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Neuro-Endocrinology of Amphibians and Reptiles: An Overview

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Abstract: This review describes the anatomy and histology of the organs that make up the nervous and endocrine systems in amphibians and reptiles. It also includes the effects of the various substances produced by these organs during the ontogeny of both classes of vertebrates.

Keywords: Amphibians, Reptiles, Nervous system, Endocrine system, Neuroendocrinology, Hormones, Ontogeny, Reproduction, Biology, Calcitonin, Parathyroid hormone, Prolactin, Pineal, Pituitary

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Introduction

In vertebrates, the control of various biological processes, among which reproduction stands out, resides in brain structures with secretory activity: the pineal gland, hypothalamus, and pituitary. The pineal organ or pineal gland produces and secretes, among other substances, melatonin, which acts as a regulator -transducer- of the biological clock of vertebrates. The structure of the brain called the hypothalamus is the region where the nervous and endocrine systems are both morphological and functionally integrated in such a way that the cells that make up this orchestrating center synthesize and secrete hormones (neurohormones).

The other relevant structure in the nervous system (NS) is hypophysis. This gland also called the pituitary gland, is made up of two regions separated anatomically and functionally. The anterior lobe is called adenohypophysis, and the posterior lobe as neurohypophysis. Together, the pituitary produces, stores, and secretes at least ten hormones. The secretion or inhibition of these is due to the action of hypothalamic hormones or factors called releasing hormones or inhibitory

factors, respectively.

On the other hand, the response to the hormones of the NS (pineal, hypothalamus, and hypophysis or pituitary) occurs in the first instance in target tissues of the endocrine glands, standing out for their function at different stages -ontogeny- of the biology of amphibians and reptiles, for example, thyroid, parathyroid, adrenals (interrenal) and gonads. Therefore, the neuroendocrine system links the central nervous system with the endocrine system, and when the effectors of the external and internal environment are transduced, allowing the individual to respond differentially during the ontogeny, based on various physiological processes.

This review focus on how some hormones, both from NS glands and endocrine glands, have effects on the biology of amphibians and reptiles.

Pineal Gland:

Even tough in higher vertebrates it refers to specific structures, the pineal organ, pineal gland, or pineal complex of amphibians and reptiles refers to-(i) an epithalamic structure, the epiphysis, (ii) having a secretory function, or (iii) because there is more than one structure in the epithalamus, respectively (Gorbman *et al*., 1983). The pineal organ -and the parapineal- is an evagination or compaction of the dorsal button of the roof of the diencephalon -epithalamus- communicated with the third ventricle. It has photosensory cells -photoreceptors-, which can form an "eye" (Gorbman *et al*., 1983; Norris, 1997; Bentley, 1998). The main part of the pineal is called the epiphysis or pineal body and the structure is the pineal complex. For this reason, the pineal gland is also called epiphysis. The pineal complex is connected to a structure adjacent to complex support cells - the ependyma - called the subcommissural organ whose ependymal cells produce and secrete a fiber-forming substance, Reissner's fiber. This can extend into the spinal cord, and possibly form part of the cerebrospinal fluid that in amphibians is sensitive to temperature, in addition to containing biogenic amines (e.g. epinephrine and norepinephrine), and in reptiles, it is related to the subcommissural organ with the seasonal secretory activity of corticosteroids and sex steroid hormones (Saarela and Reiter, 1991; Norris, 1997).

The pineal gland consists of neuroglia and secretory cells called pinealocytes. It also receives sympathetic postganglionic fibers from the superior cervical ganglion (Gorbman *et al*., 1983; Delgado and Vivien-Roels, 1989; D'Istria *et al*., 1994; Bentley, 1998; Fernández and Ramos, 2003). In amphibians, particularly anurans, and reptiles, the pineal is connected by a nervous tract to an extracranial frontal organ, on the surface of the skull and below the skin: the parietal parapineal organ (absent in crocodiles) that contains photosensitive cells. In squamous reptiles like lizards and tuatara, *Sphenodon punctatus* (Rhyncocephalia), the parietal eye (or "third eye") is very well developed, containing a cornea, lens, and a cone-like structure connected to the retina (Gorbman *et al*., 1983; Bentley, 1998). The parietal eye acts as a dosimeter for photo-thermal radiation sensing (Norris, 1997).

The pineal has a circadian secretion of the hormone melatonin due to the regulation of the biotransformation of serotonin, therefore, the regulation in the pineal of the synthesis/secretion of this hormone is due to two types of biological clocks: (i) an external one acting via photosensory (circadian-circannual), and (ii) the internal one regulating the neuroendocrine (circadian) function. Melatonin has high-affinity sites -receptors- in brain regions such as the suprachiasmatic nucleus (circadian rhythm regulatory center) and in the midbrain where the hypothalamus is located (a regulatory center that is the internal oscillator of the rhythms of neuroendocrine processes) (e.g. amphibians- Wiechmann and Wirsig-Wiechmann 1993; reptiles- Wiechmann and Wirsig-Wiechmann 1994), as well as in extrahypothalamic regions such as the median eminence, pituitary, and gonads (Cohen *et al*., 1978; Laudon and Zisapel, 1986; Vaněček *et al*., 1987; Tavolaro *et al*., 1995).

Melatonin provides information to various tissues of the body, including other endocrine glands -e.g. thyroid-, giving rise to the idea that the pineal has been considered as a neuroendocrine transducer (Wurtman and Anton-Tay, 1969) sensing temperature and day length = light/dark time = circadian cycle (Reiter, 1986, 1991; Panda *et al*., 2002) and therefore the season of the year (pineal rhythm in amphibians: Rawding and Hutchinson, 1992; Fernández and Ramos, 2003; pineal rhythm in reptiles: Firth *et al*., 1979; Gorbman *et al*., 1983; Underwood and Hyde, 1989).

In anuran tadpoles, pineal homogenates induce paleness (lightens melanocytes) of their skin as a response to melanin aggregation in melanophores. This phenomenon was initially demonstrated by McCord and Allen (1917) in three species of anurans (*Rana pipiens*, *R. cantabridgensis* and *Bufo americana*), and two other animal species. After the characterization of the factor that induces this phenomenon, it was called melatonin by Lerner *et al*. (1958, 1960; taking "mela" for its effect on amphibian melanophores and "tonin" for being a serotonin derivative, Reiter *et al*., 2018).

Melatonin synthesis-secretion can occur in at least three ways: (i) increase in the second half of darkness -scotophase-; (ii) be secreted at the onset of darkness and increase in the middle of scotophase and decrease before the start of the light period, and (iii) increase once the light has ceased and maintain a high concentration during scotophase until shortly before the start of the light period (Reiter, 1991; Norman and Litwack, 1997; Norris, 1997). In such a way that melatonin secretion is also correlated with environmental light conditions and body temperature (Filadelfi and Castrucci, 1996; Lutterschmidt *et al*., 2003).

Melatonin is a powerful antioxidant and like other hypothalamic neuropeptides, it is related to energy balance and acts as a regulator of body temperature (Lutterschmidt *et al*., 2003; Navarro *et al*., 2006). Therefore, animal species at night, during cold spells, or in hibernation can cope with the physiological state of ischemia and thus modulate the overnight metabolism (MacNab, 2002).

Melatonin has also been shown to participate in metamorphosis (Wright, 2002), causes inhibition of thyroid function via TRH (Gordon *et al*., 1980; Sakamoto *et al*., 2000), and affects the action of ACTH by increasing the secretion of adrenocorticoids -corticosteroids- (Norman and Litwack, 1997; Norris, 1997), in addition to being able to have a negative effect on reproductive biological functions. In this sense, *in vivo* and *in vitro* studies have shown that melatonin alone or in conjunction with other metoxindoles and neuropeptides like de pineal-derived AVT (Pavel, 1978; Norris, 1997), inhibits GnRH and gonadotropin secretion, affecting both male and female gonadal function to produce gametes and sex steroids hormones that have been shown to be negatively affected also to temperature (amphibians: Alonso-Bedate *et al*., 1988, 1990; Delgado and Vivian-Roels, 1989; Paniagua *et al*., 1990; Udaykumar and Joshi, 1997; d´Istria *et al*., 2003, 2004; Izzo *et al*., 2004; reptiles: Haldar-Misra and Thapliyal, 1981; Haldar and Pandey, 1988, 1989; Lutterschmidt *et al*., 2002; Seebacher and Franklin, 2005).

Hypothalamic Hormones:

The hypothalamus, which can be considered a "non-classical" endocrine organ (Ojeda and Griffin, 1992), is an orchestrating center that receives nerve impulses from other regions of the brain such as the limbic system, the cerebral cortex, the thalamus, and the spinal cord of reticular activation, as well as external and internal sensory signals. It contains two main types of neurons: (i) those that transmit nerve impulses and (ii) those that have a neurosecretory function. The latter can be regulated by substances such as paracrine and/or autocrine nitric oxide (NO) controlling their secretion as well as other specific ligands. Some of these neurons in the hypothalamus produce and secrete neurotransmitters -amines- such as acetylcholine, dopamine, norepinephrine, serotonin, histamine, and gamma-aminobutyric acid (GABA). Other neurons secrete peptides such

as arginine vasopressin (AVP) or oxytocin, as well as peptides with a releasing (or inhibitory) function, as is the case of some members of the RF-amide peptides superfamily like GnIH/RFRP and kisspeptin. These amines act as hormones or factors for the release of adenohypophyseal hormones or even act as hormones in extrahypophyseal tissues, as is the case of gonads. This group of peptide hormones includes- (i) growth hormone-releasing hormone (GHRH); (ii) somatostatin or growth hormone-inhibiting hormone (GHIH); (iii) thyroid-releasing hormone or thyrotropin (TRH); (iv) prolactin-releasing hormone (PRH) and prolactin-inhibiting hormone (PIH); (v) corticotropin-releasing hormone (CRH), and (vi) gonadotropin-releasing hormone (GnRH).

The secretion of these hormones is in response to both external environmental factors (exteroceptive stimuli), and internal factors of the individual or interoceptive stimuli (Bentley, 1998). Exteroceptive stimuli include light, climatic stimuli such as temperature, dryness-humidity, atmospheric pressure, and those inherent to the acquisition of food and water, as well as those related to territory defense and mating events. On the other hand, interoceptive stimuli are those that evoke physicochemical changes in the homeostasis of the internal environment of the individual, ranging from those that influence the intermediary metabolism to those related to neuroendocrinology. The interoceptive stimuli are linked to the exteroceptive ones due to the circannual changes, and together, give the guidelines for the life cycles of the animal species to be carried out.

Growth hormone-releasing hormone (*GHRH*):

It has been identified in vertebrates (Gorbman *et al*., 1983; Norris, 1997; Montero *et al*., 2000). In humans, it is known that a gene for GHRH -or somatocrinin or somatoliberin- codes for a mature 45 amino acid-long protein, whereas the one for salmon has 38 residues (Miyata *et al*., 1989; Norris, 1997; Bentley, 1998). In *in vitro* pituitary assays, both polypeptide chains can activate adenylate cyclase, hence, its acronym PACAP (pituitary adenylate cyclase-activating peptide) (Rawlings and Hezareh, 1996). In the anuran *Rana ridibunda,* PACAP promotes the release and modulates the response of growth hormone (GH), as well as corticotropin and luteinizing hormone *in vitro* (Chartrel *et al*., 1991; Bentley, 1998). In addition to the hypothalamus of anurans, a peptide of the RFamide family has been isolated that causes GH secretion in the pituitary (Koda *et al*., 2002; Ukena *et al*., 2003).

Somatostatin:

Originally identified in the mammalian hypothalamus as having an inhibitory activity on growth hormone release, thus also given the name growth hormone-inhibiting-releasing hormone (GH-R-RH; GHRIH or SS) and is currently called somatostatin. It has been identified in the brain of several vertebrate species. In amphibians, it is located as a fully functional peptide of 14 aa residues in the preoptic nucleus and pars nervosa (King and Millar, 1979 a; Norris, 1997; Bentley, 1998).

Thyrotropin-releasing hormone (*TRH*):

This tripeptide has been identified in the hypothalamus of amphibians and reptiles (Licht and Papkoff, 1985; Mimnagh *et al*., 1987). In anurans, it has been detected in the skin, pineal, neurohypophysis, and spinal cord. It has also been suggested that probably it could act as a neurotransmitter and neuromodulator (Jackson and Reichlin, 1974; Roseghini *et al*., 1989; Norris, 1997; Bentley, 1998). In reptiles, it is in the septum and median eminence, hypothalamic paraventricular and periventricular nuclei, amygdala, and retina (Mimnagh *et al*., 1987; López *et al*., 2008). Hypothalamic neurons secreting norepinephrine stimulate TRH release, and dopamine-secreting neurons inhibit this release (Norris, 1997). In non-mammals, the effect of TRH has been both hard to identify and diverse due to its different functions, for example, in the anuran pituitary, it promotes the release of growth hormone and prolactin instead of their respective releasing factors (Gorbman *et al*., 1983; Harvey,

1990; Castano *et al*., 1992, 1993; Nakajima *et al*., 1993; Norris, 1997; Bentley, 1998). Isolated or synthetic TRH *in vivo* and *in vitro* stimulates the release of TSH and PRL, and therefore the secretion of thyroid hormones (MacKenzie *et al*., 1981; Kuhn *et al*., 1985; Seki and Kikuyama, 1986; Malagon *et al*., 1989; Castano *et al*., 1992; Jacobs and Kuhn, 1992; Norris, 1997; Akgun-Dar *et al*., 2004; Okada *et al*., 2004). In amphibians and reptiles, corticotropin-releasing hormone (CRH) is the hormone that mainly causes TSH secretion (Norris, 1997).

Prolactin-releasing hormone (*PRH*):

In amphibians, the secretion of prolactin (PRL) is regulated in the hypothalamus by a TRH stimulator and a dopamine inhibitor (Norris, 1997). In reptiles, a PRL-stimulating neurohormone has been documented (Fiorindo, 1980). In anurans, the TRH causes an increase in PRL in the blood (Kuhn *et al*., 1985; Castano *et al*., 1992; Nakajima *et al*., 1993; Akgun-Dar *et al*., 2004), and pimozide, a dopaminergic antagonist, increases the PRL systemic concentration, whereas bromocliptin, a dopaminergic agonist, decreases it. (Kikuyama *et al*., 2003).

Temperature acts on PRL secretion and can be mediated by TRH. At low temperatures, there is a dominant stimulatory control in the synthesis and secretion of PRL while at high temperatures the inhibitory control predominates. This pattern is found in urodeles; in *Triturus carnifex* during the winter PRL secretion increases while in *Cynops pyrrhogaster* it decreases in summer (Kikuyama *et al*., 2003). In male urodeles, pituitary PRL mRNA and blood-plasma PRL increases in February coincidently with low temperatures and their reproductive season whereas in May, a nonreproductive season characterized by higher temperatures, PRL mRNA and systemic levels are low. Keeping males at a low temperature (4 °C) for an additional month after the reproductive season increases PRL-mRNA levels but not plasma PRL content. These data indicate that temperature is an epigenetic regulator of prolactin production-secretion (Kikuyama *et al*., 2003).

Corticotropin-releasing hormone (*CRH*):

It has been identified in several vertebrates (Lederis, 1987; Stenzel-Poor *et al*., 1992; Bentley, 1998), as well as two corticotropin-releasing hormones (or factor) receptors, CRFR1 and CRFR2, cloned from cDNA of the anuran hypothalamus of *Rana castebeiana*; CRF1 is located exclusively in the brain and pituitary, and CRFR2 in peripheral tissues and brain and pituitary (Ito *et al*., 2006). CRH is made up of 41 aa and bears similarity to a neuropeptide called sauvagine isolated from anuran skin (Bentley, 1998). In amphibians and reptiles, CRH inhibits LH release, activates corticotrophs for ACTH (corticotropin) and/or vasotocin (VT or AVP) secretion, and TSH secretion in thyrotrophs (Jacobs and Kuhn, 1992; Kikuyama *et al*., 2003). CRH in the interrenal gland stimulates the secretion of corticosterone and aldosterone (Norris, 1997; Kikuyama *et al*., 2003). Steroid hormones modulate the metamorphosis induced by thyroid hormones -which can be regulated by CRH- either antagonistically or synergistically depending on the stage of development. Therefore, CRH acts as a modulator of metamorphosis (Kikuyama *et al*., 2003). Another aspect to consider is that corticosteroids like corticosterone, are involved in responses to stress; therefore, the CRH during stress would be a regulator in its own synthesis and secretion. In addition to increasing the secretion of CRH during stress conditions, it would cause the alteration of reproduction via the gonadotropin inhibitory pathway (Norris, 1997; Bentley, 1998).

Gonadotropin-releasing hormone (*GnRH*):

GnRH, also called LH-releasing hormone, luteinizing hormone (LHRH), LH/FSH-RH, or luliberin because it was first studied in the release of these gonadotropins, is a family of decapeptides made up of ten variants or isoforms: lamprey (lGnRH I and lGnRH III); fish: catfish (cGnRH), dogfish (dgGnRH), and salmon (sGnRH); chicken (cGnRH I and cGnRH II), and mammal (mGnRH in two isoforms GnRH I and GnRH II) (King and Millar, 1979 b, 1980; Sherwood and Sower, 1985;

Sherwood *et al*., 1986, 1993; Demski, 1987; Norris, 1997; Bentley, 1998; Neill *et al*., 2001; Kikuyama *et al*., 2003). This decapeptide, in addition to acting as a hormone, has also action as a neurotransmitter or neuromodulator (King and Millar, 1980; Licht *et al*., 1987, 1994; Norris, 1997). Its ontogeny has been described profusely in amphibians (Crim, 1985; Muske and Moore, 1990; Northcutt and Muske, 1994; D´Aniello *et al*., 1995; Di Fiore *et al*., 1996; Somoza *et al*., 1996; Rastogi *et al*., 1998; Forlano *et al*., 2000; Yuanyou and Haoran, 2000), and reptiles (D´Aniello *et al*., 1994).

