# Review

# Prolactin (*PRL*) and Prolactin Receptor (*PRLR*) Genes and their Role in Poultry Production Traits

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Prolactin (PRL), secreted from the anterior pituitary, plays extensive roles in osmoregulation, corpus luteum formation, mammogenesis, lactogenesis, lactopoiesis, and production of crop milk. In birds, prolactin (PRL) is generally accepted as crucial to the onset and maintenance of broodiness. All the actions of prolactin (PRL) hormone are mediated by its receptor (PRLR), which plays an important role in the PRL signal transduction cascade. It has been well established that the *PRL* gene is closely associated to the onset and maintenance of broody behavior, and could be a genetic marker in breeding against broodiness in chickens. Meanwhile, the prolactin receptor (*PRLR*) gene is regarded as a candidate genetic marker for reproductive traits. *PRLR* is also an important regulator gene for cell growth and differentiation. The identified polymorphism of this gene is mainly viewed in terms of egg production traits. Due to different biological activities attributed to *PRL* and *PRLR*, they can be used as major candidate genes in molecular animal breeding programs. Characterization of *PRL* and *PRLR* genes helps to elucidate their roles in birds and provides insights into the regulatory mechanisms of *PRL* and *PRLR* expression conserved in birds and mammals.

Key words: *PRL* and *PRLR* genes, polymorphism, prolactin, prolactin receptor, poultry, productive traits, polymorphism.

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An important purpose of modern breeding in the poultry industry is to create high-performance poultry lines and breeds in two main directions of productivity - meat and eggs (KULIBABA & POD-STRESHNYI 2012). The productive value of animals is determined by their ability to meet certain production demands, measured by the quality and quantity of the product obtained during a given period. The production potential of domestic fowl is controlled by several parameters, including those related to their reproductive potential. Production of table and hatching eggs is crucial for poultry producers. The process in which egg number and egg components are formed, the rate of lay, egg fertility and hatchability are dependent on a multitude of synchronized metabolic and physiological processes. These traits are known to be significantly affected by many factors, especially environmental factors (BRAH & SANDHU 1989; WEIS

1991; MAHMOUD et al. 1996). However, the results of experiments conducted to date confirm that both production and reproductive parameters are also dependent on genetic factors (KING'ORI 2011; MIAZI et al. 2012). Among the genes that have significant effects on egg production are the prolactin (PRL) gene and the prolactin receptor (PRLR) gene (REDDY et al. 2002; WANG et al. 2011). Consistent research on these genes, which are involved in many physiological pathways, contributes to understanding the molecular basis of useful production traits. The use of these molecular genetic markers potentially will greatly increase the intensity of selection and will most effectively uncover the productive potential of birds. Additionally, studies of candidate genes and their effect on the phenotypic manifestations of interest to researchers are the basis for market-associated selection (MAS) (KULIBABA & POD- STRESHNYI 2012).

## PRL gene and prolactin

Mammals have a single prolactin-encoding gene (PRL), which is found on chromosome 6 in humans (GOFFIN et al. 1996), on chromosome 13 in mice (WIEMERS et al. 2003), on chromosome 7 in pigs (VINCENT et al. 1998) and on chromosome 2 in birds (ALIPANAH et al. 2011; MIAO et al. 1999). So far, the *PRL* gene has been cloned in a variety of avian species, examples among the latter include the domestic chicken, turkey, quail, duck, and pigeon (LIU et al. 2008). The avian PRL gene consists of five exons and four introns (LI et al. 2009; YOUSEFI et al. 2012). This gene contains two regulatory regions, the proximal and distal enhancers (CAO et al. 1987; LUFKIN & BANCROFT 1987). In studies with rats, in vitro transcription analysis showed that the distal segment of the prolactin gene is responsible for 99% of transcriptional activity (NELSON et al. 1986; CAO et al. 1987).

