Additionally, in many cases, novel fusion proteins also overcome resistance to TRAIL.

Summary of the Disclosure

In a first aspect, there is provided 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 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 or N – terminus of domain (a).

In a second aspect, there is provided an isolated polynucleotide sequence, coding the fusion protein as defined herein.

In a third aspect, there is provided an expression vector, comprising polynucleotide sequence as defined herein.

In a fourth aspect, there is provided a host cell, comprising the expression vector as defined herein, wherein the host cell is not within a human body.

In a fifth aspect, there is provided a pharmaceutical composition, comprising as an active ingredient the fusion protein as defined herein, in combination with any pharmaceutically acceptable carrier.

In a sixth aspect, there is provided the use of a fusion protein as defined herein for the manufacture of a medicament for the treatment of neoplastic diseases in mammals, including humans.

Description of Figures

The invention will now be described in detail with reference to the Figures of the drawing.

Fig. 1 presents a schematic structure of fusion proteins of the invention according to Ex. 1, Ex. 2 , Ex. 3 , Ex. 4 , Ex. 5 and Ex. 6..

Fig. 2 presents a schematic structure of fusion proteins of the invention according to Ex. 7, Ex. 8 , Ex. 9, Ex. 10 and Ex. 11 .

Fig. 3 presents a schematic structure of fusion proteins of the invention according to Ex. 12 , Ex. 13 , Ex. 14 i Ex. 15. .

Fig. 4 shows circular dichroism spectra for rhTRAIL95-281 and fusion proteins of Ex. 1, Ex. 4Ex. 5, Ex. 9 and Ex. 14 expressed in specific ellipticity.

Fig. 5 presents tumor volume changes (% of initial stage) in Crl:CD1-Foxn1nu mice burdened with colon cancer HCT116 treated with fusion proteins of the invention of Ex. 1, Ex. 4, Ex. 5 and Ex. 9 compared to rhTRAIL114-281

Fig. 6 presents the tumor growth inhibition values (%TGI) in Crl:CD1-*Foxn1*^{nu} 1 mice burdened with colon cancer HCT116 treated with fusion proteins of the invention of z Ex. 1, Ex. 4 , Ex. 5 and Ex. 9 compared to rhTRAIL114-281.

Fig. 7 presents tumor volume changes (% of initial stage) in Crl:CD1-Foxn1nu mice burdened with lung cancer A549 treated with fusion proteins of the invention of Ex. 1 compared to rhTRAIL114-281

Fig. 8 presents the tumor growth inhibition values (%TGI) in Crl:CD1-*Foxn1*^{nu} 1 mice burdened with lung cancer A549 treated with fusion proteins of the invention of Ex. 1 compared to rhTRAIL114-281.

Fig. 9 presents a schematic structure of fusion proteins of the invention according to Ex. 16, Ex. 17 , Ex. 18 , and Ex. 19..

Fig. 10 presents tumor volume changes (% of initial stage) in Crl:CD1-Foxn1nu mice burdened with colon cancer HCT116 treated with fusion proteins of the invention from Ex. 5. , Ex. 4. Ex. 9 , and Ex. 1 compared to rhTRAIL114-281.