thereof according to any one of Example [1] to Example [28], a nucleic acid molecule according to Example [29], a vector according to Example [30], and a recombinant cell according to Example [31] when culturing the cells.

Example [46] The method according to Example [45], wherein said contacting is carried out for the purpose of promoting growth or inducing differentiation of the vertebrate-derived cells.

Example [47] The method according to Example [45] or Example [46], wherein the anti-IGF-I receptor antibody, fragment, or derivative is adsorbed by, or immobilized to, a solid phase.

Example [48] A transgenic animal comprising an IGF-I receptor gene which has been mutated in a CR domain thereof via gene engineering such that the CR domain includes an amino acid sequence represented by ProSerGlyPheIleArgAsnGlySerGlnSerMet.

Example [49] A transgenic animal into which a heterologous IGF-I receptor gene has been transfected, wherein the amino acid sequence encoded by the heterologous IGF-I receptor gene differs from the amino acid sequence encoded by the animal's inherent IGF-I receptor gene in amino acid residue(s) X_1 and/or X_2 of a sequence represented by ProSerGlyPheIleArgAsnX_1X_2GlnSerMet in a CR domain.

Example [50] In one aspect, the present disclosure refers to an anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof which specifically binds to binding sites in the CR domain including the amino acids at positions 315 and 316 of an amino acid sequence of a wild-type human IGF-I receptor defined in SEQ ID NO:2, and exhibits an activity to induce growth of human-derived cells, and consisting of an amino acid sequence comprising: as a heavy chain variable region CDR-1 (CDR-H1) sequence, an amino acid sequence defined in SEQ ID NO:3; as a heavy chain variable region CDR-2 (CDR-H2) sequence, an amino acid sequence defined in SEQ ID NO:4; as a heavy chain variable region CDR-3 (CDR-H3) sequence, an amino acid sequence defined in SEQ ID NO:5; as a light chain variable region CDR-1 (CDR-L1) sequence, an amino acid sequence defined in SEQ ID NO:6; as a light chain variable region CDR-2 (CDR-L2) sequence, an amino acid sequence defined in SEQ ID NO:7; and as a light chain variable region CDR-3 (CDR-L3) sequence, an amino acid sequence defined in SEQ ID NO:8.

Example [51] In another aspect, the present disclosure refers to a nucleic acid molecule consisting of a polynucleotide sequence encoding an anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof as described herein.

Example [52] In another aspect, the present disclosure refers to a cloning vector or expression

vector comprising at least one nucleic acid molecule as described herein.

Example [53] In another aspect, the present disclosure refers to a recombinant cell derived from a host cell via transfection of a vector as described herein.

Example [54] In another aspect, the present disclosure refers to a process of producing an anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof as described herein, comprising: culturing a recombinant cell as described herein; and
purifying the anti-IGF-I receptor antibody, fragment, or derivative produced from the recombinant cell.

Example [55] In another aspect, the present disclosure refers to a pharmaceutical composition comprising an anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof as described herein, a nucleic acid molecule as described herein, a vector as described herein, or a recombinant cell as described herein.

Example [56] In yet another aspect, the present disclosure refers to an anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof as described herein, a nucleic acid molecule as described herein, a vector as described herein, or a recombinant cell as described herein for use in therapy.

Example [57] In yet another aspect, the present disclosure refers to a use of the anti-IGF-I receptor antibody or its antigen binding fragment or the derivative thereof as described herein, the nucleic acid molecule as described herein, the vector as described herein, or the recombinant cell as described herein in the manufacture of a medicament for the treatment or prevention of a condition associated with IGF-I, wherein said condition is selected from the group consisting of: disuse muscle atrophy, dwarfism, diabetic nephropathy, chronic renal failure, Laron syndrome, hepatic cirrhosis, hepatic fibrosis, intrauterine growth restriction (IUGR), neurological disease, cerebral stroke, spinal cord injury, cardiovascular protection, diabetes, insulin resistant, metabolic syndrome, osteoporosis, cystic fibrosis, wound healing, myotonic dystrophy, AIDS-associated sarcopenia, HIV-associated fat redistribution syndrome, burn, Crohn's disease, Werner's syndrome, X-linked combined immunodeficiency disease, hearing loss, anorexia nervosa and retinopathy of prematurity, Turner's syndrome, Prader-Willi syndrome, Silver-Russell syndrome, idiopathic short stature, obesity, multiple sclerosis, fibromyalgia, ulcerous colitis, low muscle mass, myocardial ischemia and decreased bone density.

