GHRELIN, LEPTIN AND OBESTATIN PEPTIDES OFFERED BY BACHEM

Ghrelin is an endogenous peptide discovered by Kojima et al. in 1999 during the search for an unknown endogenous ligand of a receptor of known structure and function. It is a 28 amino acid peptide with an essential n-octanoyl modification on the hydroxy group of Ser3. It displays strong growth hormone-releasing activity mediated by the growth hormone secretagogue receptor 1a (GHS-R1a). Ghrelin participates in the regulation of energy homeostasis, increases food intake, and decreases energy expenditure by lowering the catabolism of fat. Several years after the isolation of ghrelin a second peptide derived from preproghrelin was isolated from rat stomach. This 23 amino acid peptide named obestatin was initially considered to oppose the orexigenic (appetite-stimulating) effects of ghrelin. It was also reported to be the cognate ligand for the G-protein-coupled receptor GPR39. Later studies, however, cast doubt on the initial findings as subsequent studies failed to confirm the anorexigenic effects of obestatin. Leptin, a satiety hormone produced by white adipose tissue, was discovered in 1994 and represents another appetite regulator. Leptin and ghrelin are supposed to share hypothalamic pathways regulating food intake and energy homeostasis.
Isolation of Ghrelin

Studies on peptidyl growth hormone (GH) secretagogues (GHS), initially discovered by Bowers and Momany in 1976, led to the identification of the GHS receptor in 1996. The GHS receptor belongs to the family of G-protein-coupled receptors containing seven transmembrane (TM) domains and three intracellular and extracellular loops. Despite intensive search by various groups, the endogenous ligand of the GHS receptor could not be isolated for a long time. Only synthetic ligands, such as growth hormone-releasing peptide-6 (GHRP-6), or hexarelin were known for this receptor.

The cloning of the GHS receptor in 1996 was an important step towards the identification of the endogenous ligand. In 1999, a Japanese group of scientists (Kojima et al.) succeeded in the purification and identification of a peptide in rat stomach that could stimulate the GHS receptor stably transfected into Chinese hamster ovary (CHO) cells. The purified ligand was found to be a peptide of 28 amino acids, called ghrelin (.ghre' is a word root in Proto-Indo-European languages, meaning ‘growth’, the suffix ‘relin’ indicates that a peptide is a releasing hormone). The side chain of serine in position 3 of ghrelin was demonstrated to be modified by an octanoyl group. This unusual esterification has not been described before.

By using the rat cDNA sequence for screening a human stomach cDNA library under low stringency conditions, the human ghrelin sequence was subsequently identified. The human ghrelin gene is localized on chromosome 3 at position p25-26 and comprises five exons. Human ghrelin is derived from a 117 amino acid precursor ovary (CHO) cells. The purified ligand was found to be a peptide of 28 amino acids, called ghrelin (.ghre' is a word root in Proto-Indo-European languages, meaning ‘growth’, the suffix ‘relin’ indicates that a peptide is a releasing hormone). The side chain of serine in position 3 of ghrelin was demonstrated to be modified by an octanoyl group. This unusual esterification has not been described before.

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Ghrelin, Leptin and Obestatin

Ghrelin, Leptin and Obestatin

4

... that inhibits the secretion but not the synthesis of GH. Together with GHRH, ghrelin acts synergistically to stimulate the release of GH from the somatotrophic cells of the hypophysis.

Amongst a range of tested neuropeptides only GHSs bound specifically to the GHS receptor. GHRH, somatostatin, and ghrelin mediate their effects through G-protein-coupled receptors. GHRH activates adenyl cyclase, cyclic AMP, and protein kinase A pathways, whereas ghrelin stimulates phospholipase C activity leading to production of inositol-1,4,5-trisphosphate and diacylglycerol, increase in cytosolic calcium levels, and GH release. Somatostatin acts through an inhibitory G-protein-coupled receptor thus blocking GH secretion.

**Influence of food intake and energy balance**

Ghrelin not only stimulates GH secretion, it also increases food intake and weight gain in experimental animals and induces hunger in humans.

Ghrelin is part of a complex neuroendocrine network involved in the regulation of appetite and energy homeostasis. Peripheral ghrelin may exert its effects on the CNS by crossing the blood brain barrier (BBB) although the rate at which it passes the BBB is very low. Several studies suggested that the orexigenic signal of ghrelin secreted from the stomach is transmitted to the brain via the vagal afferent nerve. This was supported by the finding that vagotomy inhibits the ability of ghrelin to stimulate food intake. However, other studies concluded that abdominal vagal afferents are not required for the acute eating-stimulatory effect of ghrelin.

