Effects of Glucose Metabolism and Utilization on Dairy Cattle Production (Postprint)

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Abstract

Glucose is the primary energy substrate for brain cells, the central nervous system, and embryos, and also serves as a precursor for lactose synthesis in lactating dairy cows. It is closely associated with milk fat and milk protein synthesis, thereby exerting crucial nutritional and physiological functions in lactating dairy cows. To improve lactation performance and physiological health, in-depth investigation of glucose nutrition and physiological functions in dairy cows is warranted. This review synthesizes current knowledge on glucose metabolism and utilization in lactating dairy cows, covering aspects of glucose production, mammary glucose metabolism and regulation, and the influence of glucose metabolism on dairy cow production, thereby providing a reference framework for further elucidation of glucose metabolic mechanisms, improvement of glucose utilization efficiency, and promotion of dairy cow productivity.

Full Text

Effects of Glucose Metabolism and Utilization on Dairy Cow Production

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Abstract

Glucose serves as the primary energy substrate for brain cells of the central nervous system and embryos in dairy cows, as well as the precursor for lactose synthesis and is closely associated with milk fat and protein synthesis, thus playing crucial nutritional and physiological roles in lactating dairy cows. To

improve lactation performance and physiological health, it is necessary to investigate the nutritional and physiological functions of glucose in dairy cows. This review examines glucose generation, metabolism and utilization in the mammary gland, and the effects of glucose metabolism on dairy cow production, providing a reference for further elucidating glucose metabolic mechanisms, improving glucose utilization efficiency, and promoting dairy cow productivity.

Keywords: dairy cows; glucose; gluconeogenesis; mammary gland; regulation

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In mammals, glucose serves as the primary precursor for lactose and as a substrate for milk protein and fat synthesis in mammary epithelial (alveolar) secretory cells. During lactation, lactose is synthesized in the Golgi apparatus and vesicles of mammary alveolar epithelial secretory cells. Since the mammary gland lacks glucose-6-phosphatase, it cannot synthesize glucose from other precursors[1-2] and must rely on blood supply to meet its glucose demands. In the dietary nutritional requirements of 8-10 month old Holstein heifers, a dietary metabolizable glucose level of 113.59 g/kg can meet the needs for daily gain of 0.8-1.0 kg/d[3], while a level of 99.27 g/kg can significantly improve milk yield and feed intake[4]. For dairy cows producing an average of 40 kg/d of milk, up to 3 kg of glucose must be extracted daily from mammary blood[5-6]. Mammary glucose uptake from blood is a passive and facilitated transport process[7] mediated by glucose transporters (GLUT). Glucose extracted by the mammary gland can account for 60%-85% of total glucose entering the blood[6]. Lactose maintains the osmotic pressure of milk, and the rate of lactose synthesis is a major controlling factor for milk yield[8]; consequently, mammary glucose uptake is considered the rate-limiting step for milk production[5,9]. This review therefore focuses on glucose metabolic patterns and mechanisms in dairy cows (rumen propionate production, hepatic gluconeogenesis, and mammary glucose metabolism) and their relationship with dairy cow production.

1. Glucose Sources

Glucose is an indispensable nutrient for animal life and production activities, directly participating in metabolic processes as a vital monosaccharide. It also serves as a fundamental fuel in energy metabolism and synthetic pathways of all mammalian cells[10] and must be continuously maintained at adequate levels in the bloodstream. Animal glucose originates from three primary pathways: 1) glucose produced from dietary carbohydrate digestion, where dietary carbohydrates are broken down by digestive enzymes in the gastrointestinal tract, absorbed by intestinal epithelium into the bloodstream, and then enter systemic metabolic processes; 2) glucose produced through hepatic gluconeogenesis, where dietary carbohydrates are digested into propionate or lactate in the digestive tract, absorbed, and undergo gluconeogenesis in the liver; and 3) glucose produced from glucogenic amino acids, where dietary or microbial proteins are digested into glucogenic amino acids that are converted to glucose via

gluconeogenesis. Glucose from the first pathway is termed exogenous glucose, while that from the latter two pathways is collectively called endogenous glucose. In ruminants, endogenous glucose production consists primarily of rumen propionate production (glucose precursor) and hepatic gluconeogenesis.

