

(12) PATENT APPLICATION
(19) AUSTRALIAN PATENT OFFICE

(11) Application No. AU 200151994 A1

(54) Title
Use of polypeptides or nucleic acids for the diagnosis or treatment of skin disorders and wound healing and for the identification of pharmacologically active substances

(51)⁷ International Patent Classification(s)
A61K 038/18 A61K 038/57
A61K 031/7105 A61K 039/395
A61K 038/39 A61K 039/44
A61K 038/50 A61P 017/02
A61K 038/53

(21) Application No: **200151994**

(22) Application Date: **2001.06.19**

(30) Priority Data

(31) Number	(32) Date	(33) Country
10030149	2000.06.20	DE
60222081	2000.08.01	US

(43) Publication Date : **2002.08.01**

(43) Publication Journal Date : **2002.08.01**

(71) Applicant(s)
Switch Biotech AG

(72) Inventor(s)
Eckard Wolf; Sabine Werner; Jorn-Peter Halle; Johannes Regenbogen; Andreas Goppelt

(74) Agent/Attorney
WATERMARK PATENT and TRADEMARK ATTORNEYS, Locked Bag 5, HAWTHORN VIC 3122

Abstract

Use of polypeptides or nucleic acids encoding these for the diagnosis and/or prevention and/or treatment of diseases of skin cells and/or of wound healing and/or
5 its pathological disorders, and their use for the identification of pharmacologically active substance.

AUSTRALIA

Patents Act 1990

**ORIGINAL
COMPLETE SPECIFICATION
STANDARD PATENT**

Application Number:

Lodged:

Invention Title:

Use of polypeptides or nucleic acids for the diagnosis or treatment of skin disorders and wound healing and for the identification of pharmacologically active substances

The following statement is a full description of this invention, including the best method of performing it known to :- us

Use of polypeptides or nucleic acids for the diagnosis or treatment of skin disorders and wound healing and for the identification of pharmacologically active substances

5

The invention relates to the use of polypeptides selected from SEQ ID No. 1 to SEQ ID No. 26 and/or SEQ ID No. 29 to SEQ ID No. 48 and/or SEQ ID No. 55 to SEQ ID No. 58 and/or SEQ ID No. 63 to SEQ ID No. 73 and/or SEQ ID No. 80 to SEQ ID No. 82 and/or of a nucleic acids encoding these, and/or
10 of a cell expressing said polypeptide or said nucleic acid, for the diagnosis, prevention and/or treatment of disorders, in particular skin disorders, wound healing, and/or wound healing disorders, and/or for the identification of pharmacologically active substances.

Wounds in general heal without therapeutic intervention. However,
15 there are numerous disorders in which wound healing plays a role, such as, for example, diabetes mellitus, arterial occlusive diseases, psoriasis, Crohn's disease, epidermolysis bullosa, age-related skin changes or innervation disorders. Wound healing disorders lead to a delayed healing of wounds or to chronic wounds. These disorders can be caused by the nature of the wound (e.g. large-area wounds,
20 deep and mechanically expanded operation wounds, burns, trauma, decubitus), medicinal treatment of the patients (e.g. with corticoids) but also by the nature of the disorder itself. For example, 25% of the patients with Type II diabetes thus frequently suffer from chronic ulcers ("diabetic foot"), of which approximately half necessitate expensive hospitalized treatments and nevertheless finally heal
25 poorly. Diabetic foot causes more stays in hospital than any other complication associated with diabetes. The number of these cases in diabetes Type I and II is on the increase and represents 2.5% of all hospital admissions. Moreover, wounds heal more poorly with increasing age of the patients. An acceleration of the natu-

ral wound healing process is often desirable as well in order to decrease, for example, the danger of bacterial infections or the rest periods of the patients.

Further disorders can also occur after successful wound closure. While foetal skin wounds heal without scar formation, after injuries in the post-natal period formation of scars always occurs, which often represent a great cosmetic problem. In the case of patients with large-area burn wounds, the quality of life can moreover be dramatically adversely affected, especially as in scarred skin the appendages, such as hair follicles, sweat and sebaceous glands are missing. In the case of appropriate genetic disposition, keloids can also occur, hypertrophic scars which proliferate into the surrounding skin.

The process of skin healing requires complex actions and interactions of various cell types which proceed in a coordinated manner. In the wound healing process, the following steps are differentiated: blood clotting in the area of the wound, the recruitment of inflammatory cells, reepithelialization, the formation of granular tissue and matrix remodeling. Little is known up to now about the exact reaction pattern of the cell types involved during the phases of proliferation, migration, matrix synthesis and contraction, just like about the regulation of genes such as, for example, growth factors, receptors and matrix proteins.

Thus until now only a few satisfactory therapies have been developed in order to treat wound healing disorders. Established forms of therapy are restricted to physical assistance of wound healing (e.g. dressings, compresses, gels) or the transplantation of skin tissues, cultured skin cells and/or matrix proteins. In recent years, growth factors have been tested for improving wound healing without, however, improving the conventional therapy decisively. The diagnosis of wound healing disorders is also based on not very meaningful optical analyses of the skin, since a deeper understanding of the gene regulation during wound healing was lacking until now.

Not very satisfactory therapies have been developed until now for other disorders of regenerative processes as well. Here too, the knowledge of gene regulation is advantageous for the development of diagnostics and therapies. It has

been shown (Finch et al., 1997, Am. J. Pathol. 151: 1619-28; Werner, 1998, Cytokine Growth Factor Rev. 9: 153-165) that genes relevant to wound healing also play a crucial role in dermatological disorders which are based on disorders of the regeneration of the skin, and generally in regenerative processes. Thus the growth factor KGF not only plays a crucial role in the regulation of the proliferation and differentiation of keratinocytes during wound healing, but is also an important factor in the hyperproliferation of the keratinocytes in psoriasis and regenerative processes in the intestine (in Crohn's disease and ulcerative colitis).

It is therefore the object of the present invention to make available polypeptides and nucleic acids encoding these which are involved in processes in disorders of skin cells, in wound healing and/or in wound healing disorders, and whose use decisively improves the diagnosis, prevention and/or treatment, and also the identification and development of pharmaceuticals which are effective in connection with these disorders.

Diseases of the skin, wound healing and its pathological disorders within the meaning of the invention are to be discriminated from skin diseases which are accompanied by uncontrolled cell proliferation and cell differentiation, in particular by skin cancer. In the latter disease, transformation of individual cells occurs, which therefore begin to proliferate in an uncontrolled, autonomous manner, i.e. isolated from interactions with other cell types, and at the same time transmit the pathological changes to the daughter cells. It is thus a disorder which is accompanied by a loss of interactions, for example of cell-cell adhesion and of typical cell properties. In contrast, diseases within the meaning of the invention are based on disorders of cell-cell interactions. The formation of skin diseases within the meaning of the invention is caused by a large number of factors. Thus in the case of psoriasis, for example, genetic predispositions and malfunctions of the T cells, fibroblasts and keratinocytes probably both play an important role (see, for example, Nair et al., 1997; Hum. Molec. Genet. 6: 1349-1356; Gottlieb et al., 1995, Nat. Med. 1: 442-447; Saiag et al., 1985, Science, 230: 669-672; Pittelkow, 1998, in Roenigk 1998: 225-246). The course of wound healing can also

be modulated by various endogenous and exogenous factors. Even small perturbations of the interactions between the different cell types of the dermis and epidermis themselves, but also of interactions with other tissues and organs such as the blood vessel system, the nervous system and the connective tissue, can lead to disturbed wound healing followed by scar formation. Furthermore, infections, aging, disorders such as diabetes and immune disorders and also vitamin deficiencies can adversely affect the wound-healing process. Similarly complex interactions are also described for other skin diseases such as vitiligo and atopic dermatitis. This essentially differentiates the skin diseases from cancer of these organs. Preferred examples of skin diseases encompass psoriasis, eczema, especially atopic eczema and disorders of pigmentation of the skin, especially vitiligo. Examples of disorders of wound healing are wounds of patients suffering from diabetes or alcoholism, wounds infected with microorganisms, ischemic wounds and wounds of patients with impaired circulation or venous stasis. Especially preferred examples of badly healing wounds are diabetic, neuropathic, venous and arterial ulcers, especially diabetic ulcers.

The autonomous character of carcinomatous disorders is also seen at the therapeutic level. In the case of non-metastasizing tumors, cancer can be treated surgically. This physical treatment is possible, as no interactions take place between tumor cells and the surrounding cells and tissues, so that the patient can be cured by simple excision of the tumor, whereas this is not possible in the case of skin diseases within the meaning of the invention – the pathological disorders of the cell-cell and/or tissue-tissue interactions cannot be abolished by excision of affected skin sites. The fact that the diseases compared are diseases which are based on a fundamentally different mechanism becomes clear if the therapeutic approaches are compared. In cancer disorders and diseases which are accompanied by uncontrolled cell proliferation, therapy is directed at the destruction of rapidly growing cells, e.g. by means of cytostatics. These toxic substances prevent the growth of actively proliferating cells while cells in the G0 phase of the cell cycle are not affected. In contrast, the treatment of disorders of skin cells within the meaning of the invention aims at the modulation of the interactions between

the different cell types, for example by affecting the migration, proliferation and differentiation of *individual* cell types. Skin diseases within the meaning of the invention cannot be cured by general inactivation of proliferating cells. The methodological approach to the identification of the nucleic acids used according to the invention, which are involved in wound healing and/or in processes of the skin diseases within the meaning of the invention, differs clearly from procedures which are suitable for identifying nucleic acids which are involved in processes of the carcinomatous disorders. The latter can be identified by analysis of genes of the cell type affected by cancer which are expressed in differential form. The aim of the assay of the present invention is, however, rather to identify, by comparison of the expression in diseased and healthy tissue biopsies, genes which are involved in the complex processes of the skin diseases and/or in wound healing and/or its pathological disorders. This procedure would be unsuitable for the identification of genes relevant to cancer.

15 In the analysis of gene expression during the wound healing process it was surprisingly possible to identify genes, that until now were not connected with diagnosis, prevention and/or treatment of disorders, of wound healing and/or of disorders of wound healing, and for the identification of pharmacologically active substances but whose regulation is essential for the healing process and which are thus in a causal relationship with diagnosis, prevention and/or treatment of disorders, disorders of the skin, in wound healing and/or disorders of wound healing, and for the identification of pharmacologically active substances. The polypeptides of these genes do not belong to the targets known until now for diagnosis - such as, for example, the indication - and/or the treatment - such as, 20 for example, the modulation - of disorders or wound healing, of disorders of wound healing or for the identification of pharmacologically active substances, such that completely novel therapeutic approaches result from this invention.

The object is therefore achieved according to the invention by the use of one or more polypeptides selected from a sequence of SEQ ID No. 55 to 30 SEQ ID No. 58 or functional variants thereof and/or of a nucleic acid or a variant

thereof encoding these, and/or of a cell expressing said polypeptide or a functional variant thereof or said nucleic acid or a variant thereof, if appropriate combined or together with suitable additives and/or auxiliaries, for the diagnosis, treatment and/or prevention of diseases, in particular diseases of skin cells, of wound healing and/or its pathological disorders, and/or its use for the identification of pharmacologically active substances.

The exact biological functions of the polypeptides selected from a sequence of SEQ ID No. 55 to SEQ ID No. 58 used according to the invention are unknown. In the investigations in the context of this invention, it was possible for the first time to determine a relationship of the polypeptides according to the invention with disorders, for example skin diseases. The accession numbers of the polypeptide sequences according to the invention and their cDNAs, if known, are listed in Table 3. The cDNA sequences of the polypeptides of SEQ ID No. 55 to 57 are listed under SEQ ID No. 50 to 52. Figure 2 and Figure 3 show the comparison of human and murine polypeptide sequences.

In the analysis of gene expression during the wound-healing process, it was possible to identify further genes whose already known and described functions have previously not been connected with skin diseases or wound healing, for example with disturbed wound healing, but whose regulation is essential for the wound-healing process and which have thus been brought for the first time into causal relationship with skin diseases, for example with disturbed wound healing. The polypeptides of these genes do not belong to the previously known targets of skin disease therapies and/or wound healing or its disorders, so that completely new therapeutic approaches result from this invention.

The object of the invention is furthermore achieved by the use of at least one polypeptide selected from a sequence of SEQ ID No. 1 to SEQ ID No. 20 and/or SEQ ID No. 31 to SEQ ID No. 48 and/or SEQ ID No. 63 to SEQ ID No. 70 and/or SEQ ID No. 80 to SEQ ID No. 82 or functional variants thereof and/or nucleic acids or variants encoding these, and/or of a cell expressing said polypeptide or a functional variant thereof or said nucleic acid or variants thereof,

if appropriate combined or together with suitable additives and/or auxiliaries, for the diagnosis, prevention and/or treatment of diseases of skin cells, of wound healing and/or its pathological disorders, and/or its use for the identification of pharmacologically active substances.

5 The following polypeptides can be used according to the invention:

- The tumor susceptibility gene TSG 101 from mouse (SEQ ID No. 1) or human (SEQ ID No. 2) that is known from WO 97/18333 and US 5,892,016 (Li and Cohen, 1996, Cell 85:319-329; Li et al., 1997, Cell 88:143-154). The functional inactivation of TSG 101 in fibroblasts leads to cellular transformation and to the ability to form metastasizing tumors. TSG 101-deficient neoplastic cells show abnormalities in mitosis associated processes (Xie et al., 10 1998, Proc. Natl. Acad. Sci. U.S.A. 95:1595-1600). Furthermore, a role as transcriptional modulator is assumed (Sun et al., 1999, Cancer 86:689-696). In addition to the human polypeptide according to SEQ ID No. 2, the splice variant according to SEQ ID No. 82 (SWISSProt: Q99816) can also be used.
- The tumor suppressor protein MASPIN, that is known from US 5,905,023, US 5,801,001, US 5,470,970 and WO 94/05804 from mouse (SEQ ID No. 3) or human (SEQ ID No. 4) (Zou et al., 1994, Science, 263, 526-529). MASPIN is a serine protease inhibitor (Zhang et al., 1997, Mol. Med. 3:49- 15 59) that is expressed in normal breast and prostate epithelial cells (Zhang et al., 1997, Proc. Natl. Acad. Sci. U.S.A. 94:5673-5678) and plays an essential role in the development of the breast gland (Zhang et al., 1999, Dev. Biol. 215:278-287).
- The RNA-polymerase I termination factor TTF-I from mouse (SEQ ID No. 5) or human (SEQ ID No. 6) (Evers and Grummt, 1995, Proc. Natl. Acad. Sci. U.S.A. 92:5827-5831). The protein mediates the termination of transcription of ribosomal genes (Kuhn et al., 1990, Nature 344:559-62) as well as the tran- 20 scriptional activation of ribosomal genes in chromatin (Langst et al., 1998, EMBO J. 17:3135-45).
- The protooncogen B-raf from mouse (SEQ ID No. 7) or human (SEQ ID No. 8), that is known from WO 91/02077 and US 7,745,381 (Miki et al., 1991, 25 30

- Proc. Natl. Acad. Sci. U.S.A. 88:5167-5171; Stephens et al., 1992, Mol. Cell. Biol. 12:3733-3742). The B-raf protooncogene belongs to the Raf-family comprising serine/threonine protein kinases that link the stimulation of growth factor receptors and the activation of mitogen-activated protein kinases (Ma-
- 5 son et al., 1999, EMBO J. 18:2137-48). Furthermore, B-Raf can inhibit apoptosis (Erhardt et al., 1999, Mol. Cell. Biol. 19:5308-15).
- Prothymosin alpha from mouse (SEQ ID No. 9) or human (SEQ ID No. 10), that is known from US 4,716,148 and US 4,659,694 (Schmidt and Werner, 1991, Biochim. Biophys. Acta. 1088:442-444; Eschenfeldt and Berger, 1986, 10 Proc. Natl. Acad. Sci. U.S.A. 83:9403-9407). It codes for a small acidic nuclear protein that has a role in the proliferation of cells (Tao et al., 1999, J. Cell Physiol. 178:154-63).
 - The GOGLI 4-TRANSMEMBRANE SPANNING TRANSPORTER or MTP (mouse transporter protein) from mouse (SEQ ID No. 11) or human (SEQ ID 15 No. 12) (Hogue et al., 1996, J. Biol. Chem. 271:9801-9808; Nagase et al., 1995, DNA Res. 2:37-43). It is a strongly conserved membrane protein, that is localized in lysosomes and endosomes of mammalian cells. The protein is responsible for the subcellular distribution of a number of different small hydrophobic molecules and contributes to the sensitivity respectively resistance of 20 mammalian cells towards particular active substances (Hogue et al., 1999, J. Biol. Chem. 274:12877-82). For the mouse homologue, an alternative polypeptide truncated at the C terminus by 89 amino acids is formed by an alternative translation initiation site (see SwissProt: Q60961). This murine polypeptide can also be used according to the invention.
 - 25 - CCR-1 from mouse (SEQ ID No. 13) or human (SEQ ID No. 14) (Post et al., 1995, J. Immunol. 155:5299-5305) that is an eosinophilic receptor for the CC-chemokine eotaxin (Gao et al., 1996, Biochem. Biophys. Res. Comm. 223:679-84). CCR-1 is expressed in heart, spleen and lung (Gao and Murphy, 1995, Genomics 29:294-96).
 - 30 - The nucleosome binding protein HMG-14 from mouse (SEQ ID No. 15) or human (SEQ ID No. 16) (Landsman and Bustin, 1990, Nucleic Acids Res.

18:5311; Landsman et al., 1986, J. Biol. Chem. 261:16082-16086), that opens up higher order chromatin structures and thus increases the transcription and replication potential of chromatin (Herrera et al., 1999, Mol. Cell. Biol. 19:3466-73).

- 5 - Split hand/foot deleted 1 from mouse (SEQ ID No. 17) or human (SEQ ID No. 18), that is a candidate gene for the autosomal dominant form of "split hand/split foot malformation disorder" that is expressed in limb buds, in the "cranofacial primordia" and in the skin (Crackower et al., 1996, Hum. Mol. Genet. 5:571-9).
- 10 - The orphan receptor TAK1 or TR4 from mouse (SEQ ID No. 19) or human (SEQ ID No. 20) (Hirose et al., 1995, Gene 163:239-242; Hirose et al., 1994, Mol. Endocrinol. 8:1667-1680), that belongs to the superfamily of nuclear hormone receptors (Hirose et al., 1994, Mol. Endocrinol. 8:1667-80). As a homodimer, TR4 influences the multitude of signal transduction pathways, among them retinoic acids, thyroid hormone, vitamin D3 and "ciliary neutrophilic factor". Additionally TR4 forms heterodimers with the androgen receptor (Lee et al., 1999, Proc. Natl. Acad. Sci. U.S.A. 96:14724-9).
- 15 - BAF57 from mouse (SEQ ID No. 31) or human (SEQ ID No. 32), that is known from WO 95/14772, which is a part of the chromatin remodeling SWI/SNF complex of higher eukaryotes (Wang et al., 1998, Proc. Natl. Acad. Sci. U.S.A. 95:492-498.) The SWI/SNF complexes regulate the transcription of specific genes by relieving chromatin mediated repression of transcription (Wolffe and Guschin, 2000, J. Struct. Biol. 129:102-122). Additionally, a role has been shown for the switch from expression of fetal to adult globin in mice (Armstrong et al., 1999, Proc. Natl. Acad. Sci. U.S.A. 96:349-54). In addition to the known human and mouse polypeptides, the closely related novel human polypeptide having a significantly different sequence (SEQ ID No. 80) can also be used. The cDNA encoding the polypeptide according to SEQ ID No. 80 is indicated under SEQ ID No. 83.
- 20 - BAF57 from mouse (SEQ ID No. 31) or human (SEQ ID No. 32), that is known from WO 95/14772, which is a part of the chromatin remodeling SWI/SNF complex of higher eukaryotes (Wang et al., 1998, Proc. Natl. Acad. Sci. U.S.A. 95:492-498.) The SWI/SNF complexes regulate the transcription of specific genes by relieving chromatin mediated repression of transcription (Wolffe and Guschin, 2000, J. Struct. Biol. 129:102-122). Additionally, a role has been shown for the switch from expression of fetal to adult globin in mice (Armstrong et al., 1999, Proc. Natl. Acad. Sci. U.S.A. 96:349-54). In addition to the known human and mouse polypeptides, the closely related novel human polypeptide having a significantly different sequence (SEQ ID No. 80) can also be used. The cDNA encoding the polypeptide according to SEQ ID No. 80 is indicated under SEQ ID No. 83.
- 25 - BAF57 from mouse (SEQ ID No. 31) or human (SEQ ID No. 32), that is known from WO 95/14772, which is a part of the chromatin remodeling SWI/SNF complex of higher eukaryotes (Wang et al., 1998, Proc. Natl. Acad. Sci. U.S.A. 95:492-498.) The SWI/SNF complexes regulate the transcription of specific genes by relieving chromatin mediated repression of transcription (Wolffe and Guschin, 2000, J. Struct. Biol. 129:102-122). Additionally, a role has been shown for the switch from expression of fetal to adult globin in mice (Armstrong et al., 1999, Proc. Natl. Acad. Sci. U.S.A. 96:349-54). In addition to the known human and mouse polypeptides, the closely related novel human polypeptide having a significantly different sequence (SEQ ID No. 80) can also be used. The cDNA encoding the polypeptide according to SEQ ID No. 80 is indicated under SEQ ID No. 83.
- 30 - Epidermal growth factor receptor kinase substrate EPS 8 from mouse (SEQ ID No. 33) or human (SEQ ID No. 34), that is known from US 7,935,311, which

amplifies the EGF dependent mitogenic signals (Wong et al., 1994, Onco-
gene 9:3057-3061; Fazioli et al., 1993, EMBO J. 12:3799-3808). Both over-
expression as well as constitutive phosphorylation of EPS 8 has been de-
scribed in connection with tumor development (Matoskova et al., 1995, Mol.
5 Cell Biol. 15:3805-3812).

- KIAA1247 from human (SEQ ID No. 36), that according to WO 99/34004 can
be applied as a marker protein for cancer metastasis. Additionally, a
KIAA1247 homologue from rat is known as protein from WO 98/53071,
whose expression is induced in injured or regenerating tissue, in particular
10 from kidney tissue of the rat. In addition to the known polypeptide from hu-
man, the polypeptide from mouse (SEQ ID No. 35) that is mentioned for the
first time in this work can also be used. In addition two human splice variants
of the gene encoding the polypeptide of SEQ ID No. 36, which are mentioned
for the first time in this work, can be used according to the invention. These
15 splice variants encode shorter variants of SEQ ID No. 36: the amino acids 652
to 654 and 664 to 681 or the amino acids 664 to 681 of the polypeptide of
SEQ ID No. 36, respectively, are deleted in these variants. In addition, other
KIAA1247 polypeptides can be used according to the invention, which result
from alternative translation initiation ATG-codon. Examples of such variants
20 are disclosed in WO 00/73454 and in WO 00/58473.

- Phospholipase inhibitor GIPL from human (SEQ ID No. 38), that is known
from US 5,948,626, US 5,663,059 and US 5,811,520. In addition to the al-
ready known polypeptide from human the polypeptide from mouse (SEQ ID
No. 37), that is mentioned in this work for the first time, and the closely re-
25 lated polypeptides with a significantly divergent sequence (SEQ ID No. 45
and SEQ ID No. 81), which are mentioned in this work for the first time, can
be used. The cDNA encoding the polypeptide according to SEQ ID No. 81 is
indicated under SEQ ID No. 84.

- EAT/MCL-1 from mouse (SEQ ID No. 39) or human (SEQ ID No. 40), that is
30 known from WO 95/28497, which is expressed in numerous tissues (Krajew-

ski et al., 1995, Am. J. Pathol. 146:1309-19) and that plays role in cutaneous malignant melanoma (Tang et al., 1998, Clin. Cancer Res. 4:1865-71).

- TSC-22 (TGF- beta-stimulated clone 22 gene) from human (SEQ ID No. 42) and mouse (SEQ ID No. 41) (Jay et al., 1996, Biochem. Biophys. Res. Commun. 222:821-826; Shibamura et al., 1992, J. Biol. Chem. 267:10219-10224), that belongs to the "leucine-zipper" family of transcription factors (Kester et al., 1999, J. Biol. Chem. 274:27439-47). Transcription of TSC-22 is induced by variety of stimuli as, for instance, growth inhibitors (Kester et al., 1999, J. Biol. Chem. 274:27439-47). Additionally an increased expression of TSC-22 during development of the mouse embryo was observed at locations where mesenchymal-epithelial interaction occurs (Dohrmann et al., 1999, Mech. Dev. 84:147-51).
- Gamma-sarcoglycan from human (SEQ ID No. 44) or mouse (SEQ ID No. 43) (Noguchi et al., 1995, Science 270:819-822; Noguchi et al., 1999, Biochem. Biophys. Res. Commun. 262:88-93), that is known from JP 100 57 065 and US 5,837,537. Gamma-sarcoglycan is a component of the sarcoglycan complex that again is a subcomplex of the dystrophin glycoprotein complex. This establishes a connection between the extracellular matrix and the actin cytoskeleton (Hack et al., 2000, Microsc. Res. Tech. 48:167-80). Mutation of gamma-sarcoglycan has been described as a primary genetic defect of a muscular dystrophy (SCARMD) (Noguchi et al., 1995, Science 270:819-822).
- Cysteine proteinase inhibitor cystatin C from human (SEQ ID No. 47) or mouse (SEQ ID No. 46) (Abrahamson et al., 1987, FEBS Lett. 216:229-233; Solem et al., 1990, Biochem. Biophys. Res. Commun. 172:945-951), that is known from WO 99/38882, WO 88/09384, DE 372 4 581, JP 012 02 287, JP 010 74 988 and US 5,212,297. Cystein protease inhibitors play a role in inflammatory disorders as, for example, rheumatism (Lenarcic et al., 1988, Biol. Chem. Hoppe Seyler 369 (Suppl.):257-261) and in vascular disorders (Shi et al., 1999, J. Clin. Invest. 104:1191-1197). In addition to the known polypeptide variant from mouse (SEQ ID No. 46) (Solem et al., 1990, Biochem. Biophys. Res. Commun. 172:945-951) the closely related polypeptide with a di-

vergent sequence, that has been described in this work for the first time (SEQ ID No. 48) can also be used.

- The tyrosine kinase Fer from mouse (SEQ ID No. 63) or human (SEQ ID No. 64) (SwissProt: P70451; Hao et al., 1989, Mol. Cell. Biol. 9:1587-1593), that is both localized in the nucleus as well as in the cytoplasm (Hao et al., 1991, Mol. Cell. Biol. 11:1180-1183). A role for Fer has been postulated both for cell-cell-adhesion (Rosato et al., 1998, Mol. Cell. Biol. 18:5762-5770) as well as a role as proto-oncogen (Morris et al., 1990, Cytogenet. Cell. Genet. 53:196-200).
- The C-C cytokine MRP-3 (macrophage inflammatory protein 3) from mouse (SEQ ID No. 65) or human (SEQ ID No. 66), that is known from WO 99/28473, WO 96/34891 and WO 98/14582, that is also called C10, MPIF-1 (Myeloid Progenitor Inhibitory Factor-1), CK-beta-8 or small inducible cytokine A23 (Orlowski et al., 1991, Cell Regul. 2:403-412; Li and Ruben, 1996, US 5,504,003). A high expression of MRP-3 in macrophages has been observed in chronic infection of the peritoneum (Wu et al., 1999, Cytokine 11:523-30). As a typical C-C cytokine MRP-3 is a chemoattractant for leukocytes (Haelens et al., 1996, Immunobiology 195:499-521) but it also effects osteoclasts (Votta et al., 2000, J. Cell Physiol. 183:196-207). In addition it has been observed that MRP-3 mRNA is not significantly upregulated by stimuli, that are connected to wound healing (Orlowski et al., Cell Regul., 1991, 2:403-412).
- The nicotinamide N-methyltransferase NNMT from mouse (SEQ ID No. 67) or human (SEQ ID No. 68) (Aksoy et al., 1994, J. Biol. Chem. 269:14835-14840; Yan et al., 1997, Biochem. Pharmacol. 54:1139-1149), that catalyzes the methyltransfer of S-adenosylmethionine to nicotineamide. There are several pieces of evidence, that NNMT can regulate the growth of liver cells (Seifert et al., 1984, Biochim. Biophys. Acta 801:259-64). In addition a role of the enzyme in liver cancer has been proposed (Hoshino et al., Biochim. Biophys. Acta 719:518-526).

- The ubiquitin protein ligase UBC9 from mouse (SEQ ID No. 69) or human (SEQ ID No. 70) (Yasugi and Howley; 1996, Nucleic Acids Res. 24:2005-2010; SwissProt: P50550), that is an important component of the proteasome mediated protein degradation (Hershko and Ciechanover, 1998, Annu. Rev. Biochem. 67:425-479). The ubiquitin dependent protein degradation plays a role in most divergent processes like cell cycle control, signal transduction or immune response. There are indications that UBC9 plays a role in accelerated aging (Kawabe et al., 2000, J. Biol. Chem.). In addition UBC9 catalyzes the sumoylation of p53 and thus activates its function as transcription factor (Rodriguez et al., 1999, EMBO J. 18:6455-61).

For none of these polypeptides, nucleic acids coding for them or the described cDNA a connection with skin disorders or wound healing or its disorders has been described or suggested. Therefore, it was unexpected that this compounds could be used according to the present invention. The accession numbers of the polypeptides according to the invention and the cDNAs are indicated in Table 4. The cDNA sequences of the polypeptides in SEQ ID No. 31, SEQ ID No. 35 and SEQ ID No. 37, SEQ ID No. 80 and SEQ ID No. 81, are indicated in SEQ ID No. 53 and SEQ ID No. 54 and SEQ ID No. 83 and SEQ ID No. 84.

During the analysis of gene expression during the wound healing processes it was possible to identify additional genes whose already known and described functions until now were not connected with wound healing, but whose regulation is essential for the wound healing process and which are thus brought for the first time in a causal relationship with wound healing. The polypeptides of these genes do not belong to the targets known until now for therapy in connection with pathological change of wound healing, such that completely novel therapeutic approaches result from this invention.

The object of the invention is therefore additionally achieved by the use of at least one polypeptide selected from a sequence of SEQ ID No. 21 to SEQ ID No. 26 and/or SEQ ID No. 29 to SEQ ID No. 30 and/or SEQ ID No. 71 to SEQ ID No. 73 or functional variants thereof and/or nucleic acids or variants thereof encoding these, and/or of a cell expressing said polypeptide or a functional

variant thereof or said nucleic acid or variants thereof, if appropriate combined or together with suitable additives and/or auxiliaries, for the diagnosis, prevention and/or treatment in wound healing and/or its pathological disorders, or for the identification of pharmacologically active substances.

5 The following polypeptides can be used according to the invention.

- The monocyte chemotactic protein-3, MCP-3 from mouse (SEQ ID No. 21) or human (SEQ ID No. 22) (Kulmburg et al., 1992, J. Exp. Med. 176:1773-1778; Minty et al., 1993, Eur. Cytokine Netw. 4:99-110), that is known from WO 95/04158, WO 99/12968 and EP 0 488 900. MCP-3 is a CC-chemokine that serves the chemoattraction and activation of monocytes, T-lymphocytes, eosinophiles and basophilic granulocytes, natural killer cells and dendritic cells. The activation of the target cells is effected through the chemokine receptors CCR2 and CCR3 (Wang et al., 2000 Biochim. Biophys. Acta 1500:41-8). MCP-3 plays a role in allergic reactions of the skin (Ying et al., 1999, J. Immunol. 163:3976-84).
- The alpha-chain of the heterodimeric Interleukin-5 receptor of mouse (SEQ ID No. 23) or human (SEQ ID No. 24) (Takaki 1990, EMBO J. 9:4367-4374; Tavernier et al., 1992, Proc. Natl. Acad. Sci. U.S.A. 89:7041-7045), that is known from EP 0 475 746 and WO 98/47923. It mediates the specific binding of the ligand Interleukin-5 (Van Ostade et al., 1999, Eur. J. Biochem. 259:954-60) and is expressed on the cell membrane of eosinophiles (Weltman & Karim, 1998, Allergy Asthma Proc. 19:257-61). A role of the Interleukin-5 receptors has been described for Atopic Dermatitis (Taha et al., 1998, J. Allergy Clin. Immunol. 102:245-50) Interleukin-5 plays an essential role in the differentiation, proliferation and functional activation of eosinophiles (Iwama et al., 1999, Mol. Cell. Biol. 19:3940-50) and in contrast to the receptor, that is described here, a function in wound healing has been described for Interleukin-5 (Yang et al., 1997, Am. J. Pathol. 151:813-9).
- The integral membrane protein Dad1 from mouse (SEQ ID No. 25) or human (SEQ ID No. 26) (Nakashima et al., 1993, Mol. Cell. Biol. 13:6367-6374;

- Apte et al., 1995, FEBS Lett. 363:304-306). It is a component of the oligosaccharyltransferase enzyme complexes, that initiates the N-glycosylation (Sanjay et al., 1998, J. Biol. Chem. 273:26094-9). Dad1 plays a role in inhibition of apoptosis in particular cell types (Hong et al., 1999, J. Immunol. 163:1888-93) and in keloids (Sayah et al., 1999, J. Surg. Res. 87:209-16).
- 5
- MCP-2 (C-C chemokine monocyte chemotactic protein 2) from human (SEQ ID No. 30) or mouse (SEQ ID No. 29) (van Coillie et al., 1997, Genomics 40:323-331; EMBL: AB023418) that is known from EP 0 905 240, EP 0 905 241, WO 98/02459, EP 0 906 954, WO 95/04158, WO 99/12968 and WO 97/25427. MCP-2 belongs to the C-C chemokines and acts as a chemoattractant for different cells like macrophages, basophiles and eosinophiles (Taub et al., 1995, J. Clin. Invest. 95:1370-6; Proost et al., 1996, J. Leukoc. Biol. 59:67-74). MCP-2 is a signal molecule that stimulates the directed migration of T-cells and monocytes in processes of inflammation and recruits them (Taub et al., 1995, J. Clin. Invest. 95:1370-6). In addition to the known polypeptide variants of human (SEQ ID No. 31) (Van Coillie et al., 1997 Genomics 40:323-331) the closely related polypeptide with a divergent sequence (SEQ ID No. 71), that is described in this work for the first time, can also be used.
- 10
- The cysteine protease cathepsin C from mouse (SEQ ID No. 72) or human (SEQ ID No. 73) (Paris et al., 1995, FEBS Lett. 369:326-330; McGuire et al., 1997, Biochim. Biophys. Acta 1351:267-273), that is known from WO 96/33278, which is present in the lysosomes of different cells (Turk et al., 1997, Biol. Chem. 378:141-150). Cathepsin C plays an important role in the activation of granzym A and B and, thus, in induction of apoptosis through cytotoxic lymphocytes (Pham and Ley, 1999, Proc. Natl. Acad. Sci. U.S.A. 96:8627-8632). In addition it was observed that a "loss-of-function" mutation in the cathepsin C gene leads to palmoplantar keratosis and periodontitis (Hart et al., 1999, J. Med. Genet. 36:881-887; Toomes et al., 1999, Nat. Genet. 23:421-424).
- 15
- 20
- 25
- 30

For none of the polypeptides or nucleic acids coding for them a connection with wound healing was described or suggested until now. It was, therefore, unexpected that these polypeptides can be used according to the present invention. The accession numbers of the polypeptides according to the present invention and their cDNAs are indicated in Table 5.

Generally, the analysis of differentially expressed genes in tissues is affected by markedly more errors in the form of false-positive clones than the analysis of cell culture systems. This problem cannot be circumvented by the use of a defined cell culture system, as existing, simple cell culture systems cannot adequately simulate the complexity of the wound-healing process in the tissue.

The problem exists in particular in the skin, which consists of a multiplicity of different cell types. Moreover, the process of wound healing is a highly complicated process which includes temporal and spatial changes of cellular processes, such as proliferation and differentiation, in the different cell types. The approach to investigate not only the complex cell system skin, but moreover the physiological process of wound healing and even different wound-healing stages at the level of differentially expressed genes is therefore not a promising strategy for a person skilled in the art. On account of these difficulties, the success of the screening was significantly dependent on the choice of the experimental parameters. While the methods used (e.g. subtractive hybridization) are standard methods, the screening and verification strategy is already inventive per se owing to the thought-out and defined choice of parameters. For example, the time of biopsy taking is critical for the success of the screening: wound-healing disorders and skin diseases are often based on disorders in cell proliferation and cell migration. These processes are initiated one day after wounding, which is why analysis of the molecular processes before this time would yield little information about the processes which are essential for normally proceeding wound healing. On the other hand, in the course of wound healing, the composition of the cell types in the wound changes greatly later than one day after wounding. This can lead to a differential expression of a specific gene in the wound being measured which is based not on altered expression in the cells, but only on the different cell compo-

sition. This illustrates that the choice of the day of biopsy taking crucially affected the success of the screening. Despite the defined parameters, an overrepresentation of genes was observed, which are differentially expressed during wound healing, but which are unsuitable for use in wound healing or in skin diseases.

5 These genes include, for example, genes which code for enzymes of the primary metabolism, such as glycolysis, citrate cycle, gluconeogenesis and respiratory chain, but also genes which code for ribosomal proteins, e.g. L41 and S20. Only a comparatively small number of genes were identified as suitable. An identification of the genes useable according to the invention as genes relevant to wound
10 healing was therefore surprising.

Moreover, there are enormous variabilities in the state of the wound at the time of a possible biopsy of the patient on initial contact with the physician. An animal model was therefore used for the identification of the previously described nucleic acids. BALB/c mice were wounded and wound biopsies
15 were taken at different times. This procedure has the advantage that conditions such as genetic background, nature of the wound, time of the biopsy etc. can be exactly controlled and so only allow a reproducible analysis of gene expression. Even under the defined mouse conditions, further methodical problems arise such as redundancy of the analyzed clones and underrepresentation of weakly ex-
20 pressed genes, which make the identification of relevant genes difficult.

The nucleic acids of the polypeptides useable according to the invention were isolated from cDNA libraries which prepared from intact and wounded skin. The cDNAs selected here were those which have different frequency rates in well-healing wounds in comparison to poorly healing wounds (ex-
25 amples 1 and 3). This was carried out, for example, with the aid of subtractive hybridization (Diatchenko et al., 1996, Proc. Natl. Acad. Sci. USA 93: 6025-30) and/or using the comparative counting of clones in cDNA libraries by means of analysis of restriction fragment patterns (Halle et al., 1999, EP 0965642A1) and/or with the aid of "differential display RT-PCR" (Liang et al., 1992, Cancer
30 Res. 52: 6996-6998; Liang and Pardee, 1992, Science 257: 967-971; Prashar and

Weissman, 1996, Proc. Natl. Acad. Sci. USA 93: 659-663). The cDNAs thus selected originate from genes which are either more strongly or more weakly expressed in wound healing disorders than in wound healing which proceeds normally.

5 After the primary identification of a gene, it is necessary to confirm wound healing-specific expression by a further method. This was carried out with the aid of "reverse Northern blots" and "TaqMan analysis". Using these methods, the amount of mRNA in tissues from various wound-healing states and in skin diseases (psoriasis) was determined or skin disease-specific local alterations in the
10 expression pattern were detected in biopsies (Examples 2, 4 to 7).

 In the present analysis of gene expression during the wound-healing process, besides genes whose function was completely unknown until now, genes were also identified which had previously not been linked to wound-healing disorders. Novel variants of known genes were furthermore identified
15 having sequences which differed significantly from the previously published and/or patented sequences.

 Of the part of the identified genes previously not connected with wound-healing disorders, it was hitherto known that they have a function in proliferation (Tsg101: Xie et al., Proc. Natl. Acad. Sci. USA 95: 1595-1600;
20 MASPIN: Sager et al., 1997, Adv. Exp. Med. Biol. 425:77-88; B-Raf: Mason et al., 1999, EMBO J. 18:2137-48; Ikawa et al., 1988, Mol. Cell Biol. 8:2651-2654; Prothymosin alpha: Tao et al., 1999, J. Cell Physiol. 178:154-163; Eps8: Wong et al., 1994, Oncogene 9:3057-3061; KIAA1247: WO 99/34004; EAT/MCL-1: Tang et al., 1998, Clin. Cancer Res. 4:1865-1871; TSC-22: Kester et al., 1999, J. Biol.
25 Chem. 274:27439-47; Fer: Morris et al., 1990, Cytogenet. Cell. Genet. 53:196-200), differentiation (MASPIN: Zhang et al., 1999, Dev. Biol. 215:278-87; Split hand/foot deleted 1: Crackower et al., 1996, Hum. Mol. Genet. 5:571-9), cell migration (MRP-3: Haelens et al., 1996, Immunobiology 195:499-521; MCP-3: Taub et al., 1995, J. Clin. Invest. 95:1370-6; MCP-2: Taub
30 et al., 1995, J. Clin. Invest. 95:1370-6) and/or apoptosis (B-Raf: Erhardt et al.,

1999, Mol. Cell. Biol. 19:530815). These genes, however, were previously not linked to wound healing.

In addition to the known polypeptides of human phospholipase inhibitor GIPL (US 5,948,626), MCP-2 (van Coillie et al., 1997, Genomics 40: 323-331), BAF57 (WO 95/14772) and mouse cystatin C (Solem et al., 1990, Biochem. Biophys. Res. Commun. 172:945-951), closely related polypeptides having a significantly different sequence were identified. Of the known polypeptides of human phospholipase GIPL (US 5,948,626) and human KIAA1247 (WO 99/34004), the sequences of the corresponding mouse polypeptide were identified for the first time.

The polypeptides of these genes do not include the previously known targets of therapies of wound-healing disorders, so that completely new therapeutic approaches result from this invention. Of the remaining identified genes, no description of function yet exists (Table 3).

For the checking or generation of full-length cDNA sequences of the previously described nucleic acids, full-length clones were generated with the aid of colony hybridization (Sambrook et al., 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor, Cold Spring Harbor Laboratory Press, New York, chapter 8-10) and/or PCR-based methods ("RACE", Frohman et al., 1988, Proc. Natl. Acad. Sci. USA 85: 8998-9002, Chenchik et al., 1996, in A Laboratory Guide to RNA: Isolation, Analysis, and Synthesis, Ed. Krieg, Wiley-Liss, pages 272-321; "LDPCR", Barnes, 1994, Proc. Natl. Acad. Sci. USA 91: 2216-20) both for the mouse genes and also for the human genes and the sequence of these clones was determined.

The term "functional variants" of a polypeptide within the meaning of the present invention includes polypeptides which are regulated, for example, like the polypeptides used according to the invention during disease, in particular skin diseases, or in regenerative processes of the skin, but in particular in wound-healing disorders. Functional variants, for example, also include polypeptides which are encoded by a nucleic acid which is isolated from non-skin-specific tis-

sue, e.g. embryonic tissue, but after expression in a cell involved in wound healing or skin disease have the designated functions.

Functional variants within the meaning of the present invention are also polypeptides which have a sequence homology, in particular a sequence identity, of about 70%, preferably about 80%, in particular about 90%, especially about 95%, with the polypeptide having the amino acid sequence according to one of SEQ ID No. 1 to SEQ ID No. 48 and SEQ ID No. 55 to SEQ ID No. 58 and SEQ ID No. 63 to SEQ ID No. 73 and SEQ ID No. 80 to SEQ ID No. 82. Examples of such functional variants are accordingly the polypeptides homologous to a polypeptide useable according to the invention, which originate from organisms other than the human or the mouse, preferably from non-human mammals such as, for example monkeys, pigs and rats. Other examples of functional variants are polypeptides which are encoded by different alleles of the gene, in different individuals or in different organs of an organism.

Sequence identity is understood as degree of identity (= % positives) of two sequences, that in the case of polypeptides can be determined by means of for example BlastP 2.0.1 and in the case of nucleic acids by means of for example BLASTN 2.014, wherein the Filter is set off (Altschul et al., 1997, Nucleic Acids Res., 25:3389-3402).

"Functional Variants" of the polypeptide can also be parts of the polypeptide used according to the invention with at least 6 amino acids length, preferably with at least 8 amino acids length, in particular with at least 12 amino acids length. Also included are deletions of the polypeptides used accordingly to the invention, in the range from about 1-60, preferably from about 1-30, in particular from about 1-15, especially from about 1-5 amino acids. For example, the first amino acid methionine can be absent without the function of the polypeptide being significantly altered.

In order to decide, whether a candidate polypeptide is a functional variant, the activity of the candidate functional variant polypeptide may be compared with the activity of a polypeptide useable according to the invention in

functional assays such as for example single cell or cell culture systems or standard wound healing assays. Assuming that the candidate functional variant polypeptide fulfills the criteria of a functional variant on the level of % sequence identity listed above the candidate functional variant molecule represents a functional
5 variant if the activity in the functional assays is similar to or identical with the activity exhibited by the polypeptide useable according to the invention.

Such standard wound healing assays comprise for example the application of the an expression vector containing a nucleic acid coding for the candidate polypeptide or the application of the candidate polypeptide itself or of an
10 antibody directed against the candidate polypeptide or of an antisense oligonucleotide to punched wounds, and after incubation for example of an expression vector comparing the progress of wound healing of wounds that have been injected with expression vectors containing e.g. the nucleic acid coding for the candidate functional variant polypeptide, with the progress of wound healing of
15 wounds injected with an expression vector containing the nucleic acid coding for the polypeptide useable according to the invention, or containnig a control vector with no insert. Such assays may also be applied test the activity of candidate functional variant polypeptides in the case of disorders of wound healing employing for example badly healing wounds of dexamethasone-treated animals.
20 For example, it was demonstrated that application of the polypeptide-variants PDGF-A and PDGF-B on badly healing rabbit wounds resulted in a comparable wound healing response (J. Surg. Res., 2000, 93:230-236). Similar tests can be carried out for skin disorders, for example Psoriasis. In this case, an expression vector containing a nucleic acid coding for the candidate polypeptide or the candidate polypeptide itself or an antibody directed against the candidate polypeptide
25 or an antisense oligonucleotide are applied to for example human afflicted skin areas transplanted onto SCID mice and the course of the skin disorder, for example the healing, is determined, for example by measuring PASI-score in the case of psoriasis.

The term "coding nucleic acid" relates to a DNA sequence which codes for an isolatable bioactive polypeptide according to the invention or a precursor. The polypeptide can be encoded by a sequence of full length or any part of the coding sequence as long as the specific, for example enzymatic, activity is retained.

It is known that small alterations in the sequence of the nucleic acids described above can be present, for example, due to the degeneration of the genetic code, or that untranslated sequences can be attached to the 5' and/or 3' end of the nucleic acid without its activity being significantly altered. Also included are modifications that are carried out as described below. This invention, therefore, also comprises so-called "variants" of the nucleic acids described above

"Variants" are understood as meaning all DNA sequences which are complementary to a DNA sequence, which hybridize with the reference sequence under stringent conditions and have a similar activity to the corresponding polypeptide according to the invention.

"Stringent hybridization conditions" are understood as meaning for example those conditions in which hybridization takes place at 60°C in 2.5 × SSC buffer, followed by a number of washing steps at 37°C in a lower buffer concentration, and remains stable.

Variants of the nucleic acids can also be parts of the nucleic acids used according to the present invention with at least 8 nucleotides length, preferably with at least 18 nucleotides length, in particular with at least 24 nucleotides length particularly preferred with at least 30 nucleotides, and especially preferred with at least 42 nucleotides.

The term " pharmacologically active substance" in the sense of the present invention is understood as meaning all those molecules, compounds and/or compositions and substance mixtures which can interact under suitable conditions with the nucleic acids, polypeptides or antibodies or antibody fragments described above, if appropriate together with suitable additives and/or aux-

iliaries. Possible pharmacologically active substances are simple chemical organic or inorganic molecules or compounds, but can also include peptides, proteins or complexes thereof. Examples of pharmacologically active substances are organic molecules that are derived from libraries of compounds that have been analyzed
5 for their pharmacological activity. On account of their interaction, the pharmacologically active substances can influence the function(s) of the nucleic acids, polypeptides or antibodies in vivo or in vitro or alternatively only bind to the nucleic acids, polypeptides or antibodies or antibody fragments described above or enter into other interactions of covalent or non-covalent manner with them.

10 The term "regulation" is understood, for example, as meaning the raising or lowering of the amount of polypeptide or nucleic acid encoding this. This may occur, for example, on the transcriptional or translational level.

