PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OR PREVENTION OF A MALIGNANT TUMOR

The present invention relates to a pharmaceutical composition intended for the curative treatment or the prevention of a malignant tumor, more especially of a carcinoma and most especially of a breast cancer.

Most tumor cells express antigens at their surface which differ either qualitatively or quantitatively from the antigens present at the surface of the corresponding normal cells. These antigens are specific when they are expressed only by tumor cells. When they are present on both normal and tumor cells, these antigens are said to be associated with the tumor; in this case, they are present either in larger amounts or in a different form in the tumor cells.

The large majority of tumor antigens which have been characterized to date in man are human antigens associated with a tumor (hereinafter referred to as associated antigens). Among these, the following may be highlighted:

- oncofetal antigens, such as carcinoembryonic antigen, which are present in fetal tissues and absent or in the trace state in the corresponding adult tissues; their expression is induced again in an aberrant manner during the development of a tumor;

- differentiation antigens, which are normally expressed only during certain stages of maturation of a particular cell type; tumor cells which express such an antigen are considered to have their origin in a cell blocked in its differentiation;

- the products of oncogenes which are beginning to be identified.

The specificity of an antigen associated with a tumor is hence quantitative rather than qualitative, since it may be present in a normal individual in a localized manner or intermittently (feto-embryonic period) or in the trace state, and becomes hyperexpressed (expression increased by a factor of 10 to 1000 times)

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only during a process of tumorigenesis. When this antigen is expressed normally, it is recognized by the immune system as part of the "Self", while its hyperexpression or its aberrant expression can trigger a humoral or cellular immune response.

Generally speaking, there are two major types of immune response: the humoral type response which is characterized by the production of antibodies by B lymphocytes, and the cell-mediated immune response which involves effector cells, i.e. essentially macrophages and cytotoxic T lymphocytes, as well as cells that regulate the immune response, i.e. helper and suppressor T lymphocytes.

A cell-mediated immune response necessitates the cooperation of helper T lymphocytes and effector cells. This cooperation takes place, in particular, as a result of interleukin-2 and various other lymphokines which are secreted by activated helper T lymphocytes. Interleukin-2 thereafter induces the action of cytotoxic T lymphocytes, and the lymphokines trigger the phagocytosis response of the macrophages. Concomitantly, there likewise exists a mechanism that suppresses the cell-mediated immune response which employs suppressor T lymphocytes.

It is now well known that patients suffering from a cancer may develop a humoral and cell-mediated immune response. This has been revealed, in particular, by demonstrating that the serum of some patients contained anti-tumor antigen antibodies, and that their serum was capable of inhibiting the growth of cancer cells in vitro. Nevertheless, inasmuch as spontaneous tumor regressions are extremely rare, it appears that the immune response observed in vitro remains ineffective in vivo. Similarly, it is also known that tumor grafts are not often rejected, even in immune animals, whereas allografts always are.

Although an immune response may develop against a tumor, it is doubtful whether it is of real benefit to the patient. Everything seems to indicate that a tumor

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eludes the body's mechanisms of immune surveillance. Various models have been proposed, to explain this phenomenon; for a complete and detailed review, see Scientific American, Medecine, Chapter 6, VIII Tumor Immunology, 1990. In principle, tumor antigens are considered to play a not insignificant part in modifying or diverting the immune response in favor of the tumor rather than in favor of the individual.

In the light of the complexity of the immune response against tumors and the mediocre state of current knowledge in this field, the use of an anticancer vaccine is not at all obvious. Animal studies have shown that immunization using living or killed cancer cells could lead to rejection of a subsequent tumor graft. Attempts at immunization using acellular products have generally been less successful.

To date, the possibility of manufacturing a vaccine against a cancer employing an antigen associated with this cancer hence remains controversial. A major theoretical objection to this method of treatment lies in the fact that an immune response is not considered to be sufficient to prevent or treat a tumor and that it is highly doubtful that a vaccine could be protective, that is to say capable of preventing or retarding the development of a tumor.

Nevertheless, it has now been found that a tumor antigen associated, inter alia, with breast cancer can, in vaccinal or therapeutic form, induce an immune response which protects against a subsequent tumor attack or one in the process of development. The antigen in question is, more specifically, the one recognized by the monoclonal antibody H23 derived from hybridoma ATCC No. HB 8630, deposited for the purposes of Patent Application EPA 174,534 and available to the public for experimental research work. Antibody H23 is, moreover, commercially available from Teva Pharmaceutical Industries Ltd, 5 Basel Street, Petah Tiqva, P.O. Box 1424, Tel-Aviv, Israel.

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Antibody H23 was generated against particulate material present in the supernatant of in vitro cultures of the mammary tumor cell line T47D. Subsequently, it was shown that antibody H23 reacted markedly with a large majority of mammary tumor biopsies, as well as with the serum and other physiological fluids of patients with a breast cancer. In contrast, antibody H23 does not detect an antigen, or detect antigen only in the trace state, in the case of healthy individuals.

The tumor antigen recognized by antibody H23 is hence expressed in an aberrant manner by the epithelial cells of the cancerous mammary tissue in approximately 90% of cases of breast cancer whereas, in a normal individual, its expression is very low if not zero. Its presence in significant amounts has also been detected in tumoral epithelial tissues other than mammary epithelial tissues.

In a given patient, the tumor antigen recognized by antibody H23 exists in two forms: a transmembrane form and a secreted form, the amino acid sequences of which are shown, respectively, in the sequence identifiers (SI) Nos. 1 and 2. The transmembrane form and the secreted form both exhibit a high degree of polymorphism. In effect, the sequence of both forms of antigen comprises one particular subunit of 20 amino acids which is shown boxed in each SI and which may be repeated in tandem several times. The sequence of this subunit is of the formula (I): Pro-Gly-Ser-Thr-Ala-Pro-X-Ala-His-Gly-Val-Thr-Ser-Ala-Pro-Asp-Y-Arg-Pro-X in which X is Pro or Ala and Y is Thr or Asn. From one individual to another, the number of tandem repeats can vary from 20 to 80 approximately and can, inter alia, characterize the polymorphic type. Lastly, it can happen that, from one repeat to another, a minimum number of amino acids (most often 1,2 or 3 amino acids) is modified.

Moreover, it was established that the subunit of 20 amino acids described above was specific to the tumor antigen reacting with antibody H23, since this subunit

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contains the epitope recognized by this antibody.

