Short title: Fetal programming in meat production

Fetal programming in meat production

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Abstract:

Nutrient fluctuations during the fetal stage affects fetal development, which has long-term impacts on the production efficiency and quality of meat. During the early development, a pool of mesenchymal progenitor cells proliferate and then diverge into either myogenic or adipogenic/fibrogenic lineages. Myogenic progenitor cells further develop into muscle fibers and satellite cells, while adipogenic/fibrogenic lineage cells develop into adipocytes, fibroblasts and resident fibro-adipogenic progenitor cells. Enhancing the proliferation and myogenic commitment of progenitor cells during fetal development enhances muscle growth and lean production in offspring. On the other hand, promoting the adipogenic differentiation of adipogenic/fibrogenic progenitor cells inside muscle increases intramuscular adipocytes and reduces connective tissue, which improves meat marbling and tenderness. Available studies in mammalian livestock, including cattle, sheep and pigs, clearly show the link between maternal nutrition and the quantity and quality of meat production. Similarly, chicken muscle fibers develop before hatching and, thus, egg and yolk sizes and hatching temperature affect long-term growth performance and meat production of chicken. On the contrary, because fishes are able to generate new muscle fibers lifelong, the impact of early nutrition on fish growth performance is expected to be minor, which requires further studies.

Key words: Adipogenesis; Fetal programming; Meat; Myogenesis; Progenitor cells; Quality

1. Introduction

Forage and feed deficiency is a common occurrence in the livestock industry in many areas of the world. Such deficiency could be due to drought which results in a significant reduction in forage production subjecting cows and ewes to nutrient deficiency during gestation (Du et al., 2013). In addition, nutrient deficiency could also be due to the lack of feeds and the poor quality of feeds, rendering sows and hens to nutrient deficiency (Altmann et al., 2012).

Fetal programming, also called developmental programming or fetal developmental programming, is the response to a specific challenge to the mammalian organism during a critical developmental time window that alters the trajectory of development qualitatively and/or quantitatively with resulting persistent effects (Nathanielsz, Poston, & Taylor, 2007). Studies linking fetal programming to animal performance in livestock and other experimental species were initiated relatively recently. In these studies, both malnutrition and over-nutrition during gestation impacts offspring growth performance (Benyshek, Johnston, & Martin, 2004; Bieswal et al., 2006; Bispham et al., 2003; Desai, Gayle, Babu, & Ross, 2005; Fernandez-Twinn, Ekizoglou, Wayman, Petry, & Ozanne, 2006; Fernandez-Twinn et al., 2005; Ford et al., 2007; King, 2006; Long, Shasa, Ford, & Nathanielsz, 2012; Long, Tousley, et al., 2012; Meyer et al., 2013; Reynolds et al., 2010; Symonds, Pearce, Bispham, Gardner, & Stephenson, 2004; Vonnahme et al., 2013; Yan et al., 2013; Zambrano et al., 2006). Therefore, in addition to genetic background, proper fetal development is also important to maximize the growth potential of animals.

Meat animals are raised for their skeletal muscle. The fetal stage is crucial for skeletal muscle development in mammalian livestock, because there is no net increase in the muscle fiber number after birth (Stickland, 1978; Zhu, Ford, Nathanielsz, & Du, 2004). A decrease in the

number of muscle fibers due to fetal programming permanently reduces muscle mass and negatively affects animal performance.

Marbling (intramuscular fat) is crucial for meat palatability and the fetal and neonatal stages are major stages for generation of intramuscular adipocytes (Tong et al., 2008), which provide the sites for intramuscular fat accumulation or marbling formation during fattening. Hence, fetal programming also affects the marbling in offspring cattle. In addition, the overall fat accumulation in offspring is also affected by maternal nutrition (Zhu et al., 2006).

In this review, we summarize recent progress in the impact of maternal nutrition on fetal development, focusing on myogenesis and intramuscular adipogenesis, as well as the impacts of fetal programming on the growth performance and meat quality of offspring of mammalian livestock. In the end, as a comparison, we also discuss the possible impacts of fetal programming on poultry and fish production.

