

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
20 June 2002 (20.06.2002)

PCT

(10) International Publication Number  
**WO 02/48182 A2**

- (51) International Patent Classification<sup>7</sup>: **C07K 14/00**
- (21) International Application Number: PCT/GB01/05496
- (22) International Filing Date:  
11 December 2001 (11.12.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
0030184.6 11 December 2000 (11.12.2000) GB
- (71) Applicant (for all designated States except US):  
**PHARMA PACIFIC PTY. LTD** [AU/AU]; 103-105  
Pipe Road, Laverton North, VIC 3026 (AU).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **MERITET, Jean-Francois** [FR/FR]; 62, rue de Picpus, F-75012 Paris (FR). **DRON, Michel** [FR/FR]; 22, avenue des Cottages, F-92340 Bourg la Reine (FR). **TOVEY, Michael, Gerard** [GB/FR]; 7, rue Lagrange, F-75005 Paris (FR).
- (74) Agent: **IRVINE, Jonquil, Claire**; J.A. Kemp & Co., 14 South Square, Gray's Inn, London WC1R 5JJ (GB).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



**WO 02/48182 A2**

(54) Title: INTERFERON-ALPHA INDUCED GENE

(57) Abstract: The present invention relates to identification of a gene upregulated by interferon- $\alpha$  administration corresponding to the cDNA sequence set forth in SEQ.ID. No. 1. Determination of expression products of this gene is proposed as having utility in predicting responsiveness to treatment with interferon- $\alpha$  and other interferons which act at the Type 1 interferon receptor. Therapeutic use of the protein encoded by the same gene is also envisaged.

## INTERFERON-ALPHA INDUCED GENE

### Field of the Invention

The present invention relates to identification of a human gene upregulated by interferon- $\alpha$  (IFN- $\alpha$ ) administration, the coding sequence of which is believed to be previously unknown. Detection of expression products of this gene may find use in predicting responsiveness to IFN- $\alpha$  and other interferons which act at the Type 1 interferon receptor. Therapeutic use of the isolated novel protein encoded by the same gene is also envisaged.

### Background of the Invention

IFN- $\alpha$  is widely used for the treatment of a number of disorders. Disorders which may be treated using IFN- $\alpha$  include neoplastic diseases such as leukemia, lymphomas, and solid tumours, AIDS-related Kaposi's sarcoma and viral infections such as chronic hepatitis. IFN- $\alpha$  has also been proposed for administration via the oromucosal route for the treatment of autoimmune, mycobacterial, neurodegenerative, parasitic and viral disease. In particular, IFN- $\alpha$  has been proposed, for example, for the treatment of multiple sclerosis, leprosy, tuberculosis, encephalitis, malaria, cervical cancer, genital herpes, hepatitis B and C, HIV, HPV and HSV-1 and 2. It has also been suggested for the treatment of arthritis, lupus and diabetes. Neoplastic diseases such as multiple myeloma, hairy cell leukemia, chronic myelogenous leukemia, low grade lymphoma, cutaneous T-cell lymphoma, carcinoid tumours, cervical cancer, sarcomas including Kaposi's sarcoma, kidney tumours, carcinomas including renal cell carcinoma, hepatic cellular carcinoma, nasopharyngeal carcinoma, haematological malignancies, colorectal cancer, glioblastoma, laryngeal papillomas, lung cancer, colon cancer, malignant melanoma and brain tumours are also suggested as being treatable by administration of IFN- $\alpha$  via the oromucosal route, i.e. the oral route or the nasal route.

IFN- $\alpha$  is a member of the Type 1 interferon family, which exert their characteristic biological activities through interaction with the Type 1 interferon receptor. Other Type 1 interferons include IFN- $\beta$ , IFN- $\omega$  and IFN- $\tau$ .

Unfortunately, not all potential patients for treatment with a Type 1 interferon such as interferon- $\alpha$ , particularly, for example, patients suffering from chronic viral hepatitis, neoplastic disease and relapsing remitting multiple sclerosis, respond favourably to Type 1 interferon therapy and only a fraction of those who do respond exhibit long-term benefit. The inability of the physician to confidently predict the therapeutic outcome of Type 1 interferon treatment raises serious concerns as to the cost-benefit ratio of such treatment, not only in terms of wastage of an expensive biopharmaceutical and lost time in therapy, but also in terms of the serious side effects to which the patient is exposed. Furthermore, abnormal production of IFN- $\alpha$  has been shown to be associated with a number of autoimmune diseases. For these reasons, there is much interest in identifying Type 1 interferon responsive genes since Type 1 interferons exert their therapeutic action by modulating the expression of a number of genes. Indeed, it is the specific pattern of gene expression induced by Type 1 interferon treatment that determines whether a patient will respond favourably or not to the treatment.

### **Summary of the Invention**

A human gene cDNA has now been identified as corresponding to a mouse gene upregulated by administration of IFN- $\alpha$  by an oromucosal route or intravenously and is believed to represent a novel DNA. The corresponding human gene is thus now also designated an IFN- $\alpha$  upregulated gene.

The HuIFRG 70 gene encodes a protein of 618 amino acids and is referred to below as HuIFRG 70 protein. This protein shows homology to a 470 amino acid protein (AB033094), a 419 amino acid protein (AK022542) and a 373 amino acid protein (AK001770) all of unknown function. HuIFRG 70 protein, and functional variants thereof, are now envisaged as therapeutic agents, in particular for use as an anti-viral,

anti-tumour or immunomodulatory agent. For example, they may be used in the treatment of autoimmune, mycobacterial, neurodegenerative, parasitic or viral disease, arthritis, diabetes, lupus, multiple sclerosis, leprosy, tuberculosis, encephalitis, malaria, cervical cancer, genital herpes, hepatitis B or C, HIV, HPV, HSV-1 or 2, or neoplastic disease such as multiple myeloma, hairy cell leukemia, chronic myelogenous leukemia, low grade lymphoma, cutaneous T-cell lymphoma, carcinoid tumours, cervical cancer, sarcomas including Kaposi's sarcoma, kidney tumours, carcinomas including renal cell carcinoma, hepatic cellular carcinoma, nasopharyngeal carcinoma, haematological malignancies, colorectal cancer, glioblastoma, laryngeal papillomas, lung cancer, colon cancer, malignant melanoma or brain tumours. In other words, such a protein may find use in treating any Type 1 interferon treatable disease.

Determination of the level of HuIFRG 70 protein or a naturally-occurring variant thereof, or the corresponding mRNA, in cell samples of Type 1 interferon-treated patients, e.g. patients treated with IFN- $\alpha$ , e.g. such as by the oromucosal route or intravenously, may also be used to predict responsiveness to such treatment. It has additionally been found that alternatively, and more preferably, such responsiveness may be judged, for example, by treating a sample of human peripheral blood mononuclear cells *in vitro* with a Type 1 interferon and looking for upregulation or downregulation of an expression product, preferably mRNA, corresponding to the HuIFRG 70 gene.

According to a first aspect of the invention, there is thus provided an isolated polypeptide comprising;

- (i) the amino acid sequence of SEQ ID NO: 2;
- (ii) a variant thereof having substantially similar function, e.g. an immunomodulatory activity and/or an anti-viral activity and/or an anti-tumour activity; or
- (iii) a fragment of (i) or (ii) which retains substantially similar function, e.g. an immunomodulatory activity and/or an anti-viral activity and/or an anti-tumour activity.

The invention also provides such a protein for use in therapeutic treatment of a human or non-human animal, more particularly for use as an anti-viral, anti-tumour or immunomodulatory agent. As indicated above, such use may extend to any Type 1 interferon treatable disease.

According to another aspect of the invention, there is provided an isolated polynucleotide encoding a polypeptide of the invention as defined above or a complement thereof. Such a polynucleotide will typically include a sequence comprising:

- (a) the nucleic acid of SEQ. ID. No. 1 or the coding sequence thereof and/or a sequence complementary thereto;
- (b) a sequence which hybridises, e.g. under stringent conditions, to a sequence complementary to a sequence as defined in (a);
- (c) a sequence which is degenerate as a result of the genetic code to a sequence as defined in (a) or (b);
- (d) a sequence having at least 60% identity to a sequence as defined in (a), (b) or (c).

The invention also provides;

- an expression vector which comprises a polynucleotide of the invention and which is capable of expressing a polypeptide of the invention;
- a host cell containing an expression vector of the invention;
- an antibody specific for a polypeptide of the invention;
- a method of treating a subject having a Type 1 interferon treatable disease, which method comprises administering to the said patient an effective amount of HuIFRG 70 protein or a functional variant thereof
- use of such a polypeptide in the manufacture of a medicament for use in therapy as an anti-viral or anti-tumour or immunomodulatory agent, more particularly for use in treatment of a Type 1 interferon treatable disease;
- a pharmaceutical composition comprising a polypeptide of the invention and a pharmaceutically acceptable carrier or diluent;
- a method of producing a polypeptide of the invention, which method comprises maintaining host cells of the invention under conditions

suitable for obtaining expression of the polypeptide and isolating the said polypeptide;

- a polynucleotide of the invention, e.g. in the form of an expression vector, which directs expression *in vivo* of a polypeptide as defined above for use in therapeutic treatment of a human or non-human animal, more particularly for use as an anti-viral, anti-tumour or immunomodulatory agent;
- a pharmaceutical composition comprising such a polynucleotide and a pharmaceutically acceptable carrier or diluent;
- a method of treating a subject having a Type 1 interferon treatable disease, which method comprises administering to said patient an effective amount of such a polynucleotide;
- use of such a polynucleotide in the manufacture of a medicament, e.g. a vector preparation, for use in therapy as an anti-viral, anti-tumour or immunomodulatory agent, more particularly for use in treating a Type 1 interferon treatable disease; and
- a method of identifying a compound having immunomodulatory activity and/or anti-viral activity and/or anti-tumour activity comprising providing a cell capable of expressing HuIFRG 70 protein or a naturally occurring variant thereof, incubating said cell with a compound under test and monitoring for upregulation of HuIFRG 70 gene expression.