Consequently, the invention provides a pharmaceutical composition intended for the curative treatment or the prevention of a malignant tumor, which comprises, as therapeutic agent, (i) a polypeptide recognized by antibody H23 or, alternatively, (ii) a virus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 is inserted, in combination with a diluent or vehicle which is acceptable from a pharmaceutical standpoint.

From a more general standpoint, the subject of the invention is also, as therapeutic agent for the treatment or prevention of a malignant tumor, a polypeptide recognized by antibody H23.

Similarly, the subject of the invention is also:

- the use (i) of a polypeptide recognized by antibody H23, or, alternatively, the use (ii) of a virus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 is inserted, for treating or preventing a malignant tumor;

- a method of curative treatment or prevention of a malignant tumor, which comprises the act of administering a therapeutically effective amount (i) of a polypeptide recognized by antibody H23 or, alternatively, (ii) of a virus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 is inserted, to a subject needing such a treatment. ("Therapeutically effective amount" is understood to mean an amount sufficient for implementing an effective therapy.)

A poypeptide [sic] recognized by antibody H23 can be, in particular, a polypeptide which comprises the sequence (I): Pro-Gly-Ser-Thr-Ala-Pro-X-Ala-His-Gly-Val-Thr-Ser-Ala-Pro-Asp-Y-Arg-Pro-X in which X is Pro or Ala and Y is Thr or Asn. The sequence (I) can be the complete sequence of the polypeptide recognized by antibody H23, or else can represent a single or repeated fragment of the polypeptide recognized by antibody H23.

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A preferred polypeptide recognized by antibody H23 is a polypeptide recognized by antibody H23 whose sequence exhibits a degree of homology of at least 80%, preferably of at least 90% and, as a very special preference, from 95 to 100% inclusive with the sequence of the antigen of human epithelial tissue recognized by antibody H23 (in the text hereinafter, this antigen will be designated H23 - ETA) in its transmembrane or secreted form.

As shown in SI No. 1, the transmembrane form of H23 - ETA has an amino acid sequence beginning with the threonine residue at position 1 and ending with the leucine residue at position 414 + (20 × n) whereas, as shown in SI No. 2, the secreted form of H23 - ETA has an amino acid sequence beginning with the threonine residue at position 1 and ending with the proline residue at position 246 + (20 × n). Quite generally speaking, n is a number from 1 to 80; preferably, n is a number from 1 to 40; as a very special preference, n is 2, 3 or 4.

More specifically, the transmembrane and secreted forms of H23 - ETA have in common an N-terminal region of 106 amino acids (hereinafter referred to as the N-terminal region) and a middle region corresponding to the set of repeated subunits; in contrast, their C-terminal ends differ substantially. The amino acids from position 107 + (20 × n) to position 149 + (20 × n) are identical for both forms and vary from position 150 + (20 × n).

A preferred polypeptide recognized by antibody H23 whose sequence is not identical to one of those described in SI Nos. 1 and 2 is characterized by at least one mutation of an amino acid (point mutation) distributed at random in the N- or C-terminal regions. The number of total mutations [sic] must, of course, satisfy the criterion of degree of homology as established above. "Point mutation" is understood to mean the deletion or substitution of an amino acid of the N- or C-terminal region described in SI No. 1 or 2, as well as the

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addition of an amino acid within the N- or C-terminal region described in SI No. 1 or 2.

Generally speaking, a polypeptide recognized by antibody H23 may be produced by conventional methods of chemical synthesis or else, when the amino acid sequence comprises a large number of residues, by recombinant DNA techniques. More especially, a preparation method comprises the act of culturing a host microorganism transformed with a DNA fragment coding for a polypeptide recognized by antibody H23, and the act of harvesting said polypeptide from the culture. The host organism can be any microorganism capable of being transformed, for example and without limitation, a bacterium, a yeast or alternatively a mammalian cell, insofar as the DNA fragment in question is either integrated in the genome of the host organism or inserted into a suitable expression vector, that is to say capable of replicating in the host organism. Naturally, the DNA fragment coding for the polypeptide recognized by antibody H23 is placed under the control of regions containing suitable transcription and translation signals. Expression vectors and control regions are known to a person skilled in the art.

During the last decade, the use has been proposed of recombinant viruses as agents intended for inducing an immune response against miscellaneous pathogenic organisms. To this end, adenoviruses or pox viruses are most especially suitable. For use in the present invention, avian pox viruses, canarypox virus, or vaccinia virus are highly suitable. Vaccinia virus exhibits an immune cross-reaction with smallpox virus and, as a result, has been used as an anti-smallpox vaccinal agent since the 19th century. At the beginning of the 1980s, smallpox was considered to be eradicated from the earth's surface, and the World Health Organization consequently judged it preferable to stop vaccinating against smallpox. Hence vaccinia virus is now available for use in vaccines comprising a vaccinia virus whose genome has been modified so as to express

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heterologous genes coding for antigenic determinants specific to a vector organism of a disease other than smallpox.

Thus, the therapeutic agent of a pharmaceutical composition according to the invention can be, alternatively, a virus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 has been inserted.

This type of pharmaceutical composition has the advantage of being inexpensive to produce and of great stability under miscellaneous environmental conditions. In particular, the storage conditions impose no restrictions.

The general conditions for obtaining a vaccinia virus capable of expressing a block for expression of a heterologous protein are described in European Patent EP 83,286, the content of which is incorporated herein by reference. These conditions are applicable to other viruses which are acceptable as vectors, insofar as the latter possess at least one nonessential genomic region into which an expression block may be inserted.

A vaccinia virus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 is inserted may also be used as a particular expression vector for the purpose of producing said polypeptide in culture of mammalian cells, as stated above.

A polypeptide recognized by antibody H23, or a virus into the genome of which a DNA fragment coding for said polypeptide is inserted, exhibits <u>in vivo</u> antitumor activity in the following test: C3H line mice or Fisher line rats, aged 4 to 5 weeks, are treated twice, with an interval of ten days between the two treatments, with either between 10 and 500 μg of a polypeptide recognized by antibody H23, or between 10^7 and 10^8 pfu (plaque forming units) of a virus into the genome of which a DNA fragment coding for said polypeptide is inserted. When a polypeptide is used, the treatment is preferably performed by subcutaneous injection. A scarification of the

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tail is preferable in the case of a virus. Fifteen days after the first treatment, approximately 10^4 to 10^7 syngeneic tumor cells expressing H23-ETA, which have been cultured in vitro, treated with trypsin, washed and resuspended in PBS (phosphate buffered saline) buffer, are injected subcutaneously in a volume of approximately 100 µl. In parallel, untreated animals are likewise subjected to an identical tumor attack. Approximately 20 days after injection of the cells, the size of the subcutaneous tumors is smaller in the animals treated with a polypeptide or a virus than in untreated animals.

