

HORMONES, PITUITARY-LIKE HORMONES

Hormones with structural and functional similarities to the hormones of the anterior pituitary gland (see Hormones, anterior pituitary hormones) fall into two main categories, ie, proteins of the prolactin/growth hormone (PRL/GH) family, and glycoproteins. These hormones are produced in the placenta by chorionic tissue, and so are normally found in the female during pregnancy. Placental lactogens, members of the PRL/GH family, support growth and development of mammary tissue in preparation for lactation. Chorionic gonadotropin (CG) is similar in structure to luteinizing hormone (LH) and supports the maintenance of early pregnancy. Chorionic gonadotropin [9002-70-4] is found in humans (hCG) and lower primates, as well as in horses (eCG). Additional members of the PRL/GH family of hormones with unknown biologic function have been discovered. Commercial sources are provided herein when available. Additional information on primary structure, glycosylation, and disulfide bonding relating to the bioactivity of PRL/GH-related hormones and glycoprotein hormones is available (see Hormones, anterior pituitary hormones).

1. Prolactin/Growth Hormone Family

1.0.1. Chorionic Somatomammotropin

Three genes encode human chorionic somatomammotropin [11085-36-2] (hCS). These are located within a cluster of genes on human chromosome 17 which code for pituitary growth hormone [12629-01-5] (GH-N), placental GH [109675-94-7] (GH-V), and three hCS molecules, ie, hCS-A, hCS-B, and hCS-V (1–3), also referred to as human placental lactogens. All of these molecules are closely related to GH in structure (Fig. 1). Placental lactogens also exist in rodents and ruminants; however, these hormones are more closely related to prolactin than GH.

The amino acid sequences of hCS-A, hCS-B, and hCS-V are shown in relation to GH in Figure 1. The sequence of hCS-V is predicted from the DNA coding sequence and apparently does not possess amino acids 8–55 relative to GH and the other hCS molecules. It is not certain whether hCS-V is expressed or what function it may have. Human CS-A and hCS-B share approximately 85% identity with GH and also possess the disulfide bonds between Cys 53–165 and Cys 182–189 which produce the long and short S—S loops characteristic of the PRL/GH family.

Chorionic somatomammotropin is detectable in maternal serum by immunoassay (qv) at about two weeks of pregnancy. Its secretion increases thereafter to very high levels, 20 $\mu\text{g/mL}$ serum, prior to delivery (4). Human CS does not bind the GH receptor significantly, even though there is high sequence homology between hCS and GH. Existing structure—function data, particularly from hydrophobicity evaluations, suggest that four amino acid substitutions relative to GH, ie, Asp-104, Asp-109, Asp-110, and His-112, may result in the lack of growth-promoting activity of hCS (5). Human CS behaves much like prolactin in a number of assay systems. Accordingly, hCS is thought to contribute to the development of mammary tissue in preparation for postnatal nursing. Some of the metabolic effects of GH may be conserved in hCS. Human CS is thought to contribute to the commonly observed resistance to insulin in the mother, which serves to divert carbohydrate