Localization in the hypothalamus of GnRH isoforms has been widely described in amphibians and reptiles. In both classes of vertebrates, some neurons can have one, two -or even three- isoforms, characteristic of the species and, as we will describe later, have different functions (amphibians: Lovejoy *et al*., 1991; Muske and Moore, 1994; Bentley, 1998; Kikuyama *et al*., 2003; reptiles: Powell *et al*., 1986; Sherwood and Whittier, 1988; Masucci *et al*., 1992; Tsai and Licht, 1993 a, b; Lescheid *et al*., 1997; Montaner *et al*., 2000; Ikemoto and Park, 2003).

In amphibians (urodeles, anurans, and caecilians), GnRH has been demonstrated, mainly, of at least two of the following three isoforms: sGnRH, cGnRH II, and mGnRH (Conlon *et al*., 1993; Collin *et al*., 1995; Di Matteo *et al*., 1996; Miranda *et al*., 1998; Kikuyama *et al*., 2003), and in reptiles, they are cGnRH I and/or II (Powell *et al*., 1986; Sherwood and Whittier, 1988; Masucci *et al*., 1992; Lescheid *et al*., 1997).

In male *Rana esculenta*, the interannual profile of cGnRH II and mGnRH content in the brain, pituitary, and nasal tissue has been determined (Rastogi *et al*., 1997), as well as in *Rana pipiens*, *R. esculenta* and *R. ridibunda*, the sGnRH, cGnRH II and mGnRH isoforms have been found in different concentrations (Licht *et al*., 1994).

In the urodele *Triturus carnifex*, cGnRH II is localized in the nerve terminal, anterior preoptic area, and preoptic nucleus, as well as in spermatocytes, spermatozoa, and theca externa cell layer (Battisti *et al*., 1997). It has also been detected in oocytes and granulosa cells from *Rana esculenta* (Battisti *et al*., 1994). In general, mGnRH localizes to the telencephalon, median septal nucleus, ventral preoptic area of the anterior hypothalamus toward the infundibulum, and system of the terminal nerve -septo- preoptic. On the other side, cGnRH II in four species of *Triturus* and two Genera (*Ambystoma* and *Salamandra*), is located in the midbrain (posterior diencephalon), paraventricular and periventricular organ of the posterior tubercle, and infundibulum (Muske *et al*., 1994; Kikuyama *et al*., 2003). In addition, GnRH stimulates the biosynthesis of gonadotropins in the pituitary in anurans (*Rana pipiens* -Stamper and Licht, 1990, 1993 1994). Experimentally, when GnRH (LHRH) is injected into the intraparaventricular zone in *Taricha granulosa* males, it regulated sexual behavior and stimulated androgen secretion (Moore *et al*., 1982).

In *Rana esculenta* cGnRH II and mGnRH are localized to neurons and fibers in the area nasal, anterior preoptic area, mid-septal area, dorsal caudal preoptic region, and the median eminence whereas sGnRH is in the dorsal region, mGnRH in the dorsal part of the preoptic region and the median eminence, and cGnRH II in interstitial cells of the testis and germinal compartment (Cariello *et al*., 1989; Battisti *et al*., 1994; D´Aniello *et al*., 1995; Di Matteo *et al*., 1996; for *Bufo arenarum* Miranda *et al*., 1998, *Pachymedusa dacnicolor* Iela *et al*., 1991, 1996; *Rana ridibunda* Conlon *et al*., 1993; Collin *et al*., 1995). In the brain of *Pachymedusa dacnicolor*, there are sGnRH, cGnRH II, and mGnRH, located in the anterior preoptic area, infundibulum, and median eminence (Iela *et al*., 1991, 1996). Evaluation of the contents of mGnRH and cGnRH during larval development, metamorphosis, and before the reproductive activity of *Rana sculenta*, allowed for ascertaining their profiles in the brain, pituitary and nasal area (Di Fiore *et al*., 1996).

In the caecilian *Typhlonectes natans* - a

viviparous species - mGnRH is predominantly in the septum-preoptic area and a few bodies in the lateral hypothalamus and ventral thalamic eminence. For its part, cGnRH is in the dorsal hypothalamus, ventral thalamus of the midbrain tegmentum. sGnRH is not located in the neural bodies of the terminal field (Ebersole and Boyd, 2000).

In addition to the fact that in amphibians some isoforms of GnRH are located in the nervous system -the hypothalamus, pituitary, neurons of the nasal cavity, and in the spinal cord and sympathetic ganglia (Lascar *et al*., 1996; Troskie *et al*., 1997; Chartel *et al*., 1998 a, b;), it can be detected in the interstitial cells and spermatocytes and spermatozoa of the testis; theca interna and granulosa cells, and perinuclear zone of oocytes, and the placenta (Cariello *et al*., 1989; Di Matteo *et al*., 1990, 1996; Fasano *et al*., 1990; Battisti *et al*., 1994, 1997; Kikuyama *et al*., 2003).

In reptiles, the isoforms have been localized in various brain regions such as the anterior and medial preoptic area, hindbrain, and cerebellum (Masucci *et al*., 1992), as well as in the spinal cord (Bennis *et al*., 1989, 1998; Chartrel *et al*., 1998 a, b). Brain distribution of cGnRH I is similar for amphibians, birds, and mammals (Smith *et al*., 1997). In the freshwater turtle *Trachemys scripta*, this isoform prevails in the median eminence (more in females than in males) while cGnRH II is in regions of the caudal brain, especially the cerebellum and spinal cord (more in adult females than in juveniles) (Tsai and Licht, 1993 a, b). In saurians, there is only cGnRH II in their hindbrain e.g. hypothalamus (Lescheid *et al*., 1997), and in snakes (*Thamnophis sirtalis parietalis*), there is only cGnRH I (Smith *et al*., 1997).

The fact that there are isoforms of GnRH and they have a different distribution in the NS of vertebrates, indicates that they have particular functions (e.g. Kaiser *et al*., 1997; Kauffman, 2004), which may depend on the season of the year when reproduction takes place (Fasano *et al*., 1995). In amphibians, mGnRH, considered to be the main regulator of gonadotropin release, is found mainly in the hypothalamus (Miranda *et al*., 1998; Yuanyou and Haoran, 2000), and cGnRH II, which is located essentially in the midbrain and posteriorly, it would play a neuromodulatory role and since this isoform is in the sympathetic ganglion, it would participate as a neuro-transmitter (Troskie *et al*., 1997; Yuanyou and Haoran, 2000). In addition to this, there is the fact that the isoforms cGnRH I and II and mGnRH in amphibians stimulate the secretion of both LH and FSH in the adenohypophysis, but GnRH III stimulates only the secretion of FSH (Kikuyama *et al*., 2003). But when assessing the levels of GnRH isoforms and their relationship with the pituitary and the circulating content of testosterone, it has been found that in *Rana esculenta*, cGnRH II -and sGnRH and mGnRH- have hypophysiotropic activity, favoring the steroidogenesis of androgens (D'Antonio *et al*., 1992; Fasano *et al*., 1993, 1995), and mGnRH acts as a neurotransmitter and/or neuromodulator (Fasano *et al*., 1995).

In reptiles, the mGnRH isoform sGnRH and cGnRH I that are located in the median eminence are considered to be responsible for the secretion of gonadotropins, whereas the cGnRH II, located extrahypothalamically in the olfactory region, acts as neurotransmitter or neuromodulator (Norris, 1997).

On the other hand, in amphibians and reptiles, GnRH, is in the terminal nerve that innervates the epithelium of the nasal cavity and fibers of the palatine ganglion that do so with the constrictor nasalis muscle that when secreted in response to odors and pheromones via the vomeronasal organ, would act as a neuromodulator along with other neuropeptides and AVT, causing specific responses of individuals during reproductive events as is the case of the sounds emitted during courtship and amplexus in amphibians (Wilczynski *et al.*, 1993; Wirsig-Wiechmann 1993; Dawley and Crowder, 1995; Propper and Dixon, 1997; Kawamura and Kikuyama 1998; Wirsig-Wiechmann and Ebadifar 2002; Ford *et al*., 2003, 2004; Kikuyama *et al*., 2003; Park *et al*., 2003; Burmeister and Wilcynski, 2005), and reptiles

(Rosen *et al*., 1997).

GnRH can also control the movements of the oculomotor muscle and the vestibular nucleus that have a role in the reproductive behavior of saurians (Rosen *et al*., 1997), as well as stimulate the development of steroidogenic interstitial tissue and spermatogonia in amphibians as evidenced by the regulation of the cFos-oncoprotein pathway (Minucci *et al*., 1986, 1992; Moya *et al*., 1987; Fasano *et al*., 1988; Cobellis *et al*., 2003). It has also been shown that in amphibian gonads, a GnRH-like molecule regulates the testicular function in a paracrine cycle (Di Matteo *et al*., 1990; Minucci *et al*., 1996). As a partial conclusion, it has been shown that there are two different GnRH peptides (GnRH I and GnRH II) that regulate different functions. GnRH I regulates the secretion of gonadotropins and GnRH II regulates the processes in those areas related to sexual behavior.

GnRH receptors are members of the G protein-coupled protein superfamily that act via adenylate cyclase/protein kinase A (AC/PKA) or phospholipase C/protein kinase C (PLC/PKC) (Neves *et al*., 2002), in addition to being able to be desensitized or sequestered by cellular internalization (Bentley, 1998; Troskie *et al*., 1998; Hislop *et al*., 2000, 2005; Millar, 2003; Pawson *et al*., 2003; Millar *et al*., 2004; Caunt *et al*., 2006). Based on the presence of at least two GnRH, two subtypes of receptors have been identified as type I and II, respectively (Troskie *et al*., 1997, 1998; Millar, 2003).

In amphibians, three receptors have been identified in various cell types designated bfGnRHR-1, bfGnRH-2, and bfGnRH-3 from the bullfrog *Rana castebeiana*; the type bfGnRH-2 act through the PKA signaling pathway whereas the types 1 and 3 act through the PKC signaling, so they have different cellular and physiological responses. It has been documented that their stimulatory effects are quickly desensitize and the receptors are removed by enter into the target cell (Fasano *et al*., 1990; Troskie *et al*., 2000; Hislop *et al*., 2000, 2005; Wang *et al*., 2001 a, b; Archarjee *et al*., 2002; Oh *et al*., 2003; Maiti *et al*., 2003; Finch *et al*., 2004; Morgan and Millar, 2004; Sedgley *et al*., 2006). Additionally, the presence of its receptor in different tissues of the gonad in the testicles of *Rana esculenta* has been shown by inducing GnRH-mediated steroidogenesis and spermatogenesis (Di Matteo *et al*., 1988). In reptiles, especially in several cell types of the gecko *Eublepharis macularius*, the GnRH receptor has been characterized (Ikemoto *et al*., 2004).

RF-amide peptides:

In recent years a group of neuropeptides has gained relevance in animal reproductive biology, the RF-amide peptide superfamily. Once the "peak C" cardioexitator peptide was purified and sequenced as phe-met-arg-phe from the cerebral ganglion of the mollusk *Macrocallista nimbosa*, was called FMRFamide (Price and Greenberg, 1977). From this discovery, structurally similar neuropeptides have been identified in various animal species, which together are called FMRFamide-related peptides (FaRPs) or FMRFamide-like peptides (FLPs).

GnIH:

In vertebrates, the first member of the RF-amide (RFa) family was isolated and sequenced from the chicken brain (Dockray *et al*., 1983). Subsequently, when a neuropeptide with an RFa motif at the terminal carboxyl end corresponding to that of the chicken was isolated and characterized from the quail brain, it inhibited *in vitro* the release of LH in the quail adenohypophysis. The neuropeptide was named gonadotropin-inhibitory hormone, GnIH (Tsutsui *et al*., 2000), and its receptor was later identified (Yin *et al*., 2005).

In amphibians, an RF-amide peptide with high similarity to quail's GnIH was isolated from the hypothalamus of *Rana catesbeiana* (Koda *et al*., 2002). In this case, this neuropeptide had growth hormone-releasing activity (GH) and therefore was named frog GH-releasing peptide or fGRP (Koda *et al*., 2002). There are three putative peptides related to the fGRP neuropeptide: fGRP-RP1; fGRP-RP2 and fGRP-RP3, all four

neuropeptides have a common carboxy-terminal LPXRFamide with avian and mammalian GnIH (Sawada *et al*., 2002; Ukena *et al*., 2003); LPXRFamide corresponds to the group of genes in mammals for RF-amides called farp (Tsutsui *et al*., 2018). The neuropeptides fGRP and fGRP-RP2 *in vitro* and *in vivo* stimulate the release of GH and/or prolactin (PRL), whereas fGRP-RP1 and fGRP-RP3 have no effect (Ukena *et al*., 2006), and none of the four affect the release/inhibition of gonadotropins (Ukena *et al*., 2003). The location of fGRPs in the amphibian brain is mainly restricted to the periventricular region of the hypothalamus (Koda *et al*., 2002; Pinelli *et al*., 2015). The presence of GnIH, nLPXRFa-1, nLPXRFa-2, nLPXRFa-3 y nLPXRFa-4 in areas of the brain such as the suprachiasmatic nucleus of *Cynops pyrrhogaster*, has been demonstrated (Chowdhury *et al*., 2011).

In reptiles, three GnIH neuropeptides (GnIH, GnIH-RP-1, and GnRH-RP-2) have been characterized in the tortoise *Trachemys scripta elegans* (Ukena *et al*., 2016), the Chinese softshell turtle (*Pelodiscus sinensis*) and the anole lizard (*Anolis carolinensis*). They all possess the common carboxy-terminal LPXRFamide motif, like the avian and mammalian peptides (Osugi *et al*., 2014; Tsutsui *et al*., 2018). Cerebral localization of GnIH has been reported in the lizard *Takidromus tachydromoides* (Kawano *et al*., 2006) and in the tortoise *Trachemys scripta elegans* (Ukena *et al*., 2016). In the lizard *Calotes versicolor*, GnIH has been located in the ovary in addition to repressing the expression of the GnRH receptor in the gonad (Singh *et al*., 2008).

KiSS peptides:

Another of the RFa superfamily neuropeptides of current importance in animal reproductive biology is kisspeptin. Lee *et al*. (1996) identified a metastasis suppressor gene for melanoma cells and named it KiSS-1. This name was given because the Institute to which the authors belong is in the city of Hershey, Pennsylvania, where the famous chocolate fudge kiss is made. The KiSS-1 gene encodes a 54-amino acid peptide which may be further processed into shorter peptides of 13 and 14 amino acids all designated as kisspeptins and the 54 aa residues peptide was also named metastin (Kotani *et al*., 2001; Ohtaki *et al*., 2001). The 10-amino acid carboxy-terminal fragment of kisspeptins (or kiss peptides) carries the biological activity (Kotani *et al*., 2001). It was later discovered that kisspeptin was involved in some reproductive biology processes, for example, the inactivation of kisspeptin receptor (GPR54) leads to hypogonadotropic hypogonadism in human patients (de Roux *et al*., 2003). Anomalies were found in the development of genitalia and gonads of both male and female mice (Funes *et al*., 2003; d´Anglemont de Tassigny *et al*., 2007), as well as in the regulation of GnRH during puberty and sexual maturation in humans and mice (Seminara *et al*., 2004). Mutations leading to higher resistance of kisspeptin to degradation or prolonged activation of GPR54 can induce precocious puberty onset in humans (Teles *et al*., 2008; Silveira *et al*., 2010).

The kisspeptin system (ligand and receptor) is a stimulator of the gonadotropic axis via the induction of GnRH in rodents, sheep, and primates. In most mammals, Kisspeptin-10 (KiSS-10 o Kp-10) can stimulate LH and FSH as has been documented for rodents (Matsui *et al*., 2004; Thompson *et al*., 2004; Messager *et al*., 2005; Navarro *et al*., 2005), bovine and porcine (Suzuki *et al*., 2008), ovine (Smith *et al*., 2008), and baboons (Luque *et al*., 2011).

Three KiSS genes have been evolutionarily characterized: KiSS1, KiSS2, and KiSS3 altough their numbers and type varies; in coelacanths, there are 3 genes; in amphibians up to 3 genes. In sauropsid reptiles, data are contrasting since whereas some authors are not able to found any Kiss gene, others found 1 or 2 genes. No rodents mammals have 1 or 2 genes (Dufour *et al*., 2020). Regarding the kisspeptin receptor (KissR) gene, there have been isolated three forms from amphibians, and one or two in sauropsid reptiles (Pasquier *et al*., 2014).

In amphibians, the Kisspeptin GPR54 receptor gene was expressed in the pituitary, spinal cord,

ovary, and testes of *Rana sculenta* (Chianese *et al*., 2013). The KiSS1 and GPR54 genes were expressed in the testes in *Pelophylax sculentus*, during their annual sexual cycle (Chinease *et al*., 2017). When analyzing the effect of Kisspeptin on gonadal function in *Rana esculenta*, it has been shown that treatment with KiSS-10 *in vitro* induced in the testis the expression of both the GPR54 receptor gene and of the alpha gene for the estrogen receptor (ERα; Chianese *et al*., 2013). *In vivo* and *in vitro* studies on testicles of the frog *Pelophylax sculentus*, have shown that estradiol stimulates the expression of KiSS-1 and GPR54, and Kp-10, in an exposure time. It also stimulates steroidogenic enzymes and increases the expression of testicular ERβ, GNRH 1 and 2, and its three types of receptors, rendering a global spermatogenesis regulation effect (Chianese *et al*., 2015, 2017).