 The polypeptides according to the invention can furthermore be characterized in that they are synthetically prepared. Thus, the entire polypeptide
15 or parts thereof can be synthesized, for example, with the aid of the conventional synthesis (Merrifield technique). Parts of the polypeptides according to the invention are particularly suitable to obtain antisera, with whose aid suitable gene expression banks can be searched in order thus to arrive at further functional variants of the polypeptide according to the invention.

20 Preferentially, the nucleic acids used according to the invention are DNA or RNA, preferably a DNA, in particular a double-stranded DNA. The sequence of the nucleic acids can furthermore be characterized in that it has at least one intron and/or one polyA sequence. The nucleic acids according to the invention can also be used in the form of their antisense sequence.

25 For the expression of the gene concerned, in general a double-stranded DNA is preferred, the DNA region coding for the polypeptide being particularly preferred. This region begins with the first start codon (ATG) lying in a Kozak sequence (Kozak, 1987, Nucleic. Acids Res. 15: 8125-48) up to the next stop codon (TAG, TGA or TAA), which lies in the same reading frame to the
30 ATG.

A further use of the nucleic acid sequences according to the invention is the construction of anti-sense oligonucleotides (Zheng and Kemeny, 1995, Clin. Exp. Immunol. 100: 380-2; Nellen and Lichtenstein, 1993, Trends Biochem. Sci. 18: 419-23; Stein, 1992, Leukemia 6: 967-74) and/or ribozymes (Amarzguioui, et al. 1998, Cell. Mol. Life Sci. 54: 1175-202; Vaish, et al., 1998, Nucleic Acids Res. 26: 5237-42; Persidis, 1997, Nat. Biotechnol. 15: 921-2; Couture and Stinchcomb, 1996, Trends Genet. 12: 510-5). Using anti-sense oligonucleotides, the stability of the nucleic acid used according to the invention can be decreased and/or the translation of the nucleic acid used according to the invention inhibited.

Thus, for example, the expression of the corresponding genes in cells can be decreased both in vivo and in vitro. Oligonucleotides can therefore be suitable as therapeutics. This strategy is suitable, for example, for skin, epidermal and dermal cells, in particular if the antisense oligonucleotides are complexed with liposomes (Smyth et al., 1997, J. Invest. Dermatol. 108: 523-6; White et al., 1999, J. Invest. Dermatol. 112: 699-705; White et al., 1999, J. Invest. Dermatol. 112: 887-92). For use as a sample or as an "antisense" oligonucleotide, a single-stranded DNA or RNA is preferred.

Furthermore, a nucleic acid which has been prepared synthetically can be used for carrying out the invention. Thus, the nucleic acid according to the invention can be synthesized, for example, chemically with the aid of the DNA sequences described in Tables 3 to 5 and/or with the aid of the protein sequences likewise described in these tables with reference to the genetic code, e.g. according to the phosphotriester method (see, for example, Uhlmann, E. & Peyman, A. (1990) Chemical Reviews, 90, 543-584, No. 4).

As a rule, oligonucleotides are rapidly degraded by endo- or exonucleases, in particular by DNases and RNases occurring in the cell. It is therefore advantageous to modify the nucleic acid in order to stabilize it against degradation, so that a high concentration of the nucleic acid is maintained in the cell over a long period (Beigelman et al., 1995, Nucleic Acids Res. 23: 3989-94; Dudycz, 1995, WO 95/11910; Macadam et al., 1998, WO 98/37240; Reese et al., 1997,

WO 97/29116). Typically, such a stabilization can be obtained by the introduction of one or more internucleotide phosphorus groups or by the introduction of one or more non-phosphorus internucleotides.

Suitable modified internucleotides are summarized in Uhlmann and
5 Peymann (1990 Chem. Rev. 90, 544) (see also Beigelman et al., 1995 Nucleic
Acids Res. 23: 3989-94; Dudycz, 1995, WO 95/11910; Madadam et al., 1998,
WO 98/37240; Reese et al., 1997, WO 97/29116). Modified internucleotide phos-
phate radicals and/or non-phosphorus bridges in a nucleic acid which can be em-
ployed in one of the uses according to the invention contain, for example, methyl-
10 phosphonate, phosphorothioate, phosphoramidate, phosphorodithioate, phosphate
ester, while non-phosphorus internucleotide analogues, for example, contain si-
loxane bridges, carbonate bridges, carboxymethyl esters, acetamidate bridges
and/or thioether bridges. It is also intended that this modification should improve
the stability of a pharmaceutical composition which can be employed in one of the
15 uses according to the invention.

In a further embodiment of the use according to the invention, the
nucleic acids are comprised in a vector, preferably in a "shuttle" vector,
phagemid, cosmid, expression vector or vector applicable in gene therapy. Fur-
thermore, the above mentioned nucleic acids can be included in "knock-out" gene
20 constructs or expression cassettes.

Preferably, the vector applicable in gene therapy contains wound-
or skin-specific regulatory sequences which are functionally associated with the
nucleic acid according to the invention.

The expression vectors can be prokaryotic or eukaryotic expression
25 vectors. Examples of prokaryotic expression vectors are, for expression in *E. coli*,
e.g. the vectors pGEM or pUC derivatives, examples of eukaryotic expression
vectors are for expression in *Saccharomyces cerevisiae*, e.g. the vectors
p426Met25 or p426GAL1 (Mumberg et al. (1994) Nucl. Acids Res., 22, 5767-
5768), for expression in insect cells, e.g. *Baculovirus* vectors such as disclosed in
30 EP-B1-0 127 839 or EP-B1-0 549 721, and for expression in mammalian cells,

e.g. the vectors Rc/CMV and Rc/RSV or SV40 vectors, which are all generally obtainable.

In general, the expression vectors also contain promoters suitable for the respective host cell, such as, for example, the trp promoter for expression
5 in *E. coli* (see, for example, EP-B1-0 154 133), the MET 25, GAL 1 or ADH2 promoter for expression in yeasts (Russel et al. (1983), J. Biol. Chem. 258, 2674-2682; Mumberg, supra), the Baculovirus polyhedrin promoter, for expression in insect cells (see, for example, EP-B1-0 127 839). For expression in mammalian cells, for example, suitable promoters are those which allow a constitutive, regu-
10 latable, tissue-specific, cell-cycle-specific or metabolically specific expression in eukaryotic cells. Regulatable elements according to the present invention are promoters, activator sequences, enhancers, silencers and/or repressor sequences.

Examples of suitable regulatable elements which make possible constitutive expression in eukaryotes are promoters which are recognized by the
15 RNA polymerase III or viral promoters, CMV enhancer, CMV promoter, SV40 promoter or LTR promoters, e.g. from MMTV (mouse mammary tumor virus; Lee et al. (1981) Nature 214, 228-232) and further viral promoter and activator sequences, derived from, for example, HBV, HCV, HSV, HPV, EBV, HTLV or HIV.

20 Examples of regulatable elements which make possible regulatable expression in eukaryotes are the tetracycline operator in combination with a corresponding repressor (Gossen M. et al. (1994) Curr. Opin. Biotechnol. 5, 516-20).

Preferably, the expression of wound-healing-relevant genes takes place under the control of tissue-specific promoters, wherein skin-specific pro-
25 moters such as, for example, the human K10 promoter (Bailleul et al., 1990. Cell 62: 697-708), the human K14 promoter (Vassar et al., 1989, Proc. Natl. Acad. Sci. USA 86: 1563-67), the bovine cytokeratin IV promoter (Fuchs et al., 1988; The biology of wool and hair (ed. G.E. Rogers, et al.), pp. 287-309. Chapman and Hall, London/New York) are particularly to be preferred.

Further examples of regulatable elements which make possible tissue-specific expression in eukaryotes are promoters or activator sequences from promoters or enhancers of those genes which code for proteins which are only expressed in certain cell types.

5 Examples of regulatable elements which make possible cell cycle-specific expression in eukaryotes are promoters of the following genes: cdc25A, cdc25B, cdc25C, cyclin A, cyclin E, cdc2, E2F-1 to E2F-5, B-myb or DHFR (Zwicker J. and Müller R. (1997) Trends Genet. 13, 3-6). The use of cell cycle regulated promoters is particularly preferred in cases, in which expression of the
10 polypeptides or nucleic acids used according to the invention is to be restricted to proliferating cells.

 An example of an regulatable element which makes possible the keratinocyte-specific expression in the skin, is the FiRE-element (Jaakkola et al., 2000, Gen. Ther., 7: 1640-1647). The FiRE element is a AP-1-driven, FGF-
15 inducible response element of the Syndecan-1 gene (Jaakkola et al., 1998, FASEB J., 12: 959-9).

 Examples of regulatable elements which make possible metabolically specific expression in eukaryotes are promoters which are regulated by hypoxia, by glucose deficiency, by phosphate concentration or by heat shock.

20 In order to make possible the introduction of nucleic acids as described above and thus the expression of the polypeptide in a eu- or prokaryotic cell by transfection, transformation or infection, the nucleic acid can be present as a plasmid, as part of a viral or non-viral vector. Suitable viral vectors here are particularly: baculoviruses, vaccinia viruses, adenoviruses, adeno-associated vi-
25 ruses and herpesviruses. Suitable non-viral vectors here are particularly: virosomes, liposomes, cationic lipids, or poly-lysine-conjugated DNA.

 Examples of vectors having gene therapy activity are virus vectors, for example adenovirus vectors or retroviral vectors (Lindemann et al., 1997, Mol. Med. 3: 466-76; Springer et al., 1998, Mol. Cell. 2: 549-58). Eukaryotic expres-

sion vectors are suitable in isolated form for gene therapy use, as naked DNA can penetrate into skin cells on topical application (Hengge et al., 1996, *J. Clin. Invest.* 97: 2911-6; Yu et al., 1999, *J. Invest. Dermatol.* 112: 370-5).

Vectors having gene therapy activity can also be obtained by complexing the nucleic acid with liposomes, since a very high transfection efficiency, in particular of skin cells, can thus be achieved (Alexander and Akhurst, 1995, *Hum. Mol. Genet.* 4: 2279-85). In the case of lipofection, small unilamellar vesicles are prepared from cationic lipids by ultrasonic treatment of the liposome suspension. The DNA is bound ionically to the surface of the liposomes, namely in such a ratio that a positive net charge remains and the plasmid DNA is complexed to 100% of the liposomes. In addition to the lipid mixtures DOTMA (1,2-dioleoyloxypropyl-3-trimethylammonium bromide) and DPOE (dioleoylphosphatidylethanolamine) employed by Felgner et al. (1987, *supra*), meanwhile numerous novel lipid formulations were synthesized and tested for their efficiency in the transfection of various cell lines (Behr et al. 1989, *Proc. Natl. Acad. Sci. USA* 86: 6982-6986; Felgner et al., 1994, *J. Biol. Chem.* 269:2550-2561; Gao, X. and Huang, 1991, *Biochim. Biophys. Acta* 1189:195-203). Examples of the novel lipid formulations are DOTAP N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium ethyl-sulphate or DOGS (TRANSFECTAM; dioctadecylamidoglycylspermine). Other lipids suitable for transfection in keratinocytes in vivo and in vitro are the cationic lipids Cytofectin GS 2888 (US 5,777,153; Lewis et al., 1996, *Proc. Natl. Acad. Sci. USA*, 93: 3176-3181). Auxiliaries which increase the transfer of nucleic acids into the cell can be, for example, proteins or peptides which are bound to DNA or synthetic peptide-DNA molecules which make possible the transport of the nucleic acid into the nucleus of the cell (Schwartz et al., 1999, *Gene Therapy* 6:282; Brandén et al., 1999, *Nature Biotech.* 17:784). Auxiliaries also include molecules which make possible the release of nucleic acids into the cytoplasm of the cell (Planck et al., 1994, *J. Biol. Chem.* 269:12918; Kichler et al. (1997) *Bioconj. Chem.* 8:213) or, for example, liposomes (Uhlmann and Peymann, 1990, *supra*). Another particularly suitable form of gene therapy vectors can be obtained by applying the above described nucleic

acid to gold particles and shooting these into tissue, preferably into the skin, or cells with the aid of the so-called gene gun (Wang et al., 1999, J. Invest. Dermatol. 112: 775-81, Tuting et al., 1998, J. Invest. Dermatol. 111: 183-8).

5 A further form of a vector applicable in gene therapy can be prepared by the introduction of "naked" expression vectors into a biocompatible matrix, for example a collagen matrix. This matrix can be introduced into wounds in order to transfect the immigrating cells with the expression vector and to express the polypeptides according to the invention in the cells (Goldstein and Banadio, US 5,962,427).

10 For gene therapy use of the above described nucleic acid, it is also advantageous if the part of the nucleic acid which codes for the polypeptide contains one or more non-coding sequences including intron sequences, preferably between promoter and the start codon of the polypeptide, and/or a polyA sequence, in particular the naturally occurring polyA sequence or an SV40 virus
15 polyA sequence, especially at the 3' end of the gene, as a stabilization of the mRNA can be achieved thereby (Palmiter et al., 1991, Proc. Natl. Acad. Sci. USA 88:478-482; Jackson, 1993, Cell 74:9-14).

Knock-out gene constructs are known to the person skilled in the art, for example, from the US patents 5,625,122; US 5,698,765; US 5,583,278 and
20 US 5,750,825.

A further preferred embodiment of the present invention is the use of a cell, preferentially of an autologous or heterologous cell, in particular a skin cell, which is transformed with a vector useable according to the invention or with a knock-out gene construct, for the diagnosis and/or prevention and/or treatment
25 of diseases of skin cells and/or of wound healing and/or of their pathological disorders, and/or for the identification of pharmacologically active substances. Cells can be either prokaryotic or eukaryotic cells; examples of prokaryotic cells are *E. coli* and of eukaryotic cells are *Saccharomyces cerevisiae* or insect cells.

A particularly preferred transformed host cell is a transgenic embryonic non-human stem cell, which is characterized in that it comprises at least one knock-out gene construct and/or an expression cassette as described above. Processes for the transformation of host cells and/or stem cells are well known to
5 the person skilled in the art and include, for example, electroporation or microinjection.

The genome of transgenic non-human mammals comprises at least one knock-out gene construct and/or an expression cassette as described above. Transgenic animals in general show a tissue-specifically increased expression of
10 the nucleic acids and/or polypeptides and can be used for the analysis of wound healing disorders. Thus, for example, an activin A transgenic mouse exhibits improved wound healing (Munz et al., 1999, EMBO J. 18: 5205-15) while a transgenic mouse having a dominantly negative KGF receptor exhibits delayed wound healing (Werner et al., 1994, Science 266: 819-22).

15 Processes for the preparation of transgenic animals, in particular of transgenic mice, are likewise known to the person skilled in the art from DE 196 25 049 and US 4,736,866; US 5,625,122; US 5,698,765; US 5,583,278 and US 5,750,825 and include transgenic animals which can be produced, for example, by means of direct injection of expression vectors (see above) into embryos or
20 spermatocytes or by means of the transfection of expression vectors into embryonic stem cells (Polites and Pinkert: DNA Microinjection and Transgenic Animal Production, page 15 to 68 in Pinkert, 1994: Transgenic animal technology: a laboratory handbook, Academic Press, London, UK; Houdebine, 1997, Harwood Academic Publishers, Amsterdam, The Netherlands; Doetschman: Gene Transfer in
25 Embryonic Stem Cells, page 115 to 146 in Pinkert, 1994, supra; Wood: Retrovirus-Mediated Gene Transfer, page 147 to 176 in Pinkert, 1994, supra; Monastyrsky: Gene Transfer Technology; Alternative Techniques and Applications, page 177 to 220 in Pinkert, 1994, supra).

If the above described nucleic acids are integrated into so-called
30 "targeting" vectors or "knock-out" gene constructs (Pinkert, 1994, supra), it is

possible after transfection of embryonic stem cells and homologous recombination, for example, to generate knock-out mice which, in general, as heterozygous mice, show decreased expression of the nucleic acid, while homozygous mice no longer exhibit expression of the nucleic acid. The animals thus produced can also
5 be used for the analysis of wound healing disorders. Thus, for example, the eNOS (Lee et al., 1999, Am. J. Physiol. 277: H1600-1608), Nf-1 (Atit et al., 1999, J. Invest. Dermatol. 112: 835-42) and osteopontin (Liaw et al., 1998, J. Clin. Invest. 101: 967-71) knock-out mice exhibit impaired wound healing. Here too, a tissue-specific reduction of the expression of wound healing-relevant genes, for example
10 in skin-specific cells using the Cre-loxP system (stat3 knock-out, Sano et al., EMBO J 1999 18: 4657-68), is particularly to be preferred. Transgenic and knock-out cells or animals produced in this way can also be used for the screening and for the identification of pharmacologically active substances vectors having gene therapy activity.

15 Polypeptides useable according to the invention can be prepared according to generally known recombinant processes. Furthermore, polypeptides useable according to the invention can be isolated from an organism or from tissue or cells and used according to the invention. Thus, it is possible, for example, to purify polypeptides useable according to the invention from mammal tissue, for
20 example from skin or body fluids such as for example blood, serum, saliva, synovial fluid, wound liquid. Furthermore, starting from cells expressing polypeptides useable according to the invention, cell lines can be prepared which can then be used for the isolation of polypeptides useable according to the invention. For example skin cells, such as for example HaCaT cells can be transformed with ex-
25 pression vectors containing nucleic acids useable according to the invention. The expression can be for example constitutive or inducible.

The polypeptide is prepared, for example, by expression of the above described nucleic acids in a suitable expression system, as already mentioned above, according to the methods generally known to the person skilled in
30 the art. Suitable host cells are, for example, the *E.coli* strains DHS, HB101 or

BL21, the yeast strain *Saccharomyces cerevisiae*, the insect cell line Lepidoptera, e.g. from *Spodoptera frugiperda*, or the animal cells COS, Vero, 293, HaCaT, and HeLa, which are all generally obtainable.

5 A further embodiment relates to the use of the polypeptides according to the invention, the polypeptides being employed in the form of a fusion protein. Fusion proteins useable according to the invention can be prepared, for example, by expressing nucleic acids useable according to the invention of a suitable cell.

10 The fusion proteins useable according to the invention themselves already having the function of a polypeptide of the invention or the specific function being functionally active only after cleavage of the fusion portion. Especially included here are fusion proteins having a proportion of about 1-300, preferably about 1-200, in particular about 1-100, especially about 1-50, foreign amino acids. Examples of such peptide sequences are prokaryotic peptide sequences, which can
15 be derived, for example, from the galactosidase of *E.coli*. Furthermore, viral peptide sequences, such as, for example, of the bacteriophage M13 can also be used in order thus to produce fusion proteins for the phage display process known to the person skilled in the art.

Further preferred examples of peptide sequences for fusion proteins
20 are peptides, that facilitate easier detection of the fusion proteins, these are, for example, "Green-fluorescent-protein" or functional variants thereof (WO 95/07463).

For the purification of the proteins described above (a) further polypeptide(s) (tag) can be attached. Protein tags according to the invention allow,
25 for example, high-affinity absorption to a matrix, stringent washing with suitable buffers without eluting the complex to a noticeable extent and subsequently targeted elution of the absorbed complex. Examples of the protein tags known to the person skilled in the art are a (His)₆ tag, a Myc tag, a FLAG tag, a haemagglutinin tag, glutathione transferase (GST) tag, intein having an affinity chitin-binding tag

or maltose-binding protein (MBP) tag. These protein tags can be situated N- or C-terminally and/or internally.

A further embodiment of the invention relates to the use of an antibody or an antibody fragment directed against a polypeptide useable according to the invention or a functional variant thereof, preferably of a polyclonal or monoclonal antibody or antibody fragment, for the analysis, diagnosis, prevention and/or treatment of diseases of skin cells, of wound healing and/or disorders of wound healing, and its use for the identification of pharmacologically active substances, if appropriate combined or together with suitable additives and/or auxiliaries.

Thus the local injection, for example, of monoclonal antibodies against TGF beta 1 in the animal model can improve wound healing (Ernst et al., 1996, Gut 39:172-5).

The process for manufacturing an antibody or an antibody fragment is carried out according to methods generally known to the person skilled in the art by immunizing a mammal, for example a rabbit, with said polypeptide or parts thereof having at least 6 amino acid length, preferably having at least 8 amino acid length, in particular having at least 12 amino acid length, if appropriate in the presence of, for example, Freund's adjuvant and/or aluminium hydroxide gels (see, for example, Diamond et al., 1981, The New England Journal of Medicine, 1344-1349). The polyclonal antibodies formed in the animal as a result of an immunological reaction can then be easily isolated from the blood according to generally known methods and purified, for example, by means of column chromatography. Monoclonal antibodies can be produced, for example, according to the known method of Winter & Milstein (Winter, G. & Milstein, C. (1991) Nature, 349, 293-299). As alternatives to the classical antibodies, for example, "anticalins" based on lipocalin can be used (Beste et al., 1999, Proc. Natl. Acad. Sci. USA, 96:1898-1903). The natural ligand-binding sites of the lipocalins, such as the retinol-binding protein or the bilin-binding protein can be modified, for example, by a "combinatorial protein design" approach in a manner such that they bind

to selected haptens, for example to the polypeptides useable according to the invention (Skerra, 2000, Biochim. Biophys. Acta 1482:337-50). Further known "scaffolds" are known as alternatives for antibodies for molecular recognition (Skerra, J. Mol. Recognit., 2000, 13:167-187).

5 The antibody useable according to the invention or the antibody fragment is directed against a polypeptide according to the invention and reacts specifically with the polypeptides according to the invention, where the above mentioned parts of the polypeptide either are immunogenic themselves or can be rendered immunogenic or increased in their immunogenicity by coupling to suitable carriers, such as bovine serum albumin. This antibody useable according to 10 the invention is either polyclonal or monoclonal; a monoclonal antibody is preferred. The term antibody or antibody fragment is understood according to the present invention as also meaning antibodies or antigen-binding parts thereof prepared by genetic engineering and optionally modified, such as chimeric antibodies, humanized antibodies, multifunctional antibodies, bi- or oligospecific anti- 15 bodies, single-stranded antibodies, F(ab) or F(ab)₂ fragments (see, for example, EP-B1-0 368 684, US 4,816,567, US 4,816,397, WO 88/01649, WO 93/06213, WO 98/24884).

20 The identified pharmacologically active substances can be used, if appropriate combined or together with suitable additives and/or auxiliaries, for the production of a diagnostic or of a medicament for the prevention, treatment and/or diagnosis of diseases of skin cells and/or in wound healing and/or their pathological disorders.

25 In order to use nucleic acids as a diagnostic the polymerase chain reaction can be employed as described below. For the use of nucleic acids as a medicament, a vector applicable for gene therapy or antisense nucleotides can be utilized as described.

30 In order to use other organic or anorganic pharmacologically active substances as a medicament, they can be applied as described above. Antibodies can be utilized as a diagnostic by means of immunological techniques as de-

scribed above, for example by using antibodies that are labeled with an enzyme. The specific antibody-peptide complex can be determined easily and quickly by means of an enzymatic color-reaction.

In order to use pharmacologically active substances as a diagnostic,
5 substances may contain a detectable marker, for example the substance may be radioactively labeled, fluorescence-labeled or luminescence-labeled. In addition substances may be coupled to enzymes, that allow indirect detection, for example by enzymatic catalysis by means of peroxidase-assay using a chromogenic substrate as described above or by binding of a labeled or detectable antibody. The
10 substances can be brought into contact with the sample and thus the amount of polypeptides useable according to the invention or a functional variant thereof or nucleic acids coding for this or a variant thereof, or a cell containing a polypeptide useable according to the invention or a functional variant thereof or a nucleic acid coding for this, or an antibody directed against a polypeptide useable according to
15 the invention or a fragment thereof, can be determined. The result of the sample, being isolated from an organism to be analyzed, can be compared with the result of a sample, of a healthy or a pathological organism.

The present invention also relates to the use of at least one polypeptide useable according to the invention or a functional variant thereof and/or of
20 a nucleic acid encoding this or a variant thereof, and/or of a cell expressing a polypeptide useable according to the invention or of a functional variant thereof or a nucleic acid encoding this or a variant thereof, and/or of an antibody or an antibody fragment directed against a polypeptide useable according to the invention, optionally combined or together with suitable additives and/or auxiliaries, for the
25 production of a medicament for the prevention and/or treatment of diseases of skin cells, of wound healing and/or their pathological disorders.

The medicament useable according to the invention may be used for the prevention and/or treatment of diseases of skin cells, of wound healing and/or their pathological disorders, wherein at least one polypeptide useable according to the invention or a functional variant thereof or a nucleic acid encoding
30

this, and/or a cell expressing a polypeptide useable according to the invention or a functional variant thereof or a nucleic acid encoding this or a variant thereof, and/or an antibody or an antibody fragment directed against a polypeptide useable according to the invention or a functional variant thereof, if appropriate combined
5 or together with suitable additives and/or auxiliaries, is being employed.

The therapy of the disorders, of skin disorders, of wound healing and/or disorders of wound healing, can be carried out in a conventional manner, e.g. by means of dressings, plasters, compresses or gels which contain the medicaments according to the invention. It is thus possible to administer the pharmaceuticals containing the suitable additives and/or auxiliaries, such as, for example,
10 physiological saline solution, demineralized water, stabilizers, proteinase inhibitors, gel formulations, such as, for example, white petroleum jelly, highly liquid paraffin and/or yellow wax, etc., topically and locally in order to influence wound healing immediately and directly. The administration of the medicaments according
15 to the invention can furthermore also be carried out topically and locally in the area of the wound, if appropriate in the form of liposome complexes or gold particle complexes. Furthermore, the treatment can be carried out by means of a transdermal therapeutic system (TTS), which makes possible a temporally controlled release of the medicaments according to the invention. The treatment by means of
20 the medicaments according to the invention, however, can also be carried out by means of oral dosage forms, such as, for example, tablets or capsules, by means of the mucous membranes, for example the nose or the oral cavity, or in the form of dispositories implanted under the skin. TTS are known for example, from EP 0 944 398 A1, EP 0 916 336 A1, EP 0 889 723 A1 or EP 0 852 493 A1.

25 For gene therapy use in humans, an especially suitable medicament is one which contains the described nucleic acid in naked form or in the form of one of the vectors having gene therapy activity described above or in a form complexed with liposomes or gold particles. The pharmaceutical carrier is, for example, a physiological buffer solution, preferably having a pH of about 6.0-8.0, preferably of about 6.8-7.8, in particular of about 7.4, and/or an osmolality of about
30

200-400 milliosmol/liter, preferably of about 290-310 milliosmol/liter. In addition, the pharmaceutical carrier can contain suitable stabilizers, such as nuclease inhibitors, preferably complexing agents such as EDTA and/or other auxiliaries known to the person skilled in the art.

5 The nucleic acid described is optionally administered in the form of the virus vectors described above in greater detail or as liposome complexes or a gold particle complex, customarily topically and locally in the area of the wound. It is also possible to administer the polypeptide itself with suitable additives and/or auxiliaries, such as physiological saline solution, demineralized water, sta-
10 bilizers, protease inhibitors, gel formulations, such as white petroleum jelly, highly liquid paraffin and/or yellow wax, etc., in order to affect wound healing immediately and directly.

 Examples of disorders of skin cells within the meaning of the invention is understood as psoriasis, eczema, especially atopic eczema, acne, Urti-
15 caria, disorders of pigmentation of the skin, especially vitiligo, senile skin and disorders of hair growth and hair metabolism.

 Wound healing within the meaning of the invention is understood as the healing process of a mechanical wound of the skin, such as for example laceration, skin abrasion or excoriation of the skin, for example by means of a
20 permanent load, for example decubitus or necrotic processes, for example *Necrobiosis lipoidica*.

 Examples of disorders of wound healing in the meaning of the invention comprise wounds of patients suffering from diabetes or alcoholism, wounds infected with organisms or viruses, ischemic wounds, wounds of patients
25 suffering from arterial disorders, or venous insufficiency, and scars, preferably overshooting scars, especially keloids. Especially preferred badly healing wounds comprise diabetic, neuropathic, venous or arterial ulcers, especially diabetic ulcers.

The present invention furthermore relates to the use of at least one polypeptide useable according to the invention or a functional variant thereof and/or of a nucleic acid encoding this or a variant thereof, and/or of a cell expressing a polypeptide useable according to the invention or a functional variant thereof or a nucleic acid encoding this or a variant thereof, and/or of an antibody or of an antibody fragment directed against a polypeptide useable according to the invention or a functional variant thereof, if appropriate combined or together with suitable additives and/or auxiliaries, for the production of a diagnostic for the diagnosis of diseases of skin cells and/or in wound healing and/or their pathological disorders.

For example, it is possible according to the present invention to prepare a diagnostic based on the polymerase chain reaction (Examples 2, 4 to 7, PCR diagnostic, e.g. according to EP 0 200 362) or an RNase protection assay (see, for instance, Sambrook et al., supra chapter 7, page 7.71-7.78, Werner et al., 1992, Growth Factor and Receptors: A Practical Approach 175-197, Werner, 1998, Proc. Natl. Acad. Sci. U.S.A. 89: 6896-699) with the aid of a nucleic acid as described above. These tests are based on the specific hybridization of a nucleic acids with its complementary counter strand, usually of the corresponding mRNA or its cDNA. The nucleic acid described above can in this case also be modified, such as disclosed, for example, in EP 0 063 879. Preferably a DNA fragment is labeled according to generally known methods by means of suitable reagents, e.g. radioactively with α -P³²-dCTP or non-radioactively with biotin or digoxigenin, and incubated with isolated RNA, which has preferably been bound beforehand to suitable membranes of, for example, cellulose or nylon. With the same amount of investigated RNA from each tissue sample, the amount of mRNA which was specifically labeled by the sample can thus be determined. Alternatively, the determination of mRNA amount can also be carried directly out in tissue sections with the aid of in situ hybridization (Werner et al., 1992, Proc. Natl. Acad. Sci. USA 89: 6896-6900).

The diagnostic useable according to the invention is used for the diagnosis of diseases of skin cells and/or in wound healing and/or their pathological disorders, wherein at least one polypeptide useable according to the invention or a functional variant thereof and/or a nucleic acid encoding this or a variant thereof, and/or a cell expressing a polypeptide useable according to the invention or a functional variant thereof or nucleic acid coding for this or a variant thereof, and/or an antibody or an antibody fragment directed against a polypeptide useable according to the invention or a functional variant thereof, if appropriate combined or together with suitable additives and/or auxiliaries, is employed.

The diagnostic useable according to the invention, can thus also be used to specifically measure the strength of expression in a tissue sample in order to be able to safely diagnose, for example, a wound healing disorder or dermatological disorders (Examples 2, 4 to 7). Such a process is particularly suitable for the early prognosis of disorders.

A preferred diagnostic useable according to the invention contains the described polypeptide or the immunogenic parts thereof described in greater detail above. The polypeptide or the parts thereof, which are preferably bound to a solid phase, e.g. of nitrocellulose or nylon, can be brought into contact in vitro, for example, with the body fluid to be investigated, e.g. wound secretion, in order thus to be able to react, for example, with autoimmune antibodies. The antibody-peptide complex can then be detected, for example, with the aid of labeled anti-human IgG or antihuman IgM antibodies. The labeling involves, for example, an enzyme, such as peroxidase, which catalyses a color reaction. The presence and the amount of autoimmune antibody present can thus be detected easily and rapidly by means of the color reaction.

A further diagnostic useable according to the invention, that is that subject matter of the present invention, contains the antibodies useable according to the invention themselves. With the aid of these antibodies, it is possible, for example, to easily and rapidly investigate a tissue sample as to whether the concerned polypeptide is present in an increased amount in order to thereby obtain an

indication of possible disorders, in particular skin disorder, and wound healing disorder. In this case, the antibodies according to the invention are labeled, for example, with an enzyme, as already described above. The specific antibody-peptide complex can thereby be detected easily and also rapidly by means of an enzymatic color reaction.

A further diagnostic useable according to the invention comprises a sample, preferably a DNA sample, and/or primer. This opens up a further possibility of obtaining the described nucleic acids, for example by isolation from a suitable gene bank, for example from a wound-specific gene bank, with the aid of a suitable sample (see, for example, J. Sambrook et al., 1989, Molecular Cloning. A Laboratory Manual 2nd edn., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY Chapter 8 page 8.1 to 8.81, Chapter 9 page 9.47 to 9.58 and Chapter 10 page 10.1 to 10.67).

Suitable samples are, for example, DNA or RNA fragments having a length of about 100-1000 nucleotides, preferably having a length of about 200-500 nucleotides, in particular having a length of about 300-400 nucleotides, whose sequence can be derived from the polypeptides according to SEQ ID No. 1 to SEQ ID No. 48, SEQ ID No. 55 to SEQ ID No. 58 and SEQ ID No. 63 to SEQ ID No. 73 and SEQ ID No. 80 to SEQ ID No. 82 of the sequence protocol and/or with the aid of the cDNA sequences of the database entries indicated in Tables 3 to 5 or with the aid of the sequence protocol according to SEQ ID No. 50 to SEQ ID No. 54 and SEQ ID No. 83 to SEQ ID No. 84.

The present invention also relates to the use of at least one antibody or antibody fragment directed against a polypeptide useable according to the invention for the identification of pharmacologically active substances, wherein the antibody/antibodies or antibody fragment(s) is/are bound to a solid phase.

Alternatively, it is possible with the aid of the derived nucleic acid sequences to synthesize oligonucleotides which are suitable as primers for a polymerase chain reaction. Using this, the nucleic acid described above or parts of this can be amplified and isolated from cDNA, for example wound-specific cDNA

(Example 2). Suitable primers are, for example, DNA fragments having a length of about 10 to 100 nucleotides, preferably having a length of about 15 to 50 nucleotides, in particular having a length of 20 to 30 nucleotides, whose sequence can be derived from the polypeptides according to SEQ ID No. 1 to SEQ ID No. 48, SEQ ID No. 55 to SEQ ID No. 58 and SEQ ID No. 63 to SEQ ID No. 73 and SEQ ID No. 80 to SEQ ID No. 82 of the sequence protocol and/or with the aid of the cDNA sequences of the database entries indicated in Tables 3 to 5 or with the aid of the sequence protocol according to SEQ ID No. 50 to SEQ ID No. 54 and SEQ ID No. 83 to SEQ ID No. 84.

10 The present invention furthermore relates to the use of at least one polypeptide useable according to the invention or a functional variant thereof and/or of a nucleic acid encoding this or a variant thereof, and/or of a cell expressing a polypeptide useable according to the invention or a functional variant thereof or a nucleic acid coding for this or a variant thereof, and/or of an antibody
15 or an antibody fragment directed against a polypeptide useable according to the invention or a functional variant thereof, if appropriate combined or together with suitable additives and/or auxiliaries, for the production of a test for finding pharmacologically active substances in connection with skin diseases and/or in connection with wound healing, in particular wound healing disorders.

20 At least one polypeptide useable according to the invention or a functional variant thereof and/or of a nucleic acid encoding this or a variant thereof, and/or of a cell expressing a polypeptide useable according to the invention or a functional variant thereof or a nucleic acid coding for this or a variant thereof, and/or of an antibody or an antibody fragment directed against a polypeptide useable according to the invention or a functional variant thereof, if appropriate combined or together with suitable additives and/or auxiliaries, may be
25 used in the form of a test for finding pharmacologically active substances in connection with diseases of skin cells and/or in wound healing and/or their pathological disorders.

In a preferred embodiment of the invention the test system comprises at least one polypeptide useable according to the invention and/or at least one antibody or antibody fragment useable according to the invention, which is bound to a solid-phase.

5 In an other preferred embodiment of the invention the test system comprises at least one cell expressing at least one polypeptide useable according to the invention or a nucleic acid coding for this.

A suitable system can be produced, for example, by the stable transformation of epidermal or dermal cells with expression vectors which contain
10 selectable marker genes and the described nucleic acids. In this process, the expression of the described nucleic acids is altered in the cells such that it corresponds to the pathologically disturbed expression in vivo. Anti-sense oligonucleotides which contain the described nucleic acid can also be employed for this purpose. It is therefore of particular advantage for these systems to know the ex-
15 pression behavior of the genes in disturbed regenerative processes, such as disclosed in this application. Often, the pathological behavior of the cells in vitro can thus be mimicked and substances can be sought which reproduce the normal behavior of the cells and which have a therapeutic potential.

Suitable cells for these test systems useable according to the inven-
20 tion are, for example, HaCaT cells, which are generally obtainable, and the expression vector pCMV4 (Anderson et al., 1989, J. Biol. Chem. 264: 8222-9). The nucleic acid as described above can in this case be integrated into the expression vectors both in the sense and in the anti-sense orientation, such that the functional concentration of mRNA of the corresponding genes in the cells is either increased,
25 or is decreased by hybridization with the antisense RNA. After the transformation and selection of stable transformants, the cells in culture in general show an altered proliferation, migration and/or differentiation behavior in comparison with control cells. This behavior in vitro is often correlated with the function of the corresponding genes in regenerative processes in the body (Yu et al., 1997, Arch.
30 Dermatol. Res. 289: 352-9; Mils et al., 1997, Oncogene 14: 15555-61; Charvat et

al., 1998, *Exp Dermatol* 7: 184-90; Werner, 1998, *Cytokine Growth Factor Rev.* 9: 153-65; Mythily et al., 1999, *J. Gen. Virol.* 80: 1707-13;) and can be detected using tests which are simple and rapid to carry out, such that test systems for pharmacologically active substances based thereon can be constructed. Thus, the proliferation behavior of cells can be detected very rapidly by, for example, the incorporation of labeled nucleotides into the DNA of the cells (see, for example, Savino and Dardenne, 1985, *J. Immunol. Methods* 85: 221-6; Perros and Weightman, 1991, *Cell Prolif.* 24: 517-23; Fries and Mitsuhashi, 1995, *J. Clin. Lab. Anal.* 9: 89-95), by staining the cells with specific stains (Schulz et al., 1994, *J. Immunol. Methods* 167: 1-13) or by means of immunological processes (Frahm et al., 1998, *J. Immunol. Methods* 211: 43-50). The migration can be detected simply by the migration index test (Charvat et al., *supra*) and comparable test systems (Benestad et al., 1987, *Cell Tissue Kinet.* 20: 109-19, Junger et al., 1993, *J. Immunol. Methods* 160: 73-9). Suitable differentiation markers are, for example, keratin 6, 10 and 14 and also loricrin and involucrin (Rosenthal et al., 1992, *J. Invest. Dermatol.* 98: 343-50), whose expression can be easily detected, for example, by means of generally obtainable antibodies.

Another suitable test system systems useable according to the invention is based on the identification of interactions using the so-called two-hybrid system (Fields and Sternglanz, 1994, *Trends in Genetics*, 10, 286-292; Colas and Brent, 1998 *TIBTECH*, 16, 355-363). In this test, cells are transformed using expression vectors which express fusion proteins from the polypeptide according to the invention and a DNA binding domain of a transcription factor such as, for example, Gal4 or LexA. The transformed cells additionally contain a reporter gene, whose promoter contains binding sites for the corresponding DNA binding domains. By transformation of a further expression vector which expresses a second fusion protein from a known or unknown polypeptide having an activation domain, for example of Gal4 or *Herpes simplex* virus VP16, the expression of the reporter gene can be greatly increased if the second fusion protein interacts with the polypeptide according to the invention. This increase in expression can be utilized in order to identify novel pharmacologically active sub-

stances, for example by preparing a cDNA library from regenerating tissue for the construction of the second fusion protein. Moreover, this test system can be utilized for the screening of substances which inhibit an interaction between the polypeptide according to the invention and pharmacologically active substance.

5 Such substances decrease the expression of the reporter gene in cells which express fusion proteins of the polypeptide according to the invention and of the pharmacologically active substance (Vidal and Endoh, 1999, Trends in Biotechnology; 17: 374-81). Novel active compounds which can be employed for the therapy of disorders of regenerative processes can thus be rapidly identified.

10 Furthermore a test system may be based on binding a polypeptide useable according to the invention, or a functional variant thereof and/or a nucleic acid coding for this or a variant thereof, and/or an antibody or an antibody fragment directed against a polypeptide useable according to the invention or a functional variant thereof, to a solid phase and test substances for interactions, for example for binding or for changes of the conformation. Suitable systems such as
15 affinity chromatography and fluorescence spectroscopy are known to the person skilled in the art.

Solid-phase bound polypeptides useable according to the invention, or functional variants thereof or nucleic acids coding for these or variants thereof,
20 or antibodies or antibody fragments directed against polypeptides useable according to the invention or functional variants thereof can also be part of an array.

In a preferred embodiment of the invention at least one polypeptide useable according to the invention or a nucleic acid coding for this, or at least one antibody or antibody fragment useable according to the invention may be used in
25 the form of an array fixated to a carrier, for the annalysis in connection with diseases of skin cells, of wound healing and/or disorders of wound healing.

Processes for the production of arrays by means of solid-phase chemistry and photolabile protecting groups are known from US 5,744,305. Such arrays can also be brought into contact with substances or libraries of substances

in order to test the substances for interactions, for example for binding or for changes of the conformation.

A substance to be tested may for example contain a detectable marker, for example a substance which is radioactively labeled, fluorescence-labeled or luminescence-labeled. Furthermore substances may be coupled to proteins, that allow indirect detection, for example by enzymatic catalysis using a peroxidase-assay with a chromogenic substrate or by binding of a detectable antibody. Modifications of the conformation of a polypeptide useable according to the invention can be detected by interaction with a suitable test-substance that for example changes fluorescence of an endogenous tryptophan within the molecule.

Pharmacologically active substances of the polypeptides according to the invention can also be nucleic acids which are isolated by means of selection processes, such as, for example, SELEX (see Jayasena, 1999, Clin. Chem. 45: 1628-50; Klug and Famulok, 1994, M. Mol. Biol. Rep. 20: 97-107; Toole et al., 1996, US 5,582,981). In the SELEX process, typically those molecules which bind to a polypeptide with high affinity (aptamers) are isolated by repeated amplification and selection from a large pool of different, single-stranded RNA molecules. Aptamers can also be synthesized and selected in their enantiomorphic form, for example as the L-ribonucleotide (Nolte et al., 1996, Nat. Biotechnol. 14: 1116-9; Klussmann et al., 1996, Nat. Biotechnol. 14: 1112-5). Thus isolated forms have the advantage that they are not degraded by naturally occurring ribonucleases and therefore have greater stability.

In a preferred embodiment of the invention, a test for identifying pharmacologically active substances is used, where candidate substances are tested for their influence on the expression of at least one nucleic acid useable according to the invention.

Assays for the identification of pharmacologically active substances, which influence the expression of genes are known to the person skilled in the art (see for example Sivaraja et al., 2001, US 6,183,956).

It is possible for example to cultivate cells, which express nucleic acids useable according to the invention, for example HeLa cells as a test system for the analysis of gene expression in vitro. Preferably the cells are skin cells, even more preferably they are keratinocytes, fibroblasts or endothelial cells. A possible test system constitutes the human keratinocyte cell line HaCat which is generally available.

The analysis of gene expression can be performed for example on the mRNA or protein level. Here, the amount of nucleic acid or protein useable according to the invention is measured after the application of one or more candidate substances to the cell culture and is then compared with the amount in a control cell culture. This can be performed for example by hybridization of an antisense probe which can be used to detect mRNA of target genes useable according to the invention in cell lysates. Quantification can be performed for example by binding of a specific antibody to the mRNA-probe complex (see Stuart and Frank, 1998, US 4,732,847). It is possible to perform the analysis as a high-throughput analysis to test a lot of substances with respect to their suitability as modulator of gene expression of nucleic acids useable according to the invention (Sivaraja et al., 2001, US 6,183,956). The substances to be analysed can be taken from substance libraries (see for example. DE19816414, DE19619373) which contain several thousand, often very heterogeneous substances. Alternatively, the total RNA or mRNA can be isolated from cells and subsequently the absolute or relative amount of mRNA of a target gene useable according to the invention can be determined for example by the use of quantitative RT-PCR (see EP 0 200 362; Wittwer et al., 1997, BioTechniques 22:130-8; Morrison et al., 1998, BioTechniques 24: 954-62) or RNase Protection Assays (see for example Sambrook et al., 1989, Molecular cloning: A Laboratory Manual, Cold Spring Harbor, Cold Spring Harbor Laboratory Press, New York, chapter 7; EP 0 063 879). Another possibility constitutes the detection of the amount of protein in cell lysate by the use of an antibody which specifically detects the protein useable according to the invention. The quantification can for example be performed by the use of an ELISA or Western blot analysis, which are generally known to a person skilled in the art. To

determine the specificity of the substances for the expression of nucleic acids useable according to the invention, the influence of the candidate substances on the target gene expression can be compared to the influence on the expression on other genes, for example genes of the cell metabolism like GAPDH. This can be performed in separately or in parallel to the analysis of the nucleic acids useable according to the invention.

The pharmacologically active substances identified with the aid of the test procedures useable according to the invention can be used, if appropriate combined or together with suitable additives and/or auxiliaries, for the production of a diagnostic or medicament for the diagnosis, prevention and/or treatment of diseases of skin cells, of wound healing and/or their pathological disorders.

A further subject of the invention relates to the use of at least one polypeptide useable according to the invention or of a functional variant thereof and/or of a nucleic acid encoding this or a variant thereof, and/or of an antibody or an antibody fragment directed against a polypeptide useable according to the invention or a functional variant thereof, if appropriate combined or together with suitable additives and/or auxiliaries, for the production of an array attached to a carrier material for analysis in connection with diseases of skin cells and/or of wound healing and/or their pathological disorders.

Processes for preparing such arrays are known, for example, from US 5,744,305 by means of solid-phase chemistry and photolabile protective groups.

The present invention furthermore relates to the use of at least one polypeptide useable according to the invention or a functional variant thereof and/or of a nucleic acid encoding this or a variant thereof, and/or of an antibody or an antibody fragment directed against a polypeptide useable according to the invention or a functional variant thereof, if appropriate combined or together with suitable additives and/or auxiliaries, in the form of an array for analysis in connection with diseases of skin cells, in wound healing and/or their pathological disorders.

For analysis in connection with diseases of skin cells and/or of wound healing and/or their pathological disorders, it is also possible to use, for example, DNA chips and/or protein chips which comprise at least one nucleic acid, at least one polypeptide, and/or at least one antibody or antibody fragment,
5 as described above. DNA chips are disclosed, for example, in US 5,837,832.

The invention will now be further illustrated below with the aid of the figures and examples, without the invention being restricted thereto.

Description of the tables, figures and sequences:

- 10 Table 1: Tabulation of the differential expression of various genes relevant for wound healing in wounds of 10 weeks old BALB/c mice and in wounds of young (4 weeks of age) and old (12 months) mice, as well as in intact skin and wounds of dexamethasone-treated, badly healing wounds and of control mice.
- 15 Table 2: Tabulation of the differential expression of various genes that are relevant for wound healing in intact skin and in wounds of mice with diabetes and of control mice.
- Table 3: Tabular survey of polypeptide sequences with unknown biological function that were identified during the analysis of gene expression during wound healing, and their cDNAs and accession numbers or
20 SEQ ID numbers.
- Table 4: Tabular survey of the polypeptide sequences with already known and described functions identified in the analysis of gene expression during the wound healing process and their cDNAs and accession numbers or SEQ ID numbers.
- 25 Table 5: Tabular survey of the polypeptide sequences with already known and described functions, that were additionally identified in the

analysis of gene expression during the wound-healing process, and their cDNAs and accession numbers or SEQ ID numbers.

Table 6: Analysis of the kinetics of wound-relevant genes during wound healing in the mouse by means of "TaqMan analysis".

5 Table 7: Analysis of the kinetics of wound-relevant genes during wound healing in humans relative to Cyclophilin by means of "TaqMan analysis".

Table 8: Analysis of the expression of genes useable according to the invention in the wound ground and the wound edge relative to intact skin of ulcer patients.

10 Table 9: Analysis of the expression of genes useable according to the invention in intact skin of healthy persons, as well as in lesional and non-lesional skin of psoriasis patients.

Figure 1: Autoradiograms of hybridizations of membranes (mouse ATLAS Array, Clontech Laboratories GmbH, Heidelberg) with an identical pattern of applied cDNA fragments using four different samples. All samples were prepared from cDNAs which originated from subtractive hybridizations. A: wound-specific sample (subtraction wound versus intact skin), B: skin-specific sample (subtraction intact skin versus wound), C: sample specific for poorly healing wounds (subtraction wound dexamethasone-treated animals versus wound control animals), D: sample specific for well-healing wounds (subtraction wound control animals versus wound dexamethasone-treated animals). The positions of the TTF-I cDNAs (each loaded twice) are indicated with arrows.

