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Review: Animal model and the current understanding of molecule dynamics of adipogenesis

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Among several potential animal models that can be used for adipogenic studies, Wagyu cattle is the one that presents unique molecular mechanisms underlying the deposit of substantial amounts of intramuscular fat. As such, this review is focused on current knowledge of such mechanisms related to adipose tissue deposition using Wagyu cattle as model. So abundant is the lipid accumulation in the skeletal muscles of these animals that in many cases, the muscle cross-sectional area appears more white (adipose tissue) than red (muscle fibers). This enhanced marbling accumulation is morphologically similar to that seen in numerous skeletal muscle dysfunctions, disease states and myopathies; this might indicate cross-similar mechanisms between such dysfunctions and fat deposition in Wagyu breed. Animal models can be used not only for a better understanding of fat deposition in livestock, but also as models to an increased comprehension on molecular mechanisms behind human conditions. This revision underlies some of the complex molecular processes of fat deposition in animals.

Keywords: wagyu, adipogenesis, lipodystrophies, obesity

Implications

Because adipose tissue studies have grown over the years due to its huge importance in the context of fat deposition, improving the knowledge of genetic differences between breeds can have a significant impact of beef production. This review summarizes several issues regarding to Wagyu beef and other breeds related to intramuscular fat, since animals of this breed stand out for having higher marbling. The benefits of the use of Wagyu breed for adipogenic studies are also discussed.

Introduction

Fat found in skeletal muscle includes intramyocellular fat droplets (occurring in lower abundance) and adipose tissue between muscle fibers, which is usually referred to as intramuscular fat (IMF). Adipose tissue is derived from the mesenchyme (Fehrer and Lepperdinger, 2005) with a supportive stroma (Romao *et al*., 2011) and is easily isolated (Hausman and Dodson, 2012) for *in vitro* studies. Adipocytes appear to be dynamic; a renewed search for the origin of adipocyte progenitors has demonstrated high incidences of cellular plasticity, even in adult adipose tissue (Fernyhough *et al*., 2005 and 2008; Hausman *et al*., 2009). As such, adipose tissue may represent a source of stem cells that can have far-reaching effects on several fields (Zuk *et al*., 2002). Furthermore, adipose tissue has the potential to be a source of cells for tissue engineer purposes, as it appears to contain cells able to act as functional and vascular building blocks for several tissues (Fraser *et al*., 2006). The potential for cellular development of adipocytes is believed to be fixed relatively early in life, with changes thereafter in either the size or number of cells that occur in proportion to the initial cell number and lipogenic proteins (Caserta *et al*., 2001; Pethick *et al*., 2004; Wang *et al*., 2009). Moreover, dysfunction of the adipose compartment (cells and metabolism) is central to the pathology associated with metabolic diseases such as obesity, type II diabetes (Edelman, 1998), cancer cachexia and lipodystrophies (Cristancho and Lazar, 2011).

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Regarding to IMF in production animals, we can highlight the Wagyu beef cattle, which can be considered a model for the studies of adipose tissue deposition. This is a composite breed comprised of four *Bos taurus* breeds: Japanese Black, Japanese Brown, Japanese Shorthorn and Japanese Polled. Originally bred for strength and endurance, by the 20th century, Wagyu cattle were mostly selected for their desirable marbling characteristics, with strict geographic restraints resulting in a sharp decline in genetic diversity (further amplified by artificial insemination), such that the offspring of five sires accounted for 42% registered Wagyu (Scraggs *et al*., 2014). The importation of Wagyu cattle to the United States in 1973 has allowed for the expansion of the population from the initial individuals in 1994 to an estimated 700 purebred animals in 2009 (Scraggs *et al*., 2014). Wagyu cattle are now highly valued for their tender meat (Yang *et al*., 1999) and their ability to deposit extremely high amounts of IMF (Fernyhough *et al*., 2008; Shirouchi *et al*., 2014).

