CLAIMS

1. A Cas13 protein, wherein the amino acid sequence of the Cas13 protein has at least 90% sequence identity compared to SEQ ID NO: 1.

2. The Cas13 protein according to claim 1, wherein the Cas13 protein can form a CRISPR complex with a guide polynucleotide comprising a direct repeat sequence linked to a guide sequence, wherein the guide sequence is engineered to guide the sequence-specific binding of the CRISPR complex to a target RNA;

and/or, the Cas13 protein comprises one or more mutations in a catalytic domain and has reduced RNA cleavage activity;

and/or, the Cas13 protein comprises one or more mutations in one or two HEPN domains and substantially lacks RNA cleavage activity.

3. The Cas13 protein according to claim 1, wherein:

(a) the Cas13 protein comprises at least one mutation at the location corresponding to amino acid residue positions 40-91, 146-153, 158-176, 182-209, 216-253, 271-287, 341-353, 379-424, 456-477, 521-557, 575-588, 609-625, 700-721, 724-783, 796-815, 828-852 or 880-893 of the reference protein as shown in SEQ ID NO: 1;

(b) the Cas13 protein comprises one or more mutations at the location corresponding to the following amino acid residues of the reference protein as shown in SEQ ID NO: 1: R11, N34, R35, R47, R58, R63, R64, N68, N87, N265, N274, R276, R290, R294, N299, N303, R308, R314, R320, R328, N332, R341, N346, R358, N372, N383, N390, N394, R47+R290, R47+R314, R290+R314, R47+R290+R314, R308+N68, N394+N68, N87+N68, R308+N265, N394+N265, N87+N265, R308+N68+N265, N87+N68+N265, T7, A16, S260, A263, M266, N274, F288, M302, N303, L304, V305, I311, D313, H324, P326, H327, N332, N346, T353, T360, E365, A373, M380, S382, K395, Y396, D402, D411, and

S418; and/or,

(c) the Cas13 protein comprises a mutation at the location corresponding to the RxxxxH motif at positions 210-215, 750-755 and/or 785-790 of the reference protein as shown in SEQ ID NO: 1;

preferably, the mutation is selected from R11A, N34A, R35A, R47A, R58A, R63A, R64A, N68A, N87A, N265A, N274A, R276A, R290A, R294A, N299A, N303A, R308A, R314A, R320A, R328A, N332A, R341A, N346A, R358A, N372A, N383A, N390A, N394A, R47A+R290A, R47A+R314A, R290A+R314A, R47A+R290A+R314A, R308A+N68A, N394A+N68A, N87A+N68A, R308A+N265A, N394A+N265A, N87A+N265A, R308A+N68A+N265A, N87A+N68A+N265A, T7S, A16S, S260E, A263K, M266I, N274K, F288Y, M302F, N303S, L304I, V305K, I311M D313E, H324Y, P326S, H327V, N332Y, N346D, T353L, T360S, E365D, A373E, M380K, S382R, K395G, Y396D, D402L, D411E, and S418K.

4. A fusion protein comprising the Cas13 protein according to any one of claims 1 to 3 or a functional fragment thereof, fused to a protein domain and/or a polypeptide tag; optionally, the original function of the Cas13 protein and/or the functional fragment thereof is not altered after fusion.

5. The fusion protein according to claim 4, wherein the Cas13 protein or the functional fragment thereof is fused to a nuclear localization signal (NLS);

and/or, the Cas13 protein or the functional fragment thereof is fused to a nuclear export signal (NES);

and/or, the Cas13 protein or the functional fragment thereof is covalently linked to the protein domain.

and/or, the Cas13 protein or the functional fragment thereof is fused to any one or more of the following protein domains and/or polypeptide tags: a cytosine deaminase domain, an adenosine deaminase domain, a translational activation

domain, a translational repression domain, an RNA methylation domain, an RNA demethylation domain, a nuclease domain, a splicing factor domain, a reporter domain, an affinity domain, a subcellular localization signal, a reporter tag, and an affinity tag.

6. A guide polynucleotide comprising (i) a direct repeat sequence having at least 50% sequence identity compared to any one of SEQ ID NO: 3 and SEQ ID NOs: 80-87, wherein the direct repeat sequence is linked to (ii) a guide sequence engineered to hybridize with a target RNA, wherein the guide polynucleotide can form a CRISPR complex with a Cas13 protein and guide the sequence-specific binding of the CRISPR complex to the target RNA;

optionally, the Cas13 protein is Cas13a, Cas13b, Cas13c, or Cas13d;

optionally, the Cas13 protein has at least 90%, at least 95%, at least 98%, or at least 99% sequence identity compared to the amino acid sequence of SEQ ID NO: 1;

optionally, the base at position 26 corresponding to SEQ ID NO: 3 in the direct repeat sequence is A;

optionally, the direct repeat sequence is $GGAAGATN_1ACTCTACAAACCTGTAGN_2GN_3N_4N_5N_6N_7N_8N_9N_{10}N_{11}$;

wherein N_1 and N_3-N_{11} are independently any one selected from A, C, G, and T; and N_2 is any one selected from A and G;

optionally, the direct repeat sequence is $GGAAGATN_{12}ACTCTACAAACCTGTAGN_{13}GN_{14}N_{15}N_{16}N_{17}N_{18}N_{19}N_{20}N_{21}N_{22}$;

wherein N_{12}, N_{13}, N_{19}, and N_{21} are independently any one selected from A and G, N_{14} is any one selected from A and T, N_{15} and N_{16} are independently any one selected from C and T, N_{17} and N_{18} are independently any one selected from G and T, and N_{20} and N_{22} are independently any one selected from C and G.