Figure 2: Comparison of the polypeptide sequences of the identified proteins of SW1136 from mouse (murine) and human. Differences to the human sequence of SW1136 are indicated.

Figure 3: Comparison of the polypeptide sequences of the identified proteins of SW1295 from mouse (murine) and human. Differences to the human sequence of SW1295 are indicated.

5 SEQ ID No. 1 to SEQ ID No. 58 and SEQ ID No. 63 to SEQ ID No. 73 and SEQ ID No. 80 to SEQ ID No. 84 show the polypeptide or cDNA sequences useable according to the invention from human or mouse.

SEQ ID No. 59 to SEQ ID No. 62 and SEQ ID No. 74 to SEQ ID No. 79 show DNA sequences of oligonucleotides which were used for the experiments of the present invention.

10

Examples

Example 1: Enrichment of wound-relevant cDNA by means of subtractive hybridization and identification of TTF-I as wound-relevant gene

15

Total RNA was isolated from intact skin and from wound tissue (wounding on the back 1 day before tissue sampling by scissors cut) of BALB/c mice by standard methods (Chomczynski and Sacchi, 1987, Anal. Biochem. 162: 156-159, Chomczynski and Mackey, 1995, Anal. Biochem. 225: 163-164). In order to obtain tissue of mice with poorly healing wounds, BALB/c mice were treated before wounding with dexamethasone (injection of 0.5 mg of dexamethasone in isotonic saline solution per kg of body weight twice per day for 5 days). The RNAs were then transcribed into cDNA with the aid of a reverse transcriptase. The cDNA synthesis was carried out using the "SMART PCR cDNA synthesis kit" from Clontech Laboratories GmbH, Heidelberg, according to the directions of the corresponding manual.

20

25

In order to identify those cDNAs which occurred with differing frequency in the cDNA pools, a subtractive hybridization (Diatchenko et al.,

1996, Proc. Natl. Acad. Sci. U.S.A. 93: 6025-30) was carried out. This was effected using the "PCR select cDNA subtraction kit" from Clontech Laboratories GmbH, Heidelberg, according to the directions of the corresponding manual, the removal of excess oligonucleotides after the cDNA synthesis being carried out by means of agarose gel electrophoresis. Four cDNA pools were set up, which were enriched for wound-relevant genes, where one pool was enriched for cDNA fragments which are expressed more strongly in the wound tissue in comparison with intact skin ("wound-specific cDNA pool"), one pool was enriched in cDNA fragments which are more strongly expressed in intact skin in comparison with wound tissue ("skin-specific cDNA pool"), one pool was enriched in cDNA fragments which are more strongly expressed in well-healing wounds in comparison with poorly healing wounds ("well healing cDNA pool") and one pool was enriched in cDNA fragments which are more strongly expressed in poorly healing wounds in comparison with well-healing wounds ("poorly healing cDNA pool").

In order to identify those genes which were contained in the cDNA pools relevant to wound healing, the presence of the corresponding cDNAs in the pools was analysed in "reverse Northern blot". Here, the cDNA fragments are immobilized on membranes in the form of arrays of many different cDNAs, and hybridized with a complex mixture of radio-labeled cDNA (Sambrook et al., 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor, Cold Spring Harbor Laboratory Press, New York, Chapter 9 page 9.47 to 9.58 and Chapter 10 page 10.38 to 10.50; Anderson and Young: Quantitative filter hybridisation; in: Nucleic Acids Hybridisation, A Practical Approach, 1985, Eds. Hames and Higgins, IRL Press Ltd.; Oxford, Chapter 4, page 73 to 112). For example, commercially available membranes were used (mouse ATLAS array, Clontech).

For the preparation of suitable hybridization samples, the subtracted cDNA pools were treated with the restriction endonuclease RsaI and purified by means of agarose gel electrophoresis (Sambrook et al., supra, Chapter 6, page 6.1 to 6.35) in order to separate the cDNA synthesis and amplification primer (see manual "PCR-Select cDNA Subtraction Kit", Clontech). The cDNAs

were then radio-labeled using the "random hexamer priming" method (Feinberg and Vogelstein, 1983, Anal. Biochem. 132: 6-13) in order to prepare hybridization samples.

The membrane was preincubated in 25 ml of hybridization solution
5 for 30 min at 65°C (25 mM sodium phosphate, pH = 7.5, 125 mM NaCl, 7% SDS). The hybridization sample was denatured at 100°C for 10 min, then cooled on ice, about 100 CPM ("counts per minute") per ml were added to the hybridization solution and the hybridization was carried out in a hybridization oven for 16 hours at 65°C. The membrane was then washed twice with the hybridization solution without sample at 65°C for 10 min. The membrane was then washed at 65°C
10 a number of times for 10 min in each case in wash solution (2.5 mM sodium phosphate, pH = 7.5, 12.5 mM NaCl, 0.7% SDS) until it was no longer possible to detect any activity in the solution poured off. The radioactive signals were analyzed using a phosphorimager (BioRad, Quantity One®) (Figure 1). Those cDNAs
15 were then selected which produced different signal intensities with the various samples. This resulted at the position of TTF-I on the membrane, in a significantly stronger signal intensity with the skin specific cDNA pool in comparison to the wound specific cDNA pool (Figure 1A, B). The analysis of the experiment, in which hybridization was performed in parallel with the "poorly healing" cDNA
20 pool and the "well healing" cDNA pool, showed, that the hybridization sample of the "poorly healing" cDNA pool hybridized significantly stronger at the position of TTF-I (Figure 1 C, D). Therefore, differential expression of TTF-I was observed at two different wound healing states.

25 Example 2: Verification of the expression pattern of TTF-I by means of „real-time quantitative RTPCR“

A verification of the differential expression of the nucleic acids described above as well as the investigation of further wound healing states was carried out by real-time RTPCR in the ABI Prism 7700 sequence detection system
30 (PE Applied Biosystems). The apparatus was equipped with the ABI Prism

7200/7700 SDS software version 1.6.3 (1998). The detection of PCR products was carried out during the amplification of the cDNA with the aid of the stain SYBR Green 1, whose fluorescence is greatly increased by binding to double-stranded DNA (Karlsen et al. 1995, J. Virol. Methods. 55: 153-6; Wittwer et al.,
5 1997, BioTechniques 22: 130-8, Morrison et al., 1998, BioTechniques 24: 954-62). The basis for the quantification is the PCR cycle (threshold cycle, CT value) which is reached when the fluorescence signal exceeds a defined threshold. The analysis is carried out by means of the Δ -CT method (User Bulletin #2, Relative Quantitation of Gene Expression, PE Applied Biosystems, 1997). The abundances
10 of the cDNAs were determined relative to an endogenous reference (GAPDH). The results are shown in Tables 1 and 2.

To obtain tissue from mice with poorly healing wounds, BALB/c mice were treated prior to wounding with dexamethasone (injection of 0.5 mg dexamethasone in isotonic salt solution per kg body weight twice a day for 5
15 days). To obtain wound tissue from young and old mice, day 1 wounds from 4 weeks and 12 months old BALB/c mice were employed. To obtain wound tissue from mice with diabetes, day 1 wounds of 10 weeks old C57-BL/Ks-*db/db*/OLA mice were used. Total RNA was obtained from skin and wound tissue as described above and 1 μ g of total RNA was subjected to reverse transcription in a
20 thermocycler (GeneAmp PCR system 9700, Perkin Elmer) using the TaqMan reverse transcription reagent kit (Perkin Elmer) according to the recommendations of the manufacturer (SYBR Green PCR and RT-PCR Reagents Protocol, PE Applied Biosystems, 1998). The primers for the amplification of the TTF-I cDNA (*TTF-I*-Primer 1: CGAGCGCTACATTGTCGCT (SEQ ID No. 59), *TTF-I*-Primer
25 2: GTCTTAAATTTGCTTGTGCCCC (SEQ ID No. 60)) and the reference (GAPDH primer 1: ATCAACGGGAAGCCCATCA (SEQ ID No. 61), GAPDH primer 2: GACATACTCAGCACCGGCCT (SEQ ID No. 62)) were selected with the aid of the Primer Express software for Macintosh PC Version 1.0 (PE Applied Biosystems, P/N 402089, 1998) based on the nucleic acid described above and the
30 known sequence of GAPDH. For the PCR, the SYBR Green PCR Core Reagents Kit (4304886, PE Applied Biosystems) was used. The concentration of the prim-

ers in the PCR was initially optimized in the range from 50 nM to 600 nM and the specificity of the PCR was tested by analysis of the length of the amplified products in an agarose gel electrophoresis. The efficiency of the PCR system was then determined by means of a dilution series (User Bulletin #2, Relative Quantitation
5 of Gene Expression, PE Applied Biosystems, 1997). It became apparent that for both cDNAs the efficiency of the amplification was 100%, i.e. at each 1:2 dilution of the cDNA one more cycle was needed in order to exceed the fluorescence threshold value.

For the quantification, each batch of cDNA was amplified from 10
10 ng of reverse-transcribed total RNA in a total volume of 25 µl. The running conditions for the PCR corresponded to the details of the manufacturer (PE Applied Biosystems, SYBR Green® PCR and RT-PCR Reagents Protocol, 1998). The CT values were analysed and the abundance of *TTF-I* relative to GAPDH was calculated. On the one hand the decrease of *TTF-I* in wounds in comparison to intact
15 skin from control animals as well as of young mice was confirmed (Table 1, compare to Figure 1 A, B). On the other hand again an increase of expression of *TTF-I* was observed in poorly healing wounds of dexamethasone treated mice in comparison to well healing wounds of control animals (Table 1, compare to Figure 1 B, C). In addition a decrease of *TTF-I* could be measured in mice with diabetes
20 (Table 2). Therefore, the regulation of expression of *TTF-I* in different wound healing states was verified.

Example 3: Identification of MCP-2 as gene relevant for wounds using comparison counting of clones in cDNA libraries through the analysis of restriction fragment patterns
25

BALB/c mice were treated with dexamethasone (injection of 0.5 mg dexamethasone per kg body weight twice a day for 5 days) and subsequently wounded to obtain tissue of poorly healing day 1 wounds. The generation of cDNA of the total RNA isolated from the tissue as well as all further steps was
30 performed as described in EP 0 965 642: the cDNA was cloned in defined orien-

tation in a suitable vector and the thus obtained plasmid was transformed into a suitable *E. coli* strain. 100 *E. coli* clones respectively were mixed, and the plasmid DNA was isolated. The DNA was separated into three portions and subsequently hydrolyzed with the restriction endonuclease BglI and labeled with a fluorescent dye. Subsequently each portion was divided into two portions and then hydrolyzed with one of the restriction endonuclease BfaI, DpnI, RsaI, DdeI, AluI and HinfI. The portioned nucleic acids were separated electrophoretically and the pattern of the separated nucleic acids was analyzed. The restriction fragment pattern of clone mixture was compared with the patterns of single cDNA clone analysis and thus the cDNAs were identified. Those nucleic acids were selected which restriction fragment pattern was identified with a different abundance in cDNA pools of poorly healing and well healing wounds. During the analysis of 37000 cDNAs the pattern of MCP-2 (DdeI:196.23±0.3 base pairs; AluI: 67.51±0.5 base pairs; HinfI: 349.88±0.7 base pairs; BfaI: 531.02±2.0 base pairs; DpnI: 245.02±0.3 base pairs; RasI: 254.23±0.3 base pairs) was identified three times in the cDNA pool of poorly healing wounds, while the pattern was not observed in the cDNA pool of well healing wounds.

Example 4: Analysis of the kinetics of wound-relevant genes during wound healing in the mouse by means of "TaqMan analysis"

The kinetics of the regulation of the expression of wound-relevant genes during normal wound healing in the mouse was investigated by means of "TaqMan analysis" using the GeneAmp5700 from Applied Biosystems. Normally healing wound biopsies from various time points after wounding and intact skin were obtained from 6 10 week-old BALB/c mice treated with isotonic saline solution by scissors cut as described in Example 1. The RNA was isolated by homogenizing the biopsies in RNAClean buffer (AGS, Heidelberg), to which 1/100 part by volume of 2-mercaptoethanol had been added using a disperser. The RNA was then extracted by treating with phenol twice by means of acidic phenol saturated with water and extracted in the presence of 1-bromo-3-chloropropane. An

isopropanol and an ethanol precipitation were then carried out and the RNA was washed with 75% ethanol. After this, a DNase I digestion of the RNA was carried out. For this, 20 µg of RNA (to 50 µl with DEPC-treated water) were incubated at 37°C for 20 min with 5.7 µl of transcription buffer (Roche), 1 µl of RNase inhibitor (Roche; 40 U/µl) and 1 µl of DNase I (Roche; 10 U/µl). 1 µl of DNase I was then added again and the mixture was incubated at 37°C for a further 20 min. The RNA was then treated with phenol, ethanol-precipitated and washed. All above mentioned steps were carried out using DEPC (diethyl pyrocarbonate)-treated solutions or liquids containing no reactive amino groups. cDNA was then prepared from the extracted RNA. This was carried out in the presence of 1 × TaqMan RT buffer (Applied Biosystems), 5.5 mM MgCl₂ (Perkin Elmer), 500 µM each of dNTPs (Perkin Elmer), 2.5 µM of random hexamers (Perkin Elmer), 1.25 U/µl of MultiScribe Reverse Transcriptase (50 U/µl, Perkin Elmer), 0.4 U/µl RNase inhibitor (20 U/µl, Perkin Elmer), 20 µl of RNA (50 ng/µl) and DEPC-treated water (to 100 µl volume). After addition of the RNA and thorough mixing, the solution was divided in 2 0.2 ml wells (50 µl each) and the reverse transcription was carried out in a thermo cycler (10 min at 25°C; 30 min at 48°C and 5 min at 95°C). The cDNA was subsequently quantified by means of quantitative PCR using SYBR green PCR master mixes (Perkin Elmer), a triplicate determination (in each case with target primers and GAPDH primers) being carried out for each cDNA species to be determined. The stock solution for each triplet contained, in a total volume of 57 µl, 37.5 µl of 2 × SYBR master mix, 0.75 µl of AmpErase UNG (1 U/µl) and 18.75 µl of DEPC-treated water. Per triplicate determination, 1.5 µl each of forward and reverse primer were added to 57 µl of stock solution in a previously optimized concentration ratio. 60 µl each of the stock solution/primer mixture were mixed with 15 µl of cDNA solution (2 ng/µl) and subdivided into 3 reaction wells. Parallel to this, a stock solution with primers was prepared as a reference for the determination of GAPDH (SEQ ID No. 61 and SEQ ID No. 62), mixed with a further 15 µl of the same cDNA solution and subdivided into 3 reaction wells. In addition, in order to set up a standard curve for

the GAPDH-PCR, various cDNA solutions were prepared as a dilution series (4 ng/μl; 2 ng/μl; 1 ng/μl; 0.5 ng/μl and 0.25 ng/μl). 15 μl each of these cDNA solutions were mixed with 60 μl of stock solution/primer mixture for the determination of GAPDH and subdivided into 3 reaction wells. Likewise, a standard curve for the PCR of the genes to be investigated was set up in each case; the same dilutions which were also employed for the GAPDH standard curve were used here. The control used was a PCR batch without cDNA. 15 μl each of DEPC water were added to 60 μl in each case of stock solution/primer mixture of target and GAPDH in each case, mixed and in each case subdivided into 3 reaction wells.

10 The amplification of the batches was carried out in the GeneAmp 5700 (2 min at 50°C; 10 min at 95°C, followed by 3 cycles of 15 sec at 96°C and 2 min at 60°C; then 37 cycles of 15 sec at 95°C and 1 min at 60°C). The analysis was carried out by the determination of the relative abundance of each target gene with respect to the GAPDH reference. For this, a standard curve was first set up by plotting the

15 C_T values of the dilution series against the logarithm of the amount of cDNA in the PCR batch (ng of transcribed RNA) and the slope(s) (s) of the straight lines was determined. The efficiency (E) of the PCR then results as follows: $E = 10^{-1/s} - 1$. The relative abundance (X) of the cDNA species (Y) investigated in relation to GAPDH is then: $X = (1 + E_{GAPDH})^{C_T(GAPDH)} / (1 + E_Y)^{C_T(Y)}$. The numerical values were

20 then standardized by setting the amount of cDNA from intact skin of the 10 week-old BALB/c control animals equal to 1. The relative changes in the target gene expression in various wound healing states are compiled in Table 6. Thus it is clear, for example, in the case of the tyrosine kinase Fer that the expression of skin disease-relevant targets is specifically regulated during wound healing. In

25 this target, even one hour after wounding, a greatly decreased expression of mRNA occurs which lasts during the entire observation period of 14 d. This shows that differential regulation over the entire period of wound healing is essential for the normal course of wound healing.

A similar kinetic, i.e. a reduced expression upon wounding that

30 lasted for days was observed in a plurality of genes, for example for KIAA1247,

Cystatin C, SW1136, SW1295, Baf57, TSC-22, Split hand foot deleted 1, Nicotinamid N-Methyl-Transferase, UBC9, tsq101, HMG-14, TAK1 and Golgi-4-transmembrane spanning transporter. This demonstrates that differential regulation of these genes is required over the entire period of wound healing. However
5 complex kinetics have also been observed, for example phospholipase inhibitor exhibited an upregulation of the expression 1 h after wounding as well as 7 and 14 days after wounding. This clearly shows, that the differential expression of phospholipase inhibitor can lead to disorders of the wound healing process directly after wounding as well as during later phases of wound healing and that disorders
10 of the expression and/or activity of phospholipase inhibitor may lead to disorders of the wound healing directly after wounding as well as in later phases of wound healing.

Example 5: Differential expression of wound-relevant genes in human wounds

15 With the aid of the normally healing wounds, it should now be investigated whether a differential regulation of the expression of the genes identified as wound-relevant verified in Example 4 can also be observed in humans. For this, 4 mm biopsies of intact skin were taken from 6 patients as described above, and also 6 mm biopsies from the same patients at the time points T=1 h, 1 d, 5 d
20 and 14 d. The biopsies of a given time point were pooled and the cDNA was isolated as described above. Then the quantification was done by means of TaqMan analysis as described above, except that the abundance of the target species to be determined was determined relative to cyclophilin (EMBL: Y00052). The primers used for this are cyclophilin primer 1: TCTTAACCAC CAGATCATTC CTTCT
25 (SEQ ID No. 78) and cyclophilin primer 2: GGATACTGCG AGCAAATGGG (SEQ ID No. 79). The analysis of the experiment is shown in Table 7. In the case of CCR-1 (CCR-1 Primer 1: CCCAATGGGA ATTCATTCAC C (SEQ ID Nr. 76); CCR-1 Primer 2: GCTTCCACTC TCGTAGGCTT TC (SEQ ID Nr. 77)), a strong increase in CCR-1 expression until 24 h after wounding followed by a slow
30 decrease in CCR-1 expression was observed in human. This is fully consistent with the kinetics of CCR-1 expression in murine wound biopsies (Table 6). Also,

it was possible to show, for example, in the case of the Golgi 4 transmembrane spanning transporter that differential regulation of expression during wound healing can be detected both in the mouse and in man. Thereby, it was thus possible to verify the relevance of the target to wound healing and skin diseases. Also
5 the other genes analyzed showed a differential regulation upon wounding. Thus it was possible to demonstrate that the targets are relevant for wound healing and for skin disorders. The genes showed complex kinetics of expression with transient changes, such as for example in the case of Eps8, Phospholipase Inhibitor, TSC-22, Cathepsin C and HMG-14 as well as a steady increase in expression spanning
10 the time of investigation such as in the case of KIAA1247 and Cystatin C. This demonstrates, that the precise regulation of the expression and/or activity of the targets is essential for the normal course of the wound healing process both in mice and humans.

15 Example 6: Differential expression of wound-relevant genes in human ulcers

In order to show that the genes identified as wound-relevant are differentially regulated not only in normally proceeding wound healing but also in the case of a wound-healing disorder, biopsies from patients having chronic venous ulcers were taken at the same time from intact skin and from the wound
20 ground and the wound edge and were investigated for expression of the target genes. From each group (intact skin, wound edge, wound ground), the biopsies of 6 subjects in each case were pooled. RNA was isolated from all biopsies as described in Example 4 transcribed into cDNA. The quantification of wound healing-relevant cDNAs was carried out also as described in Example 5, the amount
25 of cyclophilin mRNA being used for the calculation of the relative amount of the target gene cDNA. The results of the experiments are compiled in Table 8. Thus, in the case of KIAA1247, for example, a dysregulation of the expression in the ulcers was found in comparison to the normally healing wound (Table 7): while in the normally healing wound a steady increase in the KIAA1247 was observed, a
30 markedly reduced expression was found at the wound edge. This shows that the

differential expression of KIAA1247 is essential not only for wound healing, but that dysregulations can lead to severe wound-healing disorders. The experiment illustrates that KIAA1247 can be used for the diagnosis, prevention and/or treatment of wound-healing disorders and/or skin diseases.

5

Example 7: Differential regulation of genes useable according to the invention in lesional and non-lesional skin of psoriasis patients in comparison with intact skin of healthy patients

It should now be verified with the aid of psoriasis patients that
10 genes useable according to the invention play an important part not only in wound healing and wound-healing disorders but also in other skin diseases. For this, 4 mm punch biopsies both of lesional and non-lesional skin were taken from psoriasis patients as described in Example 5. As a control, biopsies of intact skin were taken from healthy subjects. The isolation of the mRNA from the individual biop-
15 sies was carried out by embedding the biopsies in tissue freezing medium (Jung), the reduction of the biopsy into pieces using a microtome and the subsequent mRNA isolation by means of Dynabeads-Oligo dT (Dyna). The hacked biopsies were first suspended in lysis-buffer and then homogenized using the Polytron. In order to fragment the genomic DNA, the solution is centrifuged through Qia-
20 Shredder columns and additionally sheared a number of times in a syringe with a needle. The Dynabeads were pretreated according to the instructions of the manufacturer and mixed with the lysis homogenate (250 µl of the stock suspension), incubated and washed (final volume 250 µl). The suspension was then divided into one portion each of 240 µl and of 10 µl (as a control). For the first strand
25 synthesis, the following components were mixed: 20 µl of 10 × TaqMan RT buffer, 44 µl of 25 mM MgCl₂, 40 µl of dNTP mix (2.5 mM/dNTP), 87 µl of DEPC-H₂O, 4 µl of RNase inhibitor (20 U/µl) and 5 µl of MultiScribe transcriptase (50 U/µl). 195 µl of the reaction mix were then added to the 240 µl batch and 20 µl to the control batch, mixed and incubated at 48°C for 45 min. The Dyna-
30 beads were then pelleted in a magnetic particle collector and the supernatant was

withdrawn. 20 µl of Tris-HCl buffer were then added and the suspension was incubated at 95°C for 1 min. The Dynabeads were immediately pelleted in a magnetic particle collector and the mRNA in the supernatant was withdrawn. The cDNA/Dynabeads were then washed 3× with TE buffer. For the second strand
5 synthesis, the cDNA/Dynabeads were washed 2× in 1× EcoPol buffer and a solution of the following components was added: 23 µl of 10× EcoPol buffer; 4.6 µl of dNTP mix (25 mM/dNTP); 11.5 µl of random hexamers; 118.7 µl of DEPC-H₂O. The suspension was mixed briefly with the aid of a vortexer and 9.2 µl of Klenow fragment (5 U/µl) were then added. 200 µl of this solution were added to
10 the batch, 20 µl to the control batch, and the suspensions were incubated at 37°C for 1 h. The DNA was then melted at 94°C for 1 min and the Dynabeads were pelleted in a magnetic particle collector. The supernatant was transferred to a new reaction vessel and the enzyme was inactivated at 75°C for 10 min. The sense DNA strands contained in the supernatant were then employed for the TaqMan
15 analysis.

The TaqMan analysis was carried out as described in Example 5, the amount of GAPDH (hGAPDH-Primer 1: CCTCCCCTCTTCAAGGGTCTA (SEQ ID Nr. 74); hGAPDH-Primer 2: AGGAGTAAGACCCCTGGACCA (SEQ ID Nr. 75) being used for the calculation of the relative abundance of the respective mRNA species in the individual biopsies. Since a far greater amount of total
20 mRNA is isolatable from the skin biopsies of psoriasis patients, in particular from lesional skin, than from intact skin of healthy subjects, a standardization to identical amounts of mRNA is necessary, the amount of GAPDH mRNA being assumed as a housekeeping gene as a marker for the amount of total mRNA. A total
25 of 4 biopsies of intact skin of healthy subjects were analyzed, and also 8 biopsies in each case of lesional and non-lesional skin from psoriasis patients. The abundances of target gene cDNA in the individual groups (intact skin, lesional skin, non-lesional skin) were then standardized to the total amount of the abundances of the cDNAs measured on a microtiter plate. These analyses were carried out for
30 Eps8 (EMBL: U12535); KIAA1247 (GB: AB033073; WO 99/63088) and

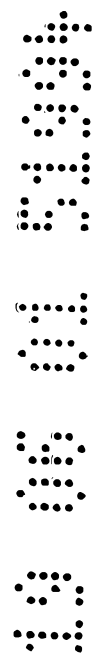
MASPIN (EMBL: U04313); the average values of the results are compiled in Table 9. It is clear that in both genes useable according to the invention a clear and statistically significant ($p < 0.05$, paired t-test) reduced regulation in lesional skin of 8 psoriasis patients is observed compared with non-pathological skin of the same patients in each case. This illustrates that a dysregulation of these genes can lead to skin diseases and that the genes useable according to the invention are therefore suitable for the prevention and/or treatment and/or diagnosis of skin diseases. In the case of psoriasis patients, the aim is to modulate, preferably to activate, the expression and/or activity of KIAA1247 and/or Eps8 and/or MASPIN. Modulation in the skin, in particular the lesional skin, of the psoriasis patients is preferred here.

As exemplified by KIAA1247, the relationship between dysregulation of the gene and psoriatic disease should now be demonstrated. Here, the conductivity of the skin (a measure of the moisture of the skin) was determined as a measurement parameter and compared with the KIAA1247 expression of the gene in this part of the skin. The conductivity of the skin was determined using a corneometer according to the instructions of the manufacturer (Courage and Khazaka Electronics). It was found here that a statistically significant positive correlation ($p = 0.000659$, Pearson Product Moment Correlation) is observed between conductivity of the biopsy investigated in each case and the KIAA1247 expression: in very dry biopsies of lesional psoriatic skin having a low conductivity, a correspondingly low KIAA1247 mRNA expression was measured, while in more moist skin, i.e. in non-pathogenic skin of the psoriatic patients and in intact skin of healthy subjects, a markedly stronger KIAA1247 expression is detectable. This verifies the relevance of KIAA1247 expression for the pathogenesis of skin diseases.

It will be apparent to those skilled in the art that various modifications and variations can be made to the compositions and processes of this invention. Thus, it is intended that the present invention cover such modifications and

variations, provided they come within the scope of the appended claims and their equivalents.

All publications cited herein are incorporated in their entireties by reference.



Page(s) 145-148 are claims pages
They appear after the table listings &
Sequence listing

Table 1

Genes differentially expressed	Intact skin	Wound	Intact skin	Wound
	control animals	control animals	dexamethasone	dexamethasone
TTF-1	1,00	0,81	1,00	1,31
CCR-1	1,00	31,84	0,45	76,74
MASPIN	1,00	0,76	1,00	1,03
B-Raf	1,00	0,77	0,77	0,71
Prothymosin alpha	1,00	0,97	0,91	1,90
Eps8	1,00	0,70	0,60	0,20
KIAA1247	1,00	0,30	0,90	0,20
Cystatin C	1,00	0,77	0,74	2,21
SW1136	1,00	0,83	0,58	1,43
SW1295	1,00	0,80	0,55	4,39
BAF57	1,00	0,98	0,93	0,54
EAT/MCL-1	1,00	1,99	0,79	2,55
Phospholipase Inhibitor	1,00	0,19	1,35	0,23
TSC-22	1,00	0,60	0,56	2,31
Split hand/foot deleted 1	1,00	1,89	0,98	10,53
Gamma Sarcoglycan	1,00	0,47	1,51	0,46
Nicotinamid N-Methyltransferase	1,00	0,93	1,00	2,15
Golgi 4-Transmembrane spanning transporter	1,00	0,57	0,28	2,00
UBC9	1,00	0,95	1,06	1,91
Cathepsin C	1,00	1,68	1,58	1,09
tsg101	1,00	0,94	1,03	2,06
DAD-1	1,00	1,07	0,93	1,93
HMG-14	1,00	0,61	0,43	2,11
TAK1	1,00	0,64	0,90	0,46
IL-5Ralpha	1,00	5,89	0,84	1,12
Fer	1,00	0,72	0,46	0,33

Genes differentially expressed	Intact skin	Wound	Intact skin	Wound
	young mice	young mice	old mice	old mice
TTF-1	1,87	0,78	0,84	0,65
CCR-1	1,07	22,22	0,84	24,18
MASPIN	2,00	0,39	1,18	0,45
B-Raf	1,29	0,63	0,61	0,70
Prothymosin alpha	1,36	0,67	0,78	0,48
Eps8	0,80	0,40	0,60	0,60
KIAA1247	2,20	0,70	1,00	0,20
Cystatin C	0,76	0,37	0,91	0,26
SW1136	1,05	0,33	0,44	0,26
SW1295	0,73	0,50	0,70	0,35
BAF57	1,82	0,54	0,70	0,92
EAT/MCL-1	2,67	1,79	1,42	1,12
Phospholipase Inhibitor	6,03	0,11	0,59	0,23
TSC-22	1,23	0,42	0,42	0,55
Split hand/foot deleted 1	1,48	0,94	0,83	0,55
Gamma Sarcoglycan	0,43	0,48	0,44	0,14
Nicotinamid N-Methyltransferase	1,14	0,86	0,92	0,78
Golgi 4-Transmembrane spanning transporter	0,53	0,26	0,27	0,11
UBC9	1,76	0,94	1,40	0,64
Cathepsin C	2,20	1,61	0,75	0,89
tsg101	1,80	0,92	0,96	0,48
DAD-1	1,32	1,04	0,87	0,61
HMG-14	1,03	0,40	0,50	0,20
TAK1	1,75	0,74	0,93	0,74
IL-5Ralpha	1,38	1,66	2,61	1,74
Fer	0,48	0,22	0,40	0,37

Table 2

Genes differentially expressed	Intact skin	Wound	Intact skin	Wound
	control animals	control animals	diabetic mice	diabetic mice
TTF-1	1,00	0,61	1,57	0,54
CCR-1	1,00	23,51	2,26	20,66
MASPIN	1,00	0,30	1,54	0,38
B-Raf	1,00	1,25	1,66	1,05
Prothymosin alpha	1,00	0,58	1,26	0,83
Eps8	1,00	2,50	0,70	1,40
KIAA1247	1,00	0,30	1,50	0,50
Cystatin C	1,00	0,49	1,35	0,57
SW1136	1,00	0,31	1,15	0,48
SW1295	1,00	0,39	1,00	0,65
BAF57	1,00	0,45	1,15	0,51
EAT/MCL-1	1,00	1,36	1,54	1,56
Phospholipase Inhibitor	1,00	0,31	1,14	0,28
TSC-22	1,00	0,43	1,70	0,60
Split hand/foot deleted 1	1,00	0,41	0,35	0,79
Gamma Sarcoglycan	1,00	0,04	0,33	0,08
Nicotinamid N-Methyltransferase	1,00	0,77	3,26	1,88
Golgi 4-Transmembrane spanning transporter	1,00	0,22	0,35	0,40
UBC9	1,00	0,63	1,66	0,63
Cathepsin C	1,00	0,89	0,58	0,34
tsg101	1,00	0,64	1,53	0,53
DAD-1	1,00	0,96	1,84	1,43
HMG-14	1,00	0,31	1,56	0,58
TAK1	1,00	0,35	1,30	0,46
Fer	1,00	0,27	1,35	0,31

19 06 01 51994

- 67 -

Table 3

No. NAME	PROTEIN- MOUSE*	Seq ID No.	PROTEIN- HUMAN*	Seq ID No.	CDNA-MOUSE*	CDNA-HUMAN*
1. SW1136	Seq ID Nr. 55	55	Seq ID Nr. 56	56	Seq ID Nr. 50	Seq ID Nr. 51
2. SW1295	Seq ID Nr. 57	57	trembl: Q9Y6H1	58	Seq ID Nr. 52	EMBL :AF078845

*: pir: PIR-databank

5 EMBL: EMBL-databank

trembl: translated EMBL-databank

Table 4

No.	NAME	PROTEIN- MOUSE*	Seq ID No.	PROTEIN- HUMAN*	Seq ID No.	CDNA-MOUSE*	CDNA-HUMAN*
3.	tumor susceptibility gene 101 (TSG101)	SP: Q61187	1	SP: Q99816	2	EMBL: U52945	EMBL: U82130
4.	MASPIN	SP: P70124	3	SP: P36952	4	EMBL: U54705	EMBL: U04313
5.	Transcription Termination Factor 1	SP: Q62187	5	SP: Q15361	6	EMBL: X83974	EMBL: X83973
6.	B-Raf	SP: P28028	7	SP : P15056	8	GB: M64429	GB: M95712
7.	Prothymosin alpha	SP: P26350	9	SP: P06454	10	GB: X56135	GB: M14630
8.	Golgi 4-transmembrane spanning transporter (MTP)	SP: Q60961	11	SP: Q15012	12	EMBL: U34259	EMBL: D14696
9.	CCR-1	SP: P51675	13	SP: P32246	14	EMBL: U29678	EMBL: L09230
10.	HMG-14	SP: P18608	15	SP: P05114	16	EMBL: X53476	EMBL: J02621
11.	Split hand/Foot deleted 1	GP: NP_033195	17	SP: Q13437	18	EMBL: U41626	EMBL: U41515
12.	TAK1	SP: P49117	19	SP: P49116	20	EMBL: U11688	EMBL: U10990
13.	BAF57	trembl:O54941	31	trembl: O43539	32	GB: AF035263	GB: AF035262
14.	EPS8	SP: Q08509	33	SP: Q12929	34	EMBL: L21671	EMBL: U12535
15.	KIAA1247	Seq ID Nr. 36	35	GP: BAA86561	36	Seq ID 53	GB: AB033073
16.	Phospholipase Inhibitor	Seq ID Nr. 38	37	US 5,948,626	38	Seq ID 54	US 5,948,626
17.	EAT/MCL-1	trembl: P97287	39	SP: Q07820	40	EMBL: U35623	EMBL: L08246
18.	TSC-22	SP: Q00992	41	SP: Q15714	42	EMBL: X62940	EMBL: U35048

19. Gamma-Sarcoglycan	trembl: P82348	43	trembl: Q13326	44	EMBL: AB024922	EMBL: U34976
20. Cystatin C	SP: P21460	46	SP: P01034	47	EMBL: M59470	EMBL: X05607
21. Fer	trembl: P70451	63	SP: P16591	64	EMBL: U76762	EMBL: J03358
22. MRP-3	SP: P27784	65	SP: P55773	66	EMBL: M58004	EMBL: U85767
23. NNMT	trembl: O55239	67	SP: P40261	68	EMBL: U86105	EMBL: U08021
24. UBC9	SP: P50550	69	SP: P50550	70	EMBL: X99739	EMBL: X96427

*: pir: PIR-databank

EMBL: EMBL-databank

trembl: translated EMBL-databank

GB: GeneBank nucleic acids

5 GP: GeneBank polypeptide

19 06 01 5:00

- 70 -

Table 5

No.	NAME	PROTEIN- MOUSE*	Seq ID No.	PROTEIN- HUMAN*	Seq ID No.	CDNA- MOUSE*	CDNA- HUMAN*
25.	MCP-3	SP: Q03366	21	SP: P80098	22	EMBL: X70058	EMBL: X71087
26.	IL-5Ralpha	SP: P21183	23	SP: Q01344	24	EMBL: D90205	EMBL: M96652
27.	DAD-1	SP: P46966	25	SP: P46966	26	EMBL: U22107	EMBL: D15057
29.	MCP-2	trembl: Q9Z121	29	SP: P80075	30	GB: AB023418	GB: X99886
30.	Cathepsin C	SP: P97821	72	SP: P53634	73	GB: U89269	GB: X87212

*: pir: PIR-databank

5 EMBL: EMBL-databank

GB: GeneBank nucleic acid

GP: GeneBank polypeptide

trembl: translated EMBL-databank

Table 6

Differentially expressed genes	Intakt skin	Wound 1 h	Wound 7 h	Wound 15 h	Wound 24 h	Wound 3 d	Wound 5 d	Wound 7 d	Wound 14 d
B-Raf	1,00	1,30	0,79	0,89	0,87	0,94	1,21	0,72	0,93
KIAA1247	1,00	0,67	0,53	0,30	0,31	0,44	0,67	1,11	0,97
Cystatin C	1,00	0,78	0,69	0,69	0,60	0,68	0,88	1,05	0,89
SW1136	1,00	0,48	0,36	0,15	0,15	0,23	0,31	0,33	0,20
SW1295	1,00	0,43	0,33	0,28	0,22	0,27	0,35	0,66	0,44
BAF57	1,00	0,76	0,57	0,54	0,42	0,67	0,93	1,19	0,94
EAT/MCL-1	1,00	0,58	0,81	1,08	0,75	0,85	1,16	0,66	0,66
Phospholipase Inhibitor	1,00	14,47	1,00	0,23	0,88	1,34	1,49	3,67	21,93
TSC-22	1,00	0,68	0,66	0,43	0,40	0,43	0,70	0,88	0,95
Split hand/foot deleted 1	1,00	0,57	0,40	0,42	0,43	0,53	0,67	0,62	0,66
Nicotinamide N-Methyl- transferase	1,00	0,36	0,60	0,46	0,43	0,71	0,43	0,80	0,62
Golgi 4- Transmem- brane span- ning trans- porter	1,00	0,67	0,69	0,34	0,26	0,33	0,46	0,50	0,48
UBC9	1,00	0,72	0,68	0,49	0,51	0,81	0,87	0,95	1,18
Cathepsin C	1,00	0,83	0,29	0,26	1,54	0,81	1,29	1,07	3,88
tsg101	1,00	0,71	0,51	0,45	0,33	0,62	0,53	0,66	0,83
DAD-1	1,00	0,84	0,76	0,74	0,84	1,07	1,10	1,36	1,18
HMG-14	1,00	0,55	0,31	0,29	0,33	0,46	0,49	0,45	0,62
TAK1	1,00	0,49	0,62	0,28	0,39	0,54	0,64	0,71	0,65
Fer	1,00	0,17	0,15	0,09	0,13	0,17	0,22	0,25	0,08
EPS8	1,00	0,60	1,10	1,00	0,70	0,70	1,00	0,70	0,90
CCR-1	1,00	1,40	5,90	19,00	17,00	16,00	13,00	5,50	3,70

MASPIN	1,00	0,60	0,50	0,30	0,30	0,30	0,40	0,50	0,80
TTF-1	1,00	0,80	0,60	0,50	0,40	0,50	0,60	0,60	0,90

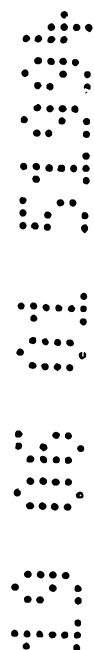


Table 7

cDNA expression in human biop- sies relative to Cyclophilin	Time after wounding				
	Intact skin	wound 1 h	wound 24 h	wound 5 d	wound 14 d
Eps8	1,00	1,41	0,74	1,3	1,29
KIAA1247	1,00	0,92	1,22	1,02	1,58
Phospholipase Inhibitor	1,00	1,24	0,64	0,57	0,85
Cystatin C	1,00	0,86	1,27	1,79	2,33
TSC-22	1,00	1,34	0,91	1,29	1,98
Golgi 4- Transmem- brane spanning transporter	1,00	0,69	0,63	0,59	0,72
Cathepsin C	1,00	0,86	2,96	4,09	2,67
HMG-14	1,00	1,87	0,56	0,98	0,87
Nicotinamide N-Methyltrans- ferase	1,00	1,74	6,20	9,74	5,15
UBC9	1,00	0,98	1,39	1,43	1,45
CCR-1	1,00	1,28	10,56	7,78	5,66
tsg101	1,00	1,09	1,07	1,24	1,27
MASPIN	1,00	1,62	0,38	1,11	0,61
TTF-1	1,00	0,55	0,95	0,74	1,45
B-Raf	1,00	1,82	0,89	1,45	1,30
DAD-1	1,00	0,66	1,47	1,61	1,46
Fer	1,00	8,07	0,83	3,35	5,06
Split hand/foot deleted 1	1,00	0,98	0,79	1,31	1,20
Gamma Sarcoglycan	1,00	1,13	0,29	0,67	0,89
TAK1	1,00	1,08	0,89	1,37	1,56

Table 8

Gen useable according to the invention	Intact skin of ulcer patients	wound edge of ulcer patients	wound ground of ulcer patients
Eps8	1,00	0,88	0,89
KIAA1247	1,00	0,38	1,1
Phospholipase Inhibitor (Variant SEQ ID Nr. 45)	1,00	0,54	0,48
Phospholipase Inhibitor (Variant SEQ ID Nr. 81)	1,00	1,54	1,18
Cystatin C	1,00	0,66	0,52
TSC-22	1,00	0,64	0,70
Golgi 4-Transmembrane spanning transporter	1,00	1,15	0,85
Cathepsin C	1,00	0,6	1,07
HMG-14	1,00	1,64	0,87
Nicotinamid N-Methyltransferase	1,00	2,28	1,49
UBC9	1,00	0,72	0,74
CCR-1	1,00	6,00	16,80
tsg101	1,00	0,54	0,50
MASPIN	1,00	0,29	0,04
TTF-1	1,00	0,40	0,60
B-Raf	1,00	0,76	0,31
DAD-1	1,00	0,97	0,65
Fer	1,00	0,80	0,26
Split hand/foot deleted 1	1,00	0,19	0,16
Gamma Sarcoglycan	1,00	0,10	0,05
TAK1	1,00	0,27	0,41

Table 9

Gen useable according to the invention	standardized relative amount		
	Intact healthy skin	Lesional skin of psoriasis patients	Non-lesional skin of psoriasis patients
KIAA1247	9,69E-02	6,23E-02	1,39E-01
Eps8	1,10E-01	5,36E-02	1,41E-01
MASPIN	7,55E-02	8,60E-02 1,26E-01	1,26E-01

SEQUENCE LISTING

<110> Switch Biotech AG

<120> Method of using polypeptides nucleic acids encoding said polypeptides, and/or of a cell expressing said polypeptide or said nucleic acid, for the diagnosis, prevention and/or treatment of skin diseases, of wound healing and/or its pathological disorders, and/or for the identification of pharmacologically active substances.