Comparisons between Wagyu cattle and other breeds regarding cell biology and general adipogenesis have been reported in several studies, such as those by Oikawa *et al.* (2000), Hausman *et al.* (2009), Dodson *et al.* (2010a) and Duarte *et al.* (2013). Some studies comparing Wagyu cattle with other breeds (Hausman *et al.,* 2009; Dodson *et al.,* 2010a; Duarte *et al.,* 2013) have emphasized the uniqueness of this breed and the importance of better understanding adipogenesis, mainly because its increased accumulation of fat within the skeletal muscle, which seems to not follow the same pattern of other adipose tissue depots. Consequently, Wagyu cattle may present a highly marbled beef without an increase of overall fatness, making this breed an unique animal model for the understanding of this phenomena.

Adipogenesis and IMF

In humans, the subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) have been identified as the main fat depots. These depots differ in terms of their turnover. Adipose cells derived from VAT, in particular, have higher levels of metabolic activity and have been shown to hypertrophy in obese individuals. In addition to VAT and SAT, intermuscular adipose tissue and IMF are also measured in farm animal species such as swine and cattle (Komolka *et al*., 2014).

IMF deposition is achieved at the cellular level through adipogenesis, the process of proliferation and differentiation of preadipocytes, and lipogenesis, the subsequent assimilation of lipid (Harper and Pethick, 2004; Hausman *et al*., 2009; Dodson *et al*., 2010b). Previous studies have suggested that the high deposition of IMF in Wagyu is related to the differential expression of specific genes (Hudson *et al*., 2014). In most cattle breeds, IMF is first visible at about 11 months, with the greatest increases between 15 and 24 months. However, when they are finished on concentrated grain, Wagyu deposit more IMF at an earlier age when compared with other cattle breeds (Wertz *et al*., 2002; Shirouchi *et al*., 2014). Dietary conditions, particularly energy density, affect carcass adipose tissue deposition in beef cattle (Yamada *et al*., 2009). Thus, cattle that are fed low energy through the finishing phase with forage and pasture type diets seldom show the desired marbling. Moreover, the level of dietary starch that is fed to young cattle may alter gene networks associated with adipocyte differentiation and energy metabolism (Graugnard *et al*., 2010). Thus, high energy diets (finishing diets usually only during the last 4 to 6 months before harvest) have been used as a production strategy for enhancing intramuscular adipose tissue in beef cattle. Exposure to high-starch diets during the early growth phase of cattle might induce precocious preadipocyte differentiation and lipid filling (Graugnard *et al*., 2010).

Marbling is an important component of livestock production, as it is a major factor in the overall meat quality (flavor and tenderness), nutrition (protein and fat levels and fatty acid composition) and economic value (Pena *et al*., 2013; Hudson *et al*., 2014; Sadkowski *et al*., 2014). An increase in IMF has been proposed to occur either through the myogenic transdifferentiation of myogenic stem cells (MSC) in skeletal muscle through a complex regulatory pathway, which remains unclear, or through the multi-step process of adipogenic determination and differentiation of fibroblast-like preadipocytes into mature adipocytes assimilating lipid (Du and Zhu, 2010; Du *et al*., 2013).

Myoblasts and adipocytes have been shown to utilize intercellular communication, which directly affects the growth and development of these cells (Kokta *et al*., 2004; Muthuraman, 2014). Furthermore, when in close proximity, these cells perform a paracrine function by altering the growth, development or energy storage of each other based on the chemical factors that are released (Kokta *et al*., 2004; Muthuraman, 2014). Myoblasts have been shown to regulate the growth, development, differentiation and lipid assimilation of adipocytes through intercellular communication (Muthuraman, 2014).

