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GLUT4 TRANSLOCATION AND ITS IMPLICATIONS ON SWINE MUSCLE TISSUE

(*Translocação de glut4 e suas implicações no tecido muscular de suínos*)

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ABSTRACT

This study had as objective to describe, through a bibliographic review, of how the GLUT4 glucose-transporter protein's metabolical process contributes for the skeletal muscular tissue development through the addition of iodine in the nourishment, causing the liberation of the hormones Triiodothyronine (T3) and Thyroxine (T4), stimulators of the GLUT4 protein. The synthesis of these hormones consists of the metabolism of iodine, through the transport of extracellular iodides to the glandular cells and to the thyroid follicles and can induce the muscular action in the swine species of GLUT4 glucose transporters, that are abundantly present in the cellular membranes of skeletal and cardiac muscles, as well as adipose tissue. Articles, periodicals and studies were used to carry out this research. The aim of this research was to present the producer with options to maintain the excellence of his product and to ensure that it reaches the market with quality and low production costs It was concluded that, by inducing thyroid hormones, there could be an increase in muscle hypertrophy through GLUT4 translocation.

Keywords: *Glucose transporters, iodine, muscle growth, thyroid hormones; animal production.*

RESUMO

Este estudo teve como objetivo descrever, através de uma revisão bibliográfica, como o processo do metabolismo de translocação da proteína transportadora de glicose GLUT4 contribui para o desenvolvimento do tecido muscular esquelético através de uma adição de iodo na nutrição, causando a liberação dos hormônios Triiodotironina (T3) e Tiroxina (T4), estimuladores da proteína GLUT4. A síntese destes hormônios consiste no metabolismo de iodo, através do transporte de iodetos extracelulares para as células glandulares e para os folículos da tireoide podendo induzir a ação muscular na espécie suína dos transportadores de glicose GLUT4 que são abundantemente presentes nas membranas celulares dos músculos esquelético e cardíaco, além do tecido adiposo. Para a realização dessa pesquisa, foram utilizados artigos, periódicos e estudos. A proposta dessa pesquisa visou apresentar opções para que o produtor consiga manter a qualidade de seu produto e que esse chegue ao mercado com qualidade e baixo custo de produção. Concluiu-se que, através da indução dos hormônios tireoidianos, pode haver um aumento de hipertrofia muscular pela translocação da GLUT4.

Palavras-chave: Transportadores de glicose, iodo, crescimento muscular, hormônios tireóide, produção animal.

INTRODUCTION

Glucose transport in the body is extremely important in cellular energy metabolism. The glycolytic route is employed through glucose transporters until the degradation of this molecule to supply energy in the form of ATP (adenosine triphosphate). With the technological increase and the demand for production of good quality meat, the physiological area emerges as an alternative to develop strategies to increase muscle growth from a low-cost food source, without reducing the quality of the product (GU *et al.*, 2023).

In general, GLUTs are induced by the thyroid hormones triiodothyronine (T3) and thyroxine (T4), essential for normal metabolism in all cells (ZAMONER *et al.*, 2007). The synthesis of T3 and T4 consists of iodine metabolism, through the transport of extracellular iodides to the glandular cells and thyroid follicles (SUZUKI and KOHN, 2006). In this work,

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it was studied more specifically the muscle action in the porcine species of GLUT4 glucose transporters, which are insulin-dependent and abundantly present in the cell membranes of skeletal and cardiac muscle, as well as adipose tissue (BRYANT and GOULD, 2020).

Thus, the objective was to evaluate, through a literature review, how the process of translocation metabolism of the glucose transporter protein GLUT4 contributes to the development of skeletal muscle tissue through an addition of iodine in the diet, causing the release of the thyroid hormones T3 and T4, stimulators of GLUT4 protein, generating a higher protein rate in the cell, thus benefiting skeletal muscle growth (BUCCI *et al.*, 2006).

DEVELOPMENT

The transformation of iodine/iodide and the expression of thyroid hormones

For the formulation of healthy diets, minerals must be inserted in a way that meets the stipulated requirements, so that there are no metabolic consequences and that they do not harm the animal's health. Among several minerals, one of the most important is iodine, which when it does not reach its requirements is the cause of goiter and hypothyroidism, negatively influencing the health and weight gain of the animal (WHO, 2007). According to the NRC (1996), the swine species has a requirement of 0.14mg/kg and in this species shows toxicity from a concentration of 400ppm. Iodine deficiency affects reproductive characteristics, in addition to losses in productive traits (MEHDI and DUFRASNE, 2016).

