Postprint: Regulation of Embryonic Nutritional Environment on Postnatal Nutritional Metabolism in Animals

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Abstract

The nutritional environment of animal embryos is influenced by two aspects: maternal nutrition supply and placental nutrient transport. Adequate and appropriate maternal nutrition supply is essential for the healthy development of embryos; the placenta is responsible for transporting nutrients from the mother, and the efficiency of this transport determines the nutrient supply to the embryo. Embryonic development is inseparable from the nutritional environment it experiences, and an adverse embryonic nutritional environment can program embryonic development and persistently affect metabolism, leading to chronic diseases in adulthood. Therefore, in-depth investigation into the long-term effects of maternal nutrition supply on offspring metabolism not only contributes to the healthy growth of offspring but also effectively reduces the incidence of metabolic diseases after birth. This article reviews the effects of insufficient maternal nutrition supply on postnatal nutrient metabolism in animals and provides a preliminary overview of the underlying mechanisms of nutritional programming.

Full Text

Preamble

Effects of Embryonic Nutrition Environment on Postnatal Animal Nutritional Metabolism

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Abstract: The embryonic nutritional environment is influenced by both maternal nutrient supply and placental nutrient transport. Adequate and appropriate maternal nutrition is essential for healthy embryonic development, while the placenta is responsible for transferring nutrients from the mother. The efficiency of this transport determines the nutrient supply available to the embryo. Embryonic development is inseparable from its nutritional environment, and adverse conditions can program embryonic development, exerting lasting effects on metabolism and leading to chronic diseases in adulthood. Therefore, in-depth investigation of the long-term effects of maternal nutrition on offspring metabolism will not only promote healthy growth in future generations but also effectively reduce the incidence of metabolic diseases after birth. This article reviews the impact of insufficient maternal nutrition supply on postnatal nutritional metabolism and discusses the underlying mechanisms of nutritional programming.

Keywords: maternal nutrition; embryonic development; metabolic programming; nutritional metabolism

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1 Maternal Nutrition Supply

Pregnancy represents a critical period for both maternal growth and embryonic development. Maternal nutrient intake must satisfy not only the mother' s basic metabolic needs but also provide continuous nourishment for embryonic development. To maintain normal embryonic development, the mother must supply appropriate amounts of glucose, amino acids, and fatty acids through the placenta. During pregnancy, the mother naturally enters an insulin-resistant state, creating a concentration gradient between maternal and embryonic blood glucose that drives nutrient transport across the placenta to meet embryonic growth demands. As pregnancy progresses, this concentration gradient gradually increases to ensure substantial nutrient uptake by the embryo. Concurrently, embryonic weight increases while water content decreases. By one-third of gestation, white adipose tissue (WAT) begins rapid deposition, a process that consumes substantial energy. By the end of pregnancy, 90% of the energy required for embryonic development is utilized for WAT formation. Both insufficient and excessive energy intake can progressively affect embryonic gene expression, alter metabolic patterns, and cause intrauterine growth restriction or overgrowth. Intrauterine growth retardation (IUGR) embryos typically exhibit depleted fat and glycogen reserves, generally resulting from inadequate intrauterine nutrient supply. Conversely, maternal nutrient excess leads to intrauterine overgrowth, with body fat content exceeding that of normal embryos [4]. Additionally, maternal body mass index, gestational weight gain, and behavioral habits also influence embryonic growth and development.

1.1 Effects of Maternal Nutrition Insufficiency on Postnatal Nutritional Metabolism

Numerous epidemiological cases and animal experiments have confirmed the existence of metabolic programming, establishing that "embryonic programming" represents the origin of multiple diseases. Insufficient intrauterine nutrient supply [4], hypoxia, and toxin exposure [5] during gestation all increase the incidence of heart disease and metabolic disorders—including hyperphagia, obesity, endocrine and metabolic abnormalities, type II diabetes, insulin resistance, hypertension, and ischemic heart disease—in offspring. Maternal nutrition during pregnancy exerts programming effects on embryonic fat metabolism, as both nutrient excess and deficiency can alter adipocyte development, affecting both the capacity for adipose tissue to generate new adipocytes and lipid storage in existing adipocytes.

