

What is claimed is:

1. An antibody that specifically binds human glucagon receptor (GCGR; SEQ ID NO:223), which comprises:
 - (a) a heavy chain variable region comprising a heavy chain variable region CDR1 comprising GFTFTNHWLG (SEQ ID NO:1), a heavy chain variable region CDR2 comprising DIYPGGYYINYNEKFKG (SEQ ID NO:2), and a heavy chain variable region CDR3 comprising HTNYGSDY (SEQ ID NO:3); and
 - (b) a light chain variable region comprising a light chain variable region CDR1 comprising RSSQSIVDSYGNTFLE (SEQ ID NO:4), a light chain variable region CDR2 comprising KVSNRLS (SEQ ID NO:5), and a light chain variable region CDR3 comprising FQGSHPVWT (SEQ ID NO:6).
2. The antibody of claim 1, wherein:
 - (a) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:25;
 - (b) the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:26;
 - (c) the heavy chain variable region comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:25;
 - (d) the light chain variable region comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:26;
 - (e) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:25;
 - (f) the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:26;

- (g) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:25 and the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:26;
- (h) the heavy chain variable region comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:25 and the light chain variable region comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:26;
- (i) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:220;
- (j) the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:221;
- (k) the heavy chain variable region comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:220;
- (l) the light chain variable region comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:221;
- (m) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:220 and the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:221; or
- (n) the heavy chain variable region comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:220 and the light chain variable region comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:221.

3. The antibody of claim 1, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:25 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:26.
4. The antibody of claim 1, where the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:220.
5. The antibody of claim 1, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:221.
6. The antibody of any one of claims 1 to 5, which is a monoclonal antibody, a chimeric antibody, a bispecific antibody, a multispecific antibody, an IgG antibody, or an antibody fragment comprising at least one antigen-binding site.
7. The antibody of any one of claims 1 to 3, which is a humanized antibody.
8. An antibody that specifically binds human glucagon receptor (GCGR; SEQ ID NO:223), which comprises: a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO:220 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO:221.
9. The antibody of any one of claims 1 to 8, which comprises an IgG1 heavy chain constant region.
10. The antibody of claim 9, wherein the IgG1 heavy chain constant region is a human IgG1 heavy chain constant region.
11. The antibody of any one of claims 1 to 8, which comprises a kappa light chain constant region.
12. The antibody of claim 11, wherein the kappa light chain constant region is a human kappa light chain constant region.
13. The antibody of any one of claims 1 to 8, which comprises an IgG1 heavy chain constant region and a kappa light chain constant region.

14. The antibody of claim 13, wherein the IgG1 heavy chain constant region is a human IgG1 heavy chain constant region and the kappa light chain constant region is a human kappa light chain constant region.
15. The antibody of any one of claims 1 to 5 and 8, which comprises a heavy chain that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO:234.
16. The antibody of any one of claims 1 to 5 and 8, which comprises a light chain that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO:236.
17. The antibody of any one of claims 1 to 5 and 8, which comprises: (i) a heavy chain that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO:234; and (ii) a light chain that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO:236.
18. The antibody of claim 1, which comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:234.
19. The antibody of claim 1, which comprises a light chain comprising the amino acid sequence set forth in SEQ ID NO:236.
20. An antibody that specifically binds human glucagon receptor (GCGR; SEQ ID NO:223), which comprises: (i) a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:234; and (ii) a light chain comprising the amino acid sequence set forth in SEQ ID NO:236.
21. An antibody that competes with the antibody of any one of claims 1 to 20 for specific binding to GCGR.
22. An antibody that specifically binds human glucagon receptor (GCGR; SEQ ID NO:223), which comprises :
 - (a) a heavy chain variable region comprising a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:27, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:28, and a heavy chain variable region CDR3 comprising the amino acid

- sequence set forth in SEQ ID NO:29, and a light chain variable region comprising a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:30, a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:31, and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:32;
- (b) a heavy chain variable region comprising a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:53, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:54, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:55, and a light chain variable region comprising a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:56, a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:31, and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:32;
- (c) a heavy chain variable region comprising a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:73, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:74, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:75, and a light chain variable region comprising a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:76, a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:77, and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:78;
- (d) a heavy chain variable region comprising a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:99, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:100, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:101, and a light chain variable region comprising a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:102, a light chain variable region CDR2

comprising the amino acid sequence set forth in SEQ ID NO:103, and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:104;

- (e) a heavy chain variable region comprising a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:124, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:125, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:126, and a light chain variable region comprising a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:127, a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:128, and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:6;
- (f) a heavy chain variable region comprising a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:146, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:147, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:148, and a light chain variable region comprising a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:149, a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:128, and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:6;
- (g) a heavy chain variable region comprising a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:166, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:167, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:168, and a light chain variable region comprising a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:169, a light chain variable region CDR2

comprising the amino acid sequence set forth in SEQ ID NO:170, and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:171;

- (h) a heavy chain variable region comprising a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:190, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:191, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:192, and a light chain variable region comprising a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:169, a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:128, and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:193; or
- (i) a heavy chain variable region comprising a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:190, a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:205, and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:206, and a light chain variable region comprising a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO:207, a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO:128, and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO:6.