When inserted into the diet, iodine is converted into iodide in the gastrointestinal tract prior to its absorption. Upon entering the bloodstream, iodide is transported into the follicle cells by the sodium/iodide co-transporter (NIS), which is embedded in the basolateral membrane of the thyrocyte (SPITZWEG and MORRIS, 2002). The activity of NIS is electrogenic and depends on the Na^+ gradient produced by the Na^+/K^+ ATPase pump.

With a negative electrical potential relative to the interstitium and follicular lumen maintained within the cell, iodide is transported against this electronegative potential, but in favor of the electrochemical gradient generated by Na^+. Thus, NIS activity is related to the Na^+/K^+ ATPase pump (DOHAN *et al*., 2003). The adenohypophyseal hormone thyrotropin (TSH) stimulates iodide transport by NIS. In addition to serum TSH concentration, iodide transport is also regulated by the autoregulatory mechanism of the thyrocyte, where NIS activity varies inversely with glandular iodine content (ENG *et al.*, 1999).

After this process, through pendrin, which is a highly expressed anion transporter in the thyroid gland, where it performs the Cl^-/I^- exchange, iodide is directed into the follicular lumen (NOFZIGER *et al.*, 2011). The organification of iodide and its oxidation are accomplished at the apical surface of the follicular cell, where the reactions are catalyzed by thyrooperoxidase (TPO). The literature indicates that TPO is responsible for the oxidation of iodide and its incorporation into thyroglobulin tyrosyl radicals (LARSEN *et al.*, 2003). This reaction takes advantage of the hydrogen peroxide (H_2O_2) formed by the H_2O_2 generating system, DUOX (VAISMAN *et al.*, 2004).

The H_2O_2 is essential as an oxidant in the oxidation reaction of iodide performed by TPO and, when intracellular iodide levels are regular, the generation of H_2O_2 becomes the limiting step in the biosynthesis of thyroid hormones (Fig. 01) (CORVILAIN *et al.*, 1988).

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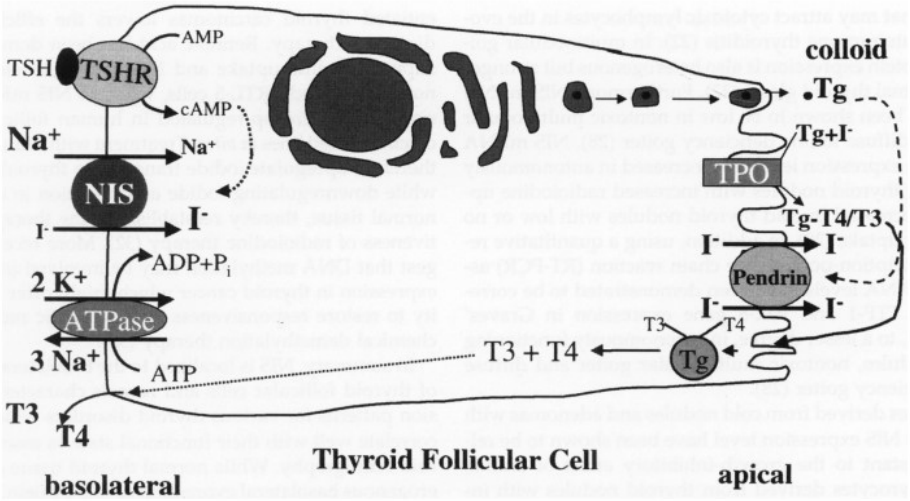
These hormones (TH) reach the cell interior through monocarboxylate transporters 8 (MCT8) (BRENT, 2012) and after being taken up, they undergo the deiodation process, and T3 may be translocated to the cell nucleus, where four isoforms of thyroid hormone (TR) receptors have already been well characterized in animals: (TRα1 TRα2, TRβ1 and TRβ2) (WILLIAMS, 2000).



(**Source:** SPITZWEG *et al.*, 2000)

Figure 01: Localization of proteins involved in iodide transport and metabolism in the thyroid cell.

The most widespread mechanism of thyroid hormone action involves the formation of the TR-T3 complex, forming a heterodimer in specific regions of DNA, known as thyroid hormone response elements (TREs). The interaction of TR with T3 favors heterodimer formation with the Retinoid X receptor (RXR), and, during this process, coactivator proteins are recruited to the promoter region of the target gene. This mechanism leads to a modification in chromatin and the regulation of gene transcription (DAVIS *et al.*, 2008).

The T4 hormone also acts through nuclear receptors, however, the binding affinity of these receptors for T3 is much higher than for T4. Thus, T3 is the natural ligand for TRs (DAVIS *et al.*, 2008).