2. Programming of skeletal muscle and adipose tissue development

2.1. Fetal programming of skeletal muscle development

Muscle cells, adipocytes and fibroblasts are all derived from the mesoderm. Specifically, skeletal muscle cells are developed from dermomyotome during the early embryonic development, while adipocyte progenitors are derived from lateral mesoderm (Fig. 1). Mesoderm cells undergoing myogenic commitment initially become Pax3⁺ and then Pax7⁺; and the subsequent expression of Myf5 commits these cells to the myogenic lineage. Myogenic differentiation involves the sequential expression of MyoD, myogenin and MYF-4 (Buckingham et al., 2003; Collins et al., 2009). These myogenic transcription factors then initiate the expression of myogenic specific genes including embryonic myosin heavy chain. Interestingly,

brown adipocytes can be developed from Myf5⁺ cells during fetal development (Seale et al., 2008). Recently, there is a new pool of brown-like adipocytes identified in adipose tissue, so called beige adipocytes. These cells also express UCP-1, generating heat (Harms & Seale, 2013). Selected markers for satellite cells, muscle fibers, fibroblasts, brown and beige adipocytes are listed in Table 1.

Ontogenetically, the early skeletal muscle development can be separated into primary myogenesis and secondary myogenesis. Primary myofibers form first during the embryonic stage, followed by the formation of secondary myofibers which accounts for the majority of muscle fibers in adults (Beermann, Cassens, & Hausman, 1978). There is no further increase in muscle fibers after birth, and postnatal muscle growth is mainly due to increase in muscle fiber size without forming new muscle fibers (Karunaratne, Ashton, & Stickland, 2005; Stickland, 1978). Satellite cells are derived from fetal myoblasts, which become quiescent and locate surrounding mature muscle fibers in postnatal muscle. The asymmetrical proliferation and myogenic differentiation of satellite cells, and their fusion with existing muscle fibers are crucial for postnatal muscle growth (Kuang, Kuroda, Le Grand, & Rudnicki, 2007).

Since the majority of muscle fibers, if not all, form during the fetal stage and myogenesis requires large amount of nutrients (Rehfeldt & Kuhn, 2006), muscle development during this stage is vulnerable to maternal nutrient deficiency (Zhu et al., 2004). Furthermore, skeletal muscle has a lower priority in nutrient partitioning during fetal development when compared to organs, such as the brain, heart and liver, which render skeletal muscle development particularly vulnerable to nutrient availability (Zhu et al., 2006). In the bovine fetus, primary muscle fibers form within the first 2 month post-conception, which only accounts for a limited number of muscle fibers (Russell & Oteruelo, 1981). Conversely, the majority of muscle fibers form in the

fetal stage between 2 and 7 months of gestation in cattle (Russell & Oteruelo, 1981). Reduction in the formation of muscle fibers during this stage reduces muscle fiber number and muscle mass, negatively affecting growth performance of offspring (Stannard & Johnson, 2004; Zambrano et al., 2005; Zhu et al., 2006). Skeletal muscle matures at late gestation in sheep (approximately day 105 of gestation) and cattle (approximately day 210 of gestation or slightly earlier) (Picard, Gagniere, Robelin, & Geay, 1995), and nutrient restriction after this stage has no major impact on muscle fiber number. Maternal nutrient restriction during the late gestation reduces fetal sheep muscle fiber size but not the number (Du et al., 2010). However, based on rodent studies, maternal nutrient restriction during late gestation reduces satellite cell density, which may affect postnatal muscle growth and muscle regeneration (Woo et al., 2011).

2.2. Fetal programming of fat and connective tissue development

Intramuscular fat (i.e., marbling) is crucial for the palatability of beef because marbling contributes to both flavor and juiciness. The amount of intramuscular fat is determined by the number and size of intramuscular adipocytes. Fetal programming has a major effect on the number of adipocytes in offspring. Adipocyte progenitors are derived from lateral mesoderm, and likely have an endothelial origin. These progenitor cells also have fibrogenic capacity and named fibro/adipogenic progenitors (**FAPs**) (Joe et al., 2010; Uezumi, Fukada, Yamamoto, Takeda, & Tsuchida, 2010; Uezumi et al., 2011). Platelet derived growth factor receptor α (**PDGFR α**) positive cells are progenitors for adipogenesis (Table 1) (Catalano & Hauguel-De Mouzon, 2011; Joe et al., 2010; Uezumi et al., 2010; Uezumi et al., 2011). Stem cell antigen-1 (**Sca-1**) is another marker for adipogenic progenitors, and PDGFR α + / CD45- and Sca-1+ / CD34+ / CD45- mark the similar pool of progenitor cells possessing high adipogenic capacity

