What is Claimed is:

1. Use of a chimeric peptide sequence in the manufacture of a medicament for modulating bile acid homeostasis or treating a bile-acid related or associated disorder, said chimeric peptide sequence comprising:

    a) an N-terminal region comprising at least seven amino acid residues, the N-terminal region having a first amino acid position and a last amino acid position, wherein the N-terminal region comprises DSSPL (SEQ ID NO:121) or DASPH (SEQ ID NO:122); and

    b) a C-terminal region comprising a portion of SEQ ID NO:99 [FGF19], the C-terminal region having a first amino acid position and a last amino acid position, wherein the C-terminal region comprises amino acid residues 16-29 of SEQ ID NO:99 [FGF19], WGDPIRLRHLYTSG (SEQ ID NO:169), wherein the W residue corresponds to the first amino acid position of the C-terminal region.

2. Use of a chimeric peptide sequence in the manufacture of a medicament for modulating bile acid homeostasis or treating a bile-acid related or associated disorder, said chimeric peptide sequence comprising:

    a) an N-terminal region comprising a portion of SEQ ID NO:100 [FGF21], the N-terminal region having a first amino acid position and a last amino acid position, wherein the N-terminal region comprises amino acid residues GQV, and wherein the V residue corresponds to the last amino acid position of the N-terminal region; and

    b) a C-terminal region comprising a portion of SEQ ID NO:99 [FGF19], the C-terminal region having a first amino acid position and a last amino acid position, wherein the C-terminal region comprises amino acid residues 21-29 of SEQ ID NO:99 [FGF19], RLRHLYTSG (SEQ ID NO:185), and wherein the R residue corresponds to the first position of the C-terminal region.

3. Use of a chimeric peptide sequence in the manufacture of a medicament for modulating bile acid homeostasis or treating a bile-acid related or associated disorder, said chimeric peptide sequence comprising:

a) an N-terminal region comprising a portion of SEQ ID NO:100 [FGF21], the N-terminal region having a first amino acid position and a last amino acid position, wherein the N-terminal region comprises at least 5 contiguous amino acids of SEQ ID NO:100 [FGF21] including the amino acid residues GQV, and wherein the V residue corresponds to the last amino acid position of the N-terminal region; and

b) a C-terminal region comprising a portion of SEQ ID NO:99 [FGF19], the C-terminal region having a first amino acid position and a last amino acid position, wherein the C-terminal region comprises amino acid residues 21-29 of SEQ ID NO:99 [FGF19], RLRHLYTSG (SEQ ID NO:185), and wherein the R residue corresponds to the first position of the C-terminal region.

4. The use of claim 3, wherein the N-terminal region comprises at least 6 contiguous amino acids of SEQ ID NO:100 [FGF21] including the amino acid residues GQV.

5. The use of claim 3, wherein the N-terminal region comprises at least 7 contiguous amino acids of SEQ ID NO:100 [FGF21] including the amino acid residues GQV.

6. Use of a peptide sequence in the manufacture of a medicament for modulating bile acid homeostasis or treating a bile-acid related or associated disorder, said peptide sequence comprising or consisting of any of:

a) a FGF19 sequence variant having one or more amino acid substitutions, insertions or deletions compared to a reference or wild type FGF19;

b) a FGF21 sequence variant having one or more amino acid substitutions, insertions or deletions compared to a reference or wild type FGF21;

c) a portion of an FGF19 sequence fused to a portion of an FGF21 sequence; or

d) a portion of an FGF19 sequence fused to a portion of an FGF21 sequence, wherein the FGF19 and/or FGF21 sequence portion(s) have one or more amino acid substitutions, insertions or deletions compared to a reference or wild type FGF19 and/or FGF21.

7. The use of claim 6, wherein the peptide sequence has amino-terminal amino acids 1-16 of SEQ ID NO:100 [FGF21] fused to carboxy-terminal amino acids 21-194 of SEQ ID NO:99 [FGF19], or wherein the peptide sequence has amino-terminal amino acids 1-147 of SEQ ID

NO:99 [FGF19] fused to carboxy-terminal amino acids 147-181 of SEQ ID NO:100 [FGF21] (M41), or wherein the peptide sequence has amino-terminal amino acids 1-20 of SEQ ID NO:99 [FGF19] fused to carboxy-terminal amino acids 17-181 of SEQ ID NO:100 [FGF21] (M44), or wherein the peptide sequence has amino-terminal amino acids 1-146 of SEQ ID NO:100 [FGF21] fused to carboxy-terminal amino acids 148-194 of SEQ ID NO:99 [FGF19] (M45), or wherein the peptide sequence has amino-terminal amino acids 1-20 of SEQ ID NO:99 [FGF19] fused to internal amino acids 17-146 of SEQ ID NO:100 [FGF21] fused to carboxy-terminal amino acids 148-194 of SEQ ID NO:99 [FGF19] (M46).

8. The use of claim 6, wherein the peptide sequence comprises at least one amino acid substitution to amino acid residues 125-129 of SEQ ID NO:99 [FGF19], EIRPD; at least one amino acid substitution to amino acid residues 126-128 of SEQ ID NO:99 [FGF19], IRP; or at least one amino acid substitution to amino acid residues 127-128 of SEQ ID NO:99 [FGF19], RP.

9. The use of claim 8, wherein the peptide sequence comprises a substitution to one of amino acid residues 127-128 of SEQ ID NO:99 [FGF19], IRP, wherein at least one amino acid substitution is R127L or P128E

10. The use of claim 9, wherein the peptide sequence comprises RPLAFSDAGPHVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSL LEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEILEDGYNVYR SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLE TDSMDPFGLVTGLEAVRSPSFEK (M3) (SEQ ID NO:3); or RPLAFSDAGPHVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSL LEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIREDGYNVYR SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLE TDSMDPFGLVTGLEAVRSPSFEK (M140) (SEQ ID NO:194).

11. The use of claim 8, wherein the peptide sequence further comprises at least one amino acid substitution to amino acid residues 1-124 of SEQ ID NO:99 [FGF19] and/or to amino acid residues 130-194 of SEQ ID NO:99 [FGF19].

12. The use of claim 11, wherein the peptide sequence is RPLAFSDAGPHVHYGWGDPIRQRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSL LEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEILEDGYNVYR SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLE TDSMDPFGLVTGLEAVRSPSFEK (M160) (SEQ ID NO:196).

