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Structural and functional characteristics of prolactin and its gene in the American mink (*Neovison vison* Schreb., 1777). A rewiev

Charakterystyka strukturalna i funkcjonalna prolaktyny i jej genu u norki amerykańskiej (*Neovison vison* Schreb., 1777). Praca przeglądowa

Summary. Prolactin belongs to a group of hormones having the most comprehensive, systemic biological activity. PRL functions can be divided into two groups – activities associated with the maintenance of homeostasis (osmotropic, somatotrophic and metabotropic activity, impact on behavior, immunomodulation) and related with reproduction (effects on mammary gland, ovary and uterus, effect on physiology of pregnancy, effect on testes and accessory sex glands, impact on behavior related to reproduction and parenthood). Prolactin gene occurs in American mink in one copy and is located in chromosome 13. Because of the many functions of *PRL*, its gene is considered as a gene conditioning quantitative traits. It seems desirable to pay particular attention to the relationship of high level of lactation yield of mink females with features conditioning their vigor and vitality during offspring feeding. It is important because of the particularly heavy burden on the female body during this period, observed in carnivorous fur-bearing animals.

Key words: prolactin, prolactin gene, peptide structure, functional characteristic, gene structure, secretion, signal transduction, *Neovison vison*

INTRODUCTION

Prolactin (PRL, also called lactotropin, lactogenic hormone, mammotropin, luteotropin, luteotropic hormone/LTH) is a peptide hormone secreted by eosinophilic lactotropic cells of anterior lobe of the pituitary gland (Lat. *adenohypophysis*) [Konturek 2000]. The number of lactotropic cells increases significantly during pregnancy [Krzymowski and Przała 2005]. In addition to pituitary, prolactin occurs in the uterine decidua, placenta, prostate, testes, adrenal gland, pancreas, intestine, brain, immune system tissues,

as well as in the milk of mammals, cerebrospinal fluid and amniotic fluid. Prolactin receptor (PRLR) is present on the cells of almost all tissue types [Bole-Feysot *et al*. 1998]. Prolactin content in 1 g of the pituitary gland of sheep and cows is about 0.9-1.7 mg [Ślebodziński 1979].

Prolactin is a very comprehensive and systemic hormone, which regulates more than 300 different biological processes in mammals [Dusza and Ciereszko 2007]. The most important function of the hormone is to initiate and maintain lactation, as well as participation in the processes of reproduction [Michalik and Bartoszewicz 2002]. Functionally, prolactin belongs to the so-called somatotropic axis, which also includes somatoliberin (GHRH), growth hormone (GH) and its receptor (GHR), prolactin receptor (PRLR), insulin-like growth factor-I (IGF-I), a transcription factor Pit-I and the transcription factor STAT5 [Parmentier *et al.* 1999].

Lactogenic hormone was first identified by Stricker and Grueter in the twenties of the last century [Stricker and Grueter 1928]. In 1933, Riddle, Bates and Dykshorn isolated protein hormone in pure form and, due to the originally described function, gave it the name commonly used today – prolactin. The standard method for the prolactin content determination, based on a measurement of the pigeon crop growth, was developed two years later by Lyons and Page [Ślebodziński 1979]. In 1937, Azimov and Krouze observed stimulation of milk production under the influence of a pituitary gland extract in cows during lactation.

Structural characteristics of prolactin polypeptide

American mink's PRL polypeptide chain is made of 199 amino acids and contains four evolutionarily conserved regions, forming a crucial domain for binding PRL to its receptor [Sotowska-Brochocka 2001]. The molecular weight of prolactin is about 23 kDa [Kooijman *et al.* 2000].