A polypeptide recognized by antibody H23, or a virus into the genome of which a DNA fragment coding for said polypeptide is inserted, is, as a result, useful for the purpose of treating or preventing a cancerous condition, more especially a carcinoma type tumor (tumor developed by epithelial cells), for example a mammary tumor.

For these indications, the appropriate dosage varies in accordance, for example, with the polypeptide or virus employed, the individual being treated, the mode of administration, the use as a vaccine or as a treatment, and the nature and severity of the tumor condition which is being treated. However, in general, the indications are that satisfactory vaccination results in mammals, for example humans, may be obtained with a virus, into the genome of which a DNA fragment coding for said polypeptide is inserted, at a single dosage, or dosage repeated once or twice at intervals of approximately 1 to 3 weeks, of approximately 10^4 pfu/kg to approximately 10^8 pfu/kg of body weight of the mammal.

A pharmaceutical composition according to the invention may be administered by any conventional route, especially the subcutaneous route, for example in the form of an injectable solution or suspension. As a vaccine, a composition according to the invention may be administered according to the modes conventionally implemented for already known vaccines, for example in a

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single dose or dose repeated one or several times after a certain lapse of time. When a composition according to the invention is being used in the curative treatment of a cancer, it may be administered frequently for a sufficient period for the treatment to be effective. Such a composition may advantageously be injected intratumorally.

A pharmaceutical composition according to the invention may be prepared according to conventional techniques. When the therapeutic agent is a vaccinia virus, this virus is preferably in attenuated live form. Attenuated viral strains are available at the present time; for example, the thymidine kinase-negative Copenhagen strain. To obtain the recombinant viruses needed for using a composition according to the invention, it suffices to use such a strain. Lastly, a recombinant virus may be attenuated by a suitable chemical treatment known to a person skilled in the art.

The invention is illustrated below, reference being made to Figure 1.

Figure 1 shows diagrammatically a genomic DNA fragment coding for the secreted form of H23-ETA (→ 1) or for the transmembrane form of H23-ETA (→ 2). The blocks and the gaps symbolize the exons and the introns, respectively. The black background corresponds to the signal sequence and the shaded background denotes the repeat sequences (of which there are 4: a, b, c and d). The DNA fragments Nos. 1 and 2 are used for the construction of a complete fragment coding for the secreted form of H23-ETA, whereas the fragments Nos. 3 to 5 are used for constructing a complete fragment coding for the transmembrane form of H23-ETA. The restriction sites shown in this figure are also to be found in SI Nos. 1 and 2.

Example 1

Complementary and genomic DNA fragments coding for portions of H23 are isolated according to the procedure described in Wreschner et al., Eur. J. Biochem, (1990) 189: 463. These fragments are thereafter used to

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reconstruct a DNA fragment coding for the complete H23-ETA antigen in its secreted or transmembrane form.

The plasmid constructions are described below, reference being made to Figure 1.

A. Preparation of a vaccinia virus capable of promoting the synthesis of the secreted form of H23-ETA.

An EcoRI-PvuII complementary DNA fragment (No. 1) is introduced between the EcoRI and PvuII sites of the multiple insertion region of the vector pPolyII described in Lathe et al., Gene (1987) 57: 193 to give plasmid pETA-5'. A PvuII genomic DNA fragment (No. 2), containing 4 repeat units, is introduced into the PvuII site of the multiple insertion region of pETA-5', downstream of the fragment No. 1 and in the appropriate orientation. In the repeat units a, b, c and d, the codons xxx_1 and xxx_2 are, respectively, CCA (Pro) and CCC (Pro), CCA and CCC, GCA (Ala) and GCC, CCA and GCC. Likewise, the codon yyy is ACC (Thr) in the repeat units a, b and c; the codon yyy is AAC (Asn) in the unit d.

A BamHI-SalI fragment coding for the complete secreted form of H23-ETA is excised from the plasmid finally obtained. This fragment is then inserted between the BamHI and SalI sites of the transfer vector ptg194-poly described in Kieny et al., Bio/Technology, (1986) 4:790, downstream of the vaccinia virus promoter E7.5k and inside the vaccinia virus gene coding for thymidine kinase.

The transfer vector obtained in the above paragraph is thereafter used to transfer the block for expression of the secreted form of H23-ETA into the genome of vaccinia virus, Copenhagen strain, according to the method described in Kieny et al., Nature (1984) 312: 163. The vaccinia virus VV-ETA-S is thereby obtained.

B. Preparation of a vaccinia virus capable of promoting the synthesis of the transmembrane form of H23-ETA.

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A PvuII-PstI genomic DNA fragment (No. 3), containing 4 repeat units, is introduced between the PvuII and PstI sites of the multiple insertion region of pETA-5', downstream of the fragment No. 1 and in the appropriate orientation. In the repeat units a, b, c and d, the codons xxx_1 and xxx_2 are, respectively, CCA (Pro) and CCC (Pro), CCA and CCC, GCA (Ala) and GCC, CCA and GCC. Likewise, the codon yyy is ACC (Thr) in the repeat units a, b and c; the codon yyy is AAC (Asn) in the unit d.

An EcoRI-PstI fragment corresponding to the cloned fragments is excised from the final plasmid obtained. The EcoRI cohesive end is converted to a blunt end by treatment with Klenow polymerase. This fragment is then introduced between the XhoI site, treated beforehand with Klenow polymerase, and the PstI site of the multiple insertion region of the vector pPolyII-Sfi/Not-14 described in Lathe et al., supra, to give plasmid pETA-T-5'.

A PstI-BalI complementary DNA fragment (No. 4) is introduced between the PstI and BalI sites of pETA-T-5'. A BalI-BalI complementary DNA fragment (No. 5) is then inserted into the BalI site of the plasmid finally obtained.

A BglII-SStI fragment coding for the complete transmembrane form of H23-ETA is excised from the plasmid obtained in the above paragraph; it is then introduced between the BamHI and SstI sites of the transfer vector ptg186-poly described in Kieny et al., (1986), supra, downstream of the vaccinia virus promoter E7.5k and inside the vaccinia virus gene coding for thymidine kinase.

