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What is Claimed:

1. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a human G protein-coupled receptor 156 (GPR156) protein, wherein the protein comprises an aspartic acid at a position corresponding to position 533 according to SEQ ID NO:4, or the complement of the nucleic acid sequence.
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2. The isolated nucleic acid molecule according to claim 1, wherein the nucleic acid molecule comprises DNA.
- 10 3. The isolated nucleic acid molecule according to claim 2, wherein the nucleic acid molecule is cDNA.
4. The isolated nucleic acid molecule according to claim 1, wherein the nucleic acid molecule comprises RNA.
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5. The isolated nucleic acid molecule according to any one of claims 1 to 4, wherein the nucleic acid sequence comprises DNA and the aspartic acid is encoded by the codon GAT or GAC, or wherein the nucleic acid sequence comprises RNA and the aspartic acid is encoded by the codon GAU or GAC.
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6. The isolated nucleic acid molecule according to any one of claims 1 to 5, wherein the aspartic acid is encoded by the codon GAT.
7. The isolated nucleic acid molecule according to any one of claims 1 to 6, wherein the
25 GPR156 protein comprises the amino acid sequence of SEQ ID NO:4, or an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:4 and comprises an aspartic acid at the position corresponding to position 533 according to SEQ ID NO:4.
8. A vector comprising the isolated nucleic acid molecule according to any one of claims 1
30 to 7.
9. The vector according to claim 8, wherein the vector is a plasmid.

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10. The vector according to claim 8, wherein the vector is a virus.

11. A host cell comprising the isolated nucleic acid molecule according to any one of claims 1 to 7.

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12. A host cell comprising the vector according to any one of claims 8 to 10.

13. The host cell according to claim 11 or claim 12, wherein the nucleic acid sequence is operably linked to a promoter active in the host cell.

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14. The host cell according to claim 13, wherein the promoter is an exogenous promoter.

15. The host cell according to claim 13 or claim 14, wherein the promoter is an inducible promoter.

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16. The host cell according to any one of claims 12 to 15, wherein the host cell is a mammalian cell.

17. A cDNA comprising a nucleic acid sequence encoding at least a portion of the human
20 GPR156 protein, wherein the portion comprises an aspartic acid at a position corresponding to position 533 according to SEQ ID NO:4.

18. The cDNA according to claim 17, wherein the cDNA encodes a full length human GPR156 protein comprising an aspartic acid at the position corresponding to position 533
25 according to SEQ ID NO:4.

19. The cDNA according to claim 17 or claim 18, wherein the aspartic acid is encoded by the codon GAT.

30 20. The cDNA according to any one of claims 17 to 20, wherein the cDNA comprises the nucleic acid sequence of SEQ ID NO:16, or a nucleic acid sequence having at least 90% sequence

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identity to SEQ ID NO:16, wherein the cDNA encodes a GPR156 protein which comprises aspartic acid at the position corresponding to position 533 according to SEQ ID NO:4.

21. The cDNA according to claim 17 or claim 18, wherein the aspartic acid is encoded by
5 the codon GAC.
22. The cDNA according to claim 17, 18 or 21, wherein the cDNA comprises the nucleic acid sequence of SEQ ID NO:17, or a nucleic acid sequence having at least 90% sequence identity to SEQ ID NO:17, wherein the cDNA encodes a GPR156 protein which comprises
10 aspartic acid at the position corresponding to position 533 according to SEQ ID NO:4.
23. A vector comprising the cDNA according to any one of claims 17 to 22.
24. The vector according to claim 23, wherein the vector is a plasmid.
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25. The vector according to claim 23, wherein the vector is a virus.
26. A host cell comprising the cDNA according to any one of claims 17 to 22.
- 20 27. A host cell comprising the vector according to any one of claims 23 to 25.
28. The host cell according to claim 26 or claim 27, wherein the cDNA is operably linked to a promoter active in the host cell.
- 25 29. The host cell according to claim 28, wherein the promoter is an exogenous promoter.
30. The host cell according to claim 28 or claim 29, wherein the promoter is an inducible promoter.
- 30 31. The host cell according to any one of claims 26 to 30, wherein the host cell is a mammalian cell.

