Claims

1. A fusion protein comprising:

- domain (a) comprising a functional fragment of soluble hTRAIL protein sequence starting with amino acid in a position not lower than hTRAIL95 or a ~~homolog of said functional fragment~~ *sequence* having at least 70% sequence identity *with said functional fragment*; and

- domain (b) constituting a sequence of anti-angiogenic effector peptide *which is the inhibitor of growth factor receptor and is selected from the group of growth factor fragments consisting of VEGF fragment of SEQ. No. 17, PDGF fragment of SEQ. No. 22 and EGF fragment of SEQ. No. 23*;

wherein the sequence of domain (b) is attached at C - terminus ~~and/~~or N - terminus of domain (a)~~, and wherein effector peptide is not selected from the group consisting of calreticulin, tumstatin 183-230, kininogen D5, vasostatin, kininostatin and canstatin.~~

2. A fusion protein according to claim 1, wherein domain (a) comprises ~~a~~ *the* fragment of soluble hTRAIL ~~(SEQ. No. 16)~~ protein sequence starting with *an* amino acid ~~in a range~~ *from the range* hTRAIL95 to hTRAIL121, inclusive, and ending with *the* amino acid *hTRAIL* 281.

3. A fusion protein according to claim 1 or 2, wherein domain (a) is selected form the group consisting of hTRAIL95-281, hTRAIL119-281, hTRAIL120-281 and hTRAIL121-281.

~~4. A fusion protein according to claims 1 to 3, wherein domain (b) is selected form the group consisting of:~~

~~- inhibitors of receptors for growth factors selected from receptors for VEGF, PDGF and EGF;~~

~~- fragments of tumstatin, and~~

~~- inhibitors of aminopeptidase N (CD13).~~

~~5. A fusion protein according to claims 1 do 4, wherein domain (b) consisting of the group of inhibitors of growth factors is selected from VEGF, PDGF and EGF and consist of SEQ. No. 17, SEQ. No. 22 and SEQ. No. 23.~~

~~6. A fusion protein according to claims 1 do 4, wherein domain (b) consisting of tumstatin or fragments thereof consist of SEQ. No 18 and SEQ. No. 19 representing respectively tumstatin fragment I and tumstatin fragment II .~~

~~7. A fusion protein according to claims 1 do 4, wherein domain (b) consisting of inhibitors of aminopeptidase N (CD13) consist of SEQ. No. 20 and SEQ. No. 21.~~

4. ~~8.~~ A fusion protein according to any of the claims 1 to *3* ~~7~~, wherein the fusion

protein between the domain (a) and domain (b) contains domain (c) comprising a protease cleavage site, selected from a sequence recognized by metalloprotease MMP, a sequence recognized by urokinase uPA, and combinations thereof.

5. ~~9.~~ A fusion protein according to claim 4 ~~8~~, wherein the sequence recognized by metalloprotease MMP is SEQ. No. 24, SEQ. No. 55 or SEQ. No.56, the sequence recognized by urokinase uPA is SEQ. No. 25.

6. ~~10~~. A fusion protein according to claims 4 or 5 ~~8 or 9~~, wherein domain (c) is a combination of located next to each other sequences recognized by metalloprotease MMP and urokinase uPA.

7. ~~11~~. A fusion protein according to any of the preceding claims, wherein the protein between domains (a), (b), (c) and/or (d) comprises additionally glycine, glycine-serine or cysteine flexible steric linker or combinations thereof

8. ~~12~~. A fusion protein according to claim 7 ~~11~~, wherein flexible steric linker is selected from the group consisting of GG, E, GGGCAAACAAC (SEQ. No. 26), GGCAAACAAC (SEQ. No. 27), GGGGG (SEQ. No. 28), GGGG (SEQ. No. 29), GGG (SEQ. No. 30) and GSG (SEQ. No. 54).