Example [58] In yet another aspect, the present disclosure refers to a use of the anti-IGF-I receptor antibody or its antigen binding fragment or the derivative thereof as described herein, the nucleic acid molecule as described herein, the vector as described herein, or the recombinant cell as described herein in the manufacture of a medicament for the treatment or prevention of a disease caused by an effect of IGF-I or IGF-II on an IGF-I receptor, wherein said disease is selected from the group consisting of: liver cancer, neuroblastoma, striated muscle sarcoma,

bone cancer, childhood cancer, acromegalia, ovary cancer, pancreas cancer, benignant prostatic hypertrophy, breast cancer, prostate cancer, bone cancer, lung cancer, colorectal cancer, cervix cancer, synovial sarcoma, urinary bladder cancer, stomach cancer, Wilms' tumor, diarrhea associated with metastatic carcinoid and vasoactive intestinal peptide secreting tumor, vipoma, Verner-Morrison syndrome, Beckwith-Wiedemann syndrome, kidney cancer, renal cell cancer, transitional cell cancer, Ewing's sarcoma, leukemia, acute ymphoblastic leukemia, brain tumor, glioblastoma, non-glioblastomatic brain tumor, meningioma, pituitary adenoma, vestibular schwannoma, primitive neuroectodermal tumor, medulloblastoma, astrocytoma, oligodendroglioma, ependymoma, choroid plexus papilloma, gigantism, psoriasis, atherosclerosis, vascular smooth muscle restenosis, inappropriate microvascular growth, diabetic retinopathy, Graves' disease, multiple sclerosis, systemic lupus erythematosus, chronic thyroiditis, myasthenia gravis, autoimmune thyroiditis and Behcet's disease.

EFFECT OF THE DISCLOSURE

[0019]

The anti-IGF-I receptor antibody or its fragment or a derivative thereof according to the present disclosure has an effect of specifically binding to an IGF-I receptor of a vertebrate.

BRIEF EXPLANATION OF THE DRAWINGS

[0020]

Figure 1 illustrates aligned amino acid sequences of CR domains of the mouse, rat, human, guinea pig and rabbit IGF-I receptors, in which the amino acid sequences are indicated using the one letter code;

Figure 2 is a graph indicating the results of ELISA using variants of a presumptive epitope of IGF11-16;

Figure 3 is a graph indicating the growth activity of human myoblasts after removal of IGF11-16 and IGF-I;

Figure 4 is a graph indicating the glucose uptake effect by human differentiated muscle cells after addition of IGF-I and IGF11-16;

Figure 5 is a graph indicating the weights of extensor digitorum longus muscles of guinea pigs which received sustained administration of IGF-I using an osmotic pump for two weeks or

CLAIMS

[Claim 1]
An anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof which specifically binds to binding sites in the CR domain including the amino acids at positions 315 and 316 of an amino acid sequence of a wild-type human IGF-I receptor defined in SEQ ID NO:2, and exhibits an activity to induce growth of human-derived cells, and consisting of an amino acid sequence comprising:
as a heavy chain variable region CDR-1 (CDR-H1) sequence, an amino acid sequence defined in SEQ ID NO:3;
as a heavy chain variable region CDR-2 (CDR-H2) sequence, an amino acid sequence defined in SEQ ID NO:4;
as a heavy chain variable region CDR-3 (CDR-H3) sequence, an amino acid sequence defined in SEQ ID NO:5;
as a light chain variable region CDR-1 (CDR-L1) sequence, an amino acid sequence defined in SEQ ID NO:6;
as a light chain variable region CDR-2 (CDR-L2) sequence, an amino acid sequence defined in SEQ ID NO:7; and
as a light chain variable region CDR-3 (CDR-L3) sequence, an amino acid sequence defined in SEQ ID NO:8.