In a still further aspect, the invention provides a method of predicting responsiveness of a patient to treatment with a Type 1 interferon, e.g. IFN- $\alpha$  treatment (such as IFN- $\alpha$  treatment by the oromucosal route or a parenteral route, for example, intravenously, subcutaneously, or intramuscularly), which comprises determining the level of HuIFRG 70 protein or a naturally-occurring variant thereof, e.g. an allelic variant, or the corresponding mRNA, in a cell sample from said patient, e.g. a blood sample, wherein said sample is obtained from said patient following administration of a Type 1 interferon, e.g. IFN- $\alpha$  by an oromucosal route or intravenously, or is treated prior to said determining with

a Type 1 interferon such as IFN- $\alpha$  *in vitro*. The invention also extends to kits for carrying out such testing.

### **Brief description of the Sequences**

SEQ. ID. No.1 is the amino acid sequence of human protein HuIFRG 70 and its encoding cDNA.

SEQ. ID. No.2 is the amino acid sequence alone of HuIFRG 70 protein.

### **Detailed Description of the Invention**

As indicated above, human protein HuIFRG 70 and functional variants thereof are now envisaged as therapeutically useful agents, more particularly for use as an anti-viral, anti-tumour or immunomodulatory agent.

A variant of HuIFRG 70 protein for this purpose may be a naturally occurring variant, either an allelic variant or species variant, which has substantially the same functional activity as HuIFRG 70 protein and is also upregulated in response to administration of IFN- $\alpha$ . Alternatively, a variant of HuIFRG 70 protein for therapeutic use may comprise a sequence which varies from SEQ. ID. No. 2 but which is a non-natural mutant.

The term " functional variant" refers to a polypeptide which has the same essential character or basic function of HuIFRG 70 protein. The essential character of HuIFRG 70 protein may be deemed to be as an immunomodulatory peptide. A functional variant polypeptide may show additionally or alternatively anti-viral activity and/or anti-tumour activity.

Desired anti-viral activity may, for example, be tested as follows. antiviral activity may be monitored as follows. A sequence encoding a variant to be tested is cloned into a retroviral vector such as a retroviral vector derived from the Moloney murine leukemia virus (MoMuLV) containing the viral packaging signal  $\psi$ , and a drug-resistance marker. A pantropic packaging cell line containing the viral *gag*, and *pol*,

genes is then co-transfected with the recombinant retroviral vector and a plasmid, pVSV-G, containing the vesicular stomatitis virus envelope glycoprotein in order to produce high-titre infectious replication incompetent virus (Burns *et al.*, Proc. Natl. Acad. Sci. USA **84**, 5232-5236). The infectious recombinant virus is then used to transfect interferon sensitive fibroblasts or lymphoblastoid cells and cell lines that stably express the variant protein are then selected and tested for resistance to virus infection in a standard interferon bio-assay (Tovey *et al.*, Nature, **271**, 622-625, 1978). Growth inhibition using a standard proliferation assay (Mosmann, T., J. Immunol. Methods, **65**, 55-63, 1983) and expression of MHC class I and class II antigens using standard techniques may also be determined.

A desired functional variant of HuIFRG 70 may consist essentially of the sequence of SEQ. ID. No. 2. A functional variant of SEQ. ID. No.2 may be a polypeptide which has a least 60% to 70% identity, preferably at least 80% or at least 90% and particularly preferably at least 95%, at least 97% or at least 99% identity with the amino acid sequence of SEQ. ID. No. 2 over a region of at least 20, preferably at least 30, for instance at least 100 contiguous amino acids or over the full length of SEQ. ID. No. 2. Methods of measuring protein identity are well known in the art.

Amino acid substitutions may be made, for example from 1, 2 or 3 to 10, 20 or 30 substitutions. Conservative substitutions may be made, for example according to the following Table. Amino acids in the same block in the second column and preferably in the same line in the third column may be substituted for each other.

ALIPHATIC	Non-polar	G A P
		I L V
	Polar-uncharged	C S T M
		N Q
	Polar-charged	D E
		K R
AROMATIC		H F W Y

Variant polypeptide sequences for therapeutic use in accordance with the invention may be shorter polypeptide sequences, for example, a peptide of at least 20 amino acids or up to 50, 60, 70, 80, 100, 150 or 200 amino acids in length is considered to fall within the scope of the invention provided it retains appropriate biological activity of HuIFRG 70 protein. In particular, but not exclusively, this aspect of the invention encompasses the situation when the variant is a fragment of a complete natural naturally-occurring protein sequence.

Also encompassed by the invention are modified forms of HuIFRG 70 protein and fragments thereof which can be used to raise anti-HuIFRG 70 protein antibodies. Such variants will comprise an epitope of the HuIFRG 70 protein.

Polypeptides of the invention may be chemically modified, e.g. post-translationally modified. For example, they may be glycosylated and/or comprise modified amino acid residues. They may also be modified by the addition of a sequence at the N-terminus and/or C-terminus, for example by provision of histidine residues or a T7 tag to assist their purification or by the addition of a signal sequence to promote insertion into the cell membrane. Such modified polypeptides fall within the scope of the term "polypeptide" of the invention.

A polypeptide of the invention may be labelled with a revealing label. The revealing label may be any suitable label which allows the polypeptide to be detected. Suitable labels include radioisotopes such as  $^{125}\text{I}$ ,  $^{35}\text{S}$  or enzymes, antibodies, polynucleotides and linkers such as biotin. Labelled polypeptides of the invention may be used in assays. In such assays it may be preferred to provide the polypeptide attached to a solid support. The present invention also relates to such labelled and/or immobilised polypeptides packaged in the form of a kit in a container. The kit may optionally contain other suitable reagent(s), control(s) or instructions and the like.

The polypeptides of the invention may be made synthetically or by recombinant means. Such polypeptides of the invention may be modified to include non-naturally occurring amino acids, e.g. D amino acids. Variant polypeptides of the invention may have modifications to increase stability *in vitro* and/or *in vivo*. When the polypeptides are produced by synthetic means, such modifications may be introduced during production. The polypeptides may also be modified following either synthetic or recombinant production.

A number of side chain modifications are known in the protein modification art and may be present in polypeptides of the invention. Such modifications include, for example, modifications of amino acids by reductive alkylation by reaction with an aldehyde followed by reduction with  $\text{NaBH}_4$ , amidination with methylacetimidate or acylation with acetic anhydride.

Polypeptides of the invention will be in substantially isolated form. It will be understood that the polypeptides may be mixed with carriers or diluents which will not interfere with the intended purpose of the polypeptide and still be regarded as substantially isolated. A polypeptide of the invention may also be in substantially purified form, in which case it will generally comprise the polypeptide in a preparation in which more than 90%, for example more than 95%, 98% or 99%, by weight of polypeptide in the preparation is a polypeptide of the invention.

### Polynucleotides

The invention also includes isolated nucleotide sequences that encode HuIFRG 70 protein or a variant thereof as well as isolated nucleotide sequences which are complementary thereto. The nucleotide sequence may be DNA or RNA, single or double stranded, including genomic DNA, synthetic DNA or cDNA. Preferably the nucleotide sequence is a DNA sequence and most preferably, a cDNA sequence.

As indicated above, such a polynucleotide will typically include a sequence comprising:

- (a) the nucleic acid of SEQ. ID. No. 1 or the coding sequence thereof and/or a sequence complementary thereto;
- (b) a sequence which hybridises, e.g. under stringent conditions, to a sequence complementary to a sequence as defined in (a);
- (c) a sequence which is degenerate as a result of the genetic code to a sequence as defined in (a) or (b);
- (d) a sequence having at least 60% identity to a sequence as defined in (a), (b) or (c).

Polynucleotides comprising an appropriate coding sequence can be isolated from human cells or synthesised according to methods well known in the art, as described by way of example in Sambrook *et al.* (1989) *Molecular Cloning: A Laboratory Manual*, 2<sup>nd</sup> edition, Cold Spring Harbor Laboratory Press.

Polynucleotides of the invention may include within them synthetic or modified nucleotides. A number of different types of modification to polynucleotides are known in the art. These include methylphosphonate and phosphothioate backbones, addition of acridine or polylysine chains at the 3' and/or 5' ends of the molecule. Such modifications may be carried out in order to enhance the *in vivo* activity or lifespan of polynucleotides of the invention.

