◀Review▶

Prolactin and Growth Hormone in Birds: Protein Structure, Gene Structure and Genetic Variation

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Prolactin (PRL) and Growth hormone (GH) are secreted from the anterior pituitary gland and affect a wide variety of physiological functions in birds. A causal relationship between plasma PRL concentration and broody behaviour is well known. Similarly, a relationship between plasma GH concentration and body growth is well documented. Following the cloning of cDNA of PRL and GH in the chicken and turkey, the levels of mRNA were measured. Levels of PRL or GH mRNA in the anterior pituitary gland were generally correlated with the plasma levels of PRL or GH. Using the PRL or GH cDNA clone as a probe, the genomic DNA clone of PRL and GH was obtained in several galliform species. The availability of cDNA and genomic DNA sequence also allowed the determination of sequence variation of PRL and GH genes in chicken and turkey. The genetic variation of the turkey and chicken PRL promoter and allelic variation of PRL have been shown to be associated with the plasma levels of PRL and expression of incubation behaviour. Likewise, allelic variants of the GH have been proposed as a mechanism to explain variation in egg production in the chicken. Recently, the duck PRL and GH gene was cloned and sequenced. Genetic variations were also detected in the duck GH gene. The presence of variation and/or polymorphic sequence may be important since a variety of body types and egg production traits are found among the duck breeds. Thus, genetic variation in the PRL and GH genes of domestic fowl may be applicable to marker assisted selection. Cloning of cDNA and genomic DNA of PRL and GH was conducted mainly in the domestic species. The sequence information of PRL and GH in the domestic species makes it possible to clone and characterize the PRL and GH in altricial species. The sequence of PRL and GH in the various avian species will provide useful information for studying the physiological function and general and species specific mechanisms of gene expression in birds.

Key words: glycosylation, growth hormone, prolactin, variation

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Introduction

Prolactin (PRL) and Growth Hormone (GH) are considered to belong to the same hormonal family because they share a number of common biological, immunological, and structural features (Niall *et al.*, 1971; Miller and Eberhardt, 1983; Nicoll *et al.*, 1986). PRL and GH are mainly, though not exclusively, produced in the anterior pituitary gland and are synthesized via gene transcription and mRNA translation in lactotrobes or sommatotrobes, respectively. In birds, PRL mRNA expression is observed mainly in the cephalic lobe of the anterior pituitary gland, whereas, GH mRNA is expressed in the caudal lobe.

Both PRL and GH affect a wide range of target tissues. The most studied effects of PRL involve crop-sac development in columbiforms, the induction and maintenance of

broody behaviour, regulation of gonadal function and immune responsiveness in a variety of species. On the other hand, the major effects of GH involve synthesis of protein and nucleic acid, increase in use of lipid for energy production, osmoregulation and reproduction. The wide diversity of physiological functions of PRL and GH are supported by the ubiquitous expression of their receptor mRNA in various tissues. In the domestic fowl, growth and egg production performance are important traits from the aspect of the breeder. Low growth and/or egg production performance cost extra time and feed. Since PRL and GH are associated with egg production and growth parameters, selection for genetic variants of these hormones may result in higher performance and profitability to the breeder. Accordingly we will briefly consider genetic aspects of PRL and GH in birds.

Protein Structure

Prolactin

Cloning of PRL cDNA in avian species was conducted in the chicken (Hanks *et al.*, 1989; Watahiki *et al.*, 1989),

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Table 1. Amino acid similarity of bird PRL

	Chicken	J. quail	Turkey	Duck	Comb duck	Goose	Ostrich	Budgerigar
Chicken		95.2	92.6	93.4	93.0	93.4	91.7	93.9
J. quail	96.5		93.0	93.4	93.0	93.4	91.3	92.6
Turkey	93.0	92.5		91.3	91.7	92.1	89.1	91.3
Duck	96.0	95.5	92.5		98.7	98.3	91.7	94.8
Comb duck	95.0	94.5	92.5	99.0		98.7	92.2	94.3
Goose	95.0	94.5	92.5	99.0	99.0		92.2	94.8
Ostrich	94.0	93.5	91.5	95.0	95.0	95.0		90.0
Budgerigar	95.0	94.0	92.0	97.5	96.5	96.5	93.5	

