

WHAT IS CLAIMED

1. An FN3 polypeptide that binds to human CD71 at a site on human CD71 that does not compete with transferrin binding to human CD71, wherein the FN3 polypeptide comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of

MLPAPKNLVVSRVTEDSARLSWTAPDAAFDSFX₁IX₂YX₃EX₄X₅X₆X₇GEAIX₈L
X₉VPGSERSYDLTGLKPGTEYX₁₀VX₁₁IX₁₂X₁₃VKGGX₁₄X₁₅SX₁₆PLX₁₇AX₁₈FTT
(SEQ ID NO: 273), provided that:

X₈, X₉, X₁₇, and X₁₈ are each, independently, any amino acid other than M or P,

X₁ is selected from D, F, Y, or H,

X₂ is selected from Y, G, A, or V,

X₃ is selected from I, T, L, A, or H,

X₄ is selected from S, Y or P,

X₅ is selected from Y, G, Q, or R,

X₆ is selected from G or P,

X₇ is selected from A, Y, P, D, or S,

X₁₀ is selected from W, N, S, or E,

X₁₁ is selected from L, Y, or G,

X₁₂ is selected from D, Q, H, or V,

X₁₃ is selected from G or S,

X₁₄ is selected from R, G, F, L, or D,

X₁₅ is selected from W, S, P, or L, and

X₁₆ is selected from T, V, M, or S.

2. The FN3 polypeptide of claim 1, wherein the FN3 polypeptide comprises the amino acid sequence selected from SEQ ID NO: 209, 104, 105, 106, 112, 113, 115, 116, 117, 118, 119, 120, 122, 124, 125, 127, 128, 129, 11, 133, 134, 135, 137, 138, 141, 143, 144, 145, 146, 147, 148, 149, 150, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 164, 165, 166, 167, 168, 169, 170, 171, 176, 177, 178, 180, 181, 182, 183, 184, 185, 186, 188, 189, 190, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 206, 207, 211, 212, 213, 214, 215, 216, 217, 218, 219, 224, 225, 226, 227, 228, 229, 230, 233, 234, 236, 237, 238, 239, 240, 242, 244, 245, 246, 247, 248, 249, 250, 252, 253, 254, 256, 257, 258, 259, 261, 262, 263, 264, 265, 266, 267, 268, or 269.
3. The FN3 polypeptide of any one of claims 1 or 2, wherein the FN3 polypeptide is conjugated to a detectable label, an oligonucleotide, a therapeutic agent, or any combination thereof.
4. The FN3 polypeptide of claim 3, wherein the detectable label is a radioactive isotope, magnetic beads, metallic beads, colloidal particles, a fluorescent dye, an electron-dense reagent, an enzyme, biotin, digoxigenin, or hapten.
5. The FN3 polypeptide of claim 3, wherein the therapeutic agent is auristatin, monomethyl auristatin phenylalanine, or dolastatin.
6. The FN3 polypeptide of claim 3, wherein the therapeutic agent is a chemotherapeutic agent, a drug, an antibody, a growth inhibitory agent, a toxin, a radioactive isotope, an anti-tubulin agent, a polynucleotide, an siRNA molecule, an siRNA sense strand, an siRNA antisense strand, an RNA molecule, a DNA molecule, a DNA minor groove binder, a DNA replication inhibitor, an alkylating agent, an antibiotic, an antifolate, an antimetabolite, a chemotherapy sensitizer, a topoisomerase inhibitor, or a vinca alkaloid.
7. The FN3 polypeptide of claim 3, wherein the therapeutic agent can elicit one or more cytotoxic effects by modulating gene expression, RNA expression or levels, tubulin binding, DNA binding, topoisomerase inhibition, DNA cross linking, chelation, spliceosome inhibition, NAMPT inhibition, or HDAC inhibition.

8. The FN3 polypeptide of any of claims 1-7, further comprising a methionine at the N-terminus of the FN3 polypeptide.
9. The FN3 polypeptide of any of claims 1-8, wherein the FN3 polypeptide is coupled to a half-life extending moiety.
10. The FN3 polypeptide of claim 9, wherein the half-life extending moiety is an albumin binding molecule, a polyethylene glycol (PEG), albumin, albumin variant, at least a portion of an Fc region of an immunoglobulin.
11. The FN3 polypeptide of claim 10, wherein the albumin binding molecule is a second polypeptide that binds albumin or an albumin variant.
12. The FN3 polypeptide of claim 1, wherein the FN3 polypeptide is coupled to an oligonucleotide.
13. The FN3 polypeptide of claim 1, wherein the FN3 polypeptide is coupled to an siRNA molecule, wherein the siRNA molecule comprises a sense strand and an antisense strand.
14. The FN3 polypeptide of claim 13, wherein the FN3 polypeptide is coupled to the sense strand of the siRNA molecule.
15. The FN3 polypeptide of claim 14, wherein the FN3 polypeptide is coupled to a 3' end of the sense strand of the siRNA molecule.
16. The FN3 polypeptide of claim 14, wherein the FN3 polypeptide is coupled to a 5' end of the sense strand of the siRNA molecule.
17. The FN3 polypeptide of claim 1, wherein the FN3 polypeptide is coupled to an antisense molecule.
18. The FN3 polypeptide of claim 1, wherein the FN3 polypeptide is coupled to a DNA molecule.

19. An isolated polynucleotide encoding the FN3 polypeptide of any one of claims 1-18.
20. A vector comprising the polynucleotide of claim 19.
21. A host cell comprising the vector of claim 30.
22. A method of producing an FN3 polypeptide that binds CD71, comprising culturing the isolated host cell of claim 21 under conditions that the FN3 polypeptide is expressed, and purifying the FN3 polypeptide.
23. A pharmaceutical composition comprising the FN3 polypeptide of any one of claims 1-18 and a pharmaceutically acceptable carrier.
24. A kit comprising the FN3 polypeptide of any one of claims 1-18.
25. Use of the pharmaceutical composition of claim 23 for the manufacture/preparation of a medicament for the treatment of a neurological disease and/or a brain tumor.
26. The use of claim 25, wherein the brain tumor is a nonmalignant, a benign, or a malignant brain tumor.
27. The use of claim 26, wherein the malignant brain tumor is astrocytoma, medulloblastoma, glioma, ependymoma, germinoma (pinealoma), glioblastoma multiform, oligodendroglioma, schwannoma, retinoblastoma, cancer of the spinal cord, neurofibroma, meningioma, glioma, or sarcoma.
28. The use of claim 26, wherein the brain tumor is a congenital tumor.
29. The use of claim 25, wherein the neurological disease is stroke, seizures, hypertensive encephalopathy, acquired immunodeficiency syndrome, traumatic brain injuries, multiple sclerosis, Parkinson's disease (PD), or Alzheimer disease.