

Single exon genes encoding novel bio-active peptides

5 The present invention relates to novel bio-active peptide hormone, process for the production of the same, and use of the same. The present invention identified novel bioactive peptide precursor and salts thereof which can be used as drugs, for example therapeutic polypeptides, ligands to discover relevant targets (e.g. GPCRs) or targets for drug intervention.

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The present invention relates to novel bio-active peptide hormone, a process for the production of the same, and use of the same. More particularly, the present invention relates to a method for the identification of bioactive peptide hormones derived from precursor proteins that can be used as therapeutic polypeptides, targets for drug
15 intervention, ligands to discover relevant targets (e.g. GPCR deorphaning) or biomarkers to monitor diseases.

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Many biologically active peptides exhibit profound effects both in health and disease, either by growth stimulation, growth inhibition, or the regulation of critical metabolic pathways.

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Peptide hormones are produced as precursors in different cell types and organs like glands, neurons, intestine, brain; etc. Peptide hormones are initially synthesized as larger precursors, or prohormones, and may acquire a number of post-translational modifications during transportation through the ER and Golgi stacks. They are
25 processed and transported to their final destination to act as active substances (first messengers) to trigger a cellular response by binding to a cell surface receptor. They play a key role in physiological processes that are relevant to many areas of biomedical research such as Diabetes (Insulin), blood pressure regulation
30 (Angiotensin), Anemia (Erythropoietin- α), Multiple Sclerosis (Interferon- β) and others.

The recent sequencing of the human genome has revealed around 30,000 genes, far fewer than would be predicted from the complexity of human biological processes. Alternative splicing of these genes prior to translation would likely generate up to

200,000 primary transcripts. It is now widely accepted that post translational modifications to the protein products coded by these genes represents the additional level of complexity required, to explain the diversity of function.

- 5 Gene finding typically refers to the area of computational biology that is concerned with algorithmically identifying stretches of sequence, usually genomic DNA, that are biologically functional. This especially includes protein-coding genes, but may also include other functional elements such as RNA genes and regulatory regions. Gene finding is one of the first and most important steps in understanding the genome of a
10 species once it has been sequenced.

In extrinsic gene finding systems, the target genome is searched for sequences that are similar to extrinsic evidence in the form of the known sequence of a messenger RNA (mRNA) or protein product. Given an mRNA sequence, it is critical to derive a
15 unique genomic DNA sequence from which it had to have been transcribed. Given a protein sequence, a family of possible coding DNA sequences can be derived by reverse translation of the genetic code. Once candidate DNA sequences have been determined, it is an algorithmic problem to efficiently search a target genome for matches, complete or partial, and exact or inexact. BLAST is a widely used system
20 designed for this purpose.

A high degree of similarity to a known messenger RNA or protein product is strong evidence in many cases that a region of a target genome is a protein-coding gene. However, to apply this approach systemically requires extensive sequencing of
25 mRNA and protein products. Not only is this expensive, but in complex organisms, only a subset of all genes in the organism's genome are expressed at any given time, meaning that extrinsic evidence for many genes is not readily accessible in any single cell culture. Thus, in order to collect extrinsic evidence for most or all of the genes in a complex organism, many hundreds or thousands of different cell types
30 must be studied, which itself presents further difficulties. For example, some human genes may be expressed only during development as an embryo or fetus. Despite these difficulties, extensive transcript and protein sequence databases have been generated for human as well as other important model organisms in biology, such as mice and yeast. For example, the RefSeq database contains transcript and

protein sequence from many different species and the Ensembl system comprehensively maps this evidence to human and several other genomes.

5 Because of the inherent expense and difficulty in obtaining extrinsic evidence for many genes, it is also necessary to resort to *ab initio* gene finding, in which genomic DNA sequence alone is systematically searched for certain telltale signs of protein-coding genes. These signs can be broadly categorized as either signals, specific sequences that indicate the presence of a gene nearby, or content, statistical properties of protein-coding sequence itself. *Ab initio* gene finding might be more
10 accurately characterized as gene prediction, since extrinsic evidence is generally required to conclusively establish that a putative gene is functional.

Ab initio gene finding in eukaryotes, especially complex organisms like humans, is considerably more challenging for several reasons. First, the promoter and other
15 regulatory signals in these genomes are more complex and less well-understood than in prokaryotes, making them more difficult to reliably recognize. Two classic examples of signals identified by eukaryotic gene finders are CpG islands and binding sites for a poly (A) tail.

20 Second, splicing mechanisms employed by eukaryotic cells mean that a particular protein-coding sequence in the genome is divided into several parts (exons), separated by non-coding sequences (introns). Splice sites are themselves another signal that eukaryotic gene finders are often designed to identify. A typical protein-coding gene in human might be divided into a dozen exons, each less than two
25 hundred base pairs in length, and some as short as twenty to thirty. It is therefore much more difficult to detect periodicities and other known content properties of protein-coding DNA in eukaryotes.

Advanced gene finders for both prokaryotic and eukaryotic genomes typically use
30 complex probabilistic models, such as hidden Markov Models, in order to combine information from a variety of different signal and content measurements. The Glimmer system is a widely used and highly accurate gene finder for prokaryotes. Eukaryotic *ab initio* gene finders, by comparison, have achieved only limited success; a notable example is the GENSCAN program.

The present invention identified novel bioactive peptide hormone precursors by means of identification of novel single exon genes that encode for peptide hormone precursor sequences. To find novel single exon genes, the human genome (NCBI 33
5 assembly, 1st of July 2003) and the mouse genome (NCBI 30 assembly, 1st of July 2003), both were translated into all six reading frames using the standard genetic code. Only sequence fragments starting with the amino acid Methionine and with a length between 50 and 200 amino acids were selected. The human and the mouse set were compared to each other using the program BLAST in order to find closely
10 related sequences in both organisms. Only sequences that appear in both organisms (human and mouse) were selected. To filter for secreted proteins, potential signal sequences were predicted with the program signalP and the absence of potential membrane spanning regions was confirmed by the program TMHMM. In addition, an InterPro search was performed on the selected sequences in order to rule out the
15 presence of readily described protein domains (e.g. kinase domain etc). The novelty of the remaining sequences was verified by sequence comparison to publicly available databases such as UNIPROT. These in silico analysis suggested the discovery of novel secreted proteins that lack any previously described protein domains.

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It is generally understood, that peptide hormones are characterized by their high specificity as well as their effectiveness in very low concentrations. Another characteristic of peptide hormones is that their corresponding mRNA is expressed in a small number of distinct tissues. A ubiquitous expression pattern of peptide
25 hormones is rarely observed in mammalian systems.

To determine the tissues transcribing the 8 novel genes in the human body, commonly used in vitro transcription assays were performed on a panel of human tissues (see figure 1-6). Using specific probe / primer sets, the mRNA encoding the
30 gene of interest can be detected and quantified. However, it must be noted that the gene expression data can be influenced by the transcription of genes located in the same locus on the genome. In addition the tissue panel used in the present invention is not comprehensive.

Bioactive peptides hormones have a tremendous use in biomedical research and are therefore of interest to the pharmaceutical industry. Various peptide hormones are used for treatment of diseases.

Whereas WO2004039956 (Title: "compositions and methods for treatment of immune related diseases") disclose several bioactive polypeptide sequences, the method of identification and the use of such sequences had been made however no reference to.

The present invention identified novel genes encoding for bioactive peptide hormone precursors. Peptide hormones are characterized by their high specificity as well as their effectiveness in very low concentrations. Bioactive peptides hormones have a tremendous use in biomedical research. Various peptide hormones are used for treatment of diseases or to monitor a disease states. Such polypeptide sequences can be used in therapeutically effective amounts as medicines and medicaments for immune related diseases.

