

Claims

[Claim 1]

A pharmaceutical composition for use in preventing or treating cancer, comprising, as an active ingredient,

a fusion protein dimer comprising a CD80 protein fragment, and a variant of IL-2 protein,

wherein the fusion protein dimer is to be administered in combination with an anticancer agent,

and wherein the fusion protein is represented as following structural formula (I):

$N'-X-[linker(1)]_n-Fc\ domain-[linker(2)]_m-Y-C'$ (I)

wherein,

N' is the N-terminus of the fusion protein,

C' is the C-terminus of the fusion protein,

X is the CD80 fragment, wherein the CD80 fragment is an extracellular domain of CD80 protein consisting of the 35th to 242nd amino acid of SEQ ID NO: 11;

Y is the variant of IL-2 protein comprising substitutions of R38A and F42A in the amino acid of SEQ ID NO: 10,

the linker (1) is a peptide linker consisting of 30 amino acids,

the linker (2) is a peptide linker consisting of 5 amino acids,

n and m are 1.

[Claim 2]

A pharmaceutical composition for use in preventing or treating cancer, comprising an anticancer agent as an active ingredient,

wherein the anticancer agent is to be administered in combination with a fusion protein dimer comprising a CD80 protein fragment and a variant of IL-2 protein,

and wherein the fusion protein is represented as following structural formula (I):

$N'-X-[linker(1)]_n-Fc\ domain-[linker(2)]_m-Y-C'$ (I)

wherein,

N' is the N-terminus of the fusion protein,

C' is the C-terminus of the fusion protein,

X is the CD80 fragment, wherein the CD80 fragment is an extracellular domain of

CD80 protein consisting of the 35th to 242nd amino acid of SEQ ID NO: 11;

Y is the variant of IL-2 protein comprising substitutions of R38A and F42A in the amino acid of SEQ ID NO: 10,

the linker (1) is a peptide linker consisting of 30 amino acids,

the linker (2) is a peptide linker consisting of 5 amino acids,

n and m are 1.

[Claim 3]

The pharmaceutical composition of claim 1, wherein the anticancer agent is any one selected from the group consisting of an anticancer chemotherapeutic agent, a target anticancer agent, an anticancer virus, an antibody therapeutic agent, a cell therapeutic agent, and an immune checkpoint inhibitor.

[Claim 4]

The pharmaceutical composition of claim 3, wherein the anticancer chemotherapeutic agent is any one selected from the group consisting of an alkylating agent, a microtubule inhibitor, an anti-metabolite, and a topoisomerase inhibitor.

[Claim 5]

The pharmaceutical composition of claim 4, wherein the anticancer chemotherapeutic agent is any one selected from the group consisting of Mechlorethamine, Cyclophosphamide, Ifosfamide, Melphalan, Chlorambucil, Thiotepa, Altretamine, Procarbazine, Busulfan, Streptozocin, Carmustine, Lomustine, Dacarbazine, Cisplatin, Carboplatin, Oxaliplatin, Docetaxel, Velban, Oncovin, Navelbine, Fluorouracil, Capecitabine, Cytarabine, Gemcitabine, Fludarabine, Methotrexate, Pemetrexed, Hycamtin, Camptosar, Vepesid, Paclitaxel, Blenoxane, Adriamycin, and Cerubidine.

[Claim 6]

The pharmaceutical composition of claim 3, wherein the target anticancer agent targets any one protein selected from the group consisting of EGFR, VEGFR, CD20, CD38, RNAK-L, BTK, Bcr-abl, PDGFR/FGFR family, MEK/RAF, HER2/Neu, Ubiquitin, JAK, ALK, PARP, TGFβR, Proteasome, Bcl-2, C-Met, VR1, VR2, VR3, c-kit, AXL, RET, Braf, DNMT, CDK4/6,

and STING.

[Claim 7]

The pharmaceutical composition of claim 6, wherein the target anticancer agent is any one selected from the group consisting of Cetuximab, Trastuzumab, Pertuzumab, Axitinib, Lenvatinib, Bevacizumab, Ramucirumab, Afibercept, Rituximab, Obinutuzumab, Daratumumab, Denosumab, Ibrutinib, Dasatinib, Nilotinib, Imatinib, Bosutinib, Galunisertib, Vactosertib, Nintedanib, Sunitinib, Sorafenib, Cabozantinib, Regorafenib, Masitinib, Semaxanib, Tivozanib, Vandetanib, Pazopanib, Trametinib, Dabrafenib, Afatinib, Lapatinib, Neratinib, Lenalidomide, Ixazomib, Ruxolitinib, Lestaurtinib, Pacritinib, Cobimethinib, Selumetinib, Trametinib, Binimetinib, Alectinib, Crizotinib, Venetoclax, Crizotinib, Cabozantinib, Bemcentinib, Gilteritinib, Selpercatinib, Pralsetinib, Vemurafenib, Olaparib, Talazoparib, Niraparib, Rucaparib, Azacitidine, Decitabine, Guadecitabine, Abemaciclib, Ribociclib, Palbociclib, CDNs, SB11285, and DMXAA.