Values above and under the diagonal represent amino acids sequence similarity of all and mature regions, respectively.

turkey (Wong *et al.*, 1991), Japanese quail (AB162003), domestic duck (Kansaku *et al.*, 2005), comb duck (AM180924), goose (DQ345783) and budgerigar (AB362879). In the ostrich, the structure of PRL is predicted based on the genomic sequence (AB362880). Only ostrich have 31 amino acid residues in the signal peptide, whereas, other avian species have 30 amino acids. On the other hand, all species have 199 amino acid residues for the mature protein. Avian PRLs are highly conserved and have over 88% amino acid sequence similarity to each other (Table 1). Similar to mammalian PRLs, avian PRL has 6 cysteines, which form 3 intra molecular disulfide bonds, and 5 highly conserved regions (residues of mature PRL 11–51, 58–71, 80–98, 108–133, and 160–192) are present which are likely essential for the biological properties of PRL (Fig. 1). Different molecular size of PRLs were detected in the anterior pituitary gland of chicken, turkey and duck (Bedecarrats *et al.*, 1999a, b; Kansaku *et al.*, 2005). Since N-glycosidase F treatment resulted in one single clear signal by western blot analysis, glycosylation is considered as the major post-translational modification of PRL in the chicken, turkey and duck. Although domestic duck, comb duck, goose, ostrich and Budgerigar have a N-linked glycosylation consensus sequence (Asn-Gly-Ser) at position 6 of the mature PRL, galliform species lack the consensus sequence. Thus, an alternative glycosylation site (Asn-X-Cys) has been proposed (Corcoran and Proudman, 1991). All birds have this sequence at position 56. Interestingly, turkey has another site at position 197. To date, the precise site of glycosylation has not been determined and it is not known whether both putative sites of the turkey PRL are glycosylated. In our study, several sizes of the glycosylated form of chicken PRL were detected by western blot analysis in addition to the 23 kDa non-glycosylated form (Fig. 2A). Following neuraminidase treatment the glyco-forms were resolved as a single immunoreactive band (Fig. 2B). Following the 2-dimensional PAGE analysis, different isoelectric point variants were detected both in glycosylated PRL and non-glycosylated PRL (Fig. 3). These results clearly indicate that the glycosylated form of PRL consists of several different sizes of glyco-chain, which

Budgerigar	1	LPICPAGNSV	QQVSLGELFD	RAVLSIYIH	FLSSEMFNEF	DERYAQGRGF	50
Ostrich	1	PN-V- -Y-G- -K-	F- -I- - - - -	- - - - -	- - - - -	- - - - -	50
Goose	1	PN-A- -Y-G- -K-	F- -M- - - - -	- - - - -	- - - - -	- - - - -	50
Comb duck	1	PN-A- -Y-G- -K-	F- -M- - - - -	- - - - -	- - - - -	- - - - -	50
Duck	1	PN-A- -Y-G- -K-	F- -M- - - - -	- - - - -	- - - - -	- - - - -	50
Turkey	1	SS-V- -Y-G- -R-	F- -I- - - - -	- - - - -	- - - - -	- - - - -	50
J. Quail	1	PS-V- -M-A- -K-	Y- -I- - - - -	- - - - -	- - - - -	- - - - -	50
Chicken	1	PI-V- -Y-G- -K-	Y- -I- - - - -	- - - - -	- - - - -	- - - - -	50
Budgerigar	51	ITKAVNGCHT	SSLTPPEKE	QAQTHIEDL	LNLIIGVLR	WNPDIHLAS	100
Ostrich	51	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	100
Goose	51	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	100
Comb duck	51	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	100
Duck	51	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	100
Turkey	51	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	100
J. Quail	51	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	100
Chicken	51	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	100
Budgerigar	101	EVQRKEAPD	TILWAVEIE	EQKRLLEG	EKIVGRVISG	EIGNEIYSPW	150
Ostrich	101	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	150
Goose	101	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	150
Comb duck	101	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	150
Duck	101	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	150
Turkey	101	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	150
J. Quail	101	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	150
Chicken	101	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	150
Budgerigar	151	EGLPSQLQDD	EDSRLFAFYN	LJHCLRRISH	KIDNYLKVLE	CRLIHDSNC	199
Ostrich	151	A- - - - -	R- - - - -	L- - - - -	L- - - - -	S- - - - -	199
Goose	151	E- - - - -	R- - - - -	L- - - - -	V- - - - -	S- - - - -	199
Comb duck	151	E- - - - -	R- - - - -	L- - - - -	V- - - - -	S- - - - -	199
Duck	151	E- - - - -	R- - - - -	L- - - - -	V- - - - -	S- - - - -	199
Turkey	151	D- - - - -	R- - - - -	L- - - - -	V- - - - -	N- - - - -	199
J. Quail	151	D- - - - -	R- - - - -	F- - - - -	V- - - - -	S- - - - -	199
Chicken	151	D- - - - -	R- - - - -	L- - - - -	V- - - - -	S- - - - -	199