The non-genomic or non-classical actions (independent of nuclear receptors), have evolved over time suggesting that TH could cause a rapid stimulus in Ca^{2+} uptake, which would be independent of protein synthesis, thus involving the activation of phospholipase C (PLC), with release of inositol triphosphate (IP3), and consequent activation of protein kinase C (PKC) (SEGAL and INGBAR, 1989). T4 triggers effects at basal physiological concentrations, whereas T3 produces a similar effect at supraphysiological concentrations, evidencing the preference of T4 for non-genomic actions. The identification of Ca^{2+} as the first messenger for T3 action at the plasma membrane emphasizes Ca^{2+} uptake as a pioneering event after the hormone binds to the respective membrane receptor and can also be bound to red blood cells, or even influence intracellular calcium homeostasis, including energy production, metabolism and apoptosis, which influence mitochondrial actions (MARCHI *et al*., 2018; VAFAI and MOOTHA, 2012).

Plow *et al.* (2000) described an αvβ3 integrin heterodimer, located in the ArgGly-Asp recognition region (RGD), responsible for binding to several extracellular matrix proteins, such

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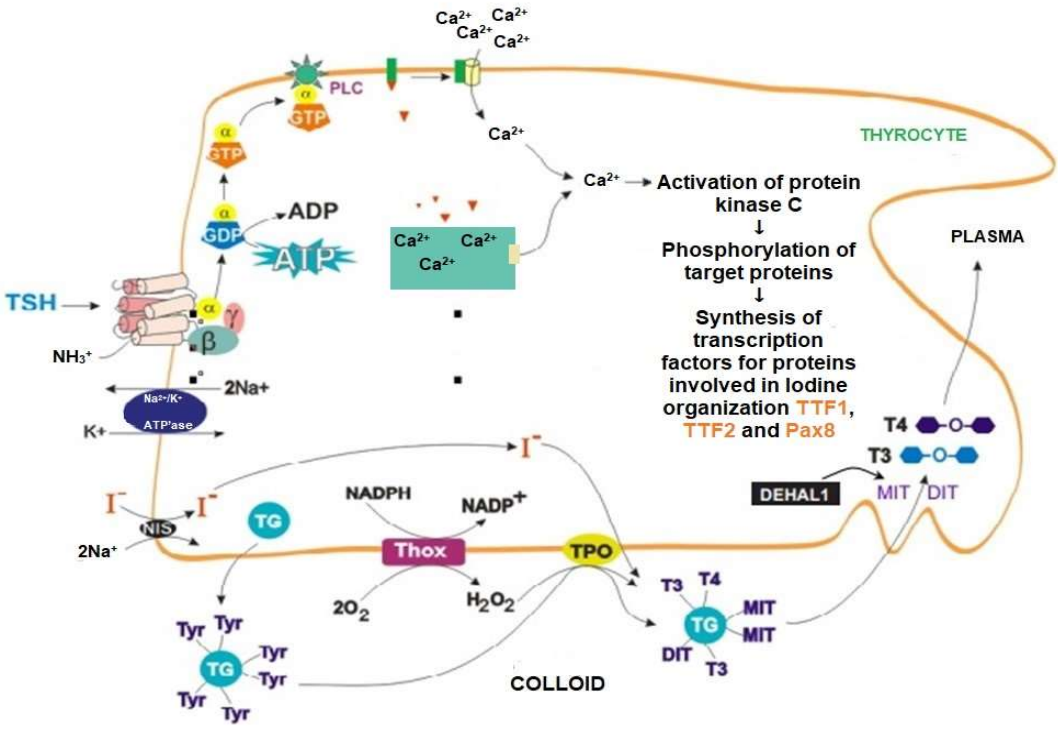
as growth hormone. THs can still connect to nuclear transduction events by activating one or more signaling pathways, potentially resulting in DNA-dependent effects, or encompassing effects that do not directly involve gene expression. These non-genomic responses are generally associated with second messenger signaling that include the PLC, IP3, phosphatidylinositol 3-kinase (PI3K), diacylglycerol (DAG), protein kinase C (PKC), protein kinase A (PKA), cyclic AMP (cAMP), cAMP response element binding protein (CREB), Ras, Raf1 serine/threonine kinase (ZAMONER and PESSOA-PUREUR, 2011) pathways.

The TSH and iodine at high concentrations (5mM) can increase pendrin mRNA expression when these are in the presence of TG (SUZUKI and KOHN, 2006). For the efflux of iodide by pendrin to occur, it is necessary to have the presence of chloride in the follicular lumen, where the exchange occurs by 1 iodide/1 chloride (SHCEYNIKOV *et al.*, 2008). However, although pendrin is placed as the main transporter to perform this iodide efflux, it is not the only pathway where this can occur (OHANA *et al.*, 2009).