Myostatin, a growth differentiation factor secreted by myoblasts, suppresses proliferation of preadipocytes in muscle tissue through direct down-regulation of adipogenic transcription factors, thus decreasing the overall IMF (Komolka *et al*., 2014). Furthermore, co-culture of myoblasts and adipocytes results in an upregulation of peroxisome proliferator activating receptor γ (*PPAR*γ), CCAAT enhancer binding protein α (*C/EBP*α) and fatty acid binding protein 4 (*FABP4*), possibly indicating myoblasts' promotion of adipogenic specific transcription factors leading to increased IMF or allowing for MSC transdifferentiation as a mechanism for increasing IMF (Muthuraman, 2014). In both cases, myogenic and adipogenic contributions to marbling appear to be mediated by the transcription factors, *PPAR*γ, *C/EBP*α and *FABP4*. Fibroblasts like preadipocytes, in response to the aforementioned transcription factors, differentiate from progenitor cells and undergo adipogenesis and assimilation of lipid (Du *et al*., 2010). Similarly, MSCs respond to high concentrations of the same transcription factors. However, these factors appear to inhibit myogenic differentiation

stimulating adipogenesis and also appears to inhibit myogenic differentiation, while ensuring adipogenic differentiation (Teboul *et al*., 1995; Taylor-Jones *et al*., 2002; Singh *et al*., 2007; Du *et al*., 2010). Considering this, the study of adipogenesis and its effects on the accumulation of IMF can be used not only to understand fat deposition in livestock, but also for a better comprehension of the differentiation process in mesenchymal stem cells.

Stem cells

Skeletal muscle is derived from the mesoderm and is postnatally surrounded by small multipotent myogenic satellite cells (SC) that play an important role in muscle hypertrophy and regeneration (Kook *et al*., 2006; Du *et al*., 2010; Lee *et al*., 2012; Duarte *et al*., 2014). SC are multipotent cells capable of transdifferentiating into intramuscular adipocytes when exposed to local cellular signaling (Taylor-Jones *et al*., 2002; Singh *et al*., 2007; Du *et al*., 2010; Lee *et al*., 2012; Ryan *et al*., 2013). Moreover, muscle side population (SP) cells are multipotent stem cells that can participate in myogenesis and muscle regeneration upon transplantation (Penton *et al*., 2013). Interestingly, SP cells in skeletal muscle tissue have not only the ability to transdifferentiate into cells from myogenic but also in hematopoietic lineage (Reecy *et al*., 2003). *In vivo* studies using mice as a molecular model, have confirmed the hematopoietic stem cell potential of SP cells, as these present a regenerative capacity for blood, bone and lymph cells (Reecy *et al*., 2003). These studies have implied that SP cells may be an important resident source of transdifferentiation within skeletal muscle, and may be less differentiated than other previously discovered SC populations (Reecy *et al*., 2003).

The regenerative capacity of skeletal muscle decreases with age, thereby resulting in an overall loss of muscle mass over time and an increase in lipid content (Teboul *et al*., 1995; Kook *et al*., 2006; Aguiari *et al*., 2008; Ryan *et al*., 2013). This might not be totally accountable by the decrease in stem cell activity; myogenic transdifferentiation into adipocytes also play a role in this phenomena. Since MSCs are multipotent, their transdifferentiation into intramuscular adipocytes is feasible, depending on different cellular signaling exposure, thereby leading to greater amounts of IMF (if the adipocytes invade the perimysium) (Taylor-Jones *et al*., 2002; Singh *et al*., 2007; Aguiari *et al*., 2008; Du *et al*., 2010; Lee *et al*., 2012).

Adipogenic markers

A major marker of adipogenesis (or lack thereof) is preadipocyte factor-1 (pref-1), as this membrane protein is expressed on preadipocytes and acts to prevent adipogenesis. It has been reported that pref-1 inhibits adipocyte differentiation via sex determining region Y-box 9, which binds to its binding sites at the *C/EBP* β and δ promoter regions to suppress their transcription (Sul, 2009). In addition, it appears to be depot specific, as high levels of pref-1 expression were observed in smaller adipocytes (Yamada *et al*., 2014). Early and late differentiation are marked by the expression of the C/EBP family, which in turn is greater in fat depots of Wagyu when compared with Holstein cattle, as they are responsible for the increased proliferation potential of Wagyu preadipocytes *in vitro* (Yamada *et al*., 2009). Meanwhile, PPARs act as transcription factors to regulate gene expression by acting on lipid metabolism and adipocyte filling. Indeed, both *C/EBP*α and *PPAR*γ from the IMF of Wagyu are increased when compared with the IMF of Angus cattle (May *et al*., 1994; Yamada *et al*., 2007; Duarte *et al*., 2013).