[Claim 2]
The anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof according to claim 1 further comprises a framework sequence of immunoglobulin.

[Claim 3]
The anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof according to claim 2, wherein the framework sequence of immunoglobulin is a framework sequence of each class of immunoglobulin from a human or a non-human animal including a guinea pig, a monkey, a rabbit, a cow, a pig, a horse, a sheep, a dog, a fowl, a mouse, or a rat.

[Claim 4]
The anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof according to any one of claims 1 to 3, which consists of an amino acid sequence comprising:
as a heavy chain variable region, an amino acid sequence defined in SEQ ID NO:9 or an amino acid sequence having a similarity of 90% or more to SEQ ID NO:9; and

as a light chain variable region, an amino acid sequence defined in SEQ ID NO:10 or an amino acid sequence having a similarity of 90% or more to SEQ ID NO:10.

[Claim 5]
The anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof according to any one of claims 1 to 4 further comprising a constant region of each class of immunoglobulin a human or a non-human animal including a guinea pig, a monkey, a rabbit, a cow, a pig, a horse, a sheep, a dog, a fowl, a mouse, or a rat.

[Claim 6]
The anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof according to any one of claims 1 to 5, which is a Fab, scFv, diabody or bispecific antibody, or a derivative thereof.

[Claim 7]
A nucleic acid molecule consisting of a polynucleotide sequence encoding an anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof according to any one of claims 1 to 6.

[Claim 8]
A cloning vector or expression vector comprising at least one nucleic acid molecule according to claim 7.

[Claim 9]
A recombinant cell derived from a host cell via transfection of a vector according to claim 8.

[Claim 10]
A process of producing an anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof according to any one of claims 1 to 6, comprising:
culturing a recombinant cell according to claim 9; and
purifying the anti-IGF-I receptor antibody, fragment, or derivative produced from the recombinant cell.

[Claim 11]
A pharmaceutical composition comprising an anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof according to any one of claims 1 to 6, a nucleic acid molecule according to claim 7, a vector according to claim 8, or a recombinant cell

according to claim 9.

[Claim 12]
The pharmaceutical composition according to claim 11, further comprising an additional active ingredient other than the anti-IGF-I receptor antibody, antigen binding fragment, or derivative according to any one of claims 1 to 6, the nucleic acid molecule according to claim 7, the vector according to claim 8, or the recombinant cell according to claim 9.

[Claim 13]
The pharmaceutical composition according to claim 12, wherein the active ingredient is one or more selected from a growth hormone or an analog thereof, insulin or an analog thereof, IGF-II or an analog thereof, an anti-myostatin antibody, a myostatin antagonist, an anti-activin type IIB receptor antibody, an activin type IIB receptor antagonist, a soluble activin type IIB receptor or an analog thereof, ghrelin or an analog thereof, follistatin or an analog thereof, a beta 2 agonist, and a selective androgen receptor modulator.

[Claim 14]
The pharmaceutical composition according to claim 12 or 13, wherein the active ingredient comprises an ingredient selected from the group consisting of: corticosteroid, ondansetron hydrochloride, granisetron hydrochloride, metoclopramide, domperidone, haloperidol, cyclizine, lorazepam, prochlorperazine, dexamethasone, levomepromazine, tropisetron, GM-CSF inhibitor, GM-CSF DNA vaccine, dendritic cell vaccine, recombinant virus vaccine, heat shock protein (HSP) vaccine, homologous tumor vaccine, autologous tumor vaccine, ibuprofen, naproxen, choline magnesium trisalicylate, oxycodone hydrochloride, anti-angiogenic, antithrombotic, anti-PD-1 antibody, nivolumab, pembrolizumab, anti-PD-L1 antibody, atezolizumab, anti-CTLA4 antibody, ipilimumab, anti-CD20 antibody, rituximab, anti-HER2 antibody, trastuzumab, anti-CCR4 antibody, mogamulizumab, anti-VEGF antibody, bevacizumab, anti-VEGF receptor antibody, soluble VEGF receptor fragment, anti-TWEAK antibody, anti-TWEAK receptor antibody, soluble TWEAK receptor fragment, AMG 706, AMG 386, farnesyl protein transferase inhibitor, alpha v beta 3 inhibitor, alpha v beta 5 inhibitor, p53 inhibitor, Kit receptor inhibitor, ret receptor inhibitor, PDGFR inhibitor, growth hormone secretion inhibitor, angiopoietin inhibitor, tumor-infiltrating macrophage inhibitor, c-fms inhibitor, anti-c-fms antibody, CSF-1 inhibitor, anti-CSF-1 antibody, soluble c-fms fragment, pegvisomant, gemcitabine, panitumumab, irinotecan, and SN-38.