23. The antibody of claim 22, wherein:

- (a) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:51 and the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:52;

- (b) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:71 and the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:72;
- (c) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:97 and the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:98;
- (d) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:122 and the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:123;
- (e) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:144 and the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:145;
- (f) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:164 and the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:165;
- (g) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:188 and the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:189;

- (h) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:203 and the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:204; or
 - (i) the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:218 and the light chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:219.
24. The antibody of claim 22, wherein:
- (a) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:51 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:52;
 - (b) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:71 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:72;
 - (c) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:97 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:98;
 - (d) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:122 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:123;
 - (e) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:144 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:145;

- (f) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:164 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:165;
 - (g) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:188 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:189;
 - (h) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:203 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:204; or
 - (i) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:218 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:219.
25. An antibody that binds the same epitope on GCGR as the antibody of any one of claims 1 to 20.
26. The antibody of any one of claims 1 to 25, which:
- (a) inhibits GCGR signaling in cells expressing GCGR;
 - (b) inhibits GCGR activity in a cell;
 - (c) inhibits GCGR activity in a cell wherein the GCGR activity is induced by glucagon; and/or
 - (d) inhibits cAMP activity.
27. The antibody of any one of claims 1 to 25, which:
- (i) reduces blood glucose levels;
 - (ii) increases the level of C-peptide; and/or
 - (iii) increases the level of insulin.

28. A pharmaceutical composition comprising the antibody of any one of claims 1 to 27 and a pharmaceutically acceptable carrier.
29. An isolated polynucleotide molecule comprising a polynucleotide encoding the antibody of any one of claims 1 to 27.
30. A vector comprising the polynucleotide molecule of claim 29.
31. A cell comprising the polynucleotide molecule of claim 29.
32. A cell comprising or producing the antibody of any one of claims 1 to 27.
33. A method of making the antibody of any one of claims 1 to 27, comprising: (a) culturing (i) a cell comprising a polynucleotide molecule comprising a polynucleotide encoding the antibody of any one of claims 1 to 8 and 15 to 26, or (ii) a cell comprising or producing the antibody of any one of claims 1 to 8 and 15 to 25, and (b) isolating the antibody.
34. Use of the antibody of any one of claims 1 to 27 for the preparation of a medicament for the treatment of diabetes in a subject.
35. The use of claim 34, wherein the diabetes is Type 1 diabetes or Type 2 diabetes.
36. The use of claim 34 or 35, wherein the medicament is for administration to the subject in combination with at least one additional therapeutic agent to the subject.
37. The use of claim 36, wherein the at least one additional therapeutic agent is a diabetes or hyperglycemia drug.
38. The use of claim 37, wherein the diabetes or hyperglycemia drug is a biguanide, a sulfonylurea, a meglitinide derivative, an alpha-glucosidase inhibitor, a thiazolidinedione (TZD), a glucagon-like peptide-I (GLP-1) agonist, a dipeptidyl peptidase 4 (DPP-4) inhibitor, a selective sodium-glucose transporter-2 (SGLT-2) inhibitor, an insulin or insulin mimetic, an amylinomimetic, a bile acid sequestrant, and/or a dopamine agonist.
39. The use of any one of claims 34 to 38, wherein the subject is a human.

40. Use of the antibody of any one of claims 1 to 27 for the preparation of a medicament for reducing or lowering blood glucose levels in a subject.
41. The use of claim 40, wherein the subject is a human.
42. Use of the antibody of any one of claims 1 to 27 for the preparation of a medicament for increasing the level of C-peptide in the blood of a subject.
43. The use of claim 42, wherein the subject is a human.
44. Use of the antibody of any one of claims 1 to 27 for the preparation of a medicament for increasing the level of insulin in the blood of a subject.
45. The use of claim 44, wherein the subject is a human.
46. Use of the antibody of any one of claims 1 to 27 for the preparation of a medicament for treating hyperglycemia in a subject.
47. The use of claim 46, wherein the subject is a human.
48. Use of the antibody of any one of claims 1 to 27 for the preparation of a medicament for treating a disease, disorder, or condition associated with beta cell dysfunction in a subject.
49. The use of claim 48, wherein the subject is a human.
50. Use of the antibody of any one of claims 1 to 27 for the preparation of a medicament for treating a beta cell defective disease, disorder, or condition in a subject.
51. The use of claim 50, wherein the subject is a human.
52. Use of the antibody of any one of claims 1 to 27 for the preparation of a medicament for improving beta cell function in a subject.
53. The use of claim 52, wherein the subject is a human.