Previous studies have suggested that the high deposition of IMF in Wagyu cattle is related to the differential expression of specific genes such as *C/EBP*α and *PPAR*γ (late adipogenic markers) as well as an early adipogenic marker *zinc finger protein 423* (Duarte *et al*., 2013). Table 1 shows the differences in adipogenic gene expression between Wagyu and other cattle breeds. Moreover, the expression of adipogenesis and the lipid droplet associated genes, perilipin 1 (*PLIN1*) and adipose differentiation-related protein (*ADFP*), are upregulated as markers of the overall amount of IMF (Shirouchi *et al*., 2014). *PLIN1* is a major protein that resides on the surface of mature adipocyte lipid droplets and plays an integral role in triacylglycerol storage and breakdown (Shirouchi *et al*., 2014). The largest lipid droplets in mature adipocytes are exclusively coated with *PLIN1*. Moreover, *PLIN1* promotes skeletal muscle lipid deposition by partitioning excess fatty acids towards triacylglycerol storage (Shirouchi *et al*., 2014). *ADFP* functions similarly to *PLIN1* but it is ubiquitous, whereas *PLIN1* appears to be found only on adipocytes (Shirouchi *et al*., 2014).

Several genes are well known for their correlation with obesity and other metabolic disorders; these genes include *PPAR*γ (Dodson *et al*., 2010b), leptin (*LEP*) (Duarte *et al*., 2007), adiponectin (*ADIPOQ*), *FABP4* (Wang *et al*., 2005), bone morphogenetic protein 4 (*BMP4*) (Majka *et al*., 2011), fat mass and obesity associated (*FTO*) (Fischer *et al*., 2009), *C/EBP*β (Cristancho and Lazar, 2011) and v-akt murine thymoma viral oncogene homolog 2 (*AKT2*). Three of the genes that are reported above (*BMP4, C/EBP*β and *AKT2*) are found in many reports related to fat storage in humans. Five of them (*PPAR*γ, *FABP4, ADIPOQ, FTO* and *LEP*) are mentioned both in connection with human disorders and adipogenesis in *B. taurus*. In particular, the role of the *ADIPOQ* gene is well described in Wagyu cattle (Jordan *et al*., 2011).

Adipogenesis and lipid metabolism: Wagyu as a model

Although research in humans and farm animals ultimately have different goals – identification of potential drug targets for metabolic diseases *v.* optimization of meat quality – the same tissue can be the focus of both research efforts (Komolka *et al*., 2014). Bovine adipocytes are a cell model for studying adipogenesis and lipid metabolism for improving animal production and also serving human health (Duarte *et al*., 2013).

Table 1 *Differences of adipogenic gene expression between Wagyu and other cattle breeds*

