

intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal administration.

In one embodiment, the TRAIL receptor agonist protein is administered as a single bolus. In another embodiment, TRAIL receptor agonist protein may be administered over several divided doses. The TRAIL receptor agonist protein can be administered at about 0.1-100 mg/kg. In one embodiment, the TRAIL receptor agonist protein can be administered at a dosage selected from the group consisting of: about 0.1-0.5, 0.1-1, 0.1-10, 0.1-20, 0.1-50, 0.1-75, 1-10, 1-15, 1-7.5, 1.25-15, 1.25-7.5, 2.5-7.5, 2.5-15, 5-15, 5-7.5, 1-20, 1-50, 7-75, 1-100, 5-10, 5-15, 5-20, 5-25, 5-50, 5-75, 10-20, 10-50, 10-75, and 10-100 mg/kg. In other embodiments, the TRAIL receptor agonist protein is present in pharmaceutical compositions at about 0.1-100 mg/ml. In one embodiment, the TRAIL receptor agonist protein is present in pharmaceutical compositions at an amount selected from the group consisting of: about 0.1-0.5, 0.1-1, 0.1-10, 0.1-20, 0.1-50, 0.1-75, 1-10, 1-20, 1-50, 1-75, 1-100, 5-10, 5-15, 5-20, 5-25, 5-50, 5-75, 10-20, 10-50, 10-75, or 10-100 mg/ml. In other embodiments, a therapeutically effective amount of TRAIL receptor agonist protein is administered to a subject. In another embodiment, a prophylactically effective amount of TRAIL receptor agonist protein is administered to a subject.

In another aspect, the present invention provides the use of an effective amount of the TRAIL receptor agonist protein as disclosed herein in the manufacture of a medicament for treating a subject having a TRAIL-associated disease or disorder.

Description of the Figures

Figure 1 Domain structure of a single-chain fusion polypeptide comprising three TRAIL domains. I., II., III. Soluble TRAIL domains.

Figure 2 Schematic picture representing the general structure of TRAIL.

- ■ ■ Cell membrane, N-terminus located within the cell,
- 1. anti-parallel β -fold of receptor-binding domain (RBD),
- 2. interface of RBD and cell membrane,
- 3. protease cleavage site.

11. A cell comprising the nucleic acid molecule of claim 9.
12. The cell of claim 11, which is a eukaryotic cell.
13. The cell of claim 11, wherein the cell is a mammalian cell.
14. The cell of claim 11, wherein the cell is a Chinese Hamster Ovary (CHO) cell.
15. ~~A method of treating a subject having a TRAIL-associated disease or disorder, the method comprising administering to the subject~~Use of an effective amount of the TRAIL receptor agonist protein of any one of claims 1-7 in the manufacture of a medicament for treating a subject having a TRAIL-associated disease or disorder.
16. The ~~method~~use of claim 15, wherein the disease or disorder is selected from the group consisting of: tumors, infectious diseases, inflammatory diseases, metabolic diseases, autoimmune disorders, degenerative diseases, apoptosis-associated diseases, and transplant rejections.
17. The ~~method~~use of claim 16, wherein the tumors are solid tumors.
18. The ~~method~~use of claim 16, wherein the tumors are lymphatic tumors.
19. The ~~method~~use of claim 16, wherein the autoimmune disorders are rheumatoid diseases, arthritic diseases, or rheumatoid and arthritic diseases.
20. The ~~method~~use of claim 16, wherein the disease or disorder is rheumatoid arthritis.
21. The ~~method~~use of claim 16, wherein the degenerative disease is a neurodegenerative disease.
22. The ~~method~~use of claim 16, wherein the neurodegenerative disease is multiple sclerosis.