1.1 Rumen Propionate Production

In ruminants, propionate is mainly produced through rumen microbial fermentation and serves as the primary precursor for hepatic gluconeogenesis[11]. Propionate supply significantly influences gluconeogenesis[12], and increasing propionate availability can enhance hepatic gluconeogenic activity[13]. Lemosquet et al.[14] investigated the effects of ruminal propionate infusion on glucose metabolism and mammary energy metabolism in lactating dairy cows, finding that propionate affected whole-body glucose turnover, enhanced gluconeogenic capacity, and maintained stable lactose, milk protein, and milk yield. Other reports indicate that ruminal butyrate infusion can also decrease blood glucose concentration and consequently reduce lactose synthesis[15]. Wang et al.[16] found that rumen propionate concentration and blood glucose concentration were significantly lower in cows fed rice straw diets compared to alfalfa diets, suggesting that cows fed rice straw may have reduced glucose synthesis due to insufficient propionate supply. Plant essential oils such as capsaicin can regulate rumen fermentation patterns, maintaining propionate-type fermentation[17]. However, research on rumen fermentation pattern regulation in periparturient cows remains limited due to the unique and complex metabolic characteristics of this period. Therefore, establishing a rumen fermentation regulation model for periparturient cows and investigating fermentation patterns and regulatory mechanisms through in vivo experiments could provide scientific support for promoting hepatic gluconeogenesis and efficient glucose utilization.

1.2 Hepatic Gluconeogenesis

Glucose production in ruminants mainly originates from hepatic gluconeogenesis, a process where propionate transported to the liver via the portal venous system is synthesized into glucose under the action of various enzymes[18]. Several key rate-limiting enzymes in gluconeogenesis include glucose-6-phosphatase (G6Pase), phosphoenolpyruvate carboxykinase (PEPCK), and pyruvate carboxylase (PC), with their activities reflecting the extent of gluconeogenesis. The mRNA expression abundance of key gluconeogenic enzymes can reportedly reflect their enzymatic activity[19]. Hepatic glycogen content is relatively high before calving, decreases significantly after parturition, and then gradually increases. Specifically, PEPCK mRNA expression abundance increases markedly during the periparturient period as glucogenesis intensifies[19-21], while PC mRNA expression abundance in mid-lactation cows shows significant upregulation under feed restriction due to negative feedback regulation[22]. Nutrient substrates, enzymes, and hormones can jointly regulate hepatic gluconeogenesis in ruminants, with increased substrates, enhanced enzyme

activity, or exogenous hormone injection all promoting glucose production to maintain glucose metabolic homeostasis. White et al.[23] found that replacing corn with glycerol could increase PEPCK expression in dairy cow liver, indicating that different dietary energy sources can regulate hepatic gene expression. In vitro liver cell models have demonstrated that propionate can promote PEPCK gene expression by regulating the mitochondrial PEPCK promoter[24], while other studies found that PC expression can be regulated by enhancing PC promoter 1 during the early postpartum period in dairy cows[25]. Wang[26] reported that the mRNA expression abundance of mitochondrial PEPCK and PC was significantly lower in liver cells of cows fed rice straw diets compared to alfalfa diets, suggesting that feeding rice straw diets may weaken hepatic gluconeogenic activity, leading to insufficient glucose supply. Dietary protein levels can promote secretion of these enzymes by affecting amino acid metabolism and increasing glucogenic amino acid levels[19]. Other studies have shown that dietary propylene glycol supplementation increased hepatic glycogen content and gluconeogenic rate-limiting enzyme activity on days 7, 21, and 35 postpartum[21]. Rhoads et al.[27] investigated the effects of exogenous growth hormone on hepatic glucose metabolism in dairy cows and found that growth hormone could promote hepatic gluconeogenesis and increase the supply of available glucose.