[Claim 15]
An anti-IGF-I receptor antibody or its antigen binding fragment or a derivative thereof according to any one of claims 1 to 6, a nucleic acid molecule according to claim 7, a vector according to claim 8, or a recombinant cell according to claim 9 for use in therapy.

[Claim 16]
Use of the anti-IGF-I receptor antibody or its antigen binding fragment or the derivative thereof according to any one of claims 1 to 6, the nucleic acid molecule according to claim 7, the vector according to claim 8, or the recombinant cell according to claim 9 in the manufacture of a medicament for the treatment or prevention of a condition associated with IGF-I, wherein said condition is selected from the group consisting of: disuse muscle atrophy, dwarfism, diabetic nephropathy, chronic renal failure, Laron syndrome, hepatic cirrhosis, hepatic fibrosis, intrauterine growth restriction (IUGR), neurological disease, cerebral stroke, spinal cord injury, cardiovascular protection, diabetes, insulin resistant, metabolic syndrome, osteoporosis, cystic fibrosis, wound healing, myotonic dystrophy, AIDS-associated sarcopenia, HIV-associated fat redistribution syndrome, burn, Crohn's disease, Werner's syndrome, X-linked combined immunodeficiency disease, hearing loss, anorexia nervosa and retinopathy of prematurity, Turner's syndrome, Prader-Willi syndrome, Silver-Russell syndrome, idiopathic short stature, obesity, multiple sclerosis, fibromyalgia, ulcerous colitis, low muscle mass, myocardial ischemia and decreased bone density.

[Claim 17]
The use according to claim 16, wherein the medicament is to be parenterally administered.

[Claim 18]
Use of the anti-IGF-I receptor antibody or its antigen binding fragment or the derivative thereof according to any one of claims 1 to 6, the nucleic acid molecule according to claim 7, the vector according to claim 8, or the recombinant cell according to claim 9 in the manufacture of a medicament for the treatment or prevention of a disease caused by an effect of IGF-I or IGF-II on an IGF-I receptor, wherein said disease is selected from the group consisting of: liver cancer, neuroblastoma, striated muscle sarcoma, bone cancer, childhood cancer, acromegalia, ovary cancer, pancreas cancer, benignant prostatic hypertrophy, breast cancer, prostate cancer, bone cancer, lung cancer, colorectal cancer, cervix cancer, synovial sarcoma, urinary bladder cancer, stomach cancer, Wilms' tumor, diarrhea associated with metastatic carcinoid and vasoactive intestinal peptide secreting tumor, vipoma, Verner-Morrison syndrome, Beckwith-Wiedemann syndrome, kidney cancer, renal cell cancer, transitional cell cancer, Ewing's sarcoma, leukemia, acute

ymphoblastic leukemia, brain tumor, glioblastoma, non-glioblastomatic brain tumor, meningioma, pituitary adenoma, vestibular schwannoma, primitive neuroectodermal tumor, medulloblastoma, astrocytoma, oligodendroglioma, ependymoma, choroid plexus papilloma, gigantism, psoriasis, atherosclerosis, vascular smooth muscle restenosis, inappropriate microvascular growth, diabetic retinopathy, Graves' disease, multiple sclerosis, systemic lupus erythematosus, chronic thyroiditis, myasthenia gravis, autoimmune thyroiditis and Behcet's disease.