CLAIMS

[Claim 1]

~~A~~An isolated polypeptide wherein an N-terminal portion of DCTN1 protein is fused to a C-terminal portion of RET protein.

[Claim 2]

The isolated polypeptide according to claim 1, which is selected from the following (a) to (c):

(a) a polypeptide comprising the amino acid sequence represented by SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24;

(b) a polypeptide comprising an amino acid sequence wherein ~~one or several~~1 to 10 amino acids are substituted, deleted, or added in the amino acid sequence represented by SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24 ; and

(c) a polypeptide comprising an amino acid sequence that has at least 90% identity with the amino acid sequence represented by SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24.

[Claim 3]

An expression vector comprising a polynucleotide ~~encoding~~, wherein the ~~polypeptide according to claim 1 or 2.~~

~~[Claim 4]~~

~~The~~ polynucleotide ~~according to claim 3, which~~ is selected from the following (d) to (~~f~~i):

(d) a polynucleotide encoding a polypeptide comprising the amino acid sequence represented by SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ

ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24;

(e) a polynucleotide encoding a polypeptide comprising an amino acid sequence wherein ~~one or several~~1 to 10 amino acids are substituted, deleted, or added in the amino acid sequence represented by SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24; ~~and~~

(f) a polynucleotide encoding a polypeptide comprising an amino acid sequence that has at least 90% identity with the amino acid sequence represented by SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24~~.~~;

~~[Claim 5]~~

~~The polynucleotide according to claim 3, which is selected from the following (g) to (i):~~

~~(g)~~ (g) a polynucleotide comprising the base sequence represented by SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, or SEQ ID NO: 23;

~~(h)~~ (h) a polynucleotide hybridizing under stringent conditions with a polynucleotide comprising a base sequence complementary to the base sequence represented by SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, or SEQ ID NO: 23; and

(i) a polynucleotide having at least 90% identity with the base sequence represented by SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, or SEQ ID NO: 23.

[Claim 4]

A cell transfected with a polynucleotide, wherein the polynucleotide is selected from the following (d) to (i):

(d) a polynucleotide encoding a polypeptide comprising the amino acid sequence represented by SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24;

(e) a polynucleotide encoding a polypeptide comprising an amino acid sequence wherein 1 to 10 amino acids are substituted, deleted, or added in the amino acid sequence represented by SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24;

(f) a polynucleotide encoding a polypeptide comprising an amino acid sequence that has at least 90% identity with the amino acid sequence represented by SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24;

(g) a polynucleotide comprising the base sequence represented by SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, or SEQ ID NO: 23;

(h) a polynucleotide hybridizing under stringent conditions with a polynucleotide comprising a base sequence complementary to the base sequence represented by SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, or SEQ ID NO: 23; and

(i) a polynucleotide having at least 90% identity with the base sequence represented by SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, or SEQ ID NO: 23.

[Claim ~~6~~5]

An ~~expression vector comprising the polynucleotide according to any one of claims 3 to 5.~~

~~[Claim 7]~~

~~A cell transfected with the polynucleotide according to any one of claims 3 to 5.~~

~~[Claim 8]~~

~~An~~isolated antibody that specifically binds to the sequence of amino acids containing fused point which is the point of fusion of the N-terminal portion of DCTN1 protein and the C-terminal portion of RET protein in the isolated polypeptide according to claim 1 or 2.

[Claim 6]

The isolated antibody according to claim 5 wherein the point of fusion of the N-terminal portion of DCTN1 protein and the C-terminal portion of RET protein is selected below:

(1) the point at which a polypeptide having the amino acid sequence of positions 1-1233 of SEQ ID NO: 2, which is derived from the N-terminal portion of DCTN1, is fused to a polypeptide having the amino acid sequence of positions 1234-1635 of SEQ ID NO: 2, which is derived from the C- terminal portion of RET;

(2) the point at which a polypeptide having the amino acid sequence of positions 1-1233 of SEQ ID NO: 4, which is derived from the N-terminal portion of DCTN 1, is fused to a polypeptide having the amino acid sequence of positions 1234-1593 of SEQ ID NO: 4, which is derived from the C-terminal portion of RET;