The Barker hypothesis posits that low birth weight correlates with reduced insulin tolerance, hypertension, and hyperlipidemia in adulthood [6], a proposition supported by subsequent research [7]. Insufficient maternal nutrient supply during pregnancy creates intrauterine stress, and while altered gene expression under adverse environmental factors may allow embryonic survival, it significantly increases the incidence of adult metabolic disease. The severity of adult metabolic disease is determined by the degree of mismatch between prenatal and postnatal nutritional environments. When maternal nutrient supply is inadequate during pregnancy but offspring receive adequate or excessive nutrition after birth, a pronounced catch-up growth phenomenon occurs, markedly elevating the incidence of adult metabolic disease. Birth weight serves as a direct indicator of the embryonic nutritional environment, and insufficient maternal nutrient supply during pregnancy constitutes an important cause of IUGR.

While the Barker hypothesis can explain developmental programming of adult disease, further exploration is needed to understand how organ development changes under embryonic programming and what diseases this may trigger.

1.1.1 Protein Restriction Maternal protein restriction correlates with metabolic disease in adult offspring. Feeding pregnant sows diets containing 5%–9% protein induces IUGR in offspring, and when these offspring are fostered by normally-fed lactating sows, they exhibit catch-up growth followed by insulin resistance [8-9]. Research also demonstrates that maternal protein restriction during pregnancy impairs pancreatic development in offspring, triggering hyperinsulinemia, reduced glucose tolerance, insulin signaling pathway lesions, and increased expression of lipogenic enzymes, thereby promoting fat deposition [10]. Offspring experiencing low protein during embryogenesis followed by catch-up growth show impaired development of adipose tissue insulin signaling pathways and increased incidence of adult metabolic disease [11].

However, high dietary protein levels during pregnancy are not necessarily ben-

eficial. Studies show that protein supplementation during gestation adversely affects intrauterine development, increasing both embryonic mortality and the incidence of small-for-gestational-age births, though the underlying mechanisms require further investigation [12]. Supplementing pregnant sow diets with 1% L-arginine hydrochloride enhances uterine and placental function, increasing litter size, total litter weight, and average piglet birth weight, suggesting a potential therapeutic approach for IUGR [13]. Additionally, reducing exercise before or during pregnancy can mitigate the adverse effects of low protein on offspring growth, glucose homeostasis, and leptin levels [14].

1.1.2 Energy Restriction Research indicates that reducing maternal food supply during pregnancy decreases β-cell content in newborn offspring, which cannot be restored to normal levels even with improved postnatal nutrition. Reducing dietary energy levels during late gestation causes insulin resistance and vascular dysfunction in offspring rats. Moderate to severe energy deficiency during pregnancy induces reduced offspring body weight, hyperphagia, and subsequent metabolic syndrome—including obesity, hypertension, hyperinsulinemia, hyperleptinemia, and altered neuroendocrine gene expression—though these symptoms do not occur if catch-up growth is prevented [15]. Investigations of the Dutch famine period provide compelling evidence for the maternal origins of adult metabolic disease. Pregnant women during the famine had reduced energy intake, and their offspring showed increased rates of glucose intolerance, microproteinuria, respiratory obstruction, and coronary heart disease in adulthood [16]. Animal studies also demonstrate that both offspring sex and gestational nutrient restriction affect metabolic programming differently [17], with gender-specific responses to blood leptin potentially explaining differential metabolic disease incidence.

1.1.3 High Sugar and High Fat Nutrition Excessive nutrition during embryogenesis is similarly detrimental, readily causing glucose and lipid imbalance in offspring. Studies show that high-fat diets during pregnancy lead to hypercholesterolemia [18], obesity, insulin resistance, and hypertension [19] in offspring at various ages. When rats are fed high-fat diets during pregnancy and lactation, and their offspring are fed normal diets after weaning, the offspring become highly susceptible to metabolic syndrome when later challenged with high-fat diets [20].

Brenseke et al. [21] propose that high-fat diets during pregnancy cause oxidative-antioxidant imbalance in embryos, elevating oxidative stress levels and subsequently increasing postnatal metabolic disease incidence. High-fat diets during pregnancy alter hepatic mitochondrial content and peroxisome proliferator-activated receptor gamma coactivator 1-alpha expression in offspring, triggering adult metabolic syndrome. Feeding rats fructose during pregnancy and lactation increases fasting insulin, glucose, and leptin levels in offspring at weaning [22]. During critical developmental periods, excessive fructose directly affects adipose tissue, impairs hypothalamic development, blocks hypothalamic-adipose

signaling pathways, and promotes obesity in offspring [23].