Ghrelin receptors are synthesized by a subset of vagal afferent neurons of the nodose ganglion and then transmitted to axon terminals where they bind to ghrelin. Ghrelin can influence gastric satiety signaling by altering the mechanosensitivity of gastric vagal afferents to distension.

The ghrelin receptor is expressed in several hypothalamic nuclei. Many of them are known to be involved in the regulation of food intake and body weight. Ghrelin is also synthesized locally in neurons of hypothalamic areas such as the paraventricular and the arcuate nucleus but also in the sensorimotor area of the cerebral cortex and in the cingulate gyrus.

In the arcuate nucleus, ghrelin-containing neurons send efferent fibers onto neurons expressing neuropeptide Y (NPY) and agouti-related protein (AgRP) to stimulate the release of these orexigenic peptides. This is complemented by a suppressive ef-
fect on proopiomelanocortin/cocaine- and amphetamine-regulated transcript (POMC/CART)-expressing neurons via inhibitory γ-aminobutyric acid (GABA) inputs from NPY/AgRP neurons. The hypothalamic NPY/Y1 receptor pathway is shared by leptin. Ghrelin antagonizes the anorectic effect of leptin through the activation of this pathway (Fig. 2).

Effects of ghrelin on the cardiovascular system

A study of the peripheral distribution of GHS receptors has shown that ghrelin is also present in cardiovascular tissue, which has led to the exploration of the cardiovascular functions of ghrelin and synthetic growth hormone-releasing peptides. These ligands have several cardiovascular activities, including a cardioprotective effect against myocardial ischemia, and vasoactive and cardioprotective effects in both experimental models and humans. There is evidence that certain cardioprotective effects are mediated via a novel, yet to be identified cardiac receptor distinct from the GHS receptor. This is supported by the finding that both octanoylated and non-acylated ghrelin exhibited antiapoptotic effects on cardiomyocytes which do not express the GHS receptor. Both ghrelin and non-acyl ghrelin, recognize a common high affinity binding site, although only the fatty acid modified form of ghrelin binds to the GHS receptor.

The role of the ghrelin in reproduction

Ghrelin is also supposed to be involved in the regulation of reproductive function by acting at central and peripheral levels. Ghrelin has been described to predominantly negatively modulate the hypothalamic-pituitary-gonadal (HPG) axis. Recently, kisspeptin (KiSS-1) and its G-protein-coupled receptor GPR54 (KiSS-1R) have been identified as an essential component of the HPG axis controlling gonadotrophin secretion. Ghrelin has been demonstrated to decrease KiSS-1 mRNA expression in the medial preoptic area without affecting GPR54 levels. At peripheral levels, ghrelin may also function in the direct control of follicular development, ovarian cell functions, and embryonal development. In addition, ghrelin has been suggested to influence the male reproductive axis in situations of energy deficit.

Identification of Leptin

Leptin has been discovered in 1994 by positional cloning of the mouse obese gene originally described in 1950. Mice which are homozygous for the recessive obese mutation exhibit hyperphagia and increase rapidly in weight. The ob/ob phenotype is also characterized by infertility and a form of diabetes similar to human type-II diabetes. The mouse obese gene was mapped to chromosome 6. It encodes a 167 amino acid protein containing a 21 amino acid signal sequence. The gene product was called leptin, after the Greek word leptos meaning thin. Human leptin also consist of 167 amino acids and is 83% similar to the mouse protein. The human gene resides on chromosome 7.

In 1995 the leptin receptor (Ob-R) was identified. It is a single membrane-spanning receptor and belongs to the class I cytokine receptor superfamily. The receptor is encoded by the diabetes (db) gene. Mice deficient for the leptin receptor (db/db mice) serve as a model for obesity, diabetes, and dyslipidemia. Both human and mouse leptin receptors exist in several isoforms generated by alternative splicing and can be divided into three classes: secreted, short, and long.

Physiological Functions of Leptin

Regulation of food intake and body weight

Leptin acts as a satiety hormone. It is mainly secreted by white adipose tissue and its serum levels positively correlate with the percentage of body fat. Leptin signaling is part of a feedback mechanism controlling food intake and energy homeostasis. Interestingly, elevated leptin serum levels are associated with leptin resistance in obese subjects. Leptin exerts its effects by binding to its receptor expressed in the brain and in peripheral tissues. The long form of the leptin receptor (Ob−Rb), highly expressed in the hypothalamus, is supposed to mediate most of leptin's effects. Leptin signals via the Janus Kinase / Signal Transducer and Activator of Transcription (JAK/STAT) pathway but also modulates a number of other signaling pathways in the brain, such as the PI 3-kinase,
MAPK, and mTOR pathway. In the hypothalamus leptin inhibits neuronal pathways that stimulate food intake by counteracting the orexigenic effects of NPY/AgRP neurons and by activating anorexigenic POMC/CART neurons.

