a vector that comprises a nucleic acid encoding HNF4α isoform 2.

CLAIMS

What is claimed is:

1. Use of a composition in the manufacture of a medicament for treating liver disease with cirrhosis in a subject in need thereof, wherein the composition comprises one or more expression vectors comprising one or more nucleic acids encoding one or more transcription factors selected from the group consisting of NR5A2, NR0B2, MTF1, SREBP1, EP300, and POM121C and a nucleic acid that encodes HNF4α isoform 2 (P1), wherein said composition is to be used to increase an amount or function of one or more transcription factors selected from the group consisting of NR5A2, NR0B2, MTF1, SREBP1, EP300, and POM121C in a hepatocyte.

2. The use of claim 1, wherein the vector comprises one or more nucleic acids that encode the SREBP1.

3. The use of claim 1, wherein the vector comprises one or more nucleic acids that encode the MTF1.

4. The use of claim 1, wherein the vector comprises one or more nucleic acids that encode the NR0B2.

5. The use of claim 1, wherein the vector comprises one or more nucleic acids that encode the NR5A2.

6. The use of claim 1, wherein the vector comprises one or more nucleic acids that encode the EP300.

7. The use of claim 1, wherein the vector comprises one or more nucleic acids that encode the POM121C.

8. The use of any one of claims 1-7, wherein the one or more nucleic acids are a DNA or a mRNA.

9. The use of any one of claims 1-8, wherein the administration of the composition increases an amount of HNF4α isoform 2 (P1) in a nucleus of the hepatocyte in the subject.

10. The use of any one of claims 1-9, wherein the administration of the composition does not increase a total amount of HNF4α isoform 2 (P1) in the hepatocyte.

11. The use of any one of claims 1-10, wherein the administration of the composition increases a total amount of HNF4α isoform 2 (P1) in the hepatocyte.

12. The use of any one of claims 1-11, wherein the nucleic acid that encodes HNF4α isoform 2 (P1) comprises SEQ ID NO:1.

13. The use of any one of claims 1-12, wherein the subject is a human.

14. A composition comprising a vector, wherein the vector comprises one or more nucleic acids that encode HNF4α isoform 2 (P1) and one or more transcription factors selected from the group consisting of NR5A2, NR0B2, MTF1, SREBP1, EP300, and POM121C.

15. The composition of claim 14, wherein the nucleic acid that encodes HNF4α isoform 2 (P1) comprises SEQ ID NO:1.

16. The composition of claim 14, wherein the vector comprises one or more nucleic acids that encode the SREBP1.

17. The composition of claim 14, wherein the vector comprises one or more nucleic acids that encode the MTF1.

18. The composition of claim 14, wherein the vector comprises one or more nucleic acids that encode the NR0B2.

19. The composition of claim 14, wherein the vector comprises one or more nucleic acids that encode the NR5A2.

20. The composition of claim 14, wherein the vector comprises one or more nucleic acids that encode the EP300.

21. The composition of claim 14, wherein the vector comprises one or more nucleic acids that encode the POM121C.