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32. An isolated or recombinant polypeptide comprising at least a portion of the human G protein-coupled receptor 156 (GPR156) protein, wherein the portion comprises an aspartic acid at a position corresponding to position 533 according to SEQ ID NO:4.
- 5 33. The isolated or recombinant polypeptide according to claim 32, wherein the polypeptide comprises a full-length GPR156 protein comprising an aspartic acid at the position corresponding to position 533 according to SEQ ID NO:4.
34. The isolated or recombinant polypeptide according to claim 32 or claim 33, wherein
10 the polypeptide comprises the amino acid sequence of SEQ ID NO:4, or an amino acid sequence having at least 90% sequence identity to SEQ ID NO:4, wherein the polypeptide comprises aspartic acid at the position corresponding to position 533 according to SEQ ID NO:4.
35. The isolated or recombinant polypeptide according to any one of claims 32 to 34,
15 wherein the polypeptide is fused to a heterologous polypeptide.
36. The isolated or recombinant polypeptide according to claim 35, wherein the heterologous polypeptide comprises a peptide purification tag, a fluorescent protein, or both a peptide purification tag and a fluorescent protein.
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37. The isolated or recombinant polypeptide according to any one of claims 32 to 36, wherein the polypeptide is linked to a detectable label.
38. The isolated or recombinant polypeptide according to claim 37, wherein the
25 detectable label is a fluorescent label or a radiolabel.
39. A composition comprising the isolated or recombinant polypeptide according to any one of claims 33 to 38 and a carrier.
- 30 40. A probe or primer comprising a nucleic acid sequence comprising at least about 15 nucleotides, which specifically hybridizes to a nucleic acid sequence encoding a human G protein-coupled receptor 156 (GPR156) protein comprising an aspartic acid at a position

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corresponding to position at 533 according to SEQ ID NO:4, or which specifically hybridizes to the complement of the nucleic acid sequence encoding the human GPR156 protein.

41. The probe or primer according to claim 40, wherein the probe or primer comprises
5 DNA.
42. The probe or primer according to claim 40, wherein the probe or primer comprises RNA.
- 10 43. The probe or primer according to any one of claims 40 to 42, wherein the aspartic acid is encoded by the codon GAT.
44. The probe or primer according to any one of claims 40 to 42, wherein the aspartic acid is encoded by the codon GAC.
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45. The probe or primer according to any one of claims 40 to 44, wherein the probe or primer specifically hybridizes to the nucleic acid sequence encoding the human GPR156 protein, or its complement, under stringent conditions.
- 20 46. The probe or primer according to any one of claims 40 to 45, wherein the probe or primer comprises a label.
47. The probe or primer according to claim 46, wherein the label is a fluorescent label, a radiolabel, or biotin.
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48. A support comprising a substrate to which a probe according to any one of claims 40 to 47 is attached.
49. The support according to claim 48, wherein the support is a microarray.
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50. An allele-specific probe or primer comprising a nucleic acid sequence which is complementary to a nucleic acid sequence encoding a GPR156 protein, wherein the allele-

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specific probe or primer comprises a nucleic acid sequence which is complementary to the nucleic acid codon encoding an aspartic acid at a position corresponding to position 533 according to SEQ ID NO:4.

5 51. The allele-specific primer according to claim 50, wherein the aspartic acid is encoded by the codon GAT.

52. The allele-specific primer according to claim 50, wherein the aspartic acid is encoded by the codon GAC.

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53. A method for identifying a human subject having unipolar depression or a risk for developing unipolar depression, wherein the method comprises determining in a sample obtained from the subject the presence or absence of

(i) an E533D variation within the GPR156 protein; and/or

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(ii) a nucleic acid molecule encoding an E533D variation within the GPR156 protein;

wherein the presence of said E533D variation within the GPR156 protein and/or said nucleic acid molecule encoding said E533D variation indicates that the subject has unipolar depression or a risk for developing unipolar depression.

20 54. The method according to claim 53, wherein the presence of one or more symptoms of unipolar depression indicates that the subject has unipolar depression.

55. The method according to claim 53 or claim 54, wherein the method is an *in vitro* method.

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56. The method according to any one of claims 53 to 55, wherein the determining step comprises sequencing at least a portion of the nucleic acid molecule that encodes a GPR156 protein, wherein the sequenced nucleic acid molecule encodes an amino acid sequence which comprises the position corresponding to position 533 according to SEQ ID NO:4.

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57. The method according to any one of claims 53 to 56, wherein the determining step comprises sequencing the nucleic acid molecule encoding the entire GPR156 protein.

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58. The method according to any one of claims 53 to 55, wherein the determining step comprises:

amplifying at least a portion of the nucleic acid molecule that encodes a GPR156 protein, wherein the amplified nucleic acid molecule encodes an amino acid sequence which

5 comprises the position corresponding to position 533 according to SEQ ID NO:4;

labeling the nucleic acid molecule with a detectable label;

contacting the labeled nucleic acid with a support comprising a probe, wherein the probe comprises a nucleic acid sequence which hybridizes under stringent conditions to a nucleic acid sequence encoding aspartic acid at the position corresponding to position 533

10 according to SEQ ID NO:4; and

detecting the detectable label.

59. The method according to claim 58, wherein the nucleic acid molecule is mRNA and the determining step further comprises reverse-transcribing the mRNA into a cDNA prior to the

15 amplifying step.

60. The method according to any one of claims 53 to 55, wherein the determining step comprises:

contacting the nucleic acid molecule with a probe comprising a detectable label,

20 wherein the probe comprises a nucleic acid sequence which hybridizes under stringent conditions to a nucleic acid sequence encoding an amino acid sequence which comprises aspartic acid at the position corresponding to position at 533 according to SEQ ID NO:4, and

detecting the detectable label.