<150> DE 100 30 149.5-41

<151> 2000-06-20

<150> US 60/222,081

<151> 2000-08-01

<160> 84

<170> Word 6.0, PC-DOS/MS-DOS

<210> 1

<211> 391

<212> PRT

<213> Mus musculus

<220>

<223> TUMOR SUSCEPTIBILITY PROTEIN TSG101

<400> 1

Met	Ala	Val	Ser	Glu	Ser	Gln	Leu	Lys	9
Lys	Met	Met	Ser	Lys	Tyr	Lys	Tyr	Arg	18
Asp	Leu	Thr	Val	Arg	Gln	Thr	Val	Asn	27
Val	Ile	Ala	Met	Tyr	Lys	Asp	Leu	Lys	36
Pro	Val	Leu	Asp	Ser	Tyr	Val	Phe	Asn	45
Asp	Gly	Ser	Ser	Arg	Glu	Leu	Val	Asn	54
Leu	Thr	Gly	Thr	Ile	Pro	Val	Arg	Tyr	63
Arg	Gly	Asn	Ile	Tyr	Asn	Ile	Pro	Ile	72
Cys	Leu	Trp	Leu	Leu	Asp	Thr	Tyr	Pro	81
Tyr	Asn	Pro	Pro	Ile	Cys	Phe	Val	Lys	90
Pro	Thr	Ser	Ser	Met	Thr	Ile	Lys	Thr	99
Gly	Lys	His	Val	Asp	Ala	Asn	Gly	Lys	108
Ile	Tyr	Leu	Pro	Tyr	Leu	His	Asp	Trp	117
Lys	His	Pro	Arg	Ser	Glu	Leu	Leu	Glu	126
Leu	Ile	Gln	Ile	Met	Ile	Val	Ile	Phe	135
Gly	Glu	Glu	Pro	Pro	Val	Phe	Ser	Arg	144

Pro	Thr	Val	Ser	Ala	Ser	Tyr	Pro	Pro	153
Tyr	Thr	Ala	Thr	Gly	Pro	Pro	Asn	Thr	162
Ser	Tyr	Met	Pro	Gly	Met	Pro	Ser	Gly	171
Ile	Ser	Ala	Tyr	Pro	Ser	Gly	Tyr	Pro	180
Pro	Asn	Pro	Ser	Gly	Tyr	Pro	Gly	Cys	189
Pro	Tyr	Pro	Pro	Ala	Gly	Pro	Tyr	Pro	198
Ala	Thr	Thr	Ser	Ser	Gln	Tyr	Pro	Ser	207
Gln	Pro	Pro	Val	Thr	Thr	Val	Gly	Pro	216
Ser	Arg	Asp	Gly	Thr	Ile	Ser	Glu	Asp	225
Thr	Ile	Arg	Ala	Ser	Leu	Ile	Ser	Ala	234
Val	Ser	Asp	Lys	Leu	Arg	Trp	Arg	Met	243
Lys	Glu	Glu	Met	Asp	Gly	Ala	Gln	Ala	252
Glu	Leu	Asn	Ala	Leu	Lys	Arg	Thr	Glu	261
Glu	Asp	Leu	Lys	Lys	Gly	His	Gln	Lys	270
Leu	Glu	Glu	Met	Val	Thr	Arg	Leu	Asp	279
Gln	Glu	Val	Ala	Glu	Val	Asp	Lys	Asn	288
Ile	Glu	Leu	Leu	Lys	Lys	Lys	Asp	Glu	297
Glu	Leu	Ser	Ser	Ala	Leu	Glu	Lys	Met	306
Glu	Asn	Gln	Ser	Glu	Asn	Asn	Asp	Ile	315
Asp	Glu	Val	Ile	Ile	Pro	Thr	Ala	Pro	324
Leu	Tyr	Lys	Gln	Ile	Leu	Asn	Leu	Tyr	333
Ala	Glu	Glu	Asn	Ala	Ile	Glu	Asp	Thr	342
Ile	Phe	Tyr	Leu	Gly	Glu	Ala	Leu	Arg	351
Arg	Gly	Val	Ile	Asp	Leu	Asp	Val	Phe	360
Leu	Lys	His	Val	Arg	Leu	Leu	Ser	Arg	369
Lys	Gln	Phe	Gln	Leu	Arg	Ala	Leu	Met	378
Gln	Lys	Ala	Arg	Lys	Thr	Ala	Gly	Leu	387
Ser	Asp	Leu	Tyr						391

<210> 2

<211> 390

<212> PRT

<213> Homo sapiens

<220>

<223> TUMOR SUSCEPTIBILITY PROTEIN

<400> 2

Met	Ala	Val	Ser	Glu	Ser	Gln	Leu	Lys	9
Lys	Met	Val	Ser	Lys	Tyr	Lys	Tyr	Arg	18
Asp	Leu	Thr	Val	Arg	Glu	Thr	Val	Asn	27
Val	Ile	Thr	Leu	Tyr	Lys	Asp	Leu	Lys	36
Pro	Val	Leu	Asp	Ser	Tyr	Val	Phe	Asn	45
Asp	Gly	Ser	Ser	Arg	Glu	Leu	Met	Asn	54
Leu	Thr	Gly	Thr	Ile	Pro	Val	Pro	Tyr	63
Arg	Gly	Asn	Thr	Tyr	Asn	Ile	Pro	Ile	72
Cys	Leu	Trp	Leu	Leu	Asp	Thr	Tyr	Pro	81
Tyr	Asn	Pro	Pro	Ile	Cys	Phe	Val	Lys	90
Pro	Thr	Ser	Ser	Met	Thr	Ile	Lys	Thr	99
Gly	Lys	His	Val	Asp	Ala	Asn	Gly	Lys	108

Ile	Tyr	Leu	Pro	Tyr	Leu	His	Glu	Trp	117
Lys	His	Pro	Gln	Ser	Asp	Leu	Leu	Gly	126
Leu	Ile	Gln	Val	Met	Ile	Val	Val	Phe	135
Gly	Asp	Glu	Pro	Pro	Val	Phe	Ser	Arg	144
Pro	Ile	Ser	Ala	Ser	Tyr	Pro	Pro	Tyr	153
Gln	Ala	Thr	Gly	Pro	Pro	Asn	Thr	Ser	162
Tyr	Met	Pro	Gly	Met	Pro	Gly	Gly	Ile	171
Ser	Pro	Tyr	Pro	Ser	Gly	Tyr	Pro	Pro	180
Asn	Pro	Ser	Gly	Tyr	Pro	Gly	Cys	Pro	189
Tyr	Pro	Pro	Gly	Gly	Pro	Tyr	Pro	Ala	198
Thr	Thr	Ser	Ser	Gln	Tyr	Pro	Ser	Gln	207
Pro	Pro	Val	Thr	Thr	Val	Gly	Pro	Ser	216
Arg	Asp	Gly	Thr	Ile	Ser	Glu	Asp	Thr	225
Ile	Arg	Ala	Ser	Leu	Ile	Ser	Ala	Val	234
Ser	Asp	Lys	Leu	Arg	Trp	Arg	Met	Lys	243
Glu	Glu	Met	Asp	Arg	Ala	Gln	Ala	Glu	252
Leu	Asn	Ala	Leu	Lys	Arg	Thr	Glu	Glu	261
Asp	Leu	Lys	Lys	Gly	His	Gln	Lys	Leu	270
Glu	Glu	Met	Val	Thr	Arg	Leu	Asp	Gln	279
Glu	Val	Ala	Glu	Val	Asp	Lys	Asn	Ile	288
Glu	Leu	Leu	Lys	Lys	Lys	Asp	Glu	Glu	297
Leu	Ser	Ser	Ala	Leu	Glu	Lys	Met	Glu	306
Asn	Gln	Ser	Glu	Asn	Asn	Asp	Ile	Asp	315
Glu	Val	Ile	Ile	Pro	Thr	Ala	Pro	Leu	324
Tyr	Lys	Gln	Ile	Leu	Asn	Leu	Tyr	Ala	333
Glu	Glu	Asn	Ala	Ile	Glu	Asp	Thr	Ile	342
Phe	Tyr	Leu	Gly	Glu	Ala	Leu	Arg	Arg	351
Gly	Val	Ile	Asp	Leu	Asp	Val	Phe	Leu	360
Lys	His	Val	Arg	Leu	Leu	Ser	Arg	Lys	369
Gln	Phe	Gln	Leu	Arg	Ala	Leu	Met	Gln	378
Lys	Ala	Arg	Lys	Thr	Ala	Gly	Leu	Ser	387
Asp	Leu	Tyr	390						

<210> 3

<211> 375

<212> PRT

<213> Mus musculus

<220>

<223> MASPIN PRECURSOR

<400> 3

Met	Asp	Ala	Leu	Arg	Leu	Ala	Asn	Ser	9
Ala	Phe	Ala	Val	Asp	Leu	Phe	Lys	Gln	18
Leu	Cys	Glu	Arg	Asp	Pro	Ala	Gly	Asn	27
Ile	Leu	Phe	Ser	Pro	Ile	Cys	Leu	Ser	36
Thr	Ser	Leu	Ser	Leu	Ala	Gln	Val	Gly	45
Thr	Lys	Gly	Asp	Thr	Ala	Asn	Glu	Ile	54
Gly	Gln	Val	Leu	His	Phe	Glu	Asn	Val	63

Lys	Asp	Val	Pro	Phe	Gly	Phe	Gln	Thr	72
Val	Thr	Ser	Asp	Val	Asn	Lys	Leu	Ser	81
Ser	Phe	Tyr	Ser	Leu	Lys	Leu	Val	Lys	90
Arg	Leu	Tyr	Ile	Asp	Lys	Ser	Leu	Asn	99
Pro	Ser	Thr	Glu	Phe	Ile	Ser	Ser	Thr	108
Lys	Arg	Pro	Tyr	Ala	Lys	Glu	Leu	Glu	117
Thr	Val	Asp	Phe	Lys	Asp	Lys	Leu	Glu	126
Glu	Thr	Lys	Gly	Gln	Ile	Asn	Ser	Ser	135
Ile	Lys	Glu	Leu	Thr	Asp	Gly	His	Phe	144
Glu	Asp	Ile	Leu	Ser	Glu	Asn	Ser	Ile	153
Ser	Asp	Gln	Thr	Lys	Ile	Leu	Val	Val	162
Asn	Ala	Ala	Tyr	Phe	Val	Gly	Lys	Trp	171
Met	Lys	Lys	Phe	Pro	Glu	Ser	Glu	Thr	180
Lys	Glu	Cys	Pro	Phe	Arg	Ile	Ser	Lys	189
Thr	Asp	Thr	Lys	Pro	Val	Gln	Met	Met	198
Asn	Leu	Glu	Ala	Thr	Phe	Cys	Leu	Gly	207
Asn	Ile	Asp	Asp	Ile	Ser	Cys	Lys	Ile	216
Ile	Glu	Leu	Pro	Phe	Gln	Asn	Lys	His	225
Leu	Ser	Met	Leu	Ile	Val	Leu	Pro	Lys	234
Asp	Val	Glu	Asp	Glu	Ser	Thr	Gly	Leu	243
Glu	Lys	Ile	Glu	Gln	Gln	Leu	Asn	Pro	252
Glu	Thr	Leu	Leu	Gln	Trp	Thr	Asn	Pro	261
Ser	Thr	Met	Ala	Asn	Ala	Lys	Val	Lys	270
Leu	Ser	Leu	Pro	Lys	Phe	Lys	Val	Glu	279
Lys	Met	Ile	Asp	Pro	Lys	Ala	Ser	Leu	288
Glu	Ser	Leu	Gly	Leu	Lys	Ser	Leu	Phe	297
Asn	Glu	Ser	Thr	Ser	Asp	Phe	Ser	Gly	306
Met	Ser	Glu	Thr	Lys	Gly	Val	Ser	Leu	315
Ser	Asn	Val	Ile	His	Arg	Val	Cys	Leu	324
Glu	Ile	Thr	Glu	Asp	Gly	Gly	Glu	Ser	333
Ile	Glu	Val	Pro	Gly	Ser	Arg	Ile	Leu	342
Gln	His	Lys	Asp	Glu	Phe	Asn	Ala	Asp	351
His	Pro	Phe	Ile	Tyr	Ile	Ile	Arg	His	360
Asn	Lys	Thr	Arg	Asn	Ile	Ile	Phe	Phe	369
Gly	Lys	Phe	Cys	Ser	Pro				375

<210> 4

<211> 375

<212> PRT

<213> Homo sapiens

<220>

<223> MASPIN PRECURSOR

<400> 4

Met	Asp	Ala	Leu	Gln	Leu	Ala	Asn	Ser	9
Ala	Phe	Ala	Val	Asp	Leu	Phe	Lys	Gln	18
Leu	Cys	Glu	Lys	Glu	Pro	Leu	Gly	Asn	27
Val	Leu	Phe	Ser	Pro	Ile	Cys	Leu	Ser	36

Thr	Ser	Leu	Ser	Leu	Ala	Gln	Val	Gly	45
Ala	Lys	Gly	Asp	Thr	Ala	Asn	Glu	Ile	54
Gly	Gln	Val	Leu	His	Phe	Glu	Asn	Val	63
Lys	Asp	Ile	Pro	Phe	Gly	Phe	Gln	Thr	72
Val	Thr	Ser	Asp	Val	Asn	Lys	Leu	Ser	81
Ser	Phe	Tyr	Ser	Leu	Lys	Leu	Ile	Lys	90
Arg	Leu	Tyr	Val	Asp	Lys	Ser	Leu	Asn	99
Leu	Ser	Thr	Glu	Phe	Ile	Ser	Ser	Thr	108
Lys	Arg	Pro	Tyr	Ala	Lys	Glu	Leu	Glu	117
Thr	Val	Asp	Phe	Lys	Asp	Lys	Leu	Glu	126
Glu	Thr	Lys	Gly	Gln	Ile	Asn	Asn	Ser	135
Ile	Lys	Asp	Leu	Thr	Asp	Gly	His	Phe	144
Glu	Asn	Ile	Leu	Ala	Asp	Asn	Ser	Val	153
Asn	Asp	Gln	Thr	Lys	Ile	Leu	Val	Val	162
Asn	Ala	Ala	Tyr	Phe	Val	Gly	Lys	Trp	171
Met	Lys	Lys	Phe	Pro	Glu	Ser	Glu	Thr	180
Lys	Glu	Cys	Pro	Phe	Arg	Leu	Asn	Lys	189
Thr	Asp	Thr	Lys	Pro	Val	Gln	Met	Met	198
Asn	Met	Glu	Ala	Thr	Phe	Cys	Met	Gly	207
Asn	Ile	Asp	Ser	Ile	Asn	Cys	Lys	Ile	216
Ile	Glu	Leu	Pro	Phe	Gln	Asn	Lys	His	225
Leu	Ser	Met	Phe	Ile	Leu	Leu	Pro	Lys	234
Asp	Val	Glu	Asp	Glu	Ser	Thr	Gly	Leu	243
Glu	Lys	Ile	Glu	Lys	Gln	Leu	Asn	Ser	252
Glu	Ser	Leu	Ser	Gln	Trp	Thr	Asn	Pro	261
Ser	Thr	Met	Ala	Asn	Ala	Lys	Val	Lys	270
Leu	Ser	Ile	Pro	Lys	Phe	Lys	Val	Glu	279
Lys	Met	Ile	Asp	Pro	Lys	Ala	Cys	Leu	288
Glu	Asn	Leu	Gly	Leu	Lys	His	Ile	Phe	297
Ser	Glu	Asp	Thr	Ser	Asp	Phe	Ser	Gly	306
Met	Ser	Glu	Thr	Lys	Gly	Val	Ala	Leu	315
Ser	Asn	Val	Ile	His	Lys	Val	Cys	Leu	324
Glu	Ile	Thr	Glu	Asp	Gly	Gly	Asp	Ser	333
Ile	Glu	Val	Pro	Gly	Ala	Arg	Ile	Leu	342
Gln	His	Lys	Asp	Glu	Leu	Asn	Ala	Asp	351
His	Pro	Phe	Ile	Tyr	Ile	Ile	Arg	His	360
Asn	Lys	Thr	Arg	Asn	Ile	Ile	Phe	Phe	369
Gly	Lys	Phe	Cys	Ser	Pro	375			

<210> 5

<211> 833

<212> PRT

<213> Mus musculus

<220>

<223> TRANSCRIPTION TERMINATION FACTOR 1

<400> 5

Met	Lys	Gly	Gly	Thr	Ser	Lys	Phe	Lys	9
Thr	His	Thr	Glu	Thr	Leu	Tyr	Lys	Lys	18

Lys	Lys	Trp	Ser	Ser	Val	Ser	Glu	Lys	27
Arg	Pro	Gln	Lys	Cys	Pro	Ser	Gln	Cys	36
Leu	Glu	Ser	Lys	Gln	Pro	Gln	Val	Ser	45
Val	Leu	Gly	Lys	Arg	Arg	Arg	Ala	Ser	54
Gln	Thr	Pro	Ala	Gln	Glu	Thr	Leu	Glu	63
Ser	Glu	Trp	Pro	Gln	Lys	Ala	Lys	Lys	72
Lys	Lys	Arg	Arg	Gly	Glu	Pro	Gln	Thr	81
Pro	Thr	Gln	Glu	Ser	Leu	Glu	Ser	Glu	90
Gln	Pro	Pro	Val	Ser	Leu	Leu	Gly	Lys	99
Arg	Arg	Arg	Glu	Ser	Gln	Thr	Pro	Ala	108
Gln	Glu	Asn	Ser	Glu	Ser	Glu	Gln	Pro	117
Arg	Lys	Ala	Lys	Arg	Arg	Arg	Lys	Lys	126
Arg	Lys	Gly	Ser	Gln	Gln	Pro	Thr	Ser	135
Ser	Leu	Leu	Lys	Thr	Pro	Glu	Thr	Phe	144
Leu	Lys	Ala	Lys	Lys	Thr	Thr	Ser	Ala	153
His	Lys	Lys	Lys	Lys	Asn	Ser	Val	Leu	162
Glu	Val	Asp	Met	Glu	Thr	Gly	Ile	Ile	171
Leu	Val	Asp	Lys	Glu	Asn	Met	Glu	Asn	180
Leu	Leu	Glu	Thr	Ser	Arg	Lys	Asp	Val	189
Asp	Ile	Val	Tyr	Val	Asp	Met	Ser	Lys	198
Gly	Gln	Arg	Ser	Ala	Lys	Val	Arg	Glu	207
Thr	Gly	Glu	Leu	Pro	Ala	Ala	Lys	Pro	216
Gln	Glu	His	Gly	Cys	Arg	Glu	Leu	Leu	225
Gly	Asp	Val	Arg	Ser	Arg	Lys	Lys	Gln	234
Lys	His	Leu	Gln	Lys	Val	Ala	Pro	Trp	243
Asp	Val	Val	Gln	Gly	Ser	Gln	Pro	Glu	252
Ser	Ile	Ser	Leu	Pro	Pro	Ser	Glu	Pro	261
Leu	Ser	Ser	Glu	Asp	Leu	Glu	Gly	Lys	270
Ser	Thr	Glu	Ala	Ala	Val	Phe	Cys	Lys	279
Arg	Ser	Leu	Lys	Lys	Asn	Val	Phe	Arg	288
Ser	Gln	Glu	Leu	Glu	Pro	Ile	Pro	Asp	297
Ser	Leu	Asp	Asp	Ser	Glu	Thr	Ile	Ser	306
Glu	Arg	Leu	Asp	Ser	Thr	His	His	Gly	315
Gly	Ala	Val	Gly	Ala	Gly	Glu	Cys	Glu	324
Ser	Thr	Lys	Glu	Ser	His	Ser	Ile	Lys	333
Lys	Lys	Ser	Lys	Lys	Lys	Lys	His	Lys	342
Ser	Val	Ala	Leu	Ala	Thr	Ser	Ser	Asp	351
Ser	Ala	Ser	Val	Thr	Asp	Ser	Lys	Ala	360
Lys	Asn	Ala	Leu	Val	Asp	Ser	Ser	Glu	369
Gly	Ser	Gly	Ala	Val	Arg	Glu	Glu	Asp	378
Val	Asp	His	Arg	Pro	Ala	Glu	Ala	Glu	387
Ala	Gln	Ala	Cys	Ser	Thr	Glu	Lys	His	396
Arg	Glu	Ala	Met	Gln	Arg	Leu	Glu	Pro	405
Thr	His	Glu	Glu	Glu	Ser	Asn	Ser	Glu	414
Ser	Ala	Ser	Asn	Ser	Ala	Ala	Arg	His	423
Ile	Ser	Glu	Asp	Arg	Arg	Glu	Ser	Asp	432
Asp	Ser	Asp	Val	Asp	Leu	Gly	Ser	Ala	441
Val	Arg	Gln	Leu	Arg	Glu	Phe	Ile	Pro	450
Asp	Ile	Gln	Glu	Arg	Ala	Ala	Thr	Thr	459
Ile	Arg	Arg	Met	Tyr	Arg	Asp	Asp	Leu	468
Gly	Leu	Phe	Lys	Glu	Phe	Lys	Ala	Gln	477
Gly	Val	Ala	Ile	Arg	Phe	Gly	Lys	Phe	486

Ser	Ala	Lys	Glu	Asn	Lys	Gln	Ile	Glu	495
Lys	Asn	Val	Gln	Asp	Phe	Leu	Ser	Leu	504
Thr	Gly	Ile	Glu	Ser	Ala	Asp	Lys	Leu	513
Leu	Tyr	Thr	Asp	Arg	Tyr	Pro	Glu	Glu	522
Lys	Thr	Leu	Ile	Thr	Asn	Leu	Lys	Arg	531
Lys	His	Ala	Phe	Arg	Leu	His	Ile	Gly	540
Lys	Gly	Ile	Ala	Arg	Pro	Trp	Lys	Leu	549
Val	Tyr	Tyr	Arg	Ala	Lys	Lys	Ile	Phe	558
Asp	Val	Asn	Asn	Tyr	Lys	Gly	Arg	Tyr	567
Asn	Glu	Glu	Asp	Thr	Lys	Lys	Leu	Lys	576
Ala	Tyr	His	Ser	Leu	His	Gly	Asn	Asp	585
Trp	Lys	Lys	Ile	Gly	Ala	Met	Val	Ala	594
Arg	Ser	Ser	Leu	Ser	Val	Ala	Leu	Lys	603
Phe	Ser	Gln	Ile	Gly	Gly	Thr	Arg	Asn	612
Gln	Gly	Ala	Trp	Ser	Lys	Ala	Glu	Thr	621
Gln	Arg	Leu	Ile	Lys	Ala	Val	Glu	Asp	630
Val	Ile	Leu	Lys	Lys	Met	Ser	Pro	Gln	639
Glu	Leu	Arg	Glu	Leu	Asp	Ser	Lys	Leu	648
Gln	Glu	Asp	Pro	Glu	Gly	Arg	Leu	Ser	657
Ile	Val	Arg	Glu	Lys	Leu	Tyr	Lys	Gly	666
Ile	Ser	Trp	Val	Glu	Val	Glu	Ala	Arg	675
Val	Glu	Thr	Arg	Asn	Trp	Met	Gln	Cys	684
Lys	Ser	Lys	Trp	Thr	Glu	Ile	Leu	Thr	693
Lys	Arg	Met	Thr	His	Gly	Gly	Phe	Val	702
Tyr	Arg	Gly	Val	Asn	Ala	Leu	Gln	Ala	711
Lys	Ile	Thr	Leu	Ile	Glu	Arg	Leu	Tyr	720
Glu	Leu	Asn	Val	Asn	Asp	Ala	Asn	Glu	729
Ile	Asp	Trp	Glu	Asp	Leu	Cys	Ser	Ala	738
Ile	Gly	Asp	Val	Pro	Pro	Pro	Phe	Val	747
Gln	Ala	Lys	Phe	Tyr	Lys	Leu	Lys	Ala	756
Ala	Cys	Val	Pro	Phe	Trp	Gln	Lys	Lys	765
Thr	Phe	Pro	Glu	Ile	Ile	Asp	Tyr	Leu	774
Tyr	Lys	Asn	Ser	Leu	Pro	Leu	Leu	Lys	783
Glu	Lys	Leu	Asp	Lys	Lys	Met	Lys	Lys	792
Lys	Asp	Gly	Gln	Ile	Gln	Thr	Pro	Ala	801
Ala	Pro	Lys	Gln	Asp	Phe	Leu	Phe	Lys	810
Asp	Ile	Phe	His	Cys	Asp	Asp	Asp	Ser	819
Asp	Glu	Gly	Ser	Pro	Glu	Glu	Pro	Ser	828
Ala	Ser	Asp	Val	Gln	833				

<210> 6

<211> 886

<212> PRT

<213> Homo sapiens

<220>

<223> TRANSCRIPTION TERMINATION FACTOR 1

<400> 6

Met	Glu	Gly	Glu	Ser	Ser	Arg	Phe	Glu	9
Ile	His	Thr	Pro	Val	Ser	Asp	Lys	Lys	18
Lys	Lys	Lys	Cys	Ser	Ile	His	Lys	Glu	27
Arg	Pro	Gln	Lys	His	Ser	His	Glu	Ile	36
Phe	Arg	Asp	Ser	Ser	Leu	Val	Asn	Glu	45
Gln	Ser	Gln	Ile	Thr	Arg	Arg	Lys	Lys	54
Arg	Lys	Lys	Asp	Phe	Gln	His	Leu	Ile	63
Ser	Ser	Pro	Leu	Lys	Lys	Ser	Arg	Ile	72
Cys	Asp	Glu	Thr	Ala	Asn	Ala	Thr	Ser	81
Thr	Leu	Lys	Lys	Arg	Lys	Lys	Arg	Arg	90
Tyr	Ser	Ala	Leu	Glu	Val	Asp	Glu	Glu	99
Ala	Gly	Val	Thr	Val	Val	Leu	Val	Asp	108
Lys	Glu	Asn	Ile	Asn	Asn	Thr	Pro	Lys	117
His	Phe	Arg	Lys	Asp	Val	Asp	Val	Val	126
Cys	Val	Asp	Met	Ser	Ile	Glu	Gln	Lys	135
Leu	Pro	Arg	Lys	Pro	Lys	Thr	Asp	Lys	144
Phe	Gln	Val	Leu	Ala	Lys	Ser	His	Ala	153
His	Lys	Ser	Glu	Ala	Leu	His	Ser	Lys	162
Val	Arg	Glu	Lys	Lys	Asn	Lys	Lys	His	171
Gln	Arg	Lys	Ala	Ala	Ser	Trp	Glu	Ser	180
Gln	Arg	Ala	Arg	Asp	Thr	Leu	Pro	Gln	189
Ser	Glu	Ser	His	Gln	Glu	Glu	Ser	Trp	198
Leu	Ser	Val	Gly	Pro	Gly	Gly	Glu	Ile	207
Thr	Glu	Leu	Pro	Ala	Ser	Ala	His	Lys	216
Asn	Lys	Ser	Lys	Lys	Lys	Lys	Lys	Lys	225
Ser	Ser	Asn	Arg	Glu	Tyr	Glu	Thr	Leu	234
Ala	Met	Pro	Glu	Gly	Ser	Gln	Ala	Gly	243
Arg	Glu	Ala	Gly	Thr	Asp	Met	Gln	Glu	252
Ser	Gln	Pro	Thr	Val	Gly	Leu	Asp	Asp	261
Glu	Thr	Pro	Gln	Leu	Leu	Gly	Pro	Thr	270
His	Lys	Lys	Lys	Ser	Lys	Lys	Lys	Lys	279
Lys	Lys	Lys	Ser	Asn	His	Gln	Glu	Phe	288
Glu	Ala	Leu	Ala	Met	Pro	Glu	Gly	Ser	297
Gln	Val	Gly	Ser	Glu	Val	Gly	Ala	Asp	306
Met	Gln	Glu	Ser	Arg	Pro	Ala	Val	Gly	315
Leu	His	Gly	Glu	Thr	Ala	Gly	Ile	Pro	324
Ala	Pro	Ala	Tyr	Lys	Asn	Lys	Ser	Lys	333
Lys	Lys	Lys	Lys	Lys	Ser	Asn	His	Gln	342
Glu	Phe	Glu	Ala	Val	Ala	Met	Pro	Glu	351
Ser	Leu	Glu	Ser	Ala	Tyr	Pro	Glu	Gly	360
Ser	Gln	Val	Gly	Ser	Glu	Val	Gly	Thr	369
Val	Glu	Gly	Ser	Thr	Ala	Leu	Lys	Gly	378
Phe	Lys	Glu	Ser	Asn	Ser	Thr	Lys	Lys	387
Lys	Ser	Lys	Lys	Arg	Lys	Leu	Thr	Ser	396
Val	Lys	Arg	Ala	Arg	Val	Ser	Gly	Asp	405
Asp	Phe	Ser	Val	Pro	Ser	Lys	Asn	Ser	414
Glu	Ser	Thr	Leu	Phe	Asp	Ser	Val	Glu	423
Gly	Asp	Gly	Ala	Met	Met	Glu	Glu	Gly	432
Val	Lys	Ser	Arg	Pro	Arg	Gln	Lys	Lys	441
Thr	Gln	Ala	Cys	Leu	Ala	Ser	Lys	His	450
Val	Gln	Glu	Ala	Pro	Arg	Leu	Glu	Pro	459
Ala	Asn	Glu	Glu	His	Asn	Val	Glu	Thr	468

Ala	Glu	Asp	Ser	Glu	Ile	Arg	Tyr	Leu	477
Ser	Ala	Asp	Ser	Gly	Asp	Ala	Asp	Asp	486
Ser	Asp	Ala	Asp	Leu	Gly	Ser	Ala	Val	495
Lys	Gln	Leu	Gln	Glu	Phe	Ile	Pro	Asn	504
Ile	Lys	Asp	Arg	Ala	Thr	Ser	Thr	Ile	513
Lys	Arg	Met	Tyr	Arg	Asp	Asp	Leu	Glu	522
Arg	Phe	Lys	Glu	Phe	Lys	Ala	Gln	Gly	531
Val	Ala	Ile	Lys	Phe	Gly	Lys	Phe	Ser	540
Val	Lys	Glu	Asn	Lys	Gln	Leu	Glu	Lys	549
Asn	Val	Glu	Asp	Phe	Leu	Ala	Leu	Thr	558
Gly	Ile	Glu	Ser	Ala	Asp	Lys	Leu	Leu	567
Tyr	Thr	Asp	Arg	Tyr	Pro	Glu	Glu	Lys	576
Ser	Val	Ile	Thr	Asn	Leu	Lys	Arg	Arg	585
Tyr	Ser	Phe	Arg	Leu	His	Ile	Gly	Arg	594
Asn	Ile	Ala	Arg	Pro	Trp	Lys	Leu	Ile	603
Tyr	Tyr	Arg	Ala	Lys	Lys	Met	Phe	Asp	612
Val	Asn	Asn	Tyr	Lys	Gly	Arg	Tyr	Ser	621
Glu	Gly	Asp	Thr	Glu	Lys	Leu	Lys	Met	630
Tyr	His	Ser	Leu	Leu	Gly	Asn	Asp	Trp	639
Lys	Thr	Ile	Gly	Glu	Met	Val	Ala	Arg	648
Arg	Ser	Leu	Ser	Val	Ala	Leu	Lys	Phe	657
Ser	Gln	Ile	Ser	Ser	Gln	Arg	Asn	Arg	666
Gly	Ala	Trp	Ser	Lys	Ser	Glu	Thr	Arg	675
Lys	Leu	Ile	Lys	Ala	Val	Glu	Glu	Val	684
Ile	Leu	Lys	Lys	Met	Ser	Pro	Gln	Glu	693
Leu	Lys	Glu	Val	Asp	Ser	Lys	Leu	Gln	702
Glu	Asn	Pro	Glu	Ser	Cys	Leu	Ser	Ile	711
Val	Arg	Glu	Lys	Leu	Tyr	Lys	Gly	Ile	720
Ser	Trp	Val	Glu	Val	Glu	Ala	Lys	Val	729
Gln	Thr	Arg	Asn	Trp	Met	Gln	Cys	Lys	738
Ser	Lys	Trp	Thr	Glu	Ile	Leu	Thr	Lys	747
Arg	Met	Thr	Asn	Gly	Arg	Arg	Ile	Tyr	756
Tyr	Gly	Met	Asn	Ala	Leu	Arg	Ala	Lys	765
Val	Ser	Leu	Ile	Glu	Arg	Leu	Tyr	Glu	774
Ile	Asn	Val	Glu	Asp	Thr	Asn	Glu	Ile	783
Asp	Trp	Glu	Asp	Leu	Ala	Ser	Ala	Ile	792
Gly	Asp	Val	Pro	Pro	Ser	Tyr	Val	Gln	801
Thr	Lys	Phe	Ser	Arg	Leu	Lys	Ala	Val	810
Tyr	Val	Pro	Phe	Trp	Gln	Lys	Lys	Thr	819
Phe	Pro	Glu	Ile	Ile	Asp	Tyr	Leu	Tyr	828
Glu	Thr	Thr	Leu	Pro	Leu	Leu	Lys	Glu	837
Lys	Leu	Glu	Lys	Met	Met	Glu	Lys	Lys	846
Gly	Thr	Lys	Ile	Gln	Thr	Pro	Ala	Ala	855
Pro	Lys	Gln	Val	Phe	Pro	Phe	Arg	Asp	864
Ile	Phe	Tyr	Tyr	Glu	Asp	Asp	Ser	Glu	873
Gly	Gly	Gly	His	Arg	Lys	Arg	Lys	Arg	882
Arg	Gly	Ile	Pro		886				

<210> 7

<211> 659

<212> PRT

<213> Mus musculus

<220>

<223> b-raf

<400> 7

Met	Glu	Gly	Gly	Cys	Gly	Glu	Gly	Gly	9
Gly	Gly	Thr	Gly	Ser	Gly	Arg	Ser	Ala	18
Ala	Ala	Ala	Arg	Arg	Ala	Gly	Arg	Met	27
Arg	Pro	Arg	Ala	Gln	Gly	Pro	Asp	Ser	36
Glu	Ser	Gly	Gly	Glu	Ala	Ser	Arg	Leu	45
Asn	Leu	Leu	Asp	Thr	Cys	Ala	Val	Cys	54
His	Gln	Asn	Ile	Gln	Ser	Arg	Val	Pro	63
Lys	Leu	Leu	Pro	Cys	Leu	His	Ser	Phe	72
Cys	Gln	Arg	Cys	Leu	Pro	Ala	Pro	Gln	81
Arg	Tyr	Leu	Met	Leu	Thr	Ala	Pro	Ala	90
Leu	Gly	Ser	Ala	Glu	Thr	Pro	Pro	Pro	99
Ala	Pro	Ala	Pro	Ala	Pro	Ala	Pro	Gly	108
Ser	Pro	Ala	Gly	Gly	Pro	Ser	Pro	Phe	117
Ala	Thr	Gln	Val	Gly	Val	Ile	Arg	Cys	126
Pro	Val	Cys	Ser	Gln	Glu	Cys	Ala	Glu	135
Arg	His	Ile	Ile	Asp	Asn	Phe	Phe	Val	144
Lys	Asp	Thr	Thr	Glu	Val	Pro	Ser	Ser	153
Thr	Val	Glu	Lys	Ser	Asn	Gln	Val	Cys	162
Thr	Ser	Cys	Glu	Asp	Asn	Ala	Glu	Ala	171
Asn	Gly	Phe	Cys	Val	Glu	Cys	Val	Glu	180
Trp	Leu	Cys	Lys	Thr	Cys	Ile	Arg	Ala	189
His	Gln	Arg	Val	Lys	Phe	Thr	Lys	Asp	198
His	Thr	Val	Arg	Gln	Lys	Glu	Glu	Val	207
Ser	Pro	Glu	Ala	Val	Gly	Val	Thr	Ser	216
Gln	Arg	Pro	Val	Phe	Cys	Pro	Phe	His	225
Lys	Lys	Glu	Gln	Leu	Lys	Leu	Tyr	Cys	234
Glu	Thr	Cys	Asp	Lys	Leu	Thr	Cys	Arg	243
Asp	Cys	Gln	Leu	Leu	Glu	His	Lys	Glu	252
His	Arg	Tyr	Gln	Phe	Ile	Glu	Glu	Ala	261
Phe	Gln	Asn	Gln	Lys	Val	Ile	Ile	Asp	270
Thr	Leu	Ile	Thr	Lys	Leu	Met	Glu	Lys	279
Thr	Lys	Tyr	Ile	Lys	Tyr	Thr	Gly	Asn	288
Gln	Ile	Gln	Asn	Arg	Ile	Ile	Glu	Ile	297
Asn	Gln	Asn	Gln	Lys	Gln	Val	Glu	Gln	306
Asp	Ile	Lys	Val	Ala	Ile	Phe	Thr	Leu	315
Met	Val	Glu	Ile	Asn	Lys	Lys	Gly	Lys	324
Ala	Leu	Leu	His	Gln	Leu	Glu	Lys	Thr	333
Leu	Gly	Arg	Arg	Asp	Ser	Ser	Asp	Asp	342
Trp	Glu	Ile	Pro	Asp	Gly	Gln	Ile	Thr	351
Val	Gly	Gln	Arg	Ile	Gly	Ser	Gly	Ser	360
Phe	Gly	Thr	Val	Tyr	Lys	Gly	Lys	Trp	369
His	Gly	Asp	Val	Ala	Val	Lys	Met	Leu	378
Asn	Val	Thr	Ala	Pro	Thr	Pro	Gln	Gln	387
Leu	Gln	Ala	Phe	Lys	Asn	Glu	Val	Gly	396
Val	Leu	Arg	Lys	Thr	Arg	His	Val	Asn	405

Ile	Leu	Leu	Phe	Met	Gly	Tyr	Ser	Thr	414
Lys	Pro	Gln	Leu	Ala	Ile	Val	Thr	Gln	423
Trp	Cys	Glu	Gly	Ser	Ser	Leu	Tyr	His	432
His	Leu	His	Ile	Ile	Glu	Thr	Lys	Phe	441
Glu	Met	Ile	Lys	Leu	Ile	Asp	Ile	Ala	450
Arg	Gln	Thr	Ala	Gln	Gly	Met	Asp	Tyr	459
Leu	His	Ala	Lys	Ser	Ile	Ile	His	Arg	468
Asp	Leu	Lys	Ser	Asn	Asn	Ile	Phe	Leu	477
His	Glu	Asp	Leu	Thr	Val	Lys	Ile	Gly	486
Asp	Phe	Gly	Leu	Ala	Thr	Val	Lys	Ser	495
Arg	Trp	Ser	Gly	Ser	His	Gln	Phe	Glu	504
Gln	Leu	Ser	Gly	Ser	Ile	Leu	Trp	Met	513
Ala	Pro	Glu	Val	Ile	Arg	Met	Gln	Asp	522
Lys	Asn	Pro	Tyr	Ser	Phe	Gln	Ser	Asp	531
Val	Tyr	Ala	Phe	Gly	Ile	Val	Leu	Tyr	540
Glu	Leu	Met	Thr	Gly	Gln	Leu	Pro	Tyr	549
Ser	Asn	Ile	Asn	Asn	Arg	Asp	Gln	Ile	558
Ile	Phe	Met	Val	Gly	Arg	Gly	Tyr	Leu	567
Ser	Pro	Asp	Leu	Ser	Lys	Val	Arg	Ser	576
Asn	Cys	Pro	Lys	Ala	Met	Lys	Arg	Leu	585
Met	Ala	Glu	Cys	Leu	Lys	Lys	Lys	Arg	594
Asp	Glu	Arg	Pro	Leu	Phe	Pro	Gln	Ile	603
Leu	Ala	Ser	Ile	Glu	Leu	Leu	Ala	Arg	612
Ser	Leu	Pro	Lys	Ile	His	Arg	Ser	Ala	621
Ser	Glu	Pro	Ser	Leu	Asn	Arg	Ala	Gly	630
Phe	Gln	Thr	Glu	Asp	Phe	Ser	Leu	Tyr	639
Ala	Cys	Ala	Ser	Pro	Lys	Thr	Pro	Ile	648
Gln	Ala	Gly	Gly	Tyr	Gly	Gly	Phe	Pro	657
Val	His		659						

<210> 8

<211> 765

<212> PRT

<213> Homo sapiens

<220>

<223> b-raf

<400> 8

Met	Ala	Ala	Leu	Ser	Gly	Gly	Gly	Gly	9
Gly	Gly	Ala	Glu	Pro	Gly	Gln	Ala	Leu	18
Phe	Asn	Gly	Asp	Met	Glu	Pro	Glu	Ala	27
Gly	Ala	Gly	Arg	Pro	Ala	Ala	Ser	Ser	36
Ala	Ala	Asp	Pro	Ala	Ile	Pro	Glu	Glu	45
Val	Trp	Asn	Ile	Lys	Gln	Met	Ile	Lys	54
Leu	Thr	Gln	Glu	His	Ile	Glu	Ala	Leu	63
Leu	Asp	Lys	Phe	Gly	Gly	Glu	His	Asn	72
Pro	Pro	Ser	Ile	Tyr	Leu	Glu	Ala	Tyr	81
Glu	Glu	Tyr	Thr	Ser	Lys	Leu	Asp	Ala	90
Leu	Gln	Gln	Arg	Glu	Gln	Gln	Leu	Leu	99

Glu	Ser	Leu	Gly	Asn	Gly	Thr	Asp	Phe	108
Ser	Val	Ser	Ser	Ser	Ala	Ser	Met	Asp	117
Thr	Val	Thr	Ser	Ser	Ser	Ser	Ser	Ser	126
Leu	Ser	Val	Leu	Pro	Ser	Ser	Leu	Ser	135
Val	Phe	Gln	Asn	Pro	Thr	Asp	Val	Ala	144
Arg	Ser	Asn	Pro	Lys	Ser	Pro	Gln	Lys	153
Pro	Ile	Val	Arg	Val	Phe	Leu	Pro	Asn	162
Lys	Gln	Arg	Thr	Val	Val	Pro	Ala	Arg	171
Cys	Gly	Val	Thr	Val	Arg	Asp	Ser	Leu	180
Lys	Lys	Ala	Leu	Met	Met	Arg	Gly	Leu	189
Ile	Pro	Glu	Cys	Cys	Ala	Val	Tyr	Arg	198
Ile	Gln	Asp	Gly	Glu	Lys	Lys	Pro	Ile	207
Gly	Trp	Asp	Thr	Asp	Ile	Ser	Trp	Leu	216
Thr	Gly	Glu	Glu	Leu	His	Val	Glu	Val	225
Leu	Glu	Asn	Val	Pro	Leu	Thr	Thr	His	234
Asn	Phe	Val	Arg	Lys	Thr	Phe	Phe	Thr	243
Leu	Ala	Phe	Cys	Asp	Phe	Cys	Arg	Lys	252
Leu	Leu	Phe	Gln	Gly	Phe	Arg	Cys	Gln	261
Thr	Cys	Gly	Tyr	Lys	Phe	His	Gln	Arg	270
Cys	Ser	Thr	Glu	Val	Pro	Leu	Met	Cys	279
Val	Asn	Tyr	Asp	Gln	Leu	Asp	Leu	Leu	288
Phe	Val	Ser	Lys	Phe	Phe	Glu	His	His	297
Pro	Ile	Pro	Gln	Glu	Glu	Ala	Ser	Leu	306
Ala	Glu	Thr	Ala	Leu	Thr	Ser	Gly	Ser	315
Ser	Pro	Ser	Ala	Pro	Ala	Ser	Asp	Ser	324
Ile	Gly	Pro	Gln	Ile	Leu	Thr	Ser	Pro	333
Ser	Pro	Ser	Lys	Ser	Ile	Pro	Ile	Pro	342
Gln	Pro	Phe	Arg	Pro	Ala	Asp	Glu	Asp	351
His	Arg	Asn	Gln	Phe	Gly	Gln	Arg	Asp	360
Arg	Ser	Ser	Ser	Ala	Pro	Asn	Val	His	369
Ile	Asn	Thr	Ile	Glu	Pro	Val	Asn	Ile	378
Asp	Asp	Leu	Ile	Arg	Asp	Gln	Gly	Phe	387
Arg	Gly	Asp	Gly	Gly	Ser	Thr	Thr	Gly	396
Leu	Ser	Ala	Thr	Pro	Pro	Ala	Ser	Leu	405
Pro	Gly	Ser	Leu	Thr	Asn	Val	Lys	Ala	414
Leu	Gln	Lys	Ser	Pro	Gly	Pro	Gln	Arg	423
Glu	Arg	Lys	Ser	Ser	Ser	Ser	Ser	Glu	432
Asp	Arg	Asn	Arg	Met	Lys	Thr	Leu	Gly	441
Arg	Arg	Asp	Ser	Ser	Asp	Asp	Trp	Glu	450
Ile	Pro	Asp	Gly	Gln	Ile	Thr	Val	Gly	459
Gln	Arg	Ile	Gly	Ser	Gly	Ser	Phe	Gly	468
Thr	Val	Tyr	Lys	Gly	Lys	Trp	His	Gly	477
Asp	Val	Ala	Val	Lys	Met	Leu	Asn	Val	486
Thr	Ala	Pro	Thr	Pro	Gln	Gln	Leu	Gln	495
Ala	Phe	Lys	Asn	Glu	Val	Gly	Val	Leu	504
Arg	Lys	Thr	Arg	His	Val	Asn	Ile	Leu	513
Leu	Phe	Met	Gly	Tyr	Ser	Thr	Lys	Pro	522
Gln	Leu	Ala	Ile	Val	Thr	Gln	Trp	Cys	531
Glu	Gly	Ser	Ser	Leu	Tyr	His	His	Leu	540
His	Ile	Ile	Glu	Thr	Lys	Phe	Glu	Met	549
Ile	Lys	Leu	Ile	Asp	Ile	Ala	Arg	Gln	558
Thr	Ala	Gln	Gly	Met	Asp	Tyr	Leu	His	567

Ala	Lys	Ser	Ile	Ile	His	Arg	Asp	Leu	576
Lys	Ser	Asn	Asn	Ile	Phe	Leu	His	Glu	585
Asp	Leu	Thr	Val	Lys	Ile	Gly	Asp	Phe	594
Gly	Leu	Ala	Thr	Val	Lys	Ser	Arg	Trp	603
Ser	Gly	Ser	His	Gln	Phe	Glu	Gln	Leu	612
Ser	Gly	Ser	Ile	Leu	Trp	Met	Ala	Pro	621
Glu	Val	Ile	Arg	Met	Gln	Asp	Lys	Asn	630
Pro	Tyr	Ser	Phe	Gln	Ser	Asp	Val	Tyr	639
Ala	Phe	Gly	Ile	Val	Leu	Tyr	Glu	Leu	648
Met	Thr	Gly	Gln	Leu	Pro	Tyr	Ser	Asn	657
Ile	Asn	Asn	Arg	Asp	Gln	Ile	Ile	Phe	666
Met	Val	Gly	Arg	Gly	Tyr	Leu	Ser	Pro	675
Asp	Leu	Ser	Lys	Val	Arg	Ser	Asn	Cys	684
Pro	Lys	Ala	Met	Lys	Arg	Leu	Met	Ala	693
Glu	Cys	Leu	Lys	Lys	Lys	Arg	Asp	Glu	702
Arg	Pro	Leu	Phe	Pro	Gln	Ile	Leu	Ala	711
Ser	Ile	Glu	Leu	Leu	Ala	Arg	Ser	Leu	720
Pro	Lys	Ile	His	Arg	Ser	Ala	Ser	Glu	729
Pro	Ser	Leu	Asn	Arg	Ala	Gly	Phe	Gln	738
Thr	Glu	Asp	Phe	Ser	Leu	Tyr	Ala	Cys	747
Ala	Ser	Pro	Lys	Thr	Pro	Ile	Gln	Ala	756
Gly	Gly	Tyr	Gly	Ala	Phe	Pro	Val	His	765

<210> 9

<211> 111

<212> PRT

<213> Mus musculus

<220>

<223> PROTHYMOSIN ALPHA

<400> 9

Met	Ser	Asp	Ala	Ala	Val	Asp	Thr	Ser	9
Ser	Glu	Ile	Thr	Thr	Lys	Asp	Leu	Lys	18
Glu	Lys	Lys	Glu	Val	Val	Glu	Glu	Ala	27
Glu	Asn	Gly	Arg	Asp	Ala	Pro	Ala	Asn	36
Gly	Asn	Ala	Gln	Asn	Glu	Glu	Asn	Gly	45
Glu	Gln	Glu	Ala	Asp	Asn	Glu	Val	Asp	54
Glu	Glu	Glu	Glu	Glu	Gly	Gly	Glu	Glu	63
Glu	Glu	Glu	Glu	Glu	Glu	Gly	Asp	Gly	72
Glu	Glu	Glu	Asp	Gly	Asp	Glu	Asp	Glu	81
Glu	Ala	Glu	Ala	Pro	Thr	Gly	Lys	Arg	90
Val	Ala	Glu	Asp	Asp	Glu	Asp	Asp	Asp	99
Val	Asp	Thr	Lys	Lys	Gln	Lys	Thr	Glu	108
Glu	Asp	Asp	111						

<210> 10

<211> 111

<212> PRT

<213> Homo sapiens

<220>

<223> PROTHYMOSIN ALPHA

<400> 10

Met	Ser	Asp	Ala	Ala	Val	Asp	Thr	Ser	9
Ser	Glu	Ile	Thr	Thr	Lys	Asp	Leu	Lys	18
Glu	Lys	Lys	Glu	Val	Val	Glu	Glu	Ala	27
Glu	Asn	Gly	Arg	Asp	Ala	Pro	Ala	Asn	36
Gly	Asn	Ala	Glu	Asn	Glu	Glu	Asn	Gly	45
Glu	Gln	Glu	Ala	Asp	Asn	Glu	Val	Asp	54
Glu	Glu	Glu	Glu	Glu	Gly	Gly	Glu	Glu	63
Glu	Glu	Glu	Glu	Glu	Glu	Gly	Asp	Gly	72
Glu	Glu	Glu	Asp	Gly	Asp	Glu	Asp	Glu	81
Glu	Ala	Glu	Ser	Ala	Thr	Gly	Lys	Arg	90
Ala	Ala	Glu	Asp	Asp	Glu	Asp	Asp	Asp	99
Val	Asp	Thr	Lys	Lys	Gln	Lys	Thr	Asp	108
Glu	Asp	Asp	111						

<210> 11

<211> 233

<212> PRT

<213> Mus musculus

<220>

<223> GOLGI 4-TRANSMEMBRANE SPANNING TRANSPORTER (MTP)

<400> 11

Met	Val	Ser	Met	Thr	Phe	Lys	Arg	Ser	9
Arg	Ser	Asp	Arg	Phe	Tyr	Ser	Thr	Arg	18
Cys	Cys	Gly	Cys	Phe	His	Val	Arg	Thr	27
Gly	Thr	Ile	Ile	Leu	Gly	Thr	Trp	Tyr	36
Met	Val	Val	Asn	Leu	Leu	Met	Ala	Ile	45
Leu	Leu	Thr	Val	Glu	Val	Thr	His	Pro	54
Asn	Ser	Met	Pro	Ala	Val	Asn	Ile	Gln	63
Tyr	Glu	Val	Ile	Gly	Asn	Tyr	Tyr	Ser	72
Ser	Glu	Arg	Met	Ala	Asp	Asn	Ala	Cys	81
Val	Leu	Phe	Ala	Val	Ser	Val	Leu	Met	90
Phe	Ile	Ile	Ser	Ser	Met	Leu	Val	Tyr	99
Gly	Ala	Ile	Ser	Tyr	Gln	Val	Gly	Trp	108
Leu	Ile	Pro	Phe	Phe	Cys	Tyr	Arg	Leu	117
Phe	Asp	Phe	Val	Leu	Ser	Cys	Leu	Val	126
Ala	Ile	Ser	Ser	Leu	Thr	Tyr	Leu	Pro	135
Arg	Ile	Lys	Glu	Tyr	Leu	Asp	Gln	Leu	144
Pro	Asp	Phe	Pro	Tyr	Lys	Asp	Asp	Leu	153
Leu	Ala	Leu	Asp	Ser	Ser	Cys	Leu	Leu	162
Phe	Ile	Val	Leu	Val	Phe	Phe	Val	Val	171
Phe	Ile	Ile	Phe	Lys	Ala	Tyr	Leu	Ile	180
Asn	Cys	Val	Trp	Asn	Cys	Tyr	Lys	Tyr	189

Ile	Asn	Asn	Arg	Asn	Val	Pro	Glu	Ile	198
Ala	Val	Tyr	Pro	Ala	Phe	Glu	Thr	Pro	207
Pro	Gln	Tyr	Val	Leu	Pro	Thr	Tyr	Glu	216
Met	Ala	Val	Lys	Ile	Pro	Glu	Lys	Glu	225
Pro	Pro	Pro	Pro	Tyr	Leu	Pro	Ala	233	

<210> 12

<211> 233

<212> PRT

<213> Homo sapiens

<220>

<223> GOLGI 4-TRANSMEMBRANE SPANNING TRANSPORTER MTP
(KIAA0108)