Typically a polynucleotide of the invention will include a sequence of nucleotides, which may preferably be a contiguous sequence of nucleotides, which is

capable of hybridising under selective conditions to the coding sequence or the complement of the coding sequence of SEQ. ID. No. 1. Such hybridisation will occur at a level significantly above background. Background hybridisation may occur, for example, because of other cDNAs present in a cDNA library. The signal level generated by the interaction between a polynucleotide of the invention and the coding sequence or complement of the coding sequence of SEQ. ID. No. 1 will typically be at least 10 fold, preferably at least 100 fold, as intense as interactions between other polynucleotides and the coding sequence of SEQ. ID. No. 1. The intensity of interaction may be measured, for example, by radiolabelling the probe, e.g. with  $^{32}\text{P}$ . Selective hybridisation may typically be achieved using conditions of low stringency (0.3M sodium chloride and 0.03M sodium citrate at about 40°C), medium stringency (for example, 0.3M sodium chloride and 0.03M sodium citrate at about 50°C) or high stringency (for example, 0.03M sodium chloride and 0.03M sodium citrate at about 60°C).

The coding sequence of SEQ ID No: 1 may be modified by nucleotide substitutions, for example from 1, 2 or 3 to 10, 25, 50 or 100 substitutions. Degenerate substitutions may be made and/or substitutions may be made which would result in a conservative amino acid substitution when the modified sequence is translated, for example as shown in the table above. The coding sequence of SEQ. ID. NO: 1 may alternatively or additionally be modified by one or more insertions and/or deletions and/or by an extension at either or both ends.

A polynucleotide of the invention capable of selectively hybridising to a DNA sequence selected from SEQ. ID No.1, the coding sequence thereof and DNA sequences complementary thereto will be generally at least 70%, preferably at least 80 or 90% and more preferably at least 95% or 97%, homologous to the target sequence. This homology may typically be over a region of at least 20, preferably at least 30, for instance at least 40, 60 or 100 or more contiguous nucleotides.

Any combination of the above mentioned degrees of homology and minimum sized may be used to define polynucleotides of the invention, with the more stringent combinations (i.e. higher homology over longer lengths) being preferred. Thus for

example a polynucleotide which is at least 80% homologous over 25, preferably over 30 nucleotides forms may be found suitable, as may be a polynucleotide which is at least 90% homologous over 40 nucleotides.

Homologues of polynucleotide or protein sequences as referred to herein may be determined in accordance with well-known means of homology calculation, e.g. protein homology may be calculated on the basis of amino acid identity (sometimes referred to as "hard homology"). For example the UWGCG Package provides the BESTFIT program which can be used to calculate homology, for example used on its default settings, (Devereux *et al.* (1984) *Nucleic Acids Research* **12**, 387-395). The PILEUP and BLAST algorithms can be used to calculate homology or line up sequences or to identify equivalent or corresponding sequences, typically used on their default settings, for example as described in Altschul S. F. (1993) *J. Mol. Evol.* **36**,290-300; Altschul, S. F. *et al.* (1990) *J. Mol. Biol.* **215**,403-10.

Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length *W* in the query sequence that either match or satisfy some positive-valued threshold score *T* when aligned with a word of the same length in a database sequence. *T* is referred to as the neighbourhood word score threshold (Altschul *et al.*, *supra*). These initial neighbourhood word hits act as seeds for initiating searches to find HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extensions for the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity *X* from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters *W*, *T* and *X* determine the sensitivity and speed of the alignment. The BLAST program uses as defaults a word length (*W*) of 11, the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1992) *Proc. Natl. Acad. Sci. USA* **89**,10915-10919) alignments (*B*) of 50, expectation (*E*) of 10, *M*=5, *N*=4, and a comparison of both strands.

The BLAST algorithm performs a statistical analysis of the similarity between two sequences; see e.g., Karlin and Altschul (1993) Proc. Natl. Acad. Sci. USA 90: 5873-5787. One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a sequence is considered similar to another sequence if the smallest sum probability in comparison of the first sequence to the second sequence is less than about 1, preferably less than about 0.1, more preferably less than about 0.01, and most preferably less than about 0.001.

Polynucleotides according to the invention have utility in production of the proteins according to the invention, which may take place *in vitro*, *in vivo* or *ex vivo*. In such a polynucleotide, the coding sequence for the desired protein of the invention will be operably-linked to a promoter sequence which is capable of directing expression of the desired protein in the chosen host cell. Such a polynucleotide will generally be in the form of an expression vector. Polynucleotides of the invention, e.g. in the form of an expression vector, which direct expression *in vivo* of a polypeptide of the invention having immunomodulatory activity and/or anti-viral activity and/or anti-tumour activity may also be used as a therapeutic agent.

Expression vectors for such purposes may be constructed in accordance with conventional practices in the art of recombinant DNA technology. They may, for example, involve the use of plasmid DNA. They may be provided with an origin of replication. Such a vector may contain one or more selectable marker genes, for example an ampicillin resistance gene in the case of a bacterial plasmid. Other features of vectors of the invention may include appropriate initiators, enhancers and other elements, such as for example polyadenylation signals which may be desirable, and which are positioned in the correct orientation, in order to allow for protein expression. Other suitable non-plasmid vectors would be apparent to persons skilled in the art. By way of further example in this regard reference is made again to Sambrook *et al.*, 1989 (*supra*). Such vectors additionally include, for example, viral vectors. Examples of

suitable viral vectors include herpes simplex viral vectors, replication-defective retroviruses, including lentiviruses, adenoviruses, adeno-associated virus, HPV viruses (such as HPV-16 and HPV-18) and attenuated influenza virus vectors.

Promoters and other expression regulation signals may be selected to be compatible with the host cell for which expression is designed. For example, yeast promoters include *S. cerevisiae* GAL4 and ADH promoters, *S. pombe nmt1* and *adh* promoter. Mammalian promoters include the metallothionein promoter which can be induced in response to heavy metals such as cadmium and  $\beta$ -actin promoters. Viral promoters such as the SV40 large T antigen promoter or adenovirus promoters may also be used. Other examples of viral promoters which may be employed include the Moloney murine leukemia virus long terminal repeat (MMLV LTR), the rous sarcoma virus (RSV) LTR promoter, the human cytomegalovirus (CMV) IE promoter, and HPV promoters, particularly the HPV upstream regulatory region (URR). Other suitable promoters will be well-known to those skilled in the recombinant DNA art.

An expression vector of the invention may further include sequences flanking the coding sequence for the desired polypeptide of the invention providing sequences homologous to eukaryotic genomic sequences, preferably mammalian genomic sequences, or viral genomic sequences. This will allow the introduction of such polynucleotides of the invention into the genome of eukaryotic cells or viruses by homologous recombination. In particular, a plasmid vector comprising the expression cassette flanked by viral sequences can be used to prepare a viral vector suitable for delivering the polynucleotides of the invention to a mammalian cell.

The invention also includes cells *in vitro*, for example prokaryotic or eukaryotic cells, which have been modified to express the HuIFRG 70 protein or a variant thereof. Such cells include stable, e.g. eukaryotic, cell lines wherein a polynucleotide encoding HuIFRG 70 protein or a variant thereof is incorporated into the host genome. Host cells of the invention may be mammalian cells or insect cells, lower eukaryotic cells, such as yeast or prokaryotic cells such as bacterial cells. Particular examples of cells which may be modified by insertion of vectors encoding for a polypeptide according to the invention include mammalian HEK293T, CHO, HeLa and COS cells. Preferably a cell line may

be chosen which is not only stable, but also allows for mature glycosylation of a polypeptide. Expression may, for example, be achieved in transformed oocytes.

A polypeptide of the invention may be expressed in cells of a transgenic non-human animal, preferably a mouse. A transgenic non-human animal capable of expressing a polypeptide of the invention is included within the scope of the invention.

Polynucleotides according to the invention may also be inserted into vectors as described above in an antisense orientation in order to provide for the production of antisense sequences. Antisense RNA or other antisense polynucleotides may also be produced by synthetic means.

A polynucleotide, e.g. in the form of an expression vector, capable of expressing *in vivo* an antisense sequence to a coding sequence for the amino acid sequence defined by SEQ. ID. No. 2, or a naturally-occurring variant thereof, for use in therapeutic treatment of a human or non-human animal is also envisaged as constituting an additional aspect of the invention. Such a polynucleotide will find use in treatment of diseases associated with upregulation of HuIFRG 70 protein.

Polynucleotides of the invention extend to sets of primers for nucleic acid amplification which target sequences within the cDNA for a polypeptide of the invention, e.g. pairs of primers for PCR amplification. The invention also provides probes suitable for targeting a sequence within a cDNA or RNA for a polypeptide of the invention which may be labelled with a revealing label, e.g. a radioactive label or a non-radioactive label such as an enzyme or biotin. Such probes may be attached to a solid support. Such a solid support may be a micro-array (also commonly referred to as nucleic acid, probe or DNA chip) carrying probes for further nucleic acids, e.g. mRNAs or amplification products thereof corresponding to other Type 1 interferon upregulated genes, e.g. such genes identified as upregulated in response to oromucosal or intravenous administration of IFN- $\alpha$ . Methods for constructing such micro-arrays are well-known (see, for example, EP-B 0476014 and 0619321 of Affymax Technologies N.V. and Nature Genetics Supplement January 1999 entitled "The Chipping Forecast").