Fig. 1. Comparison of amino acid sequences for mature PRL in avian species. Dashes indicate amino acids that are common to all avian species.

originated from a different number of sialic acid residues. However, the observation of similar molecular mass but different isoelectric point variants of non-glycosylated PRL is indicative of alternative post-translational modifications such as phosphorylation. Since the general structure of bird PRL is well conserved, the different positions or degrees of glycosylation and different sizes or forms of glyco-chain may affect the binding ability of PRL to its receptor. Moreover, post-translational modification other than glycosylation may affect biological activity due to potential differences in binding affinity.

Growth Hormone

The amino acid sequence of GH was deduced from cDNA sequence of chicken (Baum *et al.*, 1990), turkey (Foster *et al.*, 1990), duck (Chen *et al.*, 1988), goose (AY

149895) and ostrich (AB028191). In the pied flycatcher, the structure of GH is predicted based on the genomic sequence (Buggiotti *et al.*, 2006). The number of amino acids residue show slight differences among the species. Goose, duck, ostrich and pied flycatcher have 26 residues of signal peptide, whereas, chicken and turkey have 25 residues. On the other hand, the mature protein of pied flycatcher, duck and goose has 190 amino acids, whereas chicken, turkey and ostrich have 191 residues (Fig. 4). Thus, the number of amino acids ranges from 216 to 218 in birds. Although there are minor differences of amino acid number, bird GHs are highly conserved (Table 2) and have 4 cysteines, which are located in almost similar

positions and are likely involved in the formation of intra-molecular disulphide bonds. Various size variants of GH have been detected in the chicken anterior pituitary gland by western blot analyses under non-reducing conditions. The 22 kDa, 44 kDa, 66 kDa, and 88 kDa immunoreactive bands are presumed to represent monomeric, dimeric, trimeric, and tetrameric forms of GH, respectively (Aramburo *et al.*, 2000). Molecular variants of GH were detected in the serum (Montiel *et al.*, 1992). In addition, a 29 kDa form was detected which disappeared following treatment by N-glycosidase F. Since chicken GH has a consensus sequence for N-linked glycosylation at position 188, the 29 kDa band is likely glycosylated GH. This pu-

Fig. 2. Western blot analyses of PRL in Nagoya-Chochin chicken pituitary extracts. Out of lay, laying and incubating hens are represented in lanes 1 to 3, respectively. (A) Without neuraminidase treatment, (B) With neuraminidase treatment.

Fig. 3. Analysis of PRL variants in a Nagoya-Chochin incubating hen by two-dimensional electrophoresis and western blot. Fifty μ g of pituitary extract were electrophoresed and the isoelectric points and molecular mass are indicated on the top and right, respectively.