Characteristic for PRL's protein secondary structure are four α-helical segments, representing about 50% of the protein chain. The remainder of the polypeptide exists in the form of loops [Dusza and Ciereszko 2007]. Typical is also presence of three intramolecular disulfide bonds between the six cysteines' residues in position Cys^{4}-Cys^{11}, Cys^{58}-Cys^{174} and Cys^{191}-Cys^{199} [Konturek 2000, Michalik and Bartoszewicz 2002]. In the model of the tertiary structure of human prolactin, created on the basis of structural and functional homology with the growth hormone polypeptide, characteristic are four α-helical domains, two of which are oriented antiparallel with respect to the other two [Goffin *et al.* 1995]. A very important feature of the PRL is its high heterogeneity, that is a multitude of structural forms (structural polymorphism), explaining the functional diversity of the hormone [Dusza and Ciereszko 2007]. It is suggested that prolactin is a prohormone, from which various functional forms of the hormone arise [Sotowska-Brochocka 2001]. This is possible thanks to posttranslational modifications (proteolysis, dimerization and polymerization, glycolysation, phosphorylation, sulfatation, deamidation), presence of several variants of the PRL gene and the possibility of prolactin mRNA alternative splicing [Michalik and Bartoszewicz 2002]. The major forms of prolactin are as follow: base form with a mass of 23 kDa [Kooijman *et al*. 2000], small forms with mass of 14 kDa, 16 kDa and 22 kDa, resulting from proteolysis of the basic form (16 kDa form shows increased mitotic activity in mammary gland and has the ability to inhibit angiogenesis, as well as inhibit the growth of endothelial cells, having a

specific receptor for this form) [Freeman et al. 2000, Sotowska-Brochocka 2001, Fiedorowicz 2004], large forms (48 to over 100 kDa), resulting from dimerization, polymerization and aggregation of PRL particles (have low biological activity and most probably are used to storage and to modify the prolactin) [Sinha 1995], glycolysed form (GPRL), which may constitute up to 60% of the systemic prolactin and has lower biological activity and reduced affinity for PRL receptor [Haro *et al.* 1990], phosphorylated form, showing a reduced biological activity and, through an inhibitory effect on GH3 line cells proliferation, being an autocrine regulator of PRL secretion in the pituitary [Freeman et al. 2000, Sotowska-Brochocka 2001], sulfated form, that may have an impact on the binding with the PRLR [Kohli *et al.* 1988], deaminated form, showing a reduced biological activity (deamidation can also affect the binding of PRL to its receptor) [Freeman *et al.* 2000], form associated with the prolactin-binding protein (PBP), showing a high similarity to the PRLR [Cohen *et al*. 1993], form associated with antibodies directed against it, stimulating proliferation of lymphocytes (prolactin-immunoreactive form – PRL-ir) [Fiedorowicz 2004].

The versatility of prolactin is also possible thanks to existence of several isoforms of PRLR and PRL ability to activate various intracellular signalling pathways [Dusza and Ciereszko 2007].

Regulation of PRL secretion and signal transduction

Regulation of prolactin secretion is a highly complex and comprehensive process, including environmental, behavioral and hormonal factors, as well as lactotropic cells proliferation [Sotowska-Brochocka 2001]. The environmental factors include photoperiod (melatonin) and stress [Sotowska-Brochocka 2001]. Among the behavioral factors, that stimulate the secretion of PRL, the most important are nipple stimulation (suckling), scent (pheromones) and acoustic (offspring sounds) stimuli, copulation, stimuli associated with oestrus, pregnancy and birth [Dusza and Ciereszko 2007]. Mitotic and proliferative activity of lactotropic cells is affected by estrogen, galanin and TGF-α [Takahashi *et al.* 2002].

Hormonal regulation of prolactin secretion involves hypothalamic neurohormones and neurotransmitters, pituitary hormones and peripheral endocrine glands hormones [Sotowska-Brochocka 2001]. All these factors can be divided into factors inhibiting secretion of PRL (prolactostatines, called PIF – *Prolactin Inhibiting Factors*) and factors stimulating secretion of PRL (prolactoliberines, called PRF – *Prolactin Releasing Factors*). The first group include: dopamine, γ-aminobutyric acid (GABA), somatostatin, acetylcholine, calcitonin, oreksin A, neuropeptide Y, angiotensin II, bombesin, Gastrin-releasing peptide (GRP), ghrelin, atrial natriuretic peptide (ANP) [Bartke *et al*. 1998, Demaria *et al*. 2000, Russell *et al*. 2000]. The second group includes: hypothalamic prolactin releasing hormon (PRLH), thyroliberin (TRH), vasoactive intestinal peptide (VIP), hypothalamic prolactin releasing peptide (PrRP), serotonin, histamine, oxytocin and vasopressin, galanin, opioids, adrenaline and norepinephrine, aspartate and glutamate (neurotransmitters of the central nervous system), cholecystokinin [Hinuma *et al*. 1998, Freeman *et al*. 2000, Perumal and Vrontakis 2003, Krzymowski and Przała 2005, Nagy *et al*. 2005].