2. Glucose Transport

As a polar hydrophilic molecule, glucose cannot traverse the hydrophobic lipid bilayer of the plasma membrane through simple diffusion[28]; therefore, transmembrane glucose transport represents the rate-limiting step for efficient glucose utilization. Glucose transport across biological membranes requires specific mechanisms and transport proteins. In mammalian cells, glucose uptake occurs through two independent mechanisms mediated by two classes of glucose transporters—sodium-dependent glucose transporters (SGLT) and facilitated glucose transporters (GLUT)[29]. 1) Sodium (Na^+)-dependent transport: Glucose transport across the apical membrane of intestinal epithelial cells, choroid plexus, and renal proximal tubules depends on a Na^+-linked secondary active transport mechanism via Na^+/glucose cotransporters, protein symbol SGLT, gene symbol SLC5[30-32]. The SLC5 family currently comprises 12 structurally related members (SGLT1-6, SMIT1, NIS, SMVT, CH1, SMCT1, and SMCT2)[32] with different tissue distributions and substrate specificities. Among these transporters, SGLT1 (SLC5A1), SGLT2 (SLC5A2), SGLT3 (SLC5A4), SGLT4 (SLC5A9), SGLT5 (SLC5A10), and SMIT1 (SLC5A3) have demonstrated glucose transport activity. SGLT1 is primarily expressed in the brush border membrane of mature small intestinal epithelial cells and plays a major role in glucose and galactose absorption[31]. 2) Facilitated transport: Present in the basolateral membrane of intestinal epithelial cells, choroid plexus, renal proximal tubule membranes, and almost all other cell plasma membranes, this process is mediated by facilitated glucose transporters, protein symbol GLUT, gene symbol SLC2. In facilitated diffusion, glucose is

transported bidirectionally along its concentration gradient without requiring energy. The GLUT family belongs to one of the largest membrane transporter families, with 14 GLUT proteins identified in mammals, named GLUT1-12, GLUT14, and HMIT[33]. GLUT1 is the main isoform with a Michaelis constant (Km) of 10 mmol/L and is ubiquitously expressed in many tissues and cells, playing an important role in glucose uptake and transport across tissue-blood barriers[34-35]. In addition to its presence on the plasma membrane, GLUT1 is also expressed on the Golgi membrane of mammary epithelial cells, likely participating in glucose and galactose uptake at the site of lactose synthesis. Since lactose synthesis affects milk yield, investigating the mechanisms of glucose transporter expression and transport is crucial for dairy cow production.

The mammary gland primarily expresses GLUT1 and GLUT8[36]. Mammary glucose transport activity increases dramatically from the non-lactating to the lactating state, accompanied by increased GLUT expression. GLUT1 is expressed in bovine mammary glands at different developmental stages, with higher expression during lactation and peak expression at 140 days of lactation[37]. Zhao et al.[38] used human cDNA probes to investigate GLUT1-5 expression in lactating bovine mammary gland via Northern blot analysis, finding that lactating mammary tissue expressed abundant GLUT1 and small amounts of GLUT3-5. Interestingly, a different-sized 38 kDa GLUT1 was also detected in non-lactating mammary gland[39]. After the discovery of new GLUTs, moderate to low levels of GLUT8 and GLUT12 mRNA were detected in lactating bovine mammary gland[40]. Additionally, low levels of SGLT2 mRNA have been detected in bovine mammary gland[41], though the physiological role of SGLT2 in mammary tissue requires further investigation.

Regulating GLUT quantity and activity to enhance glucose transport capacity represents an important approach to ensure adequate energy supply to the mammary gland and maintain metabolic balance. Insulin and glucagon are key hormones that maintain blood glucose balance and regulate carbohydrate metabolism, and their regulation of glucose metabolism is inevitably accompanied by spatiotemporal changes in GLUT expression. Insulin levels can affect GLUT4 expression and transport[42]. Zhao[43] found that high-dose prolactin significantly decreased GLUT8 gene expression, while insulin promoted GLUT8 gene expression. With increasing hydrocortisone concentration, both GLUT1 and GLUT8 gene expression showed a trend of initial increase followed by decrease. The study also identified a significant interaction between insulin and hydrocortisone, with hydrocortisone antagonizing the effect of insulin in increasing GLUT8 gene expression. Wang[26] found that different quality forage diets had no significant effects on mRNA expression abundance of GLUT1, GLUT3, and GLUT8 in mammary gland.

3.1 Mammary Glucose Uptake

Mammary glucose uptake is influenced by numerous factors, including mammary developmental stage, nutritional status, and mammary metabolism. In

goats, mammary glucose uptake increases more than 20-fold from pregnancy to peak lactation, then gradually declines with decreasing milk yield[44]. Cant et al.[45] used isotope-labeled glucose infusion experiments to demonstrate that in lactating Holstein cows, mammary glucose uptake of approximately 300 mmol/h could support a milk yield of 0.6 kg/h. This finding aligns with earlier observations that bovine mammary gland extracts 72 g of glucose to produce 1 kg of milk[5]. Glucose uptake by the mammary gland of lactating ruminants can account for 60%-85% of total glucose entering the bloodstream[6,46]. Increasing milking intervals reduces mammary glucose uptake by decreasing mammary blood flow and extraction rate[47]. Some studies have reported that mammary glucose uptake in dairy cows partially depends on acetate uptake[48], indicating an interaction between these two nutrients in bovine mammary gland. However, mammary glucose uptake is hardly affected by amino acids, as infusing amino acids into the abomasum of dairy cows does not significantly alter mammary glucose uptake[49-50]. Mammary glucose uptake can be stimulated by growth hormone and thyroxine[51], but not by insulin[44].

