

What is claimed is:

1. Use of a compound comprising a polynucleotide in the manufacture of a medicament for treating fatty liver disease in a subject in need thereof, wherein the compound is effective in lowering the expression of *Pleckstrin and Sec7 Domain Containing 3* (PSD3), wherein the compound is to be administered to the subject.
2. Use of a compound comprising a polynucleotide effective in lowering PSD3 expression in the manufacture of a medicament for inhibiting expression or activity of PSD3 in a cell, wherein the compound is to be contacted with the cell, wherein the compound is capable of inhibiting expression or activity of PSD3 in the cell.
3. Use of a compound in the manufacture of a medicament for reducing activation of ADP-ribosylation factor 6 (ARF6) in a subject, wherein the compound comprises a polynucleotide effective for lowering the PSD3 expression in the subject, wherein lower PSD3 expression provides for reduced activation of ARF6, wherein the compound is to be administered to the subject.
4. Use of a compound in the manufacture of a medicament for lowering intracellular fat content in a liver cell in a subject, wherein the compound comprises a polynucleotide effective for lowering PSD3 expression in the subject, wherein the compound is to be administered to the subject.
5. Use of a compound in the manufacture of a medicament for lowering cholesterol in a subject, wherein the compound comprises a polynucleotide effective for lowering PSD3 expression in the subject, wherein the compound is to be administered to the subject.
6. A method of identifying a subpopulation of subjects having fatty liver disease for whom PSD3 reduction therapy is a suitable treatment, the method comprising;
 - a. diagnosing whether a subject has fatty liver disease;
 - b. determining whether the subject has the 186T allelic variant of PSD3 protein or the 186L allelic variant of PSD3 protein;wherein if the subject has the 186L allelic variant of PSD3 protein, then the subject is included in the subpopulation of subjects having fatty liver disease for whom PSD3 reduction therapy is a suitable treatment; and

wherein if the subject has the 186T allelic variant of PSD3 protein, then the subject is not included in the subpopulation of subjects having liver disease for whom PSD3 reduction therapy is a suitable treatment.

7. Use of a compound comprising a polynucleotide effective for lowering PSD3 expression in the manufacture of a medicament for treating fatty liver disease in a subject, wherein;
 - a. the subject having the 186T allelic variant of PSD3 protein or the 186L allelic variant of PSD3 protein is to be determined; and
 - b. the compound is to be administered only if the subject has the 186L allelic variant of PSD3 protein.
8. The use in any of claims 1-5 and 7, or the method of claim 6, wherein the compound is selected from an antisense oligonucleotide, an siRNA, and an ssRNAi.
9. The use or method of claim 8, wherein the compound comprises an antisense RNAi polynucleotide consisting of 17 to 30 linked nucleosides, wherein the nucleobase sequence of the antisense RNAi polynucleotide comprises a targeting region comprising at least 15 contiguous nucleobases complementary to an equal portion of a PSD3 RNA, and wherein the antisense RNAi polynucleotide is at least 90%, at least 95%, or 100% complementary to an equal portion of any of SEQ ID NO: 2-18.
10. The use or method in any of claims 1-9, wherein the polynucleotide has:
 - a gap segment consisting of linked deoxynucleosides;
 - a 5' wing segment consisting of linked nucleosides;
 - a 3' wing segment consisting linked nucleosides;wherein the gap segment is positioned immediately adjacent to and between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.
11. Use of a compound effective in lowering the expression of *Pleckstrin and Sec7 Domain Containing 3* (PSD3) in the manufacture of a medicament for treating a fatty liver disease, wherein the compound comprises a polynucleotide.

12. Use of a compound effective in lowering the expression of *Pleckstrin and Sec7 Domain Containing 3* (PSD3) for the treatment of a fatty liver disease, wherein the compound comprises a polynucleotide.
13. Use of a compound effective in reducing activation of ADP-ribosylation factor 6 (ARF6) in the manufacture of a medicament for treating a fatty liver disease, wherein the compound comprises a polynucleotide.
14. Use of a compound effective in reducing activation of ADP-ribosylation factor 6 (ARF6) for the treatment of a fatty liver disease, wherein the compound comprises a polynucleotide.
15. Use of a compound effective in lowering intracellular fat content in a liver cell in a subject in the manufacture of a medicament for treating a fatty liver disease, wherein the compound comprises a polynucleotide.
16. Use of a compound effective in lowering intracellular fat content in a liver cell in a subject for the treatment of a fatty liver disease, wherein the compound comprises a polynucleotide.
17. Use of a compound effective in lowering cholesterol in a subject in the manufacture of a medicament for treating a fatty liver disease, wherein the compound comprises a polynucleotide.
18. Use of a compound effective in lowering cholesterol in a subject for the treatment of a fatty liver disease, wherein the compound comprises a polynucleotide.