The problem as laid out by availability of the closest prior art (WO2004039956) could be defined as to identify novel hormone polypeptide sequences which are useful for the treatment of human diseases. The present invention solves that problem by providing 8 novel peptide hormone precursors and fragments thereof which could be used to interfere with physiological factors that increase the risk of arteriosclerosis, inflammation or uncontrolled cell division. According to the invention it will provide a new reservoir of hormonal polypeptides that could be used for treatment of human disease in the field of biomedical research.

Summary

The present disclosure therefore refers to polypeptide chain consisting of an amino acid sequence according Seq id no 1-8 or an amino acid sequence derived therefrom by deletion, substitution or insertion of at least one amino acid residue, its amide or ester or a salt of said peptide.

In a first aspect, there is provided a polypeptide chain comprising an amino acid sequence according to Seq Id no 1. or an amino acid sequence derived therefrom by deletion, substitution or insertion of at least one amino acid residue, its amide or ester or a salt of said peptide, whereby the polypeptide comprising an amino acid sequence derived from Seq Id no. 1 has hormonal activity.

An embodiment of present disclosure refers to a polypeptide chain consisting of the following amino acid sequence:

MYWMALRRISTLGSRWLGLSRVLLFRASKASFTFLSLRFSLSVAARRRSTDTDFLLH
TLHAHGRHWPGQCSGVPSPLSSRGPGASGLRVSSVRS

Another embodiment of present disclosure relates to a polypeptide consisting of following amino acid sequence:

MGSGCARARLGLLSWLAASSGSEDALASSISVKLALELAEVAWSEGDEAEGLAPWL
SPLVQGRDSGEDREQLEAACLKRGSWAGAGKARELSPTAPKWLEEAEERLTLRSI
PL

Another embodiment of present disclosure relates to a polypeptide consisting of the following amino acid sequence:

MLLAMSSISIFSSLFSFSSFCFTRCRLSICSPSSATLSACFFLRVAAVASCCRVASSR
SLRIFWNSASLFLFISIWAEVAPLASSSSLISSSSLARSERCFSILALSVCSASISSSS
SSMRA

Another embodiment of present disclosure relates to a polypeptide consisting of the following amino acid sequence:

MATSWAGSAAPPASAAKS VVGTRPSRPGGPRSAWRRRRATLAAWTGPARAATAT
TTRAAARRPVAARTPARLAATSRATHARTWPMASPRASVTTCTCAFRAARASPALS
S

Another embodiment of present disclosure relates to a polypeptide consisting of the following amino acid sequence:

MPRSAPRAAAAPARAPAAAVACACCPNSAPDFFMVCGGHVRS LAGKRLFSSPPR
PACSGPNDLRSSGVSGGAVRPAARTRRRAQGEVEEEEASCGEKGRRTAERMGPVA
AARAGLDAAWARRCEVPKVTTIPTRQPRAPARPGAPRRI

Another embodiment of present disclosure relates to a polypeptide consisting of the following amino acid sequence:

MPKWRLAWPKQTRASSCGLSLPSISCASSCSASRNGGDRC SLRTTTTRHTR

Another embodiment of present disclosure relates to a polypeptide consisting of the following amino acid sequence:

MSVWTF LKCRGNSSLLKNLLQVKVKAELLLLCLLVTHSLWSSTWSPPGVAAVRSAS

TVPEENCSGSKLYVCVAKSMNSPSMLLDSEMTWPLSSLKAHWRVVLMRSDLGRS
STVIPKSEVSTALCSLGLQLNMASSRARRFPQ

Another embodiment of present disclosure relates to a polypeptide consisting of the following amino acid sequence:

MASAAGEPFMYLASAAAALCTPTASARKARGRLRTEPLDEVLARGGPAASTLWCR
CRLWPKASLYPGARKPCLAASGSDSSTSGGSATDTGPD LTPWKEVDS DLSASMQL
LMIWLTSLSTSLAMVEISATELWLSGPGRPSSQSLRSGGSPVRTSM

An embodiment of the disclosure also provides a DNA comprising of a nucleotide base sequence according to Seq Id no 9 to 16 encoding a polypeptide chain comprising an amino acid sequences represented by Seq Id no 1-8 or its amide, ester or a salts thereof.

In a second aspect, there is provided a DNA consisting of a nucleotide base sequence according to Seq Id no 9 encoding a polypeptide chain as defined above consisting of an amino acid sequence represented by Seq Id no 1 or its amide, ester or a salts thereof.

The disclosure relates to a DNA that consist of a nucleotide base sequence according to Seq Id no 9, encoding a polypeptide chain that consist of an amino acid sequence according to Seq Id no 1 or its amide, ester or a salts thereof.

This Present disclosure relates to a DNA that consists of a nucleotide base sequence according to Seq Id no 10, encoding polypeptide chain described in paragraph 1 that consists of an amino acid sequence according to Seq Id no 2 or its amide, ester or a salts thereof.

Another embodiment of present disclosure relates to a DNA that consist of a nucleotide base sequence according to Seq Id no 11, encoding polypeptide chain that consist of an amino acid sequence according to Seq Id no 3 or its amide, ester or a salts thereof.

Another embodiment of present disclosure relates to a DNA that consist of a nucleotide base sequence according to Seq Id no 12, encoding polypeptide chain that consist of an amino acid sequence according to Seq id no 4 or its amide, ester or a salts thereof.

Another embodiment of present disclosure relates to a DNA that consist of a nucleotide base sequence according to Seq Id no 13, encoding polypeptide chain that consist of an amino acid sequence according to Seq Id no 5 or its amide, ester or a salts thereof.

Another embodiment of present disclosure relates to a DNA that consist of a nucleotide base sequence according to Seq Id no 14, encoding polypeptide chain that consist of an amino acid sequence according to Seq Id no 6 or its amide, ester or a salts thereof.

Another embodiment of present disclosure relates to a DNA that consist of a nucleotide base sequence according to Seq Id no 15, encoding polypeptide chain that consist of an amino acid sequence according to Seq Id no 7 or its amide, ester or a salts thereof.

Another embodiment of present disclosure relates to a DNA that consist of a nucleotide base sequence according to Seq Id no 16, encoding polypeptide chain that consist of an amino acid sequence according to Seq Id no 8 or its amide, ester or a salts thereof.

In a third aspect, there is provided the use of a DNA as defined above for preparing a recombinant vector, wherein said recombinant vector comprises

1. a DNA as defined above, and
- for introducing said recombinant vector in to a host cell, wherein said host cell comprises said recombinant vector.

In a fourth aspect, there is provided a method for manufacturing of a polypeptide as defined above wherein said method comprises the step of:

- i. providing the amino acid
- ii. synthesizing the amino acid by solid phase or liquid phase synthesis
 1. extraction of polypeptide
- iii. purification of the polypeptide

Present disclosure refers to a method for manufacturing of a polypeptide wherein the said method comprises the step of providing the amino acid, synthesizing the amino acid by solid phase or liquid phase synthesis, extraction of polypeptide, purification of the polypeptide

In a fifth aspect, there is provided a method of producing the peptide, precursor or salt thereof as defined above which comprises subjecting an amino terminus-constituting amino acid or peptide and a carboxyl terminus-constituting amino acid or peptide to condensation, optionally followed by intramolecular disulfide bond formation.

Present disclosure also provides a method of producing the peptide, precursor or salt thereof which comprises subjecting an amino terminus-constituting amino acid or peptide and a carboxyl terminus-constituting amino acid or peptide to condensation, optionally followed by intramolecular disulfide bond formation.

In a sixth aspect, there is provided a pharmaceutical composition comprising as the active agent a polypeptide chain or precursor, or pharmaceutically acceptable amide, ester, or a salt thereof wherein said polypeptide chain consists of an amino acid sequence according Seq Id no 1.

An embodiment of the disclosure provides a pharmaceutical composition comprising as the active agent a polypeptide chain or precursor, or pharmaceutically acceptable amide, ester, or a salt thereof wherein said polypeptide chain consists of an amino acid sequence according Seq Id no 1-8.

