Journal of Animal and Veterinary Advances 14 (4): 81-90, 2015
ISSN: 1680-5593
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Role of Leptin in Cattle Production: Review

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Abstract: Leptin is produced in the adipose tissue and other organs. Its main function is to maintain glucose homeostasis indicating the status of the reserve of energy to ventromedial nucleus of the hypothalamus; target of leptin which regulates eating behavior, so this is considered a sensor of energy balance. This hormone is involved in the onset of puberty and acts as a critical hormonal signal of nutritional status in the neuroendocrine regulation of pulsatile secretion of Growth Hormone (GH) and release of Gonadotropin-Releasing factor (GHRH) mediated by Neuropeptide Y (NPY). This hormone is involved in the onset of puberty and acts as a critical hormonal signal of nutritional status in the neuroendocrine regulation of pulsatile secretion of GH and release of GHRH mediated by NPY. Leptin also controls the hypothalamic-hypophysis-gonadal axis through synthesis and release of hypothalamic and hypophyseal gonadotrophins (GnRH, FSH and LH) and potentiates the effects of insulin through which regulates the synthesis of blood glucose. The regulation of secretion of this hormone is at long term and depends on the variation in body mass and stimulating effects of insulin because of this, it has great importance in the transition period in dairy cattle in which during the time of drying the body condition and fat reserves are recovered for postpartum performance. The cattle breed tically determines the amount of body fat and leptin secretion which in turn determines the quality of the carcass.

Key words: Leptin, bovine, meat and milk production, carcass, stimulating effects

INTRODUCTION

In the animal industry, production efficiency is built upon healthy animals which will present regular reproductive cycles (pregnancy, childbirth, cyclical-ovarian reactivation, fertilization, new pregnancy). In dairy cattle, the increase in production was accompanied by a Negative Energy Balance (NEB) acute and pronounced during early lactation and a decrease in fertility (Wettemann and Bossis, 2000; Liefers *et al*., 2005; Nakada, 2006), this as a result of environmental changes and changes in the animal itself (for example, the tic potential for milk production has increased, the herds are now larger, systems of exploitation now have more technology and intensive total feeding has expanded) and it is unclear how far animals have adapted to these changes (Nakada, 2006; Wyle, 2011). Furthermore, until now, the reproduction management was carried out by monitoring the behavior of cows and/or using hormonal protocols and this has given acceptable results.

Nevertheless, reproductive disorders by multifactorial causes (Roche, 2006) is the most common reason for culling in herds. The trend today is to prevent this aspect to increase reproductive efficiency while providing welfare to the animals.

Within the production cycle, the dairy cow passes for three critical stages as to their metabolic functions are concerned. In the peripartum period are carried out dramatic changes in both energy metabolism and within the reproductive physiology (Wettemann and Bossis, 2000; Liefers *et al*., 2005; Kadokawa *et al*., 2006; Nakada, 2006; Roche, 2006) as a result of the transition from the gestational to non-gestational state it is given the increase in fetal-placental mass, preparation for delivery, synthesis of colostrum and delivery, demands of energy, protein and minerals by the fetus are increased and the capacity of gastrointestinal tract is endangered due to the increase in the size of the fetus (Giblin *et al*., 2010). In this sense, the nutritional management in these stages is critical for the future performance of the animal (maintenance, production and reproduction).

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The management of the dry period in dairy cows is a key to reducing the negative effects of these changes postpartum; stage in which the cow must accumulate energy reserves (weight gain, adipose tissue, bone mineral reserves and rest of the mammary gland). At the beginning of lactation, the energy requirements are quadrupled by the need of precursors for the synthesis of colostrum and then milk in the mammary gland and the cell oxidation processes in increase (Block *et al*., 2001; Leury *et al*., 2003) as feed intake by the animal is not sufficient for these demands, the deficit is covered by the mobilization of endogenous reserves and the change in the pattern of nutrients used by non-mammary tissues for maintenance functions. Peripheral mechanisms that orchestrate these adaptations in ruminants before and after birth have been extensively studied and which essentially involve changes in the concentration and action of hormones.