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1	15
GH-N:Phe-Pro-Thr-Ile-Pro-Leu-Ser-Arg-Leu-Phe-Asp-Asn-Ala-Met-Leu	
GH-V: * * * * *	
CS-A: Val-Gln * -Val * * * * *	
CS-B: Val-Gln * -Val * * * * *	
CS-V: Val-Gln * -Val * * * * *	
16	30
GH-N:Arg-Ala-His-Arg-Leu-His-Gln-Leu-Ala-Phe-Asp-Thr-Tyr-Gln-Glu	
GH-V: * * * -Arg * * * -Tyr * * * * *	
CS-A: Gln * * * * -Ala * * * * -Ile * * * * *	
CS-B: Gln * * * * -Ala * * * * -Ile * * * * *	
CS-V: Gln * * * * -Ala * * * * -Ile * * * * *	
31	45
GH-N:Phe-Glu-Glu-Ala-Tyr-Ile-Pro-Lys-Glu-Gln-Lys-Tyr-Ser-Phe-Leu	
GH-V: * * * * * -Leu * * * * *	
CS-A: * * * * -Thr * * * * *	
CS-B: * * * * -Thr * * * * -Asp * * * * *	
CS-V: * -Ile-Ser-Ser-Trp-Gly-Met - - - - -	
46	60
GH-N:Gln-Asn-Pro-Gln-Thr-Ser-Leu-Cys-Ser-Glu-Ser-Ile-Pro-Thr	
GH-V: * * * * * * * * * * * * * * * * *	
CS-A: His-Asp-Ser * * * * -Phe * * * * -Asp * * * * *	
CS-B: His-Asp-Ser * * * * -Phe * * * * -Asp * * * * *	
CS-V: * * * * * -Asp * * * * *	
61	75
GH-N:Pro-Ser-Asn-Arg-Glu-Glu-Thr-Gln-Gln-Lys-Ser-Asn-Leu-Glu-Leu	
GH-V: * * * * * -Val-Lys * * * * *	
CS-A: * * * * -Met * * * * *	
CS-B: * * * * -Met * * * * *	
CS-V: Ser * -Asn-Met * * * * *	
76	90
GH-N:Leu-Arg-Ile-Ser-Leu-Leu-Leu-Ile-Gln-Ser-Trp-Leu-Glu-Pro-Val	
GH-V: * * * * * * * * * * * * * * * * *	
CS-A: * * * * * * * * * * * * * * * * *	
CS-B: * * * * * * * * * -Glu * * * * *	
CS-V: * -His * * * * * -Glu * -Arg * * * * *	
91	105
GH-N:Gln-Phe-Leu-Arg-Ser-Val-Phe-Ala-Asn-Ser-Leu-Val-Tyr-Gly-Ala	
GH-V: * -Leu * * * * * -Trp * * * * *	
CS-A: Arg * * * * * -Met * * * * -Asn * * * * -Asp-Thr	
CS-B: * * * * * -Met * * * * -Asn * * * * -Asp-Thr	
CS-V: Arg * * * * * -Thr * -Thr * -Asn * * * * -Asp-Thr	
106	120
GH-N:Ser-Asp-Ser-Asn-Val-Tyr-Asp-Leu-Lys-Asp-Leu-Glu-Glu-Gly	
GH-V: * * * * * * * * * * -His * * * * *	
CS-A: * * * * * -Asp-Asp * -His * * * * *	
CS-B: * * * * * -Asp-Asp * -His * * * * *	
CS-V: * * * * * -Asp-Asp * -His * * * * *	
121	135
GH-N:Ile-Gln-Thr-Leu-Met-Gly-Arg-Leu-Glu-Asp-Gly-Ser-Pro-Arg-Thr	
GH-V: * * * * * -Trp * * * * *	
CS-A: * * * * * -Arg * * * * *	
CS-B: * * * * * -Arg * * * * *	
CS-V: * * * -Met * * * * * -His-Leu * *	
136	150
GH-N:Gly-Gln-Ile-Phe-Lys-Gln-Thr-Tyr-Ser-Lys-Phe-Asp-Thr-Asn-Ser	
GH-V: * * * * * -Asn * -Ser * * * * *	
CS-A: * * * * -Leu * * * * *	
CS-B: * * * * -Leu * * * * *	
CS-V: * * * -Thr-Leu * * * * *	
151	165
GH-N:His-Asn-Asp-Asp-Ala-Leu-Leu-Lys-Asn-Tyr-Gly-Leu-Leu-Tyr-Cys	
GH-V: * * * * * * * * * * * * * * * * *	
CS-A: * * * -His * * * * *	
CS-B: * * * -His * * * * *	
CS-V: * * * -His * * * * *	
166	180
GH-N:Phe-Arg-Lys-Asp-Met-Asp-Lys-Val-Glu-Thr-Phe-Leu-Arg-Ile-Val	
GH-V: * * * * * * * * * * * * * * * * *	
CS-A: * * * * * * * * * * * -Met * *	
CS-B: * * * * * * * * * * * -Met * *	
CS-V: * * * * * * * * * * * -Met * *	
181	191
GH-N:Gln-Cys-Arg-Ser-Val-Glu-Gly-Ser-Cys-Gly-Phe	
GH-V: * * * * * * * * * * *	
CS-A: * * * * * * * * * * *	
CS-B: * * * * * * * * * * *	
CS-V: * * * * * * * * * * *	

Fig. 1. Primary structure of the human growth hormone family of proteins. GH-N=pituitary GH; GH-V=placental GH variant; CS=choriosomatotrophin; *=same amino acid as GH-N. Disulfide bonds connect Cys molecules at positions 53–165 and 182–189. Asn-140 of GH-V is underlined to indicate an N-linked glycosylation site.

energy sources to the developing fetus. Human CS is available for research purposes from a variety of sources (6), but does not have clinical applications.