Flycatcher	1	FPAIPSSLF	ANAVLRAQHL	HLLAAETQYE	LQRTYIPEEQ	RHTNKNSSQVA	50
Ostrich	1	-AM-N-	A-----	-----K-	FE-T-E-	-HA---S-	50
Goose	1	-AM-N-	A-----	-----K-	FE-S-D-	-HT---A*	50
Duck	1	-AM-N-	A-----	-----K-	FE-S-D-	-HT---A*	50
Turkey	1	-TM-N-	I-----	-----K-	FE-T-D-	-YT---A-	50
Chicken	1	-AM-N-	A-----	-----K-	FE-T-D-	-YT---A-	50
Flycatcher	51	FCYSETIPAP	MKKDDAQKS	DMELLOFSLI	LIQSWLTPVQ	YLSKMFNNL	100
Ostrich	51	-----TG-----	-----R-V-----	-----V-----	-----V-----	-----	100
Goose	51	-----TG-----	-----R-V-----	-----V-----	-----V-----	-----	100
Duck	51	-----TG-----	-----R-V-----	-----V-----	-----V-----	-----	100
Turkey	51	-----TG-----	-----R-V-----	-----M-----	-----V-----	-----	100
Chicken	51	-----TG-----	-----R-V-----	-----V-----	-----V-----	-----	100
Flycatcher	101	VFGTSDRYVE	KLKDL EEGIQ	ALMR***DRS	PRGPQLLRPT	YDKFDIHLRN	150
Ostrich	101	-----V-----	-----ELE-----	S-PL-RS-	-K-----N	-----	150
Goose	101	-----F-----	-----ELE-----	P-QI-KP-	-K-----N	-----	150
Duck	101	-----F-----	-----ELE-----	P-QL-KP-	-K-----N	-----	150
Turkey	101	-----F-----	-----ELE-----	P-QL-RP-	-R-----S	-----	150
Chicken	101	-----F-----	-----ELE-----	P-QL-RP-	-K-----N	-----	150
Flycatcher	151	EDALLKNYGL	LSCFKKDLHK	VETYLKVMKC	RRFGESNCTI		190
Ostrich	151	-E-----P-----	-----T-----				190
Goose	151	-D-----L-----	-----T-----				190
Duck	151	-D-----L-----	-----T-----				190
Turkey	151	-D-----L-----	-----N-----				190
Chicken	151	-D-----L-----	-----T-----				190

Fig. 4. Comparison of amino acid sequences for mature GH in avian species. Dashes indicate amino acids that are common to all avian species. Asterisk (*) indicates amino acid positions that are left blank to optimize alignment of amino acid sequences.

Table 2. Amino acid similarity of bird GH

	Chicken	Turkey	Duck	Goose	Ostrich	Flycatcher
Chicken		96.3	94.0	93.5	91.7	88.0
Turkey	96.8		91.7	91.2	89.4	85.7
Duck	97.9	94.7		99.1	94.0	89.9
Goose	97.4	94.2	99.5		93.1	89.4
Ostrich	94.7	91.6	94.2	93.7		88.9
Flycatcher	91.1	87.9	90.5	90.0	89.5	

Values above and under the diagonal represent amino acids sequence similarity of all and mature regions, respectively.

tative glycosylation site is located near the two cysteines which form intra molecular bonds. Glycosylation affects the tertiary structure of GH which may result in different binding affinity to its receptor and altered biological activity. Differential effects of G-GH and NG-GH on proliferation of Nb2 cells may reflect different binding activity or biological effects (Berumen *et al.*, 2004). As in PRL, different charge variants with isoelectric point was identified in both G-GH and NG-GH. These results indicate that post-translational modification other than glycosylation may affects isoelectric point of GH.