13. The use of claims 1, 2, 3 or 6, wherein the peptide sequence comprises or consists of any sequence set forth herein as M1 to M98 or M101 to M160, or SEQ ID NOs:1 to 98, 101 to 135, or 138 to 196 .

14. The use of claims 1, 2, 3 or 6, wherein the peptide sequence comprises or consists of any sequence set forth in Tables 1-10.

15. The use of claims 1, 2, 3 or 6, wherein the peptide sequence comprises or consists of any sequence set forth in the Sequence Listing herein.

16. The use of claims 1, 2 or 6, wherein the peptide sequence has a WGDPI (SEQ ID NO:170) sequence motif corresponding to the WGDPI sequence of amino acids 16-20 of SEQ ID NO:99 [FGF19].

17. The use of claim 16, wherein the peptide sequence maintains or increases an FGFR4 mediated activity.

18. The use of claims 1, 2 or 6, wherein the peptide sequence has a substituted, mutated or absent WGDPI (SEQ ID NO:170) sequence motif corresponding to FGF19 WGDPI sequence of amino acids 16-20 of FGF19.

19. The use of claim 18, wherein the WGDPI (SEQ ID NO:170) sequence has one or more amino acids substituted, mutated or absent.

20. The use of claims 1, 2 or 6, wherein the peptide sequence is distinct from an FGF 19 variant sequence having any of GQV, GDI, WGPI (SEQ ID NO:171), WGDPV (SEQ ID NO:172), WGDI (SEQ ID NO:173), GDPI (SEQ ID NO:174), GPI, WGQPI (SEQ ID NO:175), WGAPI (SEQ ID NO:176), AGDPI (SEQ ID NO:177), WADPI (SEQ ID NO:178), WGDAI (SEQ ID NO:179), WGDPA (SEQ ID NO:180), WDPI (SEQ ID NO:181), WGDI (SEQ ID

NO:182), WGDP (SEQ ID NO:183) or FGDPI (SEQ ID NO:184) substituted for the FGF19 WGDPI (SEQ ID NO:170) sequence at amino acids 16-20.

21. The use of any of claims 1 to 3 or 6, wherein the N-terminal or C-terminal region is from about 20 to about 200 amino acid residues in length.

22. The use of claim 1, wherein the N-terminal region comprises amino acid residues VHYG (SEQ ID NO:101), wherein the N-terminal region comprises amino acid residues DASPHVHYG (SEQ ID NO:102), or wherein the N-terminal region comprises amino acid residues DSSPLVHYG (SEQ ID NO:103).

23. The use of claim 22, wherein the G corresponds to the last position of the N-terminal region.

24. The use of claims 1 or 6, wherein the N-terminal region comprises amino acid residues DSSPLLQ (SEQ ID NO:104), and wherein the Q residue is the last amino acid position of the N-terminal region.

25. The use of claim 23 or 24, wherein the N-terminal region further comprises: RHPIP (SEQ ID NO:106), where R is the first amino acid position of the N-terminal region; or HPIP (SEQ ID NO:107), where H is the first amino acid position of the N-terminal region; or RPLAF (SEQ ID NO:108), where R is the first amino acid position of the N-terminal region; or PLAF (SEQ ID NO:109), where P is the first amino acid position of the N-terminal region; or R, where R is the first amino acid position of the N-terminal region.

26. The use of any of claims 1 to 3 or 6, wherein the peptide sequence comprises or consists of any of M1 to M98 or M101 to M160 variant peptide sequences, or a subsequence or fragment of any of the M1 to M98 or M101 to M160 variant peptide sequences.

27. The use of any of claims 1 to 3 or 6, wherein the peptide sequence comprises or consists of any of:

RDSSPLVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIKA
VALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSEKHR
LPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDSM
DPFGLVTGLEAVRSPSFEK (M69) (SEQ ID NO: 69);

RDSSPLLQWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIKAVAL
RTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSEKHRLPV

SLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDSMDPFG
LVTGLEAVRSPSFEK (M52) (SEQ ID NO:52);

RHPIPDSSPLLQFGGQVRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIK
AVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSEK
HRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDS
MDPFGLVTGLEAVRSPSFEK (M5) (SEQ ID NO:5);

HPIPDSSPLLQFGGQVRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIKA
VALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSEKHR
LPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDSM
DPFGLVTGLEAVRSPSFEK (M5-R) (SEQ ID NO:160);

HPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKA
LKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHSLP
LHLPGNKSPHRDPAPRGPARFLPLPGLPPALPEPPGILAPQPPDVGSSDPLSMVGPSQG
RSPSYAS (M71) (SEQ ID NO:71);
HPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKA
LKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLP
LHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQG
RSPSYAS (M72) (SEQ ID NO:72);

HPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKA
LKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLP
LHLPGNKSPHRDPAPRGPARFLPLPGLPPALPEPPGILAPQPPDVGSSDPLSMVVQDEL
QGVGGEGCHMHPENCKTLLTDIDRTHTEKPVWDGITGE (M73) (SEQ ID NO:73);

RPLAFSDASPHVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSL
LEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYR
SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLE
TDSMDPFGLVTGLEAVRSPSFEK (M1) (SEQ ID NO:1 or 139);

RPLAFSDSSPLVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLL
EIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRS
EKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLET
DSMDPFGLVTGLEAVRSPSFEK (M2) (SEQ ID NO:2 or 140);

RPLAFSDAGPHVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSL
LEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEILEDGYNVYR
SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLE
TDSMDPFGLVTGLEAVRSPSFEK (M3) (SEQ ID NO:3);

RDSSPLLQFGGQVRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIKAVA
LRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSEKHRLP
VSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDSMDPF
GLVTGLEAVRSPSFEK (M48) (SEQ ID NO:48 or 6 or 148);

RPLAFSDSSPLLQFGGQVRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEI
KAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSE
KHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETD
SMDPFGLVTGLEAVRSPSFEK (M49) (SEQ ID NO:49 or 7 or 149);

RHPIPDSSPLLQFGDQVRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIK
AVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEILEDGYNVYRSEK
HRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDS
MDPFGLVTGLEAVRSPSFEK (M50) (SEQ ID NO:50);

RHPIPDSSPLLQFGGNVRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIK
AVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSEK
HRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDS
MDPFGLVTGLEAVRSPSFEK (M51) (SEQ ID NO:51 or 36 or 155);

MDSSPLLQWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIKAVA
LRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSEKHRLP
VSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDSMDPF
GLVTGLEAVRSPSFEK (M53) (SEQ ID NO:192);

MRDSSPLVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIK
AVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSEK
HRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDS
16MDPFGLVTGLEAVRSPSFEK (M70) (SEQ ID NO:70);

RPLAFSDAGPHVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSL
LEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEILPDGYNVYR

SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLE TDSMDPFGLVTGLEAVRSPSFEK (M139) (SEQ ID NO:193);

RPLAFSDAGPHVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSL LEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIREDGYNVYR SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLE TDSMDPFGLVTGLEAVRSPSFEK (M140) (SEQ ID NO:194);

RPLAFSDAGPHVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSL LEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEILCDGYNVYR SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLE TDSMDPFGLVTGLEAVRSPSFEK (M141) (SEQ ID NO:195); or

RPLAFSDAGPHVHYGWGDPIRQRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSL LEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEILEDGYNVYR SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLE TDSMDPFGLVTGLEAVRSPSFEK (M160) (SEQ ID NO:196);

or a subsequence or fragment of any of the foregoing peptide sequences, or any of the foregoing peptide sequences wherein the R terminal residue is deleted.

28. The use of claims 1 or 2, wherein the N-terminal region comprises amino acid residues DSSPLLQFGGQV (SEQ ID NO:105), and wherein the V residue corresponds to the last position of the N-terminal region.

29. The use of any of claims 1 to 3 or 6, wherein amino acid residues HPIP (SEQ ID NO:107) are the first 4 amino acid residues of the N-terminal region.

30. The use of any of claims 1 to 3, 6 or 27, wherein the first position of the N-terminal region is an R residue, or wherein the first position of the N-terminal region is an M residue, or wherein the first and second positions of the N-terminal region is an MR sequence, or wherein the first and second positions of the N-terminal region is an RM sequence, or wherein the first and second positions of the N-terminal region is an RD sequence, or wherein the first and second positions of the N-terminal region is an DS sequence, or wherein the first and second positions of the N-terminal region is an MD sequence, or wherein the first and second positions of the N-terminal region is an MS sequence, or wherein the first

through third positions of the N-terminal region is an MDS sequence, or wherein the first through third positions of the N-terminal region is an RDS sequence, or wherein the first through third positions of the N-terminal region is an MSD sequence, or wherein the first through third positions of the N-terminal region is an MSS sequence, or wherein the first through third positions of the N-terminal region is an DSS sequence, or wherein the first through fourth positions of the N-terminal region is an RDSS (SEQ ID NO:115) sequence, or the first through fourth positions of the N-terminal region is an MDSS (SEQ ID NO:116) sequence, or the first through fifth positions of the N-terminal region is an MRDSS (SEQ ID NO:117) sequence, or the first through fifth positions of the N-terminal region is an MSSPL (SEQ ID NO:118) sequence, or the first through sixth positions of the N-terminal region is an MDSSPL (SEQ ID NO:119) sequence, or the first through seventh positions of the N-terminal region is an MSDSSPL (SEQ ID NO:120) sequence.

31. The use of any one of claims 1 to 3 or 6, wherein the last position of the C-terminal region corresponds to about residue 194 of SEQ ID NO:99 [FGF19].

32. The use of any of claims 1 to 3 or 6, wherein the peptide sequence comprises or consists of: HPIPDSSPLLQFGGQVRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIKA VALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSEKHR LPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDSM DPFGLVTGLEAVRSPSFEK (SEQ ID NO:160);

DSSPLLQFGGQVRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIKAVAL RTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSEKHRLPV SLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDSMDPFG LVTGLEAVRSPSFEK (SEQ ID NO:138 or 161);

RPLAFSDASPHVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSL LEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYR SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLE TDSMDPFGLVTGLEAVRSPSFEK (SEQ ID NO:1 or 139);

RPLAFSDSSPLVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLL EIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRS

EKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLET DSMDPFGLVTGLEAVRSPSFEK(SEQ ID NO:2 or 140); or

DSSPLVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEIKAV ALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYRSEKHRL PVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLETDSMDP FGLVTGLEAVRSPSFEK (SEQ ID NO:141);
or a subsequence or fragment of any of the foregoing peptide sequences, or any of the foregoing peptide sequences wherein the R terminal residue is deleted.

33. The use of claim 26, 27 or 32, wherein the subsequence or fragment thereof has 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more amino acid deletions from the amino terminus, the carboxy-terminus or internally.

34. The use of claims 1, 2 or 6, wherein said N-terminal region, or said C-terminal region, comprises or consists of an amino acid sequence of about 5 to 10, 10 to 20, 20 to 30, 30 to 40, 40 to 50, 60 to 70, 70 to 80, 80 to 90, 90 to 100 or more amino acids.

35. The use of claims 3 or 6, wherein said FGF19 sequence portion, or said FGF21 sequence portion, comprises or consists of an amino acid sequence of about 5 to 10, 10 to 20, 20 to 30, 30 to 40, 40 to 50, 50 to 60, 60 to 70, 70 to 80, 80 to 90, 90 to 100 or more amino acids of FGF19 or FGF21.

36. The use of any of claims 1 to 3 or 6, wherein said N-terminal region, or said C-terminal region, or said FGF19 sequence portion, or said FGF21 sequence portion, are joined by a linker or spacer.

37. The use of any of claims 1 to 3 or 6, wherein the N-terminus of the peptide sequence at comprises or consists of any of:

HPIPDSSPLLQFGGQVRLRHLYTSG (M5-R) (amino acids 1-25 of SEQ ID NO:160);
DSSPLLQFGGQVRLRHLYTSG (M6-R) (amino acids 2-22 of SEQ ID NO:6);
RPLAFSDSSPLLQFGGQVRLRHLYTSG (M7) (amino acids 1-27 of SEQ ID NO:7);
HPIPDSSPLLQWGDPIRLRHLYTSG (M8-R) (amino acids 2-26 of SEQ ID NO:8);
HPIPDSSPLLQFGWGDPIRLRHLYTSG (M9-R) (amino acids 2-28 of SEQ ID NO:9);