Mammary glucose uptake depends on both glucose supply to the mammary gland and transmembrane glucose transport. The former is determined by arterial glucose concentration and mammary blood flow. In mammals, arterial glucose concentration is regulated by insulin and other endocrine hormones and maintained within a narrow range. Studies on cattle and sheep under various experimental conditions have failed to establish a clear relationship between mammary arteriovenous glucose difference and arterial glucose concentration[44-45,48], suggesting that arterial glucose concentration may not be a primary factor affecting mammary glucose uptake under normal physiological conditions. Mammary blood flow plays an important role in regulating nutrient supply to the mammary gland[9,52] and is generally closely related to milk yield[47]. Wang et al.[52] found that feeding dairy cows diets with different quality forage sources revealed that high-quality alfalfa diets significantly increased mammary blood flow compared to straw diets, without affecting mammary transporter mRNA abundance[26]. Therefore, mammary blood flow may be a key factor influencing mammary glucose uptake in dairy cows.

3.2.1 Metabolic Pathways

After entering the mammary gland, glucose undergoes anabolic and catabolic metabolism primarily through the following pathways (Figure 1 [Figure 1: see original paper])[36]: 1) lactose synthesis; 2) entry into the tricarboxylic acid (TCA) cycle for energy production; 3) pentose phosphate pathway to generate reduced nicotinamide adenine dinucleotide phosphate (NADPH); 4) milk fat synthesis; 5) non-essential amino acid synthesis; and 6) nucleotide synthesis. During lactose synthesis, glucose is first irreversibly phosphorylated to glucose-6-phosphate, then converted to galactose in the cytoplasm. Both glucose and galactose are taken up by Golgi vesicles and used for lactose synthesis by lactose synthase on the Golgi membrane. Lactose synthase comprises two polypep-

tide subunits: α-lactalbumin (α-LA) and β-1,4-galactosyltransferase (β-4GalT1)[53]. Additionally, glucose-6-phosphate can enter glycolysis and the pentose phosphate pathway. During glycolysis, glucose-6-phosphate is converted to triose phosphate and then to pyruvate. Triose phosphate also serves as a substrate for synthesizing α-glycerophosphate, which provides a backbone for triglyceride biosynthesis. Pyruvate is extensively taken up by mitochondria to produce acetyl-coenzyme A (CoA), which enters the TCA cycle to generate ATP. Citrate, as a TCA cycle substrate, can leave mitochondria and be converted to acetyl-CoA by ATP citrate lyase in the cytoplasm, where it participates in fatty acid synthesis. Furthermore, pyruvate and TCA cycle substrates can be used to produce non-essential amino acids required for milk protein synthesis. The pentose phosphate pathway generates NADPH and ribose, with the former providing reducing power for fatty acid biosynthesis and the latter serving as a substrate for RNA synthesis.

3.2.2 Transport Regulation

From bacteria to mammals, the regulation of glucose homeostasis represents a fundamental regulatory function in all living organisms[54-55]. In lactating animals, providing glucose to the mammary gland for milk synthesis is a prioritized metabolic activity essential for species survival[56], which must be coordinated and maintained even at the expense of disrupting homeostasis. The regulation of glucose transport in the mammary gland plays a key role in fulfilling this priority. Mammary glucose transport regulation primarily includes endocrine regulation, hypoxia regulation, developmental regulation, fasting effect regulation, and other regulatory mechanisms.