<400> 12

Met	Val	Ser	Met	Ser	Phe	Lys	Arg	Asn	9
Arg	Ser	Asp	Arg	Phe	Tyr	Ser	Thr	Arg	18
Cys	Cys	Gly	Cys	Cys	His	Val	Arg	Thr	27
Gly	Thr	Ile	Ile	Leu	Gly	Thr	Trp	Tyr	36
Met	Val	Val	Asn	Leu	Leu	Met	Ala	Ile	45
Leu	Leu	Thr	Val	Glu	Val	Thr	His	Pro	54
Asn	Ser	Met	Pro	Ala	Val	Asn	Ile	Gln	63
Tyr	Glu	Val	Ile	Gly	Asn	Tyr	Tyr	Ser	72
Ser	Glu	Arg	Met	Ala	Asp	Asn	Ala	Cys	81
Val	Leu	Phe	Ala	Val	Ser	Val	Leu	Met	90
Phe	Ile	Ile	Ser	Ser	Met	Leu	Val	Tyr	99
Gly	Ala	Ile	Ser	Tyr	Gln	Val	Gly	Trp	108
Leu	Ile	Pro	Phe	Phe	Cys	Tyr	Arg	Leu	117
Phe	Asp	Phe	Val	Leu	Ser	Cys	Leu	Val	126
Ala	Ile	Ser	Ser	Leu	Thr	Tyr	Leu	Pro	135
Arg	Ile	Lys	Glu	Tyr	Leu	Asp	Gln	Leu	144
Pro	Asp	Phe	Pro	Tyr	Lys	Asp	Asp	Leu	153
Leu	Ala	Leu	Asp	Ser	Ser	Cys	Leu	Leu	162
Phe	Ile	Val	Leu	Val	Phe	Phe	Ala	Leu	171
Phe	Ile	Ile	Phe	Lys	Ala	Tyr	Leu	Ile	180
Asn	Cys	Val	Trp	Asn	Cys	Tyr	Lys	Tyr	189
Ile	Asn	Asn	Arg	Asn	Val	Pro	Glu	Ile	198
Ala	Val	Tyr	Pro	Ala	Phe	Glu	Ala	Pro	207
Pro	Gln	Tyr	Val	Leu	Pro	Thr	Tyr	Glu	216
Met	Ala	Val	Lys	Met	Pro	Glu	Lys	Glu	225
Pro	Pro	Pro	Pro	Tyr	Leu	Pro	Ala	233	

<210> 13

<211> 355

<212> PRT

<213> Mus musculus

<220>

<223> CCR-1

<400> 13

Met	Glu	Ile	Ser	Asp	Phe	Thr	Glu	Ala	9
Tyr	Pro	Thr	Thr	Thr	Glu	Phe	Asp	Tyr	18
Gly	Asp	Ser	Thr	Pro	Cys	Gln	Lys	Thr	27
Ala	Val	Arg	Ala	Phe	Gly	Ala	Gly	Leu	36
Leu	Pro	Pro	Leu	Tyr	Ser	Leu	Val	Phe	45
Ile	Ile	Gly	Val	Val	Gly	Asn	Val	Leu	54
Met	Ile	Leu	Val	Leu	Met	Gln	His	Arg	63
Arg	Leu	Gln	Ser	Met	Thr	Ser	Ile	Tyr	72
Leu	Phe	Asn	Leu	Ala	Val	Ser	Asp	Leu	81
Val	Phe	Leu	Phe	Thr	Leu	Pro	Phe	Trp	90
Ile	Asp	Tyr	Lys	Leu	Lys	Asp	Asp	Trp	99
Ile	Phe	Gly	Asp	Ala	Met	Cys	Lys	Leu	108
Leu	Ser	Gly	Phe	Tyr	Tyr	Leu	Gly	Leu	117
Tyr	Ser	Glu	Ile	Phe	Phe	Ile	Ile	Leu	126
Leu	Thr	Ile	Asp	Arg	Tyr	Leu	Ala	Ile	135
Val	His	Ala	Val	Phe	Ala	Leu	Arg	Ala	144
Arg	Thr	Val	Thr	Leu	Gly	Ile	Ile	Thr	153
Ser	Ile	Ile	Thr	Trp	Ala	Leu	Ala	Ile	162
Leu	Ala	Ser	Met	Pro	Ala	Leu	Tyr	Phe	171
Phe	Lys	Ala	Gln	Trp	Glu	Phe	Thr	His	180
Arg	Thr	Cys	Ser	Pro	His	Phe	Pro	Tyr	189
Lys	Ser	Leu	Lys	Gln	Trp	Lys	Arg	Phe	198
Gln	Ala	Leu	Lys	Leu	Asn	Leu	Leu	Gly	207
Leu	Ile	Leu	Pro	Leu	Leu	Val	Met	Ile	216
Ile	Cys	Tyr	Ala	Gly	Ile	Ile	Arg	Ile	225
Leu	Leu	Arg	Arg	Pro	Ser	Glu	Lys	Lys	234
Val	Lys	Ala	Val	Arg	Leu	Ile	Phe	Ala	243
Ile	Thr	Leu	Leu	Phe	Phe	Leu	Leu	Trp	252
Thr	Pro	Tyr	Asn	Leu	Ser	Val	Phe	Val	261
Ser	Ala	Phe	Gln	Asp	Val	Leu	Phe	Thr	270
Asn	Gln	Cys	Glu	Gln	Ser	Lys	His	Leu	279
Asp	Leu	Ala	Met	Gln	Val	Thr	Glu	Val	288
Ile	Ala	Tyr	Thr	His	Cys	Cys	Val	Asn	297
Pro	Ile	Ile	Tyr	Val	Phe	Val	Gly	Glu	306
Arg	Phe	Trp	Lys	Tyr	Leu	Arg	Gln	Leu	315
Phe	Gln	Arg	His	Val	Ala	Ile	Pro	Leu	324
Ala	Lys	Trp	Leu	Pro	Phe	Leu	Ser	Val	333
Asp	Gln	Leu	Glu	Arg	Thr	Ser	Ser	Ile	342
Ser	Pro	Ser	Thr	Gly	Glu	His	Glu	Leu	351
Ser	Ala	Gly	Phe	355					

<210> 14

<211> 355

<212> PRT

<213> Homo sapiens

<220>

<223> CCR-1

<400> 14

Met	Glu	Thr	Pro	Asn	Thr	Thr	Glu	Asp	9
Tyr	Asp	Thr	Thr	Thr	Glu	Phe	Asp	Tyr	18
Gly	Asp	Ala	Thr	Pro	Cys	Gln	Lys	Val	27
Asn	Glu	Arg	Ala	Phe	Gly	Ala	Gln	Leu	36
Leu	Pro	Pro	Leu	Tyr	Ser	Leu	Val	Phe	45
Val	Ile	Gly	Leu	Val	Gly	Asn	Ile	Leu	54
Val	Val	Leu	Val	Leu	Val	Gln	Tyr	Lys	63
Arg	Leu	Lys	Asn	Met	Thr	Ser	Ile	Tyr	72
Leu	Leu	Asn	Leu	Ala	Ile	Ser	Asp	Leu	81
Leu	Phe	Leu	Phe	Thr	Leu	Pro	Phe	Trp	90
Ile	Asp	Tyr	Lys	Leu	Lys	Asp	Asp	Trp	99
Val	Phe	Gly	Asp	Ala	Met	Cys	Lys	Ile	108
Leu	Ser	Gly	Phe	Tyr	Tyr	Thr	Gly	Leu	117
Tyr	Ser	Glu	Ile	Phe	Phe	Ile	Ile	Leu	126
Leu	Thr	Ile	Asp	Arg	Tyr	Leu	Ala	Ile	135
Val	His	Ala	Val	Phe	Ala	Leu	Arg	Ala	144
Arg	Thr	Val	Thr	Phe	Gly	Val	Ile	Thr	153
Ser	Ile	Ile	Ile	Trp	Ala	Leu	Ala	Ile	162
Leu	Ala	Ser	Met	Pro	Gly	Leu	Tyr	Phe	171
Ser	Lys	Thr	Gln	Trp	Glu	Phe	Thr	His	180
His	Thr	Cys	Ser	Leu	His	Phe	Pro	His	189
Glu	Ser	Leu	Arg	Glu	Trp	Lys	Leu	Phe	198
Gln	Ala	Leu	Lys	Leu	Asn	Leu	Phe	Gly	207
Leu	Val	Leu	Pro	Leu	Leu	Val	Met	Ile	216
Ile	Cys	Tyr	Thr	Gly	Ile	Ile	Lys	Ile	225
Leu	Leu	Arg	Arg	Pro	Asn	Glu	Lys	Lys	234
Ser	Lys	Ala	Val	Arg	Leu	Ile	Phe	Val	243
Ile	Met	Ile	Ile	Phe	Phe	Leu	Phe	Trp	252
Thr	Pro	Tyr	Asn	Leu	Thr	Ile	Leu	Ile	261
Ser	Val	Phe	Gln	Asp	Phe	Leu	Phe	Thr	270
His	Glu	Cys	Glu	Gln	Ser	Arg	His	Leu	279
Asp	Leu	Ala	Val	Gln	Val	Thr	Glu	Val	288
Ile	Ala	Tyr	Thr	His	Cys	Cys	Val	Asn	297
Pro	Val	Ile	Tyr	Ala	Phe	Val	Gly	Glu	306
Arg	Phe	Arg	Lys	Tyr	Leu	Arg	Gln	Leu	315
Phe	His	Arg	Arg	Val	Ala	Val	His	Leu	324
Val	Lys	Trp	Leu	Pro	Phe	Leu	Ser	Val	333
Asp	Arg	Leu	Glu	Arg	Val	Ser	Ser	Thr	342
Ser	Pro	Ser	Thr	Gly	Glu	His	Glu	Leu	351
Ser	Ala	Gly	Phe						355

<210> 15

<211> 96

<212> PRT

<213> Mus musculus

<220>

<223> HMG-14

<400> 15

Met	Pro	Lys	Arg	Lys	Val	Ser	Ala	Asp	9
Gly	Ala	Ala	Lys	Ala	Glu	Pro	Lys	Arg	18
Arg	Ser	Ala	Arg	Leu	Ser	Ala	Lys	Pro	27
Ala	Pro	Ala	Lys	Val	Asp	Ala	Lys	Pro	36
Lys	Lys	Ala	Ala	Gly	Lys	Asp	Lys	Ala	45
Ser	Asp	Lys	Lys	Val	Gln	Ile	Lys	Gly	54
Lys	Arg	Gly	Ala	Lys	Gly	Lys	Gln	Ala	63
Asp	Val	Ala	Asp	Gln	Gln	Thr	Thr	Glu	72
Leu	Pro	Ala	Glu	Asn	Gly	Glu	Thr	Glu	81
Asn	Gln	Ser	Pro	Ala	Ser	Glu	Glu	Glu	90
Lys	Glu	Ala	Lys	Ser	Asp				96

<210> 16

<211> 100

<212> PRT

<213> Homo sapiens

<220>

<223> HMG-14

<400> 16

Met	Pro	Lys	Arg	Lys	Val	Ser	Ser	Ala	9
Glu	Gly	Ala	Ala	Lys	Glu	Glu	Pro	Lys	18
Arg	Arg	Ser	Ala	Arg	Leu	Ser	Ala	Lys	27
Pro	Pro	Ala	Lys	Val	Glu	Ala	Lys	Pro	36
Lys	Lys	Ala	Ala	Ala	Lys	Asp	Lys	Ser	45
Ser	Asp	Lys	Lys	Val	Gln	Thr	Lys	Gly	54
Lys	Arg	Gly	Ala	Lys	Gly	Lys	Gln	Ala	63
Glu	Val	Ala	Asn	Gln	Glu	Thr	Lys	Glu	72
Asp	Leu	Pro	Ala	Glu	Asn	Gly	Glu	Thr	81
Lys	Thr	Glu	Glu	Ser	Pro	Ala	Ser	Asp	90
Glu	Ala	Gly	Glu	Lys	Glu	Ala	Lys	Ser	99
Asp									100

<210> 17

<211> 70

<212> PRT

<213> Mus musculus

<220>

<223> Deleted in split-hand/split-foot 1 region

<400> 17

Met	Ser	Glu	Lys	Lys	Gln	Pro	Val	Asp	9
Leu	Gly	Leu	Leu	Glu	Glu	Asp	Asp	Glu	18
Phe	Glu	Glu	Phe	Pro	Ala	Glu	Asp	Trp	27
Ala	Gly	Leu	Asp	Glu	Asp	Glu	Asp	Ala	36
His	Val	Trp	Glu	Asp	Asn	Trp	Asp	Asp	45
Asp	Asn	Val	Glu	Asp	Asp	Phe	Ser	Asn	54
Gln	Leu	Arg	Ala	Glu	Leu	Glu	Lys	His	63
Gly	Tyr	Lys	Met	Glu	Thr	Ser	70		

<210> 18

<211> 70

<212> PRT

<213> Homo sapiens

<220>

<223> Deleted in split-hand/split-foot 1 region

<400> 18

Met	Ser	Glu	Lys	Lys	Gln	Pro	Val	Asp	9
Leu	Gly	Leu	Leu	Glu	Glu	Asp	Asp	Glu	18
Phe	Glu	Glu	Phe	Pro	Ala	Glu	Asp	Trp	27
Ala	Gly	Leu	Asp	Glu	Asp	Glu	Asp	Ala	36
His	Val	Trp	Glu	Asp	Asn	Trp	Asp	Asp	45
Asp	Asn	Val	Glu	Asp	Asp	Phe	Ser	Asn	54
Gln	Leu	Arg	Ala	Glu	Leu	Glu	Lys	His	63
Gly	Tyr	Lys	Met	Glu	Thr	Ser	70		

<210> 19

<211> 596

<212> PRT

<213> Mus musculus

<220>

<223> TAK1

<400> 19

Met	Thr	Ser	Pro	Ser	Pro	Arg	Ile	Gln	9
Ile	Ile	Ser	Thr	Asp	Ser	Ala	Val	Ala	18
Ser	Pro	Gln	Arg	Ile	Gln	Ile	Val	Thr	27
Asp	Gln	Gln	Thr	Gly	Gln	Lys	Ile	Gln	36
Ile	Val	Thr	Ala	Val	Asp	Ala	Ser	Gly	45
Ser	Ser	Lys	Gln	Gln	Phe	Ile	Leu	Thr	54
Ser	Pro	Asp	Gly	Ala	Gly	Thr	Gly	Lys	63
Val	Ile	Leu	Ala	Ser	Pro	Glu	Thr	Ser	72
Ser	Ala	Lys	Gln	Leu	Ile	Phe	Thr	Thr	81
Ser	Asp	Asn	Leu	Val	Pro	Gly	Arg	Ile	90
Gln	Ile	Val	Thr	Asp	Ser	Ala	Ser	Val	99

Glu	Arg	Leu	Leu	Gly	Lys	Ala	Asp	Val	108
Gln	Arg	Pro	Gln	Val	Val	Glu	Tyr	Cys	117
Val	Val	Cys	Gly	Asp	Lys	Ala	Ser	Gly	126
Arg	His	Tyr	Gly	Ala	Val	Ser	Cys	Glu	135
Gly	Cys	Lys	Gly	Phe	Phe	Lys	Arg	Ser	144
Val	Arg	Lys	Asn	Leu	Thr	Tyr	Ser	Cys	153
Arg	Ser	Ser	Gln	Asp	Cys	Ile	Ile	Asn	162
Lys	His	His	Arg	Asn	Arg	Cys	Gln	Phe	171
Cys	Arg	Leu	Lys	Lys	Cys	Leu	Glu	Met	180
Gly	Met	Lys	Met	Glu	Ser	Val	Gln	Ser	189
Glu	Arg	Lys	Pro	Phe	Asp	Val	Gln	Arg	198
Glu	Lys	Pro	Ser	Asn	Cys	Ala	Ala	Ser	207
Thr	Glu	Lys	Ile	Tyr	Ile	Arg	Lys	Asp	216
Leu	Arg	Ser	Pro	Leu	Ile	Ala	Thr	Pro	225
Thr	Phe	Val	Ala	Asp	Lys	Asp	Gly	Ala	234
Arg	Gln	Thr	Gly	Leu	Leu	Asp	Pro	Gly	243
Met	Leu	Val	Asn	Ile	Gln	Gln	Pro	Leu	252
Ile	Arg	Glu	Asp	Gly	Thr	Val	Leu	Leu	261
Ala	Ala	Asp	Ser	Lys	Ala	Glu	Thr	Ser	270
Gln	Gly	Ala	Leu	Gly	Thr	Leu	Ala	Asn	279
Val	Val	Thr	Ser	Leu	Ala	Asn	Leu	Ser	288
Glu	Ser	Leu	Asn	Asn	Gly	Asp	Ala	Ser	297
Glu	Met	Gln	Pro	Glu	Asp	Gln	Ser	Ala	306
Ser	Glu	Ile	Thr	Arg	Ala	Phe	Asp	Thr	315
Leu	Ala	Lys	Ala	Leu	Asn	Thr	Thr	Asp	324
Ser	Ala	Ser	Pro	Pro	Ser	Leu	Ala	Asp	333
Gly	Ile	Asp	Ala	Ser	Gly	Gly	Gly	Ser	342
Ile	His	Val	Ile	Ser	Arg	Asp	Gln	Ser	351
Thr	Pro	Ile	Ile	Glu	Val	Glu	Gly	Pro	360
Leu	Leu	Ser	Asp	Thr	His	Val	Thr	Phe	369
Lys	Leu	Thr	Met	Pro	Ser	Pro	Met	Pro	378
Glu	Tyr	Leu	Asn	Val	His	Tyr	Ile	Cys	387
Glu	Ser	Ala	Ser	Arg	Leu	Leu	Phe	Leu	396
Ser	Met	His	Trp	Ala	Arg	Ser	Ile	Pro	405
Ala	Phe	Gln	Ala	Leu	Gly	Gln	Asp	Cys	414
Asn	Thr	Ser	Leu	Val	Arg	Ala	Cys	Trp	423
Asn	Glu	Leu	Phe	Thr	Leu	Gly	Leu	Ala	432
Gln	Cys	Ala	Gln	Val	Met	Ser	Leu	Ser	441
Thr	Ile	Leu	Ala	Ala	Ile	Val	Asn	His	450
Leu	Gln	Asn	Ser	Ile	Gln	Glu	Asp	Lys	459
Leu	Ser	Gly	Asp	Arg	Ile	Lys	Gln	Val	468
Met	Glu	His	Ile	Trp	Lys	Leu	Gln	Glu	477
Phe	Cys	Asn	Ser	Met	Ala	Lys	Leu	Asp	486
Ile	Asp	Gly	Tyr	Glu	Tyr	Ala	Tyr	Leu	495
Lys	Ala	Ile	Val	Leu	Phe	Ser	Pro	Asp	504
His	Pro	Gly	Leu	Thr	Gly	Thr	Ser	Gln	513
Ile	Glu	Lys	Phe	Gln	Glu	Lys	Ala	Gln	522
Met	Glu	Leu	Gln	Asp	Tyr	Val	Gln	Lys	531
Thr	Tyr	Ser	Glu	Asp	Thr	Tyr	Arg	Leu	540
Ala	Arg	Ile	Leu	Val	Arg	Leu	Pro	Ala	549
Leu	Arg	Leu	Met	Ser	Ser	Asn	Ile	Thr	558
Glu	Glu	Leu	Phe	Phe	Thr	Gly	Leu	Ile	567

Gly	Asn	Val	Ser	Ile	Asp	Ser	Ile	Ile	576
Pro	Tyr	Ile	Leu	Lys	Met	Glu	Thr	Ala	585
Glu	Tyr	Asn	Gly	Gln	Ile	Thr	Gly	Ala	594
Ser	Leu	596							

<210> 20
 <211> 596
 <212> PRT
 <213> Homo sapiens

<220>
 <223> TAK1

<400> 20

Met	Thr	Ser	Pro	Ser	Pro	Arg	Ile	Gln	9
Ile	Ile	Ser	Thr	Asp	Ser	Ala	Val	Ala	18
Ser	Pro	Gln	Arg	Ile	Gln	Ile	Val	Thr	27
Asp	Gln	Gln	Thr	Gly	Gln	Lys	Ile	Gln	36
Ile	Val	Thr	Ala	Val	Asp	Ala	Ser	Gly	45
Ser	Pro	Lys	Gln	Gln	Phe	Ile	Leu	Thr	54
Ser	Pro	Asp	Gly	Ala	Gly	Thr	Gly	Lys	63
Val	Ile	Leu	Ala	Ser	Pro	Glu	Thr	Ser	72
Ser	Ala	Lys	Gln	Leu	Ile	Phe	Thr	Thr	81
Ser	Asp	Asn	Leu	Val	Pro	Gly	Arg	Ile	90
Gln	Ile	Val	Thr	Asp	Ser	Ala	Ser	Val	99
Glu	Arg	Leu	Leu	Gly	Lys	Thr	Asp	Val	108
Gln	Arg	Pro	Gln	Val	Val	Glu	Tyr	Cys	117
Val	Val	Cys	Gly	Asp	Lys	Ala	Ser	Gly	126
Arg	His	Tyr	Gly	Ala	Val	Ser	Cys	Glu	135
Gly	Cys	Lys	Gly	Phe	Phe	Lys	Arg	Ser	144
Val	Arg	Lys	Asn	Leu	Thr	Tyr	Ser	Cys	153
Arg	Ser	Asn	Gln	Asp	Cys	Ile	Ile	Asn	162
Lys	His	His	Arg	Asn	Arg	Cys	Gln	Phe	171
Cys	Arg	Leu	Lys	Lys	Cys	Leu	Glu	Met	180
Gly	Met	Lys	Met	Glu	Ser	Val	Gln	Ser	189
Glu	Arg	Lys	Pro	Phe	Asp	Val	Gln	Arg	198
Glu	Lys	Pro	Ser	Asn	Cys	Ala	Ala	Ser	207
Thr	Glu	Lys	Ile	Tyr	Ile	Arg	Lys	Asp	216
Leu	Arg	Ser	Pro	Leu	Ile	Ala	Thr	Pro	225
Thr	Phe	Val	Ala	Asp	Lys	Asp	Gly	Ala	234
Arg	Gln	Thr	Gly	Leu	Leu	Asp	Pro	Gly	243
Met	Leu	Val	Asn	Ile	Gln	Gln	Pro	Leu	252
Ile	Arg	Glu	Asp	Gly	Thr	Val	Leu	Leu	261
Ala	Thr	Asp	Ser	Lys	Ala	Glu	Thr	Ser	270
Gln	Gly	Ala	Leu	Gly	Thr	Leu	Ala	Asn	279
Val	Val	Thr	Ser	Leu	Ala	Asn	Leu	Ser	288
Glu	Ser	Leu	Asn	Asn	Gly	Asp	Thr	Ser	297
Glu	Ile	Gln	Pro	Glu	Asp	Gln	Ser	Ala	306
Ser	Glu	Ile	Thr	Arg	Ala	Phe	Asp	Thr	315
Leu	Ala	Lys	Ala	Leu	Asn	Thr	Thr	Asp	324

Ser	Ser	Ser	Ser	Pro	Ser	Leu	Ala	Asp	333
Gly	Ile	Asp	Thr	Ser	Gly	Gly	Gly	Ser	342
Ile	His	Val	Ile	Ser	Arg	Asp	Gln	Ser	351
Thr	Pro	Ile	Ile	Glu	Val	Glu	Gly	Pro	360
Leu	Leu	Ser	Asp	Thr	His	Val	Thr	Phe	369
Lys	Leu	Thr	Met	Pro	Ser	Pro	Met	Pro	378
Glu	Tyr	Leu	Asn	Val	His	Tyr	Ile	Cys	387
Glu	Ser	Ala	Ser	Arg	Leu	Leu	Phe	Leu	396
Ser	Met	His	Trp	Ala	Arg	Ser	Ile	Pro	405
Ala	Phe	Gln	Ala	Leu	Gly	Gln	Asp	Cys	414
Asn	Thr	Ser	Leu	Val	Arg	Ala	Cys	Trp	423
Asn	Glu	Leu	Phe	Thr	Leu	Gly	Leu	Ala	432
Gln	Cys	Ala	Gln	Val	Met	Ser	Leu	Ser	441
Thr	Ile	Leu	Ala	Ala	Ile	Val	Asn	His	450
Leu	Gln	Asn	Ser	Ile	Gln	Glu	Asp	Lys	459
Leu	Ser	Gly	Asp	Arg	Ile	Lys	Gln	Val	468
Met	Glu	His	Ile	Trp	Lys	Leu	Gln	Glu	477
Phe	Cys	Asn	Ser	Met	Ala	Lys	Leu	Asp	486
Ile	Asp	Gly	Tyr	Glu	Tyr	Ala	Tyr	Leu	495
Lys	Ala	Ile	Val	Leu	Phe	Ser	Pro	Asp	504
His	Pro	Gly	Leu	Thr	Ser	Thr	Ser	Gln	513
Ile	Glu	Lys	Phe	Gln	Glu	Lys	Ala	Gln	522
Met	Glu	Leu	Gln	Asp	Tyr	Val	Gln	Lys	531
Thr	Tyr	Ser	Glu	Asp	Thr	Tyr	Arg	Leu	540
Ala	Arg	Ile	Leu	Val	Arg	Leu	Pro	Ala	549
Leu	Arg	Leu	Met	Ser	Ser	Asn	Ile	Thr	558
Glu	Glu	Leu	Phe	Phe	Thr	Gly	Leu	Ile	567
Gly	Asn	Val	Ser	Ile	Asp	Ser	Ile	Ile	576
Pro	Tyr	Ile	Leu	Lys	Met	Glu	Thr	Ala	585
Glu	Tyr	Asn	Gly	Gln	Ile	Thr	Gly	Ala	594
Ser	Leu								596

<210> 21

<211> 97

<212> PRT

<213> Mus musculus

<220>

<223> MCP-3

<400> 21

Met	Arg	Ile	Ser	Ala	Thr	Leu	Leu	Cys	9
Leu	Leu	Leu	Ile	Ala	Ala	Ala	Phe	Ser	18
Ile	Gln	Val	Trp	Ala	Gln	Pro	Asp	Gly	27
Pro	Asn	Ala	Ser	Thr	Cys	Cys	Tyr	Val	36
Lys	Lys	Gln	Lys	Ile	Pro	Lys	Arg	Asn	45
Leu	Lys	Ser	Tyr	Arg	Arg	Ile	Thr	Ser	54
Ser	Arg	Cys	Pro	Trp	Glu	Ala	Val	Ile	63
Phe	Lys	Thr	Lys	Lys	Gly	Met	Glu	Val	72

Cys	Ala	Glu	Ala	His	Gln	Lys	Trp	Val	81
Glu	Glu	Ala	Ile	Ala	Tyr	Leu	Asp	Met	90
Lys	Thr	Pro	Thr	Pro	Lys	Pro	97		

<210> 22
 <211> 99
 <212> PRT
 <213> Homo sapiens

<220>
 <223> MCP-3

<400> 22

Met	Lys	Ala	Ser	Ala	Ala	Leu	Leu	Cys	9
Leu	Leu	Leu	Thr	Ala	Ala	Ala	Phe	Ser	18
Pro	Gln	Gly	Leu	Ala	Gln	Pro	Val	Gly	27
Ile	Asn	Thr	Ser	Thr	Thr	Cys	Cys	Tyr	36
Arg	Phe	Ile	Asn	Lys	Lys	Ile	Pro	Lys	45
Gln	Arg	Leu	Glu	Ser	Tyr	Arg	Arg	Thr	54
Thr	Ser	Ser	His	Cys	Pro	Arg	Glu	Ala	63
Val	Ile	Phe	Lys	Thr	Lys	Leu	Asp	Lys	72
Glu	Ile	Cys	Ala	Asp	Pro	Thr	Gln	Lys	81
Trp	Val	Gln	Asp	Phe	Met	Lys	His	Leu	90
Asp	Lys	Lys	Thr	Gln	Thr	Pro	Lys	Leu	99

<210> 23
 <211> 415
 <212> PRT
 <213> Mus musculus

<220>
 <223> IL-5R-ALPHA

<400> 23

Met	Val	Pro	Val	Leu	Leu	Ile	Leu	Val	9
Gly	Ala	Leu	Ala	Thr	Leu	Gln	Ala	Asp	18
Leu	Leu	Asn	His	Lys	Lys	Phe	Leu	Leu	27
Leu	Pro	Pro	Val	Asn	Phe	Thr	Ile	Lys	36
Ala	Thr	Gly	Leu	Ala	Gln	Val	Leu	Leu	45
His	Trp	Asp	Pro	Asn	Pro	Asp	Gln	Glu	54
Gln	Arg	His	Val	Asp	Leu	Glu	Tyr	His	63
Val	Lys	Ile	Asn	Ala	Pro	Gln	Glu	Asp	72
Glu	Tyr	Asp	Thr	Arg	Lys	Thr	Glu	Ser	81
Lys	Cys	Val	Thr	Pro	Leu	His	Glu	Gly	90
Phe	Ala	Ala	Ser	Val	Arg	Thr	Ile	Leu	99
Lys	Ser	Ser	His	Thr	Thr	Leu	Ala	Ser	108

Ser	Trp	Val	Ser	Ala	Glu	Leu	Lys	Ala	117
Pro	Pro	Gly	Ser	Pro	Gly	Thr	Ser	Val	126
Thr	Asn	Leu	Thr	Cys	Thr	Thr	His	Thr	135
Val	Val	Ser	Ser	His	Thr	His	Leu	Arg	144
Pro	Tyr	Gln	Val	Ser	Leu	Arg	Cys	Thr	153
Trp	Leu	Val	Gly	Lys	Asp	Ala	Pro	Glu	162
Asp	Thr	Gln	Tyr	Phe	Leu	Tyr	Tyr	Arg	171
Phe	Gly	Val	Leu	Thr	Glu	Lys	Cys	Gln	180
Glu	Tyr	Ser	Arg	Asp	Ala	Leu	Asn	Arg	189
Asn	Thr	Ala	Cys	Trp	Phe	Pro	Arg	Thr	198
Phe	Ile	Asn	Ser	Lys	Gly	Phe	Glu	Gln	207
Leu	Ala	Val	His	Ile	Asn	Gly	Ser	Ser	216
Lys	Arg	Ala	Ala	Ile	Lys	Pro	Phe	Asp	225
Gln	Leu	Phe	Ser	Pro	Leu	Ala	Ile	Asp	234
Gln	Val	Asn	Pro	Pro	Arg	Asn	Val	Thr	243
Val	Glu	Ile	Glu	Ser	Asn	Ser	Leu	Tyr	252
Ile	Gln	Trp	Glu	Lys	Pro	Leu	Ser	Ala	261
Phe	Pro	Asp	His	Cys	Phe	Asn	Tyr	Glu	270
Leu	Lys	Ile	Tyr	Asn	Thr	Lys	Asn	Gly	279
His	Ile	Gln	Lys	Glu	Lys	Leu	Ile	Ala	288
Asn	Lys	Phe	Ile	Ser	Lys	Ile	Asp	Asp	297
Val	Ser	Thr	Tyr	Ser	Ile	Gln	Val	Arg	306
Ala	Ala	Val	Ser	Ser	Pro	Cys	Arg	Met	315
Pro	Gly	Arg	Trp	Gly	Glu	Trp	Ser	Gln	324
Pro	Ile	Tyr	Val	Gly	Lys	Glu	Arg	Lys	333
Ser	Leu	Val	Glu	Trp	His	Leu	Ile	Val	342
Leu	Pro	Thr	Ala	Ala	Cys	Phe	Val	Leu	351
Leu	Ile	Phe	Ser	Leu	Ile	Cys	Arg	Val	360
Cys	His	Leu	Trp	Thr	Arg	Leu	Phe	Pro	369
Pro	Val	Pro	Ala	Pro	Lys	Ser	Asn	Ile	378
Lys	Asp	Leu	Pro	Val	Val	Thr	Glu	Tyr	387
Glu	Lys	Pro	Ser	Asn	Glu	Thr	Lys	Ile	396
Glu	Val	Val	His	Cys	Val	Glu	Glu	Val	405
Gly	Phe	Glu	Val	Met	Gly	Asn	Ser	Thr	414
Phe	415								

<210> 24

<211> 420

<212> PRT

<213> Homo sapiens

<220>

<223> IL-5R-ALPH

<400> 24

Met	Ile	Ile	Val	Ala	His	Val	Leu	Leu	9
Ile	Leu	Leu	Gly	Ala	Thr	Glu	Ile	Leu	18
Gln	Ala	Asp	Leu	Leu	Pro	Asp	Glu	Lys	27
Ile	Ser	Leu	Leu	Pro	Pro	Val	Asn	Phe	36

Thr	Ile	Lys	Val	Thr	Gly	Leu	Ala	Gln	45
Val	Leu	Leu	Gln	Trp	Lys	Pro	Asn	Pro	54
Asp	Gln	Glu	Gln	Arg	Asn	Val	Asn	Leu	63
Glu	Tyr	Gln	Val	Lys	Ile	Asn	Ala	Pro	72
Lys	Glu	Asp	Asp	Tyr	Glu	Thr	Arg	Ile	81
Thr	Glu	Ser	Lys	Cys	Val	Thr	Ile	Leu	90
His	Lys	Gly	Phe	Ser	Ala	Ser	Val	Arg	99
Thr	Ile	Leu	Gln	Asn	Asp	His	Ser	Leu	108
Leu	Ala	Ser	Ser	Trp	Ala	Ser	Ala	Glu	117
Leu	His	Ala	Pro	Pro	Gly	Ser	Pro	Gly	126
Thr	Ser	Ile	Val	Asn	Leu	Thr	Cys	Thr	135
Thr	Asn	Thr	Thr	Glu	Asp	Asn	Tyr	Ser	144
Arg	Leu	Arg	Ser	Tyr	Gln	Val	Ser	Leu	153
His	Cys	Thr	Trp	Leu	Val	Gly	Thr	Asp	162
Ala	Pro	Glu	Asp	Thr	Gln	Tyr	Phe	Leu	171
Tyr	Tyr	Arg	Tyr	Gly	Ser	Trp	Thr	Glu	180
Glu	Cys	Gln	Glu	Tyr	Ser	Lys	Asp	Thr	189
Leu	Gly	Arg	Asn	Ile	Ala	Cys	Trp	Phe	198
Pro	Arg	Thr	Phe	Ile	Leu	Ser	Lys	Gly	207
Arg	Asp	Trp	Leu	Ser	Val	Leu	Val	Asn	216
Gly	Ser	Ser	Lys	His	Ser	Ala	Ile	Arg	225
Pro	Phe	Asp	Gln	Leu	Phe	Ala	Leu	His	234
Ala	Ile	Asp	Gln	Ile	Asn	Pro	Pro	Leu	243
Asn	Val	Thr	Ala	Glu	Ile	Glu	Gly	Thr	252
Arg	Leu	Ser	Ile	Gln	Trp	Glu	Lys	Pro	261
Val	Ser	Ala	Phe	Pro	Ile	His	Cys	Phe	270
Asp	Tyr	Glu	Val	Lys	Ile	His	Asn	Thr	279
Arg	Asn	Gly	Tyr	Leu	Gln	Ile	Glu	Lys	288
Leu	Met	Thr	Asn	Ala	Phe	Ile	Ser	Ile	297
Ile	Asp	Asp	Leu	Ser	Lys	Tyr	Asp	Val	306
Gln	Val	Arg	Ala	Ala	Val	Ser	Ser	Met	315
Cys	Arg	Glu	Ala	Gly	Leu	Trp	Ser	Glu	324
Trp	Ser	Gln	Pro	Ile	Tyr	Val	Gly	Asn	333
Asp	Glu	His	Lys	Pro	Leu	Arg	Glu	Trp	342
Phe	Val	Ile	Val	Ile	Met	Ala	Thr	Ile	351
Cys	Phe	Ile	Leu	Leu	Ile	Leu	Ser	Leu	360
Ile	Cys	Lys	Ile	Cys	His	Leu	Trp	Ile	369
Lys	Leu	Phe	Pro	Pro	Ile	Pro	Ala	Pro	378
Lys	Ser	Asn	Ile	Lys	Asp	Leu	Phe	Val	387
Thr	Thr	Asn	Tyr	Glu	Lys	Ala	Gly	Ser	396
Ser	Glu	Thr	Glu	Ile	Glu	Val	Ile	Cys	405
Tyr	Ile	Glu	Lys	Pro	Gly	Val	Glu	Thr	414
Leu	Glu	Asp	Ser	Val	Phe	420			

<210> 25

<211> 113

<212> PRT

<213> Mus musculus

<220>

<223> DEFENDER AGAINST CELL DEATH 1 (DAD-1)

<400> 25

Met	Ser	Ala	Ser	Val	Val	Ser	Val	Ile	9
Ser	Arg	Phe	Leu	Glu	Glu	Tyr	Leu	Ser	18
Ser	Thr	Pro	Gln	Arg	Leu	Lys	Leu	Leu	27
Asp	Gly	Tyr	Leu	Leu	Tyr	Ile	Leu	Leu	36
Thr	Gly	Ala	Leu	Gln	Phe	Gly	Tyr	Cys	45
Leu	Leu	Val	Gly	Thr	Phe	Pro	Phe	Asn	54
Ser	Phe	Leu	Ser	Gly	Phe	Ile	Ser	Cys	63
Val	Gly	Ser	Phe	Ile	Leu	Ala	Val	Cys	72
Leu	Arg	Ile	Gln	Ile	Asn	Pro	Gln	Asn	81
Lys	Ala	Asp	Phe	Gln	Gly	Ile	Ser	Pro	90
Glu	Arg	Ala	Phe	Ala	Asp	Phe	Leu	Phe	99
Gly	Ser	Thr	Ile	Leu	His	Leu	Val	Val	108
Met	Asn	Phe	Val	Gly	113				

<210> 26

<211> 113

<212> PRT

<213> Homo sapiens

<220>

<223> DEFENDER AGAINST CELL DEATH 1 (DAD-1)

<400> 26

Met	Ser	Ala	Ser	Val	Val	Ser	Val	Ile	9
Ser	Arg	Phe	Leu	Glu	Glu	Tyr	Leu	Ser	18
Ser	Thr	Pro	Gln	Arg	Leu	Lys	Leu	Leu	27
Asp	Ala	Tyr	Leu	Leu	Tyr	Ile	Leu	Leu	36
Thr	Gly	Ala	Leu	Gln	Phe	Gly	Tyr	Cys	45
Leu	Leu	Val	Gly	Thr	Phe	Pro	Phe	Asn	54
Ser	Phe	Leu	Ser	Gly	Phe	Ile	Ser	Cys	63
Val	Gly	Ser	Phe	Ile	Leu	Ala	Val	Cys	72
Leu	Arg	Ile	Gln	Ile	Asn	Pro	Gln	Asn	81
Lys	Ala	Asp	Phe	Gln	Gly	Ile	Ser	Pro	90
Glu	Arg	Ala	Phe	Ala	Asp	Phe	Leu	Phe	99
Ala	Ser	Thr	Ile	Leu	His	Leu	Val	Val	108
Met	Asn	Phe	Val	Gly	113				

<210> 27

<400> 27

000

<210> 28

<400> 28

000

<210> 29
<211> 97
<212> PRT
<213> Mus musculus

<220>
<223> MCP-2

<400> 29

Met	Lys	Ile	Tyr	Ala	Val	Leu	Leu	Cys	9
Leu	Leu	Leu	Ile	Ala	Val	Pro	Val	Ser	18
Pro	Glu	Lys	Leu	Thr	Gly	Pro	Asp	Lys	27
Ala	Pro	Val	Thr	Cys	Cys	Phe	His	Val	36
Leu	Lys	Leu	Lys	Ile	Pro	Leu	Arg	Val	45
Leu	Lys	Ser	Tyr	Glu	Arg	Ile	Asn	Asn	54
Ile	Gln	Cys	Pro	Met	Glu	Ala	Val	Val	63
Phe	Gln	Thr	Lys	Gln	Gly	Met	Ser	Leu	72
Cys	Val	Asp	Pro	Thr	Gln	Lys	Trp	Val	81
Ser	Glu	Tyr	Met	Glu	Ile	Leu	Asp	Gln	90
Lys	Ser	Gln	Ile	Leu	Gln	Pro	97		

<210> 30
<211> 99
<212> PRT
<213> Homo sapiens

<220>
<223> MCP-2

<400> 30

Met	Lys	Val	Ser	Ala	Ala	Leu	Leu	Cys	9
Leu	Leu	Leu	Met	Ala	Ala	Thr	Phe	Ser	18
Pro	Gln	Gly	Leu	Ala	Gln	Pro	Asp	Ser	27
Val	Ser	Ile	Pro	Ile	Thr	Cys	Cys	Phe	36
Asn	Val	Ile	Asn	Arg	Lys	Ile	Pro	Ile	45
Gln	Arg	Leu	Glu	Ser	Tyr	Thr	Arg	Ile	54
Thr	Asn	Ile	Gln	Cys	Pro	Lys	Glu	Ala	63
Val	Ile	Phe	Lys	Thr	Gln	Arg	Gly	Lys	72
Glu	Val	Cys	Ala	Asp	Pro	Lys	Glu	Arg	81
Trp	Val	Arg	Asp	Ser	Met	Lys	His	Leu	90
Asp	Gln	Ile	Phe	Gln	Asn	Leu	Lys	Pro	99

<210> 31
<211> 411
<212> PRT

<213> Mus musculus

<220>

<223> BAF57

<400> 31

Met	Ser	Lys	Arg	Pro	Ser	Tyr	Ala	Pro	9
Pro	Pro	Thr	Pro	Ala	Pro	Ala	Thr	Gln	18
Met	Pro	Ser	Thr	Pro	Gly	Phe	Val	Gly	27
Tyr	Asn	Pro	Tyr	Ser	His	Leu	Ala	Tyr	36
Asn	Asn	Tyr	Arg	Leu	Gly	Gly	Asn	Pro	45
Gly	Thr	Asn	Ser	Arg	Val	Thr	Ala	Ser	54
Ser	Gly	Ile	Thr	Ile	Pro	Lys	Pro	Pro	63
Lys	Pro	Pro	Asp	Lys	Pro	Leu	Met	Pro	72
Tyr	Met	Arg	Tyr	Ser	Arg	Lys	Val	Trp	81
Asp	Gln	Val	Lys	Ala	Ser	Asn	Pro	Asp	90
Leu	Lys	Leu	Trp	Glu	Ile	Gly	Lys	Ile	99
Ile	Gly	Gly	Met	Trp	Arg	Asp	Leu	Thr	108
Asp	Glu	Glu	Lys	Gln	Glu	Tyr	Leu	Asn	117
Glu	Tyr	Glu	Ala	Glu	Lys	Ile	Glu	Tyr	126
Asn	Glu	Ser	Met	Lys	Ala	Tyr	His	Asn	135
Ser	Pro	Ala	Tyr	Leu	Ala	Tyr	Ile	Asn	144
Ala	Lys	Ser	Arg	Ala	Glu	Ala	Ala	Leu	153
Glu	Glu	Glu	Ser	Arg	Gln	Arg	Gln	Ser	162
Arg	Met	Glu	Lys	Gly	Glu	Pro	Tyr	Met	171
Ser	Ile	Gln	Pro	Ala	Glu	Asp	Pro	Asp	180
Asp	Tyr	Asp	Asp	Gly	Phe	Ser	Met	Lys	189
His	Thr	Ala	Thr	Ala	Arg	Phe	Gln	Arg	198
Asn	His	Arg	Leu	Ile	Ser	Glu	Ile	Leu	207
Ser	Glu	Ser	Val	Val	Pro	Asp	Val	Arg	216
Ser	Val	Val	Thr	Thr	Ala	Arg	Met	Gln	225
Val	Leu	Lys	Arg	Gln	Val	Gln	Ser	Leu	234
Met	Val	His	Gln	Arg	Lys	Leu	Glu	Ala	243
Glu	Leu	Leu	Gln	Ile	Glu	Glu	Arg	His	252
Gln	Glu	Lys	Lys	Arg	Lys	Phe	Leu	Glu	261
Ser	Thr	Asp	Ser	Phe	Asn	Asn	Glu	Leu	270
Lys	Arg	Leu	Cys	Gly	Leu	Lys	Val	Glu	279
Val	Asp	Met	Glu	Lys	Ile	Ala	Ala	Glu	288
Ile	Ala	Gln	Ala	Glu	Glu	Gln	Ala	Arg	297
Lys	Arg	Gln	Glu	Glu	Arg	Glu	Lys	Glu	306
Ala	Ala	Glu	Gln	Ala	Glu	Arg	Ser	Gln	315
Ser	Ser	Met	Ala	Pro	Glu	Glu	Glu	Gln	324
Val	Ala	Asn	Lys	Ala	Glu	Glu	Lys	Lys	333
Asp	Glu	Glu	Ser	Ile	Pro	Met	Glu	Thr	342
Glu	Glu	Thr	His	Leu	Glu	Asp	Thr	Ala	351
Glu	Ser	Gln	Gln	Asn	Gly	Glu	Glu	Gly	360
Thr	Ser	Thr	Pro	Glu	Asp	Lys	Glu	Ser	369
Gly	Gln	Glu	Gly	Val	Asp	Ser	Met	Glu	378
Val	Glu	Gly	Thr	Ser	Asp	Ser	Asn	Thr	387
Gly	Ser	Glu	Ser	Asn	Ser	Ala	Thr	Val	396
Glu	Glu	Pro	Pro	Thr	Asp	Pro	Val	Pro	405

Glu Asp Glu Lys Lys Glu 411

<210> 32
 <211> 411
 <212> PRT
 <213> Homo sapiens

<220>
 <223> BAF57

<400> 32

Met	Ser	Lys	Arg	Pro	Ser	Tyr	Ala	Pro	9
Pro	Pro	Thr	Pro	Ala	Pro	Ala	Thr	Gln	18
Met	Pro	Ser	Thr	Pro	Gly	Phe	Val	Gly	27
Tyr	Asn	Pro	Tyr	Ser	His	Leu	Ala	Tyr	36
Asn	Asn	Tyr	Arg	Leu	Gly	Gly	Asn	Pro	45
Gly	Thr	Asn	Ser	Arg	Val	Thr	Ala	Ser	54
Ser	Gly	Ile	Thr	Ile	Pro	Lys	Pro	Pro	63
Lys	Pro	Pro	Asp	Lys	Pro	Leu	Met	Pro	72
Tyr	Met	Arg	Tyr	Ser	Arg	Lys	Val	Trp	81
Asp	Gln	Val	Lys	Ala	Ser	Asn	Pro	Asp	90
Leu	Lys	Leu	Trp	Glu	Ile	Gly	Lys	Ile	99
Ile	Gly	Gly	Met	Trp	Arg	Asp	Leu	Thr	108
Asp	Glu	Glu	Lys	Gln	Glu	Tyr	Leu	Asn	117
Glu	Tyr	Glu	Ala	Glu	Lys	Ile	Glu	Tyr	126
Asn	Glu	Ser	Met	Lys	Ala	Tyr	His	Asn	135
Ser	Pro	Ala	Tyr	Leu	Ala	Tyr	Ile	Asn	144
Ala	Lys	Ser	Arg	Ala	Glu	Ala	Ala	Leu	153
Glu	Glu	Glu	Ser	Arg	Gln	Arg	Gln	Ser	162
Arg	Met	Glu	Lys	Gly	Glu	Pro	Tyr	Met	171
Ser	Ile	Gln	Pro	Ala	Glu	Asp	Pro	Asp	180
Asp	Tyr	Asp	Asp	Gly	Phe	Ser	Met	Lys	189
His	Thr	Ala	Thr	Ala	Arg	Phe	Gln	Arg	198
Asn	His	Arg	Leu	Ile	Ser	Glu	Ile	Leu	207
Ser	Glu	Ser	Val	Val	Pro	Asp	Val	Arg	216
Ser	Val	Val	Thr	Thr	Ala	Arg	Met	Gln	225
Val	Leu	Lys	Arg	Gln	Val	Gln	Ser	Leu	234
Met	Val	His	Gln	Arg	Lys	Leu	Glu	Ala	243
Glu	Leu	Leu	Gln	Ile	Glu	Glu	Arg	His	252
Gln	Glu	Lys	Lys	Arg	Lys	Phe	Leu	Glu	261
Ser	Thr	Asp	Ser	Phe	Asn	Asn	Glu	Leu	270
Lys	Arg	Leu	Cys	Gly	Leu	Lys	Val	Glu	279
Val	Asp	Met	Glu	Lys	Ile	Ala	Ala	Glu	288
Ile	Ala	Gln	Ala	Glu	Glu	Gln	Ala	Arg	297
Lys	Arg	Gln	Glu	Glu	Arg	Glu	Lys	Glu	306
Ala	Ala	Glu	Gln	Ala	Glu	Arg	Ser	Gln	315
Ser	Ser	Ile	Val	Pro	Glu	Glu	Glu	Gln	324
Ala	Ala	Asn	Lys	Gly	Glu	Glu	Lys	Lys	333
Asp	Asp	Glu	Asn	Ile	Pro	Met	Glu	Thr	342