The nucleic acid sequence of such a primer or probe will preferably be at least 10, preferably at least 15 or at least 20, for example at least 25, at least 30 or at least 40 nucleotides in length. It may, however, be up to 40, 50, 60, 70, 100 or 150 nucleotides in length or even longer.

Another aspect of the invention is the use of probes or primers of the invention to identify mutations in HuIFRG 70 genes, for example single nucleotide polymorphisms (SNPs).

As indicated above, in a still further aspect the present invention provides a method of identifying a compound having immunomodulatory activity and/or antiviral activity and/or anti-tumour activity comprising providing a cell capable of expressing HuIFRG 70 protein or a naturally-occurring variant thereof, incubating said cell with a compound under test and monitoring for upregulation of HuIFRG 70 gene expression. Such monitoring may be by probing for mRNA encoding HuIFRG 70 protein or a naturally-occurring variant thereof. Alternatively antibodies or antibody fragments capable of specifically binding one or more of HuIFRG 70 and naturally-occurring variants thereof may be employed.

### Antibodies

According to another aspect, the present invention also relates to antibodies (for example polyclonal or preferably monoclonal antibodies, chimeric antibodies, humanised antibodies and fragments thereof which retain antigen-binding capability) which have been obtained by conventional techniques and are specific for a polypeptide of the invention. Such antibodies could, for example, be useful in purification, isolation or screening methods involving immunoprecipitation and may be used as tools to further elucidate the function of HuIFRG 70 protein or a variant thereof. They may be therapeutic agents in their own right. Such antibodies may be raised against specific epitopes of proteins according to the invention. An antibody specifically binds to a protein when it binds with high affinity to the protein for which it is specific but does not bind or binds with only low affinity to other proteins. A variety of protocols for

competitive binding or immunoradiometric assays to determine the specific binding capability of an antibody are well-known.

### Pharmaceutical compositions

A polypeptide of the invention is typically formulated for administration with a pharmaceutically acceptable carrier or diluent. The pharmaceutical carrier or diluent may be, for example, an isotonic solution. For example, solid oral forms may contain, together with the active compound, diluents, e.g. lactose, dextrose, saccharose, cellulose, corn starch or potato starch; lubricants, e.g. silica, talc, stearic acid, magnesium or calcium stearate, and/or polyethylene glycols; binding agents; e.g. starches, arabic gums, gelatin, methyl cellulose, carboxymethylcellulose or polyvinyl pyrrolidone; desegregating agents, e.g. starch, alginic acid, alginates or sodium starch glycolate; effervescing mixtures; dyestuffs; sweeteners; wetting agents, such as lecithin, polysorbates, laurylsulphates; and, in general, non-toxic and pharmacologically inactive substances used in pharmaceutical formulations. Such pharmaceutical preparations may be manufactured in known manner, for example, by means of mixing, granulating, tableting, sugar-coating, or film coating processes.

Liquid dispersions for oral administration may be syrups, emulsions and suspensions. The syrups may contain as carriers, for example, saccharose or saccharose with glycerine and/or mannitol and/or sorbitol.

Suspensions and emulsions may contain as carrier, for example a natural gum, agar, sodium alginate, pectin, methyl cellulose, carboxymethylcellulose, or polyvinyl alcohol. The suspensions or solutions for intramuscular injections may contain, together with the active compound, a pharmaceutically acceptable carrier, e.g. sterile water, olive oil, ethyl oleate, glycols, e.g. propylene glycol, and if desired, a suitable amount of lidocaine hydrochloride.

Solutions for intravenous administration or infusions may contain as carrier, for example, sterile water or preferably they may be in the form of sterile, aqueous, isotonic saline solutions.

A suitable dose of HuIFRG 70 protein or a functional analogue thereof for use in accordance with the invention may be determined according to various parameters, especially according to the substance used; the age, weight and condition of the patient to be treated; the route of administration; and the required regimen. Again, a physician will be able to determine the required route of administration and dosage for any particular patient. A typical daily dose may be from about 0.1 to 50 mg per kg, preferably from about 0.1mg/kg to 10mg/kg of body weight, according to the activity of the specific inhibitor, the age, weight and condition of the subject to be treated, and the frequency and route of administration. Preferably, daily dosage levels may be from 5 mg to 2 g.

A polynucleotide of the invention suitable for therapeutic use will also typically be formulated for administration with a pharmaceutically acceptable carrier or diluent. Such a polynucleotide may be administered by any known technique whereby expression of the desired polypeptide can be attained *in vivo*. For example, the polynucleotide may be introduced by injection, preferably intradermally, subcutaneously or intramuscularly. Alternatively, the nucleic acid may be delivered directly across the skin using a particle-mediated delivery device. A polynucleotide of the invention suitable for therapeutic nucleic acid may alternatively be administered to the oromucosal surface for example by intranasal or oral administration.

A non-viral vector of the invention suitable for therapeutic use may, for example, be packaged into liposomes or into surfactant containing vector delivery particles. Uptake of nucleic acid constructs of the invention may be enhanced by several known transfection techniques, for example those including the use of transfection agents. Examples of these agents include cationic agents, for example calcium phosphate and DEAE dextran and lipofectants, for example lipopfectam and transfectam. The dosage of the nucleic acid to be administered can be varied. Typically, the nucleic acid will be administered in the range of from 1pg to 1mg, preferably from 1pg to 10 $\mu$ g nucleic acid for particle-mediated gene delivery and from 10 $\mu$ g to 1 mg for other routes.

### Prediction of Type 1 interferon responsiveness

As also indicated above, in a still further aspect the present invention provides a method of predicting responsiveness of a patient to treatment with a Type 1 interferon, e.g. IFN- $\alpha$  treatment such as IFN- $\alpha$  treatment by an oromucosal route or intravenously, which comprises determining the level of HuIFRG 70 protein or a naturally-occurring variant thereof, or the corresponding mRNA, in a cell sample from said patient, wherein said sample is taken from said patient following administration of a Type 1 interferon or is treated prior to said determining with a Type 1 interferon *in vitro*.

Preferably, the Type 1 interferon for testing responsiveness will be the Type 1 interferon selected for treatment. It may be administered by the proposed treatment route and at the proposed treatment dose. Preferably, the subsequent sample analysed may be, for example, a blood sample or a sample of peripheral blood mononuclear cells (PBMCs) isolated from a blood sample.

More conveniently and preferably, a sample obtained from the patient comprising PBMCs isolated from blood may be treated *in vitro* with a Type 1 interferon, e.g. at a dosage range of about 1 to 10,000 IU/ml. Such treatment may be for a period of hours, e.g. about 7 to 8 hours. Preferred treatment conditions for such *in vitro* testing may be determined by testing PBMCs taken from normal donors with the same interferon and looking for upregulation of an appropriate expression product. Again, the Type 1 interferon employed will preferably be the Type 1 interferon proposed for treatment of the patient, e.g. recombinant IFN- $\alpha$ . PBMCs for such testing may be isolated in conventional manner from a blood sample using Ficoll-Hypaque density gradients. An example of a suitable protocol for such *in vitro* testing of Type 1 interferon responsiveness is provided in Example 3 below.

The sample, if appropriate after *in vitro* treatment with a Type 1 interferon, may be analysed for the level of HuIFRG 70 protein or a naturally-occurring variant thereof. This may be done using an antibody or antibodies capable of specifically binding one or

more of HuIFRG 70 protein and naturally-occurring variants thereof, e.g. allelic variants thereof. Preferably, however, the sample will be analysed for mRNA encoding HuIFRG 70 protein or a naturally-occurring variant thereof. Such mRNA analysis may employ any of the techniques known for detection of mRNAs, e.g. Northern blot detection or mRNA differential display. A variety of known nucleic acid amplification protocols may be employed to amplify any mRNA of interest present in the sample, or a portion thereof, prior to detection. The mRNA of interest, or a corresponding amplified nucleic acid, may be probed for using a nucleic acid probe attached to a solid support. Such a solid support may be a micro-array as previously discussed above carrying probes to determine the level of further mRNAs or amplification products thereof corresponding to Type 1 interferon upregulated genes, e.g. such genes identified as upregulated in response to oromucosal or intravenous administration of IFN- $\alpha$ .

The following examples illustrate the invention:

### **Examples**

#### **Example 1**

Previous experiments had shown that the application of 5  $\mu$ l of crystal violet to each nostril of a normal adult mouse using a P20 Eppendorf micropipette resulted in an almost immediate distribution of the dye over the whole surface of the oropharyngeal cavity. Staining of the oropharyngeal cavity was still apparent some 30 minutes after application of the dye. These results were confirmed by using  $^{125}$ I-labelled recombinant human IFN- $\alpha$ 1-8 applied in the same manner. The same method of administration was employed to effect oromucosal administration in the studies which are described below.

Six week old, male DBA/2 mice were treated with either 100,000 IU of recombinant murine interferon  $\alpha$  (IFN  $\alpha$ ) purchased from Life Technologies Inc, in phosphate buffered saline (PBS), 10 $\mu$ g of recombinant human interleukin 15 (IL-15) purchased from Protein Institute Inc, PBS containing 100  $\mu$ g/ml of bovine serum albumin (BSA), or left untreated. Eight hours later, the mice were sacrificed by cervical dislocation and the lymphoid tissue was removed surgically from the oropharyngeal

cavity and snap frozen in liquid nitrogen and stored at -80°C. RNA was extracted from the lymphoid tissue by the method of Chomczynski and Sacchi 1987, (Anal. Biochem. **162**, 156-159) and subjected to mRNA Differential Display Analysis (Lang, P. and Pardee, A.B., Science, **257**, 967-971).