1.0.2. Placental Growth Hormone

The gene for placental growth hormone (GH – V, V = variant) is found within the GH/CS gene cluster. GH-V is expressed in the placenta, but not in the anterior pituitary. The structure of GH-V differs from pituitary GH

(GH – N, N = normal), by only 12 substitutions dispersed along the length of the molecule (Fig. 1). Similarly to GH-N (see Hormones, anterior pituitary hormones), GH-V possesses both long and short disulfide loops. A consensus glycosylation site is utilized for carbohydrate attachment during post-translational processing at Asn-140 (7). A frameshift in transcription gives rise to a 230 amino acid variant of GH-V which does not possess the glycosylation site and has a dissimilar carboxy terminus relative to GH-V. Interestingly, this form of GH-V is not secreted, but is believed to be membrane-bound (2).

Antibodies have been generated which produce immunoassays that discriminate between GH-V and GH-N. These assay systems have shown that the secretion of GH-V becomes elevated at about three weeks of pregnancy and increases to approximately 15 ng/mL near term (8). The physiological role of GH-V is uncertain. Genetic deficiency of GH-V does not adversely affect pregnancy or fetal development (9). GH-V is a potent growth-stimulator but possesses considerably less lactogenic activity than GH-N (10). There are no clinical applications (ca 1993) for GH-V.

1.0.3. Placental Lactogens

The placentae of rodents and ruminants produce prolactin-related molecules called placental lactogens (11). Placental lactogens are not found in all species. Prolactin-like activity has not been demonstrated in placental extracts from rabbits, pigs, horses, or animals of the order Carnivora. Ovine [127497-22-7] (oPL) and bovine [116669-02-4] (bPL) placental lactogens have been studied extensively (12). The structures of bovine prolactin [56832-36-1] (bPRL), bPL, oPL, and bovine GH [66419-50-9] (bGH) are given in Figure 2. Bovine and ovine PL share about 50% homology with bPRL and approximately 20% homology with bGH. A short N-terminal disulfide loop exists in bPL and oPL, reflecting their relatedness to prolactin. As with other hormones of the PRL/GH family, bPL and oPL possess the long and short C-terminal loops formed by disulfide bridges. Bovine PL, but not oPL, possesses both O- and N-linked oligosaccharide moieties (13). Enzymatic deglycosylation of bPL may increase receptor binding potency, but does not appear to influence bioactivity *in vitro* (14). The carbohydrate moieties of bPL could serve to prolong the hormone's circulating half-life (15). Only the glycosylated form of bPL appears to be secreted (12).

The ruminant PLs are able to bind both GH and PRL receptors and exert lactogenic and somatogenic actions (12). As described for hCS, ruminant PLs are thought to contribute to mammary development and to alter maternal metabolism to support fetal nutrition. Evidence also suggests that ruminant PL may directly regulate fetal growth. Receptors which show greater affinity for oPL than for ovine growth hormone [37267-05-03] (oGH) and ovine prolactin [12585-34-1] (oPRL) have been identified in fetal ovine liver (16). The synthesis of hepatic glycogen, an important carbohydrate energy source, is stimulated by oPL (17). Maternal food deprivation induces a reduction of approximately 70% in PL binding to the fetal liver, perhaps contributing to the accompanying intrauterine growth retardation (18). The presence of bPL receptors in bovine endometrium (19, 20) suggests that bPL could regulate the function of maternal tissues which support pregnancy, fetal growth, and development.

There are no commercial uses for ruminant PLs. However, bPL has been shown to stimulate insulin-like growth factor I and somatic growth in rats (12), suggesting potential applications as performance stimulators in domestic animal production. Milk yield and feed intake are stimulated by the administration of bPL (21) (see Growth regulators, animal). The development of recombinant bPL for use in food animals is being investigated by Monsanto Co. (15). Limited availability of oPL has restricted opportunities for research into the pharmacologic value of this hormone. The development of a high yield expression system for oPL is in progress (22).