In a seventh aspect, there is provided the use of pharmaceutical composition as defined above, comprising as the active agent polypeptide chain or precursor, or pharmaceutically acceptable amide, ester, or a salt thereof wherein said polypeptide chain consists of an amino acid sequence according Seq Id no 1 for the preparation of a pharmaceutical composition to change physiological factors that increase the risk of arteriosclerosis, inflammation or uncontrolled cell division.

Present disclosure also refers to the use of a pharmaceutical composition, comprising as the active agent a polypeptide chain or precursor, or pharmaceutically acceptable amide, ester, or a salt thereof wherein said polypeptide chain consists of an amino acid sequence according Seq Id no 1-8, and can be used as therapeutic polypeptides, targets for drug intervention, ligands to discover relevant targets, biomarkers to monitor diseases.

The disclosure also provides the use of a peptide, precursor or salt of the invention in the production of an agent for the treatment or prevention of cardio vascular disease, hormone-producing tumors, a hormone secretion inhibitor, a tumor growth inhibitor, which comprises at least one of the amino acid sequence defined under Seq. Id 1 to 8.

In an eighth aspect, there is provided an antibody to a polypeptide chain as defined above that comprises an amino acid sequences according to Seq Id no 1, or its amide, ester or salts thereof.

An embodiment of the disclosure also provides an antibody to a polypeptide chain according to paragraph 1 that comprises an amino acid sequences according to Seq Id no 1-8, or its amide, ester or salts thereof. An antibody of the invention can be used also for detecting an inventive polypeptide present in a sample such as a body fluid or a tissue. It may be used also to produce an antibody column for purifying an inventive polypeptide, to detect an inventive polypeptide in each fraction during purification, or to analyze the behavior of an inventive polypeptide in a test cell.

The term "polypeptide" as used herein shall be taken to refer to any polymer consisting of amino acids linked by covalent bonds and this term includes within its scope parts or fragments of full length proteins, such as, for example, peptides, oligopeptides and shorter peptide sequences consisting of at least 2 amino acids, more particularly at least about 5 amino acid residues or more.

The term "polypeptide" includes all moieties containing one or more amino acids linked by a peptide bond. In addition, this term includes within its ambit polymers of modified amino acids, including amino acids which have been post- translationally modified, for example by chemical modification including but not restricted to glycosylation, phosphorylation, acetylation and/or sulphation reactions that effectively alter the basic peptide backbone. Accordingly, a polypeptide may be derived from a naturally- occurring protein, and in particular may be derived from a full-length protein

by chemical or enzymatic cleavage, using reagents such as CNBr, or proteases such as trypsin or chymotrypsin, amongst others. Alternatively, such polypeptides may be derived by chemical synthesis using well known peptide synthetic methods. Also included within the scope of the definition of a "polypeptide" are amino acid sequence variants (referred to herein as polypeptide variants). These may contain one or more preferably conservative, amino acid substitutions, deletions, or insertions, in a naturally-occurring amino acid sequence which do not alter at least one essential property of said polypeptide, such as, for example, its biological activity. Such polypeptides may be synthesised by chemical polypeptide synthesis. Conservative amino acid substitutions are well-known in the art. For example, one or more amino acid residues of a native protein can be substituted conservatively with an amino acid residue of similar charge, size or polarity, with the resulting polypeptide retaining functional ability as described herein. Rules for making such substitutions are well known. More specifically, conservative amino acid substitutions are those that generally take place within a family of amino acids that are related in their side chains. Genetically-encoded amino acids are generally divided into four groups: (1) acidic=aspartate, glutamate; (2) basic=lysine, arginine, and histidine; (3) non-polar=alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, and tryptophan; and (4) uncharged polar=glycine, asparagine, glutamine, cysteine, serine, threonine, and tyrosine. Phenylalanine, tyrosine and tryptophan are also jointly classified as aromatic amino acids. One or more replacements within any particular group such as, for example, the substitution of leucine for isoleucine or valine are alternatively, the substitution of aspartate for glutamate or threonine for serine, or of any other amino acid residue with a structurally-related amino acid residue will generally have an insignificant effect on the function of the resulting polypeptide.

Included within the scope of the definition of a "polypeptide" are amino acid sequence variants that have undergone unnatural modifications such as but not limited to protection, carboxylation, and derivatization by amide and non-amide bonds as well as covalent and non-covalent modification.

Included in the scope of the definition of the term "polypeptide" is a peptide whose biological activity is predictable as a result of its amino acid sequence corresponding to a functional domain. Also encompassed by the term "polypeptide" is a peptide

whose biological activity could not have been predicted by the analysis of its amino acid sequence.

An amino acid is any molecule that contains both amine and carboxylic acid functional groups. Amino acid residue is what is left of an amino acid once a molecule of water has been lost (an H⁺ from the nitrogenous side and an OH⁻ from the carboxylic side) in the formation of a peptide bond, the chemical bond that links the amino acid monomers in a protein chain. Each protein has its own unique amino acid sequence that is known as its primary structure. Just as the letters of the alphabet can be combined in different ways to form an endless variety of words, amino acids can be linked together in varying sequences to form a huge variety of proteins. The unique shape of each protein determines its function in the body.

A precursor is a substance from which another, usually more active or mature substance is formed. A protein precursor is an inactive protein (or peptide) that can be turned into an active form by posttranslational modification. The name of the precursor for a protein is often prefixed by pro or prepro. Precursors are often used by an organism when the subsequent protein is potentially harmful, but needs to be available on short notice and/or in large quantities.

The Polypeptide, precursors or salts thereof, of the present invention have hormonal activity. Therefore, the polypeptides, precursors and salts of the invention are useful as drugs, for example therapeutic polypeptide, ligand to discover relevant targets (e.g. GPCRs), targets for drug intervention (eg targets for monoclonal antibodies or therelike, receptor fragments), biomarkers to monitor diseases (in combination with tool antibodies to detect peptide fragments in body fluids), protein kinase inhibitors and substrates, T-cell epitopes, Peptide mimotopes of receptor binding sites, Biomarker to measure the expression level.

The DNAs coding for the peptide or precursor of the invention are useful, for example, as agents for the gene therapy or treatment or prevention of cardio vascular disease, hormone-producing tumors, diabetes, gastric ulcer and the like, hormone secretion inhibitors, tumor growth inhibitors, neural activity and so for. Furthermore, the DNAs of the invention are useful as agents for the gene diagnosis of diseases

such as cardio vascular disease, hormone-producing tumours, diabetes, gastric ulcer and the like.

A vector is a vehicle for delivering genetic material such as DNA to a cell. DNA by itself may be regarded as a vector, for example in particular when it is used for cell transformation. A vector in this sense is a DNA construct, such as a plasmid or a bacterial artificial chromosome that contains an origin of replication. An appropriate replication origin causes a cell to copy the construct along with the cell's chromosomes and to pass it along to its progeny. A single cell that has been transformed with a vector will grow into an entire culture of cells, which all contain the vector, as well as any gene attached to it within the construct. Because the constructs can be extracted from the cells by purification techniques, transformation with a vector is a way of making a small number of DNA molecules in to a much larger one. A vector can be a E. coli-derived plasmid (e.g., pBR322, pBR325, pUC12, pUC13), a Bacillus subtilis-derived plasmid (e.g., pUB110, pTP5, pC194), a yeast-derived plasmid (e.g., pSH19, pSH15), a bacteriophage such as [lambda] phage, as well as an animal virus such as retrovirus, vaccinia virus, vaculovirus and the like.

The antibodies against the peptide, precursor or salt of the invention can specifically recognize the peptide, precursor or salt of the invention. It may be used also to produce an antibody column for purifying an inventive polypeptide, to detect an inventive polypeptide in each fraction during purification, or to analyze the behavior of a novel polypeptide in a test cell. Hence it can be used for assaying the peptide or equivalent of the invention in test solutions.