In the lizard *Uta stansburiana*, intracoelomic treatment with Kisspeptin (KiSS-10) increases circulating testosterone, which correlates with their behavior (aggression) (Neuman-Lee *et al*., 2017).

Monoamines:

Nonpeptidic neurotransmitters such as monoamines (catecholamines, indolamines, and histamine), acetylcholine, and amino acids (glutamic acid and GABA) may also play a somewhat prominent role in the neuroendocrine control of reproduction (Barraclough and Wise, 1982).

Dopamine:

Dopamine is released from hypothalamic neurons in the arcuate nucleus and as a neurohormone by the paraventricular hypothalamus, which under physiological conditions increases the hypothalamus-portal-pituitary circulation causing pituitary inhibition of PRL secretion (Norris, 1997). Dopamine acts as a reproduction inhibitor in vertebrates, differentially conserving its role throughout evolution. The consensus is that the prolactin-inhibiting hormone (PRIH) is the catecholaminergic neurotransmitter dopamine (DA) since its inhibitory effect has been demonstrated *in vivo* and *in vitro* (Norris, 1997; Bentley, 1998). For example, in anurans, dopamine decreases the blood concentration of PRL (Seki and Kikuyama, 1986). In the frog *Rana temporaria*, lesions of the infundibular hypothalamus in hibernating preovulatory females cause advanced ovulation and an increase in circulating levels of GnRH and LH (Sotowska-Brochocka, 1988; Sotowska-Brochocka and Licht, 1992). This effect is mimicked by a dopaminergic antagonist and blocked by the administration of a dopaminergic agonist (Sotowska-Brochocka *et al*., 1994). The inhibitory effects of dopamine on reproduction are conserved in amphibians. For instance, in *Rana sylvatica* injection of quinpirole in females delays or inhibits oviposition (Vu and Trudeu, 2016). Coinjection of a GnRH agonist and the selective dopamine receptor D2 antagonist metoclopramide induces the release of sperm and eggs in several anurans and salamanders. This treatment has been known also as "the AMPHIPLEX method"; a derivative term from the combination of the words amphibian and amplexus (Trudeu *et al*., 2010, 2013).

Pituitary Hormones:

The pituitary gland (from Latin *pituita*, mucus), is formed from the ingrowth of brain tissue, the infundibulum, and by a raising of the roof of the mouth. Two anatomically and functionally independent regions are distinguished in the pituitary gland, the neurohypophysis, and the adenohypophysis. The posterior lobe of the hypophysis or neurohypophysis in tetrapods is made up of three regions: the median eminence or rostral part, the infundibular stem -the middle part- and the most prominent, the pars nervosa or neural lobe (Bentley, 1998). These three regions have axon terminals from neurosecretory cells of the hypothalamus and pituicytes cells that do not synthesize hormones but do store and release at least 12 peptides (Gorbman *et al*., 1983; Bentley, 1998); in amphibians and reptiles, the antidiuretic hormone (ADH) or vasotocin (VT) is somewhat important. These hormones are synthesized in the

neuronal perikaryon located in the paraventricular and supraoptic or preoptic nuclei of the hypothalamus in amphibians, whose axons form the hypothalamic-pituitary bundle that begins in the hypothalamus and ends near the blood capillaries of the neurohypophysis.

Adenohypophyseal Hormones:

The cells that produce and secrete hormones (from Greek *hormô*, excite or stimulate) (Stárka and Dušková, 2020) in this organ are called trophic cells -except those that produce GnRH in the hypothalamus = gonadotropes or gonadotrophs-, their products being called tropic substances or tropins because they act on other glands, for example, endocrine glands. The seven main tropic hormones that are produced and secreted by the five cell types of the anterior lobe of the amphibian and reptile pituitary are: in the pars distalis MSH -and endorphins-, and in the pars intermedia somatotropin, thyrotropin, prolactin, corticotropin, and gonadotropins (Naik *et al*., 1980; Gorbman *et al*., 1983; Bentley, 1998). In vertebrates, the ontogeny of the cell types that make up the adenohypophysis has been described (Saga and Yamaki, 2006).

Growth hormone or somatotropin:

This hormone -GH or hGH to refer to humans- is produced and secreted by somatotrophs. GH has been isolated from amphibians (being similar to that of humans) and, together with PRL, vitellogenin synthesis is induced in the female liver (Norris, 1997), and participates in reproduction (Polzoneti-Magni *et al*., 1995). GH in reptiles has been obtained and sequenced from the caudal lobe of the pituitary and stimulates growth and appetite (Yasuda *et al*., 1989; Norris, 1997).

In amphibian pituitary, growth hormone and PRL secretion are stimulated by TRH (Castano *et al*., 1992, 1993), POMC (N-terminal peptide of proopiomelanocortin), and ACTH (Aida *et al*., 1999), as well as by a neuropeptide RFamide (Koda *et al*., 2002; Ukena *et al*., 2003).

Through somatocrinin, or somatostatin inhibition, secreted GH acts indirectly on tissues by stimulating the synthesis and secretion of protein hormones called insulin-like growth factors (IGFs). These can be delivered into the bloodstream or act locally in the tissues as autocrine or paracrine substances. Therefore, IGFs are hormones that stimulate general body growth and regulate certain aspects of metabolism.

Thyroid-stimulating hormone (*TSH*) *or thyrotropin*:

Produced and secreted by follicular cells called thyrotrophs, this hormone in the thyroid regulates the secretion of thyroxine (T4 or T_4) and triiodothyronine (T3 or T_3). The effect of TSH from various vertebrates has been studied on the thyroid gland of amphibians and reptiles (Mackenzie and Licht, 1984). In *Chelonia mydas* and *Chelydra serpentina* the TSH isolated from the pituitary is like that of mammals (bovine) (Mackenzie *et al*., 1981). The effect of various neuropeptides, such as somatostatin on TSH secretion, has also been reported (Okada *et al*., 2006).

Prolactin (*PRL*):

It is a multifunctional hormone of the pituitary gland and has therefore been given various names, for example, ubiquitin or versitilin (Nicoll and Bern, 1972; Norris, 1997). As already mentioned, its positive and negative regulation is given by TRH and dopamine, respectively.

In amphibians, PRL and its receptor have been isolated in urodeles and anurans in the abdominal gland and kidney, and detected by RT-PCR, in the brain, liver, bladder, ovary and testis, olfactory epithelium, epidermis, intestine, tail (Kato *et al*., 1997; Kikuyama *et al*., 2000). In anuran gonadotrophs, it stimulates the secretion of gonadotropins (Oguchi *et al*., 1997). As in mammals, this protein has a powerful activity in stimulating the synthesis of collagen, increases blood Ca^{2+} concentrations, as well as having a significant effect on sodium transport in the integument and therefore in the homeostasis of ionic osmoregulation (Loretz and Bern, 1982; Brown *et al*., 1991; Kikuyama *et al*., 2003;), and

activity in reproduction (Polzonei-Magni *et al*., 1995).

In the liver, alone or together with estrogens, they control the synthesis and secretion of vitellogenin (Carnevali *et al*., 1992, 1993), induce the migration of urodeles towards the water during their mating and oviposition period, and therefore, it regulates glandular activity in their skin so that whereas the animal is in the water, it is smooth and slimy and when is out of the water, it is rough and less mucous (Bentley, 1998). In male urodeles, PRL together with gonadotropins and androgens, stimulate Mauthner cells located in the VIII cranial nerve of the medulla oblongata and causes tail vibration, a behavior characteristic of the mating season (Kikuyama *et al*., 2003).

Epithelial cells of the dorsal gland express the PRL gene and the androgen receptor indicating that these glands are regulated by PRL and androgens and stimulating the production-secretion of the pheromone soderphine in the dorsal gland (abdominal gland) of the cloaca. The pheromone would trigger the mating behavior by stimulating the sensory olfactory epithelium via the vomeronasal cavity (Kikuyama *et al*., 2003). On the other side, in the lateral gland (equivalent to the ventral gland) of the cloaca, PRL, and androgens stimulate the production and secretion of acidic mucopolysaccharides, such as hyaluronic acid and chondroitin sulfate, as well as substances that make up the structural development of spermatophores (Kikuyama *et al*., 2003). In oviductal cells, PRL *per se* or together with estradiol, stimulates the production and secretion of the jelly coat, a mucopolysaccharide-rich gelatinous layer that covers the oocytes ("eggs"). PRL and androgens stimulate the oviduct to release male attracting substances (Kikuyama *et al*., 2003).

In amphibian urodeles, PRL causes tail growth in both larvae and adults, in addition to stimulating the growth of larvae but inhibiting their metamorphosis induced by thyroid hormones (Kikuyama *et al*., 2003; Denver, 2013). Therefore, prolactin increases metamorphic climax by antagonizing thyroid hormones (T3 and T4) and thus regulating the sequence of morphogenetic changes of metamorphosis (Kikuyama *et al*., 2003).

In reptiles, the PRL and its receptors have been located (Licht and Nicoll, 1969; Kato *et al*., 2005), isolated, and sequenced in the brain (Chang and Papkoff, 1985; Yasuda *et al*., 1990). In this organ, it has been shown that it acts as a neurohormone that stimulates its secretion (Fiorindo, 1980). The PRL regulates vitellogenin production (Callard *et al*., 1990), stimulates growth, and increases appetite (Licht and Jones, 1967).

Adrenocorticotropic hormone (ACTH), adrenocorticotropin or corticotropin:

After CRH stimulation, ACTH is produced and secreted by corticotrophic cells. CRH in amphibians is an effective releaser of ACTH, participating in the metamorphosis process (Miranda *et al*., 2000). However, it has not been demonstrated in reptiles (Norris, 1997). ACTH in the adrenals regulates the production and secretion of both glucocorticoids and mineralocorticoids. Other stimuli for ACTH secretion are those related to the stress process, for example, hypoglycemia, and interleukin 1 (IL-1) produced by macrophages. In urodeles, ACTH -corticotropin-, as well as their CRH causes the production and secretion of high concentrations of corticosterone, which inhibits their amplexus or clasping mating behaviors (Kikuyama *et al*., 2003). In *Rana castebeiana*, two corticotropin-releasing factor receptors (CRFR1 and CRFR2) have been cloned from cDNA of the hypothalamus. CRF1 is located exclusively in the brain and pituitary, and CRFR2 can be found in peripheral tissues, the brain, and the pituitary (Ito *et al*., 2006). ACTH secretion can be stimulated by norepinephrine and epinephrine (Norris, 1997). Corticosteroids regulate ACTH secretion by negative feedback via inhibition of hypothalamic CRH secretion as well as by their action on corticotrophs in the pars distalis of the pituitary (Norris, 1997).

Melanocyte-stimulating hormone (*MSH*):

Some corticotropic cells are remnants of the medial lobe or pars intermedia of the pituitary gland, which produces and secrete MSH or melanotropin. This hormone increases skin pigmentation in amphibians and reptiles by stimulating the dispersion of melanin granules stored in melanosomes from cells called melanophores (melanocytes in mammals). MSH secretion is regulated by corticotropin (CRH) and/or CRH and ACTH, while dopamine inhibits it (Norris, 1997; Bentley, 1998). In amphibians, the melanophores are under endocrine control, but the release of MSH from the pars intermedia is regulated by neurons via α and/or β adrenergic receptors. In reptiles, the regulation of the pigments of the dermis includes mechanisms of neural and/or endocrine regulation (Norris, 1997). Although dopamine acts as neurohormone or releasing hormone nor a direct innervation to the neurohypophysis that stimulates MSH secretion (Norris, 1997).

Gonadotropins:

These hormones are part of a family of glycoproteins that includes TSH and chorionic gonadotropin (cGH). Hormones are made up of two subunits called α and β. The α subunit has the same primary structure for these hormones between species and is therefore highly conserved. However, the β subunit has the greatest phylogenetic divergence. This subunit is specific for each hormone and gives the biological specificity to exert its biological effect on the behavior and reproduction of vertebrates (Pierce and Parsons, 1981; Norris, 1997). Gonadotropins isolated from non-mammalian vertebrates are like those of mammals. After purification and analysis of the β-subunit, it has been proposed that the most primitive gonadotropin is LH that gives rise to other gonadotropins by gene duplication and modification first TSH and then FSH from TSH by divergence (Norris, 1997).

Bullfrog luteinizing hormone (LH) stimulates the thyroid of reptiles and birds which supports the structural relationship between LH and TSH and their actions. Therefore, the diversity of effects may be due in part to the variability of the structure of the receptor that can recognize different regions of gonadotropins or TSH (Norris, 1997).

Gonadotropins in Amphibians:

Both gonadotropins as well as β-subunit mRNAs have been isolated and purified in the same gonadotrope of the pars distalis of the pituitary of the tiger salamander *Ambystoma tigrinum*, the bullfrog *Rana castebeiana*, and leopard frog *Rana pipiens* (Licht *et al*., 1975, 1977; Daniels *et al*., 1977; Gracia-Navarro and Licht, 1987; Gracia-Navarro *et al.,* 1990; Norris, 1997). The ontogenetic cyclicity of both hormones has been shown in males and females of *Rana castebeiana* (McCreery and Licht, 1984). LH and FSH in the anuran *Rana catesbeiana* stimulate spermatogenesis and spermiation, whereas LH increases the circulating content of androgens. The same effect has been found in the neotenic urodele Ambystoma (Norris, 1997). This function also depends on environmental temperature. For example, in *Cynops* males, mammalian FSH at 18°C stimulates spermatogenesis and LH at 8°C steroidogenesis (Muller and Licht, 1980). In addition, the interannual profile of FSH and LH mRNA in the pituitary of urodeles has been described for *Cynops pyrrhogaster* (Kano *et al*., 2005), and the interannual profile of the content of both gonadotropins in plasma of anurans *Rana dybowskii* and *R. nigromaculata* (Kim *et al*., 1998) and *R. castebeiana* (Licht *et al*., 1983).

For both gonadotropins, ontological gene expression, specificity to the pituitary, and regulation have been described in *Rana pipiens* (Zhang *et al*., 2007). As noticed above, the regulation of gonadotropin secretion is primarily by GnRH. In amphibians and some mammals however, a hypothalamic neuropeptide of the RFamide family has been found to act as a hypophysiotropic factor in the regulation of gonadotropins, particularly of LH (Navarro *et al*., 2006). In *Xenopus leavis*, specific binding sites and

receptors for FSH in interstitial cells of testes has been demonstrated (Adachi *et al*., 1979). In this frog, LH has been shown to participate directly with no participation of steroid hormones, in the "courtship song" behavior (Yang *et al*., 2007).

Gonadotropins in Reptiles:

In pituitary tissue of the chelonian *Pelodiscus sinensis,* the FSH β-subunit has been cloned and it has been found that the amino acid sequence is like that corresponding to pituitarian forms of amphibians, birds, and fish (Chien *et al*., 2005). This is not the case of the Reeves´ turtle *Geoclemys reevesii* and in the squamate *Takydromus tachydromoides*, where the amino acid sequence of the FSH-β polypeptide chain corresponds to that of birds, mammals, and amphibians, whereas the LH-β is highly similar to that of amphibians, birds, and mammals. Therefore, the FSH of chelonians and lizards is more related to that of fish, birds, and mammals, and the LH with that of amphibians and birds (Aizawa and Ishii, 2003). In this class of vertebrates, it has been found that LH has thyrotropic activity due to its similarity to TSH.

Studies in *Chelonia mydas, Chelydra serpentina*, and *Geoclemis reevesi* regarding the isolation, sequencing, and physiological evaluation of FSH and LH have shown that FSH/LH cells are distributed in both zona and pars tuberalis, and caudal lobe (Papkoff *et al*., 1976; Licht and Papkoff, 1985; Mikami *et al*., 1985).

Immunolabeling studies directed to immunolocalize FSH and LH in the pituitary of squamous saurus *Podarcis sicula*. FSH specific fluorescence occupies 10% of the pars distalis and LH has a coverage of 5% LH. FSH fluorescence was found throughout this region and LH was detected only in the rostral area. This study found additionally that signal was associated with specific gonadotrophs for each gonadotropin (Desantis *et al*., 1998). FSH and LH gonadotrophs have a bimodal annual profile in size and area occupied in the par distalis. FSH and LH secreting gonadotrophs are bigger during the reproductive season and the period of gonadal recrudescence, while LH gonadotrophs increase in volume when the animal comes out of hibernation and during the post-reproductive refractory period (Desantis *et al*., 2000). The season-associated morphological variation of the LH gonadotrophs of the rostral area of the pars distalis in the pituitary of female *Uromastix acanthinurus* has been described. They are numerous and with greater secretory activity during the vitellogenic period, and decrease both in number and activity during hibernation (Hammouche *et al*., 2002). In *Anolis carolinensis*, FSH but not LH maintains testes weight, however, both gonadotropins in crocodile testes *in vitro* increase androgen concentration levels (Norris, 1997).

The gene for the FSH receptor sequence has been cloned and its expression has been demonstrated in follicular cells from the ovaries of the lizard *Podarcis sicula*, (Borrelli *et al*., 2001). On the other hand, the isolation, characterization, and effect of gonadotropins have been carried out in snakes but without convincing results (Licht *et al*., 1979). However, in the snake *Botthrops jararaca* the cloning of the gene of the receptor sequence has been described to FSH (FSHR) and demonstrated its expression in testes (Bluhm *et al*., 2004).