In addition to the above mentioned factors, with clearly defined functions of stimulating or inhibiting the secretion of PRL, there are a number of factors which modulate

the hormone secretion or affecting both stimulation as well as inhibition of this process – depending on the situation. Among them are growth factors, nitric oxide, leptin, gonadotrophin-releasing hormone (GnRH), interleukins, pituitary adenylate cyclase-activating polypeptide (PACAP-38), endothelin and neurotensin [Freeman *et al*. 2000].

Prolactin acts on the target tissues (cells) both on classical endocrine (PRL secreted into the blood reaches the specific cells and combining with membrane receptors induces them to specific effects), and also through paracrine (as a growth factor, neurotransmitter, immune-modulator) and autocrine pathway [Sotowska-Brochocka 2001]. The mechanism of action of prolactin is based on its interaction with the PRL receptor (PRLR) and, induced by this interaction, intracellular signal transduction [Watson and Burdon 1996].

PRLR belongs to the cytokine receptor of class I superfamily and bears a strong structural and functional resemblance to the growth hormone receptor (GHR) [Goffin *et al*. 1998]. PRLR is a transmembrane protein, consisting of three domains – an extracellular, ligand binding (PRL molecule), transmembrane, anchoring the receptor in the cell membrane and cytoplasmic, which is responsible for signal transduction [Michalik and Bartoszewicz 2002]. Soluble form of PRLR (PRLbp – Prolactin Binding Protein), which occurs in plasma and is similar to extracellular domain of the receptor was also described [Sotowska-Brochocka 2001]. PRL receptor is activated by dimerization induced by PRL macromolecule binding to the receptor. Prolactin polypeptide has two receptor-binding sites – the PRL-binding site 1 and PRL-binding site 2. Binding of the PRL molecule with its receptor via the PRL-binding site 1 results in formation of a hormone-receptor complex, which activates the PRL-binding site 2 [Sotowska-Brochocka 2001]. To create an active prolactin-receptor-receptor complex it is necessary to bind the other receptor macromolecule (PRLR homodimerization) by one PRL polypeptide. This complex activates tyrosine kinase JAK2 (Janus kinase 2), constitutively associated with the box1 region on both PRLR monomers. Activated JAK2 kinases phosphorylate each other, as well as cytoplasmic PRLR domaine tyrosines. Thus prepared, the receptor initiates transduction of signal into the cell, which engender a specific biological effect [Berchtold *et al*. 1998].

Signal transduction can take place through the involvement of proteins participating in signal transduction and transcription activation of STAT1, STAT3, STAT5a and STAT5b (Signal Transducer and Activator of Transcription). Phosphorylated tyrosines of PRLR allow to join the PRL-PRLR-JAK2 complex and to phosphorylate a STAT5 protein (so called MGF factor – Mammary Gland Factor), which then dissociates from the complex and undergoes dimerization with another STAT5 protein or with STAT1 and STAT2 proteins. Created dimers reach the nucleus where they bind to LHRR regions (Lactogen Hormone Response Region) of promoters of specific genes and activate them [Watson and Burdon 1996, Goffin *et al*. 1998].

PRL may also use a pathway including the mitogen-activated protein kinase (MAP). In such case, phosphorylated PRLR tyrosines enable connection Shc/Grb2/SOS adapter proteins to the PRLR-PRLPRLR complex, what in turn activates a Ras/Raf/MAP cascade. MAP kinase is responsible for the activation of many transcription factors and enzymes [Buckley *et al.* 1994].