Glu	Glu	Thr	His	Leu	Glu	Glu	Thr	Thr	351
Glu	Ser	Gln	Gln	Asn	Gly	Glu	Glu	Gly	360
Thr	Ser	Thr	Pro	Glu	Asp	Lys	Glu	Ser	369
Gly	Gln	Glu	Gly	Val	Asp	Ser	Met	Ala	378
Glu	Glu	Gly	Thr	Ser	Asp	Ser	Asn	Thr	387
Gly	Ser	Glu	Ser	Asn	Ser	Ala	Thr	Val	396
Glu	Glu	Pro	Pro	Thr	Asp	Pro	Ile	Pro	405
Glu	Asp	Glu	Lys	Lys	Glu	411			

<210> 33

<211> 821

<212> PRT

<213> Mus musculus

<220>

<223> EPS8

<400> 33

Met	Asn	Gly	His	Met	Ser	Asn	Arg	Ser	9
Ser	Gly	Tyr	Gly	Val	Tyr	Pro	Ser	Gln	18
Leu	Asn	Gly	Tyr	Gly	Ser	Ser	Pro	Pro	27
Tyr	Ser	Gln	Met	Asp	Arg	Glu	His	Ser	36
Ser	Arg	Thr	Ser	Ala	Lys	Ala	Leu	Tyr	45
Glu	Gln	Arg	Lys	Asn	Tyr	Ala	Arg	Asp	54
Ser	Val	Ser	Ser	Val	Ser	Asp	Val	Ser	63
Gln	Tyr	Arg	Val	Glu	His	Leu	Thr	Thr	72
Phe	Val	Leu	Asp	Arg	Lys	Asp	Ala	Met	81
Ile	Thr	Val	Glu	Asp	Gly	Ile	Arg	Lys	90
Leu	Lys	Leu	Leu	Asp	Ala	Lys	Gly	Lys	99
Val	Trp	Thr	Gln	Asp	Met	Ile	Leu	Gln	108
Val	Asp	Asp	Arg	Ala	Val	Ser	Leu	Ile	117
Asp	Leu	Glu	Ser	Lys	Asn	Glu	Leu	Glu	126
Asn	Phe	Pro	Leu	Asn	Thr	Ile	Ser	His	135
Cys	Gln	Ala	Val	Val	His	Ala	Cys	Ser	144
Tyr	Asp	Ser	Ile	Leu	Ala	Leu	Val	Cys	153
Lys	Glu	Pro	Thr	Gln	Ser	Lys	Pro	Asp	162
Leu	His	Leu	Phe	Gln	Cys	Asp	Glu	Val	171
Lys	Ala	Asn	Leu	Ile	Ser	Glu	Asp	Ile	180
Glu	Ser	Ala	Ile	Ser	Asp	Ser	Lys	Gly	189
Gly	Lys	Gln	Lys	Arg	Arg	Pro	Glu	Ala	198
Leu	Arg	Met	Ile	Ala	Lys	Ala	Asp	Pro	207
Gly	Ile	Pro	Pro	Pro	Pro	Arg	Ala	Pro	216
Ala	Pro	Val	Pro	Pro	Gly	Thr	Val	Thr	225
Gln	Val	Asp	Val	Arg	Ser	Arg	Val	Ala	234
Ala	Trp	Ser	Ala	Trp	Ala	Ala	Asp	Gln	243
Gly	Asp	Phe	Glu	Lys	Pro	Arg	Gln	Tyr	252
His	Glu	Gln	Glu	Glu	Thr	Pro	Glu	Met	261
Met	Ala	Ala	Arg	Ile	Asp	Arg	Asp	Val	270
Gln	Ile	Leu	Asn	His	Ile	Leu	Asp	Asp	279
Ile	Glu	Phe	Phe	Ile	Thr	Lys	Leu	Gln	288

Lys	Ala	Ala	Glu	Ala	Phe	Ser	Glu	Leu	297
Ser	Lys	Arg	Lys	Lys	Ser	Lys	Lys	Ser	306
Lys	Arg	Lys	Gly	Pro	Gly	Glu	Gly	Val	315
Leu	Thr	Leu	Arg	Ala	Lys	Pro	Pro	Pro	324
Pro	Asp	Glu	Phe	Val	Asp	Cys	Phe	Gln	333
Lys	Phe	Lys	His	Gly	Phe	Asn	Leu	Leu	342
Ala	Lys	Leu	Lys	Ser	His	Ile	Gln	Asn	351
Pro	Ser	Ala	Ser	Asp	Leu	Val	His	Phe	360
Leu	Phe	Thr	Pro	Leu	Asn	Met	Val	Val	369
Gln	Ala	Thr	Gly	Gly	Pro	Glu	Leu	Ala	378
Ser	Ser	Val	Leu	Ser	Pro	Leu	Leu	Thr	387
Lys	Asp	Thr	Val	Asp	Phe	Leu	Asn	Tyr	396
Thr	Ala	Thr	Ala	Glu	Glu	Arg	Lys	Leu	405
Trp	Met	Ser	Leu	Gly	Asp	Ser	Trp	Val	414
Lys	Val	Arg	Ala	Glu	Trp	Pro	Lys	Glu	423
Gln	Phe	Ile	Pro	Pro	Tyr	Val	Pro	Arg	432
Phe	Arg	Asn	Gly	Trp	Glu	Pro	Pro	Met	441
Leu	Asn	Phe	Met	Gly	Ala	Pro	Thr	Glu	450
Gln	Asp	Met	Tyr	Gln	Leu	Ala	Glu	Ser	459
Val	Ala	Asn	Ala	Glu	His	Gln	Arg	Lys	468
Gln	Asp	Ser	Lys	Arg	Leu	Ser	Thr	Glu	477
His	Ser	Asn	Val	Ser	Asp	Tyr	Pro	Pro	486
Ala	Asp	Gly	Tyr	Ala	Tyr	Ser	Ser	Ser	495
Met	Tyr	His	Arg	Gly	Pro	His	Ala	Asp	504
His	Gly	Glu	Ala	Ala	Met	Pro	Phe	Lys	513
Ser	Thr	Pro	Asn	His	Gln	Val	Asp	Arg	522
Asn	Tyr	Asp	Ala	Val	Lys	Thr	Gln	Pro	531
Lys	Lys	Tyr	Ala	Lys	Ser	Lys	Tyr	Asp	540
Phe	Val	Ala	Arg	Asn	Ser	Ser	Glu	Leu	549
Ser	Val	Met	Lys	Asp	Asp	Val	Leu	Glu	558
Ile	Leu	Asp	Asp	Arg	Arg	Gln	Trp	Trp	567
Lys	Val	Arg	Asn	Ala	Ser	Gly	Asp	Ser	576
Gly	Phe	Val	Pro	Asn	Asn	Ile	Leu	Asp	585
Ile	Met	Arg	Thr	Pro	Glu	Ser	Gly	Val	594
Gly	Arg	Ala	Asp	Pro	Pro	Tyr	Thr	His	603
Thr	Ile	Gln	Lys	Gln	Arg	Thr	Glu	Tyr	612
Gly	Leu	Arg	Ser	Ala	Asp	Thr	Pro	Ser	621
Ala	Pro	Ser	Pro	Pro	Pro	Thr	Pro	Ala	630
Pro	Val	Pro	Val	Pro	Leu	Pro	Pro	Ser	639
Val	Pro	Ala	Pro	Val	Ser	Val	Pro	Lys	648
Val	Pro	Ala	Asp	Val	Thr	Arg	Gln	Asn	657
Ser	Ser	Ser	Ser	Asp	Ser	Gly	Gly	Ser	666
Ile	Val	Arg	Asp	Ser	Gln	Arg	Tyr	Lys	675
Gln	Leu	Pro	Val	Asp	Arg	Arg	Lys	Ser	684
Gln	Met	Glu	Glu	Val	Gln	Asp	Glu	Leu	693
Phe	Gln	Arg	Leu	Thr	Ile	Gly	Arg	Ser	702
Ala	Ala	Gln	Arg	Lys	Phe	His	Val	Pro	711
Arg	Gln	Asn	Val	Pro	Val	Ile	Asn	Ile	720
Thr	Tyr	Asp	Ser	Ser	Pro	Glu	Glu	Val	729
Lys	Thr	Trp	Leu	Gln	Ser	Lys	Gly	Phe	738
Asn	Pro	Val	Thr	Val	Asn	Ser	Leu	Gly	747
Val	Leu	Asn	Gly	Ala	Gln	Leu	Phe	Ser	756

Leu	Asn	Lys	Asp	Glu	Leu	Arg	Ser	Val	765
Cys	Pro	Glu	Gly	Ala	Arg	Val	Phe	Asn	774
Gln	Ile	Thr	Val	Gln	Lys	Ala	Ala	Leu	783
Glu	Asp	Ser	Asn	Gly	Ser	Ser	Glu	Leu	792
Gln	Glu	Ile	Met	Arg	Arg	Arg	Gln	Glu	801
Lys	Ile	Ser	Ala	Ala	Ala	Ser	Asp	Ser	810
Gly	Val	Glu	Ser	Phe	Asp	Glu	Gly	Ser	819
Ser	His	821							

<210> 34

<211> 822

<212> PRT

<213> Homo sapiens

<220>

<223> EPS8

<400> 34

Met	Asn	Gly	His	Ile	Ser	Asn	His	Pro	9
Ser	Ser	Phe	Gly	Met	Tyr	Pro	Ser	Gln	18
Met	Asn	Gly	Tyr	Gly	Ser	Ser	Pro	Thr	27
Phe	Ser	Gln	Thr	Asp	Arg	Glu	His	Gly	36
Ser	Lys	Thr	Ser	Ala	Lys	Ala	Leu	Tyr	45
Glu	Gln	Arg	Lys	Asn	Tyr	Ala	Arg	Asp	54
Ser	Val	Ser	Ser	Val	Ser	Asp	Ile	Ser	63
Gln	Tyr	Arg	Val	Glu	His	Leu	Thr	Thr	72
Phe	Val	Leu	Asp	Arg	Lys	Asp	Ala	Met	81
Ile	Thr	Val	Asp	Asp	Gly	Ile	Arg	Lys	90
Leu	Lys	Leu	Leu	Asp	Ala	Lys	Gly	Lys	99
Val	Trp	Thr	Gln	Asp	Met	Ile	Leu	Gln	108
Val	Asp	Asp	Arg	Ala	Val	Ser	Leu	Ile	117
Asp	Leu	Glu	Ser	Lys	Asn	Glu	Leu	Glu	126
Asn	Phe	Pro	Leu	Asn	Thr	Ile	Gln	His	135
Cys	Gln	Ala	Val	Met	His	Ser	Cys	Ser	144
Tyr	Asp	Ser	Val	Leu	Ala	Leu	Val	Cys	153
Lys	Glu	Pro	Thr	Gln	Asn	Lys	Pro	Asp	162
Leu	His	Leu	Phe	Gln	Cys	Asp	Glu	Val	171
Lys	Ala	Asn	Leu	Ile	Ser	Glu	Asp	Ile	180
Glu	Ser	Ala	Ile	Ser	Asp	Ser	Lys	Gly	189
Gly	Lys	Gln	Lys	Arg	Arg	Pro	Asp	Ala	198
Leu	Arg	Met	Ile	Ser	Asn	Ala	Asp	Pro	207
Ser	Ile	Pro	Pro	Pro	Pro	Arg	Ala	Pro	216
Ala	Pro	Ala	Pro	Pro	Gly	Thr	Val	Thr	225
Gln	Val	Asp	Val	Arg	Ser	Arg	Val	Ala	234
Ala	Trp	Ser	Ala	Trp	Ala	Ala	Asp	Gln	243
Gly	Asp	Phe	Glu	Lys	Pro	Arg	Gln	Tyr	252
His	Glu	Gln	Glu	Glu	Thr	Pro	Glu	Met	261
Met	Ala	Ala	Arg	Ile	Asp	Arg	Asp	Val	270
Gln	Ile	Leu	Asn	His	Ile	Leu	Asp	Asp	279
Ile	Glu	Phe	Phe	Ile	Thr	Lys	Leu	Gln	288

Lys	Ala	Ala	Glu	Ala	Phe	Ser	Glu	Leu	297
Ser	Lys	Arg	Lys	Lys	Asn	Lys	Lys	Gly	306
Lys	Arg	Lys	Gly	Pro	Gly	Glu	Gly	Val	315
Leu	Thr	Leu	Arg	Ala	Lys	Pro	Pro	Pro	324
Pro	Asp	Glu	Phe	Leu	Asp	Cys	Phe	Gln	333
Lys	Phe	Lys	His	Gly	Phe	Asn	Leu	Leu	342
Ala	Lys	Leu	Lys	Ser	His	Ile	Gln	Asn	351
Pro	Ser	Ala	Ala	Asp	Leu	Val	His	Phe	360
Leu	Phe	Thr	Pro	Leu	Asn	Met	Val	Val	369
Gln	Ala	Thr	Gly	Gly	Pro	Glu	Leu	Ala	378
Ser	Ser	Val	Leu	Ser	Pro	Leu	Leu	Asn	387
Lys	Asp	Thr	Ile	Asp	Phe	Leu	Asn	Tyr	396
Thr	Val	Asn	Gly	Asp	Glu	Arg	Gln	Leu	405
Trp	Met	Ser	Leu	Gly	Gly	Thr	Trp	Met	414
Lys	Ala	Arg	Ala	Glu	Trp	Pro	Lys	Glu	423
Gln	Phe	Ile	Pro	Pro	Tyr	Val	Pro	Arg	432
Phe	Arg	Asn	Gly	Trp	Glu	Pro	Pro	Met	441
Leu	Asn	Phe	Met	Gly	Ala	Thr	Met	Glu	450
Gln	Asp	Leu	Tyr	Gln	Leu	Ala	Glu	Ser	459
Val	Ala	Asn	Val	Ala	Glu	His	Gln	Arg	468
Lys	Gln	Glu	Ile	Lys	Arg	Leu	Ser	Thr	477
Glu	His	Ser	Ser	Val	Ser	Glu	Tyr	His	486
Pro	Ala	Asp	Gly	Tyr	Ala	Phe	Ser	Ser	495
Asn	Ile	Tyr	Thr	Arg	Gly	Ser	His	Leu	504
Asp	Gln	Gly	Glu	Ala	Ala	Val	Ala	Phe	513
Lys	Pro	Thr	Ser	Asn	Arg	His	Ile	Asp	522
Arg	Asn	Tyr	Glu	Pro	Leu	Lys	Thr	Gln	531
Pro	Lys	Lys	Tyr	Ala	Lys	Ser	Lys	Tyr	540
Asp	Phe	Val	Ala	Arg	Asn	Asn	Ser	Glu	549
Leu	Ser	Val	Leu	Lys	Asp	Asp	Ile	Leu	558
Glu	Ile	Leu	Asp	Asp	Arg	Lys	Gln	Trp	567
Trp	Lys	Val	Arg	Asn	Ala	Ser	Gly	Asp	576
Ser	Gly	Phe	Val	Pro	Asn	Asn	Ile	Leu	585
Asp	Ile	Val	Arg	Pro	Pro	Glu	Ser	Gly	594
Leu	Gly	Arg	Ala	Asp	Pro	Pro	Tyr	Thr	603
His	Thr	Ile	Gln	Lys	Gln	Arg	Met	Glu	612
Tyr	Gly	Pro	Arg	Pro	Ala	Asp	Thr	Pro	621
Pro	Ala	Pro	Ser	Pro	Pro	Pro	Thr	Pro	630
Ala	Pro	Val	Pro	Val	Pro	Leu	Pro	Pro	639
Ser	Thr	Pro	Ala	Pro	Val	Pro	Val	Ser	648
Lys	Val	Pro	Ala	Asn	Ile	Thr	Arg	Gln	657
Asn	Ser	Ser	Ser	Ser	Asp	Ser	Gly	Gly	666
Ser	Ile	Val	Arg	Asp	Ser	Gln	Arg	His	675
Lys	Gln	Leu	Pro	Val	Asp	Arg	Arg	Lys	684
Ser	Gln	Met	Glu	Glu	Val	Gln	Asp	Glu	693
Leu	Ile	His	Arg	Leu	Thr	Ile	Gly	Arg	702
Ser	Ala	Ala	Gln	Lys	Lys	Phe	His	Val	711
Pro	Arg	Gln	Asn	Val	Pro	Val	Ile	Asn	720
Ile	Thr	Tyr	Asp	Ser	Thr	Pro	Glu	Asp	729
Val	Lys	Thr	Trp	Leu	Gln	Ser	Lys	Gly	738
Phe	Asn	Pro	Val	Thr	Val	Asn	Ser	Leu	747
Gly	Val	Leu	Asn	Gly	Ala	Gln	Leu	Phe	756

Ser	Leu	Asn	Lys	Asp	Glu	Leu	Arg	Thr	765
Val	Cys	Pro	Glu	Gly	Ala	Arg	Val	Tyr	774
Ser	Gln	Ile	Thr	Val	Gln	Lys	Ala	Ala	783
Leu	Glu	Asp	Ser	Ser	Gly	Ser	Ser	Glu	792
Leu	Gln	Glu	Ile	Met	Arg	Arg	Arg	Gln	801
Glu	Lys	Ile	Ser	Ala	Ala	Ala	Ser	Asp	810
Ser	Gly	Val	Glu	Ser	Phe	Asp	Glu	Gly	819
Ser	Ser	His	822						

<210> 35

<211> 470

<212> PRT

<213> Mus musculus

<220>

<223> KIAA1247

<400> 35

Met	Leu	Val	Glu	Thr	Gly	Glu	Leu	Asp	9
Asn	Thr	Tyr	Ile	Leu	Tyr	Thr	Ala	Asp	18
His	Gly	Tyr	His	Ile	Gly	Gln	Phe	Gly	27
Leu	Val	Lys	Gly	Lys	Ser	Met	Pro	Tyr	36
Glu	Phe	Asp	Ile	Arg	Val	Pro	Phe	Tyr	45
Val	Arg	Gly	Pro	Asn	Val	Glu	Ala	Gly	54
Ser	Leu	Asn	Pro	His	Ile	Val	Leu	Asn	63
Ile	Asp	Leu	Gly	Pro	His	His	Thr	Gly	72
Tyr	Arg	Trp	Thr	Gly	His	Pro	Cys	Arg	81
His	Gly	Arg	Glu	Val	Tyr	Ser	Gln	Thr	90
Thr	Gly	Leu	Arg	Ala	Ala	Ser	Glu	Pro	99
Val	Pro	Leu	Glu	Lys	Glu	Ala	Glu	Gly	108
Leu	Gly	Glu	Thr	Pro	Ser	Trp	Trp	Arg	117
Glu	Ala	Asn	Leu	Leu	His	Lys	Arg	Glu	126
Gly	Asp	Lys	Val	Asn	Ala	Gln	Glu	Glu	135
Asn	Phe	Leu	Pro	Lys	Tyr	Gln	Arg	Val	144
Lys	Asp	Leu	Cys	Gln	Arg	Ala	Glu	Tyr	153
Gln	Thr	Ala	Cys	Glu	Gln	Leu	Gly	Gln	162
Lys	Trp	Gln	Cys	Val	Glu	Asp	Ala	Ser	171
Gly	Thr	Leu	Lys	Leu	His	Lys	Cys	Lys	180
Gly	Pro	Met	Arg	Phe	Gly	Gly	Gly	Gly	189
Gly	Ser	Arg	Ala	Leu	Ser	Asn	Leu	Val	198
Pro	Lys	Tyr	Asp	Gly	Gln	Ser	Ser	Glu	207
Ala	Cys	Ser	Cys	Asp	Ser	Gly	Gly	Gly	216
Gly	Asp	Tyr	Lys	Leu	Gly	Leu	Ala	Gly	225
Arg	Arg	Lys	Leu	Phe	Lys	Lys	Lys	Tyr	234
Lys	Thr	Ser	Tyr	Ala	Arg	Asn	Arg	Ser	243
Ile	Arg	Ser	Val	Ala	Ile	Glu	Val	Asp	252
Gly	Glu	Ile	Tyr	His	Val	Gly	Leu	Asp	261
Thr	Val	Pro	Gln	Pro	Arg	Asn	Leu	Ser	270
Lys	Pro	His	Trp	Pro	Gly	Ala	Pro	Glu	279
Asp	Gln	Asp	Asp	Lys	Asp	Gly	Gly	Ser	288

Phe	Ser	Gly	Thr	Gly	Gly	Leu	Pro	Asp	297
Tyr	Ser	Ala	Pro	Asn	Pro	Ile	Lys	Val	306
Thr	His	Arg	Cys	Tyr	Ile	Leu	Glu	Asn	315
Asp	Thr	Val	Gln	Cys	Asp	Leu	Asp	Leu	324
Tyr	Lys	Ser	Leu	Gln	Ala	Trp	Lys	Asp	333
His	Lys	Leu	His	Ile	Asp	His	Glu	Ile	342
Glu	Thr	Leu	Gln	Asn	Lys	Ile	Lys	Asn	351
Leu	Arg	Glu	Val	Arg	Gly	His	Leu	Lys	360
Lys	Lys	Arg	Pro	Glu	Glu	Cys	Asp	Cys	369
His	???	Ile	Ser	Tyr	His	Ser	Gln	His	378
Lys	Gly	Arg	Leu	Lys	His	Lys	Gly	Ser	387
Ser	Leu	His	Pro	Phe	Arg	Lys	Gly	Leu	396
Gln	Glu	Lys	Asp	Lys	Val	Trp	Leu	Leu	405
Arg	Asp	Arg	Asn	Ala	Arg	Arg	Asn	Cys	414
Ala	Thr	Ala	Gln	Thr	Ala	Ala	Glu	Gln	423
Arg	Tyr	Val	Gln	His	Ala	Arg	Pro	His	432
Val	Leu	Tyr	Pro	Arg	Gln	Pro	Pro	Leu	441
Ala	Asp	Gly	Ala	Thr	Leu	Asp	Ala	Gly	450
Ala	Val	Leu	Arg	Leu	His	Gln	Arg	Gln	459
Gln	Gln	His	Val	Leu	Val	Leu	Glu	Asp	468
His	Lys								470

<210> 36

<211> 690

<212> PRT

<213> Homo sapiens

<220>

<223> KIAA1247

<400> 36

Glu	Lys	His	Gly	Ser	Asp	Tyr	Ser	Lys	9
Asp	Tyr	Leu	Thr	Asp	Leu	Ile	Thr	Asn	18
Asp	Ser	Val	Ser	Phe	Phe	Arg	Thr	Ser	27
Lys	Lys	Met	Tyr	Pro	His	Arg	Pro	Val	36
Leu	Met	Val	Ile	Ser	His	Ala	Ala	Pro	45
His	Gly	Pro	Glu	Asp	Ser	Ala	Pro	Gln	54
Tyr	Ser	Arg	Leu	Phe	Pro	Asn	Ala	Ser	63
Gln	His	Ile	Thr	Pro	Ser	Tyr	Asn	Tyr	72
Ala	Pro	Asn	Pro	Asp	Lys	His	Trp	Ile	81
Met	Arg	Tyr	Thr	Gly	Pro	Met	Lys	Pro	90
Ile	His	Met	Glu	Phe	Thr	Asn	Met	Leu	99
Gln	Arg	Lys	Arg	Leu	Gln	Thr	Leu	Met	108
Ser	Val	Asp	Asp	Ser	Met	Glu	Thr	Ile	117
Tyr	Asn	Met	Leu	Val	Glu	Thr	Gly	Glu	126
Leu	Asp	Asn	Thr	Tyr	Ile	Val	Tyr	Thr	135
Ala	Asp	His	Gly	Tyr	His	Ile	Gly	Gln	144
Phe	Gly	Leu	Val	Lys	Gly	Lys	Ser	Met	153
Pro	Tyr	Glu	Phe	Asp	Ile	Arg	Val	Pro	162

Phe	Tyr	Val	Arg	Gly	Pro	Asn	Val	Glu	171
Ala	Gly	Cys	Leu	Asn	Pro	His	Ile	Val	180
Leu	Asn	Ile	Asp	Leu	Ala	Pro	Thr	Ile	189
Leu	Asp	Ile	Ala	Gly	Leu	Asp	Ile	Pro	198
Ala	Asp	Met	Asp	Gly	Lys	Ser	Ile	Leu	207
Lys	Leu	Leu	Asp	Thr	Glu	Arg	Pro	Val	216
Asn	Arg	Phe	His	Leu	Lys	Lys	Lys	Met	225
Arg	Val	Trp	Arg	Asp	Ser	Phe	Leu	Val	234
Glu	Arg	Gly	Lys	Leu	Leu	His	Lys	Arg	243
Asp	Asn	Asp	Lys	Val	Asp	Ala	Gln	Glu	252
Glu	Asn	Phe	Leu	Pro	Lys	Tyr	Gln	Arg	261
Val	Lys	Asp	Leu	Cys	Gln	Arg	Ala	Glu	270
Tyr	Gln	Thr	Ala	Cys	Glu	Gln	Leu	Gly	279
Gln	Lys	Trp	Gln	Cys	Val	Glu	Asp	Ala	288
Thr	Gly	Lys	Leu	Lys	Leu	His	Lys	Cys	297
Lys	Gly	Pro	Met	Arg	Leu	Gly	Gly	Ser	306
Arg	Ala	Leu	Ser	Asn	Leu	Val	Pro	Lys	315
Tyr	Tyr	Gly	Gln	Gly	Ser	Glu	Ala	Cys	324
Thr	Cys	Asp	Ser	Gly	Asp	Tyr	Lys	Leu	333
Ser	Leu	Ala	Gly	Arg	Arg	Lys	Lys	Leu	342
Phe	Lys	Lys	Lys	Tyr	Lys	Ala	Ser	Tyr	351
Val	Arg	Ser	Arg	Ser	Ile	Arg	Ser	Val	360
Ala	Ile	Glu	Val	Asp	Gly	Arg	Val	Tyr	369
His	Val	Gly	Leu	Gly	Asp	Ala	Ala	Gln	378
Pro	Arg	Asn	Leu	Thr	Lys	Arg	His	Trp	387
Pro	Gly	Ala	Pro	Glu	Asp	Gln	Asp	Asp	396
Lys	Asp	Gly	Gly	Asp	Phe	Ser	Gly	Thr	405
Gly	Gly	Leu	Pro	Asp	Tyr	Ser	Ala	Ala	414
Asn	Pro	Ile	Lys	Val	Thr	His	Arg	Cys	423
Tyr	Ile	Leu	Glu	Asn	Asp	Thr	Val	Gln	432
Cys	Asp	Leu	Asp	Leu	Tyr	Lys	Ser	Leu	441
Gln	Ala	Trp	Lys	Asp	His	Lys	Leu	His	450
Ile	Asp	His	Glu	Ile	Glu	Thr	Leu	Gln	459
Asn	Lys	Ile	Lys	Asn	Leu	Arg	Glu	Val	468
Arg	Gly	His	Leu	Lys	Lys	Lys	Arg	Pro	477
Glu	Glu	Cys	Asp	Cys	His	Lys	Ile	Ser	486
Tyr	His	Thr	Gln	His	Lys	Gly	Arg	Leu	495
Lys	His	Arg	Gly	Ser	Ser	Leu	His	Pro	504
Phe	Arg	Lys	Gly	Leu	Gln	Glu	Lys	Asp	513
Lys	Val	Trp	Leu	Leu	Arg	Glu	Gln	Lys	522
Arg	Lys	Lys	Lys	Leu	Arg	Lys	Leu	Leu	531
Lys	Arg	Leu	Gln	Asn	Asn	Asp	Thr	Cys	540
Ser	Met	Pro	Gly	Leu	Thr	Cys	Phe	Thr	549
His	Asp	Asn	Gln	His	Trp	Gln	Thr	Ala	558
Pro	Phe	Trp	Thr	Leu	Gly	Pro	Phe	Cys	567
Ala	Cys	Thr	Ser	Ala	Asn	Asn	Asn	Thr	576
Tyr	Trp	Cys	Met	Arg	Thr	Ile	Asn	Glu	585
Thr	His	Asn	Phe	Leu	Phe	Cys	Glu	Phe	594
Ala	Thr	Gly	Phe	Leu	Glu	Tyr	Phe	Asp	603
Leu	Asn	Thr	Asp	Pro	Tyr	Gln	Leu	Met	612
Asn	Ala	Val	Asn	Thr	Leu	Asp	Arg	Asp	621
Val	Leu	Asn	Gln	Leu	His	Val	Gln	Leu	630

Met	Glu	Leu	Arg	Ser	Cys	Lys	Gly	Tyr	639
Lys	Gln	Cys	Asn	Pro	Arg	Thr	Arg	Asn	648
Met	Asp	Leu	Gly	Leu	Lys	Asp	Gly	Gly	657
Ser	Tyr	Glu	Gln	Tyr	Arg	Gln	Phe	Gln	666
Arg	Arg	Lys	Trp	Pro	Glu	Met	Lys	Arg	675
Pro	Ser	Ser	Lys	Ser	Leu	Gly	Gln	Leu	684
Trp	Glu	Gly	Trp	Glu	Gly	690			

<210> 37

<211> 212

<212> PRT

<213> Mus musculus

<220>

<223> Phospholipase Inhibitor

<400> 37

Met	Ile	Leu	Phe	Arg	Arg	His	Arg	Thr	9
Phe	Leu	Leu	Ala	Phe	Thr	Leu	Leu	Cys	18
Thr	Leu	Leu	Gly	Leu	Gly	Cys	Pro	Leu	27
Thr	Cys	Glu	Val	Cys	Lys	Gly	Ser	Gly	36
His	Thr	Cys	Ser	Gly	Lys	Met	Lys	Thr	45
Cys	Glu	Asp	Gly	Lys	Asp	Ala	Cys	Val	54
Val	Leu	Val	Ser	Glu	Ser	Ser	Thr	Lys	63
Gly	Arg	Lys	Ser	Val	Asn	Thr	Phe	Lys	72
Ala	Cys	Met	Lys	Tyr	Lys	Asp	Cys	Tyr	81
Ser	Gly	Phe	Val	Ser	Thr	Thr	Met	Thr	90
Pro	Ser	Asp	Tyr	Met	Val	Ser	Asn	Ala	99
His	Cys	Cys	Gln	Ser	Asp	Gly	Cys	Asn	108
Ser	Gly	Ser	Val	Pro	Pro	Pro	Leu	Asn	117
Asn	Arg	Thr	Glu	Asn	Gly	Leu	Met	Cys	126
Pro	Ser	Cys	Ile	Ala	Pro	Phe	Gln	Glu	135
Thr	Cys	Pro	Gly	Thr	Gln	Ala	Ala	Arg	144
Cys	Val	Gly	Arg	Glu	Thr	His	Cys	Ile	153
Tyr	Phe	Ala	Gly	Asn	Val	Gln	Ala	Gly	162
Ile	Ile	His	Thr	Lys	Phe	Ala	Thr	Arg	171
Gly	Cys	Ala	Thr	Glu	Ser	Ala	Cys	His	180
Thr	Lys	Ala	Gly	Ala	Glu	Val	Pro	Ser	189
Ala	Phe	Tyr	Leu	Tyr	Phe	Leu	Arg	Arg	198
Ala	Asp	Cys	Leu	Pro	Ala	Pro	Tyr	Pro	207
Pro	Gly	Arg	Gly	Glu	212				

<210> 38

<211> 204

<212> PRT

<213> Homo sapiens

<220>

<223> Phospholipase Inhibitor

<400> 38

Met	Arg	Leu	Ser	Arg	Arg	Pro	Glu	Thr	9
Phe	Leu	Leu	Ala	Phe	Val	Leu	Leu	Cys	18
Thr	Leu	Leu	Gly	Leu	Gly	Cys	Pro	Leu	27
His	Cys	Glu	Ile	Cys	Thr	Ala	Ala	Gly	36
Ser	Arg	Cys	His	Gly	Gln	Met	Lys	Thr	45
Cys	Ser	Ser	Asp	Lys	Asp	Thr	Cys	Val	54
Leu	Leu	Val	Gly	Lys	Ala	Thr	Ser	Lys	63
Gly	Lys	Glu	Leu	Val	His	Thr	Tyr	Lys	72
Gly	Cys	Ile	Arg	Ser	Gln	Asp	Cys	Tyr	81
Ser	Gly	Val	Ile	Ser	Thr	Thr	Met	Gly	90
Pro	Lys	Asp	His	Met	Val	Thr	Ser	Ser	99
Phe	Cys	Cys	Gln	Ser	Asp	Gly	Cys	Asn	108
Ser	Ala	Phe	Leu	Ser	Val	Pro	Leu	Thr	117
Asn	Leu	Thr	Glu	Asn	Gly	Leu	Met	Cys	126
Pro	Ala	Cys	Thr	Ala	Ser	Phe	Arg	Asp	135
Lys	Cys	Met	Gly	Pro	Met	Thr	His	Cys	144
Thr	Gly	Lys	Glu	Asn	His	Cys	Val	Ser	153
Leu	Ser	Gly	His	Val	Gln	Ala	Gly	Ile	162
Phe	Lys	Pro	Arg	Phe	Ala	Met	Arg	Gly	171
Cys	Ala	Thr	Glu	Ser	Met	Cys	Phe	Thr	180
Lys	Pro	Gly	Ala	Glu	Val	Pro	Thr	Gly	189
Thr	Asn	Val	Leu	Phe	Leu	His	His	Ile	198
Glu	Cys	Thr	His	Ser	Pro				204

<210> 39

<211> 331

<212> PRT

<213> Mus musculus

<220>

<223> EAT/MCL-1

<400> 39

Met	Phe	Gly	Leu	Arg	Arg	Asn	Ala	Val	9
Ile	Gly	Leu	Asn	Leu	Tyr	Cys	Gly	Gly	18
Ala	Ser	Leu	Gly	Ala	Gly	Gly	Gly	Ser	27
Pro	Ala	Gly	Ala	Arg	Leu	Val	Ala	Glu	36
Glu	Ala	Lys	Ala	Arg	Arg	Glu	Gly	Gly	45
Gly	Glu	Ala	Ala	Leu	Leu	Pro	Gly	Ala	54
Arg	Val	Val	Ala	Arg	Pro	Pro	Pro	Val	63
Gly	Ala	Glu	Asp	Pro	Asp	Val	Thr	Ala	72
Ser	Ala	Glu	Arg	Arg	Leu	His	Lys	Ser	81
Pro	Gly	Leu	Leu	Ala	Val	Pro	Pro	Glu	90
Glu	Met	Ala	Ala	Ser	Ala	Ala	Ala	Ala	99
Ile	Val	Ser	Pro	Glu	Glu	Glu	Leu	Asp	108

Gly	Cys	Glu	Pro	Glu	Ala	Ile	Gly	Lys	117
Arg	Pro	Ala	Val	Leu	Pro	Leu	Leu	Glu	126
Arg	Val	Ser	Glu	Ala	Ala	Lys	Ser	Ser	135
Gly	Ala	Asp	Gly	Ser	Leu	Pro	Ser	Thr	144
Pro	Pro	Pro	Pro	Glu	Glu	Glu	Glu	Asp	153
Asp	Leu	Tyr	Arg	Gln	Ser	Leu	Glu	Ile	162
Ile	Ser	Arg	Tyr	Leu	Arg	Glu	Gln	Ala	171
Thr	Gly	Ser	Lys	Asp	Ser	Lys	Pro	Leu	180
Gly	Glu	Ala	Gly	Ala	Ala	Gly	Arg	Arg	189
Ala	Leu	Glu	Thr	Leu	Arg	Arg	Val	Gly	198
Asp	Gly	Val	Gln	Arg	Asn	His	Glu	Thr	207
Ala	Phe	Gln	Gly	Met	Leu	Arg	Lys	Leu	216
Asp	Ile	Lys	Asn	Glu	Gly	Asp	Val	Lys	225
Ser	Phe	Ser	Arg	Val	Met	Val	His	Val	234
Phe	Lys	Asp	Gly	Val	Thr	Asn	Trp	Gly	243
Arg	Ile	Val	Thr	Leu	Ile	Ser	Phe	Gly	252
Ala	Phe	Val	Ala	Lys	His	Leu	Lys	Ser	261
Val	Asn	Gln	Glu	Ser	Phe	Ile	Glu	Pro	270
Leu	Ala	Glu	Thr	Ile	Thr	Asp	Val	Leu	279
Val	Arg	Thr	Lys	Arg	Asp	Trp	Leu	Val	288
Lys	Gln	Arg	Gly	Trp	Asp	Gly	Phe	Val	297
Glu	Phe	Phe	His	Val	Gln	Asp	Leu	Glu	306
Gly	Gly	Ile	Arg	Asn	Val	Leu	Leu	Ala	315
Phe	Ala	Gly	Val	Ala	Gly	Val	Gly	Ala	324
Gly	Leu	Ala	Tyr	Leu	Ile	Arg	331		

<210> 40

<211> 350

<212> PRT

<213> Homo sapiens

<220>

<223> EAT/MCL-1

<400> 40

Met	Phe	Gly	Leu	Lys	Arg	Asn	Ala	Val	9
Ile	Gly	Leu	Asn	Leu	Tyr	Cys	Gly	Gly	18
Ala	Gly	Leu	Gly	Ala	Gly	Ser	Gly	Gly	27
Ala	Thr	Arg	Pro	Gly	Gly	Arg	Leu	Leu	36
Ala	Thr	Glu	Lys	Glu	Ala	Ser	Ala	Arg	45
Arg	Glu	Ile	Gly	Gly	Gly	Glu	Ala	Gly	54
Ala	Val	Ile	Gly	Gly	Ser	Ala	Gly	Ala	63
Ser	Pro	Pro	Ser	Thr	Leu	Thr	Pro	Asp	72
Ser	Arg	Arg	Val	Ala	Arg	Pro	Pro	Pro	81
Ile	Gly	Ala	Glu	Val	Pro	Asp	Val	Thr	90
Ala	Thr	Pro	Ala	Arg	Leu	Leu	Phe	Phe	99
Ala	Pro	Thr	Arg	Arg	Ala	Ala	Pro	Leu	108
Glu	Glu	Met	Glu	Ala	Pro	Ala	Ala	Asp	117
Ala	Ile	Met	Ser	Pro	Glu	Glu	Glu	Leu	126

Asp	Gly	Tyr	Glu	Pro	Glu	Pro	Leu	Gly	135
Lys	Arg	Pro	Ala	Val	Leu	Pro	Leu	Leu	144
Glu	Leu	Val	Gly	Glu	Ser	Gly	Asn	Asn	153
Thr	Ser	Thr	Asp	Gly	Ser	Leu	Pro	Ser	162
Thr	Pro	Pro	Pro	Ala	Glu	Glu	Glu	Glu	171
Asp	Glu	Leu	Tyr	Arg	Gln	Ser	Leu	Glu	180
Ile	Ile	Ser	Arg	Tyr	Leu	Arg	Glu	Gln	189
Ala	Thr	Gly	Ala	Lys	Asp	Thr	Lys	Pro	198
Met	Gly	Arg	Ser	Gly	Ala	Thr	Ser	Arg	207
Lys	Ala	Leu	Glu	Thr	Leu	Arg	Arg	Val	216
Gly	Asp	Gly	Val	Gln	Arg	Asn	His	Glu	225
Thr	Val	Phe	Gln	Gly	Met	Leu	Arg	Lys	234
Leu	Asp	Ile	Lys	Asn	Glu	Asp	Asp	Val	243
Lys	Ser	Leu	Ser	Arg	Val	Met	Ile	His	252
Val	Phe	Ser	Asp	Gly	Val	Thr	Asn	Trp	261
Gly	Arg	Ile	Val	Thr	Leu	Ile	Ser	Phe	270
Gly	Ala	Phe	Val	Ala	Lys	His	Leu	Lys	279
Thr	Ile	Asn	Gln	Glu	Ser	Cys	Ile	Glu	288
Pro	Leu	Ala	Glu	Ser	Ile	Thr	Asp	Val	297
Leu	Val	Arg	Thr	Lys	Arg	Asp	Trp	Leu	306
Val	Lys	Gln	Arg	Gly	Trp	Asp	Gly	Phe	315
Val	Glu	Phe	Phe	His	Val	Glu	Asp	Leu	324
Glu	Gly	Gly	Ile	Arg	Asn	Val	Leu	Leu	333
Ala	Phe	Ala	Gly	Val	Ala	Gly	Val	Gly	342
Ala	Gly	Leu	Ala	Tyr	Leu	Ile	Arg	350	

<210> 41
 <211> 143
 <212> PRT
 <213> Mus musculus

<220>
 <223> TSC-22

<400> 41

Met	Lys	Ser	Gln	Trp	Cys	Arg	Pro	Val	9
Ala	Met	Asp	Leu	Gly	Val	Tyr	Gln	Leu	18
Arg	His	Phe	Ser	Ile	Ser	Phe	Leu	Ser	27
Ser	Leu	Leu	Gly	Thr	Glu	Asn	Ala	Ser	36
Val	Arg	Leu	Asp	Asn	Ser	Ser	Gly	Ala	45
Ser	Val	Val	Ala	Ile	Asp	Asn	Lys	Ile	54
Glu	Gln	Ala	Met	Asp	Leu	Val	Lys	Ser	63
His	Leu	Met	Tyr	Ala	Val	Arg	Glu	Glu	72
Val	Glu	Val	Leu	Lys	Glu	Gln	Ile	Lys	81
Glu	Leu	Ile	Glu	Lys	Asn	Ser	Gln	Leu	90
Glu	Gln	Glu	Asn	Asn	Leu	Leu	Lys	Thr	99
Leu	Ala	Ser	Pro	Glu	Gln	Leu	Ala	Gln	108
Phe	Gln	Ala	Gln	Leu	Gln	Thr	Gly	Ser	117
Pro	Pro	Ala	Thr	Thr	Gln	Pro	Gln	Gly	126

Thr	Thr	Gln	Pro	Pro	Ala	Gln	Pro	Ala	135
Ser	Gln	Gly	Ser	Gly	Ser	Thr	Ala	143	

<210> 42
 <211> 144
 <212> PRT
 <213> Homo sapiens

<220>
 <223> TSC-22

<400> 42

Met	Lys	Ser	Gln	Trp	Cys	Arg	Pro	Val	9
Ala	Met	Asp	Leu	Gly	Val	Tyr	Gln	Leu	18
Arg	His	Phe	Ser	Ile	Ser	Phe	Leu	Ser	27
Ser	Leu	Leu	Gly	Thr	Glu	Asn	Ala	Ser	36
Val	Arg	Leu	Asp	Asn	Ser	Ser	Ser	Gly	45
Ala	Ser	Val	Val	Ala	Ile	Asp	Asn	Lys	54
Ile	Glu	Gln	Ala	Met	Asp	Leu	Val	Lys	63
Ser	His	Leu	Met	Tyr	Ala	Val	Arg	Glu	72
Glu	Val	Glu	Val	Leu	Lys	Glu	Gln	Ile	81
Lys	Glu	Leu	Ile	Glu	Lys	Asn	Ser	Gln	90
Leu	Glu	Gln	Glu	Asn	Asn	Leu	Leu	Lys	99
Thr	Leu	Ala	Ser	Pro	Glu	Gln	Leu	Ala	108
Gln	Phe	Gln	Ala	Gln	Leu	Gln	Thr	Gly	117
Ser	Pro	Pro	Ala	Thr	Thr	Gln	Pro	Gln	126
Gly	Thr	Thr	Gln	Pro	Pro	Ala	Gln	Pro	135
Ala	Ser	Gln	Gly	Ser	Gly	Pro	Thr	Ala	144

<210> 43
 <211> 291
 <212> PRT
 <213> Mus musculus

<220>
 <223> gamma-Sarcoglycan

<400> 43

Met	Val	Arg	Glu	Gln	Tyr	Thr	Thr	Val	9
Thr	Glu	Gly	Thr	His	Ile	Glu	Arg	Pro	18
Glu	Asn	Gln	His	Ile	Tyr	Lys	Ile	Gly	27
Ile	Tyr	Gly	Trp	Arg	Lys	Arg	Cys	Leu	36
Tyr	Leu	Phe	Val	Leu	Leu	Leu	Leu	Ala	45
Ile	Leu	Val	Val	Asn	Leu	Ala	Leu	Thr	54
Ile	Trp	Ile	Leu	Lys	Val	Met	Trp	Phe	63
Ser	Pro	Ile	Gly	Met	Gly	His	Leu	His	72

Val	Thr	Ala	Asp	Gly	Leu	Arg	Leu	Glu	81
Gly	Glu	Ser	Glu	Phe	Leu	Phe	Pro	Leu	90
Tyr	Ala	Lys	Glu	Ile	Arg	Ser	Arg	Val	99
Asp	Ser	Ser	Leu	Leu	Leu	Gln	Ser	Thr	108
Gln	Asn	Val	Thr	Val	Ser	Ala	Arg	Asn	117
Ser	Glu	Gly	Glu	Val	Thr	Gly	Arg	Val	126
Lys	Val	Gly	Ala	Gln	Met	Val	Glu	Val	135
Gln	Ser	Gln	His	Phe	Gln	Ile	Asn	Ser	144
Glu	Asp	Gly	Lys	Pro	Leu	Phe	Ser	Ala	153
Glu	Glu	Gln	Asp	Val	Val	Val	Gly	Thr	162
Gly	Arg	Leu	Arg	Val	Thr	Gly	Pro	Glu	171
Gly	Ala	Leu	Phe	Glu	His	Ser	Val	Glu	180
Thr	Pro	Leu	Val	Arg	Ala	Asp	Pro	Phe	189
Gln	Asp	Leu	Arg	Leu	Glu	Ser	Pro	Thr	198
Arg	Ser	Leu	Ser	Met	Asp	Ala	Pro	Arg	207
Gly	Val	His	Val	Lys	Ala	Asn	Ala	Gly	216
Lys	Leu	Glu	Ala	Leu	Ser	Gln	Met	Asp	225
Ile	Ile	Leu	Gln	Ser	Ser	Glu	Gly	Val	234
Leu	Val	Leu	Asp	Ala	Glu	Thr	Val	Gly	243
Leu	Thr	Lys	Leu	Lys	Gln	Gly	Thr	Gln	252
Gly	Pro	Ala	Gly	Ser	Ser	Asn	Gly	Phe	261
Tyr	Glu	Ile	Cys	Ala	Cys	Pro	Asp	Gly	270
Lys	Leu	Tyr	Leu	Ser	Met	Ala	Gly	Glu	279
Val	Thr	Thr	Cys	Glu	Glu	His	Ser	His	288
Val	Cys	Leu	291						

<210> 44

<211> 291

<212> PRT

<213> Homo sapiens

<220>

<223> gamma-Sarcoglycan

<400> 44

Met	Val	Arg	Glu	Gln	Tyr	Thr	Thr	Ala	9
Thr	Glu	Gly	Ile	Cys	Ile	Glu	Arg	Pro	18
Glu	Asn	Gln	Tyr	Val	Tyr	Lys	Ile	Gly	27
Ile	Tyr	Gly	Trp	Arg	Lys	Arg	Cys	Leu	36
Tyr	Leu	Phe	Val	Leu	Leu	Leu	Leu	Ile	45
Ile	Leu	Val	Val	Asn	Leu	Ala	Leu	Thr	54
Ile	Trp	Ile	Leu	Lys	Val	Met	Trp	Phe	63
Ser	Pro	Ala	Gly	Met	Gly	His	Leu	Cys	72
Val	Thr	Lys	Asp	Gly	Leu	Arg	Leu	Glu	81
Gly	Glu	Ser	Glu	Phe	Leu	Phe	Pro	Leu	90
Tyr	Ala	Lys	Glu	Ile	His	Ser	Arg	Val	99
Asp	Ser	Ser	Leu	Leu	Leu	Gln	Ser	Thr	108
Gln	Asn	Val	Thr	Val	Asn	Ala	Arg	Asn	117
Ser	Glu	Gly	Glu	Val	Thr	Gly	Arg	Leu	126

Lys	Val	Gly	Pro	Lys	Met	Val	Glu	Val	135
Gln	Asn	Gln	Gln	Phe	Gln	Ile	Asn	Ser	144
Asn	Asp	Gly	Lys	Pro	Leu	Phe	Thr	Val	153
Asp	Glu	Lys	Glu	Val	Val	Val	Gly	Thr	162
Asp	Lys	Leu	Arg	Val	Thr	Gly	Pro	Glu	171
Gly	Ala	Leu	Phe	Glu	His	Ser	Val	Glu	180
Thr	Pro	Leu	Val	Arg	Ala	Asp	Pro	Phe	189
Gln	Asp	Leu	Arg	Leu	Glu	Ser	Pro	Thr	198
Arg	Ser	Leu	Ser	Met	Asp	Ala	Pro	Arg	207
Gly	Val	His	Ile	Gln	Ala	His	Ala	Gly	216
Lys	Ile	Glu	Ala	Leu	Ser	Gln	Met	Asp	225
Ile	Leu	Phe	His	Ser	Ser	Asp	Gly	Met	234
Leu	Val	Leu	Asp	Ala	Glu	Thr	Val	Cys	243
Leu	Pro	Lys	Leu	Val	Gln	Gly	Thr	Trp	252
Gly	Pro	Ser	Gly	Ser	Ser	Gln	Ser	Leu	261
Tyr	Glu	Ile	Cys	Val	Cys	Pro	Asp	Gly	270
Lys	Leu	Tyr	Leu	Ser	Val	Ala	Gly	Val	279
Ser	Thr	Thr	Cys	Gln	Glu	His	Ser	His	288
Ile	Cys	Leu	291						