7. The guide polynucleotide according to claim 15, wherein the direct repeat sequence has at least 80%, at least 90%, or at least 95% sequence identity

compared to any one of SEQ ID NOs: 3, 81, 82, 84, and 87;

and/or, the guide sequence is located at the 3' end of the direct repeat sequence;

and/or, the guide sequence comprises 15-35 nucleotides;

and/or, the guide sequence hybridizes with the target RNA with no more than one nucleotide mismatch;

and/or, the direct repeat sequence comprises 25 to 40 nucleotides;

and/or, the guide polynucleotide further comprises an aptamer sequence;

and/or, the guide polynucleotide comprises a nucleotide with modification;

and/or, the target RNA is located in nucleus of a eukaryotic cell;

and/or, the target RNA is any one or more selected from TTR RNA, SOD1 RNA, PCSK9 RNA, VEGFA RNA, VEGFR1 RNA, PTBP1 RNA, AQp1 RNA, and ANGPTL3 RNA.

8. A CRISPR-Cas13 system comprising:

the Cas13 protein according to any one of claims 1 to 3, or the fusion protein according to claim 4 or 5, or the nucleic acid encoding the Cas13 protein or the fusion protein; and

a guide polynucleotide or a nucleic acid encoding the guide polynucleotide; the guide polynucleotide comprising a direct repeat sequence linked to a guide sequence, wherein the guide sequence is engineered to hybridize with a target RNA;

the guide polynucleotide can form a CRISPR complex with the Cas13 protein or the fusion protein and guide a sequence-specific binding of the CRISPR complex to a target RNA;

optionally, the target RNA is any one or more selected from TTR RNA, SOD1 RNA, PCSK9 RNA, VEGFA RNA, VEGFR1 RNA, PTBP1 RNA, AQp1 RNA, and ANGPTL3 RNA;

optionally, the direct repeat sequence has at least 70% sequence identity

compared to any one of SEQ ID NO: 3 and SEQ ID NOs: 80-87.

9. A CRISPR-Cas13 system comprising the guide polynucleotide according to claim 6 or 7 or a nucleic acid coding the same, and a Cas13 protein or a nucleic acid coding the same.

10. A vector system comprising the CRISPR-Cas13 system according to claim 8, wherein the vector system comprises one or more vectors comprising a polynucleotide sequence encoding the Cas13 protein or the fusion protein and a polynucleotide sequence encoding the guide polynucleotide.

11. A vector system or eukaryotic cell comprising the CRISPR-Cas13 system according to claim 9; optionally, the vector is an adeno-associated viral vector comprising a DNA encoding the Cas13 protein or the fusion protein and the guide polynucleotide; optionally, the eukaryotic cell is a mammal cell;

or, the vector is a lipid nanoparticle comprising the guide polynucleotide and an mRNA encoding the Cas13 protein or fusion protein;

or, the vector is a lentiviral vector comprising the guide polynucleotide and an mRNA encoding the Cas13 protein or fusion protein; preferably, the lentiviral vector is pseudotyped with an envelope protein; optionally, the mRNA encoding a Cas13 protein or fusion protein is linked to an aptamer sequence.

12. A viral-like particle comprising the CRISPR-Cas13 system according to claim 8 or 9, wherein the viral-like particle comprises a ribonucleoprotein complex formed from the guide polynucleotide and a Cas13 protein or the fusion protein; optionally, the Cas13 protein or the fusion protein is fused to a gag protein.

13. A pharmaceutical composition comprising the Cas13 protein according to any one of claims 1 to 3, the fusion protein according to claim 4 or 5, the guide

polynucleotide according to claim 6 or 7, or the CRISPR-Cas13 system according to claim 8 or 9.

14. An isolated nucleic acid encoding the Cas13 protein according to any one of claims 1 to 3 or the fusion protein according to claim 4 or 5, or the guide polynucleotide according to claim 8 or 9.

15. The Cas13 protein according to any one of claims 1 to 3, the fusion protein according to claim 4 or 5, the guide polynucleotide according to claim 6 or 7, the CRISPR-Cas13 system according to claim 8 or 9, or the isolated nucleic acid according to claim 14 for use in detecting a target RNA in a nucleic acid sample suspected of comprising a target RNA or a target RNA in a nucleic acid sample comprising a target RNA.

16. The Cas13 protein according to any one of claims 1 to 3, the fusion protein according to claim 4 or 5, the guide polynucleotide according to claim 6 or 7, the CRISPR-Cas13 system according to claim 8 or 9, or the isolated nucleic acid according to claim 14 for use in any one of the following: cleaving one or more target RNA molecules or nicking one or more target RNA molecules; activating or upregulating one or more target RNA molecules; activating or inhibiting translation of one or more target RNA molecules; inactivating one or more target RNA molecules; visualizing, labelling or detecting one or more target RNA molecules; binding one or more target RNA molecules; transporting one or more target RNA molecules; and masking one or more target RNA molecules.

17. The Cas13 protein according to any one of claims 1 to 3, the fusion protein according to claim 4 or 5, the guide polynucleotide according to claim 6 or 7, the CRISPR-Cas13 system according to claim 8 or 9, or the isolated nucleic acid according to claim 14 for use in diagnosing, treating, or preventing diseases

or disorders associated with a target RNA.