HPIPDSSPHVHYGWGDPIRLRHLYTSG (M10-R) (amino acids 2-28 of SEQ ID NO:10);
RPLAFSDAGPLLQWGDPIRLRHLYTSG (M11) (amino acids 1-27 of SEQ ID NO:11);
RPLAFSDAGPLLQFGWGDPIRLRHLYTSG (M12) (amino acids 1-29 of SEQ ID NO:12);
RPLAFSDAGPLLQFGGQVRLRHLYTSG (M13) (amino acids 1-27 of SEQ ID NO:13);
HPIPDSSPHVHYGGQVRLRHLYTSG (M14-R) (amino acids 2-26 of SEQ ID NO:14);
RPLAFSDAGPHVHYGGQVRLRHLYTSG (M15) (amino acids 1-27 of SEQ ID NO:15);
RPLAFSDAGPHVHWGDPIRLRHLYTSG (M16) (amino acids 1-27 of SEQ ID NO:16);
RPLAFSDAGPHVGWGDPIRLRHLYTSG (M17) (amino acids 1-27 of SEQ ID NO:17);
RPLAFSDAGPHYGWGDPIRLRHLYTSG (M18) (amino acids 1-27 of SEQ ID NO:18);
RPLAFSDAGPVYGWGDPIRLRHLYTSG (M19) (amino acids 1-27 of SEQ ID NO:19);
RPLAFSDAGPVHGWGDPIRLRHLYTSG (M20) (amino acids 1-27 of SEQ ID NO:20);
RPLAFSDAGPVHYWGDPIRLRHLYTSG (M21) (amino acids 1-27 of SEQ ID NO:21);
RPLAFSDAGPHVHGWGDPIRLRHLYTSG (M22) (amino acids 1-27 of SEQ ID NO:22);
RPLAFSDAGPHHGWGDPIRLRHLYTSG (M23) (amino acids 1-27 of SEQ ID NO:23);
RPLAFSDAGPHHYWGDPIRLRHLYTSG (M24) (amino acids 1-27 of SEQ ID NO:24);
RPLAFSDAGPHVYWGDPIRLRHLYTSG (M25) (amino acids 1-27 of SEQ ID NO:25);
RPLAFSDSSPLVHWGDPIRLRHLYTSG (M26) (amino acids 1-27 of SEQ ID NO:26);
RPLAFSDSSPHVHWGDPIRLRHLYTSG (M27) (amino acids 1-27 of SEQ ID NO:27);
RPLAFSDAGPHVWGDPIRLRHLYTSG (M28) (amino acids 1-26 of SEQ ID NO:28);
RPLAFSDAGPHVHYWGDPIRLRHLYTSG (M29) (amino acids 1-28 of SEQ ID NO:29);
RPLAFSDAGPHVHYAWGDPIRLRHLYTSG (M30) (amino acids 1-29 of SEQ ID NO:30);
RHPIPDSSPLLQFGAQVRLRHLYTSG (M31) (amino acids 1-26 of SEQ ID NO:31);
RHPIPDSSPLLQFGDQVRLRHLYTSG (M32) (amino acids 1-26 of SEQ ID NO:32);
RHPIPDSSPLLQFGPQVRLRHLYTSG (M33) (amino acids 1-26 of SEQ ID NO:33);
RHPIPDSSPLLQFGGAVRLRHLYTSG (M34) (amino acids 1-26 of SEQ ID NO:34);
RHPIPDSSPLLQFGGEVRLRHLYTSG (M35) (amino acids 1-26 of SEQ ID NO:35);
RHPIPDSSPLLQFGGNVRLRHLYTSG (M36) (amino acids 1-26 of SEQ ID NO:36);
RHPIPDSSPLLQFGGQARLRHLYTSG (M37) (amino acids 1-26 of SEQ ID NO:37);
RHPIPDSSPLLQFGGQIRLRHLYTSG (M38) (amino acids 1-26 of SEQ ID NO:38);
RHPIPDSSPLLQFGGQTRLRHLYTSG (M39) (amino acids 1-26 of SEQ ID NO:39);
RHPIPDSSPLLQFGWGQPVRLRHLYTSG (M40) (amino acids 1-28 of SEQ ID NO:40);
DAGPHVHYGWGDPIRLRHLYTSG (M74-R) (amino acids 2-24 of SEQ ID NO:74);
VHYGWGDPIRLRHLYTSG (M75-R) (amino acids 2-19 of SEQ ID NO:75);

RLRHLYTSG (M77-R) (amino acids 2-10 of SEQ ID NO:77);
or any of the foregoing peptide sequences wherein the amino terminal R residue is deleted.

38. The use of any of claims 1 to 3 or 6, wherein the N-terminus of the peptide sequence comprises or consists of any of:
RHPIPDSSPLLQFGWGDPIRLRHLYTSG (M9) (amino acids 1-28 of SEQ ID NO:9);
RHPIPDSSPLLQWGDPIRLRHLYTSG (M8) (amino acids 1-26 of SEQ ID NO:8);
RPLAFSDAGPLLQFGWGDPIRLRHLYTSG (M12) (amino acids 1-29 of SEQ ID NO:12);
RHPIPDSSPHVHYGWGDPIRLRHLYTSG (M10) (amino acids 1-28 of SEQ ID NO:10);
RPLAFSDAGPLLQFGGQVRLRHLYTSG (M13) (amino acids 1-27 of SEQ ID NO:13);
RHPIPDSSPHVHYGGQVRLRHLYTSG (M14) (amino acids 1-26 of SEQ ID NO:14);
RPLAFSDAGPHVHYGGDIRLRHLYTSG (M43) amino acids 1-27 of SEQ ID NO:43); or
RDSSPLLQFGGQVRLRHLYTSG (M6) (amino acids 1-22 of SEQ ID NO:6);

or any of the foregoing peptide sequences wherein the amino terminal R residue is deleted.

39. The use of claims 37 or 38, wherein the peptide sequence further comprises the addition of amino acid residues 30-194 of SEQ ID NO:99 [FGF19] at the C-terminus, resulting in a chimeric polypeptide.

40. The use of any of claims 37 or 38, wherein the peptide sequence further comprises all or a portion of an FGF19 sequence set forth as:
PHGLSSCFLRIRADGVVDCARGQSAHSLLEIKAVALRTVAIKGVHSVRYLCMGADG
KMQGLLQYSEEDCAFEEEIRPDGYNVYRSEKHRLPVSLSSAKQRQLYKNRGFLPLSH
FLPMLPMVPEEPEDLRGHLESDMFSSPLETDSMDPFGLVTGLEAVRSPSFEK (SEQ ID NO:188) positioned at the C-terminus of the peptide, or wherein the amino terminal “R” residue is deleted from the peptide.

41. The use of any of claims 1 to 3 or 6, wherein a subsequence of a chimeric peptide sequence or peptide sequence is administered, wherein the subsequence has at least one amino acid deletion.