AN OVERVIEW OF LEPTIN

Leptin is a protein hormone produced in adipose tissue and it is important in the regulation of appetite, live weight gain, ovarian activity, growth and development of the mammary gland, distribution of nutrients between mother and fetus during pregnancy, increase of energy metabolism and muscle anabolism. However, the expression of leptin may be altered by infection or obesity (Levin *et al*., 1996; Kline *et al*., 1997; Barb *et al*., 1998; Friedman and Halaas, 1998; Houseknecht *et al*., 1998; Ramsay *et al*., 1998; Spicer and Francisco, 1998; Henry *et al*., 1999; Spicer, 2001; Oprzadek *et al*., 2003; Munzberg *et al*., 2005).

The endocrine function of adipocyte cells in rodents is clear, similarly studies in productive species show that leptin is a signal of the energy status of farm animals.

The Intracerebroventricular (ICV) bolus injection of leptin, decreases NPY levels in the Arcuate (ARC) and Paraventricular Hypothalamic Nuclei (PVN) in rats which showed the involvement of NPY and leptin in homeostasis (Erickson *et al*., 1996). NPY reduces thermosis of brown adipocyte tissue, an effect that was not a result of increase of feed intake (Billington *et al*., 1991). Leptin acts centrally on the hypothalamus to suppress the activity of NPY neurons which reduces the stimulating unit on feed intake and decreases NPY by inhibiting the cell bodies of KISS peptin.

Leptin is synthesized in adipose tissue and is secreted into the peripheral circulation and is highly correlated with live weight and the adipocyte and has been proposed that links the live weight and adipocyte to puberty (Garcia *et al*., 2002).

Leptin is synthesized in adipose tissue and is secreted into the peripheral circulation, it acts centrally on the hypothalamus to suppress the activity of NPY neurons which reduces the stimulating unit on feed intake and decreases NPY by inhibiting the Kisspeptin cell bodies. There are two distinct types of neurons in ARC that are important in control of food intake; Preopiomelanocortin (POMC) neurons activated by an orexigenic hormones and releasing α-Melanocyte-Stimulating Hormone (α-MSH) in satiety center and neurons activated by orexigenic peptides such as ghrelin that release the substances including Neuropeptide Y (NPY) and Agouti-Related Peptide (AgRP) in hunger center. ARC integrates neural (mostly vagal) and humoral inputs such as enteropeptides including orexigenic (ghrelin and orexins) and an orexigenic peptides (cholecystokinin, polypeptide YY, glucagon-like peptide-1, oxyntomodulin, leptin and others) that exert a physiological role in regulating appetite and satiety. The peripherally (gut, adipose tissue) and centrally expressed modulators of appetitive behavior act through specific receptors in the afferent (mostly vagal) nerves and hypothalamic neurons implicated in adiposity signaling and regulation of food intake.

Acting directly on POMC neurons leptin stimulates the release of α-MSH which suppresses feed intake and alters growth. The activation of POMC cell stimulates KISS peptin neurons that have axon terminals near NPY and POMC where KISS peptin cell bodies are expressed which stimulate or inhibit each. Leptin also may act directly on the sub-population of KISS peptin neurons by increasing stimulation of the GnRH release and secretion of gonadotropins from hypophysis. Leptin can enhance the secretion of LH and support reproduction acting to increase sensitivity of gonadotrophin cells in the hypophysis to GnRH. A fluctuation in the energy balance changes the secretion of leptin and alters these pathways (Nakada, 2006; Liefers *et al*., 2005; Hausman *et al*., 2012; Kuehn *et al*., 2009).