The transfer vector obtained in the above paragraph is thereafter used to transfer the block for expression of the transmembrane form of H23-ETA into the genome of vaccinia virus, Copenhagen strain (VV-O), according to the method described in Kieny et al., (1984), supra. The vaccinia virus VV-ETA-T is thereby obtained.

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Example 2: Preparation of virus stocks.

Stocks of purified viruses are prepared using BHK-21 cells. BHK-21 cells are infected with the recombinant viruses VV-ETA-S and VV-ETA-T (0.1 pfu/cell) for 48 hours. After this time, the cultures are frozen at -20°C and then thawed at room temperature. After destruction of the cell walls by 3 successive treatments with a "Potter" in a hypotonic buffer, the soluble proteins of the supernatant are loaded onto a cushion of 36% (w/v) sucrose and centrifuged (Beckman SW 28, 1h, 14 K). The pellet containing the virus is taken up in solution in 10 mM Tris-HCl pH 8 and placed on a linear (20-40%) sucrose gradient. After centrifugation (SW 28, 40 min, 14 K), the opalescent band containing the virus is withdrawn using a syringe and concentrated by centrifugation (SW 28, 20 K, 1h). The virus is lastly taken up in a small volume of 10 mM Tris-Hcl [sic] pH 8 so as to obtain a viral stock assaying at approximately 10^{10} pfu/ml.

Example 3: Tumor cell lines expressing H23-ETA.

A. Construction of eukaryotic plasmids capable of promoting the expression of H23-ETA.

A BamHI-SalI DNA fragment coding for the secreted form of H23-ETA is excised from the plasmid obtained in Example 1A, first paragraph. It is then reintroduced between the BamHI and SalI sites of the multiple insertion region of plasmid pHMG described in Gautier et al., Nucl. Acid Res., (1989) 17 (20): 83, so as to be placed under the control of the promoter of the 3-hydroxy-3-methylglutarylcoenzyme A reductase (HMGCR) gene, downstream of the signal sequence of SV40 polyA. Plasmid pHMG-ETA-S is thereby obtained.

Likewise, plasmid pHMG-ETA-T is constructed in a similar manner by insertion of a BamHI-EcoRV DNA fragment derived from the plasmid obtained in Example 1B, paragraph 2.

B. Preparation of cell lines.

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Cells of the tumor cell line FR3T3-ras-1, obtained from Fisher rat fibroblasts by Matriceau et al., EMBO J. (1985) 4: 1435, and cells of the mouse mammary carcinoma line MM5t, derived from C3H mice, are cotransfected (i) with pHMG-ETA-S and plasmid pAG60 described in Colbere-Garapin et al., J. Mol. Biol. (1981) 150: 1 which contains a gene for resistance to Geneticin (G418) or (ii) with pHMG-ETA-T and pAG60. To accomplish the transfection, the calcium phosphate precipitation method of Graham et al., Virology (1973) 52: 456 modified by Wigler et al., Cell (1978) 14: 725 is used.

The transfected clones are selected in the presence of 500 µl/ml of G418 and are thereafter cultured. Selection of the clones expressing H23-ETA is accomplished by labelling the cells with peroxidase after reaction with antibody H23. Cell lines in the pure state are obtained by the limiting dilution method, and the expression of H23-ETA is monitored.

The cell lines are designated as follows:

FR3T3-ras-1 (pAG60/pHMG-ETA-S): F-S
FR3T3-ras-1 (pAG60/pHMG-ETA-T): F-T
FR3T3-ras-1 (pAG60/pHMG): F-C
MM5tC3H (pAG60/pHMG-ETA-S): M-S
MM5tC3H (pAG60/pHMG-ETA-S): M-T
MM5tC3H (pAG60/pHMG-ETA-S): M-C

Example 4: Demonstration of the vaccinal effect of H23-ETA.

Fisher IOPS line male and female rats and C3H line female mice aged 4 to 5 weeks are immunized in the following manner: a purified viral preparation of VV-ETA-S, VV-ETA-T or VV-0 is administered to the animals, by scarification of the tail, in a volume of 10 µl corresponding to approximately 2×10^7 pfu. This treatment is repeated 10 days later.

The F-S, F-T, F-C, M-S, M-T and M-C tumor lines are cultured in modified Dulbecco medium (Gibco) supplemented with 10% of fetal calf serum, 100 units of penicillin and 100 µg/ml of streptomycin. The cultures

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are then treated with trypsin, washed and suspended in PBS (phosphate buffered saline) buffer.

14 days after the first stage of immunization, 2×10^4 F-C cells, 4×10^4 F-S cells, 1.5×10^5 F-T cells or 2×10^6 M-C, M-S or M-T cells are injected subcutaneously into an animal in a volume of 100 μl.

The appearance of the subcutaneous tumors is monitored daily. The diameter of the tumors is measured in two dimensions. The complete data for the experiment and the results are presented in Table I below:

TABLE I

Animal	Virus	Tumor cells	Number of animals having a tumor nodule relative to the total number of animals treated	Measured average diameter of the tumor nodules (in mm) x days after injection of the cells	Percentage of animals free from tumors
Fisher line male rats		F-C	4/4	31 (20 days)	0
		F-S	3/4	25 (25 days)	25
		F-T	3/6	25 (30 days)	50
	VV-ETA-S	F-C	8/8	40 (20 days)	0
		F-S	3/8	7.5 (25 days)	62.5
		F-T	1/8	0.87 (30 days)	87.5
	VV-ETA-T	F-C	8/8	32 (20 days)	0
		F-S	1/8	0.38 (25 days)	87.5
		F-T	0/8	0 (30 days)	100
		F-S	10/10	11.2 (20 days)	0
		F-T	10/10	25 (20 days)	0
	VV-ETA-S	F-S	9/10	16 (20 days)	10
		F-T	9/10	30 (20 days)	10
	VV-ETA-T	F-S	5/10	1.7 (20 days)	50
		F-T	5/10	2.8 (20 days)	50
Fisher line female rats	VV-O -	F-S	10/10	19.6 (20 days)	0
		F-T	10/10	28 (20 days)	0
	VV-ETA-S	F-S	8/10	10.6 (20 days)	20
		F-T	9/9	33.8 (20 days)	0
	VV-ETA-T	F-S	5/10	0.1 (25 days)	50
		F-T	1/10		90

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Table I shows that, when the animals are subjected to infection with F-S or F-T, the incidence of appearance of tumors in a group of animals treated beforehand using the vaccinia virus VV-ETA-S or VV-ETA-T is lower than in the groups of untreated animals or animals treated with a VV-0 vaccinia virus. Moreover, the size of the tumor nodules which appear in animals treated beforehand with VV-ETA-S or VV-ETA-T is much smaller than that of the tumor nodules observed in the untreated animals or animals treated with VV-0.