Gene Structure

Prolactin

Structure of the PRL gene was characterized in turkey (Kurima *et al.*, 1995), chicken (Ohkubo *et al.*, 1999), duck (Kansaku *et al.*, 2005) and Ostrich (AB362880). The exon/intron arrangement of the PRL gene is common and the lengths from the ATG translation starting codon to translation termination codon were about 6 kb in these species. The 5' flanking sequence of the chicken (2.6 kb), turkey (2.0 kb) and duck (0.2 kb) was reported. Chicken and turkey flanking regions show high similarity. Unlike mammals where the synthesis and release of PRL is under inhibitory control, avian PRL is under tonic regulation and the major releasing factor is vasoactive intestinal polypeptide (VIP). Kang *et al.* (2004) identified a VIP response element in the turkey PRL proximal promoter (−74/−40). Interestingly, this region is well conserved in chicken, turkey, duck, ostrich and budgerigar. Sequence similarity of the proximal region may indicate that the regulation of PRL gene expression by VIP is conserved among many avian species.

Growth Hormone

The gene encoding GH has been identified in chicken (Tanaka *et al.*, 1992) and duck (Ab158760). The gene is composed of 5 exons and 4 introns with an overall length of 4.1 kb and 5.2 kb in the chicken and duck, respectively. The reason for difference of length is partially explained by the insertion of similar sequence to *Anas platyrhynchos* interspersed repeat DNA (X57379) in intron 1 of the duck GH gene. The flanking region of GH was cloned and sequenced in the chicken (0.5 kb), turkey (0.9 kb, AF286532)

and duck (0.7 kb). The flanking region of chicken and turkey has similar structure and high identity. In addition the proximal region of the chicken (−421/−1) shows about 85% similarity to that of duck. However, the distal region of the chicken (−488/−422) and the homologous region of turkey or upstream region of turkey shows no similarity to the duck GH promoter. These results indicate that the regulation of gene expression of GH may be common amongst these species and the major control elements are located in the proximal region.

Genetic Variation And Association To Traits

Prolactin

Genetic variation within the avian PRL gene has not been well characterized. Variation within the promoter region was identified by comparison of several breeds of chickens (Kansaku *et al.*, 1999; Zadworny *et al.*, 2002). Notably, they detected a 24-bp insertion-deletion at the position −358 of the chicken PRL gene that revealed large breed differences in allelic frequencies. Recently Cui *et al.* (2006) reported the association between this 24-bp insertion-deletion and egg production. Association of PRL gene variation and egg production may be related to the antagonistic effects of PRL. Analysis of the PRL promoter of the turkey showed that 2 genetic variants were statistically associated with different plasma levels of PRL. In our recent study, difference of promoter activity was identified using luciferase assay where the 2 genetic variants showed statistically different promoter activity. Reported sequence by Kurima (1995) had about 40% greater activity than the genetic variant (Fig. 5). Furthermore, 1 of the variants was associated with higher rate of expression of broody behaviour (Guemene *et al.*, 2001). These results may provide new tools to select non-broody strains of turkey hens.

Growth Hormone

The association between allelic variants of the GH gene and production traits has been best characterized in the chicken. Four different restriction fragment polymorphisms have been described and allelic variants were observed to be associated with traits for egg production, age at first egg, size of the fat pad, and disease resistance (Kuhnlein *et al.*, 1997; Feng *et al.*, 1998; Kansaku *et al.*, 2003). These

Fig. 5. Difference of promoter activity of turkey PRL gene. Genetic variants of the turkey PRL promoter were fused to the luciferase reporter gene and transiently expressed in GH3 cells. The luciferase activity was expressed as fold changes over the pGL-3 basic plasmid. Each value is a mean $\pm$ SE of five independent transfections.

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gaaaaatacattagacaataaaagcacctgagaacaaatgtaagtaaaataatgcattg
gctgaaatttgaatcaaaagcgttacctcaaggacagaaattgttatttaaaaaaatc
gacttggtcaaaaatacccccttttgaatttttgaattttt (T)ggtagcatgacagaagt
tatgtggcagaaatgtggttcacctggcaacatccagccagctctatccccactaacgat
aaatgggaaccacacctcttttgcctttatgtcagaggtgtccagctctggttgcagccc
tgttaactgtgggcagaccctgcctggagcaggcaggaattaggagcaactttctatgc
tatgggggaaattccaccatgtaaaagcaactgatctgatttgggggtggctcttccatg
atgataaaacogttatttgcataaaacagcagaatattggagaatcattcagtgctaat
tcacccctaggcaaacatccctcccaacctttccatctatgtataaatgactacaattag
gtagaccatttgcgaacacgtgtgcatttatgcattggagaagatatagagaggttgtgt
gatcatgaacacatatatacatttttaaacagaccctgtacatataaggggtgtctaac
agttgccattaccagcctagatgaaaggaagaacatttcaattcaagcaacatctgagc
aactctccaggcagaaATGGCTCCAG