A review of the synthesis, structure, and potential functions of rodent PLs is available (11). These hormones have no commercial importance per se, but may prove useful in studies of biology and structure—function relationships essential for future practical applications of bPL and oPL. Two placental lactogens, PL-I [144591-44-6] and PL-II [121631-23-0], are produced in the rat. The production of PL-I, which is dominant

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1	15
bPRL: Thr-Pro-Val-Cys-Pro-Asn-Gly-Pro-Gly-Asn-Cys	
bPL: Val-Glu-Asp-Tyr-Ala-Tyr-Lys-Gln	
oPL: Gln-Ala-Gln-His-Pro-Tyr-Arg-Gln-Lys	
bGH: Ala-Phe-Pro	
16	30
bPRL: Gln-Val-Ser-Leu-Arg-Asp-Leu-Phe-Asp-Arg-Ala-Val-Met-Val-Ser	
bPL: Arg-Ile-Pro-Gln-Ser-Glu-Thr-Leu-Ala	
oPL: Ile-Pro-Gln-Ser-Thr-Thr-Ala	
bGH: Ala-Met-Ser-Gly-Ala-Asn-Leu-Arg-Ala	
31	45
bPRL: His-Tyr-Ile-His-Asp-Leu-Ser-Ser-Glu-Met-Phe-Asn-Glu-Phe-Asp	
bPL: Ser-Asn-Asn-Tyr-Arg-Ala-Arg-Asn	
oPL: Asn-Asn-Ser-Lys-Ala-Gly-Val-Arg	
bGH: Gln-His-Leu-Gln-Ala-Ala-Asp-Thr-Lys-Glu	
46	60
bPRL: Lys-Arg-Tyr-Ala-Gln-Gly-Lys-Gly-Phe-Ile-Thr-Met	
bPL: Gln-Phe-Gly-Glu-Asn-Thr-Ser-Lys	
oPL: Glu-Gln-Gly-Ile-Asn-Ser-Glu-Ser-Lys	
bGH: Arg-Thr-Ile-Pro-Glu-Gly-Gln-Arg-Tyr-Ser-Ile-Gln-Asn-Thr	
61	75
bPRL: Ala-Leu-Asn-Ser-Cys-His-Thr-Ser-Ser-Leu-Pro-Thr-Pro-Glu-Asp	
bPL: Phe-Ile-Glu-Phe-Met-Thr-Asn-Asn	
oPL: Val-Ile-Ile-Thr-Ile-Thr-Asn-Ser	
bGH: Gln-Val-Ala-Phe-Phe-Ser-Glu-Thr-Ile-Ala-Thr-Gly	
76	90
bPRL: Lys-Glu-Gln-Ala-Gln-Thr-His-His-Glu-Val-Leu-Met-Ser-Leu	
bPL: Ala-Ala-Asn-Glu-Asp-Ala-Leu-Arg	
oPL: Ala-Glu-Ile-Asn-Glu-Asp-Lys-Ile-Phe-Lys	
bGH: Asn-Glu-Lys-Ser-Asp-Leu-Glu-Leu-Arg-Ile	
91	105
bPRL: Ile-Leu-Gly-Leu-Leu-Arg-Ser-Trp-Asn-Asp-Pro-Leu-Tyr-His-Leu	
bPL: Val-Ile-Ser-His-Asp-Glu-His-Gln-Ala	
oPL: Val-Ile-Ser-His-Asp-Glu-His-Ala	
bGH: Ser-Leu-Ile-Gln-Leu-Gly-Gln-Phe	
106	120
bPRL: Val-Thr-Glu-Val-Arg-Gly-Met-Lys-Gly-Ala-Pro-Asp-Ala	
bPL: Leu-Leu-His-Arg-Asn-Ser-Pro-Asp	
oPL: Leu-Ala-Asn-Ser-Thr-Ser-Pro	
bGH: Ser-Arg-Val-Phe-Thr-Asn-Ser-Leu-Val-Phe-Thr-Ser-Asp-Arg	
121	135
bPRL: Ile-Leu-Ser-Arg-Ala-Ile-Glu-Ile-Glu-Glu-Glu-Asn-Lys-Arg-Leu	
bPL: Ala-Lys-Asp-Lys-Thr-Val	
oPL: Leu-Thr-Lys-Gln-Lys-Lys-Ala-Val	
bGH: Val-Tyr-Glu-Lys-Leu-Lys-Asp-Leu-Gly-Ile-Leu-Ala	
136	150
bPRL: Leu-Glu-Gly-Met-Glu-Met-Ile-Phe-Gly-Gln-Val-Ile-Pro-Gly-Ala	
bPL: Val-Val-Gln-Lys-Arg-His-Glu	
oPL: Val-Asp-Val-Gln-Lys-Arg-Ile-His-Glu	
bGH: Met-Arg-Glu-Leu-Asp-Gly-Thr-Pro-Arg-Ala-Gln	
151	165
bPRL: Lys-Glu-Thr-Glu-Pro-Tyr-Pro-Val-Trp-Ser-Gly-Leu-Pro-Ser-Leu	
bPL: Lys-Asn-Glu-Lys-Ser	
oPL: Asn-Glu-Gln-Ser	
bGH: Ile-Leu-Lys-Gln-Thr-Asp-Lys-Phe-Asp-Thr-Asn-Met	
166	180
bPRL: Gln-Thr-Lys-Asp-Glu-Asp-Ala-Arg-Tyr-Ser-Ala-Phe-Tyr-Asn-Leu	
bPL: Thr-Ala-Asp-Val-Gln-Thr-Arg-Met	
oPL: Thr-Ser-Gln-Asn-Val-Arg-Val-Arg	
bGH: Arg-Ser-Asp-Ala-Leu-Leu-Lys-Asn-Gly	
181	195
bPRL: Leu-His-Cys-Leu-Arg-Asp-Ser-Ser-Lys-Ile-Asp-Thr-Tyr-Leu	
bPL: Phe-His-Ser-Ile	
oPL: Phe-His-Tyr	
bGH: Ser-Phe-Lys-Leu-His-Thr-Glu	
196	210
bPRL: Lys-Leu-Leu-Asn-Cys-Arg-Ile-Ile-Tyr-Asn-Asn-Asn-Cys	
bPL: Asn-Lys-Phe-Thr-Pro	
oPL: Arg-Ile-Lys-Leu-Thr-Ser-Glu-Thr	
bGH: Arg-Val-Met-Lys-Arg-Phe-Gly-Glu-Ala-Ser-Ala-Phe	

