

WHAT IS CLAIMED IS:

1. A recombinant polynucleotide encoding a Ubiquitin Protein Ligase E3A (Ube3a) polypeptide or protein or a biological equivalent thereof, wherein the Ube3a polypeptide or protein or a biological equivalent thereof that comprises one or more naturally occurring or non-naturally occurring glycosylation sites.
2. The recombinant polynucleotide of claim 1, wherein the glycosylation is an N-linked glycosylation and wherein the glycosylation site comprise a consensus sequence of NXaaT or NXaaS, wherein Xaa is any amino acid residue optionally except proline (P).
3. The recombinant polynucleotide of claim 1 or 2, wherein the glycosylation sites are at amino acid (aa) positions of the polypeptide, protein or the equivalent thereof corresponding to one or more of those selected from the following:

aa62 to aa64 of SEQ ID NO: 14, aa96 to aa98 of SEQ ID NO: 14, aa102 to aa104 of SEQ ID NO: 14, aa219 to aa221 of SEQ ID NO: 14, aa354 to aa356 of SEQ ID NO: 14, aa591 to aa 593 of SEQ ID NO: 14, aa622 to aa624 of SEQ ID NO: 14, aa 805 to aa 807 of SEQ ID NO: 14;

aa85 to aa87 of SEQ ID NO: 16, aa119 to aa121 of SEQ ID NO: 16, aa125 to aa127 of SEQ ID NO: 16, aa242 to aa244 of SEQ ID NO: 16, aa377 to aa379 of SEQ ID NO: 16, aa614 to aa616 of SEQ ID NO: 16, aa645 to aa647 of SEQ ID NO: 16, aa828 to aa830 of SEQ ID NO: 16;

aa82 to aa84 of SEQ ID NO: 18, aa116 to aa118 of SEQ ID NO: 18, aa 122 to aa124 of SEQ ID NO: 18, aa239 to aa241 of SEQ ID NO: 18, aa374 to aa376 of SEQ ID NO: 18, aa611 to aa613 of SEQ ID NO: 18, aa642 to aa644 of SEQ ID NO: 18, aa825 to aa827 of SEQ ID NO: 18;

aa83 to aa85 of SEQ ID NO: 26 or 28, aa117 to aa119 of SEQ ID NO: 26 or 28, aa123 to aa125 of SEQ ID NO: 26 or 28, aa 237 to aa239 of SEQ ID NO: 26 or 28, aa372 to aa374 of SEQ ID NO: 26 or 28, aa609 to aa 611 of SEQ ID NO: 26 or 28, aa640 to aa642 of SEQ ID NO: 26 or 28, aa823 to aa825 of SEQ ID NO: 26 or 28;

aa62 to aa64 of SEQ ID NO: 30, aa96 to aa98 of SEQ ID NO: 30, aa102 to aa104 of SEQ ID NO: 30, aa216 to aa218 of SEQ ID NO: 30, aa351 to aa353 of SEQ ID NO: 30, aa588 to aa590 of SEQ ID NO: 30, aa619 to aa621 of SEQ ID NO: 30, or aa802 to aa804 of SEQ ID NO: 30,

optionally wherein any one or any two or all three amino acid residue(s) in at least one of the glycosylation sites is or are mutated compared to a wild type Ube3a polypeptide or protein, thereby constituting the glycosylation site.

4. The recombinant polynucleotide of any one of claims 1 to 3, wherein the Ube3a polypeptide, protein or the biological equivalent thereof comprises eight glycosylation sites at an amino acid (aa) positions corresponding to the eight aa positions as identified in any one of the following (a) to (e):

(a) aa62 to aa64 of SEQ ID NO: 14, aa96 to aa98 of SEQ ID NO: 14, aa102 to aa104 of SEQ ID NO: 14, aa219 to aa221 of SEQ ID NO: 14, aa354 to aa356 of SEQ ID NO: 14, aa591 to aa 593 of SEQ ID NO: 14, aa622 to aa624 of SEQ ID NO: 14, aa 805 to aa 807 of SEQ ID NO: 14;

(b) aa85 to aa87 of SEQ ID NO: 16, aa119 to aa121 of SEQ ID NO: 16, aa125 to aa127 of SEQ ID NO: 16, aa242 to aa244 of SEQ ID NO: 16, aa377 to aa379 of SEQ ID NO: 16, aa614 to aa616 of SEQ ID NO: 16, aa645 to aa647 of SEQ ID NO: 16, aa828 to aa830 of SEQ ID NO: 16;

(c) aa82 to aa84 of SEQ ID NO: 18, aa116 to aa118 of SEQ ID NO: 18, aa 122 to aa124 of SEQ ID NO: 18, aa239 to aa241 of SEQ ID NO: 18, aa374 to aa376 of SEQ ID NO: 18, aa611 to aa613 of SEQ ID NO: 18, aa642 to aa644 of SEQ ID NO: 18, aa825 to aa827 of SEQ ID NO: 18;

(d) aa83 to aa85 of SEQ ID NO: 26 or 28, aa117 to aa119 of SEQ ID NO: 26 or 28, aa123 to aa125 of SEQ ID NO: 26 or 28, aa 237 to aa239 of SEQ ID NO: 26 or 28, aa372 to aa374 of SEQ ID NO: 26 or 28, aa609 to aa 611 of SEQ ID NO: 26 or 28, aa640 to aa642 of SEQ ID NO: 26 or 28, aa823 to aa825 of SEQ ID NO: 26 or 28;

(e) aa62 to aa64 of SEQ ID NO: 30, aa96 to aa98 of SEQ ID NO: 30, aa102 to aa104 of SEQ ID NO: 30, aa216 to aa218 of SEQ ID NO: 30, aa351 to aa353 of SEQ ID NO: 30, aa588 to aa590 of SEQ ID NO: 30, aa619 to aa621 of SEQ ID NO: 30, or aa802 to aa804 of SEQ ID NO: 30.