Neurohypophysial Hormones:

They are nonapeptides, but considering the convention that two cysteines are linked by a disulfide bond forming the cystine, only one cysteine is considered, therefore these hormones are considered octapeptides. Starting from the type of amino acid at position 8 of the peptide, these hormones are divided into basic and neutral peptides according to the presence of basic (Lys, Arg), and neutral (Leu, Ile, Val, Gln) in such a way that, for example, we refer to arginine-vasotocin and arginine-vasopressin, and oxytocin and mesotocin to indicate the characteristics of the aminoacid residue at position 8.

In the most representative groups of vertebrates, 12 peptide hormones have been identified, from which their phylogenetic

distribution has been described. For example, arginine-vasopressin is only found in mammals, and its analog, arginine-vasotocin, is present in the other classes of vertebrates. Oxytocin in non-mammals exists in eight variants, one of which is mesotocin, which is found in amphibians, reptiles, and birds.

Systemic effects of neurohypophyseal hormones include control of water balance, change in blood pressure, contraction of the muscles of the uterus, and the ejection of milk in mammals. The peptide hormones secreted by the nerve terminals of the pars nervosa are synthesized in the cell bodies located in the anterior hypothalamus, whose bodies are large and called magnocellular neurons. In amphibians, these are found in the preoptic nucleus, and in reptiles in the supraoptic and paraventricular nuclei. Since these peptides are produced in the hypothalamus and stored in the pars nervosa of the pituitary gland, they are considered neurohormones (Gorbman *et al*., 1983; Norris, 1997).

Oxytocin (*OT*):

It causes smooth muscle contraction of the epididymis in males and promotes the uterotonic effect of uterine muscles of females and acts as a depressant lowering blood pressure (Norris, 1997), although it also acts as a neurotransmitter or as a neuromodulator participating in parental care behavior toward newborns (Norris, 1997).

Vasopressin or antidiuretic hormone (*ADH*):

Vasopressin (VP or arginine-vasopressin, AVP) causes the kidneys to return more water to the blood reducing the volume of urine and thus preventing dehydration and therefore has also been called the antidiuretic hormone (ADH). Contrasting the ADH or VP activity is the analog vasotocin (VT or arginine-vasotocin AVT), which phylogenetically is the most "primitive" nonapeptide of the neurohypophysis from which VP and oxytocin evolved (Gorbman *et al*., 1983). In mammals, there was the replacement of AVT by AVP so that the mammalian neurohypophysis does not have AVT as the other classes of vertebrates do (Gorbman *et al*., 1983; Bentley, 1998). The control of water balance by these hormones is more related to the habitat than to the species itself (Gorbman *et al*., 1983). For example, in *Xenopus laevis* AVT has little or no effect than in more "terrestrial" anurans. The effect of this hormone, the Brunn effect, can be induced when injecting the hormone to anurans that remain in the water. In these animals, their weight increase is due to the water that has entered their body. In the terrestrial cycle, their water requirements are minimum as water can be obtained through their skin in response to AVT (Gorbman *et al*., 1983). AVP potentiates ACTH release from the anterior pituitary gland (Gorbman *et al*., 1983; Norris, 1997).

In anurans, the AVT gene has been described as highly similar to AVP made up of three exons and two introns (Nojiri *et al*., 1987; Bentley, 1998). VP was known and named for causing an increase in blood pressure acting on arteriolar constriction (Gorbman *et al*., 1983). In addition, these hormones can have a neurotransmitter or neuromodulator function in the nervous system (Gorbman *et al*., 1983; Norris, 1997). These hormones have specific distribution in the Nervous system. For example, in amphibian males of *Taricha granulosa*, the VT is in the optic tectum, dorsal preoptic area, ventricular infundibulum, and cerebrospinal fluid. The dorsal amygdala - region homologous to the amygdala in mammals- which is sexually dimorphic to this hormone (Kikuyama *et al*., 2003).

AVP (or VT) in vertebrates not only regulates hydromineral balance or blood pressure but also acts as a neuromodulator of behavior patterns (Kikuyama, 2003). For example, in male urodeles, either single hormone treatment or with androgens, it stimulates amplexus, a behavior related to their courtship-mating and that is activated by pheromone via the olfactory sensory pathway of the vomeronasal area (Wilczynski *et al*., 1993; Kikuyama *et al*., 2003; Burmeister and Wilczynski, 2005), as well as the deposition of

spermatophores (Kikuyama, 2003). In females, VT alone or with estrogen stimulates the behavior of jelly coat deposition wrapping them with a gelatinous substance and inducing oviposition. In viviparous pregnant females, increases in VT concentration stimulate the birth of larvae because of oviposition by uterine contraction (Kikuyama, 2003). In reptiles *Anolis carolinensis*, the treatment of AVT, like the prostaglandins PGF2α and PGE2, causes tonic and rhythmic contraction of the uterus (Jones *et al*., 2006), which can be favored by the decrease in temperature environment during birth which has been observed in *Niveooscincus ocellatus* and *N. microlepidotus* (Atkins *et al*., 2006). In the sea turtles *Lepidochelys olivacea* and *Caretta caretta*, AVT participates in oviduct contractions during oviposition (Figler *et al*., 1989).

Endocrine Glands:

Thyroid gland (*Thyroid* hormones):

This gland is made up of follicles encapsulated by connective tissue. It is highly vascularized, and receives sympathetic innervation (Norris, 1997). In amphibians, it may have two lobes or be so small that it appears to be absent. In lizards and most reptiles, it may be disc- or spindle-shaped with two lobes or there may be separate, located in front of the heart and to one side of the branches of the aorta or on the trachea (Gorbman *et al*., 1983). It produces and secretes (T3) and thyroxine (T4). In vertebrates, due to its action on various tissues, it affects processes such as metabolism, metamorphosis, growth, hibernation, thermogenesis, and reproduction (Norris, 1997; Denver, 2013). In amphibians and reptiles, environmental factors such as photoperiod and temperature influence ontogenetically the synthesis and secretion of thyroid hormones via neuroendocrine stimuli (Norris, 1997). For example, in anuran larvae, the thyroid secretes thyroxine during hibernation, so this hormone reduces the somatotropic effect of prolactin, inhibiting the growth of the larvae. While the larvae is *in utero*, thyroxine stimulates the urea cycle which is excreted in the uterine fluid (Norris, 1997). The secretion of thyroid hormones is in response to TRH stimulation. TRH acts on the thyrotrophs that produce and secrete TSH. TSH stimulates the synthesis and secretion of thyroid hormones in the thyroid gland, therefore, the release of TRH depends on blood concentrations of TSH and T3.

In the thyroid gland, there are some parafollicular cells -C cells in mammals- that can be inside a follicle or arranged between them. These cells produce calcitonin (CT) or thyrocalcitonin, a hormone that decreases the concentrations of calcium, magnesium, and phosphates in the blood by inhibition of bone resorption caused by osteoclasts. Therefore, by inhibiting bone resorption, calcium uptake in the bone matrix is favored, which is related to renal function, since CT stimulates increased reabsorption of ions from urine and therefore promotes their absorption return to blood (Bentley, 1998). For example, in amphibians, CT regulates the calcium content of the lime sacs (endolymphatic sacs), as well as the permeability of their skin (Bentley, 1998; Robertson, 1969 a, b).

Parathyroid gland (*Parathyroid hormone*):

The parathyroid glands developmentally arise from pharyngeal pouch endoderm; in amphibians and reptiles they derive from the ventral wings of the third and fourth pharyngeal pouches (Gorbman *et al*., 1983; Srivastav *et al*., 1995 a, b; Chen *et al*., 2013). Among amphibians, anurans generally have two pairs of parathyroid gland located near the carotid and systemic arches and made up a single cell type; in urodeles (salamaders) appear to be similar to those reptiles (Gorbman *et al*., 1983; Srivastav *et al*., 1995a; Chen *et al*., 2013). In reptiles, there may be one or two pairs of parathyroids of variable location. Lizards, for example, have either one or two pairs, whereas crocodiles have a singl pair; the glands are located near the heart in close association with the thyroids and ultimobranchial bodies. In snakes, the anterior pair is associated with the carotid artery near the angle of the jaw (Gorbman *et al*. 1983; Srivastav *et al*., 1995b).

The parathyroid gland may have one or two cell types besides the structural-related main basal epithelia and the eosinophilic oxiphil cells rich in mitocindria; main cells are responsible to secrete parathyroid hormone (PTH) that participate in calcium homeostasis. Oxyphil cells have a higher oxidative activity (Isono *et al*., 1990; Chen *et al*., 2013).

In parathyroidectomized amphibians and reptiles a hypocalcemic effect was demonstrated, therefore it was proposed that the parathyroid could regulate calcium in the bones, kidneys, and galls of larvae (Robertson, 1969 a, b; Srivastav *et al*., 1995 a, b; Bentley, 1998). PTH was demonstrated to increase number and activity of osteoclasts, bone resorption and thus increase the release of calcium ions (hypercalcemia) and phosphate from the bone marrow. Experimental data were obtained showing the reabsorption of these minerals from the urine. Therefore, in both classes of vertebrates, PTH causes increased calcium mobilization from bone (Bentley, 1998), and in reptiles tetanic muscle contractions.

PTH in anuran and lizards is synthetized as a 80-120 amino acid preprotein with a 20 amino acid C-terminal region that allows the interaction with the receptor. Even though there is no definitive evidences in all amphibian and reptiles, the current knowledge indicates that the primary transcript has to be proteolytically processed in order to obtain the precursor PrPrTH from which the mature parathyroid protein is obtained (Pinheiro, *et al*., 2010).

Ultimobranchial gland (*Calcitonin*):

This gland develops from the last pharyngeal pouch and is not fused with the thyroid primordium, its location varies between species. As in fish, ultimobranchial cells in amphibians and reptiles are of endodermal origin; they secrete calcitonin (CT), a hormone which regulates the homeostasis of calcium and phosphate levels (Srivastav *et al*., 1998, 2000, 2011; Kameda, 2017).

In anurans the ultimobranchial gland (UBG) lies on the musculature adjacent to either side of the opening to the larynx, near the ventral pericardial region, and consist of a single follicle with a central lumen, although several secondary small follicles are occasionally present (Kameda, 2017). In salamanders the gland is composed of many small follicles (Kameda, 2017).

Reptiles possess one (on the left side) or two ultimobranchial glands (Srivastav *et al*., 1998). In most reptiles, the ultimobranchial gland is observed in close proximity with either the parathyroid or thymus but less frequently with the thyroid gland (Kameda, 2017). In turtles, this gland is situated between the subclavian artery and the carotid artery near the bifurcation of the trachea (Kameda, 2017). In snakes, together with the parathyroid IV and thymus IV derived from the fourth pharyngeal pouch, the UBG is situated at the caudal level of the thyroid (Kameda, 2017). In lizards, a single ultimobranchial gland, observed on the left side, lies opposed to the trachea or esophagus (Kameda, 2017). The ultimobranchial gland of reptiles generally consists of numerous small spherical follicles (Kameda, 2017).

In anphibians (anurans: *Rana cyanophlyctis*, Krishna and Swarup, 1985; *Rana tigrina*, Srivastav and Rani, 1989 a, b) and reptiles (lizard: *Calotes versicolor*; Srivastav *et al*., 2011), CT induced hypocalcemia and hypophosphatemia.

Adrenals (*Interrenal gland*):

These glands, named for their position adjacent to the kidney, are highly vascularized (Gorbman *et al*., 1983; Norris, 1997; Bentley, 1998), and their function is related more to habitat than to anatomy or phylogeny (Norris, 1997). Characteristically, this gland is made of chromaffin cells that secrete catecholamines, and interrenal adrenocortical cells that secrete steroid hormones. It should be noted that in mammals, chromaffin cells make up the adrenal medulla and adrenocortical cells which are the steroidogenic cells of the zona fasciculata of the adrenal cortex. In amphibians, chromaffin and adrenocortical tissue is usually associated, forming islets on the ventral surface of the kidney (Gorbman *et al*.,

1983; Norris, 1997), and even narrower in reptiles.

In amphibians, adrenocortical cells are extra-adrenal and their location is highly variable. They form irregular nodules on the ventral surface of both kidneys, constituting the inter-renal glands that in most anurans have some chromaffin cells (Norris, 1997). Adrenals in snakes, turtles, and crocodiles are paired and, in some species, they show certain regionalization in such a way that both their position and structure are similar to those of mammals (Norris, 1997). The main secretory products of these glands are Catecholamines and Adrenocorticoids.

The two catecholamines epinephrine (adrenaline) and norepinephrine (noradrenaline) contribute to the metabolism of carbohydrates and fats, as well as exert an influence on the muscle tone of some blood vessels and the heart. On the other side, corticosteroids or adrenocorticoids are grouped into mineralocorticoids and glucocorticoids. Mineralocorticoids are hormones related to electrolyte homeostasis mainly sodium and potassium ions. Glucocorticoids are related to glucose metabolism. Both have circadian and circannual regulation, the latter related to migration and reproduction processes although the difference in functions is not as precise (Chan and Phillips, 1971; Norris, 1997). For example, the mineralocorticoids corticosterone and aldosterone, both cause hyperglycemia, as well as increase liver and muscle glycogen concentration, therefore they may have both functions (Norris, 1997), while the glucocorticoid cortisol or hydrocortisone may have a more limited mineralocorticoid effect (Norris 1997; Bentley, 1998).

Regulation of adrenocortical hormones may be due to both feedback processes and the renin-angiotensin pathway (Gorbman *et al*., 1983; Norman and Litwack, 1997; Norris, 1997; Bentley, 1998). For example, low concentration of circulating adrenocorticoids stimulates the secretion of CRH by hypothalamic neurosecretory cells, a hormone that in the corticotrophs of the adenohypophysis stimulates the secretion of ACTH, which once secreted into the bloodstream acts on the adrenal glands, stimulating the synthesis of ACTH and secretion of adrenocorticoids. This positive feedback mechanism can be increased by stress due to the higher frequency of CRH and ACTH release, increasing adrenocorticoid secretion. On the other hand, high concentrations of adrenocorticoids hormones must be downregulated by a negative feedback process, for which adrenocorticoids in high concentration cause corticotrophs to decrease ACTH secretion and neurosecretory cells of the hypothalamus to inhibit ACTH secretion of CRH.

Mineralocorticoids:

The synthesis-secretion and function of corticosterone and aldosterone is generally related to electrolyte balance. Amount and relative concentration of mineralocorticoids depend on the species; in amphibians and reptiles mainly corticosterone followed by aldosterone (Norris, 1997; Bentley, 1998). In amphibians, AVT directly stimulates the secretion of both mineralocorticoids regulating diuresis. These hormones, by acting on cells of the renal tubules, increase the reabsorption of sodium ions as well as those of chloride and bicarbonate, preventing their depletion in the body. They also stimulate the secretion of potassium ions and hydrogen ions (H^+) which are excreted in the urine and thus decreasing blood pH to prevent acidosis. Corticosterone increases sodium concentrations whereas aldosterone is responsible of decreasing it (Norris, 1997). In adult anurans, corticosterone is the dominant mineralocorticoid along with the glucocorticoid cortisol during tadpole metamorphosis. In urodeles, the major mineralocorticoid is aldosterone (Norris, 1997). Ovaries produce significant amounts of deoxycorticosterone (DOC) that may be involved in female sexual maturity regulation. However, to the best of our knowledge, it is not known to have a role in ovulation as has been suggested for

teleosts (Norris, 1997). In the snake *Thamnophis sirtalis parietalis*, corticosterone participates in their courtship behavior and search for food, as well as immigration processes (Cease *et al*., 2007). Mineralocorticoids can act as a stress indicator. In the sea turtle *Lepidochelys olivacea,* increased levels of cortisone have been detected during mass nesting behavior (Valverde *et al*., 1999), and in males of the desert tortoise *Gopherus agassizii*, its circulating concentration increases more than in females during the mating season, particularly during a combat event (Lance *et al*., 2000).

Glucocorticoids:

It has been profusely documented that they regulate energy metabolism processes and resistance to stress, among other activities. The most representative glucocorticoids are cortisol or hydrocortisone and corticosterone, whose predominance is species specific. These hormones are related to activity and metabolism; promote protein proteolysis increasing the release of amino acids into the bloodstream; they regulate gluconeogenesis, increase the release of fatty acids by lipolysis; stimulate the anti-inflammatory effects by reducing the number of mast cells migration and degranulation that release histamine. They also slow down the release of lysosomal enzymes, decrease the permeability of blood capillaries and phagocytosis, and, in high concentrations, they depress immune responses.

Gonads (*Steroid hormones*):

The gonads are organs where gametogenesis and the production-secretion of protein and steroid hormones take place. Steroid hormones are part of a wide class of molecules such as sterols, bile acids, and some alkaloids. Steroids are non-saponifiable lipids, poorly soluble in water but soluble in organic solvents. They are made up of a common nucleus called cyclopentane-perhydro-phenanthrene, a cyclic hydrocarbon made up of seventeen carbon atoms (C17) arranged in three fully saturated rings of six carbons each (perhydro-phenanthrene or gonane) designated as rings A, B, and C, and a five carbon D ring (cyclopentane) (Gorbman *et al*., 1983; Kime, 1987; Norman and Litwack, 1997; Ostojic, 2012).

All steroid hormones are derived from one of the following basic hydrocarbons: cholestane, pregnane, androstane, and estrane. Cholestane or lanosterol is a 27 carbon atoms hydrocarbon (C27) that is the basic chemical structure to which cholesterol belongs. It is the characteristic sterol of animal cells that confers rigidity to cell membranes, in addition, to being the precursor molecule of steroid hormones.