Immunization using VV-ETA-S or VV-ETA-T is effective only in the case of tumors induced with cells expressing the secreted or transmembrane form of H23-ETA. The vaccinal effect of the viruses is hence very specific.

Lastly, the vaccinal effect of VV-ETA-T appears to be superior to that of VV-ETA-S, irrespective of the form of H23-ETA expressed by the cells inducing the tumors.

Example 5: Demonstration of the curative effect of H23-ETA.

Fisher line rats are infected with tumor cells as described in Example 4. As soon as tumors have appeared (10 to 15 days later), treatment is carried out using the viral preparations, as described in Example 4.

The data and results of the experiment are presented in Table II below:

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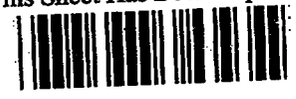


TABLE II

Virus	Tumor cells	Number of animals having a tumor nodule relative to the total number of animals treated		Measured average diameter of the tumors (in mm)	
		25 days after injection	50 days after injection	25 days after injection	50 days after injection
VV-0	F-S	10/10	10/10	27.8	all dead
	F-T	10/10	10/10	27.7	all dead
VV-ETA-S	F-S	10/10	10/10	31.5	all dead
	F-T	9/10	7/10	15.5	8.5
VV-ETA-T	F-S	9/10	10/10	26.8	50.2
	F-T	7/10	7/10	11.6	9.4

Table II shows that the treatment of an infection with VV-ETA-S or VV-ETA-T has a favorable effect on the incidence of appearance and the size of the tumors relative to the control test. Moreover, VV-ETA-T appears to be more effective than VV-ETA-S.

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SEQUENCE IDENTIFIER No. 1

Subject: The transmembrane form of the H23-ETA antigen

Sequence type: Sequence of a DNA fragment and the corresponding amino acid sequence

Molecule type: Complementary DNA

Origin: Mammary carcinoma line T47D

Characteristics of the complete DNA fragment:

EcoRI-BalI fragment

Coding sequence: from nucleotide 58 to nucleotide 1362+(60 × n)

Characteristics of the amino acid sequence:

Signal peptide: from a.a.-21 to a.a.-1

Mature form: from a.a.1 to a.a. 414*, * denoting [+(20 × n)] in which n is a number from 1 to 80

Repeat sequence: As shown boxed below, in which X_1 and X_2 are, independently, Pro or Ala and Y is Thr or Asn

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GAATTCCCTG GCTGCTTGAA TCTGTTCTGC CCCCTCCCCA CCCATTTCAC                50

CACCACC ATG ACA CCG GGC ACC CAG TCT CCT TTC TTC CTG                   90
        Met Thr Pro Gly Thr Gln Ser Pro Phe Phe Leu
        -21 -20                 -15

CTG CTG CTC CTC ACA GTG CTT ACA GTT GTT ACA GGT TCT                  129
Leu Leu Leu Leu Thr Val Leu Thr Val Val Thr Gly Ser
-10                 -5              -1   1

GGT CAT GCA AGC TCT ACC CCA GGT GGA GAA AAG GAG ACT                  168
Gly His Ala Ser Ser Thr Pro Gly Gly Glu Lys Glu Thr
      5                  10                  15

TCG GCT ACC CAG AGA AGT TCA GTG CCC AGC TCT ACT GAG                  207
Ser Ala Thr Gln Arg Ser Ser Val Pro Ser Ser Thr Glu
            20                  25
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AAG AAT GCT GTG AGT ATG ACC AGC AGC GTA CTC TCC AGC                    246
Lys Asn Ala Val Ser Met Thr Ser Ser Val Leu Ser Ser
 30                  35                  40

CAC AGC CCC GGT TCA GGC TCC TCC ACC ACT CAG GGA CAG                    285
His Ser Pro Gly Ser Gly Ser Ser Thr Thr Gln Gly Gln
         45                  50                  55

GAT GTC ACT CTG GCC CCG GCC ACG GAA CCA GCT TCA GGT                    324
Asp Val Thr Leu Ala Pro Ala Thr Glu Pro Ala Ser Gly
                 0                   65

   PvuII
TCA GCT GCC ACC [illegible] GGA CAG GAT GTC ACC TCG GTC CCA             363
Ser Ala Ala Thr [illegible] Gly Gln Asp Val Thr Ser Val Pro
     70                  75                  80

GTC ACC AGG CCA GCC CTG GGC TCC ACC ACC CCG CCA GCC                    402
Val Thr Arg Pro Ala Leu Gly Ser Thr Thr Pro Pro Ala
             85                  90

CAC GAT GTC ACC TCA GCC CCG GAC AAC AAG CCA GCC|CCG
His Asp Val Thr Ser Ala Pro Asp Asn Lys Pro Ala|Pro
 95                  100                 105

-------------------------------------------------

GGC TCC ACC GCC CCC xxx GCC CAC GGT GTC ACC TCG GCC
Gly Ser Thr Ala Pro  X1 Ala His Gly Val Thr Ser Ala

-------------------------------------------------

CCG GAC yyy AGG CCG xxx|TTG GGC TCC ACC GCC CCT CCA          459 + (60xn)
Pro Asp  Y  Arg Pro  X2|Leu Gly Ser Thr Ala Pro Pro
                       n           110*

GTC CAC AAT GTC ACC TCG GCC TCA GGC TCT GCA TCA GGC          498 + (60xn)
Val His Asn Val Thr Ser Ala Ser Gly Ser Ala Ser Gly
    115*                120*                125*

TCA GCT TCT ACT CTG GTG CAC AAC GGC ACC TCT GCC AGG          537 + (60xn)
Ser Ala Ser Thr Leu Val His Asn Gly Thr Ser Ala Arg
            130*                135*

GCT ACC ACA ACC CCA GCC AGC AAG AGC ACT CCA CCC AGC          576 + (60xn)
Ala Thr Thr Thr Pro Ala Ser Lys Ser Thr Pro Phe Ser
140*                145*                150*

ATT CCC AGC CAC CAC TCT GAT ACT CCT ACC ACC CTT GCC          615 + (60xn)
Ile Pro Ser His His Ser Asp Thr Pro Thr Thr Leu Ala
        155*                160*                165*
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AGC CAT AGC ACC AAG ACT GAT GCC AGT AGC ACT CAC CAT          654 + (50xn)
Ser His Ser Thr Lys Thr Asp Ala Ser Ser Thr His His
                170*                175*