Fig. 2. Primary structure of bPRL, bPL, oPL, and bGH. Amino acid numbers are relative to maximum homology among hormones (12). *=same amino acid as bPRL. Disulfide bonds: (Cys 8–15) (not in bGH), 65–183, 200–208. Asn-53 of bPL is underlined to indicate an N-linked glycosylation site.

at midgestation, is replaced by PL-II later in pregnancy. PL-I, but not PL-II, is glycosylated. Rodent PLs all demonstrate lactogenic activity, but do not bind GH receptors. Prolactin-like molecules support the existence and function of the corpus luteum in rodents. The maintenance of corpus luteum function, which is critical for the continuation of pregnancy, is probably mediated by PLs in mid- and late gestation.

1.0.4. Prolactin-Like Proteins

A number of prolactin-like proteins (PLPs), which are distinct from the PLs, have been identified in ruminants and rodents (11, 23). Several cDNA transcripts coding for PLPs in cattle have been identified (23). These transcripts code for proteins which possess about 40% sequence homology with bovine PRL; 60% if conservative substitutions are considered. Three glycosylated PLPs, ie, PLP-A, -B, and -C, are produced during pregnancy in the rat (11). Two additional prolactin-related molecules have been identified in the mouse (24, 25), ie, proliferin [92769-12-5] (PLF) and PLF-related protein [98724-27-7]. These are not found in other rodents and may be unique to the mouse. The functional roles of PLPs remain to be determined.