In the analysis of Fig. 02, Iodine is taken up at the basolateral membrane of the thyrocyte by the NIS where there is an electrochemical gradient energy production, being generated by the Na^+/K^+ ATPase dependent pump. On the collateral side of the thyrocyte, I^- undergoes an oxidation process by thyreoperoxidase (TPO), when H_2O_2 is present, this H_2O_2 being produced by the enzyme THOX. Reduction of H_2O_2 by the cofactor NADPH occurs. Thyroglobulin, which is secreted into the lumen of the follicle, acts as a support matrix for the synthesis of thyroid hormones (Pinto *et al.*, 2009).



(**Source:** Pinto *et al.*, 2009).

Figure 02: Main processes of thyroid hormone synthesis.

Thus, TPO catalyzes the iodination of tyrosine residues, i.e., it organifies these residues resulting in the formation of 3-monoiodotyrosine (MIT) and 3,5-diiodotyrosine (DIT).

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After this, two iodothyrosine molecules come together to generate T3 or T4 in a reaction that is also catalyzed by TPO. The iodinated thyroglobulin is retained in the lumen of the follicle and taken up by the thyrocyte by the action of pinocytosis, where the secretion of hormones that regulate this uptake. The portion of thyroglobulin that is removed from the colloid undergoes processing within the lysosomes, thus forming T3 and T4 that are released into the bloodstream. The molecules of MIT and DIT which are not used in this process, undergo deiodination by the enzyme DEHAL1 (iodothyrosine dehalogenase), where the iodine is secreted for the formation of new thyroid hormones (PINTO *et al.*, 2009).

The function of Glut4 and SLC2A4 protein

Due to its high molecular weight, glucose cannot diffuse through the membrane pores, using alternative mechanisms to be transported across the cell membrane, such as the facilitated transport that is mediated by specific membrane transporters, which is the case of GLUTs, and the co-transport with sodium ion (SGLT) (MACHEDA *et al.*, 2005).

In almost all cells, glucose is transported via transporters from an area of higher concentration to an area of lower concentration by means of facilitated membrane diffusion. All this is possible because the special binding properties of the GLUT protein mediate this entire process (BROWN, 2000).

GLUT4 is the most important and abundant transporter in the glucose displacement into the skeletal muscle and adipose cells in the postprandial period, where the skeletal muscle is the main territory involved in glucose uptake and storage as glycogen, thus being considered of paramount importance in glucose homeostatic maintenance (ZORZANO *et al.*, 2000). This transporter is found in intracellular vesicles in basal medium, but when there is an insulin stimulus or muscle contraction, these vesicles translocate to the plasma membrane, fusing and increasing the amount of GLUT4 in the membrane, allowing a sharp increase in glucose uptake (LIVINGSTONE *et al.*, 2022). This increase in muscle glucose uptake capacity is in part due to the increased content of GLUT4 in the cell (KANG and CHIANG, 2022). However, this process depends on when the SLC2a4 gene is expressed, since it encodes this protein. The regulation of how much SLC2a4 is expressed is altered by physiological, pharmacological and pathophysiological stimulus.

The region that promotes the SLC2a4 gene presents specific binding sites that anchor proteins acting as activators or repressors of gene transcription (BISNETA, 2020). Myocyte growth factor (MEF2) is a transcriptional factor that has vital role in the transmission of extracellular signals to the genome, which modulates gene programs, thus promoting muscle cell proliferation, differentiation, morphogenesis and apoptosis (MOLKETIN *et al.*, 1996). The MEF2 has 4 isoforms, where there is the importance of the MEF2A and MEF2D isoforms. When it comes to GLUT4 activation in skeletal muscle, these isoforms function as heterodimers, which in GLUT4 expression, this bond formed facilitates its expression (ISONG *et al*., 2022). The MEF2 binding site is a responsive element located in a few base pairs of the SLC2a4 gene and anchors the MEF2 factors that act in the activation and transcription of GLUT4 (MORENO *et al.*, 2003).

Another way in which GLUT4 protein is stimulated is through thyroid hormones. Thyroid hormones increase metabolic activity in nearly all tissues of the body, where mitochondrial oxygen consumption increases in hyperthyroidism, suggesting the generation of

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oxygenated water (H_2O_2), subsequently increased in hyperthyroidism (ISONG *et al*., 2022). Thyroid hormones also control a variety of physiological processes, including lipid and glucose metabolism. In hepatocytes T3 increases the expression of genes involved in lipogenesis, but also induces the expression of genes involved in fatty acid oxidation, such as CPT-1a (carnitine palmitoyltransferase-1a) (LOPEZ and NESS, 2006).