Tissue/cell type	Gene name	Variation	Reference
Sternomandibularis muscle tissue	*C/EBPα, PPARγ, Zfp423*	The mRNA expression of *C/EBPα, PPARγ* and *Zfp423* in Wagyu was higher than that of Angus at 24 months	Duarte *et al.* (2013)
Intermuscular fat tissue	*C/EBPδ*	The mRNA expression of *C/EBPδ* was higher than that of Holstein at 19 months	Yamada *et al.* (2009)
Mesenteric fat tissue	C/EBP family	The mRNA expression of C/EBP family was higher in Wagyu than that of Holstein at 19 months	Yamada *et al.* (2009)
	Pref-1	The mRNA expression of the *pref-1* gene was lower in Wagyu than that of Holstein at 19 to 24 months	Yamada *et al.* (2014)
Subcutaneous fat tissue	*PPARγ*	The protein expression of *PPARγ* in Wagyu was lower compared with that of Angus at 12 months	Wei *et al.* (2015)
	C/EBPδ	The mRNA expression of *C/EBPδ* was higher in Wagyu than that of Holstein at 19 months	Yamada *et al.* (2009)
	FABP4	The mRNA expression of *FABP4* was lower in Wagyu compared with that of Holstein	Albrecht *et al.* (2011)
Subcutaneous fat derived stromal vascular cells	*PPARγ*	The mRNA expression of *PPARγ* was lower in Wagyu when compared with that of Angus at 12 months	Wei *et al.* (2015)
	TGFB3, BMP2	The mRNA expression of *TGFB3* and *BMP2* in Wagyu was lower than that of Angus at 12 months	Wei *et al.* (2015)

C/EBPα = CCAAT enhancer binding protein α; PPARγ = peroxisome proliferator activating receptor γ; Zfp423 = zinc finger protein 423; Pref-1 = preadipocyte factor-1; FABP4 = fatty acid binding protein 4; TGFB3 = transforming growth factor 3; BMP2 = bone morphogenic protein 2.

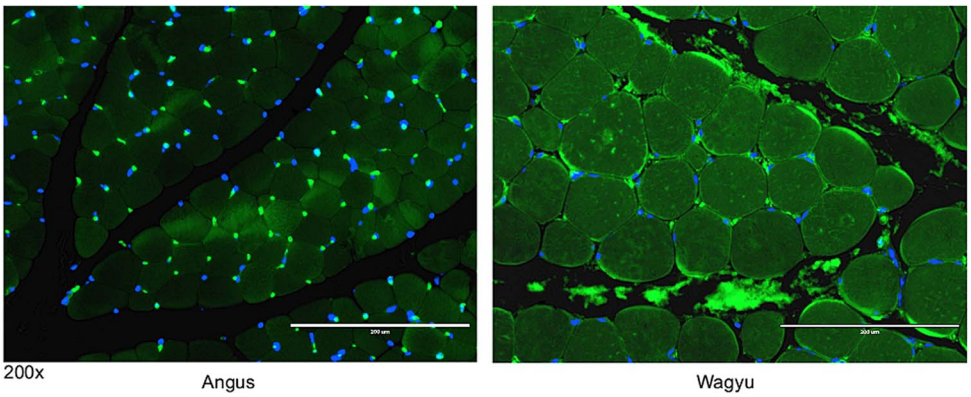

Figure 1 Immunofluorescence staining showed a greater number of fatty acid binding protein (FABP4) positive cells between muscle fibers and muscle bundles in Wagyu when compared with Angus skeletal muscle (*Sternomandibularis* muscle): FABP4 stained green and nuclei counterstained with 4',6-diamidino-2-phenylindole (DAPI). (Adapted from figure 5 in reference Duarte *et al.*, 2013, with permission. Figure provided by M. S. Duarte.)

Fat deposition in cattle typically follows the order in which perirenal fat is deposited first, followed by intermuscular, subcutaneous and finally by the IMF (Sainz and Hasting, 2000; Pethick *et al.*, 2005 and 2007; Hocquette *et al.*, 2010). Thus, as IMF deposition is time dependent in most cattle breeds and is dependent on a high energy intake, the use of cattle breeds, instead of Wagyu as models for human dysfunctions is compromised, since it would not be possible to dissociate the effect of energy intake or age from the genetic predisposition for IMF deposition abnormalities. Therefore, the use of animals that have a unique ability to deposit IMF regardless of energy intake or age, such as Wagyu cattle, may be useful in studies of adipogenesis (Lehnert *et al.*, 2006).