(3) the point at which a polypeptide having the amino acid sequence of positions 1-1099 of SEQ ID NO: 6, which is derived from the N-terminal portion of DCTN1, is fused to a polypeptide having the amino acid sequence of positions 1100-1501 of SEQ ID NO: 6, which is derived from the C-terminal portion of RET;

(4) the point at which a polypeptide having the amino acid sequence of positions 1-1099 of SEQ ID NO: 8, which is derived from the N-terminal portion of DCTN1, is fused to a polypeptide having the amino acid sequence of positions 1100-1459 of SEQ ID NO: 8, which is derived from the C-terminal portion of RET;

(5) the point at which a polypeptide having the amino acid sequence of positions 1-1208 of SEQ ID NO: 10, which is derived from the N-terminal portion of DCTN1, is fused to a polypeptide having the amino acid sequence of positions 1209-1610 of SEQ ID NO: 10, which is derived from the C-terminal portion of RET;

(6) the point at which a polypeptide having the amino acid sequence of positions 1-1208 of SEQ ID NO: 12, which is derived from the N-terminal portion of DCTN1, is fused to a polypeptide having the amino acid sequence of positions 1209-1568 of SEQ ID NO: 12, which is derived from the C-terminal portion of RET;

(7) the point at which a polypeptide having the amino acid sequence of positions 1-1094 of SEQ ID NO: 14, which is derived from the N-terminal portion of DCTN1, is fused to a polypeptide having the amino acid sequence of positions 1095-1496 of SEQ ID NO: 14, which is derived from the C-terminal portion of RET;

(8) the point at which a polypeptide having the amino acid sequence of positions 1-1094 of SEQ ID NO: 16, which is derived from the N-terminal portion of DCTN1, is fused to a polypeptide having the amino acid sequence of positions 1095-1454 of SEQ ID NO: 16, which is derived from the C-terminal portion of RET;

(9~~)~~) the point at which a polypeptide having the amino acid sequence of positions 1-1191 of SEQ ID NO: 18, which is derived from the N-terminal portion of DCTN1, is fused to a polypeptide having the amino acid sequence of positions 1192-1593 of SEQ ID NO: 18, which is derived from the C-terminal portion of RET;

(10) the point at which a polypeptide having the amino acid sequence of positions 1-1191 of SEQ ID NO: 20, which is derived from the N-terminal portion of DCTN1, is fused to a polypeptide having the amino acid sequence of positions 1192-1551 of SEQ ID NO: 20, which is derived from the C-terminal portion of RET;

(11) the point at which a polypeptide having the amino acid sequence of positions 1-1226 of SEQ ID NO: 22, which is derived from the N-terminal portion of DCTN1, is fused to a polypeptide having the amino acid sequence of positions 1227-1628 of SEQ ID NO: 22, which is derived from the C-terminal portion of RET; or

(12) the point at which a polypeptide having the amino acid sequence of positions 1-1226 of SEQ ID NO: 24, which is derived from the N-terminal portion of DCTN1, is fused to a polypeptide having the amino acid sequence of positions 1227-1586 of SEQ ID NO: 24, which is derived from the C-terminal portion of RET.

[Claim 7]

A method for detecting the presence of ~~the polypeptide according to claim 1 or 2 in a sample.~~a fusion polypeptide in a sample, the fusion polypeptide comprising an N-terminal portion of DCTN1 protein is fused to a C-terminal portion of RET protein, comprising the following steps:

(1) contacting a sample with the isolated antibody according to claim 5 or 6; and

(2) detecting the isolated antibody fused with the sample.

[Claim ~~10~~8]

A primer or probe for detecting the presence of the polynucleotide ~~according to any one of claims 3 to 5~~encoding a fusion polypeptide comprising an N-terminal portion of DCTN1 protein is fused to a C-terminal portion of RET protein in a sample, the primer or probe being a polynucleotide selected from the following~~ (j) to (l):~~:

~~(j)~~ (i) a polynucleotide comprising the base sequence represented by SEQ ID NO: 69

(ii) a polynucleotide comprising the base sequence represented by SEQ ID NO: 70

(iii) a polynucleotide ~~that is at least one probe selected from the group consisting of probes hybridizing with~~ comprising the base sequence represented by SEQ ID NO: 71.