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Fig. 6. Sites of genetic variation in the duck GH gene promoter. Potential TATA box is underlined by a dashed line. Detected sites were underlined.

associations indicate the various involvement of GH in production parameters. Genetic variation in the duck GH promoter was recently identified (Fig. 6). Since various body sizes and egg production rates are found among the duck breeds, investigation between production traits and genetic variation is very important to know the physiological mechanism of GH in bird. Characterization of variation of GH gene and investigation of association for traits may help the selection process to more rapidly establish a new strain and/or breed which shows high performance trait in the domestic birds.

Conclusion

The draft sequence of chicken genomic DNA was released. The sequence information of genomic DNA makes it possible to detect and identify genetic variation and polymorphism in many functional genes which involves expression of incubation behaviour and growth. More-

over, characterization of the structure of the functional genes in the chicken also accelerates the sequencing and characterization of homologous genes in the other avian species. Availability of structural information of functional genes make possible to identify the general and species specific mechanism of gene expression in birds. In future, identification of mechanism of gene expression assists rapid selection and development of breeds and or lines which show higher economical traits.

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References

- Arámburo C, Luna M, Carranza M, Reyes M, Martínez-Coria H and Scanes CG. Growth Hormone Size Variants: Changes in the Pituitary During Development of the Chicken. *Proceedings of the Society for Experimental Biology and Medicine*, 223: 67–74. 2000.
- Baum D, Graser G, Heib M and Krampitz G. Chicken growth hormone: cDNA-synthesis and base sequence. *Comparative Biochemistry and Physiology B*, 96: 491–495. 1990.
- Bedecarrats G, Guemene D, Kuhnlein U and Zadworny D. Changes in levels of immunoreactive prolactin isoforms during a reproductive cycle in turkey hens. *General and Comparative Endocrinology*, 113: 96–104. 1999a.
- Bedecarrats G, Guemene D, Morvan C, Crisostomo-Pinto S, Kuhnlein U and Zadworny D. In vitro release of isoforms of prolactin from pituitary glands of turkey hens at different physiological stages. *General and Comparative Endocrinology*, 113: 105–111. 1999b.
- Berumen LC, Luna M, Carranza M, Martinez-Coria H, Reyes M, Carabez A and Aramburo C. Chicken growth hormone: further characterization and ontogenic changes of an N-glycosylated isoform in the anterior pituitary gland. *General and Comparative Endocrinology*, 139: 113–123. 2004.
- Buggiotti L, Hellstrom MA and Primmer CR. Characterization of the first growth hormone gene sequence for a passerine bird—the pied flycatcher (*Ficedula hypoleuca*). *DNA Sequence*, 17: 401–406. 2006.
- Chen HT, Pan FM and Chang WC. Purification of duck growth hormone and cloning of the complementary DNA. *Biochimica et Biophysica Acta*, 949: 247–251. 1988.
- Corcoran DH and Proudman JA. Isoforms of turkey prolactin: evidence for differences in glycosylation and in tryptic peptide mapping. *Comparative Biochemistry and Physiology B*, 99: 563–570. 1991.
- Cui JX, Du HL, Liang Y, Deng XM, Li N and Zhang XQ. Association of polymorphisms in the promoter region of chicken prolactin with egg production. *Poultry Science*, 85: 26–31. 2006.
- Feng XP, Kuhnlein U, Fairfull RW, Aggrey SE, Yao J and Zadworny D. A genetic marker in the growth hormone receptor gene associated with body weight in chickens. *Journal of Heredity*, 89: 355–359. 1998.