25 61. The method according to claim 60, wherein the nucleic acid molecule is present within a cell obtained from the human subject.

62. The method according to any one of claims 53 to 61, wherein the E533D variation within the GPR156 protein is encoded by the nucleic acid sequence GAT.

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63. The method according to any one of claims 53 to 61, wherein the E533D variation within the GPR156 protein is encoded by the nucleic acid sequence GAC.

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64. A method for diagnosing unipolar depression or detecting a risk of unipolar depression in a human subject, comprising:

detecting an alteration in a nucleic acid molecule encoding a GPR156 protein obtained from the human subject, wherein the alteration encodes an aspartic acid at the position

5 corresponding to position 533 in the GPR156 protein according to SEQ ID NO:4; and

diagnosing the human subject with unipolar depression if the subject has one or more symptoms of depression, or diagnosing the human subject as at risk for unipolar depression if the subject does not have one or more symptoms of depression.

10 65. The method according to claim 64, wherein the detecting step comprises sequencing at least a portion of the nucleic acid molecule that encodes a GPR156 protein, wherein the sequenced nucleic acid molecule encodes an amino acid sequence which comprises the position corresponding to position 533 according to SEQ ID NO:4.

15 66. The method according to claim 64 or claim 65, wherein the detecting step comprises sequencing the entire nucleic acid molecule.

67. The method according to claim 64, wherein the detecting step comprises:

20 amplifying at least a portion of the nucleic acid molecule that encodes a GPR156 protein, wherein the amplified nucleic acid molecule encodes an amino acid sequence which comprises the position corresponding to position 533 according to SEQ ID NO:4;

labeling the nucleic acid molecule with a detectable label;

25 contacting the labeled nucleic acid with a support comprising a probe, wherein the probe comprises a nucleic acid sequence which hybridizes under stringent conditions to a nucleic acid sequence encoding aspartic acid at the position corresponding to position 533 according to SEQ ID NO:4; and

detecting the detectable label.

30 68. The method according to claim 67, wherein the nucleic acid molecule is mRNA and the method further comprises reverse-transcribing the mRNA into a cDNA prior to the amplifying step.

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69. The method according to claim 64, wherein the detecting step comprises:
contacting the nucleic acid molecule with a probe comprising a detectable label,
wherein the probe comprises a nucleic acid sequence which hybridizes under stringent
conditions to a nucleic acid sequence encoding an amino acid sequence which comprises
5 aspartic acid at the position corresponding to position at 533 according to SEQ ID NO:4, and
detecting the detectable label.
70. The method according to claim 69, wherein the nucleic acid molecule is present within
a cell obtained from the human subject.
- 10 71. The method according to any one of claims 64 to 70, wherein the alteration changes
the sequence of the codon encoding the position corresponding to position 533 according to
SEQ ID NO:4 to GAT.
- 15 72. The method according to any one of claims 64 to 70, wherein the alteration changes
the sequence of the codon encoding the position corresponding to position 533 according to
SEQ ID NO:4 to GAC.
- 20 73. The method according to any one of claims 64 to 72, wherein the method further
comprises treating the subject with an antidepressant when the alteration is detected in the
subject and the subject is diagnosed as having unipolar depression.
- 25 74. The method according to claim 73, wherein the antidepressant is a selective serotonin
reuptake inhibitor, a serotonin-norepinephrine reuptake inhibitor, or a norepinephrine
reuptake inhibitor.
75. An antidepressant for use in the treatment of unipolar depression in a human subject
carrying the E533D variation within the GPR156 protein.
- 30 76. The antidepressant for the use according to claim 75, wherein the human subject has
been tested positive for the E533D variation within the GPR156 protein and/or for a nucleic
acid molecule encoding the E533D variation within the GPR156 protein.

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77. The antidepressant for the use according to claim 75 or claim 76, wherein the treatment comprises the step of determining whether or not the human subject has a GPR156 protein with the E533D variation and/or a nucleic acid molecule encoding a GPR156 protein with the E533D variation.

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78. The antidepressant for the use according to any one of claims 75 to 77, wherein the human subject has been identified as having unipolar depression or as having a risk for developing unipolar depression by using the method as defined in any one of claims 53 to 74.

10 79. The antidepressant for the use according to any one of claims 75 to 78, wherein the E533D variation within the GPR156 protein is encoded by the codon GAT.

80. The antidepressant for the use according to any one of claims 75 to 78, wherein the E533D variation within the GPR156 protein is encoded by the codon GAC.

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81. The antidepressant for the use according to any one of claims 75 to 80, wherein the antidepressant is a selective serotonin reuptake inhibitor, a serotonin-norepinephrine reuptake inhibitor, or a norepinephrine reuptake inhibitor.

20 82. The antidepressant for the use according to any one of claims 75 to 80, wherein the antidepressant is lithium.

83. The method according to any one of claims 53 to 63 or the antidepressant for the use according to any one of claims 76 to 82, wherein the E533D variation refers to a variation resulting in an aspartic acid at the position corresponding to position 533 according to SEQ ID NO:4.

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