1.1.4 Trace Elements, Vitamins, and Macronutrients Trace elements play crucial roles in embryonic development, and deficiency during embryogenesis can affect metabolic pattern formation. Current research on trace elements in pregnant mothers and embryonic development remains limited, with studies on the relationship between embryonic trace elements and adult metabolic disease being particularly scarce. Iron, a critical component of hemoglobin, determines the oxygen-carrying capacity of red blood cells and affects tissue oxygen supply; iron deficiency during pregnancy readily causes abnormal embryonic development. Maternal iron deficiency in rats elevates mean arterial pressure and systolic pressure in offspring, likely due to altered renal hemodynamics affecting blood pressure. Lisle et al. [24] found that embryonic iron deficiency reduces nephron number and increases systolic pressure in 12-week-old rats. Iron deficiency during pregnancy also alters sodium handling in offspring [25], and when combined with postnatal high-fat feeding, causes visceral fat accumulation and elevated arterial pressure [26].

Chromium also plays important roles in carbohydrate and lipid metabolism, improving insulin sensitivity in diabetic patients. Studies show that restricting chromium intake by 65% before and during pregnancy in rats increases offspring body weight and body fat content, particularly visceral fat, possibly due to elevated 11β-hydroxysteroid dehydrogenase 1 and leptin expression promoting visceral fat accumulation [27].

Vitamin deficiency during pregnancy similarly affects postnatal nutritional metabolism. Restricting vitamin intake by 50% during pregnancy in rats increases offspring body fat and reduces lean body mass, indicating that vitamin deficiency can cause adult obesity [28]. Kumar et al. [29] found that maternal vitamin B12 and pantothenic acid deficiency increases offspring body fat and causes lipid metabolism abnormalities, possibly due to corticosteroid stress or altered adipocyte function. Vitamin D deficiency during pregnancy and lactation reduces muscle fiber protein content in rat offspring and may induce insulin resistance [30]. Vitamin A deficiency reduces nephron number [31] and causes hypertension [32] in offspring, while also decreasing β-cell number and reducing glucose tolerance [33].

Magnesium serves as a cofactor for carbohydrate metabolism enzymes and performs multiple biological functions through involvement in cell cycle, differentiation, and proliferation. Magnesium deficiency in pregnant sows increases offspring body fat content [34] and causes reduced glucose tolerance and insulin resistance [35]. Zinc also plays important roles in animal growth and development as an essential element for multiple enzymes. As embryos grow rapidly, zinc requirements increase progressively. Zinc deficiency in pregnant mice impairs offspring insulin sensitivity and causes abnormal weight gain [36], and offspring from zinc-deficient pregnancies develop insulin resistance when consuming excessive nutrients [37]. During late pregnancy, embryonic skeletal

development requires adequate maternal calcium supply, and maternal calcium deficiency increases offspring blood pressure [38], possibly due to altered cellular ion transport affecting hormone secretion.

1.2 Mechanisms of Embryonic Nutritional Programming

Extensive research has investigated why insufficient maternal nutrition during embryogenesis leads to adult metabolic disease, revealing that both the timing and duration of intervention affect programming outcomes. Two primary hypotheses have emerged.

Barker's "thrifty phenotype" hypothesis proposes that under adverse nutritional conditions, embryos sacrifice development of non-essential organs (pancreas, kidneys) to ensure survival and growth of critical organs (brain, heart), rendering them maladapted to postnatal nutrition and triggering adult metabolic disease. Low protein during pregnancy reduces nephron number, decreases β-cell count, enlarges and reduces hepatic lobules, decreases muscle content, and increases the proportion of large adipocytes in visceral fat, causing hypertension, hyperlipidemia, obesity, and glucose intolerance [39].

Simmons' "embryo rescue theory" attributes glucose intolerance to peripheral insulin resistance rather than impaired β-cell development [40]. Rat studies confirm that peripheral insulin resistance occurs at the expense of non-essential organs (lungs, skeletal muscle) to ensure glucose supply to critical organs [41]. IUGR rats show low tissue insulin and insulin-like growth factor-1 (IGF-1) levels during embryogenesis, but when entering the catch-up growth phase, IGF-1 rises rapidly to maintain life and combat hypoglycemia, causing insulin resistance.