- Foster DN, Kim SU, Enyeart JJ and Foster LK. Nucleotide sequence of the complementary DNA for turkey growth hormone. *Biochemical and Biophysical Research Communications*, 173: 967–975. 1990.
- Hanks MC, Alonzi JA, Sharp PJ and Sang HM. Molecular cloning and sequence analysis of putative chicken prolactin cDNA. *Journal of Molecular Endocrinology*, 2: 21–30. 1989.
- Guemene D, Kansaku N and Zadworny D. Controlling broodiness in turkey hens. *World Poultry*, 17: 14–17. 2001.
- Kang SW, Gazzillo LC, You S, Wong EA and El Halawani ME. Turkey prolactin gene regulation by VIP through 35-bp cis-acting element in the proximal promoter. *General and Comparative Endocrinology*, 138: 157–165. 2004.
- Kansaku N, Shimada K, Suzuki T, Matsuda Y, Kuhnlein U and Zadworny D. Genetic variation in the chicken prolactin promoter. *Biology of Reproduction*, 60. Sup. 253–254. 1999.
- Kansaku N, Nakada A, Okabayashi H, Guemene D, Kuhnlein U and Zadworny D. DNA polymorphism in the chicken growth hormone gene: association with egg production. *Animal Science Journal*, 74: 243–244. 2003.
- Kansaku N, Ohkubo T, Okabayashi H, Guemene D, Kuhnlein U, Zadworny D and Shimada K. Cloning of duck PRL cDNA and genomic DNA. *General and Comparative Endocrinology*, 141: 39–47. 2005.
- Kuhnlein U, Ni L, Weigend S, Gavora JS, Fairfull W and Zadworny D. DNA polymorphisms in the chicken growth hormone gene: response to selection for disease resistance and association with egg production. *Animal Genetics*, 28: 116–123. 1997.
- Kurima K, Proudman JA, El Halawani ME and Wong EA. The turkey prolactin-encoding gene and its regulatory region. *Gene*, 156: 309–310. 1995.
- Miller WL and Eberhardt NL. Structure and evolution of the growth hormone gene family. *Endocrine Review*, 4: 97–130. 1983.
- Montiel JL, Berghman LR and Aramburo C. Identification of growth hormone molecular variants in chicken serum. *General and Comparative Endocrinology*, 88: 298–306. 1992.
- Niall HD, Hogan ML, Sauer R, Rosenblum IY and Greenwood FC. Sequences of pituitary and placental lactogenic and growth hormones: evolution from a primordial peptide by gene reduplication. *Proceedings of the National Academy of Sciences of the United States of America*, 68: 866–870. 1971.
- Nicoll CS, Mayer GL and Russell SM. Structural features of prolactins and growth hormones that can be related to their biological properties. *Endocrine Review*, 7: 169–203. 1986.
- Ohkubo T, Tanaka M and Nakashima K. Molecular cloning of the chicken prolactin gene and activation by Pit-1 and cAMP-induced factor in GH3 cells. *General and Comparative Endocrinology*, 119: 208–216. 2000.
- Tanaka M, Hosokawa Y, Watahiki M and Nakashima K. Structure of the chicken growth hormone-encoding gene and its promoter region. *Gene*, 112: 235–239. 1992.
- Watahiki M, Tanaka M, Masuda N, Sugisaki K, Yamamoto M, Yamakawa M, Nagai J and Nakashima K. Primary structure of chicken pituitary prolactin deduced from the cDNA sequence. Conserved and specific amino acid residues in the domains of the prolactins. *Journal of Biological Chemistry*, 264: 5535–5539. 1989.
- Wong EA, Ferrin NH, Silsby JL and El Halawani ME. Cloning of a turkey prolactin cDNA: expression of prolactin mRNA throughout the reproductive cycle of the domestic turkey (*Meleagris gallopavo*). *General and Comparative Endocrinology*, 83: 18–26. 1991.
- Zadworny D, Kansaku N, Bedecarrats G, Guemene D and Kuhnlein U. Prolactin and its receptor in galliforms. *Avian and Poultry Biology Reviews*, 13: 223–229. 2002.