[Claim 9]

A method for detecting the presence of a polynucleotide encoding ~~DCTN1 protein, and probes hybridizing~~a fusion polypeptide in a sample, the fusion polypeptide comprising an N-terminal portion of

DCTN1 protein is fused to a C-terminal portion of RET protein, comprising the following steps:

1) contacting a sample with a ~~polynucleotide encoding RET protein;~~primer or probe according to Claim 8; and

~~(k) a polynucleotide that is a probe that hybridizes to a point of fusion between a polynucleotide encoding DCTN1 protein and a polynucleotide encoding RET protein; and~~

~~(l) a polynucleotide that is a set of a sense primer and an antisense primer designed to sandwich a point of fusion between a polynucleotide encoding DCTN1 protein and a polynucleotide encoding RET protein.~~

~~[Claim 11]~~

~~A method for~~ 2) detecting the ~~presence of~~primer or probe hybridized with the ~~polynucleotide according to any one of claims 3 to 5 in a~~ sample.

[Claim ~~12~~10]

A method for diagnosing cancer in a patient when the presence of ~~the~~a fusion polypeptide ~~according~~in which an N-terminal portion of DCTN1 protein is fused to ~~claim 1~~a C-terminal portion of RET protein or ~~2 or the~~a polynucleotide ~~according to any one of claims 3 to 5~~encoding the fusion polypeptide is detected in a sample derived from the patient by the detection method according to ~~claim 9~~claims 7 or ~~11~~9.

[Claim ~~13~~11]

A pharmaceutical composition when used for treating a patient having a cancer that is positive for a fusion gene of DCTN1 gene and RET gene and/or positive for a fusion protein of DCTN1 protein and RET protein, the composition comprising a compound that inhibits RET as an active ingredient.

[Claim ~~14~~12]

A method of screening for a compound that inhibits expression and/or activity of ~~the~~a fusion polypeptide ~~according~~in which an N-

terminal portion of DCTN1 protein is fused to ~~claim 1 or 2~~a C-terminal portion of RET protein or expression of ~~the~~a polynucleotide ~~according to any one of claims 3 to 5~~encoding the fusion polypeptide, the method comprising the following steps (1) and (2):

(1) the step of bringing the fusion polypeptide~~ according to claim 1 or 2~~, a cell expressing the fusion polypeptide ~~according to claim 1 or 2~~ or the polynucleotide ~~according to any one of claims 3 to 5~~encoding the fusion polypeptide, or the cell according to claim ~~7~~4 into contact with a test compound; and

(2) the step of measuring whether expression and/or activity of the fusion polypeptide~~ according to claim 1 or 2~~ or expression of the polynucleotide ~~according to any one of claims 3 to 5~~encoding the fusion polypeptide is inhibited in step (1), or the step of measuring whether growth of the cell in step (1) is inhibited.

[Claim ~~15~~13]

A method using ~~the~~a fusion polypeptide ~~according~~in which an N-terminal portion of DCTN1 protein is fused to ~~claim 1~~a C-terminal portion of RET protein or ~~2 or the~~a polynucleotide ~~according to any one of claims 3 to 5~~encoding the fusion polypeptide as an indicator for determining whether a chemotherapy using a compound that inhibits RET is effective,

the method comprising determining that the chemotherapy using the compound that inhibits RET is effective when the fusion polypeptide is detected in a sample by a detection method according to claim ~~1~~7, and/or ~~2~~when the presence of the polynucleotide encoding the fusion polypeptide is detected in a sample by the detection method according to claim 9~~, and/or when the presence of the polynucleotide according to any one of claims 3 to 5 is detected in a sample by the detection method according to claim 11~~.

