

CLAIMS

1. A folate receptor alpha (FOLR1) binding protein comprising an amino acid sequence having between 70% and 83% sequence identity to the amino acid sequence of SEQ ID NO: 46, wherein the amino acids corresponding to positions 9, 10, 12, 42, 44, 46, 62, 63, 64, 65, 66, 68, and 70 of SEQ ID NO: 46 are substituted as follows:

position 9 of SEQ ID NO: 46 is selected from E, L, S, or N, and

position 10 of SEQ ID NO: 46 is selected from E, Q, Y, or I, and

position 12 of SEQ ID NO: 46 is selected from Y, E, W, or D, and

position 42 of SEQ ID NO: 46 is selected from E, K, Y, Q, or M, and

position 44 of SEQ ID NO: 46 is selected from L, Y, V, or F, and

position 46 of SEQ ID NO: 46 is selected from Y, D, or S, and

position 62 of SEQ ID NO: 46 is selected from L, R, D, or I, and

position 63 of SEQ ID NO: 46 is selected from G, F, L, or A, and

position 64 of SEQ ID NO: 46 is selected from G, D, or Y, and

position 65 of SEQ IDNO: 46 is selected from A, D, Y, G, or M, and

position 66 of SEQ ID NO: 46 is selected from V, H, Y, or T, and

position 68 of SEQ ID NO: 46 is selected from K, D, P, or T, and

position 70 of SEQ ID NO: 46 is selected from Q, P, T, W, or H.
2. The FOLR1 binding protein according to claim 1 comprising an amino acid with sequence identity between 75% and 83% to SEQ ID NO: 46.
3. The FOLR1 binding protein according to claim 1 or 2, wherein the amino acid corresponding to position 11 of SEQ ID NO: 46 is selected from K or R, and the amino acid corresponding position 45 of SEQ ID NO: 46 is selected from W, R, or G.
4. The FOLR1 binding protein according to any one of claims 1 to 3, comprising amino acid residues

selected from EEKY, EERY, EQKY, LYKE, SYKW, or NIKD corresponding to positions 9, 10, 11, and 12 of SEQ ID NO: 46, and

selected from ELLWY, KLLWY, KLLRY, YLYWD, YLYGD, QLVWD, or MLFWS corresponding to positions 42, 43, 44, 45, and 46 of SEQ ID NO: 46, and

selected from LGGAVLKLQ, LGDAVLKLQ, LGGAVLKLP, RFGDHLDT, RFGYHLDT,

DLGGYLPLW, or IAYMTLTLH corresponding to positions 62, 63, 64, 65, 66, 67, 68, 69, and 70, of SEQ ID NO: 46.

5. The FOLR1 binding protein according to any one of claims 1 to 4, further comprising
5 substitutions in 1, 2, 3, 4, 5 amino acid positions, selected from positions corresponding to positions 6, 8, 13, 14, 20, 23, 24, 25, 29, 30, 31, 32, 33, 34, 48, 49, 51, 52, 58, 59, 60, 71, and 72 of SEQ ID NO:46.
6. The FOLR1 binding protein according to claim 5, wherein substitutions are selected from
10 any one of K6V, K6Q, L8R, L8E, L8Y, I13T, T14A, T14P, S20C, S20G, I23T, I23V, E24G, E24A, N25D, K29R, K29E, K29T, I30V, I30L, Q31R, D32G, D32N, K33R, K33Q, E34A, K48E, Q49R, E51K, E51D, D52G, D58N, Y59H, N60T, N60S, L71P, R72G, R72Y, or R72K.
7. The FOLR1 binding protein according to any one of claims 1 to 6, wherein the FOLR1
15 binding protein is a multimer comprising of a plurality of FOLR1 binding proteins according to any one of claims 1 to 6.
8. The FOLR1 binding protein according to claim 7, wherein the FOLR1 binding protein is a
20 dimer of the FOLR1 binding protein according to any one of claims 1 to 6.
9. The FOLR1 binding protein according to claim 8, wherein the FOLR1 binding protein is a homo-dimer of the FOLR1 binding protein according to any one of claims 1 to 6.
10. The FOLR1 binding protein according to any one of claims 1 to 9, comprising or consisting
25 of an amino acid sequence selected from the group of SEQ ID NOs: 1 to 45, 69 to 73, or selected from amino acid sequences with at least 90% identity thereto, respectively.
11. The FOLR1 binding protein according to any one of claims 1 to 10, further comprising one
30 or more coupling domain(s) of 1 to 80 amino acids comprising one or more coupling site(s) for the coupling of chemical moieties.
12. The FOLR1 binding protein according to any one of claims 1 to 11, further comprising at
35 least one diagnostically active moiety.
13. The FOLR1 binding protein according to any one of claims 1 to 11, further comprising at least one therapeutically active moiety.

14. The FOLR1 binding protein according to any one of claims 1 to 13, further comprising at least one moiety modulating pharmacokinetics.

5 15. A composition comprising a FOLR1 binding protein according to any one of claims 1 to 14.

16. A composition comprising a folate receptor alpha (FOLR1) binding protein comprising the amino acid sequence of SEQ ID NO: 2 or 30.

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17. The composition of claim 15 or 16, which is a pharmaceutical composition.

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18. Use of a FOLR1 binding protein according to claim 12 or a composition comprising said FOLR1 binding protein in the manufacture of a medicament for diagnosing a FOLR1 related tumor in a subject.

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19. Use of a FOLR1 binding protein according to claim 13 or a composition comprising said FOLR1 binding protein in the manufacture of a medicament for treating a FOLR1 related tumor in a subject.

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20. A method of producing the FOLR1 binding protein according to any one of claims 1 to 14, comprising the steps of a) culturing a host cell under conditions suitable to obtain said FOLR1 binding protein and b) isolating said FOLR1 binding protein produced.