~~13. A fusion protein according to claim 1, consisting of the amino acid sequence corresponding to the sequence selected form the group consisting of SEQ. No.1; SEQ. No.2; SEQ. No.3; SEQ. No.4; SEQ. No.5; SEQ. No.6; SEQ. No.7; SEQ. No.8; SEQ. No.9; SEQ. No.10; SEQ. No.11; SEQ. No.12; SEQ. No.13; SEQ. No.14; SEQ. No.15; SEQ. No.46; SEQ. No.47; SEQ. No.48, and SEQ. No.49.~~

9. ~~14~~. A fusion protein according to claim 1, consisting of the amino acid sequence corresponding to the sequence selected form the group consisting of SEQ. No.1; SEQ. No.2; SEQ. No.3; SEQ. No.4; SEQ. No.5; SEQ. No.6; SEQ. No.9; SEQ. No.10; SEQ. No.11; SEQ. No.14; SEQ. No.15; SEQ. No.46; No.47; SEQ. No.48, and SEQ. No.49.

~~15. A fusion protein according to claim 1, consisting of the amino acid sequence corresponding to the sequence selected form the group consisting of SEQ. No.7 and SEQ. No.8.~~

~~16. A fusion protein according to claim 1, consisting of the amino acid sequence corresponding to the sequence selected form the group consisting of SEQ. No.12 and SEQ. No.13.~~

10. ~~17~~. A fusion protein according to any of the preceding claims, which is a recombinant protein.

11. ~~18.~~ An *isolated* polynucleotide sequence, coding the fusion protein defined as in any preceding claims 1 to *9* ~~16~~.

12. ~~19.~~ A sequence according to claim *11* ~~18~~, optimized for genetic expression in *E. coli*.

~~20. A sequence according to claim 19, selected from the group consisting of SEQ. No.31; SEQ. No.32; SEQ. No.33; SEQ. No.34; SEQ. No.35; SEQ. No.36; SEQ. No.37; SEQ. No.38; SEQ. No.39; SEQ. No.40; SEQ. No.41; SEQ. No.42; SEQ. No.43; SEQ. No.44; SEQ. No.45; SEQ. No.50; SEQ. No.51; SEQ. No.52, and SEQ. No.53.~~

13. ~~21.~~ A sequence according to claim *12* ~~19~~, selected from the group consisting of SEQ. No.31; SEQ. No.32; SEQ. No.33; SEQ. No.34; SEQ. No.35; SEQ. No.36; SEQ. No.39; SEQ. No.40; SEQ. No.41; SEQ. No.44; SEQ. No.45; SEQ. No.50; SEQ. No.51; SEQ. No.52, and SEQ. No.53.

~~22. A sequence according to claim 19, selected from the group consisting of No.37 and SEQ. No.38.~~

~~23. A sequence according to claim 19, selected from the group consisting of SEQ. No.42 and SEQ. No.43.~~

14. ~~24.~~ An expression vector, comprising polynucleotide sequence according to any of the claims *11 to 13* ~~18 to 23~~.

15. ~~25.~~ A host cell, comprising the expression vector as defined in claim *14* ~~24~~, *wherein the host cell is not within a human body*.

16. ~~26.~~ A host cell according to claim *15* ~~25~~, which is a *E. coli* cell.

17. ~~27.~~ A pharmaceutical composition, comprising as an active ingredient the fusion protein as defined in any of the preceding claims 1 to *10* ~~17~~, in combination with any pharmaceutically acceptable carrier.

18. ~~28.~~ A pharmaceutical composition according to claim *17* ~~27~~, in a form for parenteral administration.

19. ~~29.~~ Use of a fusion protein as defined in any of the preceding claims 1 to *10* ~~17~~ for *the manufacture of a medicament for the* treatment of neoplastic diseases in mammals, including humans.

~~30. A method of treatment of cancer diseases in mammal, including human, in a need thereof, comprising administration to a subject an antineoplastic-effective amount of 27 or 28.~~