The role of the leptin in reproduction
Leptin is also involved in the regulation of reproductive development and function by indirectly influencing GnRH neuron activity. Leptin signaling is part of a complex neuronal network which involves NPY/AgRP, POMC/CART, and kisspeptin-1 neurons. As the kisspeptin-1 neurons express leptin receptors, they may participate in transmitting metabolic information to the GnRH neurons. Loss of KiSS-1 peptide or its receptor, GPR54, results in hypothalamic hypogonadism and infertility.

Identification of Obestatin
Obestatin was identified by Zhang et al. in 2005 on the basis of bioinformatic searches of putative hormones derived from the prepropeptides of known peptide hormones. Obestatin was predicted to be derived from a conserved region of preproghrelin that was flanked by potential convertase cleavage sites. Based on this information the peptide was subsequently isolated from rat stomach. Obestatin consists of 23 amino acid and is C-terminally amidated.

Physiological Functions of Obestatin

Influence on food intake
The newly discovered gastric peptide was initially shown to oppose the effects of ghrelin by decreasing appetite and weight gain. For this reason it was named obestatin (from the Latin word ‘obedere’, meaning ‘to devour’, and ‘statin’, denoting suppression). Similar to ghrelin, which requires posttranslational modification by acylation, the biological activity of obestatin depended on modification by C-terminal amidation. Zhang et al. (1994) showed that obestatin binds to and activates the orphan receptor GPR39. This G-protein-coupled receptor has been mapped to human chromosome 2 and is expressed in multiple tissues, including stomach, intestine, and hypothalamus. Subsequent studies, however, failed to confirm the anorexigenic effect of obestatin and activation of GPR39 and thereby questioned the role of obestatin as cognate ligand for GPR39. The controversy about this peptide as a regulator of appetite still exists as the differences in the experimental findings could not be explained by methodological variations. Obestatin has been reported to have additional roles such as the inhibition of thirst and the regulation of memory, anxiety, and sleep. It has also been shown to stimulate the proliferation of human retinal cells and to promote the survival of pancreatic β-cells and human islets (and to induce the expression of genes involved in the regulation of β-cell mass and function). Additionally, it may have functions in the regulation of adipocyte metabolism and adipogenesis.

Prospects
The increasing prevalence of obesity is a global problem. Body weight is regulated by complex mechanisms involving peptide hormones produced in the brain and gut. The discovery of ghrelin and its receptor represents a milestone in understanding the complex mechanisms involved in appetite regulation and energy homeostasis, gastrointestinal function, and growth. Ghrelin represents a major component of a neuroendocrine network. It acts at several levels and regulates food intake and energy balance. The function of obestatin is less clearly defined. Further studies are required to reconcile the controversial results concerning the physiological role of obestatin in opposing the effects of ghrelin. As ghrelin is both orexigenic and adipogenic, the ghrelin system is an ideal therapeutic target for the treatment of anorexia, cachexia, and obesity. Ghrelin's cardioactive effects will possibly allow the development of new treatment options for chronic heart failure. Leptin acts as a satiety hormone; but it is also involved in regulation of reproductive functions like ghrelin. Detailed knowledge of the molecular processes underlying these mechanisms will help to better understand the relationship between metabolism and reproduction.
REFERENCES

A.M. Ingalls et al.
Obese, a new mutation in the house mouse.
J. Hered. 41, 317-318 (1950)

C.Y. Bowers et al.
Effects of the enkephalins and enkephalin analogs on release of pituitary hormones in vitro.

Y. Zhang et al.
Positional cloning of the mouse obese gene and its human homologue.

L.A. Tartaglia et al.
Identification and expression cloning of a leptin receptor, OB-R.

M. Kojima et al.
Ghrelin is a growth-hormone-releasing acylated peptide from stomach.

I.E. Messinis and S.D. Milingos
Leptin in human reproduction.

M.A. Bednarek et al.
Structure - function studies on the new growth hormone-releasing peptide, ghrelin: Minimal sequence of ghrelin necessary for activation of growth hormone secretagogue receptor 1a.

R.R. Gonzalez et al.
Leptin and reproduction.