In summary, Wagyu cattle have a great potential to be used as animal models for adipogenesis studies due to their exceptional IMF deposition (Shirouchi *et al.*, 2014), which in turn affects carcass composition. Comparison of Wagyu animals with other popular beef breeds, such as Angus, provides a distinct basis for observation, as Wagyu presented higher feed efficiency, feed-to-gain ratio, and overall greater IMF deposits (Shirouchi *et al.*, 2014). This can be seen in Figure 1, which shows an immunofluorescent staining comparison of the adipogenic marker FABP4 in Angus and

Wagyu in the *Sternomandibularis* muscle, where the number of preadipocytes and adipocytes in Wagyu was greater than that of Angus cattle. Laboratory identification of distinct differences between Wagyu cattle and any comparable beef breed produces valuable data, which can further identify factors that either increase or inhibit adipogenesis and IMF deposition. Research with tissue and cells from Wagyu animals, can be a model to deep understanding of adipogenesis and lipid metabolism, which might be paralleled by similar studies in tissues and cells from other animal types.

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References

Aguiari P, Leo S, Zavan B, Vindigni V, Rimessi A, Bianchi K, Franzin C, Cortivo R, Rossato M, Vettor R, Abatangelo G, Pozzan T, Pinton P and Rizzuto R 2008. High glucose induces adipogenic differentiation of muscle-derived stem cells. Proceedings of the National Academy of Sciences of the United States of America 105, 1226–1231.

Albrecht E, Gotoh T, Ebara JF, Xu X, Viergutz T, Nurnberg G, Maak S and Wegner J 2011. Cellular conditions for intramuscular fat deposition in Japanese Black and Holstein steers. Meat Science 89, 13–20.

Caserta F, Tchkonia T, Civelek VN, Prentki M, Brown NF, McGarry JD, Forse RA, Corkey BE, Hamilton JA and Kirkland JL 2001. Fat depot origin affects fatty acid handling in cultured rat and human preadipocytes. American Journal of Physiology-Endocrinology and Metabolism 280, E238–E247.

Cristancho AG and Lazar MA 2011. Forming functional fat: a growing understanding of adipocyte differentiation. Nature Reviews Molecular Cell Biology 12, 722–734.

Dodson MV, Hausman GJ, Guan L, Du M, Rasmussen TP, Poulos SP, Mir P, Bergen WG, Fernyhough ME, McFarland DC, Rhoads RP, Soret B, Reecy JM, Velleman SG and Jiang Z 2010a. Lipid metabolism, adipocyte depot physiology and utilization of meat animals as experimental models for metabolic research. International Journal of Biological Sciences 6, 691–699.

Dodson MV, Vierck JL, Hausman GJ, Guan LL, Fernyhough ME, Poulos SP, Mir PS and Jiang Z 2010b. Examination of adipose depot-specific PPAR moieties. Biochemical and Biophysical Research Communications 394, 241–242.

Du M, Huang Y, Das AK, Yang Q, Duarte MS, Dodson MV and Zhu MJ 2013. Meat Science and Muscle Biology Symposium: manipulating mesenchymal progenitor cell differentiation to optimize performance and carcass value of beef cattle. Journal of Animal Science 91, 1419–1427.

Du M, Yin J and Zhu MJ 2010. Cellular signaling pathways regulating the initial stage of adipogenesis and marbling of skeletal muscle. Meat Science 86, 103–109.

Du M and Zhu MJ 2010. Cellular signaling pathways regulating adipogenesis and marbling of skeletal muscle. Meat Science 86, 103–109.

Duarte MS, Gionbelli MP, Paulino PV, Serao NV, Nascimento CS, Botelho ME, Martins TS, Filho SC, Dodson MV, Guimaraes SE and Du M 2014. Maternal overnutrition enhances mRNA expression of adipogenic markers and collagen deposition in skeletal muscle of beef cattle fetuses. Journal of Animal Science 92, 3846–3854.

Duarte MS, Paulino PV, Das AK, Wei S, Serao NV, Fu X, Harris SM, Dodson MV and Du M 2013. Enhancement of adipogenesis and fibrogenesis in skeletal muscle of Wagyu compared with Angus cattle. Journal of Animal Science 91, 2938–2946.