(Joe et al., 2010; Tan, Eminli, Hettmer, Hochedlinger, & Wagers, 2011; Uezumi et al., 2010; Uezumi et al., 2011), with more than 85% cells identical (Joe et al., 2010). Progenitors and preadipocytes account for about 15 to 50% of stromal vascular cells in adipose tissue (Catalano & Hauguel-De Mouzon, 2011; Sepe, Tchkonja, Thomou, Zamboni, & Kirkland, 2011). These cells reside in the adipose vasculature. The source of these cells remains to be established, but a large portion of FAPs are formed during fetal development (Yang et al., 2013). During the fetal stage, it appears that mesoderm-derived precursors with the capacity to differentiate into both endothelial and mesenchymal lineage cells, called mesenchymoangioblasts, are formed first, and mesenchymal cells further develop into FAPs (Fig. 1). Indeed, adipose development in the fetuses initiates with the formation of capillary vessels in the spaces between mesenchymal tissues (Hausman & Dodson, 2013) .

During postnatal development, a portion of FAPs remain in the stromal vascular fraction of adipose tissue, which becomes the source of preadipocytes and adipocytes during later adipose tissue development (Du et al., 2013; Huang, Das, Yang, Zhu, & Du, 2012). Adipogenesis can be separated into two stages, adipogenic commitment and adipogenic differentiation, which are regulated by Zfp423 and peroxisome proliferator-activated receptor γ (**PPAR γ**) respectively (Farmer, 2006; Gupta et al., 2010; Gupta et al., 2012; Rosen & MacDougald, 2006; Spiegelman & Flier, 1996; Vernochet, Peres, & Farmer, 2009).

Adipogenesis and neovascularization are temporally and spatially associated processes (Cao, 2007). During embryogenesis, the primitive fat organs are formed at the perivascular site (Hausman & Richardson, 1982). Preadipocytes migrate toward developing capillary network to develop adipose tissue, a process regulated by $\alpha v\beta 3$ integrin and plasminogen activator inhibitor 1, which are expressed in both preadipocytes and capillary endothelial cells (Crandall, Busler,

McHendry-Rinde, Groeling, & Kral, 2000). Maternal food restriction inhibits the expression of vascular epithelial growth factor (VEGF) in microvascular and aortic endothelial cells during fetal development, which decreases angiogenesis (Khorram et al., 2007). As adipose tissue development is closely associated with capillary network development, impaired neovascularization negatively affects fetal adipose development. However, because adipose tissue has high plasticity, compensatory growth of adipose tissue often result in fatter offspring born to nutrient restricted mothers. Such growth is frequently associated with increased feed intake and adipocyte hypertrophy (Gonzalez-Bulnes et al., 2012; Zhu et al., 2006).

The initial events of adipose tissue development, including the formation of a vascular network in future adipose tissue, initiates at a comparable time with primary myogenesis, (Feve, 2005; Gnanalingham, Mostyn, Symonds, & Stephenson, 2005; Muhlhausler, Duffield, & McMillen, 2006). Roughly, the stage of adipogenic commitment overlaps with the period of secondary myogenesis, and the major formation of adipocytes occurs during late gestation to early weaning stages. Thus, maternal nutritional management during this period affects adipocyte hyperplasia, which alters overall adipose tissue development, as well as intramuscular adipocyte density and thus marbling (Du et al., 2013).