5. The recombinant polynucleotide of any one of claims 1 to 4, wherein the Ube3a polypeptide, protein or the biological equivalent thereof comprises one or more of mutated amino acid residue(s) at aa position(s) corresponding to one or more of those selected from the following, thereby forming one or more of glycosylation site(s):

aa64 of SEQ ID NO: 14, aa98 of SEQ ID NO: 14, aa104 of SEQ ID NO: 14, aa221 of SEQ ID NO: 14, aa356 of SEQ ID NO: 14, aa591 of SEQ ID NO: 14, aa624 of SEQ ID NO: 14, aa 805 of SEQ ID NO: 14, aa 806 of SEQ ID NO: 14;

aa87 of SEQ ID NO: 16, aa121 of SEQ ID NO: 16, aa127 of SEQ ID NO: 16, aa244 of SEQ ID NO: 16, aa379 of SEQ ID NO: 16, aa614 of SEQ ID NO: 16, aa647 of SEQ ID NO: 16, aa828 of SEQ ID NO: 16, aa829 of SEQ ID NO: 16;

aa84 of SEQ ID NO: 18, aa118 of SEQ ID NO: 18, aa124 of SEQ ID NO: 18, aa241 of SEQ ID NO: 18, aa376 of SEQ ID NO: 18, aa611 of SEQ ID NO: 18, aa644 of SEQ ID NO: 18, aa825 of SEQ ID NO: 18, aa826 of SEQ ID NO: 18;

aa85 of SEQ ID NO: 26 or 28, aa119 of SEQ ID NO: 26 or 28, aa125 of SEQ ID NO: 26 or 28, aa239 of SEQ ID NO: 26 or 28, aa374 of SEQ ID NO: 26 or 28, aa609 of SEQ ID NO: 26 or 28, aa610 of SEQ ID NO: 26 or 28, aa642 of SEQ ID NO: 26 or 28, aa823 of SEQ ID NO: 26 or 28;

aa64 of SEQ ID NO: 30, aa98 of SEQ ID NO: 30, aa104 of SEQ ID NO: 30, aa218 of SEQ ID NO: 30, aa353 of SEQ ID NO: 30, aa588 of SEQ ID NO: 30, aa589 of SEQ ID NO: 30, aa621 of SEQ ID NO: 30, or aa802 of SEQ ID NO: 30.

6. The recombinant polynucleotide of any one of claims 1 to 5, wherein the Ube3a polypeptide, protein or the biological equivalent thereof comprises nine mutated amino acid residues at aa positions corresponding to those identified in any one of the following (a) to (e), thereby forming eight glycosylation sites:

(a) aa64 of SEQ ID NO: 14, aa98 of SEQ ID NO: 14, aa104 of SEQ ID NO: 14, aa221 of SEQ ID NO: 14, aa356 of SEQ ID NO: 14, aa591 of SEQ ID NO: 14, aa624 of SEQ ID NO: 14, aa 805 of SEQ ID NO: 14, and aa 806 of SEQ ID NO: 14;

(b) aa87 of SEQ ID NO: 16, aa121 of SEQ ID NO: 16, aa127 of SEQ ID NO: 16, aa244 of SEQ ID NO: 16, aa379 of SEQ ID NO: 16, aa614 of SEQ ID NO: 16, aa647 of SEQ ID NO: 16, aa828 of SEQ ID NO: 16, and aa829 of SEQ ID NO: 16;

(c) aa84 of SEQ ID NO: 18, aa118 of SEQ ID NO: 18, aa124 of SEQ ID NO: 18, aa241 of SEQ ID NO: 18, aa376 of SEQ ID NO: 18, aa611 of SEQ ID NO: 18, aa644 of SEQ ID NO: 18, aa825 of SEQ ID NO: 18, and aa826 of SEQ ID NO: 18;

(d) aa85 of SEQ ID NO: 26 or 28, aa119 of SEQ ID NO: 26 or 28, aa125 of SEQ ID NO: 26 or 28, aa239 of SEQ ID NO: 26 or 28, aa374 of SEQ ID NO: 26 or 28, aa609 of SEQ ID NO: 26 or 28, aa610 of SEQ ID NO: 26 or 28, aa642 of SEQ ID NO: 26 or 28, and aa823 of SEQ ID NO: 26 or 28; or

(e) aa64 of SEQ ID NO: 30, aa98 of SEQ ID NO: 30, aa104 of SEQ ID NO: 30, aa218 of SEQ ID NO: 30, aa353 of SEQ ID NO: 30, aa588 of SEQ ID NO: 30, aa589 of SEQ ID NO: 30, aa621 of SEQ ID NO: 30, and aa802 of SEQ ID NO: 30.

7. The recombinant polynucleotide of any one of claims 1 to 5, wherein the Ube3a polypeptide, protein or the biological equivalent thereof comprises eight mutated amino acid residues at aa positions corresponding to those identified in any one of the following (a) to (e), thereby forming seven glycosylation sites:

(a) aa64 of SEQ ID NO: 14, aa98 of SEQ ID NO: 14, aa221 of SEQ ID NO: 14, aa356 of SEQ ID NO: 14, aa591 of SEQ ID NO: 14, aa624 of SEQ ID NO: 14, aa 805 of SEQ ID NO: 14, and aa 806 of SEQ ID NO: 14;

(b) aa87 of SEQ ID NO: 16, aa121 of SEQ ID NO: 16, aa244 of SEQ ID NO: 16, aa379 of SEQ ID NO: 16, aa614 of SEQ ID NO: 16, aa647 of SEQ ID NO: 16, aa828 of SEQ ID NO: 16, and aa829 of SEQ ID NO: 16;

(c) aa84 of SEQ ID NO: 18, aa118 of SEQ ID NO: 18, aa241 of SEQ ID NO: 18, aa376 of SEQ ID NO: 18, aa611 of SEQ ID NO: 18, aa644 of SEQ ID NO: 18, aa825 of SEQ ID NO: 18, and aa826 of SEQ ID NO: 18;

(d) aa85 of SEQ ID NO: 26 or 28, aa119 of SEQ ID NO: 26 or 28, aa239 of SEQ ID NO: 26 or 28, aa374 of SEQ ID NO: 26 or 28, aa609 of SEQ ID NO: 26 or 28, aa610 of SEQ ID NO: 26 or 28, aa642 of SEQ ID NO: 26 or 28, and aa823 of SEQ ID NO: 26 or 28;
or

(e) aa64 of SEQ ID NO: 30, aa98 of SEQ ID NO: 30, aa218 of SEQ ID NO: 30, aa353 of SEQ ID NO: 30, aa588 of SEQ ID NO: 30, aa589 of SEQ ID NO: 30, aa621 of SEQ ID NO: 30, and aa802 of SEQ ID NO: 30.