2. Glycoprotein Family

2.0.5. Human Chorionic Gonadotropin

Human CG (hCG) is produced by syncytiotrophoblast cells of the placenta. The secretion of hCG from chorionic cells begins about 10 days after fertilization. The detection of this early rise in hCG in urine forms the basis for a variety of nonprescription home pregnancy tests. Maximum production of CG occurs at approximately 70 days of gestation and declines rapidly, reaching relatively low levels in the serum by the second trimester. The secretion of hCG early in pregnancy prolongs the lifespan of the corpus luteum, an ovarian structure which secretes the steroid hormones progesterone and estradiol, needed to maintain pregnancy. After the first two weeks, the placenta is able to produce sufficient steroid hormones to maintain pregnancy.

Human CG is purified readily from urine collected during the first trimester of pregnancy and is very similar in structure to pituitary luteinizing hormone (LH). Like LH, hCG is composed of noncovalently bound α -[56832-30-5] and β -[78690-52-6] subunits. The subunits are glycosylated during post-translational processing (26). Both subunits must be in association for the expression of biological activity. The subunits dissociate readily in the presence of chaotropic salts such as urea and guanidine—HCl. The α -subunit of hCG and the three pituitary glycoprotein hormones, ie, LH, follicle-stimulating hormone (FSH), and thyroid-stimulating hormone (TSH) (27), are coded by the same gene and therefore have identical amino acid sequences; structural information on the α -subunit is available (see Hormones, anterior pituitary hormones). The β -subunit of hCG (hCG β) is coded by a cluster of seven gene copies, some of which may be nonexpressed pseudogenes (28, 29). At least two hCG β genes are expressed and one occurs in tandem with the gene for LH β (30). As for the pituitary glycoprotein hormones, the β -subunit of hCG confers the type of biologic action which is expressed, eg, the combination of TSH α and hCG β would produce bioactive hCG. Human CG β contains a carboxy terminal peptide extension of 30 amino acids relative to hLH β [53664-53-2], which contains sites for O-linked carbohydrate attachment (Fig. 3). On a weight basis, hCG is composed of approximately one-third carbohydrate, ie, 13.8% hexose, 10.8% hexosamines, and 9.6% sialic acid. The carbohydrate component of the α -subunit is necessary for the expression of bioactivity (32). Selective elimination of N-linked glycosylation sites by site-directed mutagenesis has revealed that the absence of the oligosaccharide at Asn-52 α does not significantly affect receptor binding, yet reduces the ability of hCG to activate its target cell (33). Removal of the other carbohydrates at Asn-78 α , Asn-13 β , or Asn-30 β has minor effects on *in vitro* bioactivity (33). The high content of sialic acid confers a prolonged biological half-life which promotes biological activity *in vivo*. The complex and varied carbohydrate structures of hCG have been reviewed (34).

Human CG has considerable commercial value in clinical fertility control due to its LH-like bioactivity and natural resistance to biological degradation. The injection of hCG is used to induce ovulation following treatment with high doses of follicle-stimulating hormone (FSH) to stimulate the maturation of multiple ova. Significant producers of hCG for clinical usage are Serono (Italy) and Organon (Sweden). Human CG is available for research purposes from many suppliers (6, 35).