#### Differential Display Analysis

Differential display analysis was carried out using the "Message Clean" and "RNA image" kits of the GenHunter Corporation essentially as described by the manufacturer. Briefly, RNA was treated with RNase-free DNase, and 1 µg was reverse-transcribed in 100 µl of reaction buffer using either one or the other of the three one-base anchored oligo-(dT) primers A, C, or G. RNA was also reverse-transcribed using one or the other of the 9 two-base anchored oligo-(dT) primers AA, CC, GG, AC, CA, GA, AG, CG, GC. All the samples to be compared were reverse transcribed in the same experiment, separated into aliquots and frozen. The amplification was performed with only 1 µl of the reverse transcription sample in 10 µl of amplification mixture containing *Taq* DNA polymerase and  $\alpha$ -<sup>33</sup>P dATP (3,000 Ci/mmol). Eighty 5' end (HAP) random sequence primers were used in combination with each of the (HT11) A, C, G, AA, CC, GG, AC, CA, GA, AG, CG or GC primers. Samples were then run on 7% denaturing polyacrylamide gels and exposed to autoradiography. Putative differentially expressed bands were cut out, reamplified according to the instructions of the supplier, and further used as probes to hybridize Northern blots of RNA extracted from the oropharyngeal cavity of IFN treated, IL-15 treated, and excipient treated animals.

#### Cloning and Sequencing

Re-amplified bands from the differential display screen were cloned in the *Sfi* I site of the pPCR-Script SK(+) plasmid (Stratagene) and cDNAs amplified from the rapid amplification of cDNA ends were isolated by TA cloning in the pCR3 plasmid (Invitrogen). DNA was sequenced using an automatic di-deoxy sequencer (Perkin Elmer ABI PRISM 377).

### Isolation of Human cDNA

Differentially expressed murine 3' sequences identified from the differential display screen were compared with random human expressed sequence tags (EST) present in the dbEST database of GenBank™ of the United States National Center for Biotechnology Information (NCBI). The sequences potentially related to the murine EST isolated from the differential display screen were combined in a contig and used to construct a human consensus sequence corresponding to a putative cDNA. One such cDNA was found to be 4135 nucleotides in length. This corresponded to a mouse gene whose expression was found to be enhanced approximately 5-fold in the lymphoid tissue of the oral cavity of mice following oromucosal administration of recombinant murine IFN- $\alpha$ .

In order to establish that this putative cDNA corresponded to an authentic human gene, primers derived from the 5' and 3' ends of the consensus sequence were used to synthesise cDNA from mRNA extracted from human peripheral blood leukocytes (PBL) by specific reverse transcription and PCR amplification. A unique cDNA fragment of the predicted size was obtained, cloned and sequenced (SEQ. ID. No.1). This human cDNA contains an open reading frame (ORF) of 1857 bp in length at positions 36-1892 encoding a protein of 618 amino acids (SEQ. ID. No. 2).

### Example 2

#### Intravenous administration of IFN- $\alpha$

Male DBA/2 mice were injected intravenously with 100,000 IU of recombinant murine IFN- $\alpha$  purchased from Life Technologies Inc. in 200  $\mu$ l of PBS or treated with an equal volume of PBS alone. Eight hours later, the animals were sacrificed by cervical dislocation and the spleen was removed using conventional procedures. Total RNA was extracted by the method of Chomczynski and Sacchi (Anal. Biochem. (1987) 162,156-159) and 10.0  $\mu$ g of total RNA per sample was subjected to Northern blotting in the presence of glyoxal and hybridised with a cDNA probe for HuIFRG 70 mRNA as

described by Dandoy-Dron et al.(J. Biol. Chem. (1998) 273, 7691-7697). The blots were first exposed to autoradiography and then quantified using a PhosphorImager according to the manufacturer's instructions. Enhanced levels of mRNA for HuIFRG 70 protein (approximately 10 fold) were detected in samples of RNA extracted from spleens of IFN- $\alpha$  treated animals relative to animals treated with excipient alone.

### Example 3

#### Testing Type 1 interferon responsiveness *in vitro*

Human peripheral blood mononuclear cells (PBMCs) from normal donors were isolated on Ficoll-Hypaque density gradients and treated *in vitro* with 10,000 IU of recombinant human IFN- $\alpha$ 2 (Intron A from Schering-Plough) in PBS or with an equal volume of PBS alone. Eight hours later the cells were centrifuged (800 x g for 10 minutes) and the cell pellet recovered. Total RNA was extracted from the cell pellet by the method of Chomczynski and Sacchi and 10.0  $\mu$ g of total RNA per sample was subjected to Northern blotting in the presence of glyoxal and hybridised with a cDNA probe for HuIFRG 70 mRNA as previously described in Example 2 above. Enhanced levels of mRNA for HUIFRG 70 protein (approximately 2-fold) were detected in samples of RNA extracted from IFN- $\alpha$  treated PBMCs compared to samples treated with PBS alone.

The same procedure may be used to predict Type 1 interferon responsiveness using PBMCs taken from a patient proposed to be treated with a Type 1 interferon.

CLAIMS

1. An isolated polypeptide comprising
  - (i) the amino acid sequence of SEQ ID NO: 2;
  - (ii) a variant thereof having substantially similar function selected from immunomodulatory activity and/or anti-viral activity and/or anti-tumour activity; or
  - (iii) a fragment of (i) or (ii) which retains substantially similar function selected from immunomodulatory activity and/or anti-viral activity and/or anti-tumour activity.
2. A variant or fragment of the polypeptide defined by the amino acid sequence set forth in SEQ. ID. No. 2 suitable for raising specific antibodies for said polypeptide and/or a naturally-occurring variant thereof.
3. A polynucleotide encoding a polypeptide as claimed in claim 1 or 2.
4. A polynucleotide as claimed in claim 3 which is a cDNA.
5. A polynucleotide encoding a polypeptide as claimed in claim 1, which polynucleotide comprises:
  - (a) the nucleic acid sequence of SEQ ID NO: 1 or the coding sequence thereof and/or a sequence complementary thereto;
  - (b) a sequence which hybridises to a sequence as defined in (a);
  - (c) a sequence that is degenerate as a result of the genetic code to a sequence as defined in (a) or (b); or
  - (d) a sequence having at least 60% identity to a sequence as defined in (a), (b) or (c).
6. An expression vector comprising a polynucleotide sequence as claimed in any one of claims 3 to 5, which is capable of expressing a polypeptide according to claim 1 or 2.

7. A host cell containing an expression vector according to claim 6.
8. An antibody specific for a polypeptide as claimed in claim 1 or claim 2.
9. An isolated polynucleotide which directs expression *in vivo* of a polypeptide as claimed in claim 1.
10. A polypeptide as claimed in claim 1 or a polynucleotide as claimed in claim 9 for use in therapeutic treatment of a human or non-human animal.
11. A pharmaceutical composition comprising a polypeptide as claimed in claim 1 or a polynucleotide as claimed in claim 9 and a pharmaceutically acceptable carrier or diluent.
12. Use of a polypeptide as claimed in claim 1 or a polynucleotide as claimed in claim 9 in the preparation of medicament for use in therapy as an anti-viral, anti-tumour or immunomodulatory agent.
13. A method of treating a patient having a Type 1 interferon treatable disease, which comprises administering to said patient an effective amount of a polypeptide as claimed in claim 1 or a polynucleotide as claimed in claim 9.
14. A method of producing a polypeptide according to claim 1 or 2, which method comprises culturing host cells as claimed in claim 7 under conditions suitable for obtaining expression of the polypeptide and isolating the said polypeptide.
15. A method of identifying a compound having immunomodulatory activity and/or anti-viral activity and/or anti-tumour activity comprising providing a cell capable of expressing the polypeptide of SEQ. ID. No. 2 or a naturally-occurring variant thereof, incubating said cell with a compound under test and monitoring for upregulation of the gene encoding said polypeptide or variant.

16. A polynucleotide capable of expressing *in vivo* an antisense sequence to a coding sequence for the amino acid sequence defined by SEQ. ID. No.2 or a naturally-occurring variant of said coding sequence for use in therapeutic treatment of a human or non-human animal.
17. An antibody as claimed in claim 8 for use in therapeutic treatment.
18. A set of primers for nucleic acid amplification which target sequences within a cDNA as claimed in claim 4.
19. A nucleic acid probe derived from a polynucleotide as claimed in any one of claims 3 to 5.
20. A probe as claimed in claim 19 which is attached to a solid support.
21. A method of predicting responsiveness of a patient to treatment with a Type 1 interferon, which comprises determining the level of the protein defined by the amino acid sequence set forth in SEQ. ID. No. 2 or a naturally-occurring variant thereof, or the corresponding mRNA, in a cell sample from said patient, wherein said sample is obtained from said patient following administration of a Type 1 interferon or is treated prior to said determining with a Type 1 interferon *in vitro*.
22. A method as claimed in claim 21 wherein the interferon administered prior to obtaining said sample or used to treat said sample *in vitro* is the interferon proposed for treatment of said patient.
23. A method as claimed in claim 21 or claim 22 wherein a sample comprising peripheral blood mononuclear cells isolated from a blood sample of the patient is treated with a Type 1 interferon *in vitro*.
24. A method as claimed in any one of claims 21 to 23 wherein said determining comprises determining the level of mRNA encoding the protein defined by the

sequence set forth in SEQ. ID. No. 2 or a naturally-occurring variant of said protein.

