

Claims

1. A method for treating or limiting development of diabetes, comprising transplanting into the eye of a subject with diabetes or at risk of diabetes an amount effective to treat or limit development of diabetes of insulin-producing cells engineered to reduce expression of a $\beta 3$ subunit of Cav (Cav $\beta 3$).
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2. The method of claim 1, wherein the insulin-producing cells are engineered to disrupt each copy of the Cav $\beta 3$ gene.
- 10 3. The method of claim 1 or 2, wherein the insulin-producing cells are engineered to reduce expression of apoCIII.
4. The method of claim 3, wherein the insulin-producing cells are engineered to disrupt each copy of the apoCIII gene.
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5. The method of any one of claims 1-4, wherein the insulin-producing cells are engineered to reduce expression of one or more chemokines, including but not limited to CCL2, CCL3, CCL5, CXCL1, CXCL9, CXCL10, and/or CXCL11, and/or one or more cytokines including but not limited to IL-6 and/or IL-8.
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6. The method of claim 5, wherein the insulin-producing cells are engineered to disrupt each copy of the one or more chemokine genes and/or the one or more cytokine genes.
- 25 7. The method of any one of claims 1-6, wherein the insulin-producing cells are engineered to reduce expression of one or more major histocompatibility complex (MHC) class I proteins.
8. The method of claim 7, wherein the insulin-producing cells are engineered to disrupt
30 each copy of the one or more MHC class I proteins.
9. The method of any one of claims 1-8, wherein the insulin-producing cells are

engineered to increase expression of one or more proteins beneficial to insulin producing cells, including but not limited to GLP1 receptors, insulin receptors, and/or cytokine IL1B.

- 5 10. The method of any one of claims 1-9, wherein the insulin-producing cells comprise isolated pancreatic islets or isolated pancreatic β cells, such as isolated human pancreatic islets or isolated human pancreatic β cells.
11. The method of any one of claims 1-10, wherein the transplantation into the eye
10 involves transplantation into the anterior chamber of the eye.
12. The method of claim 11, wherein the transplantation into the anterior chamber of the eye involves injection through the cornea.
- 15 13. The method of any one of claims 1-12, wherein the subject, such as a human subject, has diabetes and the transplanting comprising transplanting into the eye of a subject with diabetes an amount effective to treat diabetes.
14. The method of claim 14, wherein the subject has type 2 diabetes.
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15. The method of claim 14, wherein the subject has type 1 diabetes.
16. The method of any one of claims 1-12, wherein the subject, such as a human subject, is at risk of diabetes and the transplanting comprising transplanting into the eye of a
25 subject at risk of diabetes an amount effective to limit development of diabetes.
17. The method of claim 16, wherein the subject is at risk of type 2 diabetes.
18. The method of claim 16, wherein the subject is at risk of type 1 diabetes.
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19. The method of any one of claims 1-18, wherein the subject, such as a human subject, overexpresses Cav β 3 compared to a control.

20. A recombinant cell comprising an insulin-producing cell engineered to reduce expression of a $\beta 3$ subunit of Cav (Cav $\beta 3$).
21. The recombinant cell of claim 20, wherein the insulin-producing cell is engineered to
5 disrupt each copy of the Cav $\beta 3$ gene.
22. The recombinant cell of claim 20 or 21, wherein the insulin-producing cell is engineered to reduce expression of apoCIII.
- 10 23. The recombinant cell of claim 22, wherein the insulin-producing cell is engineered to disrupt each copy of the apoCIII gene.
24. The recombinant cell of any one of claims 20-23, wherein the insulin-producing cell is engineered to reduce expression of one or more chemokines, including but not
15 limited to CCL2/3/5, CXCL1/9/10/11, and IL-6/8.
25. The recombinant cell of claim 24, wherein the insulin-producing cell is engineered to disrupt each copy of the one or more chemokine genes.
- 20 26. The recombinant cell of any one of claims 20-25, wherein the insulin-producing cell is engineered to reduce expression of one or more major histocompatibility complex MHC class I proteins.
27. The recombinant cell of claim 26, wherein the insulin-producing cell is engineered to
25 disrupt each copy of the one or more MHC class I proteins.
28. The recombinant cell of any one of claims 20-27, wherein the insulin-producing cells are engineered to increase expression of one or more proteins beneficial to insulin producing cells, including but not limited to GLP1 receptors, insulin receptors,
30 and/or cytokine IL1B.
29. The recombinant cell of any one of claims 20-28, wherein the insulin-producing cells comprise isolated pancreatic islets or isolated pancreatic β cells, such as isolated

human pancreatic islets or isolated human pancreatic β cells.