The 21 carbon atom pregnane (C21) is the characteristic hydrocarbon of steroid hormones with progestational and adrenocortical activity. Androstane has nineteen carbon atoms (C19) and is the basic chemical structure of steroid hormones with androgenic activity, and estrane with eighteen carbon atoms (C18) includes steroids with estrogenic activity.

Regarding the biological activity exerted by steroid hormones, they are classified into five groups: progestogens (progestagens) or natural or synthetic progestins, androgens; estrogens; glucocorticoids, and mineralocorticoids. It is important to note that progestins, androgens, and estrogens altogether are known as sex steroid hormones due to their involvement in sexual development as well as reproductive function. Glucocorticoids and mineralocorticoids together are known as corticoids or corticosteroids.

The organs that biosynthesize steroid hormones have the same capacity to do so based on similar processes that participate in each of the biotransformations, the unitary concept of steroid biosynthesis proposed by Dorfman and Ungar (1965). The qualitative and quantitative differences, regulated by genomic control mechanisms determine the particular physiological identity of each tissue and environment (Kime, 1987; Stocco and Clark 1996; Norman and Litwack, 1997; Martinez-Arguelles and Papadopoulos, 2010; Ostojic, 2012), in addition to knowing the mechanisms of action of steroid hormones (Pearce and Yamamoto, 1993;

White and Parker, 1998; Simoncini and Genazzani, 2003; Meijer *et al*., 2019).

In amphibians and reptiles, there are very extensive ontogenetic studies regarding the biosynthesis processes of steroid hormones (sexual and corticosteroids); its assessment in blood, plasma and/or serum, in urogenital tissues like gonads, mesonephros, interrenal glands, uterus, the brain or other tissues, transporter/binding molecules, among others basic aspects. With some exceptions, scarce information have been reported in the literature regarding to the isolation and characterization of hormone receptors, expression evaluation of both the genes involved in steroidogenesis and the receptors, as well as to evaluate their mechanisms of action and their effects in different ontogenetic and sex differentiation processes under both natural and experimental conditions. In such a way that citing some works that could be considered as classics, it is also necessary to cite those that allowed us to know other aspects of the functions of steroid hormones. In such a way that the state of the art regarding steroid hormones, for example, in reproductive biology is overwhelming, amphibians and reptiles being no exception. Therefore, bibliographical references are suggested that describe in detail how steroid hormones (and others) participate in reproductive biology in amphibians and reptiles (Norris and Lopez, 2010, 2011).

Conclusion

It is relevant to know the basic foundations of the neuroendocrinology of amphibians and reptiles, as well as the other classes of vertebrates. These fundamental knowledge will allow those interested in the field of management and conservation of wildlife fauna in wild or in captivity, to holistically address ecophysiological studies related to the biology of animal reproduction. They will be able to contribute to the pressing need to be able to solve the anthropogenic devastation of fauna, and flora, in the various terrestrial and aquatic ecosystems that make up our planet.

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References

Acharjee S, Maiti K, Soh JM, Im W-B, Seong JY and Kwon HB. (2002) Differential desensitization and internalization of three different bullfrog gonadotropin-releasing hormone receptors. Mol Cells 14: 1001-1007.

Adachi T, Pandey AK and Ishii S. (1979) Follicle stimulating hormone receptors in the testis of the frog *Xenopus laevis*. Gen Comp Endocrinol. 37: 177-185.

Aida T, Yamamoto K and Kikuyama S. (1999) Enhancement by proopiomelanocortin-derived peptides of growth hormone and prolactin secretion by bullfrog pituitary cells. Gen Comp Endocrinol. 115: 101-109.

Aizawa Y and Ishii S. (2003) Cloning of complementary deoxyribonucleic acid encoding follicle-stimulating hormone and luteinizing hormone β subunit precursor molecules in Reeves´s turtle (*Geoclemys reevesii*) and Japanese grass lizard (*Takydromus tachydromoides*). Gen Comp Endocrinol. 132: 465-473.

Akgun-Dar K, Erensoy N and Yilmazer S. (2004) Immunocytochemical detection of effects of TRH and T4 on prolactin- and TSH-producing cells in the pituitary gland of *Rana ridibunda*. Acta Histochem. 106: 315-323.

Alonso-Bedate M, Delgado MJ and Carballada R. (1988) *In vivo* effect of melatonin and gonadotropin-releasing hormone on testicular function in *Rana temporaria*. J Pineal Res. 5: 323-332.

Alonso-Bedate M, Carballada R and Delgado MJ. (1990) Effects of melatonin on gonadal steroids and glucose plasma levels in frogs (*Rana perezi* and *Rana temporaria*). J Pineal Res. 8: 79-89.

Atkins N, Jones SM and Guillette LJ. (2006) Timing of parturition in two species of viviparous lizard:

influences of beta-adrenergic stimulation and temperature upon uterine responses to arginine vasotocin (AVT). J Comp Physiol B Biochem Syst Environ Physiol. 176: 783-792.

Barraclough CA and Wise PM. (1982) The role of catecholamines in the regulation of pituitary luteinizing hormone and follicle-stimulating hormone secretion. Endocr Rev. 3: 91-119.

Battisti A, Vallarino M, Carnevail O, Fasano S, Polzoneti-Magni A and Pieratoni R. (1994) Detection and localization of gonadotrophin-releasing hormone (GnRH)-like material in the frog, *Rana esculenta*. Comp Biochem Physiol A Physiol. 109: 1097-1103.

Battisti A, Pieratoni R, Vallarino M, Trabucchi M, Carnevail O, Polzonetti-Magni AM and Fasano S. (1997) Detection of GnRH molecular forms in brains and gonads of the crested newt, *Triturus carnifex*. Peptides 18: 1029-1037.

Bennis M, Dubourg P, Gamrani H, Calas A and Kah O. (1989) Existence of a GnRH immunoreactive nucleus in the dorsal midbrain tegmentum of the chameleon. Gen Comp Endocrinol. 75: 195-203.

Bennis M, Repérant J and Tramu G. (1998) Evidence for co-existence of CCK-8 and GnRH in neurons of the mesencephalic tegmentum in the chameleon. Neurosci Lett. 240: 155-158.

Bentley PJ. (1998) Comparative Vertebrate Endocrinology. 3rd edn., Cambridge University Press, Cambridge, UK.

Bluhm APC, Toledo RA, Mesquita FM, Pimenta MT, Fernandes FMC, Ribela MTCP and Lazari MFM. (2004) Molecular cloning, sequence analysis and expression of the snake follicle-stimulating hormone receptor. Gen Comp Endocrinol. 137: 300-311.

Borrelli L, De Stasio R, Parisi E and Filosa S. (2001) Molecular cloning, sequence and expression of follicle-stimulating hormone receptor in the lizard *Podarcis sicula*. Gene 275: 149-156.

Brown SC, Brown PS, Yamamoto K, Matsuda K and Kikuyama S. (1991) Amphibian prolactins: activity in the eft skin transepithelial potential bioassay. Gen Comp Endocrinol. 82: 1-7.

Burmeister SS and Wilcynski W. (2005) Social signals regulate gonadotropin-releasing hormone neurons in the green treefrog. Brain Behav Evol. 65: 26-32.

Callar IP, Riley D and Perez L. (1990) Vitellogenesis in reptiles as a model for mammalian sex-differentiated hepatic protein synthesis. J Exp Zool. (Suppl) 256: 106-111.

Cariello L, Romano G, Spagnuolo A, Zanetti L, Fasano S, Minucci S, Di Matteo L, Pierantoni R and Chieffi G. (1989) Molecular forms of immnunoreactive gondotropin-releasing hormone in hypothalamus and testis of the frog, *Rana esculenta*. Gen Comp Endocrinol. 75: 343-348.

Carnevali O, Mosconi G, Yamamoto K, Kobayashi T, Kikuyama S and Polzonetti-Magni AM. (1992) Hormonal control of *in vitro* vitellogenin synthesis in *Rana esculenta* liver: effects of mammalian and amphibian growth hormone. Gen Comp Endocrinol. 88: 406-414.

Carnevali O, Mosconi G, Yamamoto K, Kobayashi T, Kikuyama S and Polzonetti-Magni AM. (1993) *In-vitro* effects on mammalian and amphibian prolactins on hepatic vitellogenin synthesis in *Rana esculenta*. J Endocrinol. 137: 383-389.

Castano JP, Ramirez LL, Malagon MM and Gracia-Navarro F. (1992) Differential response of amphibian PRL and TSH pituitary cells to *in vitro* TRH treatment. Gen Comp Endocrinol. 88: 178-187.

Castano JP, Ruiz-Navarro A, Torronteras R, Malagon MM and Gracia-Navarro F. (1993) Different exocytotic morphology in amphibian prolactin and growth hormone cells stimulated *in vitro* with TRH. Tissue Cell 25: 165-172.

Caunt CJ, Finch AR, Sedgley KR, Oakley L, Luttrell LM and McArdle CA. (2006) Arrestin-mediated ERK activation by gonadotropin-releasing hormone receptors: Receptor-specific activation mechanisms and compartmentalization. J Biol Chem. 281: 2701-2710.

Cease AJ, Lutterschmidt DI and Mason RT. (2007) Corticosterone and the transition from courtship behavior to dispersal in male red-sided garter snakes (*Thamnophis sirtalis parietalis*). Gen Comp Endocrinol. 150: 124-131.

Chan SWC and Phillips JG. (1971) Seasonal variations in production *in vitro* of corticosteroids by the frog (*Rana rigulosa*) adrenal. J Endocrinol. 50: 1-17.

Chang Y-S and Papkoff H. (1985) Isolation and properties of sea turtle (*Chelonia mydas*) pituitary prolactin. Gen Comp Endocrinol. 60: 372-379.

Chartrel N, Collin F, Huang YS, Montero M, Tonon MC, Goos HJ, Dufour S and Vaudry H. (1998a) Characterization and localization of two forms gonadoropin-releasing hormone (GnRH) in the spinal cord of the frog *Rana ridibunda*. Cell Tissue Res. 293: 235-243.

Chartrel N, Collin F, Montero M, Dufour S, Vandesande F and Vaudry H. (1998b) Biochemical characterization and regional distribution of mGnRH and cGnRH-II in the spinal cord of the frog *Rana ridibunda*. Ann N Y Acad Sci. 839: 361-362.

Chartrel N, Tonon MC, Vaudry H and Conlon JM. (1991) Primary structure of frog pituitary adenylate cyclase-

activating polypeptide (PACAP) and effects of ovine PACAP on frog pituitary. Endocrinology 129: 3367-3371.

Chen H, Senda T, Emura S and Kubo Y-Y. (2013) An update on the structure of parathyroid gland. Open Anatomy J. 5: 1-9.

Chianese R, Ciaramella V, Fasano S, Pierantoni R and Meccariello R. (2013) Kisspeptin receptor, GPR54, as a candidate for the regulation of testicular activity in the frog *Rana esculenta*. Biol Reprod. 88(3): 1-11.

Chianese R, Ciaramella V, Fasano S, Pierantoni R and Meccariello R. (2015) Kisspeptin drives germ cell progression in anuran amphibian *Pelophylax esculentus*: A study carried out in *ex vivo* testes. Gen Comp Endocrinol. 211: 81-91.

Chianese R, Ciaramella V, Fasano S, Pierantoni R and Meccariello R. (2017) Kisspeptin regulates steroidogenesis and spermiation in anuran amphibian. Reproduction 154: 403-414.

Chien JT, Shen ST, Lin YS and Yu JY. (2005) Molecular cloning of the cDNA encoding follicle-stimulating hormone beta subunit of the Chinese soft-shell turtle *Pelodiscus sinensis*, and its gene expression. Gen Comp Endocrinol. 141: 190-200.

Chowdhury VS, Ubuka T, Osugi T, Shimura T and Tsutsui K. (2011) Identification, localization and expression of LPXRFamide peptides, and melatonin-dependent induction of their precursor mRNA in the newt brain. J Endocrinol. 209: 211-220.

Cobellis G, Meccariello R, Minucci S, Palmiero C, Pierantoni R and Fasano S. (2003) Cytoplasmic versus nuclear localization of Fos-related proteins in the frog, *Rana esculenta*, testis: *in vivo* and direct *in vitro* effect of a gonadotropin-releasing hormone agonist. Biol Reprod. 68: 954-960.

Cohen M, Roselle D and Chabner B. (1978) Evidence for a cytoplasmic melatonin receptor. Nature 274: 892-993.

Collin F, Chartrel N, Fasolo A, Conlon JM, Vandesande F and Vaudry H. (1995) Distribution of two molecular forms of gonadotropin-releasing hormone (GnRH) in the central nervous system of the frog *Rana ridibunda*. Brain Res. 703: 111-128.

Conlon JM, Collin F, Chiang YC, Sower SA and Vaudry H. (1993) Two molecular forms of gonadotropin-releasing hormone from the brain of the frog, *Rana ribibunda*: purification, characterization, and distribution. Endocrinology 132: 2117-23.

Crim JW. (1985) Immunocytochemistry of luteinizing hormone-releasing hormone and sexual maturation of the frog brain: comparisons of juvenile and adult bullfrogs (*Rana catesbeiana*). Gen Comp Endocrinol. 59: 424-433.

d´Anglemont de Tassigy X, Fagg LA, Dixon JPC and Colledge WH. (2007) Hypogonadotropic hypogonadism in mice lacking a functional Kiss1 gene. Proc Natl Acad Sci USA 104: 10714-10719.

D´Antonio M, Fasano S, de Leeuw R and Pierantoni R. (1992) Effects of gonadotropin-releasing hormone variants on plasma and testicular androgen levels in intact and hypophysectomized male frog, *Rana esculenta*. J Exp Zool. 261: 34-39.

D´Aniello B, Biagio C, King JA and Rastogi RK. (1994) Neuroanatomical organization of GnRH neuronal systems in the lizard (*Podarcis s. sicula*) brain during development. Brain Res. 657: 221-226.

D´Aniello B, Pinelli C, Di Fiore MM, King JA and Rastogi RK. (1995) Development and distribution of gonadotropin-releasing hormone neuronal systems in the frog (*Rana esculenta*) brain: immunohistochemical analysis. Dev Brain Res. 89: 281-288.

d'Istria M, Monteleone P, Serino I and Chieffi G. (1994) Seasonal variations in the daily rhythm of melatonin and NAT activity in the Harderian gland, and serum of the green frog, *Rana esculenta*. Gen Comp Endocrinol. 96: 6-11.

d'Istria M, Palmiero C, Serino I, Izzo G and Minucci S. (2003) Inhibition of the basal and oestradiol-stimulated mitotic activity of primary spermatogonia by melatonin in the testis of the frog, *Rana esculenta*, *in vivo* and *in vitro*. Reproduction 126: 83-90.

d'Istria M, Serino I, Izzo G, Ferrara D, De Rienzo G and Minucci S. (2004) Effects of melatonin treatment on Leydig cell activity in the testis of the frog *Rana esculenta*. Zygote 12: 293-299.

Daniels EL, Licht P, Farmer SW and Papkoff H. (1977) Immunochemical studies on the pituitary gonadotropins follicle stimulating hormone and luteinizing hormone from the bullfrog *Rana castebeiana*. Gen Comp Endocrinol. 32: 146-157.

Dawley EM and Crowder J. (1995) Sexual and seasonal differences in the vomeronasal epithelium of the red-backed salamander (*Plethodon cinereus*). J Comp Neurol. 359: 382-390.

De Roux N, Genin E, Carel J-C and Milgrom E. (2003) Hypogonadotropic hypogonadism due to loss of function of the KiSS1-derived peptide receptor GPR54. Proc Natl Acad Sci USA 100: 10972-10976.

Delgado MJ and Vivian-Roels B. (1989) Effect of environmental temperature and photoperiod on the melatonin levels in the pineal, lateral eye, and plasma of the frog *Rana perezi*: importance of ocular melatonin. Gen Comp Endocrinol. 75: 46-53.

Demski LS. (1987) Phylogeny of luteinizing hormone-

releasing hormone systems in protochordates and vertebrates. Ann N Y Acad Sci. 519: 1-14.

Denver RJ. (2013) Neuroendocrinology of amphibian metamorphosis. Curr Top Dev Biol. 103: 195-227.

Desantis S, Labate M and Corriero A. (1998) Immunohistochemical localization of FSH and LH in the pituitary of male ruin lizards (*Podarcis sicula campestris* De Betta). Eur J Histochem. 42: 77-84.

Desantis S, Labate M, Coriero A, Labate GM and De Metrio G. (2000) Immunohistochemical evidence of seasonal changes of gonadotropes in male ruin lizard (*Podarcis simula campestres* De Betta). Eur J Histochem. 44: 385-395.

Di Fiore MM, King JA, D´Aniello B and Rastogi RK. (1996) Immunoreactive mammalian and chicken-II GnRHs in *Rana esculenta* brain during development. Regul Pept. 62: 119-124.

Di Matteo L, Minucci S, Fasano S, Pierantoni R, Varriale B and Chieffi G. (1988) A gonadotropin-releasing hormone (GnRH) antagonist decreases androgen production and spermatogonial multiplication in frog (*Rana esculenta*): indirect evidence for the existence of GnRH or GnRH-like material receptors in the hypophysis and testis. Endocrinology 122: 62-67.

