secreted by kidney cells. Moreover, we have discovered that NBL1 is also not expressed in kidney cells, but is expressed in circulating immune cells. Neutralizing NBL1 with an antagonist, either sBMP2 or anti-NBL1 monoclonal antibodies, prevents toxicity *in vitro*. Finally, we demonstrate that NBL1 is elevated in Type 1 Diabetes and Type 2 Diabetes. Inhibition of NBL1 is therefore a new therapeutic approach for preventing onset and progression of kidney damage caused by circulating NBL1, and in particular, in a patient with type 1 or type 2 diabetes. Inhibition of NBL1 will also be effective in treating non-diabetes glomerular diseases in which damage is mediated by NBL1.

[0005a] In one aspect, the present disclosure refers to a use of an antibody or antigen-binding fragment capable of inhibiting Neuroblastoma suppressor of tumorigenicity 1 (NBL1) activity in the manufacture of a medicament for delaying onset or progression of kidney damage in a subject who has type 1 diabetes or type 2 diabetes, or a non-diabetes glomerular disease in which damage is mediated by NBL1,

wherein the antibody or antigen-binding fragment comprises three heavy chain CDRs and three light chain CDRs having sequences selected from:
SEQ ID NOs: 33, 38, and 43 and SEQ ID NOs: 48, 53, and 58 (antibody H08);
SEQ ID NOs: 183, 188, and 193 and SEQ ID NOs: 198, 203, and 208 (antibody B06);
SED ID NOs: 573, 578, and 583 and SED ID NOs: 588, 593, and 598 (antibody E01),
SEQ ID NOs: 393, 398, and 403 and SEQ ID NOs: 408, 413, and 418 (antibody E04);
SEQ ID NOs: 93, 98, and 103 and SEQ ID NOs: 108, 113, and 118 (antibody A12); and
SEQ ID NOs: 543, 548, and 553 and SEQ ID NOs: 558, 563, and 568 (antibody D06).

[0006] Accordingly, in a first aspect, methods are provided for delaying onset or progression of kidney damage in a subject who has type 1 diabetes or type 2 diabetes or a glomerular disease. The method comprises administering to the subject an effective amount of an agent capable of inhibiting NBL1 activity, in particular, capable of inhibiting NBL1 toxicity on human podocytes. In some embodiments, the method prevents onset of or slows decline in kidney function.

[0007] In a further aspect, methods are provided for slowing decline in kidney function in a subject who has type 1 or type 2 diabetes or a glomerular disease. The method comprises administering to the subject an effective amount of an agent capable of inhibiting NBL1 activity, in particular, capable of inhibiting NBL1 toxicity on human podocytes.

[0008] In a yet further aspect, methods are provided for treating diabetic kidney disease (DKD) in a subject who has type 1 or type 2 diabetes or a glomerular disease. The method comprises administering to the subject an effective amount of an agent capable of inhibiting NBL1 activity, in particular, capable of inhibiting NBL1 toxicity on human podocytes.

[0009] In some embodiments of these methods, the agent is capable of binding to NBL1. In some embodiments the agent is capable of binding to human NBL1.

[0010] In some embodiments the agent is an antibody, or an antigen binding fragment of an antibody, that is capable of binding to human NBL1.

[0011] In some embodiments the antibody or antigen-binding fragment comprises three heavy chain CDRs and three light chain CDRs

having sequences selected from:

WHAT IS CLAIMED IS:

1. Use of an antibody or antigen-binding fragment capable of inhibiting Neuroblastoma suppressor of tumorigenicity 1 (NBL1) activity in the manufacture of a medicament for delaying onset or progression of kidney damage in a subject who has type 1 diabetes or type 2 diabetes, or a non-diabetes glomerular disease in which damage is mediated by NBL1,

wherein the antibody or antigen-binding fragment comprises three heavy chain CDRs and three light chain CDRs having sequences selected from:
SEQ ID NOs: 33, 38, and 43 and SEQ ID NOs: 48, 53, and 58 (antibody H08);
SEQ ID NOs: 183, 188, and 193 and SEQ ID NOs: 198, 203, and 208 (antibody B06);
SED ID NOs: 573, 578, and 583 and SED ID NOs: 588, 593, and 598 (antibody E01),
SEQ ID NOs: 393, 398, and 403 and SEQ ID NOs: 408, 413, and 418 (antibody E04);
SEQ ID NOs: 93, 98, and 103 and SEQ ID NOs: 108, 113, and 118 (antibody A12); and
SEQ ID NOs: 543, 548, and 553 and SEQ ID NOs: 558, 563, and 568 (antibody D06).

2. The use claim 1, wherein the antibody framework regions are human antibody framework regions.

3. The use of claim 1 or 2, wherein the antibody is a full length bivalent monospecific monoclonal antibody.

4. The use of claim 3, wherein the antibody comprises human IgG1, IgG2, or IgG4 heavy chain constant regions.

5. The use of claim 4, wherein the antibody comprises a human IgG1 constant region.

6. The use of any one of claims 3-5, wherein the antibody Fc region has engineered mutations that reduce antibody binding to at least one type of Fc receptor and/or reduce complement fixation.

7. The use of claim 1 or 2, wherein the antibody is a Fab, optionally wherein the Fab is PEGylated.

8. The use of any one of claims 1-7, wherein the antibody or antigen binding fragment is further capable of binding to cynomolgus monkey NBL1.

9. The use of claim 8, wherein the antibody or antigen binding fragment is further capable of binding to mouse NBL1.

10. The use of any one of claims 1-9, wherein the antibody or antigen binding fragment has a binding affinity (K_D) for human NBL1 of less than 100 nM.

11. The use of claim 10, wherein the antibody or antigen binding fragment has a binding affinity (K_D) for human NBL1 of less than 10 nM.

12. The use of claim 11, wherein the antibody or antigen binding fragment has a binding affinity (K_D) for human NBL1 of less than 5 nM.

13. The use of any one of claims 1-12, wherein the antibody or antigen binding fragment is capable of inhibiting dimerization of NBL1.

14. The use of claim 1, wherein the antibody or antigen binding fragment is capable of inhibiting NBL1 expression.

15. The use of any one of claims 1-14, wherein the antibody or antigen binding fragment is to be administered parenterally.

16. The use of claim 15, wherein the antibody or antigen binding fragment is to be administered intravenously.

17. The use of claim 15, wherein the antibody or antigen binding fragment is to be administered subcutaneously.

18. The use of any one of claims 1-17, wherein the antibody or antigen binding fragment is to be administered for at least 3 months.

19. The use of claim 18, wherein the antibody or antigen binding fragment is to be administered for at least 6 months.

20. The use of claim 19, wherein the antibody or antigen binding fragment is to be administered for at least 12 months.

21. The use of any one of claims 1-20, wherein the subject has elevated pre-treatment plasma levels of NBL1.

22. The use of any one of claims 1-21, wherein the subject has type 1 diabetes.

23. The use of any one of claims 1-21, wherein the subject has type 2 diabetes.

24. The use of any one of claims 1-23, wherein the subject has a non-diabetic glomerular disease where damage is mediated by NBL1.

25. The use of claim 24, wherein the subject with non-diabetic glomerular disease where damage is mediated by NBL1 does not have type 1 diabetes or type 2 diabetes.

26. The use of any one of claims 1-25, wherein the medicament prevents onset of or slows decline in kidney function.