As for carbohydrate metabolism, T3 participates in processes involving peripheral uptake of glucose, by increasing the expression of GLUT4 present in skeletal muscle tissue, heart and adipose tissue, and mainly responsible for maintaining glycemia in the postprandial period, as well as its use by tissues, by inducing the expression of glycolytic and oxidative enzymes, such as the pyruvate dehydrogenase complex (PDC). PDC causes decarboxylation of pyruvate to acetyl CoA, and modulation of its activity impacts both fatty acid, pyruvate, and glucose metabolism. On the other hand, T3 also promotes increased hepatic glucose production by activating the transcription of key enzymes of gluconeogenesis, such as glucose-6-phosphatase and phosphoenolpyruvate-carboxykinase (PEPCK) (BLENNEMANN *et al*., 1992).

The function of Glut4

The leading role of GLUT4 expression occurs in the regulation of insulin sensitivity in insulin-sensitive tissues and, therefore, in the regulation of glucose homeostasis. Studies in mice overexpressing GLUT4 have observed an increase of this transporter, inducing a larger amount of the protein at the plasma membrane under basal conditions (LIU *et al.*, 1993). Thus, the amount of transporter protein in the cell membrane depends on the total cellular content, which is determined by the expression pattern of the GLUT4 gene.

GLUT4 expression is known to undergo hormonal regulation. The main promoter of the SLC2a4 gene, which encodes the GLUT4 protein, has a thyroid hormone response element (TRE) where TR-α1 binds (SANTALUCIA *et al.*, 2001). Treatment for extended periods with the hormone T3 stimulates GLUT4 expression and glucose uptake by skeletal muscle tissue (KHODER *et al.*, 2022).

Activation of PI3K by insulin intercedes the translocation of GLUT4 into the plasma membrane. When PI3K is activated, AKT protein may be part of a pathway that results in GLUT4 expression, as described by Hernandez *et al.* (2001), where the authors concluded that there is implication of AKT in the expression of glucose transporters, yet AKT inhibition by ML-9 in adipocytes may prevent the increase in GLUT4 mRNA expression that is induced by insulin (Fig. 03).

The mTOR pathway is pertinent to muscle cell regeneration and differentiation (GE *et al.*, 2009), which are processes adjunct to the increased protein content of GLUT4 (MORENO *et al.*, 2003). Another important mechanism for this regulation is the insulin-controlled activation or inhibition of GLUT4 gene expression. In a region of the SLC2a4 promoter called domain 1, there are binding sites for transcription factors NF1 (nuclear factor 1) and O/E-1 (Olf-1/early B cell factor) (ZORZANO *et al.*, 2005). This region intercedes in a repressive action on the SLC2a4 gene that is induced by cAMP and by chronic insulin action (DOWELL and COOKE, 2002). The transcription factor GEF (GLUT4 enhancer factor) is also present in this region, however, it is described as an activator of GLUT4 transcription (KNIGHT *et al.*, 2003).

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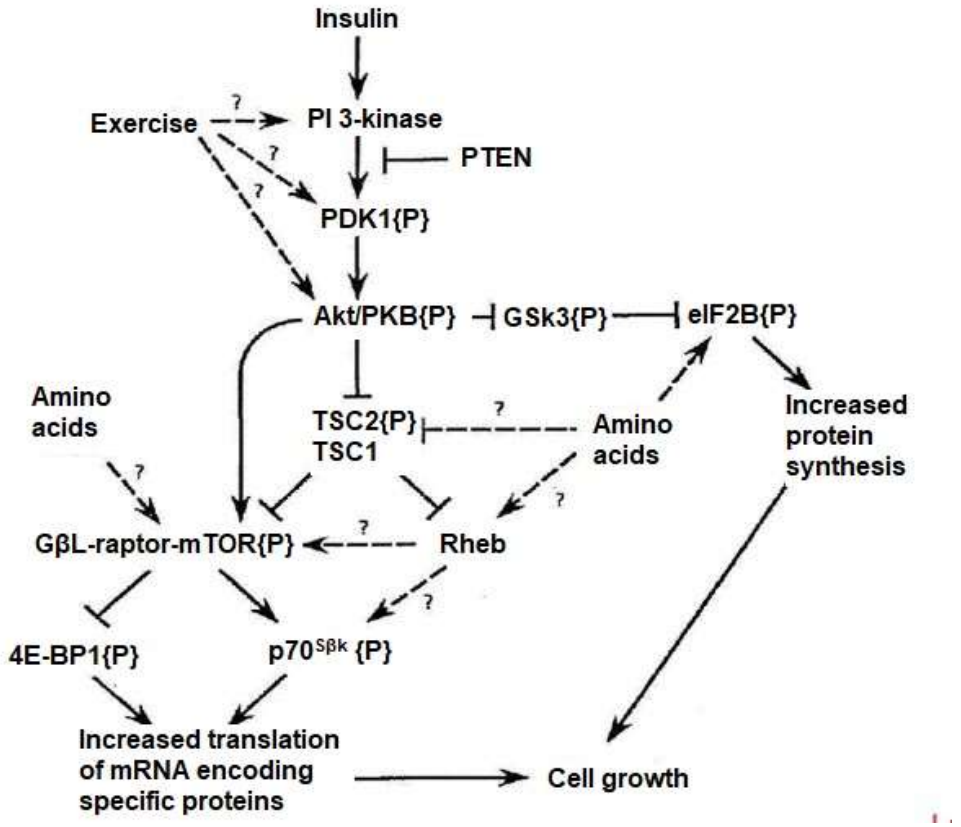