[Claim 8]

The pharmaceutical composition of claim 3, wherein the anticancer virus is any one selected from the group consisting of Talimogenem and Laherparepvec.

[Claim 9]

The pharmaceutical composition of claim 3, wherein the antibody therapeutic agent is any one selected from the group consisting of Cetuximab, Trastuzumab, Pertuzumab, Panitumumab, Emtansine, Rituximab, Daratumumab, Denosumab, Ibritumomab, Tositumomab, Brentuximab, Ofatumumab, Obinutuzumab, Necitumumab, Bevacizumab, Ramucirumab, Nivolumab, Pembrolizumab, Atezolizumab, Durvalumab, and Ipilimumab.

[Claim 10]

The pharmaceutical composition of claim 3, wherein the cell therapeutic agent is any one selected from the group consisting of Tisagenlecleucel and Axicabtagene Ciloleucel.

[Claim 11]

The pharmaceutical composition of claim 3, wherein the immune checkpoint inhibitor

is any one selected from the group consisting of an anti-CTLA-4 antibody, an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-PD-L2 antibody, an anti-B7-H4 antibody, an anti-HVEM antibody, an anti-TIM3 antibody, an anti-GAL9 antibody, an anti-LAG3 antibody, an anti-VISTA antibody, an anti-KIR antibody, an anti-BTLA antibody, and an anti-TIGIT antibody.

[Claim 12]

The pharmaceutical composition of claim 11, wherein the immune checkpoint inhibitor is any one selected from the group consisting of Ipilimumab, Pembrolizumab, Nivolumab, Cemiplimab, Atezolizumab, Avelumab, and Durvalumab.

[Claim 13]

The pharmaceutical composition of claim 1, wherein the cancer is any one selected from the group consisting of gastric cancer, liver cancer, lung cancer, colorectal cancer, breast cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer, thyroid cancer, laryngeal cancer, acute myeloid leukemia, brain tumor, neuroblastoma, retinoblastoma, head and neck cancer, salivary gland cancer, and lymphoma.

[Claim 14]

The pharmaceutical composition of claim 1, wherein the anticancer agent is an anticancer chemotherapeutic agent and a target anticancer agent; an anticancer chemotherapeutic agent and an immune checkpoint inhibitor; or an anticancer chemotherapeutic agent, a target anticancer agent, and an immune checkpoint inhibitor.

[Claim 15]

Use of a composition comprising a fusion protein dimer comprising a CD80 protein fragment and a variant of IL-2 protein in the manufacture of a medicament for the prevention or treatment of cancer,

wherein the fusion protein dimer is to be administered in combination with an anticancer agent,

and wherein the fusion protein is represented as following structural formula (I):

N'-X-[linker (1)]n-Fc domain-[linker (2)]m-Y-C' (I)

wherein,

N' is the N-terminus of the fusion protein,

C' is the C-terminus of the fusion protein,

X is the CD80 fragment, wherein the CD80 fragment is an extracellular domain of CD80 protein consisting of the 35th to 242nd amino acid of SEQ ID NO: 11;

Y is the variant of IL-2 protein comprising substitutions of R38A and F42A in the amino acid of SEQ ID NO: 10,

the linker (1) is a peptide linker consisting of 30 amino acids,

the linker (2) is a peptide linker consisting of 5 amino acids,

n and m are 1.

[Claim 16]

Use of a composition comprising an anticancer agent in the manufacture of a medicament for the prevention or treatment of cancer,

wherein the anticancer agent is to be administered in combination with a fusion protein dimer comprising a CD80 protein fragment and a variant of IL-2 protein,

and wherein the fusion protein is represented as following structural formula (I):

N'-X-[linker (1)]n-Fc domain-[linker (2)]m-Y-C' (I)

wherein,

N' is the N-terminus of the fusion protein,

C' is the C-terminus of the fusion protein,

X is the CD80 fragment, wherein the CD80 fragment is an extracellular domain of CD80 protein consisting of the 35th to 242nd amino acid of SEQ ID NO: 11;

Y is the variant of IL-2 protein comprising substitutions of R38A and F42A in the amino acid of SEQ ID NO: 10,

the linker (1) is a peptide linker consisting of 30 amino acids,

the linker (2) is a peptide linker consisting of 5 amino acids,

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