The leptin receptor was identified by Tartaglia *et al*. (1995) and is a member of the class 1 cytokines receptor family due to its structural homology with interleukin-6 and common receptors downstream on signaling pathways (Houseknecht *et al*., 1998). The leptin receptor family is composed of at least six isoforms that result from alternative splicing. Receptor isoforms include a long form (OB-rb) and several short forms with the cytoplasmic tail

lengths (OB-Ra, OB-rc, OB, OB-rd-rf and a soluble form (OB-Re), consisting of the extracellular loop and circulates in plasma (Tartaglia *et al*., 1995), leptin binding to its receptor causes stimulation of the signaling pathways of Janus Kinases (JAK), Signal Transductions and Activators of Transcription (STAT). Additionally, the short forms of receptor send signals through the Mitogen-Activated Protein Kinases (MAPK) or Phosphotidyl Inositol-3 (PI-3) (Bjorbaek *et al*., 1997; Barb and Kraeling, 2004). Fat cells release leptin into the bloodstream. The hypothalamus "reads" the amount of circulating leptin and uses this information to regulate appetite, metabolism and other processes. It is known that leptin binds to receptors of cell surface in the hypothalamus to activate through signals a molecule of STAT3, although, the role of this in mediating of various physiological effects of leptin is uncertain. However, it is known that STAT3 production is essential to reduce feed intake dramatically. In humans, obesity occurs when people become resistant to leptin which is a messenger to "control their food intake". Then, activation of STAT3 may be involved in the normalization of appetite and produce other health benefits. There is controversy whether leptin through control of glucose metabolism also regulates the production control of STAT3.

The presence of leptin, decreases feed intake, increases energy expenditure and decreases metabolic efficiency (Sartin *et al*., 2011). However, appetite is a complex process resulting from the integration of multiple factors and nerve signaling, the hypothalamus receives neurological and hormonal signals such as leptin cholecystokinin and ghrelin as well as nutritional ones as glucose, FFA, AA and VFA (Sartin *et al*., 2011).

Leptin is involved in a wide range of biological functions such as lipid and glucose metabolism, synthesis of glucocorticoids and insulin, proliferation of T CD4+lymphocytes, cytokine secretion, phagocytosis and synaptic transmission. Moreover, it regulates the hypothalamic-hypophysial-adrenal axis, maturation of the reproductive system, hematopoiesis, angiosis and fetal development. The cyclical and postpartum ovarian reactivation in cows depends on the secretion of LH, leptin promotes the secretion of hypophysial gonadotropins via the release of GnRH, although, this function depends on the animal's energy balance and body reserves (Nakada, 2006; Liefers *et al*., 2005). The concentrations of many hormones and growth factors that regulate the function of adipocytes and leptin are influenced by body weight and nutritional status. In the nuclei of the hypothalamus leptin affects the activity of some neurons which promotes the release of anabolic neuropeptides such as NPY orexins, melanin concentrating hormone and galanin, regulation of catabolic peptides which include the Corticotropin-Releasing Hormone (CRH) and Thyrotropin Releasing Hormone (TRH) (Bjorbaek and Kahn, 2004; Hausman *et al*., 2012). SNC areas involved in glucose homeostasis are the Ventromedial Nucleus (VMN), arcuate (NA) and Paraventricular (PVN). The peripheral insulin action is to ensure the maintenance of glucose homeostasis. The neuronal insulin signaling adjusts the peripheral glucose homeostasis which involves the binding of insulin to its receptor and subsequent activation of Insulin Receptor (IRS) and Protein Kinase PI3K (PKB) in the regulation of this type, IRS-1 and 2 are the common isoforms related to glucose homeostasis. The infusion of insulin or its mimetic in the third cerebral ventricle suppresses hepatic glucose production independent of alterations in body weight or changes in circulating levels of insulin and other glucoregulator hormones (Obici *et al*., 2002, Hausman *et al*., 2012).