Plasma glucose-dependent insulinotropic polypeptide concentration is significantly positively correlated with milk energy yield (r=0.67) and significantly negatively correlated with respiratory quotient (r=-0.72), indicating that plasma glucose-dependent insulinotropic polypeptide may regulate energy metabolism and potentially glucose transport in dairy cows[57]. Prolactin has been found to stimulate 2-deoxyglucose uptake in mammary explants[58]. Exogenous growth hormone injection increases mammary glucose uptake without affecting plasma glucose concentration in dairy cows[51], suggesting that growth hormone may stimulate glucose transport in the mammary gland. However, a 63-day trial of exogenous growth hormone in lactating cows did not alter mammary GLUT1 mRNA and protein expression[39], indicating that increased mammary glucose uptake may result from increased blood flow to the mammary gland[59] rather than induced GLUT expression in mammary epithelial cells. Recent studies have found that GLUT expression in mammary tissue and mammary epithelial cells is insensitive to prolactin[60]. Additionally, oxygen deficiency in the body or tissues creates a hypoxic state, a normal physiological or pathological condition during which many tissues and cells undergo physiological changes including increased glucose uptake and enhanced anaerobic metabolism to protect against insufficient oxygen supply. A new hypothesis is based on two lines of

evidence: from pregnancy to lactation, mammary metabolic rate increases to support mammary growth, lactogenesis, and milk secretion; mammary oxygen uptake increases steadily during late pregnancy and reaches its highest level during early lactation[47], supporting the role of hypoxic conditions in mammary development, GLUT1 expression, and lactation. Furthermore, glucose transporters can be glycosylated to regulate glucose transport[36].

4.1 Forage Type and Quality

Wang[26] found that rumen propionate concentration was significantly lower in cows fed rice straw diets compared to alfalfa diets. The mRNA expression abundance of pyruvate carboxylase, which reflects hepatic gluconeogenesis, was significantly lower in rice straw-fed cows than in those fed alfalfa or corn stover diets. Expression of mitochondrial phosphoenolpyruvate carboxykinase, insulin-like growth factor 1 receptor, and phosphofructokinase (liver, muscle, and pancreatic sources) was also significantly lower in rice straw-fed cows compared to alfalfa-fed cows. Mammary glucose uptake was significantly lower in cows fed corn stover and rice straw diets compared to alfalfa diets. Milk potassium ion (K^+) concentration was significantly higher in rice straw-fed cows than in alfalfa- and corn stover-fed cows. These results indicate that feeding rice straw diets leads to lower propionate production, reduced hepatic gluconeogenesis and glucose synthesis, insufficient glucose supply for mammary uptake, and ultimately inadequate lactose synthesis.

Lactose plays a major role in maintaining milk osmotic pressure, contributing approximately 50% of milk osmotic pressure[61]; therefore, lactose synthesis rate determines milk yield. Additionally, Na^+, K^+, and chloride ion (Cl^-) concentrations in milk also contribute to osmotic pressure maintenance[62]. Rice straw diets significantly reduced lactose content in cows, which was lower not only than alfalfa-fed cows but also than corn stover-fed cows with similar lactation performance. Therefore, besides insufficient glucose supply, other factors such as ions contributing to osmotic pressure must differ to maintain overall milk osmotic pressure balance. Analysis of milk ion concentrations revealed that K^+ concentration was significantly higher in rice straw-fed cows, explaining the observed changes in lactose content. Moreover, lactose content is reportedly negatively correlated with Na^+, K^+, and Cl^- concentrations in milk[62]. Peaker[63] also reported that the sum of Na^+ and K^+ concentrations in milk changes inversely with lactose content. The reduced lactose content resulting from rice straw feeding, besides being caused by insufficient glucose supply in mammary arterial blood, may be compensated by increased K^+ concentration in milk due to high K^+ content in rice straw diets, which together maintain osmotic pressure balance[26].

4.2 Rumen-Protected Starch Supply

Starch is a glucose polymer whose main degradation products in the rumen and small intestine of ruminants are propionate and glucose, respectively. Appro-

priate levels of rumen-protected starch can provide substantial exogenous glucose, reduce energy losses from gluconeogenesis, conserve glucogenic amino acids, and improve animal performance[64]. Higher levels of rumen-protected starch increase plasma insulin and decrease glucagon levels[65], indicating that appropriate dietary rumen-protected starch levels can promote glucose absorption and efficient utilization. Rumen-protected starch level determines the amount of glucose absorbable in the small intestine, thereby altering the whole-body energy supply pattern and affecting nitrogen utilization and energy-nitrogen balance[66]. Insufficient pancreatic α-amylase secretion limits small intestinal digestibility of rumen-protected starch, causing not only energy waste but also hindgut acidosis[67]. Therefore, theoretically, promoting α-amylase secretion through regulatory techniques could enhance small intestinal digestibility of rumen-protected starch, increase glucose supply, and meet the body' s glucose requirements. Xu et al.[68] found that rumen-protected starch level affects pancreatic α-amylase secretion in goats. Cholecystokinin can regulate pancreatic enzyme secretion and expression[69]. Mikuła et al.[70] investigated the effects of replacing triticale (low rumen-protected starch) with corn (high rumen-protected starch) on metabolism, lactation performance, and reproductive performance in periparturient dairy cows, concluding that corn starch is more suitable as an energy source for periparturient cows. In summary, appropriate rumen-protected starch levels and increased pancreatic α-amylase secretion can promote rumen-protected starch digestion, improve feed energy utilization efficiency, and ensure adequate energy supply during lactation.