T.L. Horvath et al.
Ghrelin and the regulation of energy balance - a hypothalamic perspective.
Endocrinology 142, 4163-4169 (2001)

M. Kojima et al.
Purification and distribution of ghrelin: the natural endogenous ligand for the growth hormone secretagogue receptor.
Horm. Res. 56 Suppl. 1, 93-97 (2001)

M. Kojima et al.
Ghrelin: discovery of the natural endogenous ligand for the growth hormone secretagogue receptor.
Trends Endocrinol. Metab. 12, 118-121 (2001)

W.A. Banks et al.
Extent and direction of ghrelin transport across the blood-brain barrier is determined by its unique primary structure.

G. Muccioli et al.
Ghrelin and des-acyl ghrelin both inhibit isoproterenol-induced lipolysis in rat adipocytes via a non-type 1a growth hormone secretagogue receptor.

D. Cocchi et al.
GH-releasing peptides and bone.
J. Endocrinol. Invest. 28 (Suppl. 8), 11-14 (2005)

A.P. Davenport et al.
International union of pharmacology. LVI. Ghrelin receptor nomenclature, distribution, and function.

F. Broglio et al.
Non-acylated ghrelin does not possess the pituitary and pancreatic endocrine activity of acylated ghrelin in humans.

M.A. Cowley et al.
The distribution and mechanism of action of ghrelin in the CNS demonstrates a novel hypothalamic circuit regulating energy homeostasis.
Neuron 37, 649-661 (2003)

M.A. Lazarczyk et al.
Ghrelin: a recently discovered gut-brain peptide (review).

B. Holst et al.
Common structural basis for constitutive activity of the ghrelin receptor family.

G. Muccioli et al.
Ghrelin and des-acyl ghrelin both inhibit isoproterenol-induced lipolysis in rat adipocytes via a non-type 1a growth hormone secretagogue receptor.

F. Lago et al.
Ghrelin, the same peptide for different functions: player or bystander?
Vitam. Horm. 71, 405-432 (2005)

R. Nogueiras and M. Tschöp
Biomedicine. Separation of conjoined hormones yields appetite rivals.
Science 310, 985-986 (2005)
Ghrelin, Leptin and Obestatin

T.L. Peeters
Ghrelin: a new player in the control of gastrointestinal functions.
Gut 54, 1638–1649 (2005)

R.G. Smith et al.
Developments in ghrelin biology and potential clinical relevance.

A.D. Strader and S.C. Woods
Gastrointestinal hormones and food intake.
Gastroenterology 128, 175–191 (2005)

M. Tena-Sempere
Ghrelin: novel regulator of gonadal function.

J.V. Zhang et al.
Obestatin, a peptide encoded by the ghrelin gene, opposes ghrelin's effects on food intake.
Science 310, 996–999 (2005)

M. Arnold et al.
Gut vagal afferents are not necessary for the eating-stimulatory effect of intraperitoneally injected ghrelin in the rat.

J.P. Camina
Cell biology of the ghrelin receptor.

J.M. Cao et al.
Effects of ghrelin and synthetic GH secretagogues on the cardiovascular system.

M.J. Kleinz et al.
Functional and immunocytochemical evidence for a role of ghrelin and des-octanoyl ghrelin in the regulation of vascular tone in man.

N. Chartrel et al.
Comment on “Obestatin, a peptide encoded by the ghrelin gene, oppos-es ghrelin's effects on food intake”.
Science 315, 766; author reply 766 (2007)

B. Holst et al.
GPR39 signaling is stimulated by zinc ions but not by obestatin.

W.K. Samson et al.
Obestatin acts in brain to inhibit thirst.

H.R. Berthoud
The vagus nerve, food intake and obesity.

R. Granata et al.
Obestatin acts in brain to inhibit thirst.

L. Jiang et al.
Leptin stimulates both JAK2-dependent and JAK2-independent signaling pathways.

M.G. Myers et al.
Mechanisms of leptin action and leptin resistance.

E.C. Villanueva and M.G. Myers, Jr.
Leptin receptor signaling and the regulation of mammalian physiology.
Int. J. Obes. (Lond) 32 Suppl 7, S8–12 (2008)

F. Cordido et al.
Ghrelin and growth hormone secretagogue, physiological and pharmacological aspects.

A. Rodriguez et al.
Acylated and desacyl ghrelin stimulate lipid accumulation in human visceral adipocytes.
Int. J. Obes. (Lond) 33, 541–552 (2009)

T.A. Dardeno et al.
Leptin in human physiology and therapeutics.