42. The use of claim 41, wherein the subsequence has 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more amino acid deletions from the amino terminus, the carboxy-terminus or internally.

43. The use of claim 6, wherein the reference or wild type FGF19 sequence is set forth as: RPLAFSDAGPHVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSL LEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYR SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSSPLE TDSMDPFGLVTGLEAVRSPSFEK (SEQ ID NO:99).

44. The use of claim 6, wherein the reference or wild type FGF21 sequence is set forth as: RHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLK ALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHG LPLHLPGNKSPHRDPAPRGPARFLPLPGLPPALPEPPGILAPQPPDVGSSDPLSMVGPS QGRSPSYAS (SEQ ID NO:100).

45. The use of any of claims 1 to 3 or 6, wherein the N-terminal region first amino acid position is a “M” residue, an “R” residue, a “S” residue, a “H” residue, a “P” residue, a “L” residue or an “D” residue, or wherein the peptide sequence does not have a “M” residue or an “R” residue at the first amino acid position of the N-terminal region.

46. The method of any of claims 1 to 3 or 6, wherein the N-terminal region comprises any one of the following sequences: MDSSPL (SEQ ID NO:119), MSDSSPL (SEQ ID NO:120), SDSSPL(SEQ ID NO:112), MSSPL (SEQ ID NO:113), or SSPL (SEQ ID NO:114).

47. The use of any of claims 1 to 3 or 6, wherein the peptide sequence has reduced hepatocellular carcinoma (HCC) formation compared to FGF19, or an FGF 19 variant sequence having any of GQV, GDI, WGPI (SEQ ID NO:171), WGDPV (SEQ ID NO:172), WGDI (SEQ ID NO:173), GDPI (SEQ ID NO:174), GPI, WGQPI (SEQ ID NO:175), WGAPI (SEQ ID NO:176), AGDPI (SEQ ID NO:177), WADPI (SEQ ID NO:178), WGDAI (SEQ ID NO:179), WGDPA (SEQ ID NO:180), WDPI (SEQ ID NO:181), WGDI (SEQ ID NO:182), WGDP (SEQ ID NO:183) or FGDPI (SEQ ID NO:184) substituted for the WGDPI (SEQ ID NO:170) sequence at amino acids 16-20 of FGF19.

48. The use of any of claims 1 to 3 or 6, wherein the peptide sequence has greater glucose lowering activity compared to FGF19, or an FGF 19 variant sequence having any of GQV, GDI, WGPI (SEQ ID NO:171), WGDPV (SEQ ID NO:172), WGDI (SEQ ID NO:173), GDPI (SEQ ID NO:174), GPI, WGQPI (SEQ ID NO:175), WGAPI (SEQ ID NO:176),

AGDPI (SEQ ID NO:177), WADPI (SEQ ID NO:178), WGDAI (SEQ ID NO:179), WGDPA (SEQ ID NO:180), WDPI (SEQ ID NO:181), WGDI (SEQ ID NO:182), WGDP (SEQ ID NO:183) or FGDPI (SEQ ID NO:184) substituted for the WGDPI (SEQ ID NO:170) sequence at amino acids 16-20 of FGF19.

49. The use of any of claims 1 to 3 or 6, wherein the peptide sequence has less lipid increasing activity compared to FGF19, or an FGF 19 variant sequence having any of GQV, GDI, WGPI (SEQ ID NO:171), WGDPV (SEQ ID NO:172), WGDI (SEQ ID NO:173), GDPI (SEQ ID NO:174), GPI, WGQPI (SEQ ID NO:175), WGAPI (SEQ ID NO:176), AGDPI (SEQ ID NO:177), WADPI (SEQ ID NO:178), WGDAI (SEQ ID NO:179), WGDPA (SEQ ID NO:180), WDPI (SEQ ID NO:181), WGDI (SEQ ID NO:182), WGDP (SEQ ID NO:183) or FGDPI (SEQ ID NO:184) substituted for the WGDPI (SEQ ID NO:170) sequence at amino acids 16-20 of FGF19.

50. The use of any of claims 1 to 3 or 6, wherein the peptide sequence has less triglyceride, cholesterol, non-HDL or HDL increasing activity compared to FGF19, or an FGF 19 variant sequence having any of GQV, GDI, WGPI (SEQ ID NO:171), WGDPV (SEQ ID NO:172), WGDI (SEQ ID NO:173), GDPI (SEQ ID NO:174), GPI, WGQPI (SEQ ID NO:175), WGAPI (SEQ ID NO:176), AGDPI (SEQ ID NO:177), WADPI (SEQ ID NO:178), WGDAI (SEQ ID NO:179), WGDPA (SEQ ID NO:180), WDPI (SEQ ID NO:181), WGDI (SEQ ID NO:182), WGDP (SEQ ID NO:183) or FGDPI (SEQ ID NO:184) substituted for the WGDPI (SEQ ID NO:170) substituted for the WGDPI sequence at amino acids 16-20 of FGF19.

51. The use of any of claims 1 to 3 or 6, wherein the peptide sequence has less lean mass reducing activity compared to FGF21.

52. The use of any of claims 47 to 51, wherein the HCC formation, glucose lowering activity, lipid increasing activity, or lean mass reducing activity is ascertained in a *db/db* mouse.

53. The use of any of claims 1 to 3 or 6, wherein the peptide sequence binds to fibroblast growth factor receptor 4 (FGFR4) or activates FGFR4, or does not detectably bind to FGFR4 or activate FGFR4.

54. The use of any of claims 1 to 3 or 6, wherein the peptide sequence binds to FGFR4 with an affinity less than, comparable to or greater than FGF19 binding affinity for FGFR4.

55. The use of any of claims 1 to 3 or 6, wherein the peptide sequence activates FGFR4 to an extent or amount less than, comparable to or greater than FGF19 activates FGFR4.

56. The use of any of claims 1 to 3 or 6, wherein the peptide sequence has 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions, deletions or insertions.

57. The use of claim 56, wherein the amino acid deletions are at the N- or C-terminus, or internal.

58. The use of claim 56, wherein the amino acid substitution, or deletion is at any of amino acid positions 8-20 of FGF19 (AGPHVHYGWGDPI) (SEQ ID NO:187).

59. The use of any of claims 1 to 3 or 6, wherein the peptide sequence comprises one or more L-amino acids, D-amino acids, non-naturally occurring amino acids, or amino acid mimetic, derivative or analogue.

60. The use of any of claims 1 to 3 or 6, wherein the chimeric peptide sequence or peptide sequence comprises a pharmaceutical composition.