25. A non-human transgenic animal capable of expressing a polypeptide that is claimed in claim 1.

SEQUENCE LISTING

<110> PHARMA PACIFY PTY

<120> INTERFERON-ALPHA INDUCED GENE

<130> N81265A JCI

<160> 3

<170> PatentIn version 3.0

<210> 1

<211> 4135

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (36)..(1892)

<400> 1

```

ccgagtggtc aataaaatat tccaggcatt ttcag atg aat ttg ccc aga agg      53
                                         Met Asn Leu Pro Arg Arg
                                         1             5

gtt aag gaa aat ctc gtc agt gac aaa ttt ccg aag gct aaa gat aca      101
Val Lys Glu Asn Leu Val Ser Asp Lys Phe Pro Lys Ala Lys Asp Thr
                    10             15             20

caa ggt ttt tat ggg act gtt tct agc cct gat tca ggt gtg tat gaa      149
Gln Gly Phe Tyr Gly Thr Val Ser Ser Pro Asp Ser Gly Val Tyr Glu
                    25             30             35

atg aag att ggc tcc atc atc ttc cag gtg gct tct gga gat atc acg      197
Met Lys Ile Gly Ser Ile Ile Phe Gln Val Ala Ser Gly Asp Ile Thr
                    40             45             50

aaa gaa gag gca gat gtg att gta aat tca aca tca aac tca ttc aat      245
Lys Glu Glu Ala Asp Val Ile Val Asn Ser Thr Ser Asn Ser Phe Asn
                    55             60             65             70

ctc aaa gca ggg gtc tcc aaa gca att tta gaa tgt gct gga caa aat      293
Leu Lys Ala Gly Val Ser Lys Ala Ile Leu Glu Cys Ala Gly Gln Asn
                    75             80             85

gta gaa agg gaa tgt tct cag caa gct cag cag cgc aaa aat gat tat      341
Val Glu Arg Glu Cys Ser Gln Gln Ala Gln Gln Arg Lys Asn Asp Tyr
                    90             95             100

ata atc acc gga ggt gga ttt ttg agg tgc aag aat atc att cat gta      389
Ile Ile Thr Gly Gly Gly Phe Leu Arg Cys Lys Asn Ile Ile His Val
                    105             110             115
    
```

att ggt gga aat gat gtc aag agt tca gtt tcc tct gtt ttg cag gag 437  
 Ile Gly Gly Asn Asp Val Lys Ser Ser Val Ser Ser Val Leu Gln Glu  
 120 125 130

tgt gaa aaa aaa aat tac tca tcc att tgc ctc cca gcc att ggg aca 485  
 Cys Glu Lys Lys Asn Tyr Ser Ser Ile Cys Leu Pro Ala Ile Gly Thr  
 135 140 145 150

gga aat gcc aaa caa cac cca gat aag gtt gct gaa gcc ata att gat 533  
 Gly Asn Ala Lys Gln His Pro Asp Lys Val Ala Glu Ala Ile Ile Asp  
 155 160 165

gcc att gaa gac ttt gtc cag aaa gga tca gcc cag tct gtg aaa aaa 581  
 Ala Ile Glu Asp Phe Val Gln Lys Gly Ser Ala Gln Ser Val Lys Lys  
 170 175 180

gtt aaa gtt gtt atc ttt ctg cct caa gta ctg gat gtg ttt tat gct 629  
 Val Lys Val Val Ile Phe Leu Pro Gln Val Leu Asp Val Phe Tyr Ala  
 185 190 195

aac atg aag aaa aga gaa ggg act cag ctt tct tcc caa cag tct gtg 677  
 Asn Met Lys Lys Arg Glu Gly Thr Gln Leu Ser Ser Gln Gln Ser Val  
 200 205 210

atg tct aaa ctt gca tca ttt ttg ggc ttt tca aag caa tct ccc caa 725  
 Met Ser Lys Leu Ala Ser Phe Leu Gly Phe Ser Lys Gln Ser Pro Gln  
 215 220 225 230

aaa aag aat cat ttg gtt ttg gaa aag aaa aca gaa tca gca act ttt 773  
 Lys Lys Asn His Leu Val Leu Glu Lys Lys Thr Glu Ser Ala Thr Phe  
 235 240 245

cgg gtg tgt ggt gaa aat gtc acg tgt gtg gaa tat gct atc tcc tgg 821  
 Arg Val Cys Gly Glu Asn Val Thr Cys Val Glu Tyr Ala Ile Ser Trp  
 250 255 260

cta caa gac ctg att gaa aaa gaa cag tgt cct tac acc agt gaa gat 869  
 Leu Gln Asp Leu Ile Glu Lys Glu Gln Cys Pro Tyr Thr Ser Glu Asp  
 265 270 275

gag tgc atc aaa gac ttt gat gaa aag gag tat cag gag ttg aat gag 917  
 Glu Cys Ile Lys Asp Phe Asp Glu Lys Glu Tyr Gln Glu Leu Asn Glu  
 280 285 290

ctg cag aag aag tta aat att aac att tcc ctg gac cat aag aga cct 965  
 Leu Gln Lys Lys Leu Asn Ile Asn Ile Ser Leu Asp His Lys Arg Pro  
 295 300 305 310

ttg att aag gtt ttg gga att agc aga gat gtg atg cag gct aga gat 1013  
 Leu Ile Lys Val Leu Gly Ile Ser Arg Asp Val Met Gln Ala Arg Asp  
 315 320 325

gaa att gag gcg atg atc aag aga gtt cga ttg gcc aaa gaa cag gaa 1061  
 Glu Ile Glu Ala Met Ile Lys Arg Val Arg Leu Ala Lys Glu Gln Glu  
 330 335 340

tcc cgg gca gat tgt atc agt gag ttt ata gaa tgg cag tat aat gac	1109
Ser Arg Ala Asp Cys Ile Ser Glu Phe Ile Glu Trp Gln Tyr Asn Asp	
345 350 355	
aat aac act tct cat tgt ttt aac aaa atg acc aat ctg aaa tta gag	1157
Asn Asn Thr Ser His Cys Phe Asn Lys Met Thr Asn Leu Lys Leu Glu	
360 365 370	
gat gca agg aga gaa aag aaa aaa aca gtt gat gtc aaa att aat cat	1205
Asp Ala Arg Arg Glu Lys Lys Lys Thr Val Asp Val Lys Ile Asn His	
375 380 385 390	
cgg cac tac aca gtg aac ttg aac aca tac act gcc aca gac aca aag	1253
Arg His Tyr Thr Val Asn Leu Asn Thr Tyr Thr Ala Thr Asp Thr Lys	
395 400 405	
ggc cac agt tta tct gtt cag cgc ctc acg aaa tcc aaa gtt gac atc	1301
Gly His Ser Leu Ser Val Gln Arg Leu Thr Lys Ser Lys Val Asp Ile	
410 415 420	
cct gca cac tgg agt gat atg aag cag cag aat ttc tgt gtg gtg gag	1349
Pro Ala His Trp Ser Asp Met Lys Gln Gln Asn Phe Cys Val Val Glu	
425 430 435	
ctg ctg cct agt gat cct gag tac aac acg gtg gca agc aag ttt aat	1397
Leu Leu Pro Ser Asp Pro Glu Tyr Asn Thr Val Ala Ser Lys Phe Asn	
440 445 450	
cag acc tgc tca cac ttc aga ata gag aag att gag agg atc cag aat	1445
Gln Thr Cys Ser His Phe Arg Ile Glu Lys Ile Glu Arg Ile Gln Asn	
455 460 465 470	
cca gat ctc tgg aat agc tac cag gca aag aaa aaa act atg gat gcc	1493
Pro Asp Leu Trp Asn Ser Tyr Gln Ala Lys Lys Lys Thr Met Asp Ala	
475 480 485	
aag aat ggc cag aca atg aat gag aag caa ctc ttc cat ggg aca gat	1541
Lys Asn Gly Gln Thr Met Asn Glu Lys Gln Leu Phe His Gly Thr Asp	
490 495 500	
gcc ggc tcc gtg cca cac gtc aat cga aat ggc ttt aac cgc agc tat	1589
Ala Gly Ser Val Pro His Val Asn Arg Asn Gly Phe Asn Arg Ser Tyr	
505 510 515	
gcc gga aag aat gcc gtg gca tat gga aag gga acc tat ttt gct gtc	1637
Ala Gly Lys Asn Ala Val Ala Tyr Gly Lys Gly Thr Tyr Phe Ala Val	
520 525 530	
aat gcc aat tat tct gcc aat gat acg tac tcc aga cca gat gca aat	1685
Asn Ala Asn Tyr Ser Ala Asn Asp Thr Tyr Ser Arg Pro Asp Ala Asn	
535 540 545 550	
ggg aga aag cat gtg tat tat gtg cga gta ctt act gga atc tat aca	1733
Gly Arg Lys His Val Tyr Tyr Val Arg Val Leu Thr Gly Ile Tyr Thr	
555 560 565	