It is assumed that via kinase c-src and Fyn may occur to the phosphorylation of insulin receptor IRS-1 (Insulin Receptor Substrate-1) substrate macromolecules' tyrosines

and phosphatidylinositol kinase [Berlanga *et al*. 1997]. PRL signal transduction is sometimes associated with changes in intracellular concentrations of potassium and calcium ions, taking place through a JAK2 kinase-dependent potassium channels and phosphatidylinositol 3-kinase (PI3K)-dependent calcium channels [Ducret *et al*. 2004].

In regulation of the PRL signal transduction are also involved factors inhibiting hormone signal, such as suppressors of cytokine signalling proteis (SOCS), CIS cytokines and tyrosine phosphatase SHP [Pezet *et al*. 1999].

Prolactin functions

As already mentioned, the PRL is one of the most versatile hormones, responsible for varied biological functions. This explains why one of the suggested names for prolactin was omnipotin or versatilin [Bern and Nicoll 1968]. Despite the great diversity of biological processes, which are determined or regulated by prolactin, they can be divided in mammals into two groups – functions related to the maintenance of homeostasis and functions associated with reproductive processes [Freeman *et al*. 2000].

Functions related to maintenance of the homeostasis include:

– osmoregulation (osmotropic activity), that is regulation of fluid and electrolyte balance by reducing excretion of sodium and chloride through sweat glands, increase water and electrolyte absorption in the intestine, stimulation of the sodium-potassium pump and decrease in sodium and potassium excretion in the kidneys, increasing the level of uric acid in the blood, regulation of the osmotic pres-sure of amniotic fluid (PRL concentration in the amniotic fluid is approximately 100 times greater than in the blood), adjustment of the secretory function of the sebaceous glands, intensification of IGF-1 synthesis [Bole-Feysot *et al*. 1998, Sotowska-Brochocka 2001];

– regulation of growth and development processes (somatotropic activity), by stimulating body growth, induction of cell proliferation (melanocytes, hepatocytes, keratinocytes, renal tubular epithelium, intestinal epithelium, vascular myocytes, astrocytes, β cells of Langerhans islands, lymphocytes), regulation of angiogenesis, mitogenic effect [Bole-Feysot *et al*. 1998, Sotowska-Brochocka 2001]; in mink prolactin also plays a role in hair growth, their density, development of hair follicles and moulting [Vardy and Farid 2002, Rose *et al*. 2006);

– effects on metabolism (metabotropic activity), including the intensification of appetite, effects on enzymes and hormones responsible for metabolism of glycogen (glycogen phosphorylase), glucose (insulin, glucokinase, glucose transporter GLUT2), lipids (lipoprotein lipase, bile), steroids (glucocorticoids, aldosterone, adrenal androgens), vitamin D (1-α-hydroxylase), calcium and iodine, ratcheting prostaglandin and surfactant synthesis, control of ATPase activity [Dave *et al*. 1982, Sotowska-Brochocka 2001];

– impact on behavior, connected with stress response (increased secretion of PRL), decreasing pain perception, influence of psychosomatic reactions (imaginary pregnancy), decreased libido, adjustment of the rhythm of sleep and wakefulness, conditioning the proper development of the neuroendocrine system, dopamine metabolism, physical exertion [Bole-Feysot *et al*. 1998, Sotowska-Brochocka 2001];

– immunomodulation associated with activation of the proliferation of T and B lymphocytes, stimulation of IgG and IgM antibodies and cytokines production, inhibition of apoptosis of lymphocytes, macrophages activation, potentiation of cytotoxicity of NK cells and stimulation of bactericidal peroxide anions [Cesano *et al*. 1994, Sotowska-

Brochocka 2001]; PRL is also associated with the pathogenesis of autoimmune diseases, and certain cancers [Bole-Feysot *et al*. 1998].

