

CLAIMS

1. An isolated fibronectin type III (FN3) domain that specifically binds to a human cluster of differentiation 8A (CD8A) protein comprising an amino acid sequence of any one of SEQ ID NO: 40-269, wherein the amino acid sequence can optionally have a residue substituted with a cysteine at a position that corresponds to residue 54 of a sequence set forth in any one of SEQ ID NOs: 79, 81, 83, 89, 122, or 68.
2. The isolated FN3 domain of claim 1, wherein the protein is conjugated to a second molecule.
3. The isolated FN3 domain of claim 2, wherein the second molecule is a detectable label.
4. The isolated FN3 domain 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 isolated FN3 domain of any one of claims 1 to 4, wherein the FN3 domain has a cysteine substitution at residue position 54 corresponding to an amino acid sequence set forth in any one of SEQ ID NOs: 79, 81, 83, 89, 122, or 68.
6. The isolated FN3 domain of any one of claims 1 to 5, further comprising a methionine at the N-terminus of the FN3 domain.
7. The isolated FN3 domain of any one of claims 1 to 6, wherein the FN3 domain is coupled to a half-life extending moiety.
8. The isolated FN3 domain of claim 7, wherein the half-life extending moiety is a CD8 binding molecule, albumin, an albumin variant, an albumin binding molecule, a polyethylene glycol (PEG), CD8, CD8 variant, or at least a portion of an Fc region of an immunoglobulin.

9. An isolated polynucleotide encoding the FN3 domain of any one of claims 1 to 8.
10. A vector comprising the polynucleotide of claim 9.
11. An isolated host cell comprising the vector of claim 10.
12. A method of producing the FN3 domain of any one of claims 1 to 8, comprising culturing an isolated host cell comprising a nucleic acid molecule encoding the FN3 domain under conditions such that the FN3 domain is expressed, and purifying the FN3 domain.
13. A diagnostic kit comprising the FN3 domain of any one of claims 1 to 8.
14. A capture agent comprising the FN3 domain of any one of claims 1 to 8.
15. The diagnostic kit of claim 13 or capture agent of claim 14, wherein the substituted cysteine is conjugated to Zr-89 or I-124.
16. A method of detecting CD8-expressing cells in a biological sample previously obtained from a subject, comprising:
 - contacting the biological sample with the capture agent of claim 15; and
 - evaluating binding of the biological sample to the FN3 domain of the capture agent.
17. The method of claim 17, wherein the capture agent has a cysteine substitution at residue position 54 corresponding to a sequence set forth in any one of SEQ ID NOs 79, 81, 83, 89, 122, or 68 and the substituted cysteine is conjugated to Zr-89 or I-124.
18. An isolated fibronectin type III (FN3) domain that specifically binds to a human cluster of differentiation 8A (CD8A) protein comprising an amino acid sequence of any one of SEQ ID NO: 229, SEQ ID NO: 230, SEQ ID NO: 231, SEQ ID NO: 232, or SEQ ID NO: 234.