Since the avian *PRL* gene was cloned and sequenced, most of the research has concentrated on identifying new polymorphic sites in this gene. Mutations in the prolactin gene sequence were found in both introns and exons (Table 1). The results of experiments on chickens showed a significant association between single nucleotide polymorphisms (SNPs) in exon 2 and body weight at hatch, age at sexual maturity, and between SNPs in exon 5 and egg number (RASHIDI *et al.* 2012). Most *PRL* gene polymorphisms were found in the 5'-flanking region, 3'-flanking region, and coding region of the signal peptide (LI *et al.* 2009). In the first maintained region of the prolactin gene, SNPs in different positions (e. g. C-2402T, C-2161G, T-2101G, C-2062G) were detected. WANG et al. (2011) demonstrated that the C-5961T polymorphism (exon 5) was significantly related with egg production and egg weight in ducks. The results of another experiment using geese suggest that egg productivity of breeds may be associated with G-10T locus (5'-untranslated region) of the prolactin gene (CHEN et al. 2011). In the works of various authors, it was found that the presence of a 24-bp insertion in the promoter region of the avian prolactin gene is positively correlated with the intensity of egg-laying activity in birds and broody behavior (KULIBABA & PODSTRESHNYI 2012; JING et al. 2009). The results of JIANG et al. (2005) have shown that *PRL* could be a genetic marker in breeding against broodiness in chickens.

Furthermore, the 5'-flanking region of the avian prolactin gene has been considered as an excellent experimental model for studying both tissue-specific and hormonally regulated activation of gene transcription. Differences were found in the length of 5' promoter between mammals and birds. Compared to the extensive research on the promoter region of the mammalian *PRL* gene, information on the 5' promoter of chicken *PRL* gene is rather limited (LIANG *et al.* 2006). Sequence variation in the 5'-flanking region of the prolactin gene may result in changes in transcription factor binding sites and contribute to the release of the hormone prolactin (RASHIDI *et al.* 2012).

It has been documented that *PRL* gene transcription is activated by the pituitary-specific transcription factor 1 (PIT-1) (OHKUBO *et al.* 2000), which

Table 1

Gene	Species	Polymorphism localiza- tion	Associated with trait	References	
PRL (chr. 2) (ALIPINAH et al. 2011, MIAO et. al.1999)	Chicken	In/Del at the site 358 of gene	Egg production	(CUI et al. 2006)	
		Promoter region	Broodiness	(JIANG <i>et al.</i> 2005)	
		Exon 2	Body weight at hatch, age at sexual maturity	(RASHIDI <i>et al.</i> 2012)	
	Goose	5' untranslated region	Egg productivity	(CHEN et al. 2011)	
		5' flanking region	Egg production	(JIANG <i>et al.</i> 2009)	
	Duck	Intron 1	Shell strength	(WANG <i>et al.</i> 2011)	
		Exon 5	Egg production, egg weight		
		Intron 1	Egg weight	(LI et al. 2009)	
<i>PRLR</i> (chr. Z) (DUNN 1998, SUZUKI <i>et al</i> .1999)	Chicken	Exon 6	Egg production, age of first egg	(LIU et al. 2012)	
		Exon 2	Body weight at hatch, age at sexual maturity	. (RASHIDI <i>et al</i> . 2012)	
		Exon 5	Egg number		
	Goose	Exon 10	Egg number	(CHEN et al. 2012)	

Examples of traits whose variation depends largely on the polymorphism identified

also binds and transactivates growth hormone (*GH*) gene promoters and thyroid stimulating hormone beta ( $\beta$ ) (NIE *et al.* 2008). Experiments with birds and mammals provide evidence that PIT-1, CCAAT-enhancer binding protein, estrogen receptors and other proteins are crucial to the regulation of *PRL* gene expression (RASHIDI *et al.* 2012). However, the molecular mechanisms of the PIT-1 protein on *PRL* gene activation are not completely understood (OHKUBO *et al.* 2000).

Studies on chickens demonstrated that the prolactin gene is expressed in the hypothalamus, pituitary, oviduct and ovary. The highest expression was observed in the pituitary gland (LI *et al.* 2009). Similarly, a study on geese (CHU *et al.* 2008) indicated that the highest levels of *PRL* were found in the pituitary gland, followed by the hypothalamus, and the least in the ovary. Moreover, the results of research conducted by ISHIDA *et al.* (1991) showed that a progressive expression of this gene in the pituitary gland occurs 1-2 days before hatching and concomitant increases in plasma concentrations of PRL may be associated with physiological changes in pulmonary respiration and hatching.