Reproductive functions of prolactin include its impact on the mammary gland, effect on the ovary and the uterus, impact on the physiology of pregnancy, as well as on testes, accessory sex glands and the impact on behavior related to reproduction and parenthood [Ciereszko 2001, Dusza and Ciereszko 2007]. It is estimated that the impact on reproductive processes represents nearly 40% of all prolactin's biological functions [Sotowska-Brochocka 2001].

One of the most important and earliest known functions of prolactin is its impact on motheroffsprings feeding in mammals, namely its mammo- and lactotropic impact [Woliński 1964]. PRL affects mammogenesis – preparation of the mammary gland for secretory function, which is done by its growth and differentiation regulation, effects on blood flow, as well as involution of mammary gland [Dusza and Ciereszko 2007]. Prolactin also determines lactogenesis (production and secretion of milk) and lactopoesis (sustaining lactation) in mink [Tauson 1997]. Lactogenic hormone affects the milk producing cells in the synthesis of basic milk ingredients – β-casein, α-lactalbumin, β-lactalbumin (ratcheting uptake of amino acids), lactose (glandular stimulation of glucose uptake) and fat (stimulation of lipoprotein lipase, pyruvate dehydrogenase, carboxylase acetyl coenzyme A, fatty acid synthase), and also affects the transport of water and electrolytes into the mammary gland. At the genetic level PRL influence milk proteins' genes transcription, stabilizes their mRNA and affects translation and post-translational modifications [Bole-Feysot *et al*. 1998, Freeman *et al.* 2000, Sotowska-Brochocka 2001].

In the ovary of the American mink PRL acts on the oocyte (stimulation of maturation), follicle and corpus luteum [Rose *et al*. 1986]. PRL has luteotropic effects in mink. It affects the differentiation of the secondary bubble, initiating luteinisation of granulosa cells, which increase the production of progesterone [Douglas *et al*. 1998]. Simultaneously, the PRL has an inhibitory effect on estrogen production [Ciereszko 2001]. Furthermore, prolactin enables to maintain the pregnancy until the acquisition by the fetus sustain of gestational corpus luteum functions [Bazer and First 1983].

Very important is the role of PRL in the physiology of pregnancy in mink. This hormone determines completion of diapause and implantation of the blastocyst, what is important for the rearing and breeding of the American mink [Desmarais *et al.* 2004].

Prolactin influences also the uterus. The hormone increases the secretory activity of endometrium, reduces the contractile activity of myometrium, participates in blastocyst implantation, increases the amount of estrogen and progesterone receptors, enhances the effects induced by progesterone (P4) and reduces its metabolism, as well as conditions the blood supply to the pregnant uterus [Bole-Feysot *et al*. 1998, Ciereszko 2001]. In mustelids, increase in the number of PRL receptors in the uterus under the influence of steroid hormones secreted by the ovary was observed [Rose *et al*. 1993].

In the American mink males PRL increases activity of the testes and stimulates spermatogenesis [Freeman *et al*. 2000]. PRL induces an increase the number of luteinizing hormone (LH) receptors and increases the aromatase activity. It also influences the secretion and release of testosterone by Leydig cells [Gancarczyk *et al*. 2006]. It was found that inhibition of PRL releasing from the pituitary, induced by short photoperiod, leads to inhibition of steroidogenesis in the testes [Bartke *et al*. 1998]. Studies show the

PRL effect on cholesterol metabolism in the mink testes [Kabbj *et al*. 2003]. Prolactin also affects the proper functioning of the prostate [Costello and Franklin 1996].

Significant, although still poorly understood, is the positive effect of prolactin on behaviour related to reproduction, especially of parenting in mammals, both in females and males [Bole-Feysot *et al*. 1998, Storey *et al*. 2006].

Prolactin levels increase during oestrus, ovulation, pregnancy and lactation, and also under the influence of copulation, after physical exertion, as a result of stress response or after a large protein meal [Sotowska-Brochocka 2001]. PRL secretion in the American mink is also correlated with the length of the day – short days are accompanied by low hormone levels, while high PRL level is observed during the spring and summer [Martinet *et al*. 1992, Persson 2007]. Ultrastructural changes in lactotropic cells are associated with this correlation [Vidal *et al.* 1997].

