concentration of 10 μg/mL, to the PBMCs (1×10^5 cells/well) and the above-described Th cell group (5×10^4 cell/well) comprising Sur/Th cells which react specifically with SU18. The resultants were co-cultured in a CO_2 incubator at 37°C for 24 hours. After the culturing, the IFN-γ contained in the culture supernatant was measured by using an ELISA kit (BD Biosciences). The results are shown in Figure 5.

[0071]

As shown in Figure 5, from the fact that IFN-γ was produced and antigen-specific reaction was observed when the overlapping peptide used was T6 (peptide in which the first two amino acids from each of the N and C terminus of SU18 were deleted), T7 (peptide in which the first one amino acid from the ~~N~~ C terminus of SU18 and the first three amino acids from the ~~C~~ N terminus of SU18 were deleted), T8 (peptide in which the first four amino acids from the ~~C~~ N terminus of SU18 were deleted), T9 (peptide in which the first five amino acids from the ~~C~~ N terminus of SU18 were deleted), T10 (peptide in which the first six amino acids from the ~~C~~ N terminus of SU18 were deleted), and T11 (peptide in which the first seven amino acids from the ~~C~~ N terminus of SU18 were deleted), it was confirmed that at least the peptide comprising the peptide of SEQ ID NO:37, GCAFLSVKKQ (G represents glycine; C cysteine; A alanine; F phenylalanine; L

performed with the PBMCs-Ad pulsed with SU18 at 1-week intervals to obtain Sur/Th cell clones.

[0074]

2) Confirmation of Recognition Site in Partially Deleted SU18

The recognition site in partially deleted SU18 was confirmed by the ELISPOT assay described below using the Sur/Th cell clones prepared in ~~this Example~~ 1) of this Example 3 and the peptides for stimulation, T1 to T10 shown in Table 3.

[0075]

[Table 3]

T1	EHKKHSSGCAFL	Sequence No. 26
T2	EHKKHSSGCAFLS	Sequence No. 27
T3	EHKKHSSGCAFLSV	Sequence No. 28
T4	EHKKHSSGCAFLSVK	Sequence No. 29
T5	HKKHSSGCAFLSVKK	Sequence No. 30
T6	KKHSSGCAFLSVKKQ	Sequence No. 31
T7	KHSSGCAFLSVKKQF	Sequence No. 32
T8	HSSGCAFLSVKKQFE	Sequence No. 33
T9	SSGCAFLSVKKQFE	Sequence No. 34
T10	SGCAFLSVKKQFE	Sequence No. 35
T11	GCAFLSVKKQFE	Sequence No. 36

[0076]

As shown in Figure 6, antigen-specific reaction was observed in T3 (peptide in which the first five amino acids from the ~~N~~ C terminus of SU18 were deleted) and T8 (peptide in which the first four amino acids from the ~~C~~ N terminus of SU18 were deleted). Hence, it was confirmed that SU18 was able to induce Survivin-specific Sur/Th cells even with deletion of the first four amino acids from the ~~C~~ N terminus or the first five amino acids from the ~~N~~ C terminus. Also, it became clear that SU18 was a polypeptide which has immunotherapeutic effect not only in patients whose HLA genotype is HLA-DRB1*0101/HLA-DRB1*0901 but also in those whose HLA genotype is HLA-DRB1*1201/HLA-DRB1*1502.

[0078]

<Example 4> Examination of HLA-DQB1*0601-Restricted SU18 Recognition Site

1) Confirmation of HLA-Restrictivity

CD4-positive T cells were prepared from the peripheral blood of healthy individual Y whose HLA genotype is HLA-DQB1*0302/HLA-DQB1*0601 by the same technique as that used in Example 1-2) and a Th cell group comprising Sur/Th cells which react specifically with SU18 was obtained by the same technique as that used in Example 1-3) and 4). HLA-restrictivity for SU18 was confirmed by using inhibitory antibodies and this Sur/Th cell group which reacts specifically with SU18.

[0079]

genotypes are HLA-DQB1*0301/HLA-DQB1*0302, HLA-DQB1*0401/HLA-DQB1*0602, HLA-DQB1*0302/HLA-DQB1*0401, and HLA-DQB1*0301/HLA-DQB1*0601. After 2-hour treatment, each resultant was co-cultured with the above-described Th cell group (5×10^4 cell/well) comprising Sur/Th cells which react specifically with SU18 in a 96-well U-bottom plate (BD Biosciences) with 200 μL of 5% human serum in AIM-V in a CO_2 incubator at 37°C for 24 hours. After the culturing, the IFN-γ contained in the culture supernatant was measured by using an ELISA kit (BD Biosciences). The results are shown in Figure 8.

[0083]

As shown in Figure 8, from the fact that IFN-g was not produced when the PBMCs whose HLA genotype is HLA-DQB1*0301/HLA-DQB1*0302 and HLA-DQB1*0302/HLA-DQB1*0401 was used and that IFN-γ was produced when the PBMC whose HLA genotype is HLA-DQB1*0301/HLA-DQB1*0601 was used, SU18 was confirmed to be restricted by HLA-DQB1*0601 among HLA-DQ.

[0084]

3) Confirmation of Recognition Site in partially deleted SU18

The recognition site in partially deleted SU18 was confirmed by using the Th cell group obtained in ~~this Example 1-1)~~ 1) of this Example 4 comprising Sur/Th cells which react specifically with SU18 and the overlapping peptides T1 to T10 shown in Table 3, which are peptides for stimulation.