[Claim ~~16~~14]

A biomarker for detecting cancer, the biomarker comprising at least one member selected from the group consisting of fusion polypeptides wherein an N-terminal portion of DCTN1 protein is fused

to a C-terminal portion of RET protein~~, and polynucleotides encoding the polypeptides~~.

[Claim ~~17~~15]

A method for treating cancer,

the method comprising

giving a chemotherapy using a compound that inhibits RET to a cancer patient who is positive for a fusion gene of DCTN1 gene and RET gene, and/or positive for a fusion protein of DCTN1 protein and RET protein.

[Claim ~~18~~16]

A method for treating cancer,

the method comprising

detecting the presence of ~~the~~a fusion polypeptide ~~according~~in which an N-terminal portion of DCTN1 protein is fused to ~~claim 1 or 2~~a C-terminal portion of RET protein, and/or the presence of ~~the~~a polynucleotide ~~according to any one of claims 3 to 5~~encoding the fusion polypeptide, in a sample derived from a test subject, and

giving a chemotherapy using a compound that inhibits RET to the test subject when the presence of the fusion polypeptide ~~according to claim 1 or 2~~ has been detected, and/or the presence of the polynucleotide ~~according to any one of claims 3 to 5~~encoding the fusion polypeptide has been detected.

[Claim ~~19~~17]

A compound that inhibits RET when used for ~~use in~~ the treatment of a cancer patient who is positive for a fusion gene of DCTN1 gene and RET gene, and/or positive for a fusion protein of DCTN1 protein and RET protein.

[Claim ~~20~~18]

Use of a compound that inhibits RET in the production of a pharmaceutical composition ~~for cancer treatment~~ for treating a cancer patient who is positive for a fusion gene of DCTN1 gene and RET gene, and/or positive for a fusion protein of DCTN1 protein and RET protein.

[Claim ~~21~~19]

A method for producing a reagent for determining whether a chemotherapy using a compound that inhibits RET is effective, using a means to detect the presence of ~~the~~a fusion polypeptide ~~according~~in which an N- terminal portion of DCTN1 protein is fused to ~~claim 1 or 2~~a C-terminal portion of RET protein in a sample~~,~~ and/or a means to detect the presence of ~~the~~a polynucleotide ~~according to any one of claims 3 to 5~~encoding the fusion polypeptide in a sample.

[Claim ~~22~~20]

A combination of an anti-DCTN1 antibody and an anti-RET antibody when used for detecting the presence of ~~the~~a fusion polypeptide in which an N-terminal portion of DCTN1 protein is fused to a C-terminal portion of RET protein and/or detecting the presence of a polynucleotide ~~according to any one of claims 3 to 5~~encoding the fusion polypeptide.

[Claim ~~23~~21]

Use of the antibody according to claim ~~8~~5, the combination of the antibodies according to claim ~~22~~20, or the primer or probe according to claim ~~10~~8 in the production of a detection reagent for detecting the presence of ~~the polypeptide according to claim 1 or 2~~, a fusion polypeptide in which an N-terminal portion of DCTN1 protein is fused to a C-terminal portion of RET protein, and/or the presence of ~~the~~a polynucleotide ~~according~~encoding the fusion polypeptide.

[Claim 22]

Use of a compound that inhibits RET in the manufacture of a medicament for treatment of cancer,

wherein the treatment is implemented by a method comprising

giving a chemotherapy using a compound that inhibits RET to a cancer patient who is positive for a fusion gene of DCTN1 gene and RET gene, and/or positive for a fusion protein of DCTN1 protein and RET protein.

[Claim 23]

Use of a compound that inhibits RET in the manufacture of a medicament for treatment of cancer,

wherein the treatment is implemented by a method comprising

detecting the presence of a fusion polypeptide in which an N-terminal portion of DCTN1 protein is fused to ~~any one of claims 3~~a C-terminal portion of RET protein and/or the presence of a polynucleotide that encodes the fusion polypeptide, in a sample derived from a test subject, and

giving a chemotherapy using a compound that inhibits RET to ~~5.~~ the test subject when the presence of the fusion polypeptide, or polynucleotide encoding the fusion polypeptide, has been detected.