61. The use of any of claims 1 to 3 or 6, wherein the bile acid associated or related disorder comprises a metabolic syndrome; a lipid or glucose disorder; cholesterol or triglyceride metabolism; type 2 diabetes; cholestasis, intrahepatic cholestasis, primary biliary cirrhosis (PBC), primary familial intrahepatic cholestasis (PFIC), progressive PFIC, primary sclerosing choangitis (PSC), pregnancy intrahepatic cholestasis (PIC), neonatal cholestasis, and drug induced cholestasis, diseases of extrahepatic cholestasis, bile cut compression from tumor, bile duct blockade by gall stones, bile acid malabsorption and other disorders involving the distal small intestine, ileal resection, inflammatory bowel diseases, Crohn’s disease, ulcerative colitis, idiopathic disorders impairing absorption of bile acids, diarrhea, bile acid diarrhea (BAD), GI symptoms, GI cancers, liver cancers, biliary cancers, colon cancer, hepatocellular cancer, bile acid synthesis abnormalities, non-alcoholic steatohepatitis (NASH), cirrhosis, portal hypertension, or any combination thereof.

62. The use of any of claims 1 to 3 or 6, wherein the bile acid associated or related disorder comprises a lipid- or glucose-related disorder.

63. The use of any of claims 1 to 3 or 6, wherein the bile acid associated or related disorder comprises bile acid malabsorption or diarrhea.

64. The use of any of claims 1 to 3 or 6, wherein the bile acid associated or related disorder comprises cholestasis or primary biliary cirrhosis.

65. The use of any of claims 1 to 3 or 6, wherein the bile acid associated or related disorder comprises primary sclerosing cholangitis.

66. The use of any of claims 1 to 3 or 6, wherein the bile acid associated or related disorder comprises PFIC or progressive PFIC.

67. A method for identifying a peptide sequence having that modulates bile acid homeostasis without having substantial HCC activity, comprising:

a) providing a candidate peptide sequence;

b) administering the candidate peptide sequence to a test animal;

c) measuring bile acid levels of the animal after administration of the candidate peptide sequence, to determine if the candidate peptide sequence modulates bile acid homeostasis; and

d) analyzing the candidate peptide sequence for induction of HCC in the animal, or expression of a marker correlating with HCC activity, wherein a candidate peptide that modulates bile acid homeostasis but does not have substantial HCC activity thereby identifies the candidate peptide sequence as a peptide sequence having that modulates bile acid homeostasis without substantial HCC activity.

68. The method of claim 67, wherein the test animal is a *db/db* mouse.

69. The method of claim 67, further comprising assessing a hepatic tissue sample obtained from the test animal to determine whether the candidate peptide sequence exhibits evidence of inducing HCC.

70. The method of claim 67, wherein the marker correlating with HCC activity comprises lipid profile, and wherein less lipid increasing activity compared to FGF19 indicates the peptide does not have substantial HCC activity.

71. The method of claim 67, wherein the marker correlating with HCC activity comprises aldo-keto reductase gene expression, and wherein up-regulating or increasing aldo-keto reductase gene expression compared to FGF19 indicates that the peptide does not have substantial HCC activity.

72. The method of claim 67, wherein the marker indicative of HCC activity comprises Slc1a2 gene expression, and wherein down-regulating or decreasing Slc1a2 gene expression compared to FGF21 indicates that the peptide does not have substantial HCC activity.

CLAIMS

1. Use of a peptide in the manufacture of a medicament for reducing bile acid synthesis in a subject, wherein said peptide comprises:

a) an N-terminal region comprising at least seven amino acid residues, the N-terminal region having a first amino acid position and a last amino acid position, wherein the N-terminal region comprises DSSPL (SEQ ID NO:121); and

b) a C-terminal region having a first amino acid position and a last amino acid position, wherein the C-terminal region comprises

(i) a first C-terminal region sequence comprising WGDPIRLRHLYTSG (amino acids 16 to 29 of SEQ ID NO:99 [FGF19]), wherein the W residue corresponds to the first amino acid position of the C-terminal region; and

(ii) a second C-terminal region sequence comprising PHGLSSCFLRIRADGVVDCARGQSAHSLLEIKAVALRTVAIK GVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNV YRSEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEE PEDLRGHLESDMFSSPLETDSMDPFGLVTGLEAVRSPSFEK (amino acid residues 30 to 194 of SEQ ID NO:99 [FGF19]);

wherein the peptide

(i) binds to fibroblast growth factor receptor 4 (FGFR4) with an affinity equal to or greater than FGF19 binding affinity for FGFR4;

(ii) activates FGFR4 to an extent or amount equal to or greater than FGF19 activates FGFR4;

(iii) has at least one of reduced hepatocellular carcinoma (HCC) formation; greater glucose lowering activity, less lipid increasing activity, less triglyceride activity, less cholesterol activity, less non-HDL activity or less HDL increasing activity, as compared to

FGF19, or as compared to an FGF19 variant sequence having any of GQV, GDI, WGPI, WGDPV, WGDI, GDPI, GPI, WGQPI, WGAPI, AGDPI, WADPI, WGDAI, WGDPA, WDPI, WGDI, WGDP or FGDPI substituted for the WGDPI sequence at amino acids 16-20 of FGF19 (SEQ ID NO:99); and/or

(iv) has less lean mass reducing activity as compared to FGF21.

2. The use of claim 1, wherein the second C-terminal region sequence of the peptide comprises from 1 to 5 amino acid substitutions, deletions or insertions.

3. The use of claim 1, wherein the peptide is less than about 250 amino acids in length.

4. The use of claim 1, wherein the N-terminal region comprises amino acid residues VHYG (SEQ ID NO:101), DASPHVHYG (SEQ ID NO:102), or DSSPLVHYG (SEQ ID NO:103).

5. The use of claim 4, wherein the G corresponds to the last position of the N-terminal region.

6. The use of claim 1, wherein the N-terminal region comprises amino acid residues DSSPLLQ (SEQ ID NO:104), and wherein the Q residue is the last amino acid position of the N-terminal region.

7. The use of claim 5, wherein the N-terminal region further comprises:

RHPIP (SEQ ID NO:106), wherein R is the first amino acid position of the N-terminal region;

HPIP (SEQ ID NO:107), wherein H is the first amino acid position of the N-terminal region;

RPLAF (SEQ ID NO:108), wherein R is the first amino acid position of the N-terminal region;

PLAF (SEQ ID NO:109), wherein P is the first amino acid position of the N-terminal region; or

R, wherein R is the first amino acid position of the N-terminal region.

