only the weight of the interleukin-2 analog site in the entire conjugate.

FIG. 7 shows the evaluation results of anti-tumor efficacy of an interleukin-2 analog long-acting conjugate in pancreatic cancer animal models. FIG. 7 shows the measurement results of the tumor size of models administered a negative control and an interleukin-2 analog conjugate 86. In FIG. 7, the dose of the long-acting conjugate was based on only the weight of the interleukin-2 analog site in the entire conjugate.

FIG. 8 shows the analysis results of the immune memory response in renal cell cancer animal models administered an interleukin-2 analog long-acting conjugate. In FIG. 8, the dose of the long-acting conjugate was based on only the weight of the interleukin-2 analog site in the entire conjugate.

【Best Mode】

In accordance with an aspect of the present invention, there is provided a composition comprising a novel interleukin-2 analog (or IL-2 analog) or a long-acting conjugate thereof. The interleukin-2 (IL-2) analog has an increased binding affinity for the interleukin-2 beta receptor compared with native interleukin-2 or aldesleukin, which is an interleukin-2 analog, and may include a sequence with a modification of at least one amino acid in the native interleukin-2.

In one specific embodiment, the interleukin-2 analog may include an amino acid sequence selected from the group consisting of SEQ ID NOS: 3 to 106.

In another embodiment, the long-acting conjugate may be represented by Chemical Formula 1 below:

[Chemical Formula 1]

X - L - F

where: X is an interleukin-2 analog including any one sequence selected from amino acid sequences of SEQ ID NOS: 3 to 106;

L is a polyethylene glycol linker;

F is a dimeric immunoglobulin Fc region, and

the - symbols represent covalent linkages between X and L and between L and F, respectively,

wherein in the long-acting conjugate, one end of L is covalently linked to only one polypeptide chain of the dimeric Fc region and X is covalently linked to the other end of L.

In the composition according to any one of the previous embodiments, the long-

acting conjugate may include as a part thereof an interleukin-2 analog having an altered binding affinity for the interleukin-2 alpha receptor, and an increased binding affinity for the interleukin-2 beta receptor compared with the native interleukin-2 or aldesleukin.

In the composition according to any one of the previous embodiments, the interleukin-2 analog may have an increased binding affinity for the interleukin-2 beta receptor compared with aldesleukin.

In the composition according to any one of the previous embodiments, the interleukin-2 analog may include any one sequence selected from the group consisting of amino acid sequences of SEQ ID NOS: 10, 13-15, 17, 20-22, 32, 35, 36, 42, 53, 54, 56, 58-60, 62, 71, 72, 74-78, 85, 87, 89, 91-94, 97-106.

In the composition according to any one of the previous embodiments, the interleukin-2 analog may include any one sequence selected from the group consisting of amino acid sequences of SEQ ID NOS: 17, 22, 42, 53, 56, 58-60, 62, 71, 72, 74-77, 87, 89, 91-93, 98-101, and 103-106.

In the composition according to any one of the previous embodiments, the interleukin-2 analog may include any one sequence selected from the group consisting of amino acid sequences of SEQ ID NOS: 22, 42, 53, 87, 105, and 106.

In the composition according to any one of the previous embodiments, the interleukin-2 analog may further include at least one amino acid at the C-terminus.

In the composition according to any one of the previous embodiments, the long-acting conjugate may include an IgG4 Fc region.

In the composition according to any one of the previous embodiments, the long-acting conjugate may include an aglycosylated immunoglobulin Fc region.

In the composition according to any one of the previous embodiments, the immunoglobulin Fc region may be derived from an aglycosylated Fc region of human IgG4.

In the composition according to any one of the previous embodiments, the immunoglobulin Fc region has a structure in which two polypeptide chains are linked through a disulfide bond, wherein the two polypeptide chains are linked through only a nitrogen atom of one of the two chains.

In the composition according to any one of the previous embodiments, the immunoglobulin Fc region may include a monomer having the amino acid sequence of SEQ ID NO: 438.

In the composition according to any one of the previous embodiments, the

71, 72, 74-78, 85, 87, 89, 91-94, 97-106, but is not limited thereto.

In another specific embodiment, the interleukin-2 analog may include, consist essentially of, or consist of any one sequence selected from the group consisting of amino acid sequences of SEQ ID NOS: 17, 22, 42, 53, 56, 58-60, 62, 71, 72, 74-77, 87, 89, 91-93, 98-101, and 103-106, but is not limited thereto.

In another specific embodiment, the interleukin-2 analog may include, consist essentially of, or consist of any one sequence selected from the group consisting of amino acid sequences of SEQ ID NOS: 10, 13, 14, 15, 16, 17, 20, 21, 22, 32, 35, 36, 42, 53, 54, 56, 58, 59, 60, 62, 71, 72, 74, 75, 76, 77, 78, 85, 87, 89, 91, 92, 93, 94, 95, 98, 99, 100, 101, 103, 104, 105, and 106, but is not limited thereto.

In another specific embodiment, the interleukin-2 analog may include, consist essentially of, or consist of any one sequence selected from the group consisting of amino acid sequences of SEQ ID NOS: 10, 13, 14, 16, 17, 20, 21, 22, 32, 35, 36, 42, 53, 54, 87, 89, 91, 92, 93, 94, 98, 99, 100, 101, 103, 104, and 105, but is not limited thereto.

In another specific embodiment, the interleukin-2 analog may include, consist essentially of, or consist of any one sequence selected from the group consisting of amino acid sequences of SEQ ID NOS: 22, 42, 53, 87, 105, and 106, but is not limited thereto.

In addition, the interleukin-2 analog may further include at least one amino acid at the C-terminus, but is not limited thereto.

Although stated as “interleukin-2 analog consisting of a specific sequence number” herein, this terminology does not exclude the addition of nonsense sequences upstream or downstream of the amino acid sequence of the corresponding sequence number or naturally-occurring mutations, or silent mutations thereof, as long as the analog has the equivalent or corresponding activity to the interleukin-2 analog consisting of the amino acid sequence of the corresponding sequence number, and it is apparent that an analog having such sequence addition or mutation falls within the scope of the present invention.

The interleukin-2 analog of the present invention may include amino acid sequences having at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% homology or identity with the amino acid sequences of