The adipose tissue development is inseparable from the connective tissue formation. Actually, adipose tissue is considered as a specialized connective tissue. Accompanying adipogenesis, fibrogenesis is also ongoing, together forming the adipose tissue and associated connective tissue. Because both adipogenesis and fibrogenesis share a common cell lineage, a positive correlation between adipogenesis and fibrogenesis is expected. Consistently, in genetically high marbling Wagyu cattle, both intramuscular adipogenesis and collagen accumulation are higher than relatively low marbling Angus cattle (Duarte et al., 2013). Fibroblasts also synthesize connective

tissue surrounding muscle bundles, together forming the basic structure of muscle. Limited studies also show that maternal nutrition alters fibrogenesis in fetal skeletal muscle and affects the collagen content in the skeletal muscle of progeny. Piglets with lower birth-weight compared to their littermates experience nutrient deficiency due to improper placental nutrient delivery. When compared to their littermates, grown pigs with lower birth-weight have a higher content of collagen in their skeletal muscle (Karunaratne et al., 2005). Overall, our understanding of fibrogenesis in livestock is very limited and more studies on the association among maternal nutrition, fibrogenesis, and collagen accumulation in offspring muscle are needed.

2.3. Competitive relationship between myogenesis, adipogenesis and fibrogenesis

As previously discussed, both skeletal muscle cells and adipocytes are derived from the mesoderm during the embryonic stage, early myogenesis and adipo/fibrogenesis can be considered as a competitive process. As much, enhanced muscle growth, such as double muscling cattle, is associated with lower marbling. Interestingly, in our studies with Wagyu cattle, we found that myogenesis was lower but intramuscular adipogenesis was higher in Wagyu cattle compared to Angus cattle (Duarte et al., 2013).

Because adipogenic and fibrogenic cells share immediate common progenitor cells, it provides an opportunity for us to manipulate the differentiation of progenitor cells to favor adipogenesis. Enhancing adipogenesis in developing muscle increases intramuscular fat, thereby improving beef flavor. On the other hand, less fibrogenic differentiation reduces intramuscular connective tissue, thereby decreasing background toughness of beef. In combination, the eating quality of beef can be improved. However, the mechanisms determining adipogenic or fibrogenic differentiation remain to be defined. In our previous studies, we found that Zfp423 is a critical

regulator of adipogenic differentiation. Over-expression of Zfp423 in stromal-vascular cells separated from beef cattle enhanced adipogenic differentiation, while knockdown of Zfp423 attenuated adipogenic capacity. Furthermore, higher adipogenic differentiation due to enhanced Zfp423 expression reduces fibrogenesis (Huang, Das, et al., 2012). Therefore, Zfp423 may provide a molecular target for enhancing intramuscular adipogenesis and marbling in beef cattle, while reducing intramuscular collagen accumulation and toughness of beef. Factors which can strengthen Zfp423 expression or enhance its function as a transcription factor are expected to enhance adipogenesis and marbling in beef cattle. For example, vitamin A supplementation can increase Zfp423 expression (Reichert et al., 2011; Yasmeen, Jeyakumar, Reichert, Yang, & Ziouzenkova, 2012), and its supplementation during a critical stage for intramuscular adipose development is expected to enhance marbling.

2.4. Long-term effect of fetal programming on offspring

Fetal programming has long-term effects on offspring performance. Lambs from dams subjected to nutrient restriction during mid-gestation were fatter and had a lower lean to fat ratio than their counterparts (Zhu et al., 2006). Piglets with lower birth-weight compared to their littermates are fatter and have a low growth efficiency compared to normal littermates (Wigmore & Stickland, 1983). Restriction in protein intake during pregnancy reduces the size of progeny pigs (Pond, Yen, Mersmann, & Maurer, 1990). Similarly, in sheep and beef cattle, nutrient deficiency impairs muscle growth and increases overall fatness (Funston, Larson, & Vonnahme, 2010; Funston & Summers, 2013; Greenwood & Cafe, 2007). Maternal nutritional status may influence fetal adipose tissue development by changing the prevailing glucose environment (Symonds & Lomax, 1992; Symonds, Pope, Sharkey, & Budge, 2012). During the early and

middle gestation, maternal nutrition restriction enhances glucose exchange capacity (Dandrea et al., 2001; Heasman, Clarke, Firth, Stephenson, & Symonds, 1998) and may increase sensitivity to insulin-like growth factor-1 (IGF1) to promote adipose development (Symonds et al., 2012). Once the maternal dietary intake is restored in the late stage of gestation, fetal glucose supply is increased and lead to fetal adiposity (Bispham et al., 2005; Zhu et al., 2006). In addition, the reduced muscle mass due to maternal nutrient deficiency reduces nutrient consumption in the muscle, and the excessive energy is diverted to adipose development and lipid accumulation, increasing the overall fatness of offspring.