Results

1.0 Description of the Computer Programs:

1.1 Signal P version 2.0

Objective: This program was used to detect potential signal sequences, it was used with a cut off score of 0.98. Signal P version 2.0 predicts the presence and location of signal peptide cleavage sites in amino acid sequences from different organisms: The method incorporates a prediction of cleavage sites and a signal peptide/non-signal

peptide prediction based on a combination of several artificial neural networks and hidden Markov models.

1.2 TMHMM version 2.0

- 5 Objective: This program was used to define possible membrane spanning regions in protein sequences. TMHMM version 2.0 is used for prediction of transmembrane helices in proteins. Predicted TM segments in the n-terminal region sometime turn out to be signal peptides.

10 1.3 ProP version 1.0

- Objective: This program was used to detect potential cleavage sites in protein sequences. It was used with a score of 0.09. This program predicts arginine and lysine propeptide cleavage sites in eukaryotic protein sequences using an ensemble of neural networks. Furin-specific prediction is the default. It is also possible to
15 perform a general proprotein convertase (PC) prediction. This program is integrated with the SignalP program predicting the presence and location of signal peptide cleavage sites.

1.4 InterPro version 12 in combination with InterProScan

- 20 InterPro is a database of protein families, domains and functional sites in which identifiable features found in known proteins can be applied to unknown protein sequences. 1.5 InterProScan is the program used to compare amino acid sequences to the InterPro database.

25 1.6 BLAST version 2.2.9

- The Basic Local Alignment Search Tool (BLAST) finds regions of local similarity between sequences. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance of matches. BLAST can be used to infer functional and evolutionary relationships between sequences as
30 well as help identify members of gene families. BLAST uses Karlin-Altschul Statistics to determine the statistical significance of the alignments it produces. The basic algorithm can be implemented in a number of ways and applied in a variety of contexts including straightforward DNA and protein sequence database searches, motif searches, gene identification searches, and in the analysis of multiple regions of

similarity in long DNA sequences. In addition to its flexibility and tractability to mathematical analysis, BLAST is an order of magnitude faster than existing sequence comparison tools of comparable sensitivity.

5 All these programs as mentioned before are accessible via the public domain internet

10 The biological role of the hormone peptides of the invention have been examined by means of expression profile studies (Fig. 1 to 6). The presence of hormone peptides could be demonstrated for several tissues to be different depending on the particular sequence. The differential expression of hormone peptides according to the invention in different tissues is regarded as strong indication for their important biological role. The adjustment of the concentration of one or several of the hormone peptides of the invention by increasing or diminishing the amount of such hormone peptides could have a strong impact to the treatment of a disease in need of diminished or
15 elevated concentrations of one or several of such hormone peptides (e.g. cardiovascular disease, metabolic disease, mental illness, cancer, viral, bacterial or yeast triggered infections and others).

2.0 Expression profiles

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2.1) Performing the tissue expression analysis

The tissue expression analysis was performed by means of TaqMan gene expression analyses

25 PCR (Polymerase Chain Reaction) is a standard technique in medical and biological research labs for a variety of tasks, such as the detection of hereditary diseases, the identification of genetic fingerprints, the diagnosis of infectious diseases, the cloning of genes, paternity testing, and DNA computing.

30 Quantitative PCR is used to rapidly measure the quantity of PCR product (preferably real-time), thus is an indirect method for quantitatively measuring starting amounts of DNA, cDNA or RNA. This is commonly used for the purpose of determining whether a sequence is present or not, and if it is present the number of copies in the sample. Description of protocol used for gene expression studies in present invention:

Sample preparation:

RNA samples from the tissues tested were purchased from different vendors.

5 DNase Digest:

All products were purchased from Ambion. DNA free DNase treatment and removal reagents (1906). DNase digest was performed using 50 µg RNA and according to the manufacturer's protocol.

10 cDNA Synthesis:

Products for cDNA were purchased from Applera Reverse Transcriptase Kit (N8080234), RNase Inhibitor (N8080119). cDNA Synthesis from 10 µg RNA was performed.

15 TaqMan Reaction Setup:

Products for the PCR were purchased from Applera. TaqMan Universal PCR Master Mix (4305719) was used in each reaction. Target forward Primer, Target reverse Primer, Target probe labeled with FAM for each gene, respectively (see Table with primer sequences). PCR was performed using the ABI Prism 7900 (Applera) under the following PCR conditions: 2 minutes at 50°C, 10 minutes at 95°C, 40 cycles with 95°C for 15 s and 1 minute at 60°C. PCR was set up as a Multiplex PCR using B2M as endogenous control for normalisation.

2.3) The following expression profiles could be gained for a gene encoding a peptide sequence according to Seq ID Nr 1 (Fig. 7). These results are exhibited as well in Fig. 1 however in another format:

Tissue Type	Mean	RPL37aMean	∆∆ Ct	Expressior
Fetal Brain	30,96	24,22	6,74	9,34
Brain	30,01	22,31	7,70	4,80
Brain Hippocampus	31,58	21,59	9,99	0,98
Cerebellum	28,74	22,28	6,47	11,29
Brain Cortex Temporal	30,15	23,05	7,10	7,29
Brain Cortex Frontal	32,02	22,81	9,20	1,70

Substantia Nigra	31,09	21,01	10,08	0,93
Dorsal Root Ganglion	33,87	21,16	12,72	0,15
Spinal Cord	34,57	21,28	13,30	0,10
Hypothalamus	32,69	21,39	11,29	0,40
Amygdala	31,25	21,07	10,18	0,86
Adrenal Gland	40,00	20,68	19,32	0,00
Salivary Gland	32,97	21,03	11,94	0,25
Thyroid	31,73	20,32	11,41	0,37
Heart	34,09	19,87	14,22	0,05
Aorta	34,96	20,66	14,30	0,05
Fetal Aorta	28,18	22,46	5,72	18,95
AoSMC	34,27	20,34	13,93	0,06
HUVEC	40,00	20,89	19,11	0,00
Adipose	33,16	19,58	13,58	0,08
Fetal Liver	34,26	21,87	12,39	0,19
Liver	34,00	20,38	13,62	0,08
Normal Spleen	34,15	18,70	15,45	0,02
Tonsil	33,53	18,82	14,71	0,04
Bone Marrow	36,58	21,18	15,40	0,00
Thymus	30,26	19,67	10,58	0,65
PBMC Control	39,54	17,77	21,77	0,00
PBMC, PHA treated	35,60	17,25	18,35	0,00
THP-1 monocytes	28,39	20,18	8,21	3,38
THP-1 macrophages	31,77	19,39	12,38	0,19
Kidney	34,59	21,75	12,84	0,14
Skeletal Muscle	24,83	21,92	2,91	133,02
Skin	30,39	20,97	9,43	1,45
Chondrocytes	30,97	20,51	10,46	0,71
Trachea	34,31	20,35	13,96	0,06
Fetal Lung	31,75	22,06	9,69	1,21
Lung	30,90	19,50	11,40	0,37
Lung COPD Control	40,00	20,36	19,64	0,00
Lung COPD	35,81	20,15	15,66	0,00
Lung Tumor Control	35,20	18,65	16,55	0,00