The expressed product of the *PRL* gene is the hormone prolactin. It is composed of 199 amino acids (LIU et al. 2008) with three disulfide bridges between six cysteines, and has a molecular weight of 23kDa (KANSAKU et al. 2008). The cDNA sequence and amino acid composition of the PRL hormone are highly homologous between different poultry species (Table 2) (KANSAKU et al. 2008). This hormone is mainly synthesized in the anterior pituitary (CUI et al. 2006; JIANG et al. 2009; WANG et al. 2009) by lactotroph cells. These cells are not the only ones to produce prolactin, because certain amounts of this hormone were also found in the thymus, spleen, lymphocytes and epithelial cells (BOLE-FEYSOT et al. 1998). Across species, prolactin secretion increases during sleep, exercise, orgasm, stimulation of nipple, pregnancy and brood (ERDOST 2005). In chickens and turkey, plasma PRL levels are generally high for the first 2 or 3 weeks after hatching, decline during the juvenile period, increase with the onset of sexual maturity, and then decline in adulthood (LIANG *et al.* 2006).

In addition, it has been observed that PRL is expressed throughout the retina, where it is proteolytically cleaved to vasoinhibins, which are emerging as natural inhibitors of the angiogenesis process. Vasoinhibins act *in vivo* and *in vitro* to block the stimulatory activity of various inducers of angiogenesis on endothelial cell proliferation, migration, and permeability, and reduce endothelial cell survival. Moreover, these inhibitors act directly on endothelial cells by blocking blood vessel growth, dilation, and by promoting apoptosis-mediated vascular regression (CLAPP *et al.* 2008).

Prolactin secretion in birds is predominantly regulated by releasing factors of which the best characterized are vasoactive intestinal peptide (VIP), dopamine (DA) and serotonine (5-HT) (KAGYA-AGYEMANG et al. 2012). Prolactin (PRL) secretion in avian species is under tonic stimulatory control exerted by the hypothalamus (DAVID et al. 2003; AL KAHTANE et al. 2005). In birds, the hypothalamus actively secretes one or more prolactin releasing factors (PRF) and the presence of a prolactin inhibiting factor (PIF) has been described (SILVER & SALDANHA 1993). The hypothalamus secretes vasoactive intestinal peptide (VIP), which has an important neuroendocrine influence on PRL secretion in birds (KUENZEL 2003). Cell bodies containing VIP are abundant in the basal hypothalamus and have terminals in the median eminence (SHARP et al. 2005). Several lines of evidence indicate that VIP is the PRLreleasing factor (PRF) in birds (OPEL & PROUDMAN 1988). In addition, VIP stimulates prolactin release and expression in vivo and in vitro in several avian species (AL KAHTANE et al. 2005). The results of research conducted by

#### Table 2

Amino acid similarity (%) and cDNA sequence homology of mature avian PRLs (LIU *et al.* 2008)

	Chicken	Goose	Duck	Turkey
Chicken	_	93.0	94.0	91.0
Goose	92.0	_	98.5	92.0
Duck	91.6	98.4	-	92.0
Turkey	94.9	92.2	91.7	_

Values above the diagonal line represent homology of amino acid similarity and values under the diagonal line represent homology of cDNA sequence.

AL KAHTANE *et al.* (2003) show that VIP treatment increased PRL release into the medium about 20- to 30-fold in comparison with that of untreated pituitary cells. Moreover, VIP increases PRL secretion from pituitary glands, especially when the pituitary gland responsiveness is enhanced with estrogen pre-treatment (SHARP *et al.* 2005). Apart from PRL-releasing ability, VIP stimulates PRL gene expression in avian species. Administration of VIP into chickens and turkey increased pituitary PRL mRNA *in vivo*.

Vasoactive intestinal peptide (VIP), a 28-amino acid peptide involved in the regulation of the secretion of prolactin, is not the main regulator of PRL release. Prolactin is under tonic inhibitory dopaminergic control exerted by the hypothalamus as well (TONG et al. 1998). Prolactin secretion is inhibited by dopamine, which is secreted by TIDA (Tuberoinfundibular Dopamine Neurons) neurons located in the hypothalamus (CHANG & SHIN 1999; FREEMAN et al. 2000). Dopamine (DA) plays a role in the control of prolactin secretion by blocking the action of VIP at the level of the anterior pituitary. Dopamine (DA) affected this blockade of PRL via D<sub>2</sub> DA receptors residing within the anterior pituitary (YOUNGREN et al. 1998; SCHNELL et al. 1999). Hens treated with dopamine receptor antagonist or receptor blocking agent resulted in terminated maintenance of broodiness by inhibiting secretion of PRL (XU et al. 2010). It has been reported that in avian species DA inhibits VIP-stimulated PRL mRNA at the transcriptional and post-transcriptional (PRL mRNA half-life) levels via pituitary D<sub>2</sub> DA receptors (AL KAHTANE et al. 2003).