The expression of leptin and its receptors was initially discovered in adipose tissue, it has been established that it has an important role throughout the body via the regulation of glucose homeostasis but the presence of this hormone is also evidenced by the placenta and other organs. Leptin levels increase during early pregnancy, even before an increase in the adipose tissue, suggesting that there are other factors that modulate their production (Hausman *et al*., 2012). However, the mechanisms of action of leptin on implantation and embryonic growth are still unknown. It has been shown that the leptin binding to its receptor causes stimulation of the signaling pathways of JAK (Janus family kinase)/STAT (Signal Transduction and Activator of Transcription), MAPK (Mitogen-Activated Protein Kinase), p38MAPK and P13K (Phosphoinositide-3-Kinase). It has also been found that leptin plays an antiapoptotic function in trophoblastic cells and exerts that function primarily through the MAPK pathway. The human Chorionic Gonadotropin (hCG) stimulates the transcription and synthesis of leptin in placenta while the AMPc inhibits the induction of leptin by hCG. The hCG effect on leptin appears to be mediated by the MAPK pathway. AMPc stimulates the expression of leptin in placenta and that the nucleotide is able to activate not only PKA signaling pathway but also that of MAPK. In this sense, it is shown that the inducing action of AMPc on leptin would be mediated by a crossover between these pathways. It has been clarified the mode of action of leptin in placenta and the mechanisms of regulation of protein expression that support the importance of leptin in reproductive biology. Insulin increases leptin production which

is associated with decreased fasting serum leptin and hyperleptinemia that exists in states of insulin resistance which can also induce a relative resistance to leptin. Proinflammatory cytokines such as TNFa and IL-1 can directly induce the expression of the *ob* gene as part of a feedback for the regulation of local immunity, inflammation and angiogenesis.

In bovines the *LEP* gene was cloned by Ji and was mapped on chromosome 4 region q32 (Pomp *et al*., 1997). It presents three exons and two introns with the coding regions located in exons 2 and 3 (Coleman, 1978). It has been described that this gene LEP has simple polymorphisms in nucleotides, a polymorphism of this type takes place in exon 2, causing physiological effects when substituted Cytosine (C) for Thymine (T). The T allele is associated with the highest fat content of the carcass (Corva *et al*., 2004). If the gene coding for the production of the protein is present on pyrimidine Cytosine base (C) common leptin is produced whereas when Thymine is present (T) leptin is modified. An animal receives one gene from each parent, the genotype may be: CC (the two genes encoding common leptin); TT (the two genes coding modified leptin) and CT (each encoding a type of leptin). The CC genotype animals fatten slowly, eat less during the lactation peak and produce less milk. Those with the TT genotype produce more milk of better quality and more carcasses with high marbling (Houseknecht *et al*., 1998; Buchanan *et al*., 2002; Corva *et al*., 2004). Animals with CT genotype can produce the two types of leptin and have intermediate behavior.

SECRETION OF LEPTIN

Leptin has a pulsatile secretion with variations according to circadian rhythm with an approximate frequency of one pulse every 45 min. Its concentration is increasing gradually during the day and reaches a peak around midnight, decreases until the start of a new cycle which begin with the appearance of sunlight. This pattern depends on feed. Circulating levels of leptin increase in the first hours after ingestion and continue rising when overfeeding. In situations of fasting leptin production decreases. It seems that changes in the pattern of secretion is associated with feeding and related to plasma concentration of insulin to body weight. This is due to the fact that insulin stimulates leptin expression in isolated adipocytes and therefore increases its circulating level (Licinio *et al*., 1997).

Leptin concentration in plasma is highly correlated with body fat mass in sheep, bovines, pigs and horses, although, it is also modified by fatness in sheep, bovines, pigs and horses as well as by simple alterations of the diet consumed in pregnant sheep and when the energy consumption is reduced, leptin concentration is reduced but when nutrient availability is increased such as lipids or glucose, the leptin concentration is increased in sheep at the end of lactation, however, the propionate is not an important regulator of leptin in dairy cattle (Blache *et al*., 2000; Delavaud *et al*., 2000; Ehrhardt *et al*., 2000; Ramsay *et al*., 1998; Buff *et al*., 2002; Nagatani *et al*., 2000; Amstalden *et al*., 2000; Barb *et al*., 2001; Piccione *et al*., 2004; Thomas *et al*., 2001; Chelikani *et al*., 2003; Archer *et al*., 2005; Bradford *et al*., 2006).

