CLAIMS

[Claim 1]

A mutant of human α-N-acetylglucosaminidase (hNAGLU) selected from the group consisting of (1) to (7) below:

(1) a mutant containing an amino acid sequence represented by SEQ ID NO: 3 in which lysine at position 36 in a wild-type hNAGLU amino acid sequence represented by SEQ ID NO: 1 is replaced with glutamic acid and proline at position 37 is replaced with serine, respectively;

(2) a mutant containing an amino acid sequence represented by SEQ ID NO: 5 in which serine is added between leucine at position 44 and glycine at position 45 in the wild-type hNAGLU amino acid sequence represented by SEQ ID NO: 1;

(3) a mutant containing an amino acid sequence represented by SEQ ID NO: 9 in which glutamine at position 209 in the wild-type hNAGLU amino acid sequence represented by SEQ ID NO: 1 is replaced with arginine;

(4) a mutant containing an amino acid sequence represented by SEQ ID NO: 11 in which glutamic acid at position 228 in the wild-type hNAGLU amino acid sequence represented by SEQ ID NO: 1 is replaced with lysine;

(5) a mutant containing an amino acid sequence represented by SEQ ID NO: 15 in which threonine at position 320 in the wild-type hNAGLU amino acid sequence represented by SEQ ID NO: 1 is replaced with proline and glutamic acid at position 321 is replaced with aspartic acid, respectively;

(6) a mutant containing an amino acid sequence represented by SEQ ID NO: 17 in which serine at position 505 in the wild-type hNAGLU amino acid sequence represented by SEQ ID NO: 1 is replaced with alanine and isoleucine at position 506 is replaced with valine; and

(7) a mutant containing an amino acid sequence represented by SEQ ID NO: 19 in which serine at position 526 in the wild-type hNAGLU amino acid sequence represented by SEQ ID NO: 1 is replaced with asparagine and alanine at position 528 is replaced with threonine, respectively.

[Claim 2]

A hNAGLU mutant containing a mutation relative to the hNAGLU mutant containing the amino acid sequence represented by SEQ ID NO: 9, selected from the group consisting of (8) to (15) below:

(8) a hNAGLU mutant containing the amino acid sequence represented by SEQ ID NO: 25 in which lysine at position 36 is replaced with glutamic acid and proline at position 37 is replaced with serine, respectively;

(9) a hNAGLU mutant containing an amino acid sequence represented by SEQ ID NO: 27 in which serine is added between leucine at position 44 and glycine at position 45;

(10) a hNAGLU mutant containing an amino acid sequence represented by SEQ ID NO: 29 in which threonine at position 320 is replaced with proline and glutamic acid at position 321 is replaced with aspartic acid;

(11) a hNAGLU mutant containing an amino acid sequence represented by SEQ ID NO: 31 in which lysine at position 36 is replaced with glutamic acid, and proline at position 37 is replaced with serine, respectively, and serine is added between leucine at position 44 and glycine at position 45;

(12) a hNAGLU mutant containing an amino acid sequence represented by SEQ ID NO: 33 in which valine at position 54 is replaced with isoleucine and arginine at position 620 is replaced with lysine, respectively;

(13) a hNAGLU mutant containing an amino acid sequence represented by SEQ ID NO: 35 in which valine at position 54 is replaced with isoleucine and serine is added between leucine at position 44 and glycine at position 45;

(14) a hNAGLU mutant containing an amino acid sequence represented by SEQ ID NO: 37 in which arginine at position 620 is replaced with lysine and serine is added between leucine at position 44 and glycine at position 45; and

(15) a hNAGLU mutant containing an amino acid sequence represented by SEQ ID NO: 39 in which valine at position 54 is replaced with isoleucine, and arginine at position 620 is replaced with lysine, respectively, and serine is added between leucine at position 44 and glycine at position 45.

[Claim 3]

A DNA comprising:

a gene encoding the hNAGLU mutant according to claim 1 or 2.

[Claim 4]

An expression vector comprising:

the DNA according to claim 3.

[Claim 5]

A mammalian cell transformed with the expression vector according to claim 4.

[Claim 6]

A method for producing a hNAGLU mutant, comprising:

a step of culturing the mammalian cell according to claim 5 in a serum-free medium.

[Claim 7]

A fusion protein of the hNAGLU mutant according to claim 1 or 2 and an antibody, wherein

the antibody binds to a receptor on cerebrovascular endothelial cells such that the fusion protein is capable of crossing a blood-brain barrier (BBB).

[Claim 8]

The fusion protein according to claim 7, wherein

the receptor on cerebrovascular endothelial cells is selected from the group consisting of an insulin receptor, a transferrin receptor, a leptin receptor, a lipoprotein receptor, and an IGF receptor.

[Claim 9]

The fusion protein according to claim 7, wherein

the receptor on cerebrovascular endothelial cells is the transferrin receptor.

[Claim 10]

The fusion protein according to any one of claims 7 to 9, wherein

the antibody is a Fab antibody, a $F(ab')_2$ antibody, a F(ab') antibody, a single domain antibody, a single chain antibody, or an Fc antibody.

[Claim 11]

The fusion protein according to any one of claims 7 to 10, wherein

the hNAGLU mutant binds to either the C-terminus side or the N-terminus side of a light chain of the antibody.

[Claim 12]

The fusion protein according to any one of claims 7 to 10, wherein

the hNAGLU mutant binds to either the C-terminus side or the N-terminus side of a heavy chain of the antibody.

[Claim 13]

The fusion protein according to any one of claims 7 to 12, wherein

the hNAGLU mutant binds to either the C-terminus side or the N-terminus side of the light chain, or either the C-terminus side or the N-terminus side of the heavy chain of the antibody, via a linker sequence.

[Claim 14]

The fusion protein according to claim 13, wherein

the linker sequence consists of 1 to 50 amino acid residues.

[Claim 15]

The fusion protein according to claim 14, wherein

the linker sequence includes an amino acid sequence selected from the group consisting of one glycine, one serine, an amino acid sequence Gly-Ser, an amino acid sequence Ser-Ser, an amino acid sequence Gly-Gly-Ser, an amino acid sequence represented by SEQ ID NO: 3, an amino acid sequence represented by SEQ ID NO: 4, an amino acid sequence represented by SEQ ID NO: 5, and an amino acid sequence consisting of 1 to 10 of consecutively-linked aforementioned amino acid sequences.

[Claim 16]

A DNA comprising:

a gene encoding the fusion protein according to any one of claims 7 to 15.

[Claim 17]

An expression vector comprising:

the DNA according to claim 16.

[Claim 18]

A mammalian cell transformed with the expression vector according to claim 17.

[Claim 19]

A method for producing a fusion protein of a hNAGLU mutant and an antibody, comprising:

a step of culturing the mammalian cell according to claim 18 in a serum-free medium.