Among neurotransmitters that stimulate PRL release in avian species is serotonine (5-hydroxytryptamine; 5-HT) (HALL et al. 1986; YOUNGREN et al. 1998). However, 5-HT does not act directly on the pituitary to cause PRL secretion. Serotonin (5-HT) facilitates the release of pituitary PRL in birds when they are treated with methysergide (PITTS et al. 1996; KAGYA-AGYEMANG et al. 2012), which can act as an antagonist at the 5- $HT_{2B}$ and 5-HT<sub>2C</sub> receptors and as a partial agonist at the 5-HT<sub>1A</sub> receptor. Moreover, serotonergic stimulation of prolactin secretion is mediated by the singular avian PRL-releasing factor, vasoactive intestinal peptide. In an experiment conducted by EL HALAWANI et al. (1995) it was confirmed that 5-HT stimulates PRL secretion in turkey via VIPergic pathways. However, other research suggests that 5-HT does not act directly upon VIP neurons, but instead uses the dopaminergic system (YOUNGREN et al. 1998).

Other factors influencing prolactin secretion include environmental ones, such as various stressors, light, and acoustic stimuli (e.g. sounds made by the offspring) (DUSZA & CIERESZKO 2007). Studies have demonstrated that stressors, in a number of forms and in a number of species, influenced circulating prolactin. In mammals, plasma prolactin levels increase rapidly during acute exposure to stressors, while in birds, prolactin levels often decrease in response to short-term stressors (ANGELIER & CHASTEL 2009). It has been observed that the diminished reproductive performance in heat-stressed poultry may, in part, be related to increased PRL secretion (ROZENBOIM et al. 2007). Another important environmental factor that stimulates PRL release in avian species is light. It has been reported that the serum prolactin level increases as a consequence of experimental photostimulation on Peking ducks, pigeons and quail (ERDOST 2005). Moreover, in an experiment by SREEKUMAR & SHARP (1998), it was observed that the photo-induced pattern of prolactin secretion in birds can be dissociated from the neuroendocrine mechanisms controlling the termination of seasonal breeding.

Prolactin (PRL) has a wide range of activities in animals. Over 300 different functions of this hormone have been documented and classified. PRL has important effects on reproductive processes and parental care in teleost fishes, birds, and mammals (WANG et al. 2009). In reptiles, amphibians and teleosts, PRL acts as an osmoregulator (ERDOST 2005; LI et al. 2009). In fish, prolactin has been observed to affect the function of different organs (gills, intestine, kidney, urinary bladder, skin), thus making it easier to adapt to aquatic life (TURNER & BAGNARA 1978). In mammals, PRL stimulates formation of the corpus luteum and its transformation into the corpus luteum graviditatis and plays a significant role in mammogenesis, lactogenesis, and lactopoiesis. In addition, it stimulates the production of progesterone, a hormone responsible mainly for the maintenance of pregnancy (FREEMAN et al. 2000).

Prolactin positively acts on hormonal and cellular immunity. Prolactin hormone has been considered as a cytokine able to modulate immune response in mammals. Furthermore, particular effects of this hormone on inflammatory response have been documented in autoimmune diseases (LÓPEZ-MEZA *et al.* 2010). The results of the experiment conducted by KANG *et al.* (2007) have shown that PRL might play an important role during the development of the immune system in chickens as well. The same study suggests that prolactin may be involved in the movement of B-cell precursors in and out of the bursa and in Band T-cell proliferation and maturation.

In birds, PRL inhibits the growth and development of ovarian follicles (CHEN *et al.* 2011). It acts synergistically with estrogen during brood patch formation. These patches of featherless skin appear on the underside of one or both sexes in many orders of bird species during brooding. It was shown that after hypophysectomy estrogen only causes vascularization of these areas, while prolactin is needed to induce edema and feather loss and does not work until the discussed area is vascularized under the influence of estrogen (BELSARE 1965).