Common endocrine disorder associated with prolactin is hyperprolactinemia (excessive secretion of PRL), caused by adenoma of pituitary gland (prolactinoma). Characteristic symptoms of this disease are galactorrhea (of females and males), reproductive disorders (non-fertility, decreased libido and abnormal estrus in females, impotence in males), hypogonadism and a decrease in bone density [Konturek 2000].

Prolactin gene

Prolactin gene in mammals occurs only in one copy, in contrast to the growth hormone gene [Miller and Eberhardt 1983]. In most mammals, this gene is located on chromosome 6 [Sotowska-Brochocka 2001], whereas in the American mink is located on the long arm of chromosome 13 [Kuznetsov *et al*. 2003].

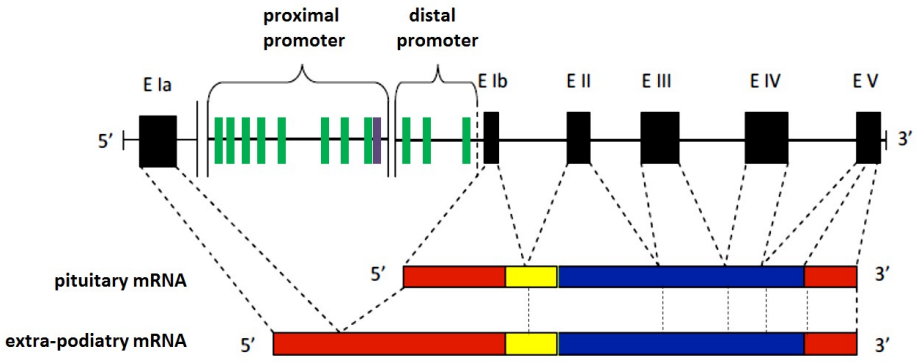

Fig. 1. Structure of human *PRL* gene: exons – marked in black, Pit-1 – marked in green, place for ecdysteroid receptor – mark in violet, signal peptide – marked in yellow, UTR – marked in orange (based on Sotowska-Brochocka 2001, Michalik and Bartoszewicz 2002)

Rys. 1. Struktura genu ludzkiej PRL: egzony – kolor czarny, miejsce Pit-1 – kolor zielony, miejsce receptora ekdysteroidowego – kolor fioletowy, peptyd sygnałowy – kolor żółty, UTR – kolor pomarańczowy (na podstawie Sotowska-Brochocka 2001, Michalik i Bartoszewicz 2002)

PRL gene in mink (GenBank: AY249860.1) has a size of 9.9 kbp and consists of five exons (E I (Ib) – 28 bp, E II – 182 bp, E III – 108 bp, E IV – 180 bp, E V – 192 bp), representing 7% of the size of the gene, and four large introns (I I – 2291 bp, I II – 1940 bp, I III – 2407 bp, I IV – 2467 bp), conditioning its large size (Fig. 1) [Vardy and Farid 2003].

cDNA of mink PRL consists of 690 nucleotides encoding the prolactin prohormone (preprolactin) built of 229 amino acids. 30 amino acids present at the N-terminus of the preprolactin macromolecule forms a signal sequence [Bondar *et al*. 1993, Vardy and Farid 2003]. Fifth exon encodes a "stop" codon and a series of nucleotides of a polyadenylation signal (AATAAA). In some tissues the presence of additional, not translated exon VI is concluded [Sotowska-Brochocka 2001].

Two promoters regulate *PRL* gene transcription – proximal (pituitary) and distal (extra-pituitary) – are located in the area of 2-2.5 kbp above the 5' region of the coding sequence [Berwaer *et al.* 1994]. In addition, there may be additional exon Ia, from which transcription of preprolactin beyond pituitary begins (Fig. 1) [Fiedorowicz 2004]. PRL gene promoter is regulated primarily by the transcription factor Pit-I [Ben-Jonathan *et al*. 1996].