Up to now, most studies in livestock focus on the effect of maternal nutrient deficiency on the performance of offspring. In addition, increasing evidence also points the impact of maternal over-nutrition on fetal development. Over-feeding of sows from conception to d 50 of gestation increased offspring fatness at birth, and the muscle fiber type composition of progeny was altered due to maternal nutritional management (Bee, 2004). Rats born to mothers fed a high fat diet either during gestation alone or during both gestation and lactation exhibited a 25% reduction in muscle cross-sectional area with approximately 20% fewer fibers compared with pups born to mothers fed a balanced chow diet (Bayol, Simbi, & Stickland, 2005). In sheep, maternal over-nutrition enhances intramuscular adipocyte density of fetuses at the late gestation (Yan et al., 2010) and also the resulting lambs (Huang, Zhao, et al., 2012; Yan et al., 2011). Besides enhanced adipocyte development due to maternal obesity, maternal over-nutrition or obesity increases fetal circulatory leptin levels (Kleiblova et al., 2010; Uzelac et al., 2010), which may induce leptin resistance in the offspring and lead to hyperphagia (Rooney & Ozanne, 2011).

The maternal impact on offspring growth and development is not only limited to the fetal

stage, and increasing evidence points to the importance of lactation nutrition on offspring adipose development. Maternal high energy intake during lactation affects milk composition, which has long-term effect on the offspring metabolism (Vogt et al., 2014). Maternal milk composition is altered by maternal diet, providing another opportunity to alter neonatal nutrition and thus, offspring development and subsequent meat production.

2.5. Application of fetal programming to meat production

In many parts of the world, drought is a recurring meteorological problem, which reduces forage production. As a result, sheep and cattle, which primarily depend on forage, undergo periodic nutrient deficiency. Due to the seasonal nature of cow and sheep reproduction, they frequently experience nutrient deficiency during pregnancy due to limited forage availability. Maternal nutrient deficiency potentially reduce muscle fiber numbers, decrease marbling and increase overall fatness of offspring animals (Du et al., 2013). To avoid negative effects of nutrient deficiency on meat production of offspring, nutrient supplementation is needed. Nutrient supplementation during the second trimester in ruminant animals promotes muscle development, which increase muscle mass and overall production efficiency of offspring (Du et al., 2010), while supplementation at late gestation only increases muscle fiber sizes without change in muscle fiber number (Du et al., 2011; Greenwood & Cafe, 2007). On the other hand, nutrient supplementation at middle to late gestation, a stage corresponding to adipose tissue development, promotes adipogenesis (Underwood et al., 2008).

Marbling is correlated with the number and size of adipocytes inside skeletal muscle. Increased adipogenesis in fetal muscle leads to an increase in the number of intramuscular adipocytes. These intramuscular adipocytes accumulate fat during post-natal growth, forming

marbling. For calves which experienced nutrient deficiency during late gestation and lactation stages, there are less intramuscular progenitors formed, which limits marbling formation during the ‘finishing’ phase. Therefore, maternal nutritional management to increase adipogenesis in fetal muscle is an effective method for promoting marbling (Du et al., 2013). The approximate timelines for muscle and adipose tissue development for beef cattle are depicted in Fig. 2. More detailed information is available in our previous publications (Du et al., 2013; Du et al., 2010).