Di Matteo L, Minucci S, Fasano S, D´Antonio M, Pierantoni R and Chieffi G. (1990) Indirect evidence for a physiological role exerted by a "Testicular gonadotropin-releasing hormone" in the frog, *Rana esculenta*. Gen Comp Endocrinol. 79: 147-153.

Di Matteo L, Vallarino M and Pierantoni R. (1996) Localization of GnRH molecular forms in the brain, pituitary, and testis on the frog, *Rana esculenta*. J Exp Zool. 274: 33-40.

Dockray GJ, Reeve JRJr, Shively J, Gayton RJ and Barnard CS. (1983) A novel active pentapeptide from chicken brain identified by antibodies to FMRFamide. Nature 305: 328-330.

Dorfman RI and Ungar F. (1965) Metabolism of Steroid Hormones. Academic Press, New York.

Dufour A, Quérat B, Tostivint H, Pascualini C, Vaudry H and Rousseau K. (2020) Origin and evolution of the neuroendocrine control of reproduction in vertebrates, with special focus on genome and gene duplications. Physiol Rev. 100: 869-943.

Ebersole TJ and Boyd SK. (2000) Immunocytochemical localization of gonadotropin-releasing hormone in the brain of a viviparous caecilian amphibian, *Typhlonectes natans* (Amphibia: Gymnophiona). Brain Behav Evol. 55: 14-25.

Fasano S, Minucci S, Pierantoni R, Fasolo A, Di Mateo L, Basile C, Varíale B, Chieffi G. (1988) Hypothalamus-hypophysis and testicular GnRH control of gonadal activity in the frog, *Rana esculenta*: Seasonal GnRH profiles and annual variations of *in vitro* androgen output by pituitary-stimulated testes. Gen Comp Endocrinol. 70: 31-40.

Fasano S, de Leeuw R, Pierantoni R, Chieffi G and Van Oordt PG. (1990) Characterization of gonadotropin-releasing hormone (GnRH) binding sites in the pituitary and testis of the frog, *Rana esculenta*. Biochem Biophys Res Commun. 168: 923-932.

Fasano S, Goos HJ, Janssen C and Pierantoni R. (1993) Two GnRHs fluctuate in correlation with androgen levels in the male frog *Rana esculenta*. J Exp Zool. 266: 277-283.

Fasano S, D´Antonio M, Chieffi P and Pierantoni CG. (1995) Chicken GnRH-II and salmon GnRH. Effects on plasma and testicular androgen concentrations in the male frog, *Rana esculenta*, during the annual reproductive cycle. Comp Biochem Physiol C Pharmacol Toxicol Endocrinol. 112: 79-86.

Fernández SN and Ramos I. (2003) Endocrinology of Reproduction. In: Reproductive Biology and Phylogeny of Anuran. Vol. 2 (ed.) Barrie G. M. Jamieson), Science Publishers, Inc. Enfield, NH, USA, pp. 73-117.

Figler RA, MacKenzie DS, Owens DW, Licht P and Amoss MS. (1989) Increased levels of arginine vasotocin and neurophysin during nesting in sea turtles. Gen Comp Endocrinol. 73: 223-232.

Filadelfi AM and Castrucci AM. (1996) Comparative aspects of the pineal/melatonin system of poikilothermic vertebrates. J Pineal Res. 20: 175-186.

Finch AR, Green L, Hislop JN, Kelly E and McArdle CA. (2004) Signaling and antiproliferative effects of type I and II gonadotropin-releasing hormone receptors in breast cancer cells. J Clin Endocrinol Metab. 89: 1823-1832.

Fiorindo RP. (1980) Further evidence for a prolactin-stimulating neurohormone in reptiles. Gen Comp Endocrinol. 40: 52-58.

Firth BT, Kennaway DJ and Roszenbilds MAM. (1979) Plasma melatonin in the scincid lizard, *Trachydosaurus rugosus*: diel rhythm, seasonally, and the effect of constant light and constant darkness. Gen Comp Endocrinol. 37: 493-500.

Ford CP, Dryden WF and Smith PA. (2003) Neurotrophic regulation of calcium channels by the peptide neurotransmitter luteinizing hormone releasing hormone. J Neurosci. 23: 7169-7175.

Ford CP, Stemkowski PL and Smith PA. (2004) Possible role of phosphatidylinositol 4,5-bisphosphate in luteinizing hormone releasing hormone-mediated

M-current inhibition in bullfrog sympathetic neurons. Eur J Neurosci. 20: 2090-2998.

Forlano PM, Maruska KP, Sower SA, King JA and Tricas TC. (2000) Differential distribution of gonadotropin-releasing hormone-immunoreactive neurons in the stingray brain: functional and evolutionary considerations. Gen Comp Endocrinol. 118: 226-248.

Funes S, Hedrick JA, Vassileva G, Markowitz L, Abbondanzo S, Golovko A, Yang S, Monsma FJ and Gustafson EL. (2003) The KiSS-1 receptor GPR54 is essential for development of the murine reproductive system. Biochem Biophys Res Commun. 312: 1357-1363.

Gorbman A, Dickhoff WW, Vigna SR, Clark NB and Ralph CL. (1983) Comparative Endocrinology. John Wiley Sons, Inc. New York.

Gordon J, Morley JE and Hershman JM. (1980) Melatonin and the thyroid. Horm Metab Res. 12: 71-73.

Gracia-Navarro F and Licht P. (1987) Subcellular localization gonadotrophic hormones LH and FSH in frog adenohypophysis using double-staining immunocytochemistry. J Histochem Cytochem. 35: 763-769.

Gracia-Navarro F, Porter D, Malagón MM and Licht P. (1990) Stereological study of gonadotropes in the frog, *Rana pipiens*, after GnRH stimulation *in vitro*. Cell Tiss Res. 262: 171-176.

Haldar-Misra C and Thapliyal JP. (1981) Response of reptilian gonad to melatonin. Neuroendocrinol. 33: 328-332.

Haldar C and Pandey R. (1988) Effect of melatonin and 5-Methoxytryptamine administration on the testis and pineal gland activity of fresh-water snake, *Natrix piscator.* Arch Anat Histol Embryol. 71: 85-95.

Haldar C and Pandey R. (1989) Effect of pinealectomy on annual testicular cycle of Indian chequered water snake, *Natrix piscator*. Gen Comp Endocrinol. 76: 214-222.

Hammouche S, Gernigon-Spychalowicz T, Khammar F and Farida J-M. (2002) Etude immunohistochimique des cellules gonadotropes chez le lizard femelle *Uromastix acanthinurus* au cours du cycle reproducteur. Bull Soc Zool. (Fr) 127: 49-55.

Harvey S. (1990) Thyrotropin-releasing hormone: a growth hormone-releasing factor. J Endocrinol. 125: 345-358.

Hislop JN, Madziva MT, Everest HM, Haring T, Uney JB, Willars GB, Millar RP, Troskie BE, Davidson JS and McArdie CA. (2000) Desensitization and internalization of human and *Xenopus* gonadotropin-releasing hormone receptors expressed in alphaT4 pituitary cells using recombinant adenovirus. Endocrinology 141: 4564-4575.

Hislop JN, Caunt CJ, Sedgley KR, Kelly E, Mundell S, Green LD and McArdie CA. (2005) Internalization of gonadotropin-releasing hormone receptors (GnRHRs): does arrestin binding to the C-terminal tail target GnRHRs for dynamin-dependent internalization? J Mol Endocrinol. 35: 177-189.

Isono H, Shoumura S and Emura S. (1990) Ultrastructure of the parathyroid gland. Histo Histopathol. 5: 95-112.

Iela L, Rastogi RK and Bagnara JT. (1991) Reproduction in the Mexican leaf frog *Pachymedusa dacnicolor*. V. Immunohistochemical localization of gonadotropin-releasing hormone in the brain. Gen Comp Endocrinol. 84: 129-134.

Iela L, Powell JF, Sherwood NM, D´Aniello B, Rastogi RK and Bagnara JT. (1996) Reproduction in the Mexican leaf frog, *Pachymedusa dacnicolor*. VI: Presence and distribution of multiple GnRH forms in the brain. Gen Comp Endocrinol. 103: 235-243.

Ikemoto T and Park MK. (2003) Identification and characterization of the reptilian GnRH-II gene in the leopard gecko, *Eublepharis macularius*, and its evolutionary considerations. Gene 316: 157-165.

Ikemoto T, Enomoto M and Park MK. (2004) Identification and characterization of a reptilian GnRH receptor from the leopard gecko. Mol Cell Endocrinol. 214: 137-147.

Ito Y, Okada R, Noriyuki T and Kikuyama S. (2006) Cloning and distribution of the bullfrog type 1 and type 2 corticotropin-releasing factor receptors. Gen Comp Endocrinol. 146: 291-295.

Izzo G, d´Istria M, Serino I and Minucci S. (2004) Inhibition of increased 17β-estradiol-induced mast cell number by melatonin in the testis of the *Rana esculenta*, *in vivo* and *in vitro*. 2004. J Exp Biol. 207: 437-441.

Jackson IMD and Reichling S. (1974) Thyrotropin-releasing hormone distribution in hypothalamic and extrahypothalamic brain tissues of mammalian and submammalian chordates. Endocrinology 95: 854-862.

Jacobs GF and Kuhn ER. (1992) Thyroid hormone feedback regulation of the secretion of bioactive thyrotropin in frog. Gen Comp Endocrinol. 88: 415-423.

Jones RE, Lopez KH, Austin HB, Orlicky DJ and Summers CH. (2006) Uterine motility in the reptile *Anolis carolinensis*: Interactive effects of tension, prostaglandins, calcium, and vasotocin. J Exp Zool. 305A: 1030-1040.

Kaiser UB, Jakubowiak A, Steinberger A and Chin WW. (1997) Differential effects of gonadotropin-releasing hormone (GnRH) pulse frequency on gonadotropin subunit and GnRH receptor messenger ribonucleic acid levels *in vitro*. Endocrinology 138: 1224-1231.

Kameda Y. (2017) Morphological and molecular evolution of the ultimobranchial gland of nonmammalian vertebrates, with special reference to the chicken C cells. Dev Dyn. 246: 719-739.

Kano Y, Nakano T, Kumakura M, Wasa T, Suzuki M, Yamauchi K and Tanaka S. (2005) Seasonal expression of LHβ and FSHβ in the male newt pituitary gonadotrophs. Gen Comp Endocrinol. 141: 248-258.

Kato K, Ikemoto T and Park MK. (2005) Identification of reptilian prolactin and its receptor cDNAs in the leopard gecko, *Eublepharis macularius*. Gene 346: 267-276.

Kato T, Matsukawa H, Shioda A, Miura S, Fujita T and Kikuyama S. (1997) Cloning and Expression of Newt Prolactin Receptor. In: Advances in Comparative Endocrinology, (eds.) Kawashima S.and Kikuyama S.). Monduzzi Editore, Bologna, Italy, pp. 979-983.

Kauffman AS. (2004) Emerging functions of gonadotropin-releasing hormone II in mammalian physiology and behavior. Neuroendocrinol. 16: 784-806.

Kawamura K and Kikuyama S. (1998) Developmental origin of the olfactory system and GnRH neurons in the amphibian. Ann N Y Acad Sci. 839: 201-204.

Kawano E, Takahata Y, Oishi T, Ukena K, Tsutsui K and Tamotsu S. (2006) Neural interaction of gonadotropin-regulating hormone immunoreactive neurons and the suprachiasmatic nucleus with the paraventricular organ in the Japanese grass lizard (*Takydromus tachydromoides*). Zool Sci. 23: 277-287.

Kikuyama S, Yazawa T, Abe S, Yamamoto K, Iwata T, Hoshi K, Hasunuma I, Mosconi G, Polozonetti-Magni AM. (2000) Newt prolactin and its involvement in reproduction. Can J Physiol Pharmacol. 78: 984-993.

Kikuyama S, Tanaka S and Moore F. (2003) Endocrinology of Reproduction. In: Reproductive Biology and Phylogeny of Anura. Vol. 1 (ed.) Barrie G. M. Jamieson), Science Publishers, Inc. Enfield, NH, USA, pp. 275-321.

Kim JW, Im WB, Choi HH, Ishi S and Kwon HB. (1998) Seasonal fluctuations in pituitary gland and plasma levels of gonadotropic hormones in Rana. Gen Comp Endocrinol. 109: 13-23.

Kime DE. (1987) The Steroids. In: Fundamentals of Comparative Vertebrate Endocrinology, (eds.) Chester-Jones I., Ingleton P. M. and Philips J. G., Plenum Press. New York, pp. 3-56.

King JA and Millar RP. (1979a) Phylogenetic and anatomical distribution of somatostatin in vertebrates. Endocrinology 105: 1322-1329.

King JA and Millar RP. (1979b) Hypothalamic luteinizing hormone-releasing hormone content in relation to the seasonal reproductive cycle of *Xenopus leavis*. Gen Comp Endocrinol. 39: 309-312.

King JA and Millar RP. (1980) Comparative aspects of luteinizing hormone-releasing hormone structure and function in vertebrate phylogeny. Endocrinology 106: 707-717.

Koda A, Ukena K, Ternishi H, Ohta S, Yamamoto K, Kikuyama S and Tsutsui K. (2002) A novel amphibian hypothalamic neuropeptide: isolation, localization, and biological activity. Endocrinology 143: 411-419.

Kotani M, Detheux M, Vandenbogaerde A, Communi D, Vanderwinden J-M, Le Poul E, Brézillon S, Tyldesley R, Suarez-Huerta N, Vandeput F, Blanpain C, Schiffmann SN, Vassart G and Parmentier M. (2001) The metastasis suppressor gene KiSS-1 encodes kisspeptins, the natural ligands of the orphan G protein-coupled receptor GPR54. J Biol Chem. 276: 34631-34636.

Krishna L and Swarup K. (1985) Response of parathyroid gland, ultimobranchial body, paravertebral lime-sacs and serum calcium level to salmon calcitonin administration in *Rana cyanophlyctis* (Anura: Amphibia). Herpetologia 41: 65-70.

Kühn ER, Kikuyama S, Yamamoto K and Darras VM. (1985) *In vivo* release of prolactin in *Rana ridibunda* following an intravenous injection of thyrotropin-releasing hormone. Gen Comp Endocrinol. 60: 86-89.

Lance VA, Grumbles JS and Rostal DC. (2000) Sex difference in plasma corticosterone in desert tortoises, *Gopherus agassizii*, during the reproductive cycle. J Exp Zool. 289: 285-289.

Lascar G, Eugene D and Taxi J. (1996) Synaptic organization of amphibian sympathetic ganglia. Micros Res Tech. 35: 157-178.

Laudon M and Zisapel V. (1986) Characterization of central melatonin receptors using ^{125}I-melatonin. FEBS Lett. 197: 9-12.

Lederis K. (1987) Non-mammalian corticotropin release-stimulating peptide. Ann N Y Acad Sci. 512: 129-138.

Lee J-H, Miele ME, Hicks DJ, Phillips KK, Trent JM, Weissman BE and Welch DR. (1996) KiSS-1, a novel human malignant melanoma metastasis-suppressor gene. J Natl Cancer Inst. 88: 1731-1737.

Lerner AB, Case JD, Takahashi Y, Lee TH and Mori W.

(1958) Isolation of melatonin, the pineal gland factor that lightens melanocytes. Am Chem Soc. 80: 2587.

Lerner AB, Case JD and TakahashiY. (1960) Isolation of Melatonin and 5-Methoxyindole-3-acetic acid from bovine pineal glands. J Biol Chem. 235: 1992-1997.

Lescheid DW, Rosen GJ, Bridge AEA, Jones RE, Warby CM and Sherwood NM. (1997) Immunoreactive gonadotropin-releasing hormone (GnRH) is detected only in the form of chicken GnRH-II within the brain of the green anole, *Anolis carolinensis*. Gen Comp Endocrinol. 108: 247-257.

Licht P and Jones RE. (1967) Effects of exogenous prolactin on reproduction and growth in adult males of the lizard *Anolis carolinensis*. Gen Comp Endocrinol. 8: 228-244.

Licht P and Nicoll CS. (1969) Localization of prolactin in the reptilian pars distalis. Gen Comp Endocrinol. 12: 526-535.

Litch P, Farmer SW and Papkoff H. (1975) The nature of the pituitary gonadotropins and their role in ovulation in a urodele amphibian (*Ambystoma tigrinum*). Life Sci. 17: 1049-1054.

Litch P, Papkoff H, Farmer SW, Muller CH, Tsui HW and Crews D. (1977) Evolution of gonadotropin structure and function. Recent Prog Horm Res. 33: 169-248.

Licht P, McCreey BR, Barnes R and Pang R. (1983) Seasonal and stress related changes in plasma gonadotropins, sex steroids, and corticosterone in the bullfrog, *Rana castebeiana*. Gen Comp Endocrinol. 50: 124-145.

Licht P and Papkoff H. (1985) Reevaluation of the relative activities of pituitary glycoprotein hormones (follicle-stimulating hormone, luteinizing hormone, and thyrotrophin) from the green sea turtle, *Chelonia mydas*. Gen Comp Endocrinol. 58: 443-451.

Licht P, Porter D and Millar RP. (1987) Specificity of amphibian and reptilian pituitaries for various forms of gonadotropin-releasing hormones *in vitro*. Gen Comp Endocrinol. 66: 248-255.

Licht P, Tsai PS and Sotowska-Brochocka J. (1994) The nature and distribution of gonadotropin-releasing hormones in brains and plasma ranid frogs. Gen Comp Endocrinol. 94: 186-198.

López JM, Domínguez L and González A. (2008) Immunohistochemical localization of thyrotropin-releasing hormone in the brain of reptiles. J Chem Neuroanat. 36: 251-263.