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	1	15
hCG β	Ser-Lys-Glu-Pro-Leu-Arg-Pro-Arg-Cys-Arg-Pro-Ile-Asn-Ala-Thr-	
hLH β	-*-Arg-*****-Trp---His-----*-lle-	
eCG β	---Arg-Gly-----*-Leu-----*-	
	16	30
hCG β	Leu-Ala-Val-Glu-Lys-Glu-Gly-Cys-Pro-Val-Cys-Ile-Thr-Val-Asn-	
hLH β	-----*------*------*------*-	
eCG β	-----Ala-----Ala-----Ile-----Phe-Thr-	
	31	45
hCG β	Thr-Thr-Ile-Cys-Ala-Gly-Tyr-Cys-Pro-Thr-Met-Thr-Arg-Val-Leu-	
hLH β	-----*------*------*------*-Met-----*-	
eCG β	---Ser-----*------*-Ser---Val-----Met-	
	46	60
hCG β	Gln-Gly-Val-Leu-Pro-Ala-Leu-Pro-Gln-Val-Val-Cys-Asn-Tyr-Arg-	
hLH β	-*Ala-----Pro-----*------*-Thr-----*-	
eCG β	Pro-Ala-Ala-----Ile-----Pro-----Thr-----*-	
	61	75
hCG β	Asp-Val-Arg-Phe-Glu-Ser-Ile-Arg-Leu-Pro-Gly-Cys-Pro-Arg-Gly-	
hLH β	-----*------*------*------*------*-	
eCG β	Glu-Leu-----Ala-----*------*-Pro-----*-	
	75	90
hCG β	Val-Asn-Pro-Val-Val-Ser-Tyr-Ala-Val-Ala-Leu-Ser-Cys-Gln-Cys-	
hLH β	-----*------*-Phe-Pro-----*------*-Arg-----*-	
eCG β	---Asp---Met-----Phe-Pro-----*------*-His-----*-	
	91	105
hCG β	Ala-Leu-Cys-Arg-Arg-Ser-Thr-Thr-Asp-Cys-Gly-Gly-Pro-Lys-Asp-	
hLH β	Gly-Pro-----*------*-Ser-----*------*-Lys-----*-	
eCG β	Gly-Pro-----Gln-Ile-Lys-----*------*-Val-Phe-Arg-----*-	
	106	120
hCG β	His-Pro-Leu-Thr-Cys-Asp-Asp-Pro-Arg-Phe-Gln-Asp-Ser-Ser-Ser-	
hLH β	-----*------*-His-----Gln	
eCG β	Gln-----Ala---Ala-Pro-Gln-Ala- <u>Ser-Ser-Ser</u> ---Lys-Asp-	
	121	135
hCG β	<u>Ser</u> -Lys-Ala-Pro-Pro-Pro- <u>Ser</u> -Leu-Pro-Ser-Pro- <u>Ser</u> -Arg-Leu-Pro-	
eCG β	Pro-Pro-Ser-Gln-----Leu- <u>Thr-Ser-Thr</u> --- <u>Thr-Pro-Thr-Pro-Gly</u> -	
	136	
hCG β	Gly-Pro- <u>Ser</u> -Asp-Thr-Pro-Ile-Leu-Pro-Gln	
eCG β	Ala- <u>Ser-Arg-Ser-Ser</u> -His-Pro-Leu-Pro-Ile-Lys- <u>Thr-Ser</u>	

Fig. 3. Human CG, hLH, and equine CG (eCG) β -subunits. Amino acid numbering is relative to maximum homology between the three subunits. Consensus glycosylation sites are at Asn-13 and 30. *=same amino acid as hCG β . Underlined Asn residues indicate attachment of N-linked carbohydrate chains. Serines at positions 121, 127, 132, and 138 of hCG β are underlined to indicate sites of O-linked carbohydrate attachment. Residues 115–118, 127–133, 137–141, 148–149 of eCG β are underlined to highlight probable locations of O-linked oligosaccharides attached to Ser or Thr (31).

2.0.6. Equine Chorionic Gonadotropin

Equine CG (eCG) is produced by trophoblast-derived structures in the endometrium known as endometrial cups. The original name of this hormone was pregnant mare serum gonadotropin (PMSG). Whereas eCG is the correct scientific name for this hormone, it is referred to by many as PMSG. Equine CG is secreted at high levels during the first trimester of the mare's pregnancy, ie, days 40–130. The high concentration of serum eCG is