cat gga aat cat tca tta att gtg cct cct tca aag aac cct caa aat	1781
His Gly Asn His Ser Leu Ile Val Pro Pro Ser Lys Asn Pro Gln Asn	
570 575 580	
cct act gac ctg tat gac act gtc aca gat aat gtg cac cat cca agt	1829
Pro Thr Asp Leu Tyr Asp Thr Val Thr Asp Asn Val His His Pro Ser	
585 590 595	
tta ttt gtg gca ttt tat gac tac caa gca tac cca gag tac ctt att	1877
Leu Phe Val Ala Phe Tyr Asp Tyr Gln Ala Tyr Pro Glu Tyr Leu Ile	
600 605 610	
acg ttt aga aaa taa cactttggta tccttccac aaaattattc tccatttgta	1932
Thr Phe Arg Lys	
615	
catatctagt tgtaaaacaa gttttagctt ttttttttaa ttcctcttaa cagatttttc	1992
taatatccaa ggatcattct ttgtcgctga agtcagctt tcttcagctt ctctttcata	2052
atggaaatga acttattatc ttgagagcaa ataacttggg aaatttaaat gagataatgc	2112
agttgcaact gtgtgtccac aagtatggac atcaaatctg tgggaaaaga acaggtttgt	2172
attttcagga aggagagaat aacagctcta tagacagagg gcacagctaa gcacagctgc	2232
cactgcagga gacaggcccc atgtcaggat gccatagtgc tgtggggagc acagtattac	2292
ccagtgggta gggcttctgt cttccctggg agcagggatg gtatcttagt caattttttt	2352
cccttgagat gaggctctgt cctgatgtac aacggatact ccataaatgt ttgacaaacc	2412
aacgaagaat gaaaaaagc ctagtcagac tcccatccaa agtaggaact atctctttaa	2472
cattcttgac tcactatcac tttacctcaa attgaacaga ttccatgacg gaacttcatt	2532
cttcacaaac tagccagtga catgtgggac agctctggcc agggctctgg gactgcagtg	2592
tacttgcgct ctgcacggtc caggagctgt gatgtggctg tggcttaggg gaatcctgcc	2652
tgccccatgg agttgcgag cacaacctg gctccaattg ccagaaggct ctttttaatg	2712
ctgaacccaa atgcgctttt ttttttttct tgagatggag tttcactctt gttgcccagg	2772
ctggagtgca atggcgcgat ctcagctcac tgcagccact gcctcccagg ttcaagtgat	2832
tctcctgcct cagcctcccg agtagctggg attacaggca tgcgctaaca caccagcta	2892
atthtgtatt tttagtagag acgaggtttc tccatgttcg acaggctggt ctggaactcc	2952
cacctcagcc tccc aaactg ctgggattac aggtgtgagc cactgtgacc agccaatgtg	3012
ccttcttata gtgtctactc attggtcttt gttctgcca gtgataacaa tgggataacg	3072
cctgctacac atcttcattg tgaaccctt cccctgtgct gagattaaat gaactctgag	3132

attattaaat agtatatntt ccttgacagc ctagegtttg atgattntaa agccttatgt 3192  
 ataaataaac caaaggaagt aagcagtcac attgctaatt tgctaactcc tatctattga 3252  
 atggtgaagt ttttaaaatt tccccagga agtntaagat tcaaacacca tctattgagc 3312  
 acctacattg tgtgccaggt agtaaaatag gtgctttcat acacattgtc tcaattcctg 3372  
 tgaggtcaga attatctctg catttgaaac ttgaggaac atgctcagag tgcaagaagc 3432  
 ttcttgcct gagatcacct agaaaggaac cctcagagcc ggcaactgaa tcttggctcc 3492  
 tgtgatgtca agcccattgc tctccactg cagaacatgg cctctagatt aatgccaccg 3552  
 attcaggaac acctccgaca gtcttgaaat accccatgt tgccttgntt gttnttct 3612  
 tctggcttct tctattacag tctcttcatt ggaagctctg taggccaagg ccagagctga 3672  
 tactgacagc gagccaatgc agatagcaca tcagatgcta ggggtcgtg ggaggattaa 3732  
 gggacttaat ctgctaggaa cacctgtact tgaagtggag gaggctaggg ggccacagtt 3792  
 gctgcttcat taacatagag gnttggatt tnttctctt gtgnttntt tnttaagtgg 3852  
 attggcagac tccttnttgc ttaagagtgg ctttctaggc aggccactgg catctgaatt 3912  
 catcattgac aataaatgta agaaattgga ataaaaaga gaggcctgct gttattcgtc 3972  
 tntgnttctc agtgatttga ttaactcagg gcaaggctga atatcagagt gtatcgcact 4032  
 gaagaataat aatccattca gtaatnttat agttatcctc aatctaaata tntcaactgt 4092  
 cnttntgcta cttntcaaat aaaatacttg aaaactgtca aaa 4135

<210> 2  
 <211> 618  
 <212> PRT  
 <213> Homo sapiens

<400> 2

Met Asn Leu Pro Arg Arg Val Lys Glu Asn Leu Val Ser Asp Lys Phe  
 1 5 10 15  
 Pro Lys Ala Lys Asp Thr Gln Gly Phe Tyr Gly Thr Val Ser Ser Pro  
 20 25 30  
 Asp Ser Gly Val Tyr Glu Met Lys Ile Gly Ser Ile Ile Phe Gln Val  
 35 40 45  
 Ala Ser Gly Asp Ile Thr Lys Glu Glu Ala Asp Val Ile Val Asn Ser  
 50 55 60  
 Thr Ser Asn Ser Phe Asn Leu Lys Ala Gly Val Ser Lys Ala Ile Leu  
 65 70 75 80

Glu Cys Ala Gly Gln Asn Val Glu Arg Glu Cys Ser Gln Gln Ala Gln  
 85 90 95  
 Gln Arg Lys Asn Asp Tyr Ile Ile Thr Gly Gly Gly Phe Leu Arg Cys  
 100 105 110  
 Lys Asn Ile Ile His Val Ile Gly Gly Asn Asp Val Lys Ser Ser Val  
 115 120 125  
 Ser Ser Val Leu Gln Glu Cys Glu Lys Lys Asn Tyr Ser Ser Ile Cys  
 130 135 140  
 Leu Pro Ala Ile Gly Thr Gly Asn Ala Lys Gln His Pro Asp Lys Val  
 145 150 155 160  
 Ala Glu Ala Ile Ile Asp Ala Ile Glu Asp Phe Val Gln Lys Gly Ser  
 165 170 175  
 Ala Gln Ser Val Lys Lys Val Lys Val Val Ile Phe Leu Pro Gln Val  
 180 185 190  
 Leu Asp Val Phe Tyr Ala Asn Met Lys Lys Arg Glu Gly Thr Gln Leu  
 195 200 205  
 Ser Ser Gln Gln Ser Val Met Ser Lys Leu Ala Ser Phe Leu Gly Phe  
 210 215 220  
 Ser Lys Gln Ser Pro Gln Lys Lys Asn His Leu Val Leu Glu Lys Lys  
 225 230 235 240  
 Thr Glu Ser Ala Thr Phe Arg Val Cys Gly Glu Asn Val Thr Cys Val  
 245 250 255  
 Glu Tyr Ala Ile Ser Trp Leu Gln Asp Leu Ile Glu Lys Glu Gln Cys  
 260 265 270  
 Pro Tyr Thr Ser Glu Asp Glu Cys Ile Lys Asp Phe Asp Glu Lys Glu  
 275 280 285  
 Tyr Gln Glu Leu Asn Glu Leu Gln Lys Lys Leu Asn Ile Asn Ile Ser  
 290 295 300  
 Leu Asp His Lys Arg Pro Leu Ile Lys Val Leu Gly Ile Ser Arg Asp  
 305 310 315 320  
 Val Met Gln Ala Arg Asp Glu Ile Glu Ala Met Ile Lys Arg Val Arg  
 325 330 335  
 Leu Ala Lys Glu Gln Glu Ser Arg Ala Asp Cys Ile Ser Glu Phe Ile  
 340 345 350  
 Glu Trp Gln Tyr Asn Asp Asn Asn Thr Ser His Cys Phe Asn Lys Met  
 355 360 365