The serum leptin concentration in sheep and cattle varies and it is a signal of the stored energy, at 65 days of restriction body fat and serum leptin concentration in ovariectomized sheep are reduced while the pregnant ewes show a decline during the negative energy balance associated with lactation (Delavaud *et al*., 2000; Liefers *et al*., 2005).

Leptin levels increase during early pregnancy, even before adipose tissue is increased, suggesting that there are other factors modulating their production (Hausman *et al*., 2012). However, the mechanisms of action of leptin on implantation and embryonic growth are still unknown. hCG stimulates the transcription and synthesis of leptin in placenta while AMPc inhibits the induction of leptin by hCG. The effect of hCG on leptin appears to be mediated by the MAPK pathway. We observed that AMPc stimulates the expression of leptin in placenta and that the nucleotide is able to activate not only PKA signaling pathway but also that of MAPK.

LEPTIN IN REPRODUCTION

The roles of leptin in reproduction was initially indicated by the observation that ob/ob homozygous cats are sterile but were corrected by leptin, it was subsequently found that leptin is closely related to GnRH neurons to facilitate secretion of gonadotrophins (Chehab *et al*., 1996; Cheung *et al*., 1997; Ingalls *et al*., 1950; Watanobe, 2002). During the development of puberty in gilts, leptin concentration increases associated with age at puberty in gilts (Qian *et al*., 1999; Wise and Klindt, 2004).

There has been a marked increase in circulating leptin and gene expression during development of puberty in heifers and it is associated with a serum increase of IGF-I and body weight (Garcia *et al*., 2002). Recent laboratory studies have demonstrated that leptin gene expression

and circulating leptin are responsive to short-term nutrient flow and are associated with changes in serum insulin, IGF-I and LH pulsating in prepubertal heifers (Amstalden *et al*., 2000).

Laboratory studies have shown that leptin gene expression and circulating leptin are responsive to short-term nutrient flow and are associated with serum changes in insulin, IGF-I and LH pulsating in pubertal heifers (Amstalden *et al*., 2000). Onset of puberty may be linked to attainment of a critical body weight or a minimum percentage of body fat (Frisch, 1984). Leptin treatment advanced sexual maturation in feed-restricted animals and in those with *ad libitum* access to feed (Barash *et al*., 1996; Ahima *et al*., 1997; Cheung *et al*., 1997).

Within the reproductive aspect, leptin is involved in a complex network of paracrine and/or endocrine interactions at multiple levels of the Hypothalamic-Hyphophysial-Gonadal axis (HHG). This hormone is mainly expressed in adipose tissue as well as in the hypothalamus, hypophysis, gastric fundic epithelium, skeletal muscle, syncytiotrophoblast and mammary epithelium. Leptin Receptors (Ob-R) have been identified in the hypothalamus, gonadotrophin cells of the adenohypophysial, granulosa cells, theca and interstitial ovarian cells, endometrium and Leydig cells. *ob* gene expression is regulated by hormones, growth factors and cytokines. Estrogens induces and androgens suppresses the leptin production which gives an explanation of sexual dimorphism in plasma leptin levels (Williams *et al*., 2002; Bjorbaek and Kahn, 2004; Gurbuz *et al*., 2005). At the level of hypothalamus leptin accelerates GnRH pulses but not their amplitude, acting directly on hypothalamic Ob-R. There is an indirect stimulation on the hypothalamus through interneurons secreting neuropeptides and of nitric oxide which induces the secretion of GnRH. Leptin also has direct action on the hypophysis stimulating release of gonadotrophins (LH and FSH).