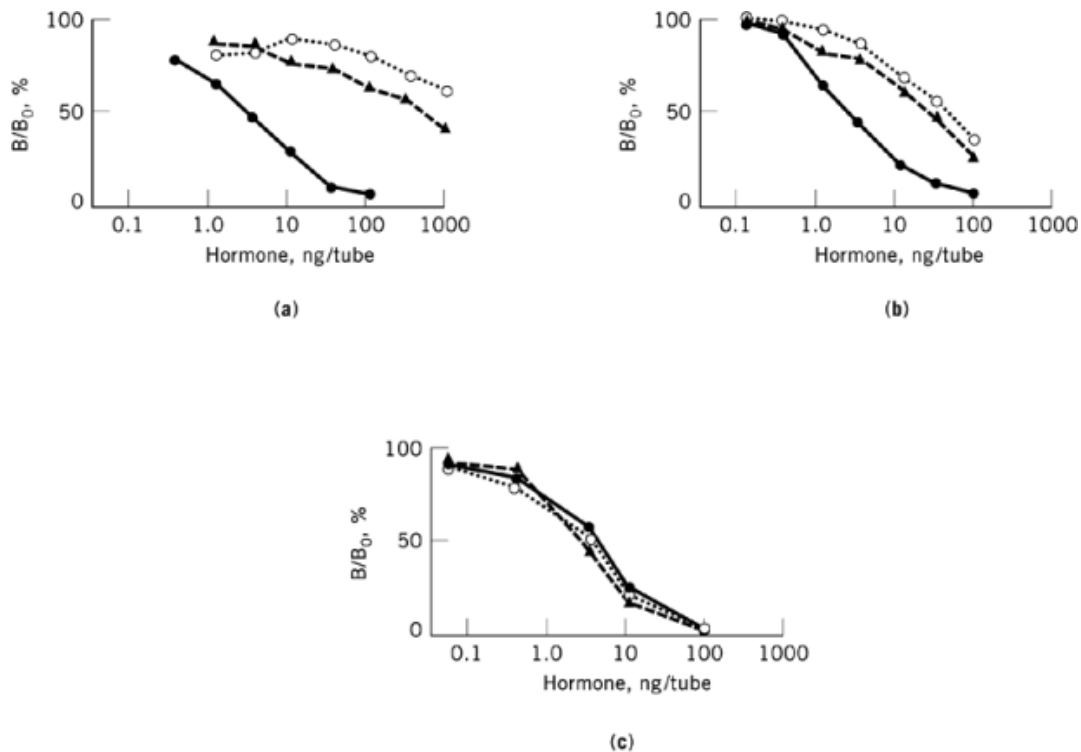


Fig. 4. FSH receptor-binding potencies of equine FSH (●), eCG purified from pregnant mare's serum (○), and endometrial cups (▲). Receptor-binding in cell membrane fractions, B/B_0 from (a) horse, (b) calf, and (c) rodent testes (40). Courtesy of Butterworth-Heinemann.

conducive to hormone extraction and purification. The purification of eCG is readily achieved by precipitation in metaphosphoric acid and ethanol, followed by ion-exchange and size-exclusion chromatography (36, 37).

Like hCG, eCG is a placental gonadotropic hormone with close structural similarity to pituitary luteinizing hormone. Equine CG is composed of noncovalently bound α -[112326-58-6] and β -[111092-61-6] subunits, which are glycosylated. Free subunits are not biologically active. Unlike hCG β , which has a different genetic code than that for hLH β , only one gene which codes for both eCG β and eLH β appears to exist (38). Accordingly, the amino acid sequence of eCG β and eLH β is identical (31, 39). Equine CG possesses an extremely high carbohydrate content, ie, 38–45% by weight, with N-linked oligosaccharides at Asn-30 β , Asn-56 α , Asn-82 α , and O-linked oligosaccharides within the last 35 C-terminal amino acids (30, 39). The structures of eCG carbohydrate moieties appear to be varied and highly complex; review of this topic offers further detail (34). The approximate contents of hexose, hexosamine, and sialic acid are 15, 14, and 12%, respectively (40). The high content of sialic acid imparts a low isoelectric point, pI, of approximately 2, and a prolonged circulating half-life (41). A half-life of six days has been reported in geldings. In laboratory species, half-lives of 24 hours have been reported.

In nonequine species, eCG exerts both LH and FSH bioactivity (42). This is reflected in the ability of eCG to bind both gonadotropin receptors. Figure 4 shows the ability of eCG purified from pregnant mare serum and endometrial cups to bind with rat, bovine, and equine FSH receptors (40). The structural component of eCG responsible for the expression of FSH activity is contained within the β -subunit, but still remains to be determined. Analysis of eLH, which is identical to eCG (38), has shown that chemical removal of the

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carboxy-terminal peptide does not eliminate FSH bioactivity (43). The prolonged biological half-life and FSH bioactivity make eCG extremely valuable commercially. This hormone is widely used internationally for the induction of superovulation in nonequine livestock. In the United States, Food and Drug Administration licensing has been issued only for the use of eCG in swine, as PG-600 (Intervet, Holland). Equine CG is readily available for research purposes from many suppliers (6, 35).

Names are necessary to report factually on available data; however, the U.S. Department of Agriculture neither guarantees nor warrants the standard of the product, and the use of the name by the U.S. Department of Agriculture implies no approval of the product to the exclusion of others that may also be suitable.

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