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[Non-Patent Literature 35] Kato, H., et al., Role of tyrosine kinase activity in signal transduction by the insulin-like growth factor-I (IGF-I) receptor. Characterization of kinase-deficient IGF-I receptors and the action of an IGF-I-mimetic antibody (alpha IR-3). *J Biol Chem*, 1993. 268(4): p. 2655-61.

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[Non-Patent Literature 37] de Bono J.S., et al., Phase II randomized study of figitumumab plus docetaxel and docetaxel alone with crossover for metastatic castration-resistant prostate cancer. *Clin Cancer Res.*, 2014.20(7): p.1925-34.

SUMMARY OF INVENTION

[0031a]

In one aspect, provided herein is an anti-IGF-I receptor humanized antibody or its fragment or a derivative thereof comprising:

as a sequence of CDR-1 of the heavy chain variable region (CDR-H1), the amino acid sequence defined in SEQ ID NO:1, or an amino acid sequence derived from the amino acid sequence defined in SEQ ID NO:1 via substitution of one amino acid residue;

as a sequence of CDR-2 of the heavy chain variable region (CDR-H2), the amino acid sequence defined in SEQ ID NO:2, or an amino acid sequence derived from the amino acid sequence defined in SEQ ID NO:2 via substitution of one or two amino acid residues;

as a sequence of CDR-3 of the heavy chain variable region (CDR-H3), the amino acid sequence defined in SEQ ID NO:3, or an amino acid sequence derived from the amino acid sequence defined in SEQ ID NO:3 via substitution of one or two amino acid residues;

as a sequence of CDR-1 of the light chain variable region (CDR-L1), the amino acid sequence defined in SEQ ID NO:4, or an amino acid sequence derived from the amino acid sequence defined in SEQ ID NO:4 via substitution of one or two amino acid residues;

as a sequence of CDR-2 of the light chain variable region (CDR-L2), the amino acid sequence defined in SEQ ID NO:5, or an amino acid sequence derived from the amino acid sequence defined in SEQ ID NO:5 via substitution of one amino acid residue; and

as a sequence of CDR-3 of the light chain variable region (CDR-L3), the amino acid sequence defined in SEQ ID NO:6, or an amino acid sequence derived from the amino acid sequence defined in SEQ ID NO:6 via substitution of one or two amino acid residues;

wherein the antibody, fragment, or derivative thereof specifically binds to a binding region containing the amino acid residues at positions 315 and 316 in the amino acid sequence of SEQ ID NO:14 (human IGF-I receptor).

[0031b]

In another aspect, provided herein is a nucleic acid molecule consisting of a polynucleotide sequence encoding an anti-IGF-I receptor humanized antibody or its fragment or a derivative thereof as described herein.

[0031c]

In another aspect, provided herein is a cloning vector or expression vector comprising at least one nucleic acid molecule as described herein.

[0031d]

In another aspect, provided herein is a recombinant cell derived by introducing a vector as described herein into a host cell.

[0031e]

In another aspect, provided herein is a process of producing an anti-IGF-I receptor humanized antibody or its fragment or a derivative thereof as described herein, comprising:

- culturing a recombinant cell as described herein; and
- purifying an anti-IGF-I receptor humanized antibody or its fragment or a derivative thereof produced by the recombinant cell.

[0031f]

In another aspect, provided herein is a pharmaceutical composition comprising, as an active ingredient, an anti-IGF-I receptor humanized antibody or its 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.

[0031g]

In another aspect, provided herein is use of a pharmaceutical composition as described herein in the manufacture of a medicament for the treatment of muscle atrophic disease or dwarfism.

[0031h]

In another aspect, provided herein is a pharmaceutical composition as described herein for use in therapy.

PROBLEM TO BE SOLVED BY THE INVENTION

[0032]

An objective of the present invention is to provide an anti-IGF-I receptor humanized antibody or its fragment or a derivative thereof which specifically binds to an IGF-I receptor of a vertebrate. Another objective of the present invention is to provide an antibody which increases the muscle mass via the IGF-I receptor while not lowering the blood glucose level.

MEANS TO SOLVE THE PROBLEM

[0033]

The present invention relates to the following aspects:

Aspect [1]

An anti-IGF-I receptor humanized antibody or its fragment or a derivative thereof comprising:

as a sequence of CDR-1 of the heavy chain variable region (CDR-H1), the amino acid sequence defined in SEQ ID NO:1, or an amino acid sequence derived from the amino acid sequence defined in SEQ ID NO:1 via substitution of one amino acid residue;

as a sequence of CDR-2 of the heavy chain variable region (CDR-H2), the amino acid sequence defined in SEQ ID NO:2, or an amino acid sequence derived from the amino acid sequence defined in SEQ ID NO:2 via substitution of one or two amino acid residues;