8. The use of claim 6, wherein the N-terminal region further comprises:

RHPIP (SEQ ID NO:106), wherein R is the first amino acid position of the N-terminal region;

HPIP (SEQ ID NO:107), wherein H is the first amino acid position of the N-terminal region;

RPLAF (SEQ ID NO:108), wherein R is the first amino acid position of the N-terminal region;

PLAF (SEQ ID NO:109), wherein P is the first amino acid position of the N-terminal region; or

R, wherein R is the first amino acid position of the N-terminal region.

9. The use of claim 1, wherein the N-terminal region comprises amino acid residues DSSPLLQFGGQV (SEQ ID NO:105), and wherein the V residue corresponds to the last position of the N-terminal region.

10. The use of claim 1, wherein amino acid residues HPIP (SEQ ID NO:107) are the first 4 amino acid residues of the N-terminal region.

11. The use of claim 1, wherein

the first position of the N-terminal region is a R or M residue;

the first and second positions of the N-terminal region is a MR, RM, RD, DS, MD or MS sequence;

the first through third positions of the N-terminal region is a MDS, RDS, MSD, MSS, or DSS sequence;

the first through fourth positions of the N-terminal region is a RDSS (SEQ ID NO:115) or MDSS (SEQ ID NO:116) sequence;

the first through fifth positions of the N-terminal region is an MRDSS (SEQ ID NO:117) sequence;

the first through sixth positions of the N-terminal region is an MDSSPL (SEQ ID NO:119) sequence; or

the first through seventh positions of the N-terminal region is an MSDSSPL (SEQ ID NO:120) sequence.

12. The use of claim 1, wherein the peptide comprises an N-terminus region and a first C-terminal region having an amino acid sequence comprising or consisting of any of:

RPLAFSDASPHVHYGWGDPIRLRHLYTSG (amino acids 1-29 of SEQ ID NO:1);

PLAFSDASPHVHYGWGDPIRLRHLYTSG (amino acids 2-29 of SEQ ID NO:1);

RPLAFSDSSPLVHYGWGDPIRLRHLYTSG (amino acids 1-29 of SEQ ID NO:2);

PLAFSDSSPLVHYGWGDPIRLRHLYTSG (amino acids 2-29 of SEQ ID NO:2);

RHPIPDSSPLLQWGDPIRLRHLYTSG (amino acids 1-26 of SEQ ID NO:8);

RHPIPDSSPLLQFGWGDPIRLRHLYTSG (amino acids 1-28 of SEQ ID NO:9);

RPLAFSDSSPLVHWGDPIRLRHLYTSG (amino acids 1-27 of SEQ ID NO:26);

PLAFSDSSPLVHWGDPIRLRHLYTSG (amino acids 2-27 of SEQ ID NO:26);

HPIPDSSPLLQWGDPIRLRHLYTSG (amino acids 1-25 of SEQ ID NO:47);

RDSSPLLQWGDPIRLRHLYTSG (amino acids 1-22 of SEQ ID NO:52);

DSSPLLQWGDPIRLRHLYTSG (amino acids 2-22 of SEQ ID NO:52);

MDSSPLVHYGWGDPIRLRHLYTSG (amino acids 1-24 of SEQ ID NO:53);

RDSSPLVHYGWGDPIRLRHLYTSG (amino acids 1-24 of SEQ ID NO:69);

DSSPLVHYGWGDPIRLRHLYTSG (amino acids 2-24 of SEQ ID NO:69);

MRDSSPLVHYGWGDPIRLRHLYTSG (amino acids 1-25 of SEQ ID NO:70);

DSSPLVHYGWGDPIRLRHLYTSG (amino acids 1-23 of SEQ ID NO:141);

or

HPIPDSSPLLQFGWGDPIRLRHLYTSG (amino acids 1-27 of SEQ ID NO:163).

13. The use of claim 1, wherein the N-terminal region first amino acid position is a methionine (M), arginine (R), serine (S), histidine (H), proline (P), leucine (L) or aspartic acid (D) residue.

14. The use of claim 1, wherein the N-terminal region does not have a methionine (M) or arginine (R) residue at the first amino acid position of the N-terminal region.

15. The use of claim 1, wherein the N-terminal region comprises any one of the following amino acid sequences: MDSSPL (SEQ ID NO:119), MSDSSPL (SEQ ID NO:120), or SDSSPL (SEQ ID NO:112).

16. The use of claim 1, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:26, SEQ ID NO:47, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:69, SEQ ID NO:70; SEQ ID NO:141 or SEQ ID NO:163.

17. The use of claim 16, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NOs:1, 2, 8, 9, 26, 52 or 69, wherein the arginine (R) residue at the first amino acid position of the N-terminal region of the sequence is deleted.

18. The use of claim 16, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NO:1.

19. The use of claim 16, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NO:2.

20. The use of claim 16, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NO:8.

21. The use of claim 16, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NO:9.

22. The use of claim 16, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NO:26.

23. The use of claim 16, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NO:47.

24. The use of claim 16, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NO:52.

25. The use of claim 16, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NO:53.

26. The use of claim 16, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NO:141.

27. The use of claim 16, wherein the peptide has an amino acid sequence comprising or consisting of SEQ ID NO:163.

28. The use of claim 1, wherein the second C-terminal region sequence comprises at least one amino acid substitution to the EIRPD sequence of SEQ ID NO:99.

29. The use of claim 28, wherein the at least one amino acid substitution is to the IRP sequence of the EIRPD sequence of SEQ ID NO:99.

30. The use of claim 28, wherein the at least one amino acid substitution is to the RP sequence of the EIRPD sequence of SEQ ID NO:99.

31. The use of claim 30, wherein the RP sequence is substituted with a LE sequence.

32. The use of claim any one of claims 1 to 31, wherein said peptide is fused with an immunoglobulin Fc region.

33. The use of any one of claims 1 to 32, wherein the peptide has at least one of reduced HCC formation; greater glucose lowering activity, or less lipid increasing activity as compared to FGF19, or as compared to an FGF19 variant having any of GQV, GDI, WGPI, WGDPV, WGDI, GDPI, GPI, WGQPI, WGAPI, AGDPI, WADPI, WGDAI,

WGDPA, WDPI, WGDI, WGDP or FGDPI substituted for the WGDPI sequence at amino acids 16-20 of FGF19 (SEQ ID NO:99).