Lung Tumor(adenocarcinoma)	34,80	18,86	15,93	0,02
Lung Tumor(carcinoma)	32,71	19,29	13,42	0,09
A549 cells	25,55	19,50	6,05	15,06
Breast	32,86	21,84	11,02	0,48
Breast Tumor Control	34,14	20,87	13,27	0,10
Breast Tumor(adenocarcinoma)	33,85	20,24	13,60	0,08
Mammary Gland	37,21	20,65	16,56	0,00
Colon	35,71	19,86	15,85	0,00
Colon IBD Control	37,82	19,17	18,65	0,00
Colon IBD	38,87	19,39	19,48	0,00
Colon Tumor Control	37,41	19,70	17,71	0,00
Colon Tumor(adenocarcinoma)	36,40	18,50	17,90	0,00
Esophagus	28,07	22,34	5,73	18,88
Stomach	38,35	20,98	17,37	0,00
Small Intestine	33,91	21,20	12,71	0,15
Pancreas	40,00	23,63	16,37	0,00
Ovary	37,02	21,12	15,89	0,00
Ovary Tumor Control	35,67	20,46	15,22	0,00
Ovary Tumor(adenocarcinoma)	31,79	19,67	12,12	0,22
Ovary Tumor(carcinoma)	31,47	18,92	12,55	0,17
Prostate	29,26	20,15	9,11	1,81
Prostate Tumor Control	40,00	20,60	19,40	0,00
Prostate Tumor(adenocarcinoma)	35,15	20,15	15,00	0,00
HeLa cells	34,97	19,45	15,51	0,02
Uterus	36,13	20,32	15,81	0,00
Placenta	32,62	22,18	10,44	0,72
Testis	29,85	22,58	7,27	6,46
Positive Control(HIPCO)	29,32	20,27	9,05	1,88

2.4) The following expression profiles could be gained for a gene encoding a peptide sequence according to Seq ID Nr 2 (Fig. 8). These results are exhibited as well in Fig. 2 however in another format:

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Tissue Type	Mean	RPL37aMean	$\Delta\Delta$ Ct	Expression
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Fetal Brain	39,66	24,66	14,99	0,00
Brain	34,18	22,90	11,29	0,40
Brain Hippocampus	33,12	21,91	11,21	0,42
Cerebellum	40,00	22,84	17,16	0,00
Brain Cortex Temporal	33,28	23,61	9,66	1,23
Brain Cortex Frontal	34,81	23,20	11,61	0,32
Substantia Nigra	40,00	21,39	18,61	0,00
Dorsal Root Ganglion	39,83	21,35	18,47	0,00
Spinal Cord	39,55	21,57	17,97	0,00
Hypothalamus	35,65	21,83	13,82	0,00
Amygdala	35,82	21,52	14,30	0,00
Adrenal Gland	40,00	21,09	18,91	0,00
Salivary Gland	40,00	21,56	18,44	0,00
Thyroid	40,00	20,52	19,48	0,00
Heart	34,96	20,69	14,26	0,05
Aorta	35,55	20,89	14,65	0,00
Fetal Aorta	35,80	22,86	12,94	0,00
AoSMC	29,23	19,25	9,98	0,99
HUVEC	40,00	21,28	18,72	0,00
Adipose	39,40	19,77	19,63	0,00
Fetal Liver	39,98	22,09	17,89	0,00
Liver	40,00	20,66	19,34	0,00
Normal Spleen	32,16	19,05	13,11	0,11
Tonsil	35,12	19,12	15,99	0,00
Bone Marrow	39,75	21,57	18,18	0,00
Thymus	38,16	20,01	18,15	0,00
PBMC Control	39,86	18,29	21,57	0,00
PBMC, PHA treated	39,83	18,11	21,72	0,00
THP-1 monocytes	39,62	20,59	19,03	0,00
THP-1 macrophages	39,80	19,82	19,98	0,00
Kidney	40,00	22,12	17,88	0,00
Skeletal Muscle	39,30	22,27	17,02	0,00
Skin	39,49	21,09	18,40	0,00
Chondrocytes	34,97	20,53	14,44	0,04

Trachea	39,64	20,70	18,94	0,00
Fetal Lung	37,09	22,44	14,65	0,00
Lung	34,54	19,60	14,93	0,03
Lung COPD Control	40,00	20,04	19,96	0,00
Lung COPD	39,00	20,28	18,72	0,00
Lung Tumor Control	35,62	18,79	16,83	0,00
Lung Tumor(adenocarcinoma)	35,29	18,81	16,47	0,00
Lung Tumor(carcinoma)	34,02	19,18	14,85	0,03
A549 cells	39,81	19,75	20,06	0,00
Breast	35,69	21,97	13,72	0,00
Breast Tumor Control	31,53	20,88	10,65	0,62
Breast Tumor(adenocarcinoma)	31,49	20,02	11,47	0,35
Mammary Gland	32,62	20,40	12,21	0,21
Colon	38,69	20,05	18,64	0,00
Colon IBD Control	35,60	19,02	16,58	0,00
Colon IBD	35,39	19,50	15,89	0,00
Colon Tumor Control	35,60	19,63	15,97	0,00
Colon Tumor(adenocarcinoma)	35,25	19,32	15,93	0,00
Esophagus	37,59	21,90	15,68	0,00
Stomach	35,13	20,88	14,25	0,00
Small Intestine	39,54	21,00	18,54	0,00
Pancreas	40,00	23,39	16,61	0,00
Ovary	39,94	21,12	18,81	0,00
Ovary Tumor Control	39,50	20,65	18,85	0,00
Ovary Tumor(adenocarcinoma)	36,06	19,50	16,56	0,00
Ovary Tumor(carcinoma)	39,67	18,95	20,72	0,00
Prostate	39,59	20,37	19,22	0,00
Prostate Tumor Control	40,00	20,54	19,46	0,00
Prostate				
Tumor(adenocarcinoma)	37,51	20,27	17,23	0,00
HeLa cells	40,00	19,34	20,66	0,00
Uterus	32,39	20,46	11,93	0,26
Placenta	35,74	22,01	13,73	0,00
Testis	32,42	22,53	9,89	1,06

Positive Control (HIPCO)	33,15	20,48	12,67	0,15
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2.5) The following expression profiles could be gained for a gene encoding a peptide sequence according to Seq ID Nr 3 (Fig. 9). These results are exhibited as well in Fig. 3 however in another format:

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Tissue Type	Mean	RPL37aMean	ΔΔ Ct	Expression
Fetal Brain	27,61	23,88	3,73	75,43
Brain	27,58	21,82	5,75	18,56
Brain Hippocampus	26,95	21,09	5,86	17,23
Cerebellum	26,98	21,83	5,15	28,14
Brain Cortex Temporal	27,87	22,74	5,13	28,48
Brain Cortex Frontal	27,92	22,36	5,57	21,10
Substantia Nigra	26,03	20,48	5,55	21,34
Dorsal Root Ganglion	24,93	20,79	4,14	56,74
Spinal Cord	25,90	20,67	5,22	26,80
Hypothalamus	26,44	20,97	5,46	22,68
Amygdala	26,70	20,75	5,95	16,20
Adrenal Gland	26,30	20,37	5,93	16,43
Salivary Gland	27,34	20,91	6,42	11,67
Thyroid	25,47	19,95	5,52	21,79
Heart	24,93	20,06	4,87	34,20
Aorta	25,44	20,08	5,36	24,31
Fetal Aorta	24,71	22,16	2,56	169,83
AoSMC	25,32	20,02	5,30	25,40
HUVEC	25,24	20,32	4,91	33,18
Adipose	23,86	19,20	4,66	39,64
Fetal Liver	26,93	21,41	5,52	21,82
Liver	27,72	20,07	7,65	4,98
Normal Spleen	25,66	18,39	7,27	6,47
Tonsil	26,10	18,32	7,78	4,54
Bone Marrow	29,36	20,50	8,86	2,15
Thymus	25,00	18,95	6,04	15,16
PBMC Control	28,79	17,48	11,32	0,39