(**Source:** VOLTARELLI E MELLO, 2008)

Figure 03: Protein synthesis via the AKT/PI3K/mTOR pathway.

According to the studies of Bucci *et al.* (2006), the increase in protein synthesis leads to an increase in contractile proteins and muscle hypertrophy, i.e. the more GLUT4 expression, the higher the level of protein synthesis in the skeletal muscle cell membrane, which will lead to a higher level of muscle hypertrophy and consequently a higher meat production after rigor mortis.

The translocation of Glut4/SLC2A4 by induction of thyroid hormones

Besides the genomic actions, there is much evidence that the TH have non-genomic actions as well, acting for example in the plasma membrane with stimulatory effects on the transport of glucose, Ca^{2+} and Na^{+}, besides the action in several cell organelles, such as in the mitochondria, facilitating the transport of ADP and subsequently the formation of ATP and in the endoplasmic reticulum, where it would increase the activity of the calcium pump (ZINMAN *et al.*, 2006). Within the first group of action, myoglobin is included (CLÉMENT *et al.*, 2002) and GLUT4 (WEINSTEIN *et al.*, 1994). In the second action group, we include the gene encoding the myosin heavy chain isoform II (MHCII) (NUNES *et al.*, 1985), and the sarcoplasmic reticulum calcium pump.

Muscle tissue is one of the main targets of T3 action, since it stands out as the tissue that uses glucose the most, influenced by T3, which can induce the expression of GLUT4, promoting its translocation towards the plasma membrane. The translocation of GLUT4

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vesicles occurs by their association to the actin cytoskeleton (TALIOR-VOLODARSKY *et al.*, 2008). Phosphorylation of the β isoform of the TH receptor, TRβ, by MAPK activation, is also involved in angiogenesis induced in the non-genomic form by T3. TH also participate in controlling the expression of genes that are involved in the maintenance of cellular architecture, exerting non-genomic effects on actin polymerization of the cytoskeleton, influencing intracellular vesicle traffic and tissue remodeling (GOULART-SILVA *et al.*, 2006).

Muscle contraction activates some kinases that participate in the translocation of GLUT4 to the plasma membrane by a mechanism that involves the reduction in the ATP/AMP ratio, where the increase in AMP activates AMPK. The phosphorylation of AMPK increases glucose transport in skeletal muscle because the translocation of GLUT4 to the plasma membrane is increased (SANTOS *et al.*, 2008). A signaling pathway activated by insulin, independent of PI3-K, influences actin polymerization by increasing GLUT4 translocation to the plasma membrane. This pathway is activated by a protein complex (CAP-Cbl-Crkll-C3G) and is called GTPase (CHANG *et al.*, 2007).

In studies with rats, T3 induces GLUT4 translocation to the plasma membrane in skeletal muscle within 30 minutes, in addition to improving insulin sensitivity in these animals (BRUNETTO *et al.*, 2012). GLUT4 translocation also occurs in response to insulin stimulation (CARVALHEIRA *et al.*, 2002), where translocation of cytoplasmic vesicles, containing GLUT4, to the plasma membrane occurs, which increases transporter density and glucose uptake (KROOK *et al.*, 2004).

The insulin receptor (IR) is a glycoprotein that contains two α and two β subunits that are linked by disulfide bonds. The α subunits are in the extracellular part possessing insulin binding site, while the β subunits cross the membrane, containing intrinsic kinase riversin activity, being responsible for the transmission of the insulin signal to the cell (BRYANT and GOULD, 2020). Phosphorylation of IR will allow binding of tyrosine residues of various intracellular protein substrates. From the phosphorylation of these substrates, recognition sites begin to exist for molecules containing specific SH2 domains, such as PI3K, which activates and mobilizes this enzyme to the plasma membrane (OLSON, 2012).