AGC ACG GTA CCT CCT CTC ACC TCC TCC AAT CAC AGC ACT          693 + (60xn)
Ser Thr Val Pro Pro Leu Thr Ser Ser Asn His Ser Thr
    180*                185*                190*

TCT CCC CAG TTG TCT ACT GGG GTC TCT TTC TTT TTC CTG          732 + (60xn)
Ser Pro Gln Leu Ser Thr Gly Val Ser Phe Phe Phe Leu
            195*                200*

TCT TTT CAC ATT TCA AAC CTC CAG TTT AAT TCC TCT CTG          771 + (60xn)
Ser Phe His Ile Ser Asn Leu Gln Phe Asn Ser Ser Leu
205*                210*                215*
                                        PstI
GAA GAT CCC AGC ACC GAC TAC TAC CAA GAG CTG CAG AGA          810 + (60xn)
Glu Asp Pro Ser Thr Asp Tyr Tyr Gln Glu Leu Gln Arg
        220*                225*                230*

GAC ATT TCT GAA ATG TTT TTG CAG ATT TAT AAA CAA GGG          849 + (60xn)
Asp Ile Ser Glu Met Phe Leu Gln Ile Tyr Lys Gln Gly
                235*                240*

GGT TTT CTG GGC CTC TCC AAT ATT AAG TTC AGG CCA GGA5         888 + (60xn)
Gly Phe Leu Gly Leu Ser Asn Ile Lys Phe Arg Pro Gly
    245*                250*                255*

TCT GTG GTG GTA CAA TTG ACT CTG GCC TTC CGA GAA GGT          927 + (60xn)
Ser Val Val Val Gln Leu Thr Leu Ala Phe Arg Glu Gly
            260*                265*

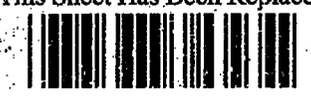
ACC ATC AAT GTC CAC GAC GTG GAG ACA CAG TTC AAT CAG          966 + (60xn)
Thr Ile Asn Val His Asp Val Glu Thr Gln Phe Asn Gln
270*                275*                280*

TAT AAA ACG GAA GCA GCC TCT CGA TAT AAC CTG ACG ATC         1005 + (60xn)
Tyr Lys Thr Glu Ala Ala Ser Arg Tyr Asn Leu Thr Ile
        285*                290*                295*

TCA GAC GTC AGC GTG AGT CAT GTG CCA TTT CCT TTC TCT         1044 + (60xn)
Ser Asp Val Ser Val Ser His Val Pro Phe Pro Phe Ser
                300*                305*

GCC CAG TCT GGG GCT GGG GTG CCA GGC TGG GGC ATC GCG         1083 + (60xn)
Ala Gln Ser Gly Ala Gly Val Pro Gly Trp Gly Ile Ala
    310*                315*                320*
                                        BalI
CTG CTG GTG CTG GTC TGT GTT CTG GTT GCG CTG GCC ATT         1122 + (60xn)
Leu Leu Val Leu Val Cys Val Leu Val Ala Leu Ala Ile
            325*                330*
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GTC TAT CTC ATT GCC TTG GCT GTC TGT CAG TGC CGC CGA          1161 + (60xn)
Val Tyr Leu Ile Ala Leu Ala Val Cys Gln Cys Arg Arg
335*                340*                345*

AAG AAC TAC GGG CAG CTG GAC ATC TTT CCA GCC CGG GAT          1200 + (60xn)
Lys Asn Tyr Gly Gln Leu Asp Ile Phe Pro Ala Arg Asp
        350*                355*                360*

ACC TAC CAT CCT ATG AGC GAG TAC CCC ACC TAC CAC ACC          1239 + (60xn)
Thr Tyr His Pro Met Ser Glu Tyr Pro Thr Tyr His Thr
                365*                370*

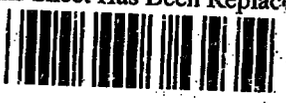
CAT GGG CGC TAT GTG CCC CCT AGC AGT ACC GAT CGT AGC          1278 + (60xn)
His Gly Arg Tyr Val Pro Pro Ser Ser Thr Asp Arg Ser
    375*                380*                385*

CCC TAT GAG AAG GTT TCT GCA GGT AAT GGT GGC AGC AGC          1317 + (60xn)
Pro Tyr Glu Lys Val Ser Ala Gly Asn Gly Gly Ser Ser
            390*                395*

CTC TCT TAC ACA AAC CCA GCA GTG GCA GCC ACT TCT GCC          1356 + (60xn)
Leu Ser Tyr Thr Asn Pro Ala Val Ala Ala Thr Ser Ala
400*                405*                410*

AAC TTG TAG GGGCACGTCG CCCTCTGAGC TGAGTGG                    1392 + (60xn)
Asn Leu Ter
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SEQUENCE IDENTIFIER NO. 2

Subject: The soluble form of the H23-ETA antigen

Sequence type: Sequence of a DNA fragment and the corresponding amino acid sequence

Molecule type: Complementary DNA

Origin: Mammary carcinoma line T47D

Characteristics of the complete DNA fragment:

EcoRI-PvuII fragment

Coding sequence: from nucleotide 58 to nucleotide 858+(60 × n)

Characteristics of the amino acid sequence:

Signal peptide: from a.a.-21 to a.a.-1

Mature form: from a.a.1 to a.a. 246*, * denoting [+(20 × n)] in which n is a number from 1 to 80