PBMC, PHA treated	24,68	17,27	7,41	5,88
THP-1 monocytes	30,34	19,53	10,82	0,55
THP-1 macrophages	30,35	18,95	11,41	0,37
Kidney	27,82	21,35	6,47	11,25
Skeletal Muscle	26,66	21,31	5,35	24,50
Skin	26,02	20,39	5,63	20,19
Chondrocytes	30,08	19,75	10,33	0,78
Trachea	25,64	20,58	5,06	29,98
Fetal Lung	23,50	22,27	1,22	428,06
Lung	24,92	19,39	5,53	21,58
Lung COPD Control	26,36	19,70	6,66	9,87
Lung COPD	25,89	20,11	5,78	18,18
Lung Tumor Control	24,46	18,90	5,56	21,24
Lung Tumor(adenocarcinoma)	25,60	18,75	6,85	8,67
Lung Tumor(carcinoma)	25,13	19,40	5,72	18,93
A549 cells	29,30	19,48	9,82	1,11
Breast	27,63	21,93	5,70	19,27
Breast Tumor Control	24,15	20,82	3,33	99,60
Breast Tumor(adenocarcinoma)	25,02	19,88	5,13	28,52
Mammary Gland	23,96	20,32	3,64	80,12
Colon	25,25	19,76	5,49	22,28
Colon IBD Control	25,44	18,98	6,46	11,35
Colon IBD	26,17	19,58	6,59	10,35
Colon Tumor Control	24,99	19,50	5,50	22,15
Colon Tumor(adenocarcinoma)	25,50	19,15	6,35	12,25
Esophagus	26,87	21,94	4,93	32,88
Stomach	25,74	21,13	4,61	40,88
Small Intestine	25,46	21,08	4,38	47,96
Pancreas	29,00	23,14	5,85	17,28
Ovary	24,37	20,93	3,44	92,12
Ovary Tumor Control	22,48	20,62	1,86	275,88
Ovary Tumor(adenocarcinoma)	26,19	19,48	6,71	9,54
Ovary Tumor(carcinoma)	26,29	19,21	7,08	7,37
Prostate	25,44	20,35	5,08	29,46

Prostate Tumor Control	25,41	20,59	4,82	35,38
Prostate				
Tumor(adenocarcinoma)	25,14	20,09	5,05	30,28
HeLa cells	29,11	19,35	9,75	1,16
Uterus	23,77	20,27	3,50	88,49
Placenta	27,73	22,13	5,59	20,74
Testis	25,44	22,28	3,16	111,93
Positive Control(HIPCO)	26,57	20,50	6,07	14,88

2.6) The following expression profiles could be gained for a gene encoding a peptide sequence according to Seq ID Nr 4 (Fig. 10). These results are exhibited as well in

5 Fig. 4 however in another format:

Tissue Type	Mean	RPL37aMean	$\Delta\Delta$ Ct	Expression
Fetal Brain	26,65	24,42	2,23	213,09
Brain	25,81	22,65	3,16	111,58
Brain Hippocampus	25,46	21,68	3,78	72,68
Cerebellum	24,21	22,63	1,58	333,75
Brain Cortex Temporal	26,22	23,25	2,97	127,57
Brain Cortex Frontal	25,85	23,02	2,84	139,77
Substantia Nigra	25,09	21,41	3,68	77,94
Dorsal Root Ganglion	26,31	21,40	4,91	33,21
Spinal Cord	25,54	21,21	4,32	49,99
Hypothalamus	25,34	21,69	3,65	79,80
Amygdala	25,59	21,41	4,18	55,15
Adrenal Gland	26,43	20,92	5,51	21,96
Salivary Gland	27,09	21,26	5,83	17,58
Thyroid	25,10	20,54	4,56	42,30
Heart	25,53	20,64	4,89	33,68
Aorta	23,48	20,64	2,84	140,12
Fetal Aorta	25,76	22,81	2,95	129,46
AoSMC	24,74	20,22	4,51	43,84
HUVEC	27,69	21,06	6,63	10,08

Adipose	24,15	19,53	4,61	40,82
Fetal Liver	26,81	21,91	4,90	33,43
Liver	27,39	20,57	6,82	8,85
Normal Spleen	26,36	18,93	7,43	5,82
Tonsil	25,40	19,02	6,38	12,02
Bone Marrow	27,72	21,20	6,52	10,89
Thymus	26,13	19,67	6,46	11,35
PBMC Control	24,51	18,28	6,23	13,33
PBMC, PHA treated	26,50	17,83	8,67	2,46
THP-1 monocytes	27,34	20,44	6,90	8,38
THP-1 macrophages	25,31	19,42	5,89	16,91
Kidney	26,42	21,98	4,44	46,00
Skeletal Muscle	26,83	21,82	5,01	31,00
Skin	26,37	20,87	5,50	22,07
Chondrocytes	25,32	20,37	4,95	32,35
Trachea	26,88	20,68	6,20	13,63
Fetal Lung	24,27	22,12	2,15	224,85
Lung	24,34	19,66	4,68	38,99
Lung COPD Control	25,91	20,04	5,87	17,08
Lung COPD	25,86	20,43	5,43	23,27
Lung Tumor Control	24,26	18,90	5,37	24,23
Lung Tumor(adenocarcinoma)	24,89	18,76	6,13	14,26
Lung Tumor(carcinoma)	24,62	19,34	5,29	25,61
A549 cells	24,30	19,69	4,61	40,86
Breast	26,25	21,79	4,47	45,26
Breast Tumor Control	25,39	21,00	4,39	47,72
Breast Tumor(adenocarcinoma)	25,06	19,91	5,15	28,22
Mammary Gland	25,45	20,47	4,99	31,54
Colon	25,67	19,89	5,78	18,14
Colon IBD Control	24,98	19,18	5,80	17,95
Colon IBD	26,45	19,46	6,98	7,91
Colon Tumor Control	24,93	19,69	5,25	26,32
Colon Tumor(adenocarcinoma)	25,21	19,41	5,80	17,93
Esophagus	27,85	22,07	5,78	18,21

Stomach	26,33	20,90	5,43	23,22
Small Intestine	26,52	21,21	5,31	25,24
Pancreas	28,54	23,50	5,03	30,53
Ovary	26,27	21,12	5,15	28,07
Ovary Tumor Control	24,96	20,85	4,11	57,84
Ovary Tumor(adenocarcinoma)	25,29	19,54	5,76	18,51
Ovary Tumor(carcinoma)	25,58	19,23	6,35	12,28
Prostate	25,83	20,29	5,55	21,42
Prostate Tumor Control	25,97	20,73	5,25	26,31
Prostate				
Tumor(adenocarcinoma)	25,30	20,36	4,94	32,52
HeLa cells	24,16	19,70	4,46	45,58
Uterus	25,44	20,46	4,98	31,72
Placenta	24,65	22,12	2,53	172,96
Testis	27,35	22,27	5,08	29,60
Positive Control(HIPCO)	24,97	20,42	4,55	42,65

2.7) The following expression profiles could be gained for a gene encoding a peptide sequence according to Seq ID Nr 5 (Fig. 11). These results are exhibited as well in Fig. 5 however in another format:

5

Tissue Type	Mean	RPL37aMean	$\Delta\Delta$ Ct	Expression
Fetal Brain	38,36	23,87	14,49	0,00
Brain	30,39	22,28	8,12	3,60
Brain Hippocampus	32,35	21,47	10,88	0,53
Cerebellum	33,44	22,32	11,12	0,45
Brain Cortex Temporal	30,48	22,87	7,61	5,12
Brain Cortex Frontal	29,54	22,87	6,67	9,85
Substantia Nigra	29,00	20,87	8,13	3,57
Dorsal Root Ganglion	33,57	21,09	12,48	0,18
Spinal Cord	34,83	21,18	13,65	0,08
Hypothalamus	33,30	21,15	12,14	0,22
Amygdala	29,81	21,10	8,71	2,39
Adrenal Gland	35,88	20,63	15,25	0,00