8. The recombinant polynucleotide of any one of claims 5 to 7, wherein the formed glycosylation site comprises a consensus sequence of NXaaT or NXaaS, wherein Xaa is any amino acid residue optionally except proline (P).

9. The recombinant polynucleotide of any one of claims 5 to 8, wherein the mutated amino acid residue(s) is/are selected from one or more of:

T or S at an aa position corresponding to aa64 of SEQ ID NO: 14, T or S at an aa position corresponding to aa98 of SEQ ID NO: 14, T or S at an aa position corresponding to aa104 of SEQ ID NO: 14, T or S at an aa position corresponding to aa221 of SEQ ID NO: 14, T or S at an aa position corresponding to aa356 of SEQ ID NO: 14, N at an aa position corresponding to aa591 of SEQ ID NO: 14, T or S at an aa position corresponding to aa624 of SEQ ID NO: 14, N at an aa position corresponding to aa 805 of SEQ ID NO: 14, and N at an aa position corresponding to aa 806 of SEQ ID NO: 14;

T or S at an aa position corresponding to aa87 of SEQ ID NO: 16, T or S at an aa position corresponding to aa121 of SEQ ID NO: 16, T or S at an aa position corresponding to aa127 of SEQ ID NO: 16, T or S at an aa position corresponding to aa244 of SEQ ID NO: 16, T or S at an aa position corresponding to aa379 of SEQ ID NO: 16, N at an aa position corresponding to aa614 of SEQ ID NO: 16, T or S at an aa position corresponding to aa647 of SEQ ID NO: 16, N at an aa position corresponding to aa828 of SEQ ID NO: 16, and N at an aa position corresponding to aa829 of SEQ ID NO: 16;

T or S at an aa position corresponding to aa84 of SEQ ID NO: 18, T or S at an aa position corresponding to aa118 of SEQ ID NO: 18, T or S at an aa position corresponding to aa124 of SEQ ID NO: 18, T or S at an aa position corresponding to aa241 of SEQ ID NO: 18, T or S at an aa position corresponding to aa376 of SEQ ID NO: 18, N at an aa position corresponding to aa611 of SEQ ID NO: 18, T or S at an aa position corresponding to aa644 of SEQ ID NO: 18, N at an aa position corresponding to aa825 of SEQ ID NO: 18, and N at an aa position corresponding to aa826 of SEQ ID NO: 18;

T or S at an aa position corresponding to aa85 of SEQ ID NO: 26 or 28, T or S at an aa position corresponding to aa119 of SEQ ID NO: 26 or 28, T or S at an aa position corresponding to aa125 of SEQ ID NO: 26 or 28, T or S at an aa position corresponding to aa239 of SEQ ID NO: 26 or 28, T or S at an aa position corresponding to aa374 of SEQ ID NO: 26 or 28, N at an aa position corresponding to aa609 of SEQ ID NO: 26 or 28, N at an aa position corresponding to aa610 of SEQ ID NO: 26 or 28, T or S at an aa position corresponding to aa642 of SEQ ID NO: 26 or 28, and N at an aa position corresponding to aa823 of SEQ ID NO: 26 or 28; or

T or S at an aa position corresponding to aa64 of SEQ ID NO: 30, T or S at an aa position corresponding to aa98 of SEQ ID NO: 30, T or S at an aa position corresponding to aa104 of SEQ ID NO: 30, T or S at an aa position corresponding to aa218 of SEQ ID NO: 30, T or S at an aa position corresponding to aa353 of SEQ ID NO: 30, N at an aa position corresponding to aa588 of SEQ ID NO: 30, N at an aa position corresponding to aa589 of SEQ ID NO: 30, T or S at an aa position corresponding to aa621 of SEQ ID NO: 30, and N at an aa position corresponding to aa802 of SEQ ID NO: 30.

10. The recombinant polynucleotide of any one of claims 1 to 6 and 8 to 9, wherein the Ube3a polypeptide, protein or the biological equivalent thereof comprises one or more non-naturally occurring glycosylation sites.

11. The recombinant polynucleotide of any one of claims 1 to 10, wherein the Ube3a polypeptide, protein or the biological equivalent thereof comprises an amino acid sequence selected from the following:

aa21 to aa 872 of SEQ ID NO: 14, aa21 to aa 895 of SEQ ID NO: 16, aa21 to aa 892 of SEQ ID NO: 18, aa21 to aa 890 of SEQ ID NO: 26, aa21 to aa 890 of SEQ ID NO: 28, aa21 to aa 869 of SEQ ID NO: 30, or a sequence having at least about 90%, or at least about 95%, or at least about 99% identity to each thereof.

12. The recombinant polynucleotide of any one of claims 1 to 11, further comprising a polynucleotide encoding a signal peptide.