Thr Asn Leu Lys Leu Glu Asp Ala Arg Arg Glu Lys Lys Lys Thr Val  
 370 375 380  
 Asp Val Lys Ile Asn His Arg His Tyr Thr Val Asn Leu Asn Thr Tyr  
 385 390 395 400  
 Thr Ala Thr Asp Thr Lys Gly His Ser Leu Ser Val Gln Arg Leu Thr  
 405 410 415  
 Lys Ser Lys Val Asp Ile Pro Ala His Trp Ser Asp Met Lys Gln Gln  
 420 425 430  
 Asn Phe Cys Val Val Glu Leu Leu Pro Ser Asp Pro Glu Tyr Asn Thr  
 435 440 445  
 Val Ala Ser Lys Phe Asn Gln Thr Cys Ser His Phe Arg Ile Glu Lys  
 450 455 460  
 Ile Glu Arg Ile Gln Asn Pro Asp Leu Trp Asn Ser Tyr Gln Ala Lys  
 465 470 475 480  
 Lys Lys Thr Met Asp Ala Lys Asn Gly Gln Thr Met Asn Glu Lys Gln  
 485 490 495  
 Leu Phe His Gly Thr Asp Ala Gly Ser Val Pro His Val Asn Arg Asn  
 500 505 510  
 Gly Phe Asn Arg Ser Tyr Ala Gly Lys Asn Ala Val Ala Tyr Gly Lys  
 515 520 525  
 Gly Thr Tyr Phe Ala Val Asn Ala Asn Tyr Ser Ala Asn Asp Thr Tyr  
 530 535 540  
 Ser Arg Pro Asp Ala Asn Gly Arg Lys His Val Tyr Tyr Val Arg Val  
 545 550 555 560  
 Leu Thr Gly Ile Tyr Thr His Gly Asn His Ser Leu Ile Val Pro Pro  
 565 570 575  
 Ser Lys Asn Pro Gln Asn Pro Thr Asp Leu Tyr Asp Thr Val Thr Asp  
 580 585 590  
 Asn Val His His Pro Ser Leu Phe Val Ala Phe Tyr Asp Tyr Gln Ala  
 595 600 605  
 Tyr Pro Glu Tyr Leu Ile Thr Phe Arg Lys  
 610 615

<210> 3  
 <211> 1857  
 <212> DNA  
 <213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1857)

<400> 3

```

atg aat ttg ccc aga agg gtt aag gaa aat ctc gtc agt gac aaa ttt      48
Met Asn Leu Pro Arg Arg Val Lys Glu Asn Leu Val Ser Asp Lys Phe
1           5           10           15

ccg aag gct aaa gat aca caa ggt ttt tat ggg act gtt tct agc cct      96
Pro Lys Ala Lys Asp Thr Gln Gly Phe Tyr Gly Thr Val Ser Ser Pro
           20           25           30

gat tca ggt gtg tat gaa atg aag att ggc tcc atc atc ttc cag gtg     144
Asp Ser Gly Val Tyr Glu Met Lys Ile Gly Ser Ile Ile Phe Gln Val
           35           40           45

gct tct gga gat atc acg aaa gaa gag gca gat gtg att gta aat tca     192
Ala Ser Gly Asp Ile Thr Lys Glu Glu Ala Asp Val Ile Val Asn Ser
           50           55           60

aca tca aac tca ttc aat ctc aaa gca ggg gtc tcc aaa gca att tta     240
Thr Ser Asn Ser Phe Asn Leu Lys Ala Gly Val Ser Lys Ala Ile Leu
65           70           75           80

gaa tgt gct gga caa aat gta gaa agg gaa tgt tct cag caa gct cag     288
Glu Cys Ala Gly Gln Asn Val Glu Arg Glu Cys Ser Gln Gln Ala Gln
           85           90           95

cag cgc aaa aat gat tat ata atc acc gga ggt gga ttt ttg agg tgc     336
Gln Arg Lys Asn Asp Tyr Ile Ile Thr Gly Gly Gly Phe Leu Arg Cys
           100          105          110

aag aat atc att cat gta att ggt gga aat gat gtc aag agt tca gtt     384
Lys Asn Ile Ile His Val Ile Gly Gly Asn Asp Val Lys Ser Ser Val
           115          120          125

tcc tct gtt ttg cag gag tgt gaa aaa aaa aat tac tca tcc att tgc     432
Ser Ser Val Leu Gln Glu Cys Glu Lys Lys Asn Tyr Ser Ser Ile Cys
           130          135          140

ctc cca gcc att ggg aca gga aat gcc aaa caa cac cca gat aag gtt     480
Leu Pro Ala Ile Gly Thr Gly Asn Ala Lys Gln His Pro Asp Lys Val
145          150          155          160

gct gaa gcc ata att gat gcc att gaa gac ttt gtc cag aaa gga tca     528
Ala Glu Ala Ile Ile Asp Ala Ile Glu Asp Phe Val Gln Lys Gly Ser
           165          170          175

gcc cag tct gtg aaa aaa gtt aaa gtt gtt atc ttt ctg cct caa gta     576
Ala Gln Ser Val Lys Lys Val Lys Val Val Ile Phe Leu Pro Gln Val
           180          185          190
    
```

ctg gat gtg ttt tat gct aac atg aag aaa aga gaa ggg act cag ctt Leu Asp Val Phe Tyr Ala Asn Met Lys Lys Arg Glu Gly Thr Gln Leu 195 200 205	624
tct tcc caa cag tct gtg atg tct aaa ctt gca tca ttt ttg ggc ttt Ser Ser Gln Gln Ser Val Met Ser Lys Leu Ala Ser Phe Leu Gly Phe 210 215 220	672
tca aag caa tct ccc caa aaa aag aat cat ttg gtt ttg gaa aag aaa Ser Lys Gln Ser Pro Gln Lys Lys Asn His Leu Val Leu Glu Lys Lys 225 230 235 240	720
aca gaa tca gca act ttt cgg gtg tgt ggt gaa aat gtc acg tgt gtg Thr Glu Ser Ala Thr Phe Arg Val Cys Gly Glu Asn Val Thr Cys Val 245 250 255	768
gaa tat gct atc tcc tgg cta caa gac ctg att gaa aaa gaa cag tgt Glu Tyr Ala Ile Ser Trp Leu Gln Asp Leu Ile Glu Lys Glu Gln Cys 260 265 270	816
cct tac acc agt gaa gat gag tgc atc aaa gac ttt gat gaa aag gag Pro Tyr Thr Ser Glu Asp Glu Cys Ile Lys Asp Phe Asp Glu Lys Glu 275 280 285	864
tat cag gag ttg aat gag ctg cag aag aag tta aat att aac att tcc Tyr Gln Glu Leu Asn Glu Leu Gln Lys Lys Leu Asn Ile Asn Ile Ser 290 295 300	912
ctg gac cat aag aga cct ttg att aag gtt ttg gga att agc aga gat Leu Asp His Lys Arg Pro Leu Ile Lys Val Leu Gly Ile Ser Arg Asp 305 310 315 320	960
gtg atg cag gct aga gat gaa att gag gcg atg atc aag aga gtt cga Val Met Gln Ala Arg Asp Glu Ile Glu Ala Met Ile Lys Arg Val Arg 325 330 335	1008
ttg gcc aaa gaa cag gaa tcc cgg gca gat tgt atc agt gag ttt ata Leu Ala Lys Glu Gln Glu Ser Arg Ala Asp Cys Ile Ser Glu Phe Ile 340 345 350	1056
gaa tgg cag tat aat gac aat aac act tct cat tgt ttt aac aaa atg Glu Trp Gln Tyr Asn Asp Asn Asn Thr Ser His Cys Phe Asn Lys Met 355 360 365	1104
acc aat ctg aaa tta gag gat gca agg aga gaa aag aaa aaa aca gtt Thr Asn Leu Lys Leu Glu Asp Ala Arg Arg Glu Lys Lys Lys Thr Val 370 375 380	1152
gat gtc aaa att aat cat cgg cac tac aca gtg aac ttg aac aca tac Asp Val Lys Ile Asn His Arg His Tyr Thr Val Asn Leu Asn Thr Tyr 385 390 395 400	1200
act gcc aca gac aca aag ggc cac agt tta tct gtt cag cgc ctc acg Thr Ala Thr Asp Thr Lys Gly His Ser Leu Ser Val Gln Arg Leu Thr 405 410 415	1248



专利名称(译)	干扰素- $\alpha$ 诱导的基因		
公开(公告)号	<a href="#">EP1341807A2</a>	公开(公告)日	2003-09-10
申请号	EP2001270548	申请日	2001-12-11
申请(专利权)人(译)	PHARMA PACIFIC PTY. LTD.		
当前申请(专利权)人(译)	PHARMA PACIFIC PTY. LTD.		
[标]发明人	MERITET JEAN FRANCOIS DRON MICHEL TOVEY MICHAEL GERARD		
发明人	MERITET, JEAN-FRANCOIS DRON, MICHEL TOVEY, MICHAEL, GERARD		
IPC分类号	A01K67/027 A61K38/00 A61K48/00 A61P31/12 A61P35/00 A61P37/02 A61P43/00 C07K14/47 C07K16/18 C12N1/15 C12N1/19 C12N1/21 C12N5/10 C12N15/09 C12P21/02 C12Q1/02 C12Q1/68 G01N33/15 G01N33/50 G01N33/53 G01N37/00 C07K14/00		
CPC分类号	C07K14/47		
优先权	2000030184 2000-12-11 GB		
外部链接	<a href="#">Espacenet</a>		

#### 摘要(译)

本发明涉及鉴定通过干扰素- $\alpha$ 给药而上调的基因，该基因对应于SEQ.ID中所示的cDNA序列。该基因的表达产物的确定被认为可用于预测对干扰素- $\alpha$ 和作用于1型干扰素受体的其它干扰素治疗的反应性。还设想了由相同基因编码的蛋白质的治疗用途。