

CLAIMS

1. An antigen-binding molecule that specifically binds to GP73, or to an antigenic portion thereof, wherein the antigen-binding molecule binds to an epitope within the amino acid sequence
 - a) SSRSVDLQTRIMELEGRVRR SEQ ID NO: 30
 - b) SSRSVELQTRIVELEGRVRR SEQ ID NO: 31; and/or
 - c) SSRSVDLQTRIVELEGRVRR SEQ ID NO: 32.
2. The antigen-binding molecule of claim 1, wherein the epitope is within the amino acid sequence RIMELEGRVRR (SEQ ID NO: 33), preferably EGRVRR (SEQ ID NO: 34).
3. The antigen-binding molecule of claim 1 or claim 2, wherein antigen-binding molecule is an antibody comprising:
 - (a) a variable heavy (VH) chain comprising CDR3 as defined in SEQ ID NO: 6 and a variable light (VL) chain comprising CDR3 as defined in SEQ ID NO: 9; or
 - (b) a variable heavy (VH) chain comprising CDR3 as defined in SEQ ID NO: 14 and a variable light (VL) chain sequence comprising CDR3 as defined in SEQ ID NO: 17.
4. The antigen-binding molecule of claim 3,
wherein the antibody of claim 3(a)
 - a) comprises a variable heavy (VH) chain comprising CDR1 as defined in SEQ ID NO: 4, CDR2 as defined in SEQ ID NO: 5 and CDR3 as defined in SEQ ID NO: 6 and a variable light (VL) chain comprising CDR1 as defined in SEQ ID NO: 7, CDR2 as defined in SEQ ID NO: 8 and CDR3 as defined in SEQ ID NO: 9; or
 - b) is an antibody binding to the same epitope as an antibody of (a);
or wherein the antibody of claim 3(b)
 - c) comprises a variable heavy (VH) chain comprising CDR1 as defined in SEQ ID NO: 12, CDR2 as defined in SEQ ID NO: 13

and CDR3 as defined in SEQ ID NO: 14 and a variable light (VL) chain sequence comprising CDR1 as defined in SEQ ID NO: 15, CDR2 as defined in SEQ ID NO: 16 and CDR3 as defined in SEQ ID NO: 17; or

d) is an antibody binding to the same epitope as an antibody of (c).

5. The antigen-binding molecule of claim 3 or claim 4, wherein the antibody

a) comprises a variable heavy (VH) chain sequence comprising the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 35 or a sequence having 90%, preferably 95% sequence identity to SEQ ID NO: 2 or SEQ ID NO: 35; and

a variable light (VL) chain sequence comprising the amino acid sequence of SEQ ID NO: 3 or SEQ ID NO: 36 or a sequence having 90%, preferably 95% sequence identity to SEQ ID NO: 3 or SEQ ID NO: 36;

b) comprises a variable heavy (VH) chain sequence comprising the amino acid sequence of SEQ ID NO: 10 or SEQ ID NO: 37 or a sequence having 90%, preferably 95% sequence identity to SEQ ID NO: 10 or SEQ ID NO: 37; and

a variable light (VL) chain sequence comprising the amino acid sequence of SEQ ID NO: 11 or SEQ ID NO: 38 or a sequence having 90%, preferably 95% sequence identity to SEQ ID NO: 11 or SEQ ID NO: 38;

or

c) is an antibody binding to the same epitope as an antibody of (a) or (b).

6. The antigen-binding molecule of any one of the preceding claims, wherein the antigen-binding molecule is internalized into a cell.

7. A polynucleotide that encodes at least one of a variable heavy (VH) chain sequence and/or a variable light (VL) chain sequence of an antibody that specifically binds to GP73, or to an antigenic portion thereof, wherein the antibody binds to an epitope within the amino acid sequence
 - a) SSRSVDLQTRIMELEGRVRR SEQ ID NO: 30
 - b) SSRSVELQTRIVELEGRVRR SEQ ID NO: 31; and/or
 - c) SSRSVDLQTRIVELEGRVRR SEQ ID NO: 32.
8. A method for producing an antibody that specifically binds to a polypeptide or to an antigenic portion thereof, comprising administering to a subject a polypeptide selected from
 - a) SSRSVDLQTRIMELEGRVRR SEQ ID NO: 30
 - b) SSRSVELQTRIVELEGRVRR SEQ ID NO: 31; and
 - c) SSRSVDLQTRIVELEGRVRR SEQ ID NO: 32.
9. An immunoconjugate comprising the antibody of any one of the preceding claims and a cytotoxic agent or a prodrug of a cytotoxic agent.
10. The immunoconjugate of claim 9 having the formula Ab(-L-D)_p, wherein:
 - a) Ab is the antibody of any one of the preceding claims;
 - b) L is a linker;
 - c) D is a cytotoxic agent; and
 - d) p ranges from 1-8.
11. An immunoconjugate comprising the antibody of any one of claims 1 to 6 and a functional agent, wherein the functional agent is an endosomal escape domain (EED) peptide.
12. A pharmaceutical composition comprising
 - a) an immunoconjugate of any one of claims 9 to 11 and a pharmaceutically acceptable carrier; or
 - b) an antigen-binding molecule of any one of claims 1 to 6 and a pharmaceutically acceptable carrier.

13. A method for identifying a subject as having disease, comprising determining the level, in a sample from the subject, of specific binding of the antigen-binding molecule of any one of claims 1 to 6 with a GP73 polypeptide or with an antigenic portion thereof, wherein detecting an altered level of the specific binding relative to a control sample identifies the subject as having disease.
14. An RNA aptamer, capable of binding to an epitope within amino acids 36 to 55 of human GP73.
15. A chimeric antigen receptor CAR T-cell, capable of binding to an epitope within amino acids 36 to 55 of human GP73.
16. An antigen-binding molecule that binds to the furin cleavage consensus sequence EGRVRR and inhibits the proteolytic cleavage of GP73 proteins.
17. An antibody that binds GP73 but not soluble GP73 (sGP73) and is thus not inhibited or neutralized by circulating sGP73.
18. Use of an antigen-binding molecule of any one of claims 1 to 6, an immunoconjugate of any one of claims 9 to 11, or a pharmaceutical composition of claim 12 in the manufacture of a medicament for treating a GP73-positive cancer.