This mobilization of PI3K ends up favoring its action on lipid substrates, such as PIP2 (phosphatidylinositol-4,5-biphosphate), which will be phosphorylated, thus originating PIP3. This new molecule recruits' proteins such as AKT/PKB (protein kinase B), by interaction with specific domains. For AKT to exert its biological effects, it needs to be activated, thus depending on two phosphorylation events, which are phosphorylation at threonine 308 and at serine 473 (KOU *et al.*, 2001).

Once AKT has been phosphorylated on either threonine or serine, several effects can occur in the muscle and fat cell, most notably translocation of vesicles that are rich in GLUT4, thus increasing the glucose taken up by the cell (Fig. 04) (OLSON, 2012).

It is worth noting that skeletal muscle tissue is an important target of the action of TH, because it induces the expression of genes involved with the control of metabolism, among which, the SLC2a4 gene, which is responsible for encoding the GLUT4 protein (WEINSTEIN *et al.*, 1994). Just like the skeletal muscle, adipose tissue also suffers from the thyroid hormone, and coincidentally, also presents the GLUT4 as one of the glucose transporters.

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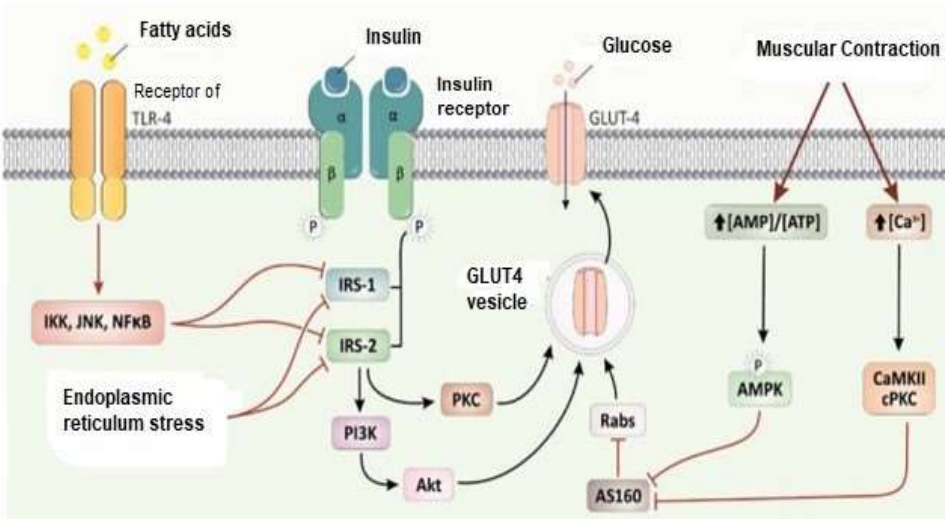


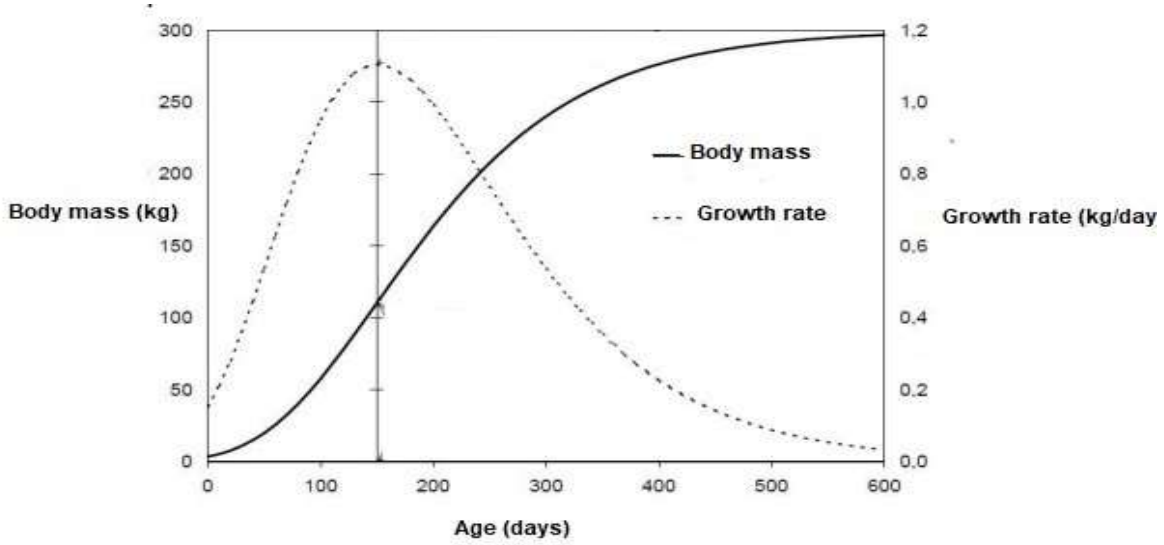
(**Source:** BARROS e NUNES, 2019).