3. Epigenetic mechanisms of fetal programming

While the genotype associated with high efficiency and quality of meat production can be improved through genetic selection, the growth efficiency of animals is also profoundly affected by epigenetic changes. Environmental factors, especially nutrients, available for fetuses shape the epigenetic landscapes of cells and tissues relevant to meat production. During animal early development, stem cells and progenitor cells maintain their pluri- or multi-potency through reversible inhibition of lineage-specific genes while allowing genes for self-renewal to express (A. Meissner et al., 2008; Mohn et al., 2008). Polycomb repression complexes (PRCs), including PRC1 and 2, are mainly responsible for reversible inhibition of genes. One core component of PRC2 is EZH2 (Enhancer of Zeste 2), which catalyzes histone 3 lysine 27 trimethylation (H3K27me3) (McCabe et al., 2012; Qi et al., 2012), a marker for gene silencing (Bernstein et al., 2006). On the other hand, trithorax group (trxG) catalyzes H3K4 trimethylation (H3K4me3), which activates gene transcription (Schuettengruber, Martinez, Iovino, & Cavalli, 2011). Interestingly, H3K4me3 and H3K27me3 co-exist, forming a ‘bivalent state’, which poise genes for activation or inhibition (A. Meissner et al., 2008; Mikkelsen et al., 2007). Most bivalent genes are key developmental genes; during differentiation, non-induced bivalent developmental genes lost active H3K4me3 but kept repressive H3K27me3 mark (Schuettengruber & Cavalli,

2009), leading to largely permanent inhibition of gene expression by inducing DNA methylation (Mohn et al., 2008).

In our previous studies, we observed that adipogenic differentiation was enhanced in fetuses of obese dams (Yan et al., 2010; Zhu et al., 2008), and increased intramuscular fat content in offspring (Yan et al., 2011), as well as overall adiposity (Samuelsson et al., 2008; Tong et al., 2011). Our bioinformatics analyses show that the Zfp423 promoter presents exceptionally rich CpG sites and islands, meeting the characteristics of “key developmental gene” with high CpG density promoters (Alexander Meissner et al., 2008). We observed that maternal obesity reduced DNA methylation in the Zfp423 promoter by about 50% (Yang et al., 2013), which aligned with the higher expression of Zfp423 in obese fetal tissue. Our data has been independently confirmed by another study in rats (Borengasser et al., 2013). In addition, the H3K27me3 and EZH2 levels in the Zfp423 promoter were lower in obese compared to control fetal tissue, consistent with the lower DNA methylation and the high expression of Zfp423. We further observed that the DNA methylation changes in adipogenic progenitor cells during the fetal stage has long-term impacts on the DNA methylation and adipogenic capacity of adipogenic progenitor cells separated from offspring fat (Unpublished data). Similar epigenetic changes likely occur in other tissues and organs (Sebert, Sharkey, Budge, & Symonds, 2011; Simmons, 2011). In summary, epigenetic changes during early fetal development alters epigenetic signature in progenitor cells and likely differentiated cells in offspring adipose tissue, providing a key mechanism linking maternal nutrition to long-term performance of offspring.

4. Fetal programming in poultry and fish

Up to date, studies on fetal programming mainly focuses on mammalian species, and the

impact of maternal nutrition on poultry is far less studied. Similar to mammals, the muscle development in chicken is mainly accomplished during the embryonic stage (*in ovo*) (Al-Musawi, Lock, Simbi, Bayol, & Stickland, 2011; Velleman, 2007), and environmental factors affect embryo development. A recent study compared the effect of exposure to high hatching temperature on the growth performance of chicken. Briefly, eggs were challenged with 39.5 °C for 12 h/d between E7 to E16 compared to 37.8 °C. Chicken were harvested at d35 and d 70, and found that the exposure to a high incubation temperature reduced abdominal fat pad by 8% but increased breast muscle yield (Loyau et al., 2013), and the feed conversion ratio was also improved (Piestun, Druyan, Brake, & Yahav, 2013), clearly showing the programming effect of early development on the subsequent performance of chicken. In another study, the impact of incubation temperature (37.5 versus 38.5 °C) on muscle development of chicken embryos of laying hens and broilers was compared, and found that high incubation temperature enhanced muscle growth only in laying chicks (Al-Musawi, Stickland, & Bayol, 2012). In a recent study, the effect of eggshell temperature on the hatchability of chicks and their growth performance was compared and found that hatching temperature affects the feed efficiency and body weight (Ipek, Sahan, Baycan, & Sozcu, 2014). Interestingly, low-protein diet to hens reduced the hatching weight of chicks; however, these chicks demonstrated faster post-hatch growth and resulted in heavier chicken at harvest (Rao et al., 2009). Besides, hatching temperature, the egg sizes determine the nutrients available for embryo development, which is expected to impact the growth performance of chicken. In summary, despite limited studies, available evidence strongly support that environmental factors during hatching has impacts on the long-term growth performance of chicks.