13. The recombinant polynucleotide of claim 12, wherein the signal peptide is a secretion signal.

14. The recombinant polynucleotide of claim 12 or 13, wherein the polynucleotide encodes a signal peptide or a secretion signal selected from the following: an antibody heavy/light chain secretion signal, a twin-arginine transport protein secretion signal, an Interleukin-2 (IL2) secretion signal, an Interleukin-4 (IL4) secretion signal, Interleukin-10 (IL10) secretion signal, an Interleukin-3 (IL3) secretion signal, an Interleukin-7 (IL7) secretion signal, an human IL2 secretion signal, a human OSM secretion signal, a VSV-G secretion signal, a Mouse Ig Kappa secretion signal, a Human IgG2 H secretion signal, a BM40 secretion signal, a Secrecon secretion signal, a Human IgKVIII secretion signal, a CD33 secretion signal, a tPA secretion signal, a Human Chymotrypsinogen secretion signal, a Human trypsinogen-2 secretion signal, a Gaussia luc secretion signal, a Albumin(HSA) secretion signal, an Influenza Haemagglutinin secretion signal, a Human insulin secretion signal, or a Silkworm Fibroin LC.

15. The recombinant polynucleotide of any one of claims 12 to 14, wherein the signal peptide or the secretion signal comprises an amino acid sequence of aa1 to aa20 of SEQ ID NO:14.
16. The recombinant polynucleotide of any one of claims 1 to 15, wherein the Ube3a polypeptide, protein or the biological equivalent thereof comprises an amino acid sequence selected from any one of SEQ ID NOs: 14, 16, 18, 26, 28 and 30, or a sequence having at least about 90%, or at least about 95%, or at least about 99% identity to each thereof.
17. The recombinant polynucleotide of any one of claims 1 to 16, comprising a nucleotide (nt) sequence selected from any one of the following:
- nt61 to nt 2619 of SEQ ID NO: 13, nt61 to nt 2688 of SEQ ID NO: 15, nt61 to nt 2679 of SEQ ID NO: 17, nt61 to nt 2673 of SEQ ID NO: 25, nt61 to nt 2673 of SEQ ID NO: 27, nt61 to nt 2610 of SEQ ID NO: 29; SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, or a sequence having at least about 90%, or at least about 95%, or at least about 99% identity to each thereof.
18. The recombinant polynucleotide of any of claims 1 to 17, wherein the Ube3a polypeptide, protein or the biological equivalent thereof is derived from a wildtype human Ube3a protein or a wildtype murine Ube3a protein.
19. The recombinant polynucleotide of claim 18, wherein the wildtype human Ube3a protein comprises an amino acid sequence of any one of SEQ ID NOs: 8, 10, or 12, and wherein the wildtype murine Ube3a protein comprises an amino acid sequence of any one of SEQ ID NOs: 20, 22 or 24.
20. The recombinant polynucleotide of any one of claims 1 to 19, further comprising a regulatory sequence which direct expression of the Ube3a polypeptide, protein or the biological equivalent thereof.

21. The recombinant polynucleotide of claim 20, wherein the regulatory sequence comprises one or more of the following: a promoter, an intron, an enhancer, a polyadenylation signal, a terminator, a silencer, a TATA box, or a Woodchuck Hepatitis Virus (WHP) Posttranscriptional Regulatory Element (WPRE).
22. The recombinant polynucleotide of claim 21, wherein the promoter is selected from the following: an MNDU3 promoter, a CMV promoter, a PGK promoter, a MNDU promoter, or an EF1alpha promoter.
23. The recombinant polynucleotide of claim 21 or 22, wherein the promoter is an MNDU3 promoter.
24. The recombinant polynucleotide of claim 22 or 23, wherein the MNDU3 promoter comprises a sequence of SEQ ID NO: 3, wherein the CMV promoter comprises a sequence selected from SEQ ID NO: 1, 2, or 34, wherein the PKG promoter comprise a sequence of SEQ ID NO: 4, wherein the MNDU promoter comprises a sequence of SEQ ID NO: 5, and wherein the EF1alpha promoter comprises a sequence of SEQ ID NO: 6.
25. The recombinant polynucleotide of any one of claims 1 to 24, further comprising one or more of the following:
- a polypurine tract sequence (PPT), a central PPT (cPPT), an R region, a U5, an encapsidation signal (Psi), a Rev-Responsive Element (RRE), a full-length U3 or a fragment thereof,
 - a detectable or selection maker, a polynucleotide encoding a detectable or selection polypeptide, a regulatory sequence directing expression of the detectable or selection polypeptide, or a coding sequence for a self-cleaving peptide located between the coding sequence for the detectable or selection polypeptide and the sequence encoding the Ube3a polypeptide or protein or a biological equivalent thereof.
26. A recombinant polynucleotide that is reverse or complement or reverse-complement to the recombinant polynucleotide of any one of claims 1 to 25.
27. A vector comprising a recombinant polynucleotide of any one of claims 1 to 26.

28. The vector of claim 27, wherein the vector is a viral vector or a non-viral vector.
29. The vector of claim 28, wherein the viral vector is selected from a retroviral vector, an adenoviral vector, an adeno-associated viral vector, or a Herpes viral vector.
30. The vector of claim 29, the retroviral vector is a lentiviral vector.
31. The vector of claim 30, wherein the lentiviral vector is a self-inactivating lentiviral vector, optionally having a U3 region lacking a TATA box and optionally one or more of transcription factor binding site(s).
32. The vector of claim 30 or 31, wherein the lentiviral vector is derived from human immunodeficiency virus (HIV).
33. The vector of claims 32, wherein non-viral vector is a plasmid.
34. The vector of any one of claims 27 to 33, further comprising a regulatory sequence operatively linked to the recombinant polynucleotide and directing the replication of the recombinant polynucleotide.
35. A recombinant Ube3a protein, polypeptide or a biological equivalent thereof comprising: one or more, or two or more, or three or more, or four or more, or five or more, or six or more, or seven or more, or eight or more, or nine or more, or ten or more, or eleven or more naturally occurring or non-naturally occurring glycosylation sites, wherein the recombinant Ube3a protein or polypeptide or a biological equivalent thereof is not a wildtype Ube3a protein.
36. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of claim 35, wherein the glycosylation is an N-linked glycosylation and wherein the glycosylation site comprise a consensus sequence of NXaaT or NXaaS, wherein Xaa is any amino acid residue optionally except proline (P).
37. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of claim 35 or 36, wherein the glycosylation sites are at amino acid (aa) positions of the polypeptide or protein corresponding to one or more of those selected from the following:

aa62 to aa64 of SEQ ID NO: 14, aa96 to aa98 of SEQ ID NO: 14, aa102 to aa104 of SEQ ID NO: 14, aa219 to aa221 of SEQ ID NO: 14, aa354 to aa356 of SEQ ID NO: 14, aa591 to aa 593 of SEQ ID NO: 14, aa622 to aa624 of SEQ ID NO: 14, aa 805 to aa 807 of SEQ ID NO: 14;

aa85 to aa87 of SEQ ID NO: 16, aa119 to aa121 of SEQ ID NO: 16, aa125 to aa127 of SEQ ID NO: 16, aa242 to aa244 of SEQ ID NO: 16, aa377 to aa379 of SEQ ID NO: 16, aa614 to aa616 of SEQ ID NO: 16, aa645 to aa647 of SEQ ID NO: 16, aa828 to aa830 of SEQ ID NO: 16;

aa82 to aa84 of SEQ ID NO: 18, aa116 to aa118 of SEQ ID NO: 18, aa 122 to aa124 of SEQ ID NO: 18, aa239 to aa241 of SEQ ID NO: 18, aa374 to aa376 of SEQ ID NO: 18, aa611 to aa613 of SEQ ID NO: 18, aa642 to aa644 of SEQ ID NO: 18, aa825 to aa827 of SEQ ID NO: 18;

aa83 to aa85 of SEQ ID NO: 26 or 28, aa117 to aa119 of SEQ ID NO: 26 or 28, aa123 to aa125 of SEQ ID NO: 26 or 28, aa 237 to aa239 of SEQ ID NO: 26 or 28, aa372 to aa374 of SEQ ID NO: 26 or 28, aa609 to aa 611 of SEQ ID NO: 26 or 28, aa640 to aa642 of SEQ ID NO: 26 or 28, aa823 to aa825 of SEQ ID NO: 26 or 28;

aa62 to aa64 of SEQ ID NO: 30, aa96 to aa98 of SEQ ID NO: 30, aa102 to aa104 of SEQ ID NO: 30, aa216 to aa218 of SEQ ID NO: 30, aa351 to aa353 of SEQ ID NO: 30, aa588 to aa590 of SEQ ID NO: 30, aa619 to aa621 of SEQ ID NO: 30, or aa802 to aa804 of SEQ ID NO: 30.

38. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of claims 35 to 37, wherein the Ube3a polypeptide or protein or a biological equivalent thereof comprises eight glycosylation sites at an amino acid (aa) positions corresponding to the eight aa positions as identified in any one of the following (a) to (e):

(a) aa62 to aa64 of SEQ ID NO: 14, aa96 to aa98 of SEQ ID NO: 14, aa102 to aa104 of SEQ ID NO: 14, aa219 to aa221 of SEQ ID NO: 14, aa354 to aa356 of SEQ ID NO: 14, aa591 to aa 593 of SEQ ID NO: 14, aa622 to aa624 of SEQ ID NO: 14, aa 805 to aa 807 of SEQ ID NO: 14;

(b) aa85 to aa87 of SEQ ID NO: 16, aa119 to aa121 of SEQ ID NO: 16, aa125 to aa127 of SEQ ID NO: 16, aa242 to aa244 of SEQ ID NO: 16, aa377 to aa379 of SEQ ID NO: 16, aa614 to aa616 of SEQ ID NO: 16, aa645 to aa647 of SEQ ID NO: 16, aa828 to aa830 of SEQ ID NO: 16;

(c) aa82 to aa84 of SEQ ID NO: 18, aa116 to aa118 of SEQ ID NO: 18, aa 122 to aa124 of SEQ ID NO: 18, aa239 to aa241 of SEQ ID NO: 18, aa374 to aa376 of SEQ ID NO: 18, aa611 to aa613 of SEQ ID NO: 18, aa642 to aa644 of SEQ ID NO: 18, aa825 to aa827 of SEQ ID NO: 18;

(d) aa83 to aa85 of SEQ ID NO: 26 or 28, aa117 to aa119 of SEQ ID NO: 26 or 28, aa123 to aa125 of SEQ ID NO: 26 or 28, aa 237 to aa239 of SEQ ID NO: 26 or 28, aa372 to aa374 of SEQ ID NO: 26 or 28, aa609 to aa 611 of SEQ ID NO: 26 or 28, aa640 to aa642 of SEQ ID NO: 26 or 28, aa823 to aa825 of SEQ ID NO: 26 or 28;

(e) aa62 to aa64 of SEQ ID NO: 30, aa96 to aa98 of SEQ ID NO: 30, aa102 to aa104 of SEQ ID NO: 30, aa216 to aa218 of SEQ ID NO: 30, aa351 to aa353 of SEQ ID NO: 30, aa588 to aa590 of SEQ ID NO: 30, aa619 to aa621 of SEQ ID NO: 30, or aa802 to aa804 of SEQ ID NO: 30.

39. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of claims 35 to 38, comprising one or more of mutated amino acid residue(s) at aa position(s) corresponding to one or more of those selected from the following, thereby forming one or more of glycosylation site(s):

aa64 of SEQ ID NO: 14, aa98 of SEQ ID NO: 14, aa104 of SEQ ID NO: 14, aa221 of SEQ ID NO: 14, aa356 of SEQ ID NO: 14, aa591 of SEQ ID NO: 14, aa624 of SEQ ID NO: 14, aa 805 of SEQ ID NO: 14, aa 806 of SEQ ID NO: 14;

aa87 of SEQ ID NO: 16, aa121 of SEQ ID NO: 16, aa127 of SEQ ID NO: 16, aa244 of SEQ ID NO: 16, aa379 of SEQ ID NO: 16, aa614 of SEQ ID NO: 16, aa647 of SEQ ID NO: 16, aa828 of SEQ ID NO: 16, aa829 of SEQ ID NO: 16;

aa84 of SEQ ID NO: 18, aa118 of SEQ ID NO: 18, aa124 of SEQ ID NO: 18, aa241 of SEQ ID NO: 18, aa376 of SEQ ID NO: 18, aa611 of SEQ ID NO: 18, aa644 of SEQ ID NO: 18, aa825 of SEQ ID NO: 18, aa826 of SEQ ID NO: 18;

aa85 of SEQ ID NO: 26 or 28, aa119 of SEQ ID NO: 26 or 28, aa125 of SEQ ID NO: 26 or 28, aa239 of SEQ ID NO: 26 or 28, aa374 of SEQ ID NO: 26 or 28, aa609 of SEQ ID NO: 26 or 28, aa610 of SEQ ID NO: 26 or 28, aa642 of SEQ ID NO: 26 or 28, aa823 of SEQ ID NO: 26 or 28;

aa64 of SEQ ID NO: 30, aa98 of SEQ ID NO: 30, aa104 of SEQ ID NO: 30, aa218 of SEQ ID NO: 30, aa353 of SEQ ID NO: 30, aa588 of SEQ ID NO: 30, aa589 of SEQ ID NO: 30, aa621 of SEQ ID NO: 30, or aa802 of SEQ ID NO: 30,

optionally wherein any one or any two or all three amino acid residue(s) in at least one of the glycosylation sites is or are mutated compared to a wild type Ube3a polypeptide or protein, thereby constituting the glycosylation site.

40. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of claims 35 to 39, comprising nine mutated amino acid residues at aa positions corresponding to those identified in any one of the following (a) to (e), thereby forming eight glycosylation sites:

(a) aa64 of SEQ ID NO: 14, aa98 of SEQ ID NO: 14, aa104 of SEQ ID NO: 14, aa221 of SEQ ID NO: 14, aa356 of SEQ ID NO: 14, aa591 of SEQ ID NO: 14, aa624 of SEQ ID NO: 14, aa 805 of SEQ ID NO: 14, and aa 806 of SEQ ID NO: 14;

(b) aa87 of SEQ ID NO: 16, aa121 of SEQ ID NO: 16, aa127 of SEQ ID NO: 16, aa244 of SEQ ID NO: 16, aa379 of SEQ ID NO: 16, aa614 of SEQ ID NO: 16, aa647 of SEQ ID NO: 16, aa828 of SEQ ID NO: 16, and aa829 of SEQ ID NO: 16;

(c) aa84 of SEQ ID NO: 18, aa118 of SEQ ID NO: 18, aa124 of SEQ ID NO: 18, aa241 of SEQ ID NO: 18, aa376 of SEQ ID NO: 18, aa611 of SEQ ID NO: 18, aa644 of SEQ ID NO: 18, aa825 of SEQ ID NO: 18, and aa826 of SEQ ID NO: 18;

(d) aa85 of SEQ ID NO: 26 or 28, aa119 of SEQ ID NO: 26 or 28, aa125 of SEQ ID NO: 26 or 28, aa239 of SEQ ID NO: 26 or 28, aa374 of SEQ ID NO: 26 or 28, aa609 of SEQ ID NO: 26 or 28, aa610 of SEQ ID NO: 26 or 28, aa642 of SEQ ID NO: 26 or 28, and aa823 of SEQ ID NO: 26 or 28; or

(e) aa64 of SEQ ID NO: 30, aa98 of SEQ ID NO: 30, aa104 of SEQ ID NO: 30, aa218 of SEQ ID NO: 30, aa353 of SEQ ID NO: 30, aa588 of SEQ ID NO: 30, aa589 of SEQ ID NO: 30, aa621 of SEQ ID NO: 30, and aa802 of SEQ ID NO: 30.

41. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of claims 35 to 39, comprising eight mutated amino acid residues at aa positions corresponding to those identified in any one of the following (a) to (e), thereby forming seven glycosylation sites:

(a) aa64 of SEQ ID NO: 14, aa98 of SEQ ID NO: 14, aa221 of SEQ ID NO: 14, aa356 of SEQ ID NO: 14, aa591 of SEQ ID NO: 14, aa624 of SEQ ID NO: 14, aa 805 of SEQ ID NO: 14, and aa 806 of SEQ ID NO: 14;

(b) aa87 of SEQ ID NO: 16, aa121 of SEQ ID NO: 16, aa244 of SEQ ID NO: 16, aa379 of SEQ ID NO: 16, aa614 of SEQ ID NO: 16, aa647 of SEQ ID NO: 16, aa828 of SEQ ID NO: 16, and aa829 of SEQ ID NO: 16;

(c) aa84 of SEQ ID NO: 18, aa118 of SEQ ID NO: 18, aa241 of SEQ ID NO: 18, aa376 of SEQ ID NO: 18, aa611 of SEQ ID NO: 18, aa644 of SEQ ID NO: 18, aa825 of SEQ ID NO: 18, and aa826 of SEQ ID NO: 18;

(d) aa85 of SEQ ID NO: 26 or 28, aa119 of SEQ ID NO: 26 or 28, aa239 of SEQ ID NO: 26 or 28, aa374 of SEQ ID NO: 26 or 28, aa609 of SEQ ID NO: 26 or 28, aa610 of SEQ ID NO: 26 or 28, aa642 of SEQ ID NO: 26 or 28, and aa823 of SEQ ID NO: 26 or 28;
or

(e) aa64 of SEQ ID NO: 30, aa98 of SEQ ID NO: 30, aa218 of SEQ ID NO: 30, aa353 of SEQ ID NO: 30, aa588 of SEQ ID NO: 30, aa589 of SEQ ID NO: 30, aa621 of SEQ ID NO: 30, and aa802 of SEQ ID NO: 30.

42. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of claim any one of claims 39 to 41, wherein the formed glycosylation site comprises a consensus sequence of NXaaT or NXaaS, wherein Xaa is any amino acid residue optionally except proline (P).

43. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of claims 39 to 42, wherein the mutated amino acid residue(s) is/are selected from one or more of:

T or S at an aa position corresponding to aa64 of SEQ ID NO: 14, T or S at an aa position corresponding to aa98 of SEQ ID NO: 14, T or S at an aa position corresponding to aa104 of SEQ ID NO: 14, T or S at an aa position corresponding to aa221 of SEQ ID NO: 14, T or S at an aa position corresponding to aa356 of SEQ ID NO: 14, N at an aa position corresponding to aa591 of SEQ ID NO: 14, T or S at an aa position corresponding to aa624 of SEQ ID NO: 14, N at an aa position corresponding to aa 805 of SEQ ID NO: 14, and N at an aa position corresponding to aa 806 of SEQ ID NO: 14;

T or S at an aa position corresponding to aa87 of SEQ ID NO: 16, T or S at an aa position corresponding to aa121 of SEQ ID NO: 16, T or S at an aa position corresponding to aa127 of SEQ ID NO: 16, T or S at an aa position corresponding to aa244 of SEQ ID NO: 16, T or S at an aa position corresponding to aa379 of SEQ ID NO: 16, N at an aa position corresponding to aa614 of SEQ ID NO: 16, T or S at an aa position corresponding to aa647 of SEQ ID NO: 16, N at an aa position corresponding to aa828 of SEQ ID NO: 16, and N at an aa position corresponding to aa829 of SEQ ID NO: 16;

T or S at an aa position corresponding to aa84 of SEQ ID NO: 18, T or S at an aa position corresponding to aa118 of SEQ ID NO: 18, T or S at an aa position corresponding to aa124 of SEQ ID NO: 18, T or S at an aa position corresponding to aa241 of SEQ ID NO: 18, T or S at an aa position corresponding to aa376 of SEQ ID NO: 18, N at an aa position corresponding to aa611 of SEQ ID NO: 18, T or S at an aa position corresponding to aa644 of SEQ ID NO: 18, N at an aa position corresponding to aa825 of SEQ ID NO: 18, and N at an aa position corresponding to aa826 of SEQ ID NO: 18;

T or S at an aa position corresponding to aa85 of SEQ ID NO: 26 or 28, T or S at an aa position corresponding to aa119 of SEQ ID NO: 26 or 28, T or S at an aa position corresponding to aa125 of SEQ ID NO: 26 or 28, T or S at an aa position corresponding to aa239 of SEQ ID NO: 26 or 28, T or S at an aa position corresponding to aa374 of SEQ ID NO: 26 or 28, N at an aa position corresponding to aa609 of SEQ ID NO: 26 or 28, N at an aa position corresponding to aa610 of SEQ ID NO: 26 or 28, T or S at an aa position corresponding to aa642 of SEQ ID NO: 26 or 28, and N at an aa position corresponding to aa823 of SEQ ID NO: 26 or 28; or

T or S at an aa position corresponding to aa64 of SEQ ID NO: 30, T or S at an aa position corresponding to aa98 of SEQ ID NO: 30, T or S at an aa position corresponding to aa104 of SEQ ID NO: 30, T or S at an aa position corresponding to aa218 of SEQ ID NO: 30, T or S at an aa position corresponding to aa353 of SEQ ID NO: 30, N at an aa position corresponding to aa588 of SEQ ID NO: 30, N at an aa position corresponding to aa589 of SEQ ID NO: 30, T or S at an aa position corresponding to aa621 of SEQ ID NO: 30, and N at an aa position corresponding to aa802 of SEQ ID NO: 30.

44. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of claims 35 to 43, comprising one or more non-naturally occurring glycosylation sites.

45. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of claims 35 to 44, comprising an amino acid sequence selected from the following:

aa21 to aa 872 of SEQ ID NO: 14, aa21 to aa 895 of SEQ ID NO: 16, aa21 to aa 892 of SEQ ID NO: 18, aa21 to aa 890 of SEQ ID NO: 26, aa21 to aa 890 of SEQ ID NO: 28, aa21 to aa 869 of SEQ ID NO: 30, or a sequence having at least about 90%, or at least about 95%, or at least about 99% identity to each thereof.

46. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of claims 35 to 45, further comprising a signal peptide.

47. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of claim 46, wherein the signal peptide is a secretion signal.

48. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of claim 46 or 47, wherein the signal peptide or the secretion signal is selected from the following: an antibody heavy/light chain secretion signal, a twin-arginine transport protein secretion signal, an Interleukin-2 (IL2) secretion signal, an Interleukin-4 (IL4) secretion signal, Interleukin-10 (IL10) secretion signal, an Interleukin-3 (IL3) secretion signal, an Interleukin-7 (IL7) secretion signal, an human IL2 secretion signal, a human OSM secretion signal, a VSV-G secretion signal, a Mouse Ig Kappa secretion signal, a Human IgG2 H secretion signal, a BM40 secretion signal, a Secrecon secretion signal, a Human IgKVIII secretion signal, a CD33 secretion signal, a tPA secretion signal, a Human Chymotrypsinogen secretion signal, a Human trypsinogen-2 secretion signal, a Gaussia luc secretion signal, a Albumin(HSA) secretion signal, an Influenza Haemagglutinin secretion signal, a Human insulin secretion signal, or a Silkworm Fibroin LC.

49. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of claims 46 to 48, wherein the signal peptide or the secretion signal comprises an amino acid sequence of aa1 to aa20 of SEQ ID NO:14.

50. The recombinant Ube3a protein, polypeptide or the biological equivalent thereof of claims 35 to 49, wherein the Ube3a polypeptide or protein or a biological equivalent thereof comprises an amino acid sequence selected from any one of SEQ ID NOs: 14, 16, 18, 26, 28 and 30, or a sequence having at least about 90%, or at least about 95%, or at least about 99% identity to each thereof.