Repeat sequence: As shown boxed below, in which X_1 and X_2 are, independently, Pro or Ala and Y is Thr or Asn

```
GAATTCCCTG GCTGCTTGAA TCTGTTCTGC CCCCTCCCCA CCCATTTCAC                50

CACCACC ATG ACA CCG GGC ACC CAG TCT CCT TTC TTC CTG                   90
        Met Thr Pro Gly Thr Gln Ser Pro Phe Phe Leu
        -21 -20                 -15

CTG CTG CTC CTC ACA GTG CTT ACA GTT GTT ACA GGT TCT                  129
Leu Leu Leu Leu Thr Val Leu Thr Val Val Thr Gly Ser
-10                 -5              -1   1

GGT CAT GCA AGC TCT ACC CCA GGT GGA GAA AAG GAG ACT                  168
Gly His Ala Ser Ser Thr Pro Gly Gly Glu Lys Glu Thr
     5                  10                  15

TCG GCT ACC CAG AGA AGT TCA GTG CCC AGC TCT ACT GAG                  207
Ser Ala Thr Gln Arg Ser Ser Val Pro Ser Ser Thr Glu
            20                  25
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AAG AAT GCT GTG AGT ATG ACC AGC AGC GTA CTC TCC AGC                    246
Lys Asn Ala Val Ser Met Thr Ser Ser Val Leu Ser Ser
 30                  35                  40

CAC AGC CCC GGT TCA GGC TCC TCC ACC ACT CAG GGA CAG                    285
His Ser Pro Gly Ser Gly Ser Ser Thr Thr Gln Gly Gln
         45                  50                  55

GAT GTC ACT CTG GCC CCG GCC ACG GAA CCA GCT TCA GGT                    324
Asp Val Thr Leu Ala Pro Ala Thr Glu Pro Ala Ser Gly
                60                  65

   PvuII
TCA GCT GCC ACC TGG GGA CAG GAT GTC ACC TCG GTC CCA                    363
Ser Ala Ala Thr Trp Gly Gln Asp Val Thr Ser Val Pro
     70                  75                  80

GTC ACC AGG CCA GCC CTG GGC TCC ACC ACC CCG CCA GCC                    402
Val Thr Arg Pro Ala Leu Gly Ser Thr Thr Pro Pro Ala
             85                  90

CAC GAT GTC ACC TCA GCC CCG GAC AAC AAG CCA GCC|CCG
His Asp Val Thr Ser Ala Pro Asp Asn Lys Pro Ala|Pro
 95                  100                 105     |___

_____________________________________________________

GGC TCC ACC GCC CCC xxx GCC CAC GGT GTC ACC TCG GCC
Gly Ser Thr Ala Pro  X1 Ala His Gly Val Thr Ser Ala
_____________________________________________________

_____________________________
CCG GAC yyy AGG CCG xxx|TTG GGC TCC ACC GCC CCT CCA        459 + (60xn)
Pro Asp  Y  Arg Pro  X2|Leu Gly Ser Thr Ala Pro Pro
_____________________________|n           110*

GTC CAC AAT GTC ACC TCG GCC TCA GGC TCT GCA TCA GGC        498 + (60xn)
Val His Asn Val Thr Ser Ala Ser Gly Ser Ala Ser Gly
    115*                120*                125*

TCA GCT TCT ACT CTG GTG CAC AAC GGC ACC TCT GCC AGG        537 + (60xn)
Ser Ala Ser Thr Leu Val His Asn Gly Thr Ser Ala Arg
            130*                135*

GCT ACC ACA ACC CCA GCC AGC AAG AGC ACT CCA TTC TCA        576 + (60xn)
Ala Thr Thr Thr Pro Ala Ser Lys Ser Thr Pro Phe Ser
140*                145*                150*

ATT CCC AGC CAC CAC TCT GAT ACT CCT ACC ACC CTT GCC        615 + (60xn)
Ile Pro Ser His His Ser Asp Thr Pro Thr Thr Leu Ala
        155*                160*                165*

AGC CAT AGC ACC AAG ACT GAT GCC AGT AGC ACT CAC CAT        654 + (60xn)
Ser His Ser Thr Lys Thr Asp Ala Ser Ser Thr His His
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```
                    170*                    175*
AGC ACG GTA CCT CCT CTC ACC TCC TCC AAT CAC AGC ACT          693 + (60xn)
Ser Thr Val Pro Pro Leu Thr Ser Ser Asn His Ser Thr
    180*                    185*                190*

TCT CCC CAG TTG TCT ACT GGG GTC TCT TTC TTT TTC CTG          732 + (60xn)
Ser Pro Gln Leu Ser Thr Gly Val Ser Phe Phe Phe Leu
            195*                    200*

TCT TTT CAC ATT TCA AAC CTC CAG TTT AAT TCC TCT CTG          771 + (60xn)
Ser Phe His Ile Ser Asn Leu Gln Phe Asn Ser Ser Leu
205*                    210*                215*

GAA GAT CCC AGC ACC GAC TAC TAC CAA GAG CTG CAG AGA          810 + (60xn)
Glu Asp Pro Ser Thr Asp Tyr Tyr Gln Glu Leu Gln Arg
        220*                    225*                230*

GAC ATT TCT GAA ATG GTG AGT ATC GGC CTT TCC TTC CCC          849 + (60xn)
Asp Ile Ser Glu Met Val Ser Ile Gly Leu Ser Phe Pro
                235*                    240*

ATG CTC CCC TGA AGCAGCCATC AGAACTGTCC ACACCCTTTG             891 + (60xn)
Met Leu Pro Ter
    245*

CATCAAGCCT GAGTCCTTTC CCTCTCACCC CAGTTTTTGC AGATTTATAA       941 + (60xn)
ACAAGGGGGT TTTCTGGGCC TCTCCAATAT TAAGTTCAGG TACAGTTCTG       991 + (60xn)
GGTGTGGACC CAGTGTGGTG GTTGGAGGGT TGGGTGGTGG TCATGACCGT      1041 + (60xn)
AGGAGGGACT GGTCGCACTT AAGGTTGGGG GAAGAGTCGT GAGCCAGAGC      1091 + (60xn)
TGGGACCCGT GGCTGAAGTG CCCATTTCCC TGTGACCAGG CCAGGATCTG      1141 + (60xn)
TGGTGGTACA ATTGACTCTG GCCTTCCGAG AAGGTACCAT CAATGTCCAC      1191 + (60xn)
GACGTGGAGA CACAGTTCAA TCAGTATAAA ACGGAAGCAG CCTCTCGATA      1241 + (60xn)
TAACCTGACG ATCTCAGACG TCAGCGGTGA GGCTACTTCC CTGGCTGCAG      1291 + (60xn)
CCCAGCACCA TGCCGGGGCC CTCTCCTTCC AGTGCCTGGG TCCCCGCTCT      1341 + (60xn)
TTCCTTAGTG CTGGCAGCGG GAGGGGCGCC TCCTCTGGGA GACTGCCCTG      1391 + (60xn)
ACCACTGCTT TTCCTTTTAG TGAGTCATGT GCCATTTCCT TTCTCTGCCC      1441 + (60xn)
AGTCTGGGGC TGGGGTGCCA GGCTGGGGCA TCGCGCTGCT GGTGCTGGTC      1491 + (60xn)
TGTGTTCTGG TTGCGCTGGC CATTGTCTAT CTCATTGCCT TGGTGAGTGC      1541 + (60xn)
AGTCCCTGGC CCTGATCAGA GCCCCCCGGT AGAAGGCACT CCATGGCCTG      1591 + (60xn)
CCATAACCTC CTATCTCCCC AGGCTGTCTG TCAGTGCCGC CGAAAGAACT      1641 + (60xn)
ACGGGCAG                                                   1649 + (60xn)
```

CLAIMS

1. A pharmaceutical composition for treating or preventing a malignant tumor, which comprises, as therapeutic agent, a polypeptide recognized by antibody H23, in combination with a diluent or vehicle which is acceptable from a pharmaceutical standpoint.