Gene for prolactin, growth hormone (*GH*) and placental lactogen (*LH*) demonstrate high structural-functional similarity and belong to one genes family [Goffin *et al*. 1995]. Numerous data indicate that these three genes evolved from one common gene, whose age is determined at 400 million years [Miller and Eberhardt 1983]. Generation of three independently regulated genes was possible mainly due to duplications, deletions and insertions that occurred in the course of its evolution [Owerbach *et al*. 1981]. It is worth noting that while the nucleotide sequence of the *PRL* gene has a relatively strong resemblance to the *GH* gene, protein products of these genes show homology of only 16% [Krzymowski and Przała 2005]. In addition to the *GH*, *PRL* and *LH* genes, to the family of *GH/PRL* genes belongs also at least 9 other genes that encode prolactin-like hormones [Lin *et al.* 1997].

Within the mink prolactin gene several single nucleotide polymorphisms (SNP) were found (4261 G/A within intron II, 5978 T/C and 6952 C/G within the intron III), and repetitive sequence polymorphism (within intron II – (GT)15/Mvi550 microsatellite area and (TTC)5(T)47; in intron IV – (CA)7(GA)14/Mvi551 microsatellite area) [Bondar *et al*. 1993, Vardy and Farid, 2002, Vardy and Farid 2003].

Possibility of practical use of *PRL* gene polymorphism

Better understanding of the correlation between the known variability of the *PRL* and occurrence of specific quantitative traits, may result to identify this gene as a gene of major effect (*Major Gene*) [Ghasemi *et al.* 2009]. Genes of large effect affect the value of quantitative traits in a significant way, while their phenotypic effect (polymorphism) is possible to identify [Montaldo and Meza-Herrera 1998].

Major Genes concern many traits categorized as productively relevant. In the case of *PRL* and American mink farming it is mainly the effect of hormone on fertility, often regarded as a decisive factor for the economic results of mink production [Skorupski and Kmieć 2012]. A key aspect in the rearing of young by the mother is the quantity and quality of produced milk [Barabasz 1984]. In Polish conditions agalactia (inhibition of lactation) is quite often stated, what results in relatively low survival rate of offspring (Krzywoszyński 1983, Bielański *et al.* 2003].

In future studies on the *PRL* gene polymorphism, it seems desirable to pay particular attention to the relationship of high level of lactation yield of females with features conditioning their vigor and vitality during offspring feeding. It is important because of the particularly heavy burden on the female body during this period, observed in carnivorous fur-bearing animals [Barabasz 1984]. The most telling is the fact that during the peak lactation N. vison females produce nearly 100 grams of milk per day, which represents approximately 10% of their body weight [Barabasz 1984].

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Streszczenie. Prolaktyna należy do grupy hormonów wykazujących najbardziej wszechstronną, ogólnoustrojową aktywność biologiczną. Funkcje PRL podzielić można na związane z utrzymaniem homeostazy organizmu (działanie osmotropowe, somatotropowe, metabotropowe, wpływ na behawior, immunomodulacja) oraz związane z rozrodem (wpływ na gruczoł mlekowy, oddziaływanie na jajnik i macicę, wpływ na fizjologię ciąży, działanie na jądra i dodatkowe gruczoły płciowe, wpływ na zachowania związane z rozrodem i rodzicielstwem). Gen prolaktyny występuje u norki amerykańskiej w jednej kopii i zlokalizowany jest w chromosomie 13. Ze względu na mnogość funkcji pełnionych przez prolaktynę gen *PRL* rozpatrywany jest jako gen warunkujący cechy ilościowe. Szczególnie istotne wydaje się poszukiwanie związku wysokiej mleczności samic norki amerykańskiej z cechami warunkującymi ich wigor i kondycję w okresie karmienia młodych, ze względu na szczególnie duże obciążenie w tym okresie organizmu samicy, obserwowane u mięsożernych zwierząt futerkowych.

Słowa kluczowe: prolaktyna, gen prolaktyny, struktura białka, charakterystyka funkcjonalna, struktura genu, sekrecja, transdukcja sygnału, *Neovison vison*