Loretz CA and Bern HA. (1982) Prolactin and osmoregulation in vertebrates. Neuroendocrinol. 35: 292-304.

Lovejoy DA, Fischer WH, Parker DB, McRory JE, Park M, Lance V, Swanson P, Rivier JE and Sherwood NM. (1991) Primary structure of two forms of gonadotropin-releasing hormone from brains of the American alligator (*Alligator mississipiensis*). Regul Pept. 33: 105-116.

Luque RM, Córdoba-Chacón J, Gahete MD, Navarro VM, Tena-Sempere M, Kinema RD and Castaño JP. (2011) Kisspeptin regulates gonadotroph and somatotroph function in nonhuman primate pituitary via common and distinct signaling mechanisms. Endocrinology 152: 957-966.

Lutterschmidt DI, Lutterschmidt WI, Ford NB and Hutchinson VH. (2002) Behavioral thermoregulation and the role of melatonin in a nocturnal snake. Horm Behav. 41: 41-50.

Lutterschmidt DI, Lutterschmidt WI and Hutchinson VH. (2003) Melatonin and thermoregulation in ectothermic vertebrates: a review. Can J Zool. 81: 1-13.

McCord CP and Allen FP. (1917) Evidence associating pineal gland function with alterations in pigmentation. J Exp Zool. 23: 207-224.

MacKenzie DS and Licht P. (1984) Studies on the specificity of thyroid response to pituitary glycoprotein hormones. Gen Comp Endocrinol. 56: 156-166.

MacKenzie DS, Licht P and Papkoff H. (1981) Purification of thyrotropin from the pituitaries of two turtles: The green sea turtle and the snapping turtle. Gen Comp Endocrinol. 45: 39-48.

Maiti K, Li JH, Wang AF, Acharjee S, Kim WP, Im WB, Kwon HB and Seong JY. (2003) GnRH-II analogs for selective activation and inhibition of non-mammalian and type-II mammalian GnRH receptors. Mol Cells 16: 173-9.

Malagon MM, Garcia-Navarro S, Ruiz-Navarro A and Gracia-Navarro F. (1989) Morphometric evaluation of subcellular changes induced by *in vivo* TRH treatment in the pituitary gland of *Rana perezi*: effects on prolactin and thyrotropic cells. Cell Tissue Res. 256: 391-398.

Martinez-Arguelles DB and Papadopoulos V. (2010) Epigenetic regulation of the expression of genes involved steroid hormone biosynthesis and action. Steroids 75: 467-476.

Masucci M, D´Aniello B, Iela L, Ciarcia G and Rastogi RK. (1992) Immunohistochemical demonstration of the presence and localization of diverse molecular forms of gonadotropin-releasing hormone in lizard *Podarcis sicula sicula* brain. Gen Comp Endocrinol. 86: 81-89.

Matsui H, Takatsu Y, Kumano S, Matsumoto H and Ohtaki T. (2004) Peripheral administration of metastin induces marked gonadotropin release and ovulation in the rat. Biochem Biophys Res Commun. 320:

383-388.

McCreery BR and Licht P. (1984) The role of androgen in the development of sexual differences in pituitary responsiveness to gonadotropin-releasing hormone (GnRH) agonist in the bullfrog, *Rana castebeiana*. Gen Comp Endocrinol. 54: 350-359.

McNab BK. (2002) The Physiological Ecology of Vertebrates: A View From Energetics. Cornell University Press, Ithaca, New York.

Meijer OC, Buurstede JC and Schaaf MJM. (2019) Corticosteroid receptors in the brain: Transcriptional mechanism for specificity and context-dependent effects. Cell Mol Neurobiol. 39: 539-549.

Messager S, Chatzidaki EE, Ma D, Hendrick AL, Zahn D, Dixon J, Thresher RR, Malinge I, Lomet D, Carlton MBL, Colledge WH, Caraty A and Aparicio SAJR. (2005) Kisspeptin directly stimulates gonadotropin-releasing hormone release via G protein-coupled receptor 54. Proc Natl Acad Sci USA 102: 1761-1766.

Mikami S, Miyasaka A and Taniguchi K. (1985) Light and electron microscopic immunocytochemistry of the pituitary gland of the tortoise. Arch Histol Jap. 48: 373-388.

Millar RP. (2003) GnRH II and type II GnRH receptors. Trends Endocrinol Metab. 14: 35-43.

Millar RP, Zhi-Liang L, Pawson AJ, Flanagan CA, Morgan K and Maudsley SR. (2004) Gonadotropin-releasing hormone receptors. Endocr Rev. 25(2): 235-275.

Mimnagh KM, Bolaffi JL and Montgomery NM. (1987) Thyrotropin-releasing hormone (TRH): Immunohistochemical distribution in tadpole and frog brain. Gen Comp Endocrinol. 66: 394-404.

Minucci S, Di Matteo L, Pierabtoni R, Varíale B, Rastogi RK and Cheffi G. (1986) *In vivo* and *in vitro* stimulatory effect of a gonadotropin-releasing hormone analog (HOE 766) on spermatogonial multiplication in the frog, *Rana esculenta*. Endocrinology 19: 731-736.

Minucci S, D´Matteo L, Fasano S, Baccari GC and Pierantoni R. (1992) Intratesticular control spermatogenesis in the frog, *Rana esculenta*. J Exp Zool. 264: 113-118.

Miranda LA, Paz DA, Affani JM and Somoza GM. (1998) Identification and neuroanatomical distribution of immunoreactivity for mammalian gonadotropin-releasing hormone (mGnRH) in the brain and neural hypophyseal lobe of the toad *Bufo arenarum*. Cell Tissue Res. 293: 419-425.

Miranda LA, Affanni JM and Paz DA. (2000) Corticotropin- releasing factor acelerates metamorphosis in *Bufo arenarum*: effect on pituitary ACTH and TSH cells. J Exp Zool. 286: 473-480.

Miyata A, Arimura A, Dahl RR, Minamto N, Uehara A, Jiang L, Culler MD and Coy DH. (1989) Isolation of a novel 38 residue-hypothalamic polypeptide which stimulates adenylate cyclase in pituitary cells. Biochem Biophys Res Commun. 164: 57-574.

Montaner AD, Gonzalez O, Paz DA, Affanni JM and Somoza GM. (2000) Gonadotropin-releasing hormone (Ngr.) variants in a lizard brain: Is mammalian GnRH being expressed? Gen Comp Endocrinol. 119: 121-131.

Montero M, Yon L, Kikuyama S, Dufour S and Vaudry H. (2000) Molecular evolution of growth hormone-releasing hormone/pituitary adenylate cyclase-activating polypeptide gene family. Functional implication in the regulation of growth hormone secretion. J Mol Endocrinol. 25: 157-168.

Moore FL, Miller JL, Spielvogel SP, Kubiak T and Folkers K. (1982) Luteinizing hormone-releasing hormone involvement in the reproductive behavior of a male amphibian. Neuroendocrinol. 35: 212-216.

Morgan K and Millar RP. (2004) Evolution of GnRH ligand precursors and GnRH receptors in protochordate and vertebrate species. Gen Comp Endocrinol. 139: 191-197.

Moya L, Guerero F, Navas P and García-Herdugo G. (1987) GnRH induces activation of Leydig-like cells in *Pleurodeles waltii*. A morphometric study. Histol Histopathol. 2: 193-198.

Muller CH and Licht P. (1980) Gonadotropin specificity of androgen secretion by amphibian testes. Gen Comp Endocrinol. 42: 365-77.

Muske LE and Moore FL. (1990) Ontogeny of immunoreactive gonadoropin-releasing hormone neuronal systems in amphibians. Brain Res. 534: 177-187.

Muske LE and Moore FL. (1994) Antibodies against different forms of GnRH distinguish different populations of cells and axonal pathways in a urodele amphibian, *Taricha granulose*. J Comp Neurol. 345: 139-147.

Muske LE, King JA, Moore FL and Millar RP. (1994) Gonadotropin-releasing hormones in microdissected brain regions of amphibians: concentration and anatomical distribution of immunoreactive mammalian GnRH and chicken GnRH II. Regul Pept. 54: 373-384.

Naik DR, Sar M and Stumpf WE. (1980) Immunohistochemical identification of cells in the pars distalis of the pituitary of the lizard *Anolis carolinensis*. Histochem. 69: 19-26.

Nakajima K, Uchida D, Sakai M, Takahashi N, Yanagisawa T, Yamamoto K and Kikuyama S. (1993) Thyrotropin-releasing hormone (TRH) is the major prolactin-releasing factor in the bullfrog hypothalamus. Gen Comp Endocrinol. 89: 1-16.

Navarro VM, Castellano JM, Fernández-Fernández R, Tovar S, Roa J, Mayen A, Nogueira R, Vazquez MJ, Barreiro ML, Magni P, Aguilar E, Dieguez C, Pinilla L and Tena-Sempere M. (2005) Characterization of the potent luteinizing hormone-releasing activity of KiSS-1 peptide, the natural ligand of GPR54. Endocrinology 146: 156-163.

Navarro VM, Fernández-Fernández R, Nogueiras R, Vigo E, Tovar S, Chartrel N, Le Marec O, Leprince J, Aguilar E, Pinilla L, Dieguez C, Vaudry H and Tena-Sempere M. (2006) Novel role f26RFa, a hypothalamic RFamide orexigenic peptide, as putative regulator of the gonadotropic axis. J Physiol. 573: 237-249.

Neill JD, Duck LW, Sellers JC and Musgrove LC. (2001) A gonadotropin-releasing hormone (GnRH) receptor specific for GnRH II in primates. Biochem Biophys Res Commun. 2821: 1012-1018.

Neuman-Lee L, Greives T, Hopkins GR and French SS. (2017) The role of the kisspeptin system in regulation of the reproductive endocrine axis and territorial behavior in male side-blotched lizards (*Uta stansburiana*). Horm Behav. 89: 48-54.

Neves SR, Ram PT and Iyengar R. (2002) G protein pathways. Science 296(5573): 1636-1639.

Nicoll CS and Bern HA. (1972) On the actions of PRL among the vertebrates; is there a common denominator. In: Lactogenic Hormones, (eds.) Wolstenholm G.E.W. and Knight J., Churchill Livingstone, Edinburgh and London, UK, pp. 299-324.

Nojiri H, Ishda I, Miyashta E, Sato M, Urano A and Deguchi T. (1987) Cloning and sequence analysis of cDNAs for neurohypophysial hormones vasotocin and mesotocin for the hypothalamus of the toad, *Bufo japonicus*. Proc Natl Acad Sci USA 84: 3043-3046.

Norman AW and Litwack G. (1997) Hormones. Academic Press. 2nd edn., San Diego, CA.

Norris DO. (1997) Vertebrate Endocrinology. Academic Press. 3rd edn., San Diego, CA.

Norris DO and Lopez KH. (2010) Hormones and Reproduction of Vertebrates, Vol 2: Amphibians, 1st edn., Academic Press, Elsevier Inc.

Norris DO and Lopez KH. (2011) Hormones and Reproduction of Vertebrates, Vol 3: Reptiles, 1st edn., Academic Press, Elsevier Inc.

Northcutt RG and Muske LE. (1994) Multiple embryonic origins of gonadotropin-releasing hormone (GnRH) immunoreactive neurons. Dev Brain Res. 78: 279-290.

Oguchi A, Tanaka S, Aida T, Yamamaoto K and Kikuyama S. (1997) Enhancement by prolactin of the GnRH-induced release of LH from dispersed anterior pituitary cells of the bullfrog (*Rana castebeiana*). Gen Comp Endocrinol. 107: 128-135.

Oh DY, Wang L, Ahn RS, Park JY, Seong JY and Kwon HB. (2003) Differential G protein coupling preference of mammalian and nonmammalian gonadotropin-releasing hormone receptors. Mol Cell Endocrinol. 205: 89-98.

Ohtaki T, Shintani Y, Honda S, Matsumoto H, Hori A, Kanehashi K, Terao Y, Kumano S, Takatsu Y, Masuda Y, Ishibashi Y, Watanabe T, Asada M, Yamada T, Suenaga M, Kitada C, Usuki S, Kurokawa T, Onda H, Nishimura O and Fujino M. (2001) Metastasis suppressor gene KiSS-1 encodes peptide ligand of a G-protein-coupled receptor. Nature 411: 613-617.

Ojeda SR and Griffin JE. (1992) Organization of the Endocrine System. In: Textbook of Endocrine Physiology, (eds.) James E. Griffin and Sergio R. Ojeda), Oxford University Press Inc., New York, pp. 3-16.

Okada R, Yamamoto K, Koda A, Ito Y, Hayashi H, Tanaka S, Hanaoka Y and Kikuyama S. (2004) Development of radioimmunoassay for bullfrog thyroid-stimulating hormone (TSH): effects of hypothalamic releasing hormones on the release of TSH from the pituitary *in vitro*. Gen Comp Endocrinol. 135: 42-50.

Okada R, Yamamoto K, Koda A, Ito Y, Chartel N, Leprince J, Fournier A, Vaudry H and Kikuyama S. (2006) Effects of pituitary adenylate cyclase-activating polypeptide, vasoactive intestinal polypeptide, and somatostatin on the release of thyrotropin from the bullfrog pituitary. Ann N Y Acad Sci. 1070: 474-480.

Ostojic S. (2012) Steroids – From Physiology to Clinical Medicine. doi: 10.5772/46119.

Osugi T, Ubuka T and Tsutsui K. (2014) Evolution of GnIH and related peptides structure and function in the chordates. Front Neurosci. 8: 255.

Panda S, Hogenesch JB and Kay SE. (2002) Circadian rhythms from flies to human. Nature 417: 329-335.

Paniagua R, Fraile B and Sáez FJ. (1990) Effects of photoperiod and temperature on testicular function in amphibians. Histol Histopathol. 5: 365-378.

Papkoff H, Farmer SW and Licht P. (1976) Isolation and characterization of a follicle stimulating hormone and luteinizing hormone and its subunits from

snapping turtle *Chelydra serpentina* pituitaries. Endocrinology 98: 767-777.

Park D and Eisthen HL. (2003) Gonadotropin releasing hormone (GnRH) modulates odorant responses in the peripheral olfactory system of axolotls. J Neurophysiol. 90: 731-738.

Park D, Zawacki SR and Eisthen HL. (2003) Olfactory signal modulation by molluscan cardioexcitatory tetrapeptide (FMRFamide) in axolotls (*Ambystoma mexicanum*). Chem Senses 28: 339-348.

Pasquier J, Kamech N, Lafont A-G, Vaudry H, Rousseau K and Dufour S. (2014) Molecular evolution of GPCRS: Kisspeptin/kisspeptin receptors. J Mol Endocrinol. 52: T101-T117.

Pavel S. (1978) Arginine vasotocin as a pineal hormone. J Neural Transm. (Suppl.) 13: 135-155.

Pawson AJ, Maudsley SR, Lopes J, Katz AA, Sun Y-M, Davidson JS and Millar RP. (2003) Multiple determinants for rapid agonist-induced internalization of a nonmammalian gonadotropin-releasing hormone receptor: A putative palmitoylation site and threonine doublet within the carboxyl-terminal tail are critical. Endocrinology 144: 3860-3871.

Pearce D and Yamamoto KR. (1993) Mineralcorticoid and glucocorticoid receptor activities distinguished by nonreceptor factors at a composite response element. Science 259: 1161-1165.

Pierce JG and Parsons TF. (1981) Glycoprotein hormones: structure and function. Ann Rev Biochem. 50: 465-495.

Pinelli C, Jadhao AG, Biswas SP, Tsutsui K and D´Aniello B. (2015) Neuroanatomical organization of the brain gonadotropin-inhibitory hormone and gonadotropin-releasing hormone systems in the frog *Pelophylax esculentus*. Brain Behav Evol. 85: 15-28.

Pinheiro PLC, Cardoso JCR, Gomes AS, Fuentes J, Power DM and Canário AVM. (2010) Gene structure, transcripts and calciotropic effects of the PTH family of peptides in *Xenopus* and chicken. BMC Evol Biol. 10: 373-387.

Polzoneti-Magni A, Carnevali O, Yamamoto K and Kikuyama S. (1995) Growth hormone and prolactin in Amphibian reproduction. Zool Sci. 12: 683-694.

Powell RC, Ciarcia G, Lance V, Millar RP and King JA. (1986) Identification of diverse molecular forms of GnRH in reptilian brain. Peptides 7: 1101-1108.

Price DA and Greenberg MJ. (1977) Structure of a molluscan cardioexcitatory neuropeptide. Science 197: 670-671.

Propper CR and Dixon TB. (1997) Differential effects of arginine vasotocin and gonadotropin-releasing hormone on sexual behaviors in an anuran amphibian. Horm Behav. 32: 99-104.

Rastogi RK, King JA, Di Fiore MM, D'Aniello B and Pinelli C. (1997) Sex and reproductive status related brain content of mammalian and chicken-II GnRHs in *Rana esculenta*. J Neuroendocrinol. 9: 519-522.

Rastogi RK, Meyer DL, Pinelli C, Fiorentino M and D'Aniello B. (1998) Comparative analysis of GnRH neuronal systems in the amphibian brain. Gen Comp Endocrinol. 112: 330-345.

Rawding RS and Hutchinson VH. (1992) Influence of temperature and photoperiod on plasma melatonin in the mudpuppy, *Necturus maculosus*. Gen Comp Endocrinol. 88: 364-374.

Rawlings SR and Hezareh M. (1996) Pituitary adenylate cyclase-activating polypeptide (PACAP) and PACAP/vasoactive intestinal polypeptide receptors: actions on the anterior pituitary gland. Endocrine Rev. 17: 4-29.