An increase in circulating PRL concentration has been suggested to cause ovarian regression (PORTER et al. 1991; EDENS 2011). Prolactin is also believed to be responsible for complete regression of the comb, which coincides with the onset of brooding, and for decreased concentrations of LH and ovarian steroids (RZASA 2007). It has been established that persistent elevation of blood PRL concentration contributes to a decrease in hypothalamic GnRH levels, suppression of LH secretion and expression of steroidogenic enzymes (RZĄSA 2007). Additionally, prolactin has been found to be involved in the regulation of waterelectrolyte metabolism (WATAHIKI et al. 1989) and energy metabolism (TURNER & BAGNARA 1976). It influences the formation of spermatozoa (MAO et al. 1999) and stimulates the growth of testes (ERDOST 2005). The physiological processes involving prolactin take a normal course only when factors affecting its secretion interact with one another and their interaction is not disturbed. Through an endocrine pathway, prolactin reaches many receptors located in the cell membrane of various organs and exerts a specific effect by coupling with them (GOFFIN et al. 1996; FREEMAN et al. 2000). Prolactin stimulates production of crop milk in columbiform birds (SILVER 1984), has an effect on the nesting instinct, and initiates broodiness (ERDOST 2005; JIANG et al. 2011).

The main functions of the endocrine system that lead to the development of broodiness are a result of increased concentration of plasma PRL (KAGYA-AGYEMANG et al. 2012). Elevated plasma prolactin inhibits gonadotropin release from the anterior pituitary causing inhibition of ovum development and ovulation leading to ovarian regression in birds (JIANG et al. 2011). Numerous reports have confirmed the relationship between plasma prolactin in the physiological range and laying performance in domestic hens (REDDY et al. 2002; ELTAYEB et al. 2010). Additionally, broodiness in domestic fowl is associated with stereotypical behaviors such as frequent nest occupancy, reduced feeding and water intake, aggressiveness or defensive behaviors, characteristic clucking and raised body temperature that can be related to elevated plasma prolactin (LIU et al. 2012). It is an important fact that increasing levels of prolactin related with complete cessation of egg production lead to significant economic losses in the poultry industry (KULIBABA & PODSTRESHNYI 2012). Blood prolactin concentration rapidly increases directly before the onset of brooding and continues to grow, after which it rapidly declines prior to hatching of chicks (RZASA 2007). It has been reported that blood levels of PRL increase 6-10 fold at the onset of reproductive behavior (REDDY *et al.* 2007). A study conducted by JIANG *et al.* (2011) demonstrated that the plasma concentration level of PRL reached its peak only at the onset of broodiness and rapidly decreased in the following 2 or 3 weeks to a normal level as in the laying period and remained unaltered until the end of broodiness.

#### PRLR gene and prolactin receptor

The pituitary hormone of PRL is a ligand of PRLR (RASHIDI et al. 2012). In hens, the prolactin receptor gene is located on the Z sex chromosome (CHENG et al. 1995; DUNN et al. 1998; SUZUKI et al. 1999), consists of 15 exons and 14 introns (RASHIDI et al. 2012), and is closely associated with production traits (CHEN et al. 2012). In humans PRLR is located on chromosome 5 (DUNN et al. 1998), on chromosome 15 in mice (BARKER et al. 1992; DUNN et al. 1998) and was mapped to chromosome 16 in pigs (VINCENT et al. 1998). The *PRLR* gene is expressed in many tissues, for example in testes, ovaries, deferent ducts, oviduct, kidneys and small and large intestine (XING et al. 2011) and also in the hypothalamus (OHKUBO et al. 2000). An experiment conducted by KANG et al. (2007), aimed at determining the expression of the PRLR gene and was quantified in lymphoid tissues from chickens at different embryonic stages and after hatching, showed that the *PRLR* gene is expressed in the bursa follicles, thymus lobules, and splenic pulp at all examined stages. Levels of PRLR expression were consistently higher in the bursa of Fabricius compared with other lymphoid organs. It has been noted that PRLR mRNA levels in avian primary lymphoid organs (bursa of Fabricius and thymus) were extremely high when compared with spleens.