51. The recombinant Ube3a protein, or polypeptide or the biological equivalent thereof of claims 35 to 50, further comprising an optional self-cleaving peptide and a detectable or selection polypeptide.

52. An isolated or engineered cell comprising one or more of the following: a recombinant polynucleotide of any one of claims 1 to 26, a vector of any one of claims 27 to 34, or a recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of claims 35 to 51, thereby expressing and secreting a recombinant Ube3a protein or polypeptide or a biological equivalent thereof of any one of 35 to 51.

53. The isolated or engineered cell of claim 52, which is a mammalian cell.

54. The isolated or engineered cell of claim 53, wherein the mammalian cell is a murine cell or a human cell.
55. The isolated or engineered cell of any one of claims 52 to 54, which is selected from a stem cell, a progenitor cell, an induced pluripotent stem cell (iPSC), an embryonic stem cell, an adult or somatic stem cell, a mesenchymal stem cell, a neural stem cell, or a progeny of each thereof.
56. The isolated or engineered cell of any one of claims 52 to 55, which is a hematopoietic stem cell or a progeny thereof.
57. The isolated or engineered cell of claim 56, which is CD34+.
58. The isolated or engineered cell of any one of claims 52 to 57, further comprising a detectable marker.
59. An isolated cell population comprising a cell of any one of claims 52 to 58 or a progeny thereof.
60. The isolated cell population of claim 59, wherein the cell population expresses CD4, CD14 and HLADR.
61. The isolated cell population of claim 60, wherein at least 90% of the cells in the population are CD4+, at least 95% of the cell in the population are CD14+ and at least 95% of the cells in the population are HLADR+.
62. The isolated cell population of any one of claims 59 to 61, deriving macrophages under a suitable condition.
63. The isolated cell population of any one of claims 59 to 62, comprising substantially macrophages.
64. The isolated cell population of any one of claims 59 to 63, which is substantially homogenous.

65. The isolated cell population of any one of claims 59 to 64, wherein the cell of the population further comprises a detectable maker.
66. A method to treat, prevent, halt or reverse Angelman syndrome in a subject carrying a defective Ube3a allele, comprising locally or systemically administering to the subject one or more of the following: a recombinant polynucleotide of any one of claims 1 to 26, a vector of any one of claims 27 to 34, a recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of 35 to 51, a cell of any one of claims 52 to 58, or a cell population of any one of 59 to 65, thereby treating Angelman syndrome in the subject.
67. A method to express a Ube3a protein or polypeptide or a biological equivalent thereof in a subject, comprising administering to the subject one or more of the following: a recombinant polynucleotide of any one of claims 1 to 26, a vector of any one of claims 27 to 34, a recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of 35 to 51, a cell of any one of claims 52 to 58, or a cell population of any one of 59 to 65, thereby expressing Ube3a in the subject.
68. The method of claim 67, wherein the subject carries a defective Ube3a gene.
69. The method of any one of claims 66 to 68, wherein the cell or cell population is administered at a dose of about 1.0×10^4 to about 1×10^{15} cells/kg body weight of the subject.
70. The method of any one of claim 66 to 69, wherein the subject is symptomatic or asymptomatic for Angelman syndrome.
71. The method of any one of claims 66 to 70, wherein the subject is a mammal.
72. The method of any one of claims 66 to 71, wherein the subject is a human.
73. The method of any one of claims 66 to 72, wherein the subject is a fetus.
74. The method of any one of claims 66 to 72, wherein the subject is an infant or a pre-pubescent subject.
75. The method of any one of claims 66 to 72, wherein the subject is an adult.

76. An isolated or engineered cell comprising one or more of the following: a recombinant polynucleotide of any one of claims 1 to 26, a vector of any one of claims 27 to 34, a recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of 35 to 51, thereby producing the polynucleotide, the vector, or the recombinant Ube3a protein or polypeptide or a biological equivalent thereof.
77. The isolated or engineered cell of claim 76, which is a eukaryotic or a prokaryotic cell.
78. The isolated or engineered cell of claim 76 or 77, which is a mammalian cell.
79. A clonal population of cells of any one of claims 76 to 78.
80. A viral packaging system comprising: (a) the vector of any one of claims 27 to 34; (b) a packaging plasmid; and (c) an envelope plasmid.
81. The viral packaging system of claim 80, further comprising (d) a packaging cell line.
82. The viral packaging system of claim 81, wherein the packaging cell line is an HEK-293 cell line.
83. A method for producing a viral particle, comprising transducing a packaging cell line with the system of claim 80 under conditions suitable to package the viral particle.
84. The method of claim 83, wherein the packaging cell line is an HEK-293 cell line.
85. A method to express a secreted Ube3a protein, polypeptide or the biological equivalent thereof comprising growing a cell of any one of claims 52 to 58 and 76 to 78 under conditions that allow for the expression of the recombinant Ube3a protein or polypeptide or a biological equivalent thereof.
86. The method of claim 85, wherein the cell is in vitro or in vivo.
87. A composition comprising a carrier and one or more of: a recombinant polynucleotide of any one of claims 1 to 26, a vector of any one of claims 27 to 34, a recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of 35 to 51, a cell of any

one of claims 52 to 58 and 76 to 78, a cell population of any one of 59 to 65, or a clonal population of claim 79.

88. The composition of claim 87, wherein the carrier is a pharmaceutically acceptable carrier.

89. A kit comprising one or more of: a recombinant polynucleotide of any one of claims 1 to 26, a vector of any one of claims 27 to 34, a recombinant Ube3a protein, polypeptide or the biological equivalent thereof of any one of 35 to 51, a cell of any one of claims 52 to 58 and 76 to 78, a cell population of any one of 59 to 65, or a clonal population of claim 79, and optionally instructions for use.