To investigate relationships between maternal nutrition and postnatal metabolism, researchers have reduced overall maternal nutrition during pregnancy or selectively restricted single nutrients while maintaining others, examining the origins of obesity and metabolic disease through several mechanisms.

1.2.1 Oxidative Stress Oxidative stress during pregnancy has been confirmed as an important cause of postnatal metabolic abnormalities [42]. Protein and trace element deficiency during gestation places embryos in an oxidative stress state, triggering metabolic abnormalities. Vitamins A, C, and E possess antioxidant functions, and clinical studies show premature infants have lower levels of these three vitamins than normal newborns [43], potentially explaining their susceptibility to oxidative stress. Insufficient maternal nutrition, hypertension, inflammation, and infection during pregnancy can all induce embryonic oxidative stress, and postnatal catch-up growth increases nutrient oxidation and consumption, gradually establishing metabolic disease.

1.2.2 Biological Rhythm Disruption Imbalanced or mismatched maternal nutrition during pregnancy can alter offspring biological rhythms, triggering

metabolic diseases such as obesity and hypertension. During late human pregnancy and early rat postnatal life, neural networks in the suprachiasmatic nucleus form to regulate circadian rhythms, determining sleep-wake cycles. These networks are highly susceptible to alteration by maternal nutrition status, which can disrupt their rhythmic regulation. Insufficient maternal nutrition during pregnancy in rats disrupts offspring feeding patterns, reducing nocturnal intake and increasing daytime feeding, causing metabolic disorders.

1.2.3 Hypothalamic-Pituitary-Adrenal Axis Activation Hypothalamic-pituitary-adrenal (HPA) axis regulation of stress responses represents a primary mechanism of metabolic abnormalities in IUGR individuals. Glucocorticoid levels are low during embryogenesis but participate in maternal metabolic regulation and are influenced by 11β-hydroxysteroid dehydrogenase 2 activity. Under stress from insufficient maternal nutrition, elevated intrauterine cortisol exerts long-term effects on embryos, causing metabolic abnormalities. Cortisol concentration correlates with both blood pressure and insulin resistance, and studies show IUGR correlates with elevated serum cortisol and blood pressure at birth. Larger birth weight associates with lower adult serum cortisol, possibly because glucocorticoids serve as important mediators and targets for early-life programming [44].

1.2.4 Appetite Regulation The hypothalamus serves as a critical center for appetite regulation and modulates leptin secretion. Leptin, an appetite-suppressing neuropeptide, participates in programming of appetite and body composition during early life. Insufficient maternal nutrition reprograms hypothalamic appetite centers, causing postnatal metabolic abnormalities. Rat nervous system development completes gradually during the neonatal period, when serum leptin levels rise dramatically (increasing 5-10 fold in female rats aged 4-10 days). Studies show leptin injection in rats from postnatal days 3-13 can reverse programming effects of maternal nutrition insufficiency, suppressing rapid weight gain in IUGR rats fed high-fat diets and normalizing energy intake, body weight, fat content, fasting glucose, insulin, and leptin levels [45].

1.2.5 Epigenetics Epigenetics regulates gene expression without altering DNA sequence, controlling DNA and histone modifications that affect chromatin accessibility and allow transcription factors to interact with their binding sites in gene regulatory regions. Epigenetics represents a cumulative effect whereby environmental factors profoundly influence all gene expression, primarily through post-translational modifications including histone N-terminal acetylation and methylation.

Maternal nutrient quantity and quality affect regulation of DNA methylation and histone acetylation, inducing metabolic programming. Embryonic nutrition can serve as a trigger for epigenetic changes that subsequently affect gene expression. Clinical statistics reveal that offspring from the Dutch famine show low insulin-like growth factor-2 methylation levels [46], while newborns with

higher retinoid X receptor and endothelial nitric oxide synthase methylation levels show greater obesity during early childhood, demonstrating that embryonic epigenetic programming affects postnatal metabolic patterns [47]. Experiments confirm that IUGR rats exhibit reduced pancreatic-duodenal homeobox 1 (Pdx1) expression [48]. Through epigenetic regulation, insufficient binding of distal Pdx1 promoter factors to upstream stimulatory factors, combined with recruitment of histone deacetylase I and corepressor Sin3A, causes deacetylation of histones H3 and H4, silencing the Pdx1 gene and reducing β-cell function. This epigenetic regulation persists from 2 weeks to 4 months of age in rats, ultimately inducing diabetes. Furthermore, multiple factors (maternal stress, nutrition insufficiency, hypoxia, harmful substance exposure) can create adverse embryonic environments that affect offspring HPA axis development through epigenetic effects, thereby increasing metabolic disease incidence.