Figure 04: Intracellular insulin signaling pathway.

Muscle growth and the effect of T3 on muscle tissue

The onset of muscle growth occurs through myogenesis in the prenatal period. The deposition of muscle tissue begins to be initiated when there is myogenesis, which can be divided into two phases, determination and differentiation. During myogenesis in the prenatal period, myoblasts multiply, migrate, differentiate, and fuse to develop myotubes and the muscle fibers. However, some myoblasts remain undifferentiated and can be used to replenish cells in situations of cell loss and muscle hypertrophy. In the second third of gestation, the remaining myoblasts use the primary myofibrils for support to align themselves and proceed with the formation of secondary fibers. These secondary fibers hypertrophy and make connections with other myoblasts, which enables communication between cells in this period (FILHO *et al.*, 2011).

After birth, the animal shows a relative growth as a function of time, represented by a sigmoid curve (Fig. 05).



(**Source:** Adapted of FIALHO, 1999)

Figure 05: Growth Stages of swine.

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At the beginning of growth, the animal's weight gain increases until the arrival of puberty, being in the acceleration phase, where weight gain increases with each passing day. When the animal reaches puberty, the weight gain becomes constant, presenting a linear characteristic (linear growth phase), where the weight gain does not change over time. When the animal starts to have a daily growth decline, the animal reaches the adult body weight, reaching the deceleration phase (FIALHO, 1999). The expression of transcription factors plays an extremely key role in muscle growth. Factors such as MyoD, Myf-5, myogenin and MRF4, which belong to the helix-loop-helix (bHLH) family of transcriptional proteins, together with other stimulating factors, activate the differentiation program by inducing the transcription of certain muscle-specific genes, influencing the myogenesis process and the formation of satellite cells as the myoblasts (FILHO, 2011).

These satellite cells remain between the membrane and the basal lamina of the muscle fiber. They have a mononuclear structure with mitotic divisions during the hypertrophy phase, i.e., they multiply after the muscle growth phase after birth. During muscle growth, the number of nuclei in the muscle fibers undergoes an increase, as satellite cells become incorporated, serving as a source of nuclei, and increasing the amount of DNA for protein synthesis (BRIDI *et al.*, 2003).

The hypertrophy first occurs in the longitudinal direction of the fiber, with the increase in the number of sarcomeres, occurring later an increase in fiber diameter by the deposition of myofibrillar proteins. Muscle fiber growth is restricted to genetic and nutritional factors that determine the muscle's ability to produce muscle proteins. Satellite cells fuse into the muscle cells, causing an increase in the number of cell nuclei, which benefits protein synthesis. The protein synthesis takes place in the cytosol of the cell and requires the participation of ribosomes, which contain ribosomal RNA (rRNA), transporter RNA (tRNA), and messenger RNA (mRNA), which also contain some amino acids, such as ATP, GTP, and various enzymes. The production of all these RNAs happens in the nucleus (FILHO *et al.*, 2011).

The muscle tissue is composed of three types of muscle fibers, which are: oxidative fibers that have slow contraction, called Type I Fibers; red and aerobic fibers; intermediate fast twitch, called Type II A Fibers, glycolytic oxidative; and the fast twitch glycolytic fibers, called Type II B Fibers, white, anaerobic (REHFELDT *et al.*, 2001). The final size and composition of the muscle, besides its metabolic and physiological characteristics, have a high dependence on the proportion and types that the constituent fibers, and the properties reflect the sum of these characteristics (SANTOS *et al.*, 2008).

Some hormones participate in muscle contraction, among them we have that the T3, activating the transcription rate of the GH gene, mechanism by which participates in the process of growth of α MHC and MHC II genes (isoforms of the myosin heavy chain type I and II) (SANTOS et al., 2001), which are responsible for increasing the speed of muscle contraction, both cardiac and skeletal, resulting in shortening the time of contraction of skeletal muscle, where, by relaxing more quickly, it is able to respond to new stimuli, this effect, which associated with the growth of genes α MHC and MHC II, increases the speed of skeletal muscle contraction (NUNES, 2003).

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FINAL CONSIDERATIONS

According to what has been presented in this work, it is concluded that it is possible that the induction of thyroid hormones by the inclusion of iodine in the diet of pigs can benefit muscle growth through the translocation of GLUT4 in muscle tissue. The source of iodine for the diet can be through iodized mineral salt, which makes the diet affordable, and can benefit the producer to obtain a better weight gain of their animals with a diet that can be cheaper or affordable. However, more research is needed to better clarify all these mechanisms.

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