<210> 45

<211> 228

<212> PRT

<213> Homo sapiens

<220>

<223> Phospholipase Inhibitor

<400> 45

Met	Trp	Val	Gln	Thr	Arg	Pro	Ser	Ser	9
Ala	Ser	Tyr	Lys	Ser	Trp	Gly	Pro	Gly	18
Thr	Ala	Asp	Thr	His	Thr	Met	Arg	Leu	27
Ser	Arg	Arg	Pro	Glu	Thr	Phe	Leu	Leu	36
Ala	Phe	Val	Leu	Leu	Cys	Thr	Leu	Leu	45
Gly	Leu	Gly	Cys	Pro	Leu	His	Cys	Glu	54
Ile	Cys	Thr	Ala	Ala	Gly	Ser	Arg	Cys	63
His	Gly	Gln	Met	Lys	Thr	Cys	Ser	Ser	72
Asp	Lys	Asp	Thr	Cys	Val	Leu	Leu	Val	81
Gly	Lys	Ala	Thr	Ser	Lys	Gly	Lys	Glu	90
Leu	Val	His	Thr	Tyr	Lys	Gly	Cys	Ile	99
Arg	Ser	Gln	Asp	Cys	Tyr	Ser	Gly	Val	108
Ile	Ser	Thr	Thr	Met	Gly	Pro	Lys	Asp	117
His	Met	Val	Thr	Ser	Ser	Phe	Cys	Cys	126
Gln	Ser	Asp	Gly	Cys	Asn	Ser	Ala	Phe	135
Leu	Ser	Val	Pro	Leu	Thr	Asn	Leu	Thr	144
Glu	Asn	Gly	Leu	Met	Cys	Pro	Ala	Cys	153
Thr	Ala	Ser	Phe	Arg	Asp	Lys	Cys	Met	162
Gly	Pro	Met	Thr	His	Cys	Thr	Gly	Lys	171
Glu	Asn	His	Cys	Val	Ser	Leu	Ser	Gly	180

His	Val	Gln	Ala	Gly	Ile	Phe	Lys	Pro	189
Arg	Phe	Ala	Met	Arg	Gly	Cys	Ala	Thr	198
Glu	Ser	Met	Cys	Phe	Thr	Lys	Pro	Gly	207
Ala	Glu	Val	Pro	Thr	Gly	Thr	Asn	Val	216
Leu	Phe	Leu	His	His	Ile	Glu	Cys	Thr	225
His	Ser	Pro	228						

<210> 46

<211> 140

<212> PRT

<213> Mus musculus

<220>

<223> Cystatin C

<400> 46

Met	Ala	Ser	Pro	Leu	Arg	Ser	Leu	Leu	9
Phe	Leu	Leu	Ala	Val	Leu	Ala	Val	Ala	18
Trp	Ala	Ala	Thr	Pro	Lys	Gln	Gly	Pro	27
Arg	Met	Leu	Gly	Ala	Pro	Glu	Glu	Ala	36
Asp	Ala	Asn	Glu	Glu	Gly	Val	Arg	Arg	45
Ala	Leu	Asp	Phe	Ala	Val	Ser	Glu	Tyr	54
Asn	Lys	Gly	Ser	Asn	Asp	Ala	Tyr	His	63
Ser	Arg	Ala	Ile	Gln	Val	Val	Arg	Ala	72
Arg	Lys	Gln	Leu	Val	Ala	Gly	Val	Asn	81
Tyr	Phe	Leu	Asp	Val	Glu	Met	Gly	Arg	90
Thr	Thr	Cys	Thr	Lys	Ser	Gln	Thr	Asn	99
Leu	Thr	Asp	Cys	Pro	Phe	His	Asp	Gln	108
Pro	His	Leu	Met	Arg	Lys	Ala	Leu	Cys	117
Ser	Phe	Gln	Ile	Tyr	Ser	Val	Pro	Trp	126
Lys	Gly	Thr	His	Ser	Leu	Thr	Lys	Phe	135
Ser	Cys	Lys	Asn	Ala	140				

<210> 47

<211> 146

<212> PRT

<213> Homo sapiens

<220>

<223> Cystatin C

<400> 47

Met	Ala	Gly	Pro	Leu	Arg	Ala	Pro	Leu	9
Leu	Leu	Leu	Ala	Ile	Leu	Ala	Val	Ala	18
Leu	Ala	Val	Ser	Pro	Ala	Ala	Gly	Ser	27
Ser	Pro	Gly	Lys	Pro	Pro	Arg	Leu	Val	36

Gly	Gly	Pro	Met	Asp	Ala	Ser	Val	Glu	45
Glu	Glu	Gly	Val	Arg	Arg	Ala	Leu	Asp	54
Phe	Ala	Val	Gly	Glu	Tyr	Asn	Lys	Ala	63
Ser	Asn	Asp	Met	Tyr	His	Ser	Arg	Ala	72
Leu	Gln	Val	Val	Arg	Ala	Arg	Lys	Gln	81
Ile	Val	Ala	Gly	Val	Asn	Tyr	Phe	Leu	90
Asp	Val	Glu	Leu	Gly	Arg	Thr	Thr	Cys	99
Thr	Lys	Thr	Gln	Pro	Asn	Leu	Asp	Asn	108
Cys	Pro	Phe	His	Asp	Gln	Pro	His	Leu	117
Lys	Arg	Lys	Ala	Phe	Cys	Ser	Phe	Gln	126
Ile	Tyr	Ala	Val	Pro	Trp	Gln	Gly	Thr	135
Met	Thr	Leu	Ser	Lys	Ser	Thr	Cys	Gln	144
Asp	Ala	146							

<210> 48

<211> 140

<212> PRT

<213> Mus musculus

<220>

<223> Cystatin C variant

<400> 48

Met	Ala	Ser	Pro	Leu	Arg	Ser	Leu	Leu	9
Phe	Leu	Leu	Ala	Val	Leu	Ala	Val	Ala	18
Trp	Ala	Ala	Thr	Pro	Lys	Gln	Gly	Pro	27
Arg	Met	Leu	Gly	Ala	Pro	Glu	Glu	Ala	36
Asp	Ala	Asn	Lys	Glu	Gly	Val	Arg	Arg	45
Ala	Leu	Asp	Phe	Ala	Val	Ser	Glu	Tyr	54
Asn	Lys	Gly	Ser	Asn	Asp	Ala	Tyr	His	63
Ser	Arg	Ala	Ile	Gln	Val	Val	Arg	Ala	72
Arg	Lys	Gln	Leu	Val	Ala	Gly	Val	Asn	81
Tyr	Phe	Leu	Asp	Val	Glu	Met	Gly	Arg	90
Thr	Thr	Cys	Thr	Lys	Ser	Gln	Thr	Asn	99
Leu	Thr	Asp	Cys	Pro	Phe	His	Asp	Gln	108
Pro	His	Leu	Met	Arg	Lys	Ala	Leu	Cys	117
Ser	Phe	Gln	Ile	Tyr	Ser	Val	Pro	Trp	126
Lys	Gly	Thr	His	Ser	Leu	Thr	Lys	Phe	135
Ser	Cys	Lys	Asn	Ala	140				

<210> 49

<400>

<210> 50

<211> 2231
<212> DNA
<213> *Mus musculus*

<220>
<223> SW1136

<400> 50

cggcgaggaa	gatggcggac	gggaaggcgg	gagaggagaa	gccagagaag	50
ccgcagcgag	ccggagccgc	cggaggacct	gaagaagaag	cagaaaaacc	100
tgtgaaaact	aagactgttt	cttccagtaa	tggaggggaa	agttccagtc	150
gcagcgctga	aaagcgatca	gctgaagacg	aagctgcaga	cctcccaaca	200
aagcctacaa	agatgtccaa	gtttggattt	gccataggta	gtcagacggc	250
acggaaagcg	tccgccatct	ccattagact	cggagcaagt	aagcctaagg	300
aaacagttcc	aactcttgct	ccaaaaactc	tgctcggtagc	agcagctttc	350
aatgaagatg	aagatagtga	gccagaagaa	atgcctccag	aagcaaaagat	400
gaggatgaag	aacattggaa	gggacacacc	aacatcagcg	ggaccaaact	450
cctttaataa	aggaagcat	ggcttttccg	ataaccagaa	gctgtgggag	500
cgaaatataa	aatctcatct	tggaaacgct	cacgaccaag	acaattaagt	550
gaagtgtctg	agactggggg	gtgggtgggt	gcagttagaa	ggagcagctc	600
cctttttgta	aagaatgggtg	taagactagc	tttggagccg	tttttctttc	650
ttcttttttt	cttttccttt	ttcttttttt	tttttttttt	ttaagattga	700
gtggtacact	aataaatgag	agtttgcaat	tagaggtaat	ttatgtttta	750
tatacagatt	tcaagacatt	tgctaatttt	gtagtttcac	atgattagtt	800
tccaagggtt	acagataata	aagaaatcac	aagtggtagc	tttctaagaa	850
ttgcatattt	ttttagacac	aactattagc	acattaagag	ggaagccaaa	900
agttattgtc	tgcttcaaac	tggaaagcag	tcctctcctg	acttctccct	950
cgttaccgga	ctgtccggct	ccctgcagca	gccttaccga	gagggagatt	1000
ggcttgagaa	gccagtgtta	ctgttgtgac	tggtggctga	gaggaagttt	1050
agatgaggtt	caagtaaacc	ctttcctgcg	ggcatttcgt	tttgtttcgg	1100
gccattctag	ctagtactgc	ttcgtctca	gtgggtaccg	atgcttgctc	1150
tgtaaaaata	aatttttttc	gttaaaaatt	cttatatgaa	gaattgagta	1200
ttatgactag	cccactctaa	cggagtgtgt	ctccgttgag	gaccttcaga	1250
ggacactatt	tgctaccaa	gtgaaccagt	attctgaatg	tgcttctctt	1300
ggtttctggt	ctagtctcta	gaagcatttc	caccagaact	tgaggcaaaa	1350
cataaggaag	ctgtttcttt	taaagtacaa	acaccaccaa	aaatatcagt	1400
gtacatagt	ctttatgtat	ttggctggct	tttatttttt	aaaaggttta	1450
aataacaaaa	aaggaaaaaa	aggtatagca	ttgtatgaag	gcagatgagg	1500
cgacacacct	gtgacatttg	aagcatttgt	gttactaact	tactagatcc	1550
ggtttggaatt	gaattcacaa	ggtttcttac	ttgtccaact	ccaggcttat	1600
tttacgtaca	tacaacctga	ccagtgggtt	caaaagcaca	tttagtgact	1650
gcaataggac	agaaatgctt	ctctagacac	atcttcattg	cgagcgtctc	1700
atcgcatatg	ctcttagagt	tctgaatgta	ggatgtttgt	tttgtatttt	1750
tgtattgtat	atgggctttt	taaatgtgac	agttaaatgc	atctttaata	1800
gtcacagaca	aaagagatga	taaaatgtcc	tttgaaaatg	gcaatggtga	1850
gtttggaggc	agcttcgggg	agtttctcgg	gtggcgatga	ttcactgggc	1900
agtttttaat	gtagtgactt	caagaagcag	cctgcggata	ttcctaacac	1950
ttggttcact	acagtttagt	ttacttcata	agccccaagt	aaaacgatgg	2000
aaatgtacat	agcactatta	gttcatacat	gatttaagta	tatcaagata	2050
cataaattta	acattttatg	ctgcaaaactg	tccatttgct	catttttactg	2100
tttgttgaaa	taacacctct	cctacatatt	ctttacttga	ctcgaataac	2150
aaattaacct	gacgtcaaga	tggagagaga	cgactgagct	gaatgtcttt	2200
actaaaatta	caataaattt	tgtcaaaactc	g		2231

<210> 51
<211> 1066
<212> DNA

<213> Homo sapiens

<220>

<223> SW1136

<400> 51

ggggaggccg	cggcggggaa	aatggcggac	gggaaggcgg	gagacgagaa	50
gcctgaaaaag	tcgcagcgag	ctggagccgc	cggaggacct	gaagaagaag	100
cagaaaaacc	tgtgaaaact	aagactgttt	cttccagtaa	tggaggggaa	150
agttccagtc	gcagcgctga	gaagcgatca	gctgaagaag	aagctgccga	200
cctcccaaca	aagcctacaa	agatctccaa	gtttggattt	gccataggtg	250
gtcagacgac	aaagaaagca	tcagccatat	ccatcaaact	tggatcaagt	300
aagcctaaaag	aaactgttcc	aactcttgct	ccaaaaactc	tttcagtagc	350
agcagctttt	aatgaagatg	aagatagtga	accagaggaa	atgcctccag	400
aagcaaaagat	gaggatgaag	aatattggaa	gggatacacc	aacatcagct	450
ggaccaaact	ccttcaataa	aggaaagcat	gggttttctg	ataaccagaa	500
gctgtgggag	cgaaatataa	aatctcatct	tggaaatgtc	catgaccaag	550
acaattaaat	gatgttttga	aattggggtg	tggggtgggt	gtaaagttaa	600
aaggaacagt	ttcctttttt	aaagaatggg	ataagactat	ctttggagcc	650
gctttttttt	tctttttcat	ttttttaaaa	gattgagtgg	tacactaata	700
aatgagagtt	tgaaattaga	ggtaatttat	gttttatata	cagatttcaa	750
gacatttgct	aattttgtag	tttcatgtga	ttagtttcca	aaggttacag	800
ataataaaga	aatcagaaat	ggtaccmatt	ttaaraattg	cycatttttt	850
ttttagagcc	camctattag	ccccmttaag	akggdgyaaa	rchaawgtat	900
aaramtrcaa	gmatgwarc	ctstctkars	tcccttatta	cctaaacttg	950
tctggctccc	aggaacagcc	ttatagagag	agggagtatt	gtattgggaa	1000
gaaaatgtta	ctgaactatt	gactgaaagt	aaatttagat	aaaatacaaa	1050
aaaaaaaaaa	aaaaaa				1066

<210> 52

<211> 773

<212> DNA

<213> Mus musculus

<220>

<223> SW1295

<400> 52

attcggatcc	ttgtagaaat	tgctggacgc	ttctgtacgt	ttcgcagttt	50
gtcttcgctg	atcggtgaga	cttcgagcag	ttaggatgcc	gcgtggaagc	100
cgaagccgca	cttcccgggt	gactcctccg	gccagccggg	cccctcagat	150
gagggctgct	ccccgaagag	cacctgcagc	tcagcctcca	gcagcagctg	200
cgccatctgc	agttggctca	cctgccgctg	cgccccggca	gccaggcctg	250
atggcccaga	tggtaccac	cgcgccgggt	gtggctgtgg	gctctgcagt	300
gggacacacc	ctgggtcacg	ccatcactgg	gggcttcagc	ggaggtggca	350
gtgctgagcc	cgcaaagccc	gacatcactt	accaggagcc	tcagggagcc	400
cagctgcaga	accagcagtc	ttttggacct	tgctctctag	agatcaagca	450
gtttctggag	tgtgctcaga	accagagcga	tgtcaagctc	tgtgagggct	500
tcaacgaggt	gctgcggcag	tgcaggattg	caaatggttt	aatgtaatca	550
agaaattcaa	gctgaagaga	tgtaacattg	gttctgtata	attgatagta	600
caagtgtgga	cccttatatt	tctaacagtt	cattgctttg	gaatggccgt	650
gaaagagatc	taactgtgga	tgcttactga	ggcttgtatg	tagtgttggg	700
tactggggaa	gtgtttgccc	tccttggaact	gtgttgtgat	tgtgagttaa	750
aaaaaataaa	ttggttattc	tga			773

<210> 53
<211> 3057
<212> DNA
<213> Mus musculus

<220>
<223> KIAA1247

<400> 53

aatgctggtg	gagacggggg	agctggacaa	cacgtacatc	ctgtacaccg	50
ccgaccacgg	ctaccacatt	ggccagtttg	ggctggtgaa	gggcaagtct	100
atgccgtatg	aattcgacat	cagagtcccg	ttctacgtga	ggggccccaa	150
cgtggaagct	ggctctctga	acccccacat	tgtcctcaac	attgacctgg	200
gccccacca	tactggatat	cgctggactg	gacatccctg	cagacatgga	250
cgggaagtct	atttctcaaac	tactggactc	agagcggcca	gtgaaccggt	300
tccacttgaa	aaagaagctg	agggctcttg	cgagactcct	tcctggtgga	350
gagaggcaaa	cttgctccac	aagagggagg	gtgacaaaagt	gaatgcccg	400
gaggagaact	tcctgcccac	gtaccagcgc	gtgaaggacc	tgtgtcagcg	450
agctgagtac	cagacagcat	gcgaacagct	ggggcagaag	tggcagtgtg	500
tggaggacgc	ttctgggacg	ctgaagctgc	acaaatgtaa	aggcccatg	550
cggtttggtg	gcggcggttg	cagcagagcc	ctctccaacc	tggtgcccaa	600
gtatgacggc	cagagcagcg	aggcctgcag	ctgtgacagt	ggcgggtggag	650
gggactacaa	actgggcctg	gctggacgcc	gtaagctctt	taagaaaaag	700
tataagacca	gctatgcccg	gaaccgctcc	atccgttccg	tggccatcga	750
ggtggacggg	gagatatacc	acgtaggctt	ggatactgtg	cctcagcccc	800
gcaacccttag	caagccgcac	tggccagggg	cccctgaaga	ccaagatgac	850
aaggatggtg	gcagtttcag	tggtagctgt	ggccttccag	attattctgc	900
ccccaatccc	atcaaaagtga	cccatcggtg	ctacatcctt	gagaatgaca	950
cagtccagtg	cgacttggtg	ctgtacaagt	ccctgcaggc	ttggaaagac	1000
cacaagctgc	acatcgacca	tgagatcgaa	accctgcaga	acaaaattaa	1050
gaaccttcga	gaagtcaggg	gtcacctgaa	gaagaagcga	ccggaagaat	1100
gtgactgcca	taraatcagt	taccacagcc	aacacaaagg	ccgtctcaag	1150
cacaaaggct	ccagcctgca	ccctttcagg	aagggtctgc	aggagaagga	1200
caagggtgtg	ctgctgcggg	acagaaacgc	aagaagaaac	tgcgcaactg	1250
ctcaaaccgg	tgcagaacaa	cgatacgtgc	agcatgcccg	gcctcacgtg	1300
ctttacccac	gacaaccacc	actggcagac	ggcgccactc	tggacgctgg	1350
ggccgttctg	cgctgcacc	agcgccaaca	acaacacgta	ctggtgcttg	1400
aggaccataa	atgagaccca	caacttcctc	ttctgcgaat	ttgcaaccgg	1450
cttcatagaa	tactttgacc	tcagtacaga	cccctaccag	ctgatgaacg	1500
cggatgaacac	actggacagg	gacgtcctta	accaactgca	cgtgcagctc	1550
atggagctaa	ggagctgtaa	aggctacaag	cagtgcgaac	cccggaccgg	1600
caacatggac	ctggggctta	gagacggagg	aagctatgaa	caatacaggc	1650
agtttcagcg	tcgaaaatgg	ccagaaatga	agagaccttc	ttccaaatca	1700
ctgggacagc	tatgggaagg	ttgggaaggc	taagcggcca	tagagagagg	1750
aacctccaaa	accagggggc	tcgtgtgggt	gccaggcca	tgcaaaaaac	1800
acccgattcc	cagaagatga	atgttggaac	tgggagacct	gacagaaggc	1850
agggtgctc	ttgggacagg	aaatcctgga	ggacagcgcc	tggactttcc	1900
gatgctcagt	ttctttgccc	tgtttgtctc	tggatcaaac	ctcactggct	1950
gctctgggat	gcgtgctcac	acctggagtc	tctgctcacc	ctttcagagg	2000
ctcacaaga	caaagggaact	aatttccatg	gacacttcct	ccagagatgg	2050
aaattgctgg	gattcgccca	ctcctcccct	gcacccctcc	cccagtcctc	2100
tagggaagca	agcttggttt	aaccttctta	ctctttggag	aaagcacgga	2150
catcccagggt	gctgtcaacc	tcacagtctt	gacaaaagtct	atagcacaaa	2200
acagtaccat	tcaccagggt	ggttgacctg	gctggctcag	aagctgcctt	2250
caccacatac	atgaccgctc	acacgtaacc	aacacaggga	attgtagggg	2300
aatctcacta	atatgaaatc	ccgcttttca	agagtcgcgg	tgtcaataaa	2350
cgtgtgggt	aggatcaagg	ataatccctt	gagctttcag	acattttattc	2400
ctgcccggga	ttcgttcctt	tgttatccat	cccagaactg	atgtttttct	2450

```

aaggtaccga aaccccaagt tgatgtgtgt cctgtgtttt aatgacattg 2500
tatttgtaaa gttttgtagt ataagtacca tcttacagtg ttcctgcccc 2550
cagccaatgt ctagctattg gtatgaaaaa aaaaatcttt gaatttttgt 2600
aaaaggcwaw mwwrrramww wwwwgctctt tattattatc atttttttct 2650
tgaagcactc aagatgttgt cgaccttcag ctgagggttg gagaagcaga 2700
gggtaataca ttaatagtaa acctctccga ttcaaggagc ctcataggta 2750
agtctcacca gctttggggc atcgatctgt gaagcaaagc atccaactgc 2800
accaaccctt tgttcatcca ggtagggtaa cctgggtcaat atggctgcca 2850
gaaagcagct gtcagagctt cggagggtgg ggtggaaatg tcagcccaac 2900
ccgactcagc agagggggct cacatttctc taaaccagca gtttttcagc 2950
tggggctcca acgacctttc acaggggtcc taaggctatc agagagcaca 3000
tttaatggta cagttcacac agtaacaatc acagctaaga agtagcacag 3050
tagcagc                                     3057

```

<210> 54

<211> 732

<212> cDNA

<213> Mus musculus

<220>

<223> Phospholipase Inhibitor

<400> 54

```

ggactacagg ttcacacacc atgattctgt ttagaagaca caggaccttc 50
ctgctggcct tcacactgct ctgtaccctc ctgggtctcg ggtgccctct 100
aacttgtagt gtgtgcaaag gctcggggca cacatgcagc ggaagatga 150
agacctgtga agacggcaaa gacgcatgct tggctcctagt gagcgagtcc 200
agcacaaaagg gccgaaagtc agtgaacacc ttcaaggcct gcatgaagta 250
caaagactgc tactcaggct tcgtatcaac caccatgact cccagtgact 300
acatgggtgc caacgcccac tgctgtcaaa gtgacgggtg caacagtggc 350
tctgtgcccc ctcccttgaa caatcggaca gagaatggcc tgatgtgtcc 400
ctcctgcatt gcgcccttcc aggagacctg tccaggaacc caggcagctc 450
gctgcgtggg ccgggaaaca cactgcatct attttgctgg caatgtgcag 500
gctggtatta tccacacgaa atttgccacg aggggctgtg ctacagagag 550
cgctgccac accaaggcag gggctgaggt cccttcagcc ttctatctct 600
acttctgctg ccgggcagac tgccttcag ccccttacc tctggcagc 650
ggagagtga gaaaccgaga agtatgtaac ttgaggagcc ctgcagcttt 700
ccagctgcct gtaaattaaa cagatygaca gt                                     732

```

<210> 55

<211> 178

<212> PRT

<213> Mus musculus

<220>

<223> SW1136

<400> 55

Met	Ala	Asp	Gly	Lys	Ala	Gly	Glu	Glu	9
Lys	Pro	Glu	Lys	Pro	Gln	Arg	Ala	Gly	18
Ala	Ala	Gly	Gly	Pro	Glu	Glu	Glu	Ala	27
Glu	Lys	Pro	Val	Lys	Thr	Lys	Thr	Val	36

Ser	Ser	Ser	Asn	Gly	Gly	Glu	Ser	Ser	45
Ser	Arg	Ser	Ala	Glu	Lys	Arg	Ser	Ala	54
Glu	Asp	Glu	Ala	Ala	Asp	Leu	Pro	Thr	63
Lys	Pro	Thr	Lys	Met	Ser	Lys	Phe	Gly	72
Phe	Ala	Ile	Gly	Ser	Gln	Thr	Ala	Arg	81
Lys	Ala	Ser	Ala	Ile	Ser	Ile	Arg	Leu	90
Gly	Ala	Ser	Lys	Pro	Lys	Glu	Thr	Val	99
Pro	Thr	Leu	Ala	Pro	Lys	Thr	Leu	Ser	108
Val	Ala	Ala	Ala	Phe	Asn	Glu	Asp	Glu	117
Asp	Ser	Glu	Pro	Glu	Glu	Met	Pro	Pro	126
Glu	Ala	Lys	Met	Arg	Met	Lys	Asn	Ile	135
Gly	Arg	Asp	Thr	Pro	Thr	Ser	Ala	Gly	144
Pro	Asn	Ser	Phe	Asn	Lys	Gly	Lys	His	153
Gly	Phe	Ser	Asp	Asn	Gln	Lys	Leu	Trp	162
Glu	Arg	Asn	Ile	Lys	Ser	His	Leu	Gly	171
Asn	Val	His	Asp	Gln	Asp	Asn	178		

<210> 56

<211> 178

<212> PRT

<213> Homo sapiens

<220>

<223> SW1136

<400> 56

Met	Ala	Asp	Gly	Lys	Ala	Gly	Asp	Glu	9
Lys	Pro	Glu	Lys	Ser	Gln	Arg	Ala	Gly	18
Ala	Ala	Gly	Gly	Pro	Glu	Glu	Glu	Ala	27
Glu	Lys	Pro	Val	Lys	Thr	Lys	Thr	Val	36
Ser	Ser	Ser	Asn	Gly	Gly	Glu	Ser	Ser	45
Ser	Arg	Ser	Ala	Glu	Lys	Arg	Ser	Ala	54
Glu	Glu	Glu	Ala	Ala	Asp	Leu	Pro	Thr	63
Lys	Pro	Thr	Lys	Ile	Ser	Lys	Phe	Gly	72
Phe	Ala	Ile	Gly	Ser	Gln	Thr	Thr	Lys	81
Lys	Ala	Ser	Ala	Ile	Ser	Ile	Lys	Leu	90
Gly	Ser	Ser	Lys	Pro	Lys	Glu	Thr	Val	99
Pro	Thr	Leu	Ala	Pro	Lys	Thr	Leu	Ser	108
Val	Ala	Ala	Ala	Phe	Asn	Glu	Asp	Glu	117
Asp	Ser	Glu	Pro	Glu	Glu	Met	Pro	Pro	126
Glu	Ala	Lys	Met	Arg	Met	Lys	Asn	Ile	135
Gly	Arg	Asp	Thr	Pro	Thr	Ser	Ala	Gly	144
Pro	Asn	Ser	Phe	Asn	Lys	Gly	Lys	His	153
Gly	Phe	Ser	Asp	Asn	Gln	Lys	Leu	Trp	162
Glu	Arg	Asn	Ile	Lys	Ser	His	Leu	Gly	171
Asn	Val	His	Asp	Gln	Asp	Asn	178		

<210> 57
<211> 153
<212> PRT
<213> Mus musculus

<220>
<223> SW1295

<400> 57

Met	Pro	Arg	Gly	Ser	Arg	Ser	Arg	Thr	9
Ser	Arg	Val	Thr	Pro	Pro	Ala	Ser	Arg	18
Ala	Pro	Gln	Met	Arg	Ala	Ala	Pro	Arg	27
Arg	Ala	Pro	Ala	Ala	Gln	Pro	Pro	Ala	36
Ala	Ala	Ala	Pro	Ser	Ala	Val	Gly	Ser	45
Pro	Ala	Ala	Ala	Pro	Arg	Gln	Pro	Gly	54
Leu	Met	Ala	Gln	Met	Ala	Thr	Thr	Ala	63
Ala	Gly	Val	Ala	Val	Gly	Ser	Ala	Val	72
Gly	His	Thr	Leu	Gly	His	Ala	Ile	Thr	81
Gly	Gly	Phe	Ser	Gly	Gly	Gly	Ser	Ala	90
Glu	Pro	Ala	Lys	Pro	Asp	Ile	Thr	Tyr	99
Gln	Glu	Pro	Gln	Gly	Ala	Gln	Leu	Gln	108
Asn	Gln	Gln	Ser	Phe	Gly	Pro	Cys	Ser	117
Leu	Glu	Ile	Lys	Gln	Phe	Leu	Glu	Cys	126
Ala	Gln	Asn	Gln	Ser	Asp	Val	Lys	Leu	135
Cys	Glu	Gly	Phe	Asn	Glu	Val	Leu	Arg	144
Gln	Cys	Arg	Ile	Ala	Asn	Gly	Leu	Met	153

<210> 58
<211> 151
<212> PRT
<213> Homo sapiens

<220>
<223> SW1295

<400> 58

Met	Pro	Arg	Gly	Ser	Arg	Ser	Arg	Thr	9
Ser	Arg	Met	Ala	Pro	Pro	Ala	Ser	Arg	18
Ala	Pro	Gln	Met	Arg	Ala	Ala	Pro	Arg	27
Pro	Ala	Pro	Val	Ala	Gln	Pro	Pro	Ala	36
Ala	Ala	Pro	Pro	Ser	Ala	Val	Gly	Ser	45
Ser	Ala	Ala	Ala	Pro	Arg	Gln	Pro	Gly	54
Leu	Met	Ala	Gln	Met	Ala	Thr	Thr	Ala	63
Ala	Gly	Val	Ala	Val	Gly	Ser	Ala	Val	72
Gly	His	Thr	Leu	Gly	His	Ala	Ile	Thr	81
Gly	Gly	Phe	Ser	Gly	Gly	Ser	Asn	Ala	90
Glu	Pro	Ala	Arg	Pro	Asp	Ile	Thr	Tyr	99
Gln	Glu	Pro	Gln	Gly	Thr	Gln	Pro	Ala	108

Gln	Gln	Gln	Gln	Pro	Cys	Leu	Tyr	Glu	117
Ile	Lys	Gln	Phe	Leu	Glu	Cys	Ala	Gln	126
Asn	Gln	Gly	Asp	Ile	Lys	Leu	Cys	Glu	135
Gly	Phe	Asn	Glu	Val	Leu	Lys	Gln	Cys	144
Arg	Leu	Ala	Asn	Gly	Leu	Ala	151		

<210> 59

<211> 19

<212> DNA

<213> Mus musculus

<220>

<223> TTF-1 Primer 1

<400> 59

cgagcgctac attgtcgct

19

<210> 60

<211> 22

<212> DNA

<213> Mus musculus

<220>

<223> TTF-1 Primer 2

<400> 60

gtcttaaatt tgcttggtgcc cc

22

<210> 61

<211> 19

<212> DNA

<213> Mus musculus

<220>

<223> GAPDH-Primer1

<400> 61

atcaacggga agcccatca

19

<210> 62

<211> 20

<212> DNA

<213> Mus musculus

<220>

<223> GAPDH-Primer2

<400> 62

gacataactca gcaccggcct

20

<210> 63

<211> 823

<212> PRT

<213> Mus musculus

<220>

<223> Fer

<400> 63

Met	Gly	Phe	Gly	Ser	Asp	Leu	Lys	Asn	9
Ser	Gln	Glu	Ala	Val	Leu	Lys	Leu	Gln	18
Asp	Trp	Glu	Leu	Arg	Leu	Leu	Glu	Thr	27
Val	Lys	Lys	Phe	Met	Ala	Leu	Arg	Ile	36
Lys	Ser	Asp	Lys	Glu	Tyr	Ala	Tyr	Thr	45
Leu	Gln	Asn	Leu	Cys	Asn	Gln	Val	Asp	54
Lys	Glu	Ser	Thr	Val	Gln	Val	Asn	Tyr	63
Val	Ser	Asn	Val	Ser	Lys	Ser	Trp	Leu	72
Leu	Met	Ile	Gln	Gln	Thr	Glu	Gln	Leu	81
Ser	Arg	Ile	Met	Lys	Thr	His	Ala	Glu	90
Asp	Leu	Asn	Ser	Gly	Pro	Leu	His	Arg	99
Leu	Thr	Met	Met	Ile	Lys	Asp	Lys	Gln	108
Gln	Val	Lys	Lys	Ser	Tyr	Val	Gly	Ile	117
His	Gln	Gln	Ile	Glu	Ala	Glu	Met	Ile	126
Lys	Val	Thr	Lys	Thr	Glu	Leu	Glu	Lys	135
Leu	Lys	Ser	Ser	Tyr	Arg	Gln	Leu	Ile	144
Lys	Glu	Met	Asn	Ser	Ala	Lys	Glu	Lys	153
Tyr	Lys	Glu	Ala	Leu	Ala	Lys	Gly	Lys	162
Glu	Thr	Glu	Lys	Ala	Lys	Glu	Arg	Tyr	171
Asp	Lys	Ala	Thr	Met	Lys	Leu	His	Met	180
Leu	His	Asn	Gln	Tyr	Val	Leu	Ala	Leu	189
Lys	Gly	Ala	Gln	Leu	His	Gln	Ser	Gln	198
Tyr	Tyr	Asp	Thr	Thr	Leu	Pro	Leu	Leu	207
Leu	Asp	Ser	Val	Gln	Lys	Met	Gln	Glu	216
Glu	Met	Ile	Lys	Ala	Leu	Lys	Gly	Ile	225
Phe	Asp	Asp	Tyr	Ser	Gln	Ile	Thr	Ser	234
Leu	Val	Thr	Glu	Glu	Ile	Val	Asn	Val	243
His	Lys	Glu	Ile	Gln	Met	Ser	Val	Glu	252
Gln	Ile	Asp	Pro	Ser	Thr	Glu	Tyr	Asn	261
Asn	Phe	Ile	Asp	Val	His	Arg	Thr	Thr	270
Ala	Ala	Lys	Glu	Gln	Glu	Ile	Glu	Phe	279
Asp	Thr	Ser	Leu	Leu	Glu	Glu	Asn	Glu	288
Asn	Leu	Gln	Ala	Asn	Glu	Ile	Met	Trp	297
Asn	Asn	Leu	Thr	Ala	Asp	Ser	Leu	Gln	306
Val	Met	Leu	Lys	Thr	Leu	Ala	Glu	Glu	315

Leu	Thr	Gln	Thr	Gln	Gln	Met	Leu	Leu	324
His	Lys	Glu	Ala	Ala	Val	Leu	Glu	Leu	333
Glu	Lys	Arg	Ile	Glu	Glu	Ser	Phe	Glu	342
Thr	Cys	Glu	Lys	Lys	Ser	Asp	Ile	Val	351
Leu	Leu	Leu	Gly	Gln	Lys	Gln	Ala	Leu	360
Glu	Glu	Leu	Lys	Gln	Ser	Val	Gln	Gln	369
Leu	Arg	Cys	Ser	Glu	Ala	Lys	Cys	Ala	378
Ala	Gln	Lys	Ala	Leu	Leu	Glu	Gln	Lys	387
Val	Gln	Glu	Asn	Asp	Gly	Lys	Glu	Pro	396
Pro	Pro	Val	Val	Asn	Tyr	Glu	Glu	Asp	405
Ala	Arg	Ser	Val	Thr	Ser	Met	Glu	Arg	414
Lys	Glu	Arg	Leu	Ser	Lys	Phe	Glu	Ser	423
Ile	Arg	His	Ser	Ile	Ala	Gly	Ile	Ile	432
Lys	Ser	Pro	Lys	Ser	Val	Leu	Gly	Ser	441
Ser	Thr	Gln	Val	Cys	Asp	Val	Ile	Ser	450
Val	Gly	Glu	Arg	Pro	Leu	Ala	Glu	His	459
Asp	Trp	Tyr	His	Gly	Ala	Ile	Pro	Arg	468
Ile	Glu	Ala	Gln	Glu	Leu	Leu	Lys	Gln	477
Gln	Gly	Asp	Phe	Leu	Val	Arg	Glu	Ser	486
His	Gly	Lys	Pro	Gly	Glu	Tyr	Val	Leu	495
Ser	Val	Tyr	Ser	Asp	Gly	Gln	Arg	Arg	504
His	Phe	Ile	Ile	Gln	Phe	Val	Asp	Asn	513
Leu	Tyr	Arg	Phe	Glu	Gly	Thr	Gly	Phe	522
Ser	Asn	Ile	Pro	Gln	Leu	Ile	Asp	His	531
His	Phe	Asn	Thr	Lys	Gln	Val	Ile	Thr	540
Lys	Lys	Ser	Gly	Val	Val	Leu	Leu	Asn	549
Pro	Ile	Pro	Lys	Asp	Lys	Lys	Trp	Val	558
Leu	Asn	His	Glu	Asp	Val	Ser	Leu	Gly	567
Glu	Leu	Leu	Gly	Lys	Gly	Asn	Phe	Gly	576
Glu	Val	Tyr	Lys	Gly	Thr	Leu	Lys	Asp	585
Lys	Thr	Pro	Val	Ala	Ile	Lys	Thr	Cys	594
Lys	Glu	Asp	Leu	Pro	Gln	Glu	Leu	Lys	603
Ile	Lys	Phe	Leu	Gln	Glu	Ala	Lys	Ile	612
Leu	Lys	Gln	Tyr	Asp	His	Pro	Asn	Ile	621
Val	Lys	Leu	Ile	Gly	Val	Cys	Thr	Gln	630
Arg	Gln	Pro	Val	Tyr	Ile	Ile	Met	Glu	639
Leu	Val	Pro	Gly	Gly	Asp	Phe	Leu	Thr	648
Phe	Leu	Arg	Lys	Arg	Lys	Asp	Glu	Leu	657
Lys	Leu	Lys	Gln	Leu	Val	Arg	Phe	Ser	666
Leu	Asp	Val	Ala	Ala	Gly	Met	Leu	Tyr	675
Leu	Glu	Ser	Lys	Asn	Cys	Ile	His	Arg	684
Asp	Leu	Ala	Ala	Arg	Asn	Cys	Leu	Val	693
Gly	Glu	Asn	Asn	Thr	Leu	Lys	Ile	Ser	702
Asp	Phe	Gly	Met	Ser	Arg	Gln	Glu	Asp	711
Gly	Gly	Val	Tyr	Ser	Ser	Ser	Gly	Leu	720
Lys	Gln	Ile	Pro	Ile	Lys	Trp	Thr	Ala	729
Pro	Glu	Ala	Leu	Asn	Tyr	Gly	Arg	Tyr	738
Ser	Ser	Glu	Ser	Asp	Val	Trp	Ser	Phe	747
Gly	Ile	Leu	Leu	Trp	Glu	Thr	Phe	Ser	756
Leu	Gly	Val	Cys	Pro	Tyr	Pro	Gly	Met	765
Thr	Asn	Gln	Gln	Ala	Arg	Glu	Gln	Val	774
Glu	Arg	Gly	Tyr	Arg	Met	Ser	Ala	Pro	783

Gln	Asn	Cys	Pro	Glu	Glu	Val	Phe	Thr	792
Ile	Met	Met	Lys	Cys	Trp	Asp	Tyr	Lys	801
Pro	Glu	Asn	Arg	Pro	Lys	Phe	Asn	Asp	810
Leu	His	Lys	Glu	Leu	Thr	Val	Ile	Lys	819
Lys	Met	Ile	Thr	823					

<210> 64

<211> 822

<212> PRT

<213> Homo sapiens

<220>

<223> Fer

<400> 64

	Met	Gly	Phe	Gly	Ser	Asp	Leu	Lys	Asn	9
Ser	His	Glu	Ala	Val	Leu	Lys	Leu	Gln	18	
Asp	Trp	Glu	Leu	Arg	Leu	Leu	Glu	Thr	27	
Val	Lys	Lys	Phe	Met	Ala	Leu	Arg	Ile	36	
Lys	Ser	Asp	Lys	Glu	Tyr	Ala	Ser	Thr	45	
Leu	Gln	Asn	Leu	Cys	Asn	Gln	Val	Asp	54	
Lys	Glu	Ser	Thr	Val	Gln	Met	Asn	Tyr	63	
Val	Ser	Asn	Val	Ser	Lys	Ser	Trp	Leu	72	
Leu	Met	Ile	Gln	Gln	Thr	Glu	Gln	Leu	81	
Ser	Arg	Ile	Met	Lys	Thr	His	Ala	Glu	90	
Asp	Leu	Asn	Ser	Gly	Pro	Leu	His	Arg	99	
Leu	Thr	Met	Met	Ile	Lys	Asp	Lys	Gln	108	
Gln	Val	Lys	Lys	Ser	Tyr	Ile	Gly	Val	117	
His	Gln	Gln	Ile	Glu	Ala	Glu	Met	Ile	126	
Lys	Val	Thr	Lys	Thr	Glu	Leu	Glu	Lys	135	
Leu	Lys	Cys	Ser	Tyr	Arg	Gln	Leu	Ile	144	
Lys	Glu	Met	Asn	Ser	Ala	Lys	Glu	Lys	153	
Tyr	Lys	Glu	Ala	Leu	Ala	Lys	Gly	Lys	162	
Glu	Thr	Glu	Lys	Ala	Lys	Glu	Arg	Tyr	171	
Asp	Lys	Ala	Thr	Met	Lys	Leu	His	Met	180	
Leu	His	Asn	Gln	Tyr	Val	Leu	Ala	Leu	189	
Lys	Gly	Ala	Gln	Leu	His	Gln	Asn	Gln	198	
Tyr	Tyr	Asp	Ile	Thr	Leu	Pro	Leu	Leu	207	
Leu	Asp	Ser	Leu	Gln	Lys	Met	Gln	Glu	216	
Glu	Met	Ile	Lys	Ala	Leu	Lys	Gly	Ile	225	
Phe	Asp	Glu	Tyr	Ser	Gln	Ile	Thr	Ser	234	
Leu	Val	Thr	Glu	Glu	Ile	Val	Asn	Val	243	
His	Lys	Glu	Ile	Gln	Met	Ser	Val	Glu	252	
Gln	Ile	Asp	Pro	Ser	Thr	Glu	Tyr	Asn	261	
Asn	Phe	Ile	Asp	Val	His	Arg	Thr	Thr	270	
Ala	Ala	Lys	Glu	Gln	Glu	Ile	Glu	Phe	279	
Asp	Thr	Ser	Leu	Leu	Glu	Glu	Asn	Glu	288	
Asn	Leu	Gln	Ala	Asn	Glu	Ile	Met	Trp	297	
Asn	Asn	Leu	Thr	Ala	Glu	Ser	Leu	Gln	306	
Val	Met	Leu	Lys	Thr	Leu	Ala	Glu	Glu	315	

Leu	Met	Gln	Thr	Gln	Gln	Met	Leu	Leu	324
Asn	Lys	Glu	Glu	Ala	Val	Leu	Glu	Leu	333
Glu	Lys	Arg	Ile	Glu	Glu	Ser	Ser	Glu	342
Thr	Cys	Glu	Lys	Lys	Ser	Asp	Ile	Val	351
Leu	Leu	Leu	Ser	Gln	Lys	Gln	Ala	Leu	360
Glu	Glu	Leu	Lys	Gln	Ser	Val	Gln	Gln	369
Leu	Arg	Cys	Thr	Glu	Ala	Lys	Phe	Ser	378
Ala	Gln	Lys	Glu	Leu	Leu	Glu	Gln	Lys	387
Val	Gln	Glu	Asn	Asp	Gly	Lys	Glu	Pro	396
Pro	Pro	Val	Val	Asn	Tyr	Glu	Glu	Asp	405
Ala	Arg	Ser	Val	Thr	Ser	Met	Glu	Arg	414
Lys	Glu	Arg	Leu	Ser	Lys	Phe	Glu	Ser	423
Ile	Arg	His	Ser	Ile	Ala	Gly	Ile	Ile	432
Arg	Ser	Pro	Lys	Ser	Ala	Val	Gly	Ser	441
Ser	Ala	Leu	Ser	Asp	Met	Ile	Ser	Ile	450
Ser	Glu	Lys	Pro	Leu	Ala	Glu	Gln	Asp	459
Trp	Tyr	His	Gly	Ala	Ile	Pro	Arg	Ile	468
Glu	Ala	Gln	Glu	Leu	Leu	Lys	Lys	Gln	477
Gly	Asp	Phe	Leu	Val	Arg	Glu	Ser	His	486
Gly	Lys	Pro	Gly	Glu	Tyr	Val	Leu	Ser	495
Val	Tyr	Ser	Asp	Gly	Gln	Arg	Arg	His	504
Phe	Ile	Ile	Gln	Tyr	Val	Asp	Asn	Met	513
Tyr	Arg	Phe	Glu	Gly	Thr	Gly	Phe	Ser	522
Asn	Ile	Pro	Gln	Leu	Ile	Asp	His	His	531
Tyr	Thr	Thr	Lys	Gln	Val	Ile	Thr	Lys	540
Lys	Ser	Gly	Val	Val	Leu	Leu	Asn	Pro	549
Ile	Pro	Lys	Asp	Lys	Lys	Trp	Ile	Leu	558
Ser	His	Glu	Asp	Val	Ile	Leu	Gly	Glu	567
Leu	Leu	Gly	Lys	Gly	Asn	Phe	Gly	Glu	576
Val	Tyr	Lys	Gly	Thr	Leu	Lys	Asp	Lys	585
Thr	Ser	Val	Ala	Val	Lys	Thr	Cys	Lys	594
Glu	Asp	Leu	Pro	Gln	Glu	Leu	Lys	Ile	603
Lys	Phe	Leu	Gln	Glu	Ala	Lys	Ile	Leu	612
Lys	Gln	Tyr	Asp	His	Pro	Asn	Ile	Val	621
Lys	Leu	Ile	Gly	Val	Cys	Thr	Gln	Arg	630
Gln	Pro	Val	Tyr	Ile	Ile	Met	Glu	Leu	639
Val	Ser	Gly	Gly	Asp	Phe	Leu	Thr	Phe	648
Leu	Arg	Arg	Lys	Lys	Asp	Glu	Leu	Lys	657
Leu	Lys	Gln	Leu	Val	Lys	Phe	Ser	Leu	666
Asp	Ala	Ala	Ala	Gly	Met	Leu	Tyr	Leu	675
Glu	Ser	Lys	Asn	Cys	Ile	His	Arg	Asp	684
Leu	Ala	Ala	Arg	Asn	Cys	Leu	Val	Gly	693
Glu	Asn	Asn	Val	Leu	Lys	Ile	Ser	Asp	702
Phe	Gly	Met	Ser	Arg	Gln	Glu	Asp	Gly	711
Gly	Val	Tyr	Ser	Ser	Ser	Gly	Leu	Lys	720
Gln	Ile	Pro	Ile	Lys	Trp	Thr	Ala	Pro	729
Glu	Ala	Leu	Asn	Tyr	Gly	Arg	Tyr	Ser	738
Ser	Glu	Ser	Asp	Val	Trp	Ser	Phe	Gly	747
Ile	Leu	Leu	Trp	Glu	Thr	Phe	Ser	Leu	756
Gly	Val	Cys	Pro	Tyr	Pro	Gly	Met	Thr	765
Asn	Gln	Gln	Ala	Arg	Glu	Gln	Val	Glu	774
Arg	Gly	Tyr	Arg	Met	Ser	Ala	Pro	Gln	783

His	Cys	Pro	Glu	Asp	Ile	Ser	Lys	Ile	792
Met	Met	Lys	Cys	Trp	Asp	Tyr	Lys	Pro	801
Glu	Asn	Arg	Pro	Lys	Phe	Ser	Glu	Leu	810
Gln	Lys	Glu	Leu	Thr	Ile	Ile	Lys	Arg	819
Lys	Leu	Thr	822						