The fish consumption is increasing rapidly, mainly due to their health beneficial effects

compared to red meat. Compared to mammalian livestock and poultry, fish has similar mechanisms regulating myogenesis and adipogenesis (Rescan, 2001). However, fish has life-long capacity to generate new muscle fibers (Rossi & Messina, 2014). Due to such plasticity in growth and development, the effects of hatching and early development on the long-term growth and performance of fish are expected to be small. However, more studies are needed to test the impact of early growth and development on the long-term growth performance of fish.

5. Conclusions

Available studies clearly show that maternal nutrition affects the development of fetal skeletal muscle and adipose tissue, which exert long-term effects on the growth performance and meat quality of offspring. In mammalian livestock and poultry, maternal under-nutrition during fetal development reduces skeletal muscle fiber number, increases fatness and reduces growth performance of progeny. Proper nutrient supplementation, however, improves fetal skeletal muscle development and adipogenesis in fetal and pre-weaning skeletal muscle, enhancing marbling in offspring. Increasing evidence also demonstrates the programming effects of hatching temperature on the growth performance of chicken. Up to now, very few evidence is available regarding to the fish. More studies on the programming effects of chicken and fish are apparently needed.

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723 **Table 1. Markers for major progenitors and differentiated cells during muscle and adipose**
724 **tissue development**

Cell name	Markers	References
Satellite cells	Pax7, Integrin $\alpha 7$	(Conboy, Cerletti, Wagers, & Conboy, 2010; Lapin, Gonzalez, & Johnson, 2013)
Muscle fibers	Myosin heavy chain	(Cassar-Malek et al., 2010; Fu et al., 2013)
Brown adipocytes	Zic1, Lhx8, UCP-1	(Petrovic et al., 2010; Wu et al., 2012)
Beige adipocytes	Cd137, Tmem26, Tbx1, UCP-1	(Lidell et al., 2013; Petrovic et al., 2010; Wu et al., 2012)
Fibroblasts	FSP1	(Strutz et al., 1995)
White adipocytes	FABP4, perilipin	(Brasaemle, Subramanian, Garcia, Marcinkiewicz, & Rothenberg, 2009; Wang, Guan, Li, & Bernlohr, 2009)
Fibro/adipogenic progenitors	PDGFR α , Sac-1	(Joe et al., 2010; Uezumi et al., 2010; Uezumi et al., 2011)
Preadipocytes	Zfp423, PPAR γ	(Huang, Das, et al., 2012; Yang et al., 2013)

725
726 Abbreviations: Cd137: Tumor necrosis factor receptor superfamily member 9; FABP4: Fatty
727 acid binding protein 4; FSP1: Fibroblast-specific protein 1; Lhx8: LIM homeobox 8; Pax7:
728 Paired box protein 7; P4H: Prolyl 4-hydroxylase; PDGFR α : Platelet-derived growth factor
729 receptor α ; Sac-1: Stem cell antigen-1; Tbx1: T-box protein 1; Tmem26: Transmembrane protein
730 26; UCP-1: Uncoupling protein-1; Zic1: Zic family member 1

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Figure legends

Figure 1. Early mesoderm development and the commitment of mesenchymal progenitor cells into myogenic and fibro-adipogenic cell lineages during fetal muscle development.

Figure 2. Approximate timelines for skeletal muscle and adipose tissue development of beef cattle. Nutrient deficiency during the specific periods of cattle development negatively affects muscle and fat development either through reducing cell numbers (hyperplasia) or sizes (hypertrophy). On the other hand, nutrient supplementation enhances muscle fiber number or sizes, or adipocyte number or sizes correspondingly.

741 **Figure 1**

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Figure 2