34. The use of claim 33, wherein the HCC formation, glucose lowering activity, or lipid increasing activity is ascertained in a *db/db* mouse.

35. The use of claim 33, wherein the peptide has less lean mass reducing activity as compared to the lean mass reducing activity of FGF21.

36. The use of claim 35, wherein the lean mass reducing activity is ascertained in a *db/db* mouse.

37. The use of any one of claims 1 to 36, wherein the peptide is formulated as a pharmaceutical composition further comprising a pharmaceutically acceptable carrier.

38. The use of any one of claims 1 to 37, wherein the medicament is prepared for administration to said subject in combination with a supplemental therapy.

39. The use of any one of claims 1 to 38, wherein the medicament modulates bile acid homeostasis in the subject.

40. The use of any one of claims 1 to 38, wherein the medicament reduces CYP7a1 level in the subject.

41. The use of any one of claims 1 to 38, wherein the medicament is for treating a bile-acid related or associated disorder in the subject.

42. The use of any one of claims 1 to 41, wherein the subject has PBC.

43. The use of any one of claims 1 to 41, wherein the subject has cholestasis.

44. The use of any one of claims 1 to 41, wherein the subject has primary sclerosing cholangitis.

45. The use of any one of claims 1 to 41, wherein the subject has BAD.

46. The use of any one of claims 1 to 41, wherein the subject has PIC.

47. The use of any one of claims 1 to 41, wherein the subject has an error of bile acid synthesis.

48. The use of any one of claims 1 to 41, wherein the subject has bile acid malabsorption.

49. The use of any one of claims 1 to 41, wherein the subject has NASH.

50. Use of a peptide in the manufacture of a medicament for reducing bile acid synthesis in a subject, wherein said peptide has an amino acid sequence comprising or consisting of MRDSSPLVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLL EIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVY RSEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFS SPLETDSMDPFGLVTGLEAVRSPSFEK (SEQ ID NO:70).

51. The use of claim 50, wherein the peptide has an amino acid sequence comprising SEQ ID NO:70.

52. The use of claim 50, wherein the peptide has an amino acid sequence consisting of SEQ ID NO:70.

53. The use of claim 50, wherein the amino acid sequence comprises at least one amino acid substitution to the EIRPD sequence of SEQ ID NO:70.

54. The use of claim 53, wherein the at least one amino acid substitution is to the IRP sequence of the EIRPD sequence of SEQ ID NO:70.

55. The use of claim 53, wherein the at least one amino acid substitution is to the RP sequence of the EIRPD sequence of SEQ ID NO:70.

56. The use of claim 55, wherein the RP sequence is substituted with a LE sequence.

57. The use of any one of claims 50 to 56, wherein said peptide is fused with an immunoglobulin Fc region.

58. The use of any one of claims 50 to 57, wherein the peptide is formulated as a pharmaceutical composition further comprising a pharmaceutically acceptable carrier.

59. The use of any one of claims 50 to 58, wherein the medicament is prepared for administration to said subject in combination with a supplemental therapy.

60. The use of any one of claims 50 to 59, wherein the medicament modulates bile acid homeostasis in the subject.

61. The use of any one of claims 50 to 59, wherein the medicament reduces CYP7a1 level in the subject.

62. The use of any one of claims 50 to 59, wherein the medicament is for treating a bile-acid related or associated disorder in the subject.

63. The use of any one of claims 50 to 62, wherein the subject has PBC.

64. The use of any one of claims 50 to 62, wherein the subject has cholestasis.

65. The use of any one of claims 50 to 62, wherein the subject has primary sclerosing cholangitis.

66. The use of any one of claims 50 to 62, wherein the subject has BAD.

67. The use of any one of claims 50 to 62, wherein the subject has PIC.

68. The use of any one of claims 50 to 62, wherein the subject has an error of bile acid synthesis.

69. The use of any one of claims 50 to 62, wherein the subject has bile acid malabsorption.

70. The use of any one of claims 50 to 62, wherein the subject has NASH.

71. Use of a peptide in the manufacture of a medicament for reducing bile acid synthesis in a subject, wherein said peptide has an amino acid sequence comprising or consisting of RDSSPLVHYGWGDPIRLRHLYTSGPHGLSSCFLRIRADGVVDCARGQSAHSLLEI KAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEEEIRPDGYNVYR SEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESDMFSS PLETDSMDPFGLVTGLEAVRSPSFEK (SEQ ID NO:69).

72. The use of claim 71, wherein the peptide has an amino acid sequence comprising SEQ ID NO:69.

73. The use of claim 71, wherein the peptide has an amino acid sequence consisting of SEQ ID NO:69.

74. The use of claim 71, wherein the amino acid sequence comprises at least one amino acid substitution to the EIRPD sequence of SEQ ID NO:69.

75. The use of claim 74, wherein the at least one amino acid substitution is to the IRP sequence of the EIRPD sequence of SEQ ID NO:69.

76. The use of claim 74, wherein the at least one amino acid substitution is to the RP sequence of the EIRPD sequence of SEQ ID NO:69.

77. The use of claim 76, wherein the RP sequence is substituted with a LE sequence.

78. The use of any one of claims 71 to 77, wherein said peptide is fused with an immunoglobulin Fc region.

79. The use of any one of claims 71 to 78, wherein the peptide is formulated as a pharmaceutical composition further comprising a pharmaceutically acceptable carrier.

80. The use of any one of claims 71 to 79, wherein the medicament is prepared for administration to said subject in combination with a supplemental therapy.

81. The use of any one of claims 71 to 80, wherein the medicament modulates bile acid homeostasis in the subject.

82. The use of any one of claims 71 to 80, wherein the medicament reduces CYP7a1 level in the subject.

83. The use of any one of claims 71 to 80, wherein the medicament is for treating a bile-acid related or associated disorder in the subject.

84. The use of any one of claims 71 to 83, wherein the subject has PBC.

85. The use of any one of claims 71 to 83, wherein the subject has cholestasis.

86. The use of any one of claims 71 to 83, wherein the subject has primary sclerosing cholangitis.

87. The use of any one of claims 71 to 83, wherein the subject has BAD.

88. The use of any one of claims 71 to 83, wherein the subject has PIC.

89. The use of any one of claims 71 to 83, wherein the subject has an error of bile acid synthesis.

90. The use of any one of claims 71 to 83, wherein the subject has bile acid malabsorption.

91. The use of any one of claims 71 to 83, wherein the subject has NASH.