<210> 65

<211> 116

<212> PRT

<213> Mus musculus

<220>

<223> MRP-3

<400> 65

Met	Arg	Asn	Ser	Lys	Thr	Ala	Ile	Ser	9
Phe	Phe	Ile	Leu	Val	Ala	Val	Leu	Gly	18
Ser	Gln	Ala	Gly	Leu	Ile	Gln	Glu	Met	27
Glu	Lys	Glu	Asp	Arg	Arg	Tyr	Asn	Pro	36
Pro	Ile	Ile	His	Gln	Gly	Phe	Gln	Asp	45
Thr	Ser	Ser	Asp	Cys	Cys	Phe	Ser	Tyr	54
Ala	Thr	Gln	Ile	Pro	Cys	Lys	Arg	Phe	63
Ile	Tyr	Tyr	Phe	Pro	Thr	Ser	Gly	Gly	72
Cys	Ile	Lys	Pro	Gly	Ile	Ile	Phe	Ile	81
Ser	Arg	Arg	Gly	Thr	Gln	Val	Cys	Ala	90
Asp	Pro	Ser	Asp	Arg	Arg	Val	Gln	Arg	99
Cys	Leu	Ser	Thr	Leu	Lys	Gln	Gly	Pro	108
Arg	Ser	Gly	Asn	Lys	Val	Ile	Ala	116	

<210> 66

<211> 120

<212> PRT

<213> Homo sapiens

<220>

<223> MRP-3

<400> 66

Met	Lys	Val	Ser	Val	Ala	Ala	Leu	Ser	9
Cys	Leu	Met	Leu	Val	Thr	Ala	Leu	Gly	18
Ser	Gln	Ala	Arg	Val	Thr	Lys	Asp	Ala	27
Glu	Thr	Glu	Phe	Met	Met	Ser	Lys	Leu	36
Pro	Leu	Glu	Asn	Pro	Val	Leu	Leu	Asp	45
Arg	Phe	His	Ala	Thr	Ser	Ala	Asp	Cys	54
Cys	Ile	Ser	Tyr	Thr	Pro	Arg	Ser	Ile	63
Pro	Cys	Ser	Leu	Leu	Glu	Ser	Tyr	Phe	72
Glu	Thr	Asn	Ser	Glu	Cys	Ser	Lys	Pro	81
Gly	Val	Ile	Phe	Leu	Thr	Lys	Lys	Gly	90

Arg	Arg	Phe	Cys	Ala	Asn	Pro	Ser	Asp	99
Lys	Gln	Val	Gln	Val	Cys	Met	Arg	Met	108
Leu	Lys	Leu	Asp	Thr	Arg	Ile	Lys	Thr	117
Arg	Lys	Asn	120						

<210> 67

<211> 264

<212> PRT

<213> Mus musculus

<220>

<223> NNMT

<400> 67

Met	Glu	Ser	Gly	Phe	Thr	Ser	Lys	Asp	9
Thr	Tyr	Leu	Ser	His	Phe	Asn	Pro	Arg	18
Asp	Tyr	Leu	Glu	Lys	Tyr	Tyr	Ser	Phe	27
Gly	Ser	Arg	His	Cys	Ala	Glu	Asn	Glu	36
Ile	Leu	Arg	His	Leu	Leu	Lys	Asn	Leu	45
Phe	Lys	Ile	Phe	Cys	Leu	Gly	Ala	Val	54
Lys	Gly	Glu	Leu	Leu	Ile	Asp	Ile	Gly	63
Ser	Gly	Pro	Thr	Ile	Tyr	Gln	Leu	Leu	72
Ser	Ala	Cys	Glu	Ser	Phe	Thr	Glu	Ile	81
Ile	Val	Ser	Asp	Tyr	Thr	Asp	Gln	Asn	90
Leu	Trp	Glu	Leu	Gln	Lys	Trp	Leu	Lys	99
Lys	Glu	Pro	Gly	Ala	Phe	Asp	Trp	Ser	108
Pro	Val	Val	Thr	Tyr	Val	Cys	Asp	Leu	117
Glu	Gly	Asn	Arg	Met	Lys	Gly	Pro	Glu	126
Lys	Glu	Glu	Lys	Leu	Arg	Arg	Ala	Ile	135
Lys	Gln	Val	Leu	Lys	Cys	Asp	Val	Thr	144
Gln	Ser	Gln	Pro	Leu	Gly	Gly	Val	Ser	153
Leu	Pro	Pro	Ala	Asp	Cys	Leu	Leu	Ser	162
Thr	Leu	Cys	Leu	Asp	Ala	Ala	Cys	Pro	171
Asp	Leu	Pro	Ala	Tyr	Arg	Thr	Ala	Leu	180
Arg	Asn	Leu	Gly	Ser	Leu	Leu	Lys	Pro	189
Gly	Gly	Phe	Leu	Val	Met	Val	Asp	Ala	198
Leu	Lys	Ser	Ser	Tyr	Tyr	Met	Ile	Gly	207
Glu	Gln	Lys	Phe	Ser	Ser	Leu	Pro	Leu	216
Gly	Trp	Glu	Thr	Val	Arg	Asp	Ala	Val	225
Glu	Glu	Ala	Gly	Tyr	Thr	Ile	Glu	Gln	234
Phe	Glu	Val	Ile	Ser	Gln	Asn	Tyr	Ser	243
Ser	Thr	Thr	Ser	Asn	Asn	Glu	Gly	Leu	252
Phe	Ser	Leu	Val	Gly	Arg	Lys	Pro	Gly	261
Arg	Ser	Glu	264						

<210> 68

<211> 264

<212> PRT

<213> Homo sapiens

<220>

<223> NNMT

<400> 68

Met	Glu	Ser	Gly	Phe	Thr	Ser	Lys	Asp	9
Thr	Tyr	Leu	Ser	His	Phe	Asn	Pro	Arg	18
Asp	Tyr	Leu	Glu	Lys	Tyr	Tyr	Lys	Phe	27
Gly	Ser	Arg	His	Ser	Ala	Glu	Ser	Gln	36
Ile	Leu	Lys	His	Leu	Leu	Lys	Asn	Leu	45
Phe	Lys	Ile	Phe	Cys	Leu	Asp	Gly	Val	54
Lys	Gly	Asp	Leu	Leu	Ile	Asp	Ile	Gly	63
Ser	Gly	Pro	Thr	Ile	Tyr	Gln	Leu	Leu	72
Ser	Ala	Cys	Glu	Ser	Phe	Lys	Glu	Ile	81
Val	Val	Thr	Asp	Tyr	Ser	Asp	Gln	Asn	90
Leu	Gln	Glu	Leu	Glu	Lys	Trp	Leu	Lys	99
Lys	Glu	Pro	Glu	Ala	Phe	Asp	Trp	Ser	108
Pro	Val	Val	Thr	Tyr	Val	Cys	Asp	Leu	117
Glu	Gly	Asn	Arg	Val	Lys	Gly	Pro	Glu	126
Lys	Glu	Glu	Lys	Leu	Arg	Gln	Ala	Val	135
Lys	Gln	Val	Leu	Lys	Cys	Asp	Val	Thr	144
Gln	Ser	Gln	Pro	Leu	Gly	Ala	Val	Pro	153
Leu	Pro	Pro	Ala	Asp	Cys	Val	Leu	Ser	162
Thr	Leu	Cys	Leu	Asp	Ala	Ala	Cys	Pro	171
Asp	Leu	Pro	Thr	Tyr	Cys	Arg	Ala	Leu	180
Arg	Asn	Leu	Gly	Ser	Leu	Leu	Lys	Pro	189
Gly	Gly	Phe	Leu	Val	Ile	Met	Asp	Ala	198
Leu	Lys	Ser	Ser	Tyr	Tyr	Met	Ile	Gly	207
Glu	Gln	Lys	Phe	Ser	Ser	Leu	Pro	Leu	216
Gly	Arg	Glu	Ala	Val	Glu	Ala	Ala	Val	225
Lys	Glu	Ala	Gly	Tyr	Thr	Ile	Glu	Trp	234
Phe	Glu	Val	Ile	Ser	Gln	Ser	Tyr	Ser	243
Ser	Thr	Met	Ala	Asn	Asn	Glu	Gly	Leu	252
Phe	Ser	Leu	Val	Ala	Arg	Lys	Leu	Ser	261
Arg	Pro	Leu							264

<210> 69

<211> 158

<212> PRT

<213> Mus musculus

<220>

<223> UBC9

<400> 69

Met	Ser	Gly	Ile	Ala	Leu	Ser	Arg	Leu	9
Ala	Gln	Glu	Arg	Lys	Ala	Trp	Arg	Lys	18
Asp	His	Pro	Phe	Gly	Phe	Val	Ala	Val	27

Pro	Thr	Lys	Asn	Pro	Asp	Gly	Thr	Met	36
Asn	Leu	Met	Asn	Trp	Glu	Cys	Ala	Ile	45
Pro	Gly	Lys	Lys	Gly	Thr	Pro	Trp	Glu	54
Gly	Gly	Leu	Phe	Lys	Leu	Arg	Met	Leu	63
Phe	Lys	Asp	Asp	Tyr	Pro	Ser	Ser	Pro	72
Pro	Lys	Cys	Lys	Phe	Glu	Pro	Pro	Leu	81
Phe	His	Pro	Asn	Val	Tyr	Pro	Ser	Gly	90
Thr	Val	Cys	Leu	Ser	Ile	Leu	Glu	Glu	99
Asp	Lys	Asp	Trp	Arg	Pro	Ala	Ile	Thr	108
Ile	Lys	Gln	Ile	Leu	Leu	Gly	Ile	Gln	117
Glu	Leu	Leu	Asn	Glu	Pro	Asn	Ile	Gln	126
Asp	Pro	Ala	Gln	Ala	Glu	Ala	Tyr	Thr	135
Ile	Tyr	Cys	Gln	Asn	Arg	Val	Glu	Tyr	144
Glu	Lys	Arg	Val	Arg	Ala	Gln	Ala	Lys	153
Lys	Phe	Ala	Pro	Ser	158				

<210> 70

<211> 158

<212> PRT

<213> Homo sapiens

<220>

<223> UBC9

<400> 70

Met	Ser	Gly	Ile	Ala	Leu	Ser	Arg	Leu	9
Ala	Gln	Glu	Arg	Lys	Ala	Trp	Arg	Lys	18
Asp	His	Pro	Phe	Gly	Phe	Val	Ala	Val	27
Pro	Thr	Lys	Asn	Pro	Asp	Gly	Thr	Met	36
Asn	Leu	Met	Asn	Trp	Glu	Cys	Ala	Ile	45
Pro	Gly	Lys	Lys	Gly	Thr	Pro	Trp	Glu	54
Gly	Gly	Leu	Phe	Lys	Leu	Arg	Met	Leu	63
Phe	Lys	Asp	Asp	Tyr	Pro	Ser	Ser	Pro	72
Pro	Lys	Cys	Lys	Phe	Glu	Pro	Pro	Leu	81
Phe	His	Pro	Asn	Val	Tyr	Pro	Ser	Gly	90
Thr	Val	Cys	Leu	Ser	Ile	Leu	Glu	Glu	99
Asp	Lys	Asp	Trp	Arg	Pro	Ala	Ile	Thr	108
Ile	Lys	Gln	Ile	Leu	Leu	Gly	Ile	Gln	117
Glu	Leu	Leu	Asn	Glu	Pro	Asn	Ile	Gln	126
Asp	Pro	Ala	Gln	Ala	Glu	Ala	Tyr	Thr	135
Ile	Tyr	Cys	Gln	Asn	Arg	Val	Glu	Tyr	144
Glu	Lys	Arg	Val	Arg	Ala	Gln	Ala	Lys	153
Lys	Phe	Ala	Pro	Ser	158				

<210> 71

<211> 109

<212> PRT

<213> Homo sapiens

<220>

<223> MCP-2

<400> 71

Met	Leu	Lys	Leu	Thr	Pro	Leu	Pro	Ser	9
Lys	Met	Lys	Val	Ser	Ala	Ala	Leu	Leu	18
Cys	Leu	Leu	Leu	Met	Ala	Ala	Thr	Phe	27
Ser	Pro	Gln	Gly	Leu	Ala	Gln	Pro	Asp	36
Ser	Val	Ser	Ile	Pro	Ile	Thr	Cys	Cys	45
Phe	Asn	Val	Ile	Asn	Arg	Lys	Ile	Pro	54
Ile	Gln	Arg	Leu	Glu	Ser	Tyr	Thr	Arg	63
Ile	Thr	Asn	Ile	Gln	Cys	Pro	Lys	Glu	72
Ala	Val	Ile	Phe	Lys	Thr	Gln	Arg	Gly	81
Lys	Glu	Val	Cys	Ala	Asp	Pro	Lys	Glu	90
Arg	Trp	Val	Arg	Asp	Ser	Met	Lys	His	99
Leu	Asp	Gln	Ile	Phe	Gln	Asn	Leu	Lys	108
Pro	109								

<210> 72

<211> 462

<212> PRT

<213> Mus musculus

<220>

<223> Cathepsin C

<400> 72

Met	Gly	Pro	Trp	Thr	His	Ser	Leu	Arg	9
Ala	Val	Leu	Leu	Leu	Val	Leu	Leu	Gly	18
Val	Cys	Thr	Val	Arg	Ser	Asp	Thr	Pro	27
Ala	Asn	Cys	Thr	Tyr	Pro	Asp	Leu	Leu	36
Gly	Thr	Trp	Val	Phe	Gln	Val	Gly	Pro	45
Arg	Ser	Ser	Arg	Ser	Asp	Ile	Asn	Cys	54
Ser	Val	Met	Glu	Ala	Thr	Glu	Glu	Lys	63
Val	Val	Val	His	Leu	Lys	Lys	Leu	Asp	72
Thr	Ala	Tyr	Asp	Glu	Leu	Gly	Asn	Ser	81
Gly	His	Phe	Thr	Leu	Ile	Tyr	Asn	Gln	90
Gly	Phe	Glu	Ile	Val	Leu	Asn	Asp	Tyr	99
Lys	Trp	Phe	Ala	Phe	Phe	Lys	Tyr	Glu	108
Val	Arg	Gly	His	Thr	Ala	Ile	Ser	Tyr	117
Cys	His	Glu	Thr	Met	Thr	Gly	Trp	Val	126
His	Asp	Val	Leu	Gly	Arg	Asn	Trp	Ala	135
Cys	Phe	Val	Gly	Lys	Lys	Val	Glu	Ser	144
His	Ile	Glu	Lys	Val	Asn	Met	Asn	Ala	153
Ala	His	Leu	Gly	Gly	Leu	Gln	Glu	Arg	162
Tyr	Ser	Glu	Arg	Leu	Tyr	Thr	His	Asn	171
His	Asn	Phe	Val	Lys	Ala	Ile	Asn	Thr	180

Val	Gln	Lys	Ser	Trp	Thr	Ala	Thr	Ala	189
Tyr	Lys	Glu	Tyr	Glu	Lys	Met	Ser	Leu	198
Arg	Asp	Leu	Ile	Arg	Arg	Ser	Gly	His	207
Ser	Gln	Arg	Ile	Pro	Arg	Pro	Lys	Pro	216
Ala	Pro	Met	Thr	Asp	Glu	Ile	Gln	Gln	225
Gln	Ile	Leu	Asn	Leu	Pro	Glu	Ser	Trp	234
Asp	Trp	Arg	Asn	Val	Gln	Gly	Val	Asn	243
Tyr	Val	Ser	Pro	Val	Arg	Asn	Gln	Glu	252
Ser	Cys	Gly	Ser	Cys	Tyr	Ser	Phe	Ala	261
Ser	Met	Gly	Met	Leu	Glu	Ala	Arg	Ile	270
Arg	Ile	Leu	Thr	Asn	Asn	Ser	Gln	Thr	279
Pro	Ile	Leu	Ser	Pro	Gln	Glu	Val	Val	288
Ser	Cys	Ser	Pro	Tyr	Ala	Gln	Gly	Cys	297
Asp	Gly	Gly	Phe	Pro	Tyr	Leu	Ile	Ala	306
Gly	Lys	Tyr	Ala	Gln	Asp	Phe	Gly	Val	315
Val	Glu	Glu	Ser	Cys	Phe	Pro	Tyr	Thr	324
Ala	Lys	Asp	Ser	Pro	Cys	Lys	Pro	Arg	333
Glu	Asn	Cys	Leu	Arg	Tyr	Tyr	Ser	Ser	342
Asp	Tyr	Tyr	Tyr	Val	Gly	Gly	Phe	Tyr	351
Gly	Gly	Cys	Asn	Glu	Ala	Leu	Met	Lys	360
Leu	Glu	Leu	Val	Lys	His	Gly	Pro	Met	369
Ala	Val	Ala	Phe	Glu	Val	His	Asp	Asp	378
Phe	Leu	His	Tyr	His	Ser	Gly	Ile	Tyr	387
His	His	Thr	Gly	Leu	Ser	Asp	Pro	Phe	396
Asn	Pro	Phe	Glu	Leu	Thr	Asn	His	Ala	405
Val	Leu	Leu	Val	Gly	Tyr	Gly	Arg	Asp	414
Pro	Val	Thr	Gly	Ile	Glu	Tyr	Trp	Ile	423
Ile	Lys	Asn	Ser	Trp	Gly	Ser	Asn	Trp	432
Gly	Glu	Ser	Gly	Tyr	Phe	Arg	Ile	Arg	441
Arg	Gly	Thr	Asp	Glu	Cys	Ala	Ile	Glu	450
Ser	Ile	Ala	Val	Ala	Ala	Ile	Pro	Ile	459
Pro	Lys	Leu	462						

<210> 73

<211> 463

<212> PRT

<213> Homo sapiens

<220>

<223> Cathepsin C

<400> 73

Met	Gly	Ala	Gly	Pro	Ser	Leu	Leu	Leu	9
Ala	Ala	Leu	Leu	Leu	Leu	Leu	Ser	Gly	18
Asp	Gly	Ala	Val	Arg	Cys	Asp	Thr	Pro	27
Ala	Asn	Cys	Thr	Tyr	Leu	Asp	Leu	Leu	36
Gly	Thr	Trp	Val	Phe	Gln	Val	Gly	Ser	45
Ser	Gly	Ser	Gln	Arg	Asp	Val	Asn	Cys	54
Ser	Val	Met	Gly	Pro	Gln	Glu	Lys	Lys	63
Val	Val	Val	Tyr	Leu	Gln	Lys	Leu	Asp	72

Thr	Ala	Tyr	Asp	Asp	Leu	Gly	Asn	Ser	81
Gly	His	Phe	Thr	Ile	Ile	Tyr	Asn	Gln	90
Gly	Phe	Glu	Ile	Val	Leu	Asn	Asp	Tyr	99
Lys	Trp	Phe	Ala	Phe	Phe	Lys	Tyr	Lys	108
Glu	Glu	Gly	Ser	Lys	Val	Thr	Thr	Tyr	117
Cys	Asn	Glu	Thr	Met	Thr	Gly	Trp	Val	126
His	Asp	Val	Leu	Gly	Arg	Asn	Trp	Ala	135
Cys	Phe	Thr	Gly	Lys	Lys	Val	Gly	Thr	144
Ala	Ser	Glu	Asn	Val	Tyr	Val	Asn	Thr	153
Ala	His	Leu	Lys	Asn	Ser	Gln	Glu	Lys	162
Tyr	Ser	Asn	Arg	Leu	Tyr	Lys	Tyr	Asp	171
His	Asn	Phe	Val	Lys	Ala	Ile	Asn	Ala	180
Ile	Gln	Lys	Ser	Trp	Thr	Ala	Thr	Thr	189
Tyr	Met	Glu	Tyr	Glu	Thr	Leu	Thr	Leu	198
Gly	Asp	Met	Ile	Arg	Arg	Ser	Gly	Gly	207
His	Ser	Arg	Lys	Ile	Pro	Arg	Pro	Lys	216
Pro	Ala	Pro	Leu	Thr	Ala	Glu	Ile	Gln	225
Gln	Lys	Ile	Leu	His	Leu	Pro	Thr	Ser	234
Trp	Asp	Trp	Arg	Asn	Val	His	Gly	Ile	243
Asn	Phe	Val	Ser	Pro	Val	Arg	Asn	Gln	252
Ala	Ser	Cys	Gly	Ser	Cys	Tyr	Ser	Phe	261
Ala	Ser	Met	Gly	Met	Leu	Glu	Ala	Arg	270
Ile	Arg	Ile	Leu	Thr	Asn	Asn	Ser	Gln	279
Thr	Pro	Ile	Leu	Ser	Pro	Gln	Glu	Val	288
Val	Ser	Cys	Ser	Gln	Tyr	Ala	Gln	Gly	297
Cys	Glu	Gly	Gly	Phe	Pro	Tyr	Leu	Ile	306
Ala	Gly	Lys	Tyr	Ala	Gln	Asp	Phe	Gly	315
Leu	Val	Glu	Glu	Ala	Cys	Phe	Pro	Tyr	324
Thr	Gly	Thr	Asp	Ser	Pro	Cys	Lys	Met	333
Lys	Glu	Asp	Cys	Phe	Arg	Tyr	Tyr	Ser	342
Ser	Glu	Tyr	His	Tyr	Val	Gly	Gly	Phe	351
Tyr	Gly	Gly	Cys	Asn	Glu	Ala	Leu	Met	360
Lys	Leu	Glu	Leu	Val	His	His	Gly	Pro	369
Met	Ala	Val	Ala	Phe	Glu	Val	Tyr	Asp	378
Asp	Phe	Leu	His	Tyr	Lys	Lys	Gly	Ile	387
Tyr	His	His	Thr	Gly	Leu	Arg	Asp	Pro	396
Phe	Asn	Pro	Phe	Glu	Leu	Thr	Asn	His	405
Ala	Val	Leu	Leu	Val	Gly	Tyr	Gly	Thr	414
Asp	Ser	Ala	Ser	Gly	Met	Asp	Tyr	Trp	423
Ile	Val	Lys	Asn	Ser	Trp	Gly	Thr	Gly	432
Trp	Gly	Glu	Asn	Gly	Tyr	Phe	Arg	Ile	441
Arg	Arg	Gly	Thr	Asp	Glu	Cys	Ala	Ile	450
Glu	Ser	Ile	Ala	Val	Ala	Ala	Thr	Pro	459
Ile	Pro	Lys	Leu		463				

<210> 74

<211> 21

<212> DNA

<213> Homo sapiens

<220>

<223> hGAPDH-Primer 1

<400> 74

CCTCCCCTCT TCAAGGGTCT A

21

<210> 75

<211> 21

<212> DNA

<213> Homo sapiens

<220>

<223> hGAPDH-Primer 2

<400> 75

AGGAGTAAGA CCCCTGGACC A

21

<210> 76

<211> 21

<212> DNA

<213> Homo sapiens

<220>

<223> CCR-1 Primer 1

<400> 76

CCCAATGGGA ATTCCTCAC C

21

<210> 77

<211> 22

<212> DNA

<213> Homo sapiens

<220>

<223> Fer Primer 2

<400> 77

GCTTCCACTC TCGTAGGCTT TC

22

<210> 78

<211> 25

<212> DNA

<213> Homo sapiens

<220>

<223> Cyclophilin Primer 1

<400> 78

TCTTAACCAC CAGATCATTC CTTCT

25

<210> 79

<211> 20

<212> DNA

<213> Homo sapiens

<220>

<223> Cyclophilin Primer 2

<400> 79

GGATACTGCG AGCAAATGGG

20

<210> 80

<211> 347

<212> Protein

<213> Homo sapiens

<220>

<223> BAF57 Variant

<400> 80

Met	Ser	Lys	Arg	Pro	Ser	Tyr	Ala	Pro	Pro	Pro	Thr	12
Pro	Ala	Pro	Ala	Thr	Gln	Met	Pro	Ser	Thr	Pro	Gly	24
Phe	Val	Gly	Tyr	Asn	Pro	Tyr	Ser	His	Leu	Ala	Tyr	36
Asn	Asn	Tyr	Arg	Leu	Gly	Gly	Asn	Pro	Gly	Thr	Asn	48
Ser	Arg	Val	Thr	Ala	Ser	Ser	Gly	Ile	Thr	Ile	Pro	60
Lys	Pro	Pro	Lys	Pro	Pro	Asp	Lys	Pro	Leu	Met	Pro	72
Tyr	Met	Arg	Tyr	Ser	Arg	Lys	Val	Trp	Asp	Gln	Val	84
Lys	Ala	Ser	Asn	Pro	Asp	Leu	Lys	Leu	Trp	Glu	Ile	96
Gly	Lys	Ile	Ile	Gly	Gly	Met	Trp	Arg	Asp	Leu	Thr	108
Asp	Glu	Glu	Lys	Gln	Glu	Tyr	Leu	Asn	Glu	Tyr	Glu	120
Ala	Glu	Lys	Ile	Glu	Tyr	Asn	Glu	Ser	Met	Lys	Ala	132
Tyr	His	Asn	Ser	Pro	Ala	Tyr	Leu	Ala	Tyr	Ile	Asn	144
Ala	Lys	Ser	Arg	Ala	Glu	Ala	Ala	Leu	Glu	Glu	Glu	156
Ser	Arg	Gln	Arg	Gln	Ser	Arg	Met	Glu	Lys	Gly	Glu	168
Pro	Tyr	Met	Ser	Ile	Gln	Pro	Ala	Glu	Asp	Pro	Asp	180

Asp	Tyr	Asp	Asp	Gly	Phe	Ser	Met	Lys	His	Thr	Ala	192
Thr	Ala	Arg	Phe	Gln	Arg	Asn	His	Arg	Leu	Ile	Ser	204
Glu	Ile	Leu	Ser	Glu	Ser	Val	Val	Pro	Asp	Val	Arg	216
Ser	Val	Val	Thr	Thr	Ala	Arg	Met	Gln	Val	Leu	Lys	228
Arg	Gln	Val	Gln	Ser	Leu	Met	Val	His	Gln	Arg	Lys	240
Leu	Glu	Ala	Glu	Leu	Leu	Gln	Ile	Glu	Glu	Arg	His	252
Gln	Glu	Lys	Lys	Arg	Lys	Phe	Leu	Glu	Ser	Thr	Asp	264
Ser	Phe	Asn	Asn	Glu	Leu	Lys	Arg	Leu	Cys	Gly	Leu	276
Lys	Val	Glu	Val	Asp	Met	Glu	Lys	Ile	Ala	Ala	Glu	288
Ile	Ala	Gln	Ala	Glu	Glu	Gln	Ala	Arg	Lys	Arg	Gln	300
Glu	Glu	Arg	Glu	Lys	Glu	Ala	Ala	Glu	Gln	Ala	Glu	312
Arg	Ser	Gln	Ser	Ser	Ile	Val	Pro	Glu	Glu	Glu	Gln	324
Ala	Ala	Asn	Lys	Gly	Glu	Glu	Lys	Lys	Asp	Asp	Glu	336
Asn	Ile	Pro	Met	Glu	Thr	Gly	Asn	Ser	Pro	Ala	347	

<210> 81

<211> 197

<212> Protein

<213> Homo sapiens

<220>

<223> Phospholipase Inhibitor GIPL, short variant

<400> 81

Met	Trp	Val	Gln	Thr	Arg	Pro	Ser	Ser	Ala	Ser	Tyr	12
Lys	Ser	Trp	Gly	Pro	Gly	Thr	Ala	Asp	Thr	His	Thr	24
Met	Arg	Leu	Ser	Arg	Arg	Pro	Glu	Thr	Phe	Leu	Leu	36
Ala	Phe	Val	Leu	Leu	Cys	Thr	Leu	Leu	Gly	Leu	Gly	48
Cys	Pro	Leu	His	Cys	Glu	Ile	Cys	Thr	Ala	Ala	Gly	60
Ser	Arg	Cys	His	Gly	Gln	Met	Lys	Thr	Cys	Ser	Ser	72
Asp	Lys	Asp	Thr	Cys	Val	Leu	Leu	Val	Gly	Lys	Ala	84
Thr	Ser	Lys	Gly	Lys	Glu	Leu	Val	His	Thr	Tyr	Lys	96
Gly	Cys	Ile	Arg	Ser	Gln	Asp	Cys	Tyr	Ser	Gly	Val	108
Ile	Ser	Thr	Thr	Met	Gly	Pro	Lys	Asp	His	Met	Val	120
Thr	Ser	Ser	Phe	Cys	Cys	Gln	Ser	Asp	Gly	Cys	Asn	132
Ser	Ala	Phe	Leu	Ser	Val	Pro	Leu	Thr	Asn	Leu	Thr	144
Glu	Asn	Gly	Leu	Met	Cys	Pro	Ala	Cys	Thr	Ala	Ser	156
Phe	Arg	Asp	Lys	Cys	Met	Gly	Pro	Met	Thr	His	Cys	168
Thr	Gly	Lys	Glu	Asn	His	Cys	Val	Ser	Leu	Ser	Gly	180
His	Val	Gln	Ala	Gly	Glu	Trp	Cys	Leu	Asn	Leu	Trp	192
Lys	Arg	Lys	Gln	Asn	197							

<210> 82

<211> 285

<212> Protein

<213> Homo sapiens

<220>

<223> tsgl01 splice variant

<400> 82

Met	Ala	Val	Ser	Glu	Ser	Gln	Leu	Lys	Lys	Met	Val	12
Ser	Lys	Pro	Gln	Ser	Asp	Leu	Leu	Gly	Leu	Ile	Gln	24
Val	Met	Ile	Val	Val	Phe	Gly	Asp	Glu	Pro	Pro	Val	36
Phe	Ser	Arg	Pro	Ile	Ser	Ala	Ser	Tyr	Pro	Pro	Tyr	48
Gln	Ala	Thr	Gly	Pro	Pro	Asn	Thr	Ser	Tyr	Met	Pro	60
Gly	Met	Pro	Gly	Gly	Ile	Ser	Pro	Tyr	Pro	Ser	Gly	72
Tyr	Pro	Pro	Asn	Pro	Ser	Gly	Tyr	Pro	Gly	Cys	Pro	84
Tyr	Pro	Pro	Gly	Gly	Pro	Tyr	Pro	Ala	Thr	Thr	Ser	96
Ser	Gln	Tyr	Pro	Ser	Gln	Pro	Pro	Val	Thr	Thr	Val	108
Gly	Pro	Ser	Arg	Asp	Gly	Thr	Ile	Ser	Glu	Asp	Thr	120
Ile	Arg	Ala	Ser	Leu	Ile	Ser	Ala	Val	Ser	Asp	Lys	132
Leu	Arg	Trp	Arg	Met	Lys	Glu	Glu	Met	Asp	Arg	Ala	144
Gln	Ala	Glu	Leu	Asn	Ala	Leu	Lys	Arg	Thr	Glu	Glu	156
Asp	Leu	Lys	Lys	Gly	His	Gln	Lys	Leu	Glu	Glu	Met	168
Val	Thr	Arg	Leu	Asp	Gln	Glu	Val	Ala	Glu	Val	Asp	180
Lys	Asn	Ile	Glu	Leu	Leu	Lys	Lys	Lys	Asp	Glu	Glu	192
Leu	Ser	Ser	Ala	Leu	Glu	Lys	Met	Glu	Asn	Gln	Ser	204
Glu	Asn	Asn	Asp	Ile	Asp	Glu	Val	Ile	Ile	Pro	Thr	216
Ala	Pro	Leu	Tyr	Lys	Gln	Ile	Leu	Asn	Leu	Tyr	Ala	228
Glu	Glu	Asn	Ala	Ile	Glu	Asp	Thr	Ile	Phe	Tyr	Leu	240
Gly	Glu	Ala	Leu	Arg	Arg	Gly	Val	Ile	Asp	Leu	Asp	252
Val	Phe	Leu	Lys	His	Val	Arg	Leu	Leu	Ser	Arg	Lys	264
Gln	Phe	Gln	Leu	Arg	Ala	Leu	Met	Gln	Lys	Ala	Arg	276
Lys	Thr	Ala	Gly	Leu	Ser	Asp	Leu	Tyr				285

<210> 83

<211> 1946

<212> DNA

<213> Homo sapiens

<220>

<223> BAF57 variant

<400> 83

CTGCCCCGGG TGTCTCAGAT TCATTCTTAA GGAAC TGAGA ACTTAATCTT CAAAATGTC 60
AAAAAGACCA TCTTATGCCC CACCTCCCAC CCCAGCTCCT GCAACACAAA TGCCCAGCAC 120
ACCAGGGTTT GTGGGATACA ATCCATACAG TCATCTCGCC TACAACAACCT ACAGGCTGGG 180
AGGGAACCCG GGCACCAACA GCCGGGTCAC GGCATCCTCT GGTATCACGA TTCCAAAACC 240
CCCCAAGCCA CCAGATAAGC CGCTGATGCC CTACATGAGG TACAGCAGAA AGGTCTGGGA 300
CCAAGTAAAG GCTTCCAACC CTGACCTAAA GTTGTGGGAG ATTGGCAAGA TTATTGGTGG 360
CATGTGGCGA GATCTCACTG ATGAAGAAAA ACAAGAATAT TTAAACGAAT ACGAAGCAGA 420
AAAGATAGAG TACAATGAAT CTATGAAGGC CTATCATAAT TCCCCGCGT ACCTTGCTTA 480
CATAAATGCA AAAAGTCGTG CAGAAGCTGC TTTAGAGGAA GAAAGTCGAC AGAGACAATC 540
TCGCATGGAG AAAGGAGAAC CGTACATGAG CATTACAGCT GCTGAAGATC CAGATGATTA 600
TGATGATGGC TTTTCAATGA AGCATACAGC CACCGCCCGT TTCCAGAGAA ACCACCGCCT 660
CATCAGTGAA ATTCTTAGTG AGAGTGTGGT GCCAGACGTT CGGTCAGTTG TCACAACAGC 720
TAGAATGCAG GTCCTCAAAC GGCAGGTCCA GTCCTTAATG GTTCATCAGC GAAAACTAGA 780
AGCTGAACTT CTTCAAATAG AGGAACGACA CCAGGAGAAG AAGAGGAAAT TCCTGGAAAG 840
CACAGATTCA TTTAACAATG AACTTAAAAG GTTGTGCGGT CTGAAAGTAG AAGTGGATAT 900
GGAGAAAATT GCAGCTGAGA TTGCACAGGC AGAGGAACAG GCCCGCAAAA GGCAGGAGGA 960
AAGGGAGAAAG GAGGCCGCAG AGCAAGCTGA GCGCAGTCAG AGCAGCATCG TTCCTGAGGA 1020
AGAACAAGCA GCTAACAAAG GCGAGGAGAA GAAAGACGAC GAGAACATTC CGATGGAGAC 1080
AGGAAACAGC CCAGCATGAC TTTAAACAAA GTGTCTAAAA GACCAACCTT ATATTATTTT 1140
TACAACTGCT TTCTCCTCGT TTAATCCATA GCACTACAGA CTAACCTCTCA TTCACTGTCC 1200
AACAGAAATA AAATGCAAGT CACGTGAAAT TTTATATTTT CTACTAGTGA CATATTTTTA 1260
AAAGTTAAGC AAAACAAGTG TTTTAACAAT ATGTTTTATT TAATTCAACA TATCCTAAAT 1320
AAAATTATTT CAACACAGAA GGAACATTTT TAAATCAGC TTTCTTTTTT TTAACAGTC 1380
TTTATACACA TCTCAATTCA GAAGCTAAAT TTTTCATCGGA AGTATTTGAT CTGCATTTAT 1440
TTAATAAATT TCATTCATTT ACAGCTAAAA AGTAGATTTT CATACCCAAA TTGTTCCAAC 1500
ATTCTTAAAA GTTCTTTAGT CGCACTGGTT CATTTTCAGGG GTTTAATAAC CACATGTGGC 1560
TAGTGGCTTC TATATTGGAC AGCACAGCTG TATACTGTCA GCATAACTAG AGTAAAATTT 1620
CATCTTGGAA CTGACAGTGA CAAATGTGTG ATTACAGAGG AGACACACCT TGAAGAAACA 1680
ACAGAGAGCC AACAGAATGG TGAAGAAGGC ACGTCTACTC CTGAGGACAA GGAGAGTGGG 1740
CAGGAGGGGG TCGACAGTAT GGCAGAGGAA GGAACCAGTG ATAGTAACAC TGGCTCGGAG 1800
AGCAACAGTG CAACAGTGGA GGAGCCACCA ACAGATCCCA TACCAGAAGA TGAGAAAAAA 1860
GAATAAGTGT TGCCTTGTTT TGTGTGTTCT AAATACTTTT TTTAATGAAA AAATGTTTTT 1920
TGGTTTTAAT GGTGTTACGT GGTTTG 1946

<210> 84

<211> 932

<212> DNA

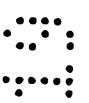
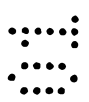
<213> Homo sapiens

<220>

<223> Phospholipase Inhibitor GIPL, short variant

<400> 84

CCGGCCGTGG	GAAAGGTGAA	TGTGGGTCCA	GACCCGCCCC	TCCTCAGCTT	CCTATAAAAG	60
CTGGGGACCA	GGTACTGCTG	ATACACACAC	CATGAGGCTC	TCCAGGAGAC	CAGAGACCTT	120
TCTGCTGGCC	TTTGTGTTGC	TCTGCACCCT	CCTGGGTCTT	GGGTGCCCAC	TACACTGCGA	180
AATATGTACG	GCGGCGGGGA	GCAGGTGCCA	TGGCCAAATG	AAGACCTGCA	GCAGTGACAA	240
GGACACATGT	GTGCTCCTGG	TCGGGAAGGC	TACTTCAAAG	GGCAAGGAGT	TGGTGCACAC	300
CTACAAGGGC	TGCATCAGGT	CCCAGGACTG	CTACTCCGGC	GTTATATCCA	CCACCATGGG	360
CCCCAAGGAC	CACATGGTAA	CCAGCTCCTT	CTGCTGCCAG	AGCGACGGCT	GCAACAGTGC	420
CTTTTTGTCT	GTTCCCTTGA	CCAATCTTAC	TGAGAATGGC	CTGATGTGCC	CCGCCTGCAC	480
TGCGAGCTTC	AGGGACAAAT	GCATGGGGCC	CATGACCCAC	TGTACTGGAA	AGGAAAACCA	540
CTGTGTCTCC	TTATCTGGAC	ACGTGCAGGC	TGGTGAGTGG	TGCCTGAATC	TCTGGAAAAG	600
GAAACAGAAC	TAGAGGTCCA	AAC TTCTAGG	TTTCATGGGA	GGAGAGGGTT	CCAGAGAAGT	660
GGGTGAGGAT	GTGTTCTGGG	ATTATGAGGA	AGAAGGGGCT	GAGGTCCCTG	ATTCCAGTCT	720
GAAATCTCCC	TTTCAGGTAT	TTTCAAACCC	AGATTTGCTA	TGCGGGGCTG	TGCTACAGAG	780
AGTATGTGCT	TTACCAAGCC	TGGTGCTGAA	GTACCCACAG	GCACCAATGT	CCTCTTCCTC	840
CATCATATAG	AGTGCACTCA	CTCCCCCTGA	AAAGCTATCT	GAACAAAGGA	AGATAATGTA	900
GTGTGAAGTC	CCCATTTGTC	CTCAGCCTGT	AA	932		



~~Patent claims~~
Patent claims

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. Use of at least one polypeptide selected from a sequence of SEQ ID No. 55 to SEQ ID No. 58 or a functional variant thereof and/or of a nucleic acid encoding said polypeptide or a variant thereof and/or of a cell expressing said polypeptide or a functional variant thereof or said nucleic acid or a variant thereof, if appropriate combined or together with suitable additives and/or auxiliaries, for the diagnosis, prevention and/or treatment of diseases, of wound healing and/or its pathological disorders, and/or for the identification of pharmacologically active substances.
2. Use of at least one polypeptide selected from a sequence of SEQ ID No. 1 to SEQ ID No. 20 and/or SEQ ID No. 31 to SEQ ID No. 48 and/or SEQ ID No. 63 to SEQ ID No. 70 and/or SEQ ID No. 80 to SEQ ID No. 82 or a functional variant thereof, or of a nucleic acid encoding said polypeptide or a variant thereof, and/or of a cell expressing said polypeptide or a functional variant thereof or said nucleic acid or a variant thereof, if appropriate combined or together with suitable additives and/or auxiliaries, for the diagnosis, prevention and/or treatment of diseases, of wound healing and/or its pathological disorders, and/or for the identification of pharmacologically active substances.
3. Use of a polypeptide selected from a sequence of SEQ ID No. 21 to SEQ ID No. 26 and/or SEQ ID No. 29 to SEQ ID No. 30 and/or SEQ ID No. 71 to SEQ ID No. 73 or a functional variant thereof and/or of a nucleic acid encoding said polypeptide or a variant thereof, and/or of a cell expressing said polypeptide or a functional variant thereof or said nucleic acid or a

variant thereof, if appropriate combined or together with suitable additives and/or auxiliaries, for the diagnosis, prevention and/or treatment of diseases, of wound healing and/or its pathological disorders, and/or for the identification of pharmacologically active substances.

5

4. Use according to at least one of the claims 1 to 3, wherein the polypeptide is used in the form of a fusion protein.

10

5. Use according to at least one of the claims 1 to 3, wherein the nucleic acid is used in the form of an expression vector, a knock-out gene construct and/or a vector which is applicable in gene therapy.

6. Use according to at least one of the claims 1 to 5, wherein said cells are autologous or heterologous cells.

15

7. Use according to claim 6, wherein said cells are skin cells.

20

8. Use of an antibody or antibody fragment directed against a polypeptide according to one of claims 1 to 4, for the analysis, diagnosis, prevention and/or treatment of diseases of skin cells, of wound healing and/or its pathological disorders, and/or its use for the identification of pharmacologically active substances, if appropriate combined or together with suitable additives and/or auxiliaries.

25

9. Use of at least one polypeptide according to at least one of the claims 1 to 4 and/or of a nucleic acid encoding this, and/or of a cell expressing said polypeptide or said nucleic acid, and/or of an antibody or an antibody

fragment directed against said polypeptide, if appropriate combined or together with suitable additives and/or auxiliaries, for the production of a diagnostic for the diagnosis of diseases of skin cells and/or of wound healing and/or its pathological disorders.

5

10. Use of at least one polypeptide according to at least one of the claims 1 to 4 and/or of a nucleic acid encoding this, and/or of a cell expressing said polypeptide or said nucleic acid, and/or of an antibody or an antibody fragment directed against said polypeptide, if appropriate combined or together with suitable additives and/or auxiliaries, for the production of a medicament for the prevention and/or treatment of diseases of skin cells, of wound healing and/or its pathological disorders.

10

11. Use of at least one polypeptide according to at least one of the claims 1 to 4 and/or of a nucleic acid encoding this, and/or of a cell expressing said polypeptide or said nucleic acid, and/or of an antibody or an antibody fragment directed against said polypeptide, if appropriate combined or together with suitable additives and/or auxiliaries, for the production of a test for finding pharmacologically active substances in connection with diseases of skin cells and/or of wound healing and/or its pathological disorders.

15

20

12. Use according to at least one of claims 1 to 3, or 11, characterized in that at least one polypeptide according to at least one of the claims 1 to 4 and/or at least one antibody or antibody fragment directed against said polypeptide, is bound to a solid-phase.

25

13. Use according to at least one of claims 1 to 3, or 11, characterized in that at least one cell expressing a polypeptide according to at least one of the claims 1 to 4 or a nucleic acid coding for this is used.
- 5 14. Use of a pharmacologically active substance identified through the use of a polypeptide, nucleic acid, and/or cell according to at least one of the claims 1 to 3, or 11 to 14, if appropriate combined or together with suitable additives and/or auxiliaries, for the production of a diagnostic or analyte and/or of a medicament for the prevention, treatment and/or diagnosis of diseases of skin cells and/or of wound healing and/or its pathological disorders.
- 10
15. Use of at least one polypeptide according to Claims 1 to 4 and/or or of a nucleic acid encoding this, and/or or of at least one said antibody or antibody fragment directed against a said polypeptide, for the production of an array attached to a carrier material for analysis in connection with diseases of skin cells and/or of wound healing and/or its pathological disorders.
- 15

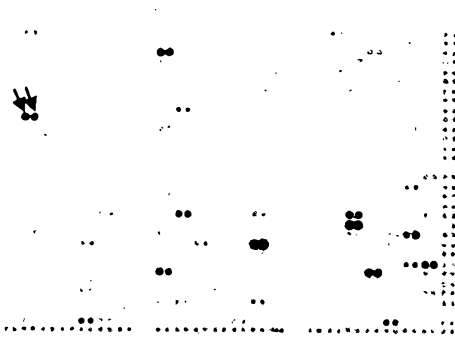
DATED this 19th day of June 2001.

SWITCH BIOTECH AG

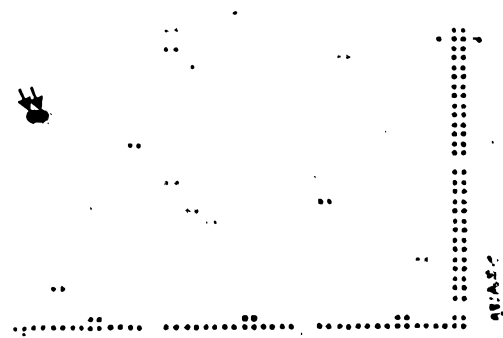
WATERMARK PATENT & TRADEMARK ATTORNEYS
290 BURWOOD ROAD
HAWTHORN. VIC. 3122.

Figure 1

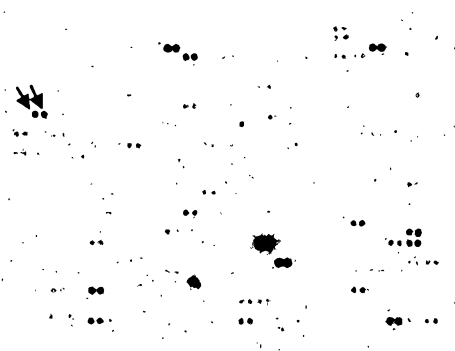
A



B



C



D



5

Figure 2

```
1  M A D G K A G D E K P E K S Q R A G A A G G P E E E A E K P SW1136_human.
1  M A D G K A G E E K P E K P Q R A G A A G G P E E E A E K P SW1136_murine

31 V K T K T V S S S N G G E S S S R S A E K R S A E E E A A D SW1136_human.
31 V K T K T V S S S N G G E S S S R S A E K R S A E D E A A D SW1136_murine

61 L P T K P T K I S K F G F A I G S Q T T K K A S A I S I K L SW1136_human.
61 L P T K P T K M S K F G F A I G S Q T A R K A S A I S I R L SW1136_murine

91 G S S K P K E T V P T L A P K T L S V A A A F N E D E D S E SW1136_human.
91 G A S K P K E T V P T L A P K T L S V A A A F N E D E D S E SW1136_murine

121 P E E M P P E A K M R M K N I G R D T P T S A G P N S F N K SW1136_human.
121 P E E M P P E A K M R M K N I G R D T P T S A G P N S F N K SW1136_murine

151 G K H G F S D N Q K L W E R N I K S H L G N V H D Q D N SW1136_human.
151 G K H G F S D N Q K L W E R N I K S H L G N V H D Q D N SW1136_murine
```

Decoration 'Decoration #1': Box residues that differ from SW1136_human.pro.l



Figure 3

```
1  M P R G S R S R T S R M A P P A S R A P Q M R A A P R P A P SW1295_human.
1  M P R G S R S R T S R V T P P A S R A P Q M R A A P R R A P SW1295_murine

31 V A Q P P A A A P P S A V G S S A A A P R Q P G L M A Q M A SW1295_human.
31 A A Q P P A A A A P S A V G S P A A A P R Q P G L M A Q M A SW1295_murine

61 T T A A G V A V G S A V G H T L G H A I T G G F S G G S N A SW1295_human.
61 T T A A G V A V G S A V G H T L G H A I T G G F S G G G S A SW1295_murine

91 E P A R P D I T Y Q E P Q G T Q P A Q Q Q Q - - P C L Y E I SW1295_human.
91 E P A K P D I T Y Q E P Q G A Q L Q N Q Q S F G P C S L E I SW1295_murine

119 K Q F L E C A Q N Q G D I K L C E G F N E V L K Q C R L A N SW1295_human.
121 K Q F L E C A Q N Q S D V K L C E G F N E V L R Q C R I A N SW1295_murine

149 G L A SW1295_human.
151 G L M SW1295_murine
```

Decoration 'Decoration #1': Box residues that differ from SW1295_human.pro.l