5. Glucose Metabolism in Transition Dairy Cows

Compared to the lactation period, dry matter intake declines sharply during the early postpartum period in dairy cows, leading to negative energy balance and hypoglycemia. Increasing small intestinal glucose supply represents the most effective strategy to address this issue. While theoretically feasible, increasing dry matter intake during the postpartum period is difficult to achieve in practice and not easily realized in the short term. Therefore, improving dietary energy supply and metabolizable glucose levels is crucial. Glucose deficiency is substantial in periparturient cows, easily leading to negative energy balance, body fat mobilization, and ketosis[71]. Additionally, insufficient nutrient intake, accelerated energy metabolism, dramatic changes in endocrine hormones, severe oxidative stress, and reduced immune and anti-inflammatory capacity make periparturient cows susceptible to mastitis, udder edema, retained placenta, and other diseases[72]. As an important energy source, glucose plays a vital role in maintaining mammary gland development, lactation, and nutrient turnover. Therefore, adequate glucose supply is an effective means to ensure energy balance and reduce disease incidence in periparturient cows. Studies have shown that supplementing postpartum cow diets with rumen-protected glucose can effectively increase milk yield and blood glucose concentration while decreasing ketone body levels and improving negative energy balance[73]. Pieper et al.[74] found that German Holstein bulls have high heritability for intravenous glucose

tolerance, providing possibilities for selecting Holstein cows with high glucose tolerance to address metabolic diseases caused by negative energy balance in periparturient cows.

Excessive energy intake during the dry period negatively affects glucose metabolism and energy balance status during the peripartum period and affects the smooth transition to early lactation. Energy intake level during the entire dry period or prepartum period does not affect glucose tolerance but is closely related to blood glucose concentration during the dry period and postpartum concentrations of insulin, glucagon, non-esterified fatty acids, and β-hydroxybutyrate[75]. Dry period duration can affect energy metabolism status before and after calving and subsequent milk yield. Liver glycogen decreases and liver fat content increases after calving, with a tendency for upregulation of hepatic PC mRNA abundance in cows with a 90-day dry period. Shortening the dry period can lead to more balanced glucose metabolism[76]. Galindo et al.[50] found that postpartum abomasal amino acid infusion increased whole-body glucose production rate in dairy cows, primarily due to increased glucose release from the portal-drained viscera to the liver. Amino acid requirements are extremely high in early lactation, and even increased amino acid supply cannot meet the demand, as cow metabolism prioritizes amino acid needs over hepatic gluconeogenesis.

The pattern of glucose metabolism in dairy cows is closely related to energy requirements and lactation performance. The entire process—from rumen production of the glucose precursor propionate, through hepatic gluconeogenesis, to glucose transport from blood in the mammary gland and its anabolic and catabolic metabolism in mammary epithelial cells—plays a critical role in lactation. As an essential and key substrate and fuel for milk synthesis, and with lactose playing an important role in osmotic pressure balance during lactation, glucose metabolism is crucial for regulating milk yield, though the underlying mechanisms remain unclear. Therefore, understanding the molecular mechanisms underlying mammary glucose uptake is essential. While significant progress has been made in glucose transporter research and it is now recognized that multiple transporters are involved, substantial knowledge gaps remain regarding the physiological and pathological roles, cellular and subcellular localization, and regulation (gene expression, subcellular trafficking, and kinetics) of each glucose transporter in mammary tissue. Additionally, the relationship between glucose metabolism and disease occurrence in dairy cows, as well as glucose metabolism during the peripartum period, require further investigation. Advances in molecular biology techniques, particularly omics technologies—for example, genomics can help select dairy cows with high glucose utilization efficiency, and metabolomics can elucidate the intrinsic molecular mechanisms linking peripartum energy metabolism disorders with cow health and lactation performance—offer promising approaches. In conclusion, more research is needed to explore the relationship between dairy cow production and glucose metabolism to ultimately provide theoretical support for healthy and efficient dairy farming.

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