D. Israel and S. Chua, Jr.
Leptin receptor modulation of adiposity and fertility.
Trends Endocrinol. Metab. 21, 10–16 (2010)

T. Kelesidis et al.
Narrative review: the role of leptin in human physiology: emerging clinical applications.

R. Granata et al.
Cardiovascular actions of the ghrelin gene-derived peptides and growth hormone-releasing hormone.

U. Gurriaran-Rodriguez et al.
Obestatin as a regulator of adipocyte metabolism and adipogenesis.

K.M. Heppner et al.

C.T. Lim et al.
The ghrelin/GOAT/GHS-R system and energy metabolism.

G.J. Morton and M.W. Schwartz
Leptin and the central nervous system control of glucose metabolism.

T. Sato et al.
Structure, regulation and function of ghrelin.

S. Kentish et al.
Diet-induced adaptation of vagal afferent function.
J. Physiol. 590, 209–221 (2012)
Bachem also offers a range of products related to obesity research such as apelin peptides, CART fragments, growth hormone releasing factors, neuropeptide Y and analogs, and orexins. For more information, please see our online shop at shop.bachem.com
**GHRELINS**

Ghrelin (human)
H-4864
GSS(octanoyl)FLSPE
HQRVQQRKESKKPPAKLQPR

Ghrelin-Cys(BMCC-biotinyl) (human)
H-6334
GSS(octanoyl)FLSPEHQRVQQRK
ESKKPPAKLQPR(BMCC-biotinyl)

(Des-octanoyl)-Ghrelin (human)
H-7746
GSSFLSPEHQRVQQRKESKKPPAKLQPR

(Des-octanoyl)-Ghrelin (human)
H-5946
GSSFLSPEHQRVQQRKESKKPPAKLQPR

([¹³C₆]Leu⁵)-Ghrelin (human)
H-7252
GSS(octanoyl)F[¹³C₆]LSPE
HQRVQQRKESKKPPAKLQPR

(Trp³,Arg⁵)-Ghrelin (1-5)
H-6456
GSWFR

Ghrelin (mouse, rat)
H-4862
GSS(octanoyl)FLSPE
HQKAQQRKESKKPPAKLQPR

(Des-octanoyl)-Ghrelin (mouse, rat)
H-6264
GSSFLSPEHQKAQQRKESKKPPAKLQPR

(Ser(Ac)³)-Ghrelin (mouse, rat)
H-7638
GSS(acetyl)FLSPEHQKAQQRKESKKPPAKLQPR

(D-Arg¹,D-Phe⁶,D-Trp⁷⁸,Leu¹¹)-Substance P
H-6935
rPKPfQwFwLL-NH₂

**OBESTATINS**

Obestatin (human)
H-6356
FNAPFDVGIKLSGVQYQQHSQAL-NH₂

Biotinyl-Obestatin (human)
H-6358
Biotinyl-FNAPFDVGIKLSGVQYQQHSQAL-NH₂

Obestatin (rat)
H-6338
FNAPFDVGIKLSGAQYQQHGRAL-NH₂

Biotinyl-Obestatin (rat)
H-6362
Biotinyl-FNAPFDVGIKLSGAQYQQHGRAL-NH₂
LEPTIN

Leptin (22–56) (human)
H-3424
VPiQKVQDDTKTLKITIVTRINDISHTQSVSSKQK

Tyr-Leptin (26–39) (human)
H-3494
YKVQDDTKTLKITIV

Leptin (93–105) (human)
H-3426
NVQISNDLENLR

Leptin (116–130) amide (mouse)
H-3966
SCSLPQTSGLQKPES-NH₂

Leptin (126–140) (human)
H-3492
ETLDSLGGVLEASGY

Leptin (138–167) (human)
H-3428
SGYSTEVVALSRQGLQDMLWQLDLSPGC

Leptin (150–167) (human)
H-3432
LQGLQDMLWQLDLSPGC

rec Leptin (human)
H-5578

rec Leptin (mouse)
H-5582

GHRP-6

(D-Trp⁷,Ala⁸,D-Phe¹⁰)-α-MSH (6–11) amide
H-9990
HwAWfK-NH₂

LEPTIN MOLECULE

Computer model showing the structure of a molecule of the hormone leptin. Leptin is produced by adipose (fat) tissue. It interacts with receptors in the brain’s hypothalamus to signal when a person is full. It also circulates in the blood at levels proportionate to body fat, which allows the brain to regulate appetite and metabolism. Mutations in the ob gene that codes for leptin are thought to be responsible for some forms of obesity.

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