Leptin plays an important role in regulating reproduction in the hypothalamic-hypophysial-gonadal axis. The hypothesis that the activity of this axis depends on the frequency of pulses of LH postpartum during the early stage of lactation (100 days) has been tested and that this event is closely related to the energy status and Free Fatty Acid (FFA) levels, insulin, Insulin-like Growth Factor I (IGF-I), leptin and GH or STH. It has also been found that leptin is involved in the secretion and regulation of the GnRH in the hypothalamus (Barb and Kraeling, 2004; Williams *et al*., 2002) and in the hypophysis modulating LH secretion. In cows, this hormone is related to the estral cycle regulation and probably is involved in the control of reproduction. There is a positive relationship between leptin levels in serum and the follicular fluid in addition to a negative relationship between the increase of levels of this hormone and estrogen levels (Gurbuz *et al*., 2005). Williams *et al*. (2002) mention that circulating leptin decreases during the follicular and luteal phase of the estrous cycle in sexually and mature heifers and cows.

Concentrations of many hormones and growth factors that regulate the function of adipocytes and leptin are influenced by body weight and nutritional status. In the nuclei of the hypothalamus leptin affects the activity of some neurons which promotes the release of anabolic neuropeptides such as NPY, orexins, melanin concentrating hormone and galanin, regulation of catabolic peptides which include Corticotropin-Releasing Hormone (CRH) and TRH (Bjorbaek and Kahn, 2004; Hausman *et al*., 2012). SNC areas involved in glucose homeostasis are the Ventromedial (VMN), Arcuate (AN) and Paraventricular (PVN) nucleus. The peripheral insulin action is to ensure the maintenance of glucose homeostasis. The neural insulin signaling regulates peripheral glucose homeostasis which involves the binding of insulin to its receptor and subsequent activation of Insulin Receptor (IRS), PI3K and Protein Kinase (PKB) in regulation of this type, IRS-1 and 2 are the common isoforms related to glucose homeostasis. The infusion of insulin or its mimetic in the third cerebral ventricle suppresses hepatic glucose production independent of changes in body weight or changes in circulating levels of insulin and other glucoregulator hormones (Obici *et al*., 2002; Hausman *et al*., 2012).

At ovarian level, leptin at high concentrations seems to antagonize the effect of IGF-I, TGFb, insulin and glucocorticoids, steroidogenesis stimulated by FSH/LH on thecal and follicular cells, so leptin in ovary can suppress estradiol production and interfere with the dominant follicle development and maturation of oocytes (Park *et al*., 2011). Thus, leptin deficiency (e.g., nutritional deficiency) can lead to a dysfunction of the HHG axis and an excess of leptin (obese) will cause gonadal inhibition giving in both cases, reproductive dysfunction. In the endometrium, leptin is important in implantation and early embryonic development. It has been found deficient Ob-R in endometrium of subfertile women. In placenta the syncytiotrophoblast secretes leptin, producing an increase in the first and second trimester of pregnancy (Cervero *et al*., 2006).

The earliest signal for the onset of puberty is leptin, however, this hormone is a necessary but not sufficient factor. It contributes to the activation of the HHG axis which increases the production of sex steroids and the

subsequent increase in Growth Hormone (GH), Insulin-like Growth Factor-I (IGF-I) and other hormonal factors (Park *et al*., 2011).

Subsequently, leptin influences menstrual cycle (woman), menopause, pregnancy and lactation. Under conditions of sub-optimal nutrition such as eating disorders (anorexia, bulimia), exercise-induced amenorrhea and functional hypothalamic amenorrhea are found under low levels of serum leptin whereas in the presence of excess of energy reserves or metabolic disorders such as obesity and syndrome of polycystic ovaries often higher leptin levels are found in blood or follicular fluid giving the possibility that a relative deficiency or leptin-resistance are responsible at least in part of the reproductive abnormalities observed in these conditions. Leptin may act as the critical link between adipose tissue and the reproductive system (Cervero *et al*., 2006; Joo *et al*., 2010; Park *et al*., 2011).

Insulin increases leptin production which is associated with serum decrease of fasting leptin and hyperleptinemia in the states of insulin-resistance. Proinflammatory cytokines such as TNFa and IL-1 can directly induce expression of the *ob* gene as part of a feedback for the regulation of local immunity, inflammation and angiogenesis. Transcription and translation of the leptin gene occurs in adipose tissue in the gastric mucosa, mammary epithelial cells, myocytes, placenta, testis, ovary, hair follicles and in the human fundic glands.