Reiter RJ. (1986) The pineal gland: An important link to the environment. News Physiol Sci. 1: 202-205.

Reiter RJ. (1991) Pineal melatonin: cell biology of its synthesis and of its physiological interactions. Endocrine Rev. 12: 151-180.

Reiter RJ, Dun-Xian T and Ramaswamy S. (2018) Historical perspective and evaluation of mechanisms by which melatonin mediates seasonal reproduction in mammals. Melatonin Res. 1: 59-77.

Robertson DR. (1969a) The ultimobranchial body of *Rana pipiens*. VIII. Effects of extirpation upon calcium distribution and bone cells types. Gen Comp Endocrinol. 12: 479-490.

Robertson DR. (1969b) The ultimobranchial body of *Rana pipiens*. IX. Effects of extirpation and transplantation on urinary calcium excretion. Endocrinology 84: 1174-1178.

Roseghini M, Erspamer G.F, Severini C and Simmaco M. (1989) Biogenic amines and active peptides in extracts of the skin of thirty-two European amphibian species. Comp Biochem Physiol C Toxicol Parmacol. 94: 455-460.

Rosen G, Sherwood N and King AJ. (1997) Immunoreactive gonadotropin-releasing hormone (GnRH) is associated with vestibular structures in the green anole (*Anolis carolinensis*). Brain Behav Evol. 50: 129-138.

Saarela S and Reiter RJ. (1994) Function of melatonin in thermoregulatory process. Life Sci. 54: 295-311.

Saga T and Yamaki K. (2006) A comparative study of the chronological appearance of adenohypophysial cells in vertebrates with emphasis on the Japanese soft-shelled turtle (*Pelodiscus sinensis japonicus*). Biomed Res. 17: 81-94.

Sakamoto S, Nakamura K, Inoue K and Sakaii T. (2000) Melatonin stimulates thyroid-stimulating hormone accumulation in the thyrotropes of rat pars tuberalis. Histochem Cell Biol. 114: 213-218.

Sawada K, Ukena K, Kikuyama S and Tsutsui K. (2002) Identification of a cDNA encoding a novel amphibian growth hormone-releasing peptide and localization of its transcript. J Endocrinol. 174: 395-402.

Sedgley KR, Finch AR, Caunt CJ and McArdle CA. (2006) Intracellular gonadotropin-releasing hormone receptors in breast cancer and gonadotrope lineage cells. J Endocrinol. 191: 625-636.

Seebacher F and Franklin CE. (2005) Physiological mechanisms of thermoregulation in reptiles: a review. J Comp Physiol. 175: 533-541.

Seki T and Kikuyama S. (1986) Effect of thyrotropin-releasing hormone and dopamine on the *in vitro* secretion of prolactin by the bullfrog pituitary gland. Gen Comp Endocrinol. 61: 197-202.

Seminara SB, Messager S, Chatzidaki EE, Thresher RR, Acierno JSJr, Shagoury JK, Bo-Abbas Y, Kuohung W, Schwinof KM, Hendrick AG, Zahn D, Dixon J, Kaiser UB, Slaugenhaupt SA, Gusella JF, O'Rahilly S, Carlton MBL, Crowley WFJr, Aparicio SAJR and Colledge WH. (2004) The GPR54 gene as a regulator of puberty. Obstet Gynecol Surv. 59: 351-353.

Sherwood NM and Sower SA. (1985) A new family member of gonadotropin-releasing hormone. Neuropeptides 6: 2005-2014.

Sherwood NM, Zoeller RT and Moore FL. (1986) Multiple forms of gonadotropin releasing hormone in amphibians brains. Gen Comp Endocrinol. 61: 313-322.

Sherwood NM and Whittier JM. (1988) Gonadotropin-releasing hormone from brains of reptiles: Turtles (*Pseudomys scrita*) and snakes (*Thamnophis sirtalis parietalis*). Gen Comp Endocrinol. 69: 319-327.

Sherwood NM, Lovejoy DA and Coe IR. (1993). Origin of mammalian gonadotropin-releasing hormones. Endocr Rev. 14: 241-245.

Silveira LG, Noel SD, Silveira-Neto AP, Abreu AP, Brito VN, Santos MG, Bianco SD, Kuohung W, Xu S, Gryngarten M, Escobar ME, Arnold IJP, Mendonca BB, Kaiser UB and Latronico AC. (2010) Mutations of the KISS1 gene in disorders of puberty. J Clin Endocrinol Metab. 95: 2276-2280.

Simoncini T and Genazzani AR. (2003) Non-genomic actions of sex steroid hormones. Eur J Endocrinol. 148: 281-292.

Sing P, Krishna A, Sridaran R and Tsutsui K. (2008) Changes in GnRH I, bradykinin and their receptors and GnIH in the ovary of *Calotes versicolor* during reproductive cycle. Gen Comp Endocrinol. 159: 158-169.

Smith MT, Moore FL and Mason RT. (1997) Neuroanatomical distribution of chicken-I gonadotropin-releasing hormone (cGnRH-I) in the brain of the male red-sided garter snake. Brain Behav Evol. 49: 137-48.

Smith JT, Rao A, Pereira A, Caraty A, Millar RP and Clarke IJ. (2008) Kisspeptin is present in ovine hypophysial portal blood but not does not increase during the preovulatory luteinizing hormone: evidence that gonadotropes are not direct targets of kisspeptin *in vivo*. Endocrinology 149: 1951-1959.

Somoza GM, Paz DA, Stefano AV and Affanni JM. (1996) Identification of immunoreactive mammalian gonadotropin-releasing hormone in the brain of metamorphic larvae of *Bufo arenarum* Hensel (Amphibia: Anura). Int J Dev Neurosci. 14: 663-672.

Sotowska-Brochocka J. (1988) The stimulatory and inhibitory role of the hypothalamus in the regulation of ovulation in grass frog, *Rana temporaria* L. Gen Comp Endocrinol. 70: 83-90.

Sotowska-Brochocka J and Licht P. (1992) Effect of infundibular lesions on GnRH and LH release in the frog, *Rana temporaria*, during hibernation. Gen Comp Endocrinol. 85: 43-54.

Sotowska-Brochocka J, Martyńska L and Licht P. (1994) Dopaminergic inhibition of gonadotropic release in hibernation frogs, *Rana temporaria*. Gen Comp Endocrinol. 93: 192-196.

Srivastav Ajai K and Rani L. (1989a) Ultimobranchial body and parathyroid gland of the frog, *Rana tigrina* in response to calcitonin administration. Biol Struct Morphog. 2: 136-40.

Srivastav Ajai K and Rani L. (1989b) Influence of calcitonin administration of serum calcium and inorganic phosphate level of the frog, *Rana tigrina*. Gen Comp Endocrinol. 74: 14-17.

Srivastav Ajai K, Das VK, Das S, Sasayama Y and Suzuki N. (1995a) Amphibian parathyroids: morphological and functional aspects. Microsc Res Tech. 32: 79-90.

Srivastav Ajai K, Sasayama Y and Suzuki N. (1995b) Morphology and physiological significance of parathyroid glands in reptilia. Microsc Res Tech. 32: 91-103.

Srivastav Ajai K, Das VK, Srivastav SK, Sasayama Y and Suzuki N. (1998) Morphological and functional aspects of reptilian ultimobranchial gland. Anat Histol Embryol. 27: 359-364.

Srivastav Ajai K, Das VK, Srivastav SK and Suzuki N. (2000) Amphibian calcium regulation: physiological aspects. Zool Pol. 45: 7-26.

Srivastav Ajai K, Srivastav B, Mishra D, Srivastav SK and Suzuki N. (2011) Calcitonin-induced alterations to the ultimobranchial and parathyroid glands in the garden lizard *Calotes versicolor*. Turk J Zool. 35: 9-14.

Stamper DL and Licht P. (1990) Effect of gonadotropin-releasing hormone on gonadotropin biosynthesis in pituitaries of frog, *Rana pipiens*. Biol Reprod. 43: 420-426.

Stamper DL and Licht P. (1993) Further studies on the influence of GnRH on the biosynthesis of gonadotropins in female frogs (*Rana pipiens*). Gen Comp Endocrinol. 92: 104-12.

Stamper DL and Licht P. (1994) Influence of androgen on the GnRH-stimulated secretion and biosynthesis of gonadotropins in the pituitary of juvenile female bullfrog, *Rana castebeiana*. Gen Comp Endocrinol. 93: 93-102.

Stárka L and Dušková M. (2020) What is a hormone? Physiol Res. 69: S183-S185.

Stenzel-Poor MP, Heldwein KA, Stenzel P, Lee S and Vale W. (1992) Characterization of the genomic corticotrophin-releasing factor (CRF) gene from *Xenopus laevis*: two members of the CRF family exist in amphibians. Mol Endocr. 6: 1716-1724.

Stocco DM and Clark BJ. (1996) Regulation of the acute production of steroids in steroidogenic cells. Endocr Rev. 17: 221-244.

Suzuki S, Kadokawa H and Hashizume T. (2008) Direct kisspeptin-10 stimulation on luteinizing hormone secretion from bovine and porcine anterior pituitary cells. Anim Reprod Sci. 103: 360-365.

Tavolaro R, Canonaco M and Franzoni MF. (1995) Comparison of melatonin-binding sites in the brain of two amphibians: an autoradiographic study. Cell Tissue Res. 279: 613-617.

Teles MG, Bianco SDC, Brito VN, Trarbach EB, Kuohung W, Xu S, Seminara SB, Mendonca BB, Kaiser UB and Latronico AC. (2008) A GPR54-activating mutation in a patient with central precocious puberty. N Engl J Med. 358: 709-715.

Thompson EL, Patterson M, Murphy KG, Smith KL, Dhillo WS, Todd JF, Ghatei MA and Bloom SR. (2004) Central and peripheral administration of kisspeptin-10 stimulates the hypothalamic-pituitary-gonadal axis. J Neuroendocrinol. 16: 850-858.

Troskie B, King JA, Millar RP, Peng YY, Kim J, Figueras H and Illing N. (1997) Chicken GnRH II-like peptides and a GnRH receptor selective for chicken GnRH II in amphibians' sympathetic ganglia. Neuroendocrinol. 65: 396-402.

Troskie B, Illing N, Rumbak E, Sun YM, Hapgood J, Sealfon S, Conklin D and Millar R. (1998) Identification of three putative GnRH receptor subtypes in vertebrates. Gen Comp Endocrinol. 112: 296-302.

Troskie BE, Hapgood JP, Millar RP and Illing N. (2000) Complementary deoxyribonucleic acid cloning, gene expression, and ligand selectivity of a novel gonadotropin-releasing hormone receptor expressed in the pituitary and midbrain of *Xenopus laevis*. Endocrinology 141: 1764-1771.

Trudeu VL, Somoza GM, Natale GS, Pauli B, Wignall J, Jackman P, Doe K and Schueler FW. (2010) Hormonal induction of spawning in 4 species of frogs by coinjection with a gonadotropin-releasing hormone agonist and a dopamine antagonist. Reprod Biol Endocrinol. 8: 36.

Trudeu VL, Schueler FW, Navarro-Martin L, Hamilton CK, Bulaeva E, Bennett A, Fletcher W and Taylor L. (2013) Efficient induction of spawning of Northern leopard frogs (*Lithobates pipiens*) during and outside the natural breeding season. Reprod Biol Endocrinol. 11: 14.

Tsai P-S and Licht P. (1993a) *In vivo* GnRH responsiveness of LH secretion in the female turtle, *Trachemys scripta*, in relation to the reproductive stage. Gen Comp Endocrinol. 90: 328-337.

Tsai P-S and Licht P. (1993b) Differential distribution of chicken-I chicken-II GnRH in the turtle brain. Peptides 14: 221-226.

Tsutsui K, Saigoh E, Ukena K, Teranishi H, Fujisawa Y, Kikuchi M, Ishii S and Sharp PJ. (2000) A novel avian hypothalamic peptide inhibiting gonadotropin release. Biochem Biophys Res Commun. 275: 661-667.

Tsutsui K, Osugi T, Son YL and Ubuka T. (2018) Structure, function, and evolution of GnIH. Gen Comp Endocrinol. 264: 48-57.

Udaykumar K and Joshi BN. (1997) Effect of exposure to continuous light and melatonin on ovarian follicular kinetics in the skipper frog, *Rana cyanophlyctis.* Biol Signals 6: 62-66.

Ukena K, Koda A, Yamamoto K, Kobayahi T, Iwakoshi-Ukena E, Minakata H, Kikuyama S and Tsutsui K. (2003) Novel neuropeptides related to frog growth hormone-releasing peptide: isolation, sequence, and functional analysis. Endocrinology 144: 3879-3884.

Ukena K, Koda A, Yamamoto K, Iwakoshi-Ukena E, Minakata H, Kikuyama S and Tsutsui K. (2006) Structures and diverse functions of frog growth hormone-releasing peptide (fGRP) and its related peptides (fGRP-RPs): a review. J Exp Zool. 305A: 815-821.

Ukena K, Iwakoshi-Ukena E, Osugi T and Tsutsui T. (2016) Identification and localization of gonadotropin-inhibitory hormone (GnIH) orthologs in the hypothalamus of the red-eared slider turtle, *Trachemys scripta elegans*. Gen Comp Endocrinol. 227: 69-76.

Underwood H and Hyde LL. (1989) The effect of day length on the pineal melatonin rhythm of the lizard *Anolis carolinensis*. Comp Biochem Physiol. A94: 53-56.

Valverde AR, Owens DW, MacKenzie DS and Amoss MS. (1999) Basal and stress-induced corticosterone levels in olive ridley sea turtles (*Lapidochelys olivacea*) in relation to their mass nesting behavior. J Exp Zool. 284: 652-662.

Vaněček J, Pavlík A and Illnerová H. (1987) Hypothalamic melatonin receptor sites revealed by autoradiography. Brain Res. 435: 359-362.

Vu M and Trudeu VL. (2016) Neuroendocrine control of spawning in amphibians and its practical applications. Gen Comp Endocrinol. 234: 28-39.

Wang L, Bogerd J, Choi HS, Seong JY, Soh JM, Chun SY, Blomenröhr M, Troskie BE, Millar RP, Yu WH, McCann SM and Kwon HB. (2001a) Three distinct types of GnRH receptor characterized in the bullfrog (*Rana catesbeiana*). Proc Natl Acad Sci USA 98: 361-366.

Wang L, Yoo MS, Kang HM, Im WB, Choi HS, Bogerd J and Kwon HB. (2001b) Cloning and characterization of cDNAs encoding the GnRH1 and GnRH2 precursors from bullfrog (*Rana catesbeiana*). J Exp Zool. 289: 190-201.

White R and Parker MG. (1998) Molecular mechanisms of steroid hormone action. Endocr Relat Cancer 5: 1-14.

Wiechmann AF and Wirsig-Wiechmann CR. (1993) Distribution of melatonin receptors in the brain of the frog *Rana pipiens* as revealed by *in vitro* autoradiography. Neuroscience 52: 469-480.

Wiechmann AF and Wirsig-Wiechmann CR. (1994) Melatonin receptor distribution in the brain and retina of lizard, *Anolis carolinensis*. Brain Behav Evol. 43: 26-33.

Wilczynski W, Allison JD and Marler CA. (1993) Sensory pathways linking social and environmental cues to endocrine control regions of amphibian forebrains. Brain Behav Evol. 42: 252-264.

Wirsig-Wiechmann CR. (1993) Peripheral projections of nervus terminalis LHRH-containing neurons in the tiger salamander, *Ambystoma tigrinum.* Cell Tissue Res. 273: 31-40.

Wirsig-Wiechmann CR and Ebadifar B. (2002) The naris muscles in tiger salamander. II. Innervation as revealed by enzyme histochemistry and immunocytochemistry. Anat Embryol. 205: 181-186.

Wright ML. (2002) Melatonin, diel rhythms, and metamorphosis in anuran amphibians. Gen Comp Endocrinol. 126: 251-254.

Wurtman RJ and Anton-Tay F. (1969) The mammalian pineal as neuroendocrine transducer. Rec Prog Horm Res. 25: 493-522.

Yang EJ, Nasipak BT and Kelley DB. (2007) Direct action of gonadotropin in brain integrates behavioral and reproductive functions. Proc Nat Acad Sci USA 104: 2477-2482.

Yasuda A, Yamaguchi K, Papkoff H, Yokoo Y and Kawauchi H. (1989) The complete amino acid sequence of growth hormone from the sea turtle (*Chelonia mydas*). Gen Comp Endocrinol. 73: 242-251.

Yasuda A, Kawauchi H and Papkoff H. (1990) The complete amino acid sequence of prolactin from the sea turtle (*Chelonia mydas*). Gen Comp Endocrinol. 80: 363-371.

Yin H, Ukena K, Ubuka T and Tsutsui T. (2005) A novel G protein-coupled receptor for gonadotropin-inhibitory hormone in the Japanese quail (*Coturnix japonica*): identification, expression and binding activity. J Endocrinol. 184: 257-266.

Yuanyou L and Haoran L. (2000) Differences in mGnRH and cGnRH-II contents in pituitaries and discrete brain areas of *Rana rugulosa* W. according to age and stage of maturity. Comp Biochem Physiol C Toxicol Pharmacol. 125: 179-188.

Zhang L, Kessler AE and Tsai PS. (2007) Characterization and steroidal regulation of gonadotropin beta subunits in the male leopard frog, *Rana pipiens.* Gen Comp Endocrinol. 150: 66-74.