2. A composition according to claim 1, in which the polypeptide recognized by antibody H23 comprises a sequence repeated n times, n being a number from 1 to 80; and of formula (I): Pro-Gly-Ser-Thr-Ala-Pro-X_1-Ala-His-Gly-Val-Thr-Ser-Ala-Pro-Asp-Y-Arg-Pro-X_2 in which X_1 and X_2 are, independently, Pro or Ala and Y is Thr or Asn.

3. A composition according to claim 2, in which the polypeptide recognized by antibody H23 is a polypeptide comprising the sequence of formula (I) repeated n times whose complete sequence exhibits a degree of homology of at least 80% with (i) the sequence as shown in SI No. 1 beginning with the threonine residue at position 1 and ending with the leucine residue at position 414 + (20 × n) or (ii) the sequence as shown in SI No. 2 beginning with the threonine residue at position 1 and ending with the proline residue at position 246 + (20 × n); the number n relating to the sequence of formula (I) of said polypeptide on the one hand and that relating to the sequence as shown in SI No. 1 or 2 on the other hand being, in a dependent manner, a number from 1 to 80.

4. A composition according to claim 3, in which the polypeptide recognized by antibody H23 is a polypeptide comprising the sequence of formula (I) repeated n times whose complete sequence exhibits a degree of homology of at least 80% with (i) the sequence as shown in SI No. 1 beginning with the threonine residue at position 1 and ending with the leucine residue at position 414 + (20 × n) or (ii) the sequence as shown in SI No. 2 beginning with the threonine residue at position 1 and ending with the proline residue at position 246 + (20 × n); the number n relating to the sequence of

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formula (I) of said polypeptide on the one hand and that relating to the sequence as shown in SI No. 1 or 2 on the other hand being, in a dependent manner, 2, 3 or 4.

5. A composition according to claim 3, in which the polypeptide recognized by antibody H23 has as its sequence (i) the sequence as shown in SI No. 1 beginning with the threonine residue at position 1 and ending with the leucine residue at position 414 + (20 × n) or (ii) the sequence as shown in SI No. 2 beginning with the threonine residue at position 1 and ending with the proline residue at position 246 + (20 × n); n being a number from 1 to 80.

6. A composition according to claim 5, in which the polypeptide recognized by antibody H23 has as its sequence (i) the sequence as shown in SI No. 1 beginning with the threonine residue at position 1 and ending with the leucine residue at position 414 + (20 × n) or (ii) the sequence as shown in SI No. 2 beginning with the threonine residue at position 1 and ending with the proline residue at position 246 + (20 × n); n being 2,3 or 4.

7. A pharmaceutical composition for treating or preventing a malignant tumor, which comprises, as therapeutic agent, a virus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 is inserted, said DNA fragment being placed under the control of suitable transcription and translation signals.

8. A composition according to claim 7, which comprises a virus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 is inserted; said polypeptide comprising a sequence repeated n times, n being a number from 1 to 80; and of formula (I): Pro-Gly-Ser-Thr-Ala-Pro-X_1-Ala-His-Gly-Val-Thr-Ser-Ala-Pro-Asp-Y-Arg-Pro-X_2 in which X_1 and X_2 are, independently, Pro or Ala and Y is Thr or Asn.

9. A composition according to claim 8, which comprises a virus into the genome of which a DNA fragment

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coding for a polypeptide recognized by antibody H23 is inserted, comprising the sequence of formula (I) repeated n times and whose complete sequence exhibits a degree of homology of at least 80% with (i) the sequence as shown in SI No. 1 beginning with the threonine residue at position 1 and ending with the leucine residue at position 414 + (20 × n) or (ii) the sequence as shown in SI No. 2 beginning with the threonine residue at position 1 and ending with the proline residue at position 246 + (20 × n); the number n relating to the sequence of formula (I) of said polypeptide on the one hand and that relating to the sequence as shown in SI No. 1 or 2 on the other hand being, in a dependent manner, a number from 1 to 80.

10. A composition according to claim 9, which comprises a virus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 is inserted, comprising the sequence of formula (I) repeated n times and whose complete sequence exhibits a degree of homology of at least 80% with (i) the sequence as shown in SI No. 1 beginning with the threonine residue at position 1 and ending with the leucine residue at position 414 + (20 × n) or (ii) the sequence as shown in SI No. 2 beginning with the threonine residue at position 1 and ending with the proline residue at position 246 + (20 × n); the number n relating to the sequence of formula (I) of said polypeptide on the one hand and that relating to the sequence as shown in SI No. 1 or 2 on the other hand being, in a dependent manner, 2, 3 or 4.

11. A composition according to claim 9, which comprises a virus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 is inserted, having as its sequence (i) the sequence as shown in SI No. 1 beginning with the threonine residue at position 1 and ending with the leucine residue at position 414 + (20 × n) or (ii) the sequence as shown in SI No. 2 beginning with the threonine residue at position 1 and ending with the proline residue at position

* C L M S *

246 + (20 × n); n being a number from 1 to 80.

12. A composition according to claim 11, which comprises a virus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 is inserted, having as its sequence (i) the sequence as shown in SI No. 1 beginning with the threonine residue at position 1 and ending with the leucine residue at position 414 + (20 × n) or (ii) the sequence as shown in SI No. 2 beginning with the threonine residue at position 1 and ending with the proline residue at position 246 + (20 × n); n being 2, 3 or 4.

13. A composition according to any one of claims 7 to 12, in which the virus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 is inserted is a poxvirus.

14. A composition according to any one of claims 7 to 12, in which the poxvirus into the genome of which a DNA fragment coding for a polypeptide recognized by antibody H23 is inserted is vaccinia virus.

15. As a therapeutic agent for the treatment or prevention of a malignant tumor, a polypeptide recognized by antibody H23.

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