1.2.6 Telomere Shortening and Apoptosis Telomeres (TL) are highly repetitive DNA sequences at chromosome ends that, with TL proteins, form a "cap" structure maintaining chromosome integrity. Each DNA replication shortens telomeres slightly, and when exhausted, cells initiate apoptosis. Embryonic nutritional programming affects telomere length, with metabolically abnormal animals showing shorter chromosome telomeres. Jennings et al. [49] found that IUGR rats from malnourished mothers had shorter renal cell chromosome telomeres and exhibited obvious catch-up growth during the neonatal period. Reports also indicate that maternal nutrition and postnatal catch-up growth affect telomere length in aortic [50] and pancreatic islet cells [51], linking early growth with cardiovascular disease. Oxidative stress and apoptosis likely cause telomere shortening in IUGR cells, and increased apoptosis rates during youth accelerate organ aging and shorten lifespan.

1.2.7 Low-Grade Inflammation Metabolically abnormal animals often suffer from low-grade inflammation. Poor growth during embryonic and neonatal periods likely affects inflammatory pathways, representing a potential mechanism linking IUGR with metabolic abnormalities. C-reactive protein (CRP), an acute-phase protein secreted by the liver, shows elevated levels that predict increased coronary artery disease and diabetes incidence. Studies reveal that adult IUGR offspring have significantly elevated CRP levels [52], indicating that maternal malnutrition during pregnancy causes low-grade inflammation in offspring. Under nutrition-deficient stress, elevated glucocorticoid levels in both maternal blood and embryos may stimulate the embryonic adrenal axis, causing persistent inflammatory responses. Intrauterine malnutrition also impairs embryonic and postnatal muscle growth, causing disproportionate abnormal fat accumulation. Inflammatory factors secreted by adipose tissue may induce low-grade chronic inflammation, causing metabolic abnormalities.

1.2.8 Mitochondrial Function Mitochondria are critical organelles for ATP generation, and mitochondrial dysfunction disrupts oxidative phosphorylation,

reducing ATP production. IUGR model animals show mitochondrial function impairment in skeletal muscle, liver, and brain [53]. IUGR rats exhibit reduced β-cell mitochondrial function, impaired insulin secretion, and increased reactive oxygen species production. Mitochondrial dysfunction readily induces adult insulin resistance and metabolic disorders, and some mitochondrial gene polymorphisms associate with multiple metabolic syndromes [54]. IUGR offspring show abnormal expression of several mitochondria-related genes.

2 Placental Nutrient Transport

Embryonic development affects postnatal metabolism, and embryonic growth depends not only on maternal nutrition status but also directly on placental nutrient transport capacity. A "placental barrier" between mother and embryo prevents direct blood contact, requiring nutrients to be delivered through transport proteins, electrochemical gradients, and diffusion channels. This transport process is complex: placental villi have inner and outer layers, and nutrients, oxygen, and water must cross both membranes to reach the embryo. The layer adjacent to maternal circulation consists of trophoblast cells called syncytiotrophoblast (SCTB), which forms the epithelium responsible for placental transport. This epithelium comprises two polarized membranes: the microvillous membrane (MVM) facing maternal blood and the basement membrane (BM) facing embryonic capillaries. Beyond SCTB membranes, nutrients must also cross embryonic capillary endothelium, whose permeability depends on solute size, allowing small molecules like amino acids and glucose to pass while blocking larger molecules. Thus, SCTB only permits free passage of small solutes, serving as the rate-limiting barrier for embryonic nutrient delivery.

Under the operation of transport proteins in MVM and BM, the placenta transports nutrients (glucose, amino acids, fatty acids) to promote embryonic development, a process inseparable from SCTB and embryonic capillary endothelium functions. SCTB directly contacts maternal blood circulation, facilitating nutrient transport across MVM. Nutrients entering the cytoplasmic space interact with BM and are taken up by embryonic capillary endothelium, completing nutrient delivery.