Today, it is known that transcription and translation of the leptin gene occurs in adipose tissue in the gastric mucosa, mammary epithelial cells, myocytes, placenta, testis, ovary, hair follicles and in the human fundic glands and that their increased levels are associated with the onset of puberty, reproductive maturity and fertility in mammals (Hausman *et al*., 2012). It is of great importance in the transition period of the milk producing cow in addition to influence carcass quality in the beef cattle producer. The hypothalamus plays a central role in regulating feed intake. The ventromedial nucleus (the satiety center), arcuate and paraventricular (centers of consumption) are the target where leptin exerts most of its effects on energy metabolism through food intake (Obici *et al*., 2002; Hausman *et al*., 2012).

Angiogenesis is associated with follicular development and is regulated independently within each follicle potential. It is critical to the vasculature of the follicle, since this determines its destiny. Thus, inhibition of Vascular Endothelial Growth Factor (VEGF), VEGF-2 receptors, the vascular endothelial cells or interference with the local vascular system can inhibit follicular development or prevent ovulation. In the ovaries, there is an intense angiogenesis and increase of permeability of blood vessels during follicular development, ovulation and later formation of the luteum corpus. Furthermore, angiogenesis is regulated independently within each follicle and of the magnitude of vascular permeability and plexus of vessels, the supply of high molecular weight of tropic factors; precursors and lipids can be controlled. This indicates that the follicular vasculature could be involved in the processes of selection, dominance and atresia (Cervero *et al*., 2006; Joo *et al*., 2010; Park *et al*., 2011).

MILK PRODUCTION

The endocrine profile of galactogenesis is PRL, STH, ACTH and indirectly TSH, insulin, glucagon and oxytocin in the galactopoiesis. Milk production is directly related to the ability of dry matter intake in animals. Leptin decreases feed intake, increases energy expenditure and decreases the efficiency of metabolism. It has been shown that this hormone participates in a wide range of biological functions such as lipid and glucose metabolism, synthesis of glucocorticoids and insulin, proliferation of T $CD4^+$ lymphocytes, cytokine secretion, phagocytosis and synaptic transmission. Moreover, it regulates the hypothalamic-hypophysial-adrenal axis, maturation of the reproductive system, hematopoiesis, angiogenesis and fetal development. The cyclical and ovarian postpartum reactivation in cows depends on the secretion of LH, leptin promotes the secretion of hypophisial gonadotrophins via the release of GnRH, although, this function depends on the animal's energy balance and body reserves (Nakada, 2006; Liefers *et al*., 2005).

Some polymorphisms as LEP-2470, LEP1238, LEP-963, Y7F and R25C are associated with the energy expenditure of lactation in cattle. Only SNP Y7F is related to energy storage. There are also associations between polymorphisms of leptin and calving difficulty, length of gestation and perinatal mortality. In the case of beef cattle, breast feeding as stimulus by itself does not appear to influence the decrease in leptin levels postpartum (Giblin *et al*., 2010).

MEAT PRODUCTION

In meat production reproductive efficiency determines profitability. The ideal in beef cattle is to ensure one delivery by year but usually not all cows are pregnant in the breeding season. This problem is attributed to poor intake of nutrients and prolonged

anestrus. Not having the necessary consumption of nutrients animals have extended periods to conceive (Wettemann and Bossis, 2000).

When food consumption is greater than that required for maintenance and production, the energy is stored as body fat. The condition of body mass is an indicator to predict the reproductive performance (Wettemann and Bossis, 2000).

By eating more nutrients after birth there is increased secretion of hormones such as the LH and FSH (Perry *et al*., 1991; Ciccioli *et al*., 2003) and the effects of nutrition on reproductive issues can be more prevalent in lean than in cows whose body mass level is appropriate.