Salivary Gland	32,11	20,86	11,25	0,41
Thyroid	30,02	20,01	10,01	0,97
Heart	22,92	20,24	2,68	155,99
Aorta	32,01	20,35	11,66	0,31
Fetal Aorta	32,25	22,20	10,05	0,95
AoSMC	36,69	20,10	16,59	0,00
HUVEC	37,96	20,81	17,15	0,00
Adipose	31,88	19,24	12,64	0,16
Fetal Liver	35,04	21,66	13,38	0,00
Liver	35,58	20,23	15,35	0,00
Normal Spleen	39,90	18,59	21,31	0,00
Tonsil	36,19	18,63	17,56	0,00
Bone Marrow	37,40	21,07	16,33	0,00
Thymus	39,63	19,29	20,34	0,00
PBMC Control	39,28	17,90	21,39	0,00
PBMC, PHA treated	39,82	17,58	22,23	0,00
THP-1 monocytes	39,31	19,99	19,32	0,00
THP-1 macrophages	37,87	19,08	18,80	0,00
Kidney	34,05	21,20	12,85	0,14
Skeletal Muscle	23,72	21,72	2,00	249,66
Skin	32,47	20,76	11,70	0,30
Chondrocytes	32,69	20,10	12,59	0,16
Trachea	34,91	20,45	14,46	0,04
Fetal Lung	38,69	22,27	16,42	0,00
Lung	33,40	19,59	13,81	0,07
Lung COPD Control	38,12	19,92	18,20	0,00
Lung COPD	39,60	20,44	19,16	0,00
Lung Tumor Control	35,64	19,07	16,57	0,00
Lung Tumor(adenocarcinoma)	36,67	18,41	18,26	0,00
Lung Tumor(carcinoma)	36,89	19,51	17,38	0,00
A549 cells	37,89	19,86	18,03	0,00
Breast	30,08	21,84	8,24	3,32
Breast Tumor Control	38,42	21,05	17,36	0,00
Breast Tumor(adenocarcinoma)	40,00	20,29	19,71	0,00

Mammary Gland	37,00	20,21	16,80	0,00
Colon	38,67	19,93	18,74	0,00
Colon IBD Control	39,98	19,15	20,84	0,00
Colon IBD	38,63	19,84	18,79	0,00
Colon Tumor Control	39,68	19,82	19,87	0,00
Colon Tumor(adenocarcinoma)	39,60	19,26	20,34	0,00
Esophagus	28,60	22,24	6,36	12,16
Stomach	36,43	21,12	15,31	0,00
Small Intestine	38,13	21,11	17,02	0,00
Pancreas	40,00	23,71	16,29	0,00
Ovary	34,51	21,07	13,43	0,09
Ovary Tumor Control	32,33	20,61	11,72	0,30
Ovary Tumor(adenocarcinoma)	39,25	19,62	19,63	0,00
Ovary Tumor(carcinoma)	37,45	19,11	18,34	0,00
Prostate	32,12	20,34	11,79	0,28
Prostate Tumor Control	39,62	20,71	18,92	0,00
Prostate Tumor(adenocarcinoma)	38,21	20,38	17,83	0,00
HeLa cells	40,00	19,38	20,62	0,00
Uterus	33,22	20,19	13,03	0,12
Placenta	39,92	22,32	17,59	0,00
Testis	33,43	22,25	11,18	0,43
Positive Control(HIPCO)	33,10	20,69	12,42	0,18

2.8) The following expression profiles could be gained for a gene encoding a peptide sequence according to Seq ID Nr 6 (Fig. 12). These results are exhibited as well in Fig. 6 however in another format:

5

Tissue Type	Mean	RPL37aMean	$\Delta\Delta$ Ct	Expression
Fetal Brain	27,34	25,41	1,93	263,22
Brain	29,19	23,30	5,88	16,95
Brain Hippocampus	28,80	22,54	6,26	13,07
Cerebellum	32,16	23,37	8,79	2,26
Brain Cortex Temporal	29,79	24,09	5,71	19,12

Brain Cortex Frontal	29,28	24,02	5,27	25,99
Substantia Nigra	28,03	22,16	5,87	17,05
Dorsal Root Ganglion	29,51	22,02	7,50	5,53
Spinal Cord	29,63	22,18	7,45	5,72
Hypothalamus	28,81	22,42	6,38	11,99
Amygdala	28,93	22,13	6,80	9,00
Adrenal Gland	33,43	21,62	11,80	0,28
Salivary Gland	34,15	22,61	11,53	0,34
Thyroid	32,85	21,28	11,57	0,33
Heart	29,36	21,31	8,05	3,76
Aorta	31,93	21,35	10,58	0,65
Fetal Aorta	28,86	23,35	5,51	21,88
AoSMC	27,84	21,18	6,66	9,92
HUVEC	30,12	21,89	8,23	3,33
Adipose	30,83	20,28	10,54	0,67
Fetal Liver	29,63	22,65	6,98	7,91
Liver	28,50	21,28	7,22	6,70
Normal Spleen	31,40	19,53	11,86	0,27
Tonsil	32,57	19,71	12,86	0,13
Bone Marrow	35,75	22,25	13,50	0,00
Thymus	30,85	20,87	9,98	0,99
PBMC Control	34,92	18,96	15,96	0,02
PBMC, PHA treated	37,76	18,82	18,93	0,00
THP-1 monocytes	32,76	21,11	11,65	0,31
THP-1 macrophages	28,51	20,16	8,35	3,05
Kidney	30,38	22,60	7,78	4,54
Skeletal Muscle	33,40	22,76	10,65	0,62
Skin	31,49	21,72	9,77	1,15
Chondrocytes	31,57	21,12	10,45	0,71
Trachea	31,85	22,03	9,82	1,11
Fetal Lung	29,20	23,75	5,45	22,83
Lung	30,97	21,01	9,96	1,01
Lung COPD Control	34,63	21,46	13,17	0,11
Lung COPD	32,57	21,55	11,02	0,48

Lung Tumor Control	32,78	20,29	12,49	0,17
Lung Tumor (adenocarcinoma)	30,87	19,82	11,05	0,47
Lung Tumor (carcinoma)	29,76	20,69	9,07	1,86
A549 cells	31,21	21,15	10,06	0,94
Breast	28,92	23,23	5,70	19,29
Breast Tumor Control	30,72	22,01	8,71	2,39
Breast Tumor (adenocarcinoma)	30,57	21,33	9,24	1,66
Mammary Gland	31,14	21,63	9,51	1,38
Colon	33,75	21,03	12,72	0,15
Colon IBD Control	33,12	20,13	12,99	0,12
Colon IBD	30,25	19,15	11,10	0,46
Colon Tumor Control	32,80	20,89	11,91	0,26
Colon Tumor (adenocarcinoma)	30,83	20,20	10,63	0,63
Esophagus	32,49	23,20	9,29	1,60
Stomach	32,13	22,16	9,96	1,00
Small Intestine	32,84	22,34	10,50	0,69
Pancreas	33,67	24,81	8,86	2,15
Ovary	31,63	22,36	9,27	1,62
Ovary Tumor Control	31,59	21,71	9,88	1,06
Ovary Tumor (adenocarcinoma)	30,43	20,50	9,94	1,02
Ovary Tumor (carcinoma)	31,36	20,21	11,15	0,44
Prostate	32,00	21,38	10,62	0,63
Prostate Tumor Control	32,00	21,95	10,04	0,95
Prostate Tumor (adenocarcinoma)	31,53	21,43	10,11	0,91
HeLa cells	31,34	20,43	10,91	0,52
Uterus	29,07	21,57	7,49	5,55
Placenta	32,19	23,28	8,92	2,07
Testis	29,04	23,44	5,60	20,60
Positive Control, HIPCO	27,78	21,54	6,24	13,27

REFERENCES:

- (1) Henrik Nielsen, Jacob Engelbrecht, Søren Brunak and Gunnar von Heijne
 "Identification of prokaryotic and eukaryotic signal peptides and prediction of
 their cleavage sites" Protein Engineering, 10:1-6, 1997.
- (2) A. Krogh, B. Larsson, G. von Heijne and E. L. L. Sonnhammer. "Predicting
 transmembrane protein topology with a hidden Markov model: Application to
 complete genomes" Journal of Molecular Biology, 305(3):567-580, January
 2001.
- (3) Peter Duckert, Søren Brunak and Nikolaj Blom, "Prediction of proprotein
 convertase cleavage sites" Protein Engineering, Design and Selection: 17:
 107-112, 2004.
- (4) Strand, F.L. Neuropeptides: Regulators of physiological processes. (1999) MIT
 Press.
- (5) Anderson, N.L. & Anderson, N.G. The human plasma proteome: history,
 character, and diagnostic prospects. Mol. Cell. Proteomics, 2002 Nov;1(11):
 845-67
- (6) Mulder NJ, Apweiler R, Attwood TK, Bairoch A, Bateman A, Binns D, Bradley
 P, Bork P, Bucher P, Cerutti L, Copley R, Courcelle E, Das U, Durbin R,
 Fleischmann W, Gough J, Haft D, Harte N, Hulo N, Kahn D, Kanapin A,
 Krestyaninova M, Lonsdale D, Lopez R, Letunic I, Madera M, Maslen J,
 McDowall J, Mitchell A, Nikolskaya AN, Orchard S, Pagni M, Ponting CP,
 Quevillon E, Selengut J, Sigrist CJ, Silventoinen V, Studholme DJ, Vaughan
 R, Wu CH. InterPro, progress and status in 2005. Nucleic Acids Res. 2005 Jan
 1;33(Database issue):D201-5.

Description of the Figures:

- Figure 1: shows mRNA Expression Profile of AC105940 on ATAQ 1 for Seq Id no 1
- Figure 2: shows mRNA Expression Profile of AC005291 on ATAQ 1for Seq Id no 3
- Figure 3: shows mRNA Expression Profile of AC090617 on ATAQ 1for Seq Id no 4
- 5 Figure 4: shows mRNA Expression Profile of AC114684 on ATAQ 1for Seq Id no 5
- Figure 5: shows mRNA Expression Profile of AC063920 on ATAQ 1 for Seq Id no 7
- Figure 6: shows mRNA Expression Profile of AC074389 on ATAQ 1 for Seq Id no 8
- Figure 7: shows amino acid sequence list for Seq Id no 1
- Figure 8: shows amino acid sequence for Seq Id no 2
- 10 Figure 9: shows amino acid sequence for Seq Id no 3
- Figure 10: shows amino acid sequence for Seq Id no 4
- Figure 11: shows amino acid sequence for Seq Id no 5
- Figure 12: shows amino acid sequence for Seq Id no 6
- Figure 13: shows amino acid sequence for Seq Id no 7
- 15 Figure 14: shows amino acid sequence for Seq Id no 8
- Figure 15: shows nucleotide sequence for Seq Id no 9
- Figure 16: shows nucleotide sequence for Seq Id no 10
- Figure 17: shows nucleotide sequence for Seq Id no 11
- Figure 18: shows nucleotide sequence for Seq Id no 12
- 20 Figure 19: shows nucleotide sequence for Seq Id no 13
- Figure 20: shows nucleotide sequence for Seq Id no 14
- Figure 21: shows nucleotide sequence for Seq Id no 15
- Figure 22: shows nucleotide sequence for Seq Id no 16
- Figure 23: shows nucleotide Probe sequence for Seq Id no 1
- 25 Figure 24: shows nucleotide Forward primer sequence for Seq Id no 1
- Figure 25: shows nucleotide Reverse primer sequence for Seq Id no 1
- Figure 26: shows nucleotide Probe sequence for Seq Id no 2
- Figure 27: shows nucleotide Forward primer sequence for Seq Id no 2
- Figure 28: shows nucleotide Reverse primer sequence for Seq Id no 2
- 30 Figure 29: shows nucleotide Probe sequence for Seq Id no 3
- Figure 30: shows nucleotide Forward primer sequence for Seq Id no 3
- Figure 31: shows nucleotide Reverse primer sequence for Seq Id no 3
- Figure 32: shows nucleotide Probe sequence for Seq Id no 4
- Figure 33: shows nucleotide Forward primer sequence for Seq Id no 4

Figure 34: shows nucleotide Reverse primer sequence for Seq Id no 4

Figure 35: shows nucleotide Probe sequence for Seq Id no 5

Figure 36: shows nucleotide Forward primer sequence for Seq Id no 5

Figure 37: shows nucleotide Reverse primer sequence for Seq Id no 5

5 Figure 38: shows nucleotide Probe sequence for Seq Id no 6

Figure 39: shows nucleotide Forward primer sequence for Seq Id no 6

Figure 40: shows nucleotide Reverse primer sequence for Seq Id no 6

Figure 41: shows nucleotide Probe sequence for Seq Id no 7

Figure 42: shows nucleotide Forward primer sequence for Seq Id no 7

10 Figure 43: shows nucleotide Reverse primer sequence for Seq Id no 7

Figure 44: shows nucleotide Probe sequence for Seq Id no 8

Figure 45: shows nucleotide Forward primer sequence for Seq Id no 8

Figure 46: shows nucleotide Reverse primer sequence for Seq Id no 8

CLAIMS

5

10

1. A polypeptide chain comprising an amino acid sequence according to Seq Id no 1. or an amino acid sequence derived there from by deletion, substitution or insertion of at least one amino acid residue, its amide or ester or a salt of said peptide, whereby the polypeptide comprising an amino acid sequence derived from Seq Id no. 1 has hormonal activity.

15

2. A polypeptide chain of claim 1 that consists of the following amino acid sequence: MYWMALRRISTLGSRWLGLSRVLLFRASKASFTFLSLRFSLVAARRRSTDTDFLLHTLHAHGRHWPGQCSGVPSPLSSRGPGASGLRVSSVRS

3. A DNA consisting of a nucleotide base sequence according to Seq Id no 9 encoding a polypeptide chain according to claim 1 or 2 consisting of an amino acid sequence represented by Seq Id no 1 or its amide, ester or a salts thereof.

4. Use of DNA according to claim 3 for preparing a recombinant vector, wherein said recombinant vector comprises
 1. a DNA according to claim 3, andfor introducing said recombinant vector in to a host cell, wherein said host cell comprises said recombinant vector.
5. A method for manufacturing of a polypeptide according to claim 1 wherein said method comprises the step of:
 - i. providing the amino acid
 - ii. synthesizing the amino acid by solid phase or liquid phase synthesis
 1. extraction of polypeptide
 - iii. purification of the polypeptide
6. A method of producing the peptide, precursor or salt thereof as claimed in Claim 1 which comprises subjecting an amino terminus-constituting amino acid or peptide and a carboxyl terminus-constituting amino acid or peptide to condensation, optionally followed by intramolecular disulfide bond formation.
7. A pharmaceutical composition comprising as the active agent a polypeptide chain or precursor, or pharmaceutically acceptable amide, ester, or a salt thereof wherein said polypeptide chain consists of an amino acid sequence according Seq Id no 1.
8. Use of pharmaceutical composition according to claim 8, comprising as the active agent polypeptide chain or precursor, or pharmaceutically acceptable amide, ester, or a salt thereof wherein said polypeptide chain consists of an amino acid sequence according Seq Id no 1 for the preparation of a pharmaceutical composition to change physiological factors that increase the risk of arteriosclerosis, inflammation or uncontrolled cell division.
9. An antibody to a polypeptide chain according to claim 1 that comprises an amino acid sequences according to Seq Id no 1, or its amide, ester or salts thereof.

Abstract

- 5 The present invention relates to novel bio-active peptide hormone, process for the production of the same, and use of the same. The present invention identified novel bioactive peptide precursor and salts thereof which can be used as drugs, for example therapeutic polypeptides, ligands to discover relevant targets (e.g. GPCRs) or targets for drug intervention.

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