2.1 Glucose

Glucose serves as the primary energy substrate for embryonic and placental growth. Embryonic gluconeogenesis is very limited, making embryonic glucose requirements almost entirely dependent on maternal blood glucose. Placental glucose transport occurs via facilitated diffusion involving glucose transporters (GLUT), with GLUT1 being the main transporter across both MVM and BM.

2.2 Amino Acids

Amino acids are essential nutrients for embryonic tissue development. Most amino acid concentrations are higher in embryonic plasma than maternal blood,

demonstrating active transport across SCTB. The placenta contains over 15 amino acid transporters, each responsible for several amino acids, with System A and System L being most extensively studied. System A is a Na+-dependent system promoting transport of small neutral amino acids (alanine, serine, glycine) into cells, active on both SCTB membranes with higher activity in MVM and regulated by hormones including insulin, leptin, IGF-1, and interleukin-6. During late pregnancy, System A has three isoforms in placenta: SNAT1, SNAT2, and SNAT4. System L is a Na+-independent carrier for large neutral amino acids, activated by glucose and insulin, with activity dependent on other transporters. System L is highly expressed in placenta to transport essential amino acids and hormones according to fetal demands, with different isoforms in different placental regions: LAT1 in MVM and LAT2, LAT3, and LAT4 in BM [55]. Currently, amino acid transport across MVM is considered the rate-limiting step for amino acid delivery. Amino acids crossing MVM then facilitate diffusion across BM via LAT3, LAT4, and TAT1 down concentration gradients into embryonic capillaries, completing nutrient transport.

2.3 Fatty Acids

Fatty acids play critical roles in embryonic growth, including brain development and fat accretion. In maternal blood, lipids exist primarily as triglycerides, phospholipids, and cholesterol esters. Triglycerides cannot cross the SCTB barrier and must first be degraded to free fatty acids (FFAs) by placental triglyceride lipases. FFAs are then taken up by the placenta via free fatty acid transport proteins to meet embryonic nutritional needs. Maternal blood triglycerides are hydrolyzed to FFAs by lipoprotein lipase and endothelial lipase, then cross MVM with assistance from fatty acid transport proteins, fatty acid translocase, and plasma membrane fatty acid-binding proteins. Intracellular FFA transport requires fatty acid transport proteins and fatty acid translocase.

2.4 Cholesterol

Cholesterol is essential for embryonic development, serving as both a critical cell membrane component and a steroid hormone precursor. Although embryos can synthesize cholesterol, this is insufficient to meet developmental requirements, necessitating maternal cholesterol delivery via lipoprotein carriers [56]. These carriers include low-density, high-density, and very low-density lipoproteins, each with specific receptors expressed in SCTB. Cholesterol transport from placenta to embryo requires specific transporters including ATP-binding cassette transporters A1 and G1 (ABCA1 and ABCG1) in endothelial and embryonic cells, with ABCA1 located in MVM [57] and ABCG1 in BM [58].

[Figure 1: see original paper] Location of key proteins involved in macronutrient (glucose, amino acids, fatty acids) transport at the MVM and BM of placenta

Adult metabolic patterns are inseparable from the embryonic nutritional environment. Maternal nutrition status directly determines embryonic nutrient

supply, and adequate, appropriate maternal nutrition is essential for embryonic development. The placenta serves as the gateway for maternal-to-embryo nutrient delivery, with multiple nutrient transporters determining transport efficiency. Together, maternal nutrient supply and placental transport efficiency determine embryonic nutrient provision. Adverse embryonic environments elevate oxidative stress, accelerate apoptosis, affect postnatal appetite, induce catch-up growth, and increase adult metabolic disease risk. In large-scale, intensive, standardized livestock production, optimizing gestational nutrition to improve postnatal growth performance can effectively enhance nutrient utilization efficiency and provide greater economic returns than direct manipulation of growing animal nutrition. Furthermore, gestational nutritional interventions that improve metabolic programming in offspring can reduce metabolic disease risk and promote healthy animal production. In-depth investigation of the embryonic origins of metabolic abnormalities enables better understanding of metabolic pattern development and provides valuable insights for human nutrition and medical research.

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Note: Figure translations are in progress. See original paper for figures.