The prolactin receptor is an important regulator gene in the process of cell growth and differentiation. It is regarded as a candidate genetic marker for reproductive traits. It is also speculated that the *PRLR* gene may be the major gene responsible for the attainment of sexual maturity (LIU *et al.* 2012). Research conducted to date has shown that polymorphisms occur in different locations of the *PRLR* gene (Table 1). For example, in an experiment by JIANG *et al.* (2005) conducted with chickens, one SNP in the exon 3(A9026G) and 2 SNPs in the exon 6 (T14771C and G14820A) of *PRLR*  were identified. In another study, polymorphisms were detected in exon 5 (RASHIDI *et al.* 2012), and exon 10 (CHEN *et al.* 2012). The identified polymorphisms in the *PRLR* gene are mainly associated with egg production traits. A study by LING-BIN *et al.* (2012), conducted on chickens, demonstrated that the G1836C polymorphism (exon 6) was significantly related with age at first egg. The results of this research showed that the *PRLR* gene may be either a major gene that influences age at first egg of chickens or a molecular marker in close linkage with such a gene.

The expressed product of the PRLR gene is a receptor protein- a single transmembrane protein belonging to class I of the cytokine receptor superfamily, which includes growth hormone receptor (GHR), interleukins, granulocyte colonystimulating factor, granulocyte macrophage colony-stimulating factor, oncostatin M, erythropoietin, thrombopoietin, gp130, ciliary neurotrophic factor, leukemia inhibiting factor (LIF) and leptin receptor (LEPR) (XING et al. 2011). Four PRLR forms have been identified to date, three of which are membrane isoforms (short, intermediate and long) and the fourth has a soluble form and contains the extracellular domain only (CLEVENGER et al. 2001). These membrane isoforms are composed of a ligand-binding extracellular domain, an intracellular catalytic domain, and a transmembrane domain. The long PRLR form is the most prevalent (DUSZA & CIERESZKO 2007). The expression of different prolactin receptor forms is dependent on female reproductive status and cell type. The different isoforms differ in the amount and amino acid composition of the receptor's cytoplasmic portion (BOLE-FEYSOT et al. 1998; MAO et al. 1999).

Avian PRLRs are extremely long (831 amino acids) compared to mammalian PRLRs (591 amino acids) (MAO et al. 1999). PRLR has been detected in most tissues and organs (CHEN et al. 2012); mainly in the brain, oviduct and ovaries (FREEMAN et al. 2000). In some mammals, the presence of PRLR was also shown in the thymus and spleen (KANG et al. 2007). Depending on the type of tissue, reproductive period, and stage of reproductive system development, different PRLR isoforms may activate various target cellsignalling pathways. The prolactin receptor has an important role in the prolactin signal transduction cascade (LING-BIN et al. 2012). Prolactin interacts with the extracellular domain of prolactin receptor which activates a cascade of intracellular events, primarily JAK-STAT signal transduction pathway, via specific sites of the PRLR cytoplasmic tail (JIANG et al. 2005). The JAK/STAT (mainly JAK2/STAT5) is the major cascade triggered by the PRLR, but many other proteins are also activated such as the MAP (Mitogen activated protein) kinase pathway (GOFFIN & KELLY 2001). An experiment conducted by GHOSH (2011) showed that MAP kinases play an important role in the regulation of proinflammatory cytokines in response to avian influenza virus (AIV) infection in chicken macrophages. In another study it was observed, with the exception of leptin and cyclin-dependent kinase (CDk), that mitogen-activated protein kinase (MAPk) is involved in the control of chicken ovarian secretory activity (release of steroids and nonapeptide hormones) (SIROTKIN & GROSSMANN 2008).

### Conclusions

Genetic improvement of farm animals, including poultry, is generally aimed at maximizing economic performance and production traits, especially in poultry breeders and table egg producing hens. The rapid development of molecular genetics has enabled scientists to obtain vast amounts of new genomic information that allows for improved estimation of an animal's genetic and breeding value with greater accuracy. A special role is played by individual genes, in particular the prolactin (PRL) gene and the prolactin receptor (PRLR) gene. Studies conducted over the last few years provide evidence that both the PRL gene and the *PRLR* gene take part, directly and indirectly, in shaping many production traits in poultry, resulting in these genes being considered as candidate markers of these traits. It is concluded that a better understanding of the described genetic and physiological factors that influence expression of *PRL* and *PRLR* genes in hens could help to develop practices to finely regulate chicken hen reproductive performance and to maintain egg production at profitable levels.

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