The accumulation of fat in the body occurs first as a result of hyperplastic adipocyte growth and is followed by hypertrophic changes (Owens *et al*., 1993). In the livestock industry, the hypertrophy of adipose tissue is fat deposition mainly involved in the finishing of animals to estimate the price of carcass in the market (Hood, 1982). However, the rate of growth of adipose tissue varies with location in the body. In beef cattle fattening, sheep and pigs, subcutaneous hypertrophy occurs faster than the intermuscular, intramuscular in kidney and pelvis (Kempster, 1981).

The adipocyte size may influence the synthesis and secretion of leptin because larger adipocytes, contain more amount of ARNm of leptin (Auwerx and Staels, 1998). According to Cianzio *et al*. (1985), adipocyte size varies with age of steers and places within the body where fat accumulates. Leptin is associated with obesity in animals, acting at both central and peripheral level, influencing on appetite and fat tissue. When leptin is given to rodents, birds, pigs and sheep feed intake is reduced and this hormone may be an important component of feedback involving key regulators of metabolism such as insulin, glucocorticoids and the sympathetic nervous system. Some *in vitro* studies suggest that leptin directly modulates energy metabolism in peripheral tissue and may be an antagonist of insulin activity in adipose tissue and muscle. These physiological properties support that the leptin gene is a candidate for the evaluation of polymorphisms that could affect the content of fat in the carcass (Buchanan *et al*., 2002). The frequencies of simple polymorphisms in nucleotides within races are consistent with an association of these polymorphisms in exon 2 and the fat content in the carcass. The British breeds have a higher frequency of thymine allele whereas the continental breeds have a higher prevalence of cytosine allele. British breeds (Angus and Hereford) are characterized by early maturity compared with continental breeds (Charolais and Simmental) giving them the ability to contain more fat at an earlier age (Gregory *et al*., 1994).

It is considered that the concentration of leptin could be related to the fat content in beef cattle. However, more information is needed to clarify whether the concentration of this hormone in serum is associated with other indicators which could favor feeding strategies, commercialization and prediction of the carcass value before slaughter (Geary *et al*., 2003).

CONCLUSION

In specialized cattle, increased milk production is accompanied by a negative energy balance more acute and prolonged as well as a decrease in fertility and consequently, the leading cause of disposal of these animals is infertility at an early age and the need of more replacement animals. As for meat production, the goal of every operation is focused on the calving interval (365 days) to achieve profitability. In these animals, adequate postpartum reproductive behavior depends on body condition or energy reserves during this period. Since, leptin discovery (1994) in adipose tissue, this has been positioned unquestionably as a molecule fundamental for reproduction. It is product of *LEP* gene whose synthesis was originally discovered in adipose tissue with the function of regulating satiety and energy balance through specific hypothalamic receptors. Today, it is known that transcription and translation of the leptin gene occurs in adipose tissue in the gastric mucosa, mammary epithelial cells, myocytes, placenta, testis, ovary, hair follicles as well as in the human fundic glands and that their increased levels are associated with the onset of puberty, reproductive maturity and fertility in mammals. It is of paramount importance in the transition period of the milk-producing cow, besides influencing carcass quality in beef cattle. The hypothalamus plays a central role in regulating food intake. The ventromedial nucleus (the satiety center), arcuate and paraventricular (centers of consumption) are the target where leptin exerts most of its effects on energy metabolism through feed consumption. Creole cattle breeds have allelic variants (alleles cytosine and thymine) that in other races are associated with meat quality. The T allele is associated with higher fat content in the carcass, animals with the TT genotype produce more and better milk and better marbled carcasses, unlike animals with CC and CT that fatten slowly, consume less feed during the peak of lactation and produce less milk. Leptin concentrations during the peripartum show marked changes are high in late gestation and decrease almost to zero level the delivery. Coincidentally dry matter intake has the same pattern in dairy cattle which is closely related to negative energy balance, uterine involution, the depth of physiological anoestrus postpartum and the resumption of cyclicity.

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