[0085]

In a 96-well U-bottom plate (BD Biosciences) with 200 μL of 5% human serum in AIM-V, each of the overlapping peptides T1 to T10 was added, to a final concentration of 10 μg/mL, to the PBMCs (1×10^5 cells/well) and the above-described Th cell group (5×10^4 cell/well) comprising Sur/Th cells which react specifically with SU18. The resultants were co-cultured in a CO_2 incubator at 37°C for 24 hours. After the culturing, the IFN-γ contained in the culture supernatant was measured by using an ELISA kit (BD Biosciences). The results are shown in Figure 9.

[0086]

As shown in Figure 9, from the fact that IFN-γ was produced and antigen-specific reaction was observed when the overlapping peptide used was T3 (peptide in which the first five amino acids from the ~~N~~ C terminus of SU18 were deleted), T4 (peptide in which the first four amino acids from the ~~N~~ C terminus of SU18 were deleted), T5 (peptide in which the first three amino acids from the ~~N~~ C terminus of SU18 and the first one amino acid from the ~~C~~ N terminus of SU18 were deleted), T6 (peptide in which the first two amino acids from each of the N and C terminus of SU18 were deleted), and T7 (peptide in which the first one amino acid from the ~~N~~ C terminus of SU18 and the first three amino acids from the ~~C~~ N terminus of SU18 were deleted), it was confirmed that at least the peptide

[0089]

As shown in Figure 10, it was confirmed that IFN-γ was hardly produced when the partially substituted peptide used was S4 (peptide in which lysine, the fourth from the ~~C~~ N terminus of SU18, was substituted with alanine), S5 (peptide in which histidine, the fifth from the ~~C~~ N terminus of ~~Su18~~ SU18, was substituted with alanine), S7 (peptide in which serine, the seventh from the ~~C~~ N terminus of SU18, was substituted with alanine), and S9 (peptide in which cysteine, the ninth from the ~~C~~ N terminus of SU18, was substituted with glycine). That is, it was confirmed that at least the peptide of SEQ ID NO:55, XXXKHXSXCXXXXXXXXXX (Xaa represents any amino acid; K lysine; H histidine; S serine; and C cysteine) was able to induce Survivin-specific Sur/Th cells.

CLAIMS

1. ~~A~~ An isolated polypeptide, ~~comprising~~ consisting of any one of the amino acid sequences a) to ~~c)~~ d) below and having a cytokine-producing activity in Th cells specific to Survivin:

a) ~~An~~ the amino acid sequence represented by SEQ ID NO:17;

b) ~~An~~ the amino acid sequence in which ~~one to several tens~~ 1 to 30 of any amino acids are added to the N terminus and/or C terminus of the amino acid sequence represented by SEQ ID No:17, provided that the sequences of EEHKKHSSGCAFLSVKKQFEELTLGEFLKLDRER, and EEHKKHSSGCAFLSVKKQFEELTLSEFLKLDKER are excluded;

c) ~~An~~ the amino acid sequence in which ~~one to four~~ 1 to 3 amino acids ~~at the~~ from N terminus and/or 1 amino acid from C terminus of the amino acid sequence represented by SEQ ID No:17 are deleted;

d) ~~An~~ the amino acid sequence in which ~~one to five~~ any one of amino ~~acids at the C terminus~~ acid residues of the amino acid sequence ~~represented by~~ at the position of 1-3, 6,8,12-18 or SEQ ID No:17 ~~are deleted;~~ is substituted with alanine or amino acid residue of the amino acid sequence at the position of 10 or 11 of SEQ ID No: 17 is substituted with glycine.

~~e) An amino acid sequence in which one to several amino acid residues of the amino acid sequence represented by SEQ ID No:17 are substituted and/or deleted;~~

~~f) An amino acid sequence in which one to several tens of any amino acids are added to the N terminus and/or C terminus of an amino acid sequence in which one to several amino acid residues of the amino acid sequence represented by SEQ ID No:17 are substituted and/or deleted; and~~

~~g) An amino acid sequence in which one to five amino acids at the N terminus and/or C terminus of the amino acid sequence represented by SEQ ID No:17 are deleted, wherein one to several amino acid residues are further substituted.~~

2. The polypeptide according to claim 1, wherein a polypeptide ~~comprising~~ consisting of the amino acid ~~sequences~~ sequence b) to ~~g)~~ d) has an epitope of a polypeptide ~~comprising~~ consisting of the amino acid sequence represented by SEQ ID No:17, the epitope inducing a Th ~~cells~~ cell specific to Survivin from a CD4-positive T ~~cells~~ cell.

3. ~~A~~ An isolated nucleic acid encoding the polypeptide according to claim 1 or 2.

4. A vector comprising the nucleic acid according to claim 3.

5. An isolated antibody that specifically binds to the polypeptide ~~according to claim 1 or 2~~ consisting of the amino acid sequence represented by SEQ ID No: 17.

6. A vaccine for immunotherapy for malignant neoplasms, comprising at least one of the polypeptides according to

claims 1 and 2 as an active ingredient.

7. A method for inducing Th cells specific to Survivin, comprising a process for incubating in vitro at least one of the polypeptides according to claims 1 and 2, antigen-presenting cells and CD4-positive T cells.

8. A therapeutic agent for malignant neoplasms, comprising the polypeptide according to claim 1 or 2 and Th cells specific to the polypeptide or Survivin.