Duarte SF, Francischetti EA, Genelhu VA, Cabello PH and Pimentel MM 2007. LEPR p.Q223R, beta3-AR p.W64R and LEP c.-2548G > A gene variants in obese Brazilian subjects. Genetics and Molecular Research 6, 1035–1043.

Edelman SV 1998. Type II diabetes mellitus. Advances in Internal Medicine 43, 449–500.

Fehrer C and Lepperdinger G 2005. Mesenchymal stem cell aging. Experimental Gerontology 40, 926–930.

Fernyhough ME, Hausman GJ, Guan LL, Okine E, Moore SS and Dodson MV 2008. Mature adipocytes may be a source of stem cells for tissue engineering. Biochemical and Biophysical Research Communications 368, 455–457.

Fernyhough ME, Helterline DL, Vierck JL, Hausman GJ, Hill RA and Dodson MV 2005. Dedifferentiation of mature adipocytes to form adipofibroblasts: more than just a possibility. Adipocytes 1, 17–24.

Fischer J, Koch L, Emmerling C, Vierkotten J, Peters T, Bruning JC and Ruther U 2009. Inactivation of the Fto gene protects from obesity. Nature 458, 894–898.

Fraser JK, Wulur I, Alfonso Z and Hedrick MH 2006. Fat tissue: an underappreciated source of stem cells for biotechnology. Trends in Biotechnology 24, 150–154.

Graugnard DE, Berger LL, Faulkner DB and Loor JJ 2010. High-starch diets induce precocious adipogenic gene network up-regulation in longissimus lumborum of early-weaned Angus cattle. British Journal of Nutrition 103, 953–963.

Harper GS and Pethick DW 2004. How might marbling begin? Australian Journal of Experimental Agriculture 44, 653–662.

Hausman GJ and Dodson MV 2012. Stromal vascular cells and adipogenesis: cells within adipose depots regulate adipogenesis. Journal of Genomics 1, 56–66.

Hausman GJ, Dodson MV, Ajuwon K, Azain M, Barnes KM, Guan LL, Jiang Z, Poulos SP, Sainz RD, Smith S, Spurlock M, Novakofski J, Fernyhough ME and Bergen WG 2009. Board-invited review: the biology and regulation of preadipocytes and adipocytes in meat animals. Journal of Animal Science 87, 1218–1246.

Hocquette JF, Gondret F, Baéza E, Médale F, Jurie C and Pethick DW 2010. Intramuscular fat content in meat-producing animals: development, genetic and nutritional control, and identification of putative markers. Animal 4, 303–319.

Hudson NJ, Reverter A, Greenwood PL, Guo B, Cafe LM and Dalrymple BP 2014. Longitudinal muscle gene expression patterns associated with differential intramuscular fat in cattle. Animal 9, 650–659.

Jordan SD, Kruger M, Willmes DM, Redemann N, Wunderlich FT, Bronneke HS, Merkwirth C, Kashkar H, Olkkonen VM, Bottger T, Braun T, Seibler J and Bruning JC 2011. Obesity-induced overexpression of miRNA-143 inhibits insulin-stimulated AKT activation and impairs glucose metabolism. Nature Cell Biology 13, 434–446.

Kokta TA, Dodson MV, Gertler A and Hill RA 2004. Intercellular signaling between adipose tissue and muscle tissue. Domestic Animal Endocrinology 27, 303–331.

Komolka K, Albrecht E, Wimmers K, Michal JJ and Maak S 2014. Molecular heterogeneities of adipose depots-potential effects on adipose-muscle cross-talk in humans, mice and farm animals. Journal of Genomics 2, 31–44.

Kook SH, Choi KC, Son YO, Lee KY, Hwang IH, Lee HJ, Chang JS, Choi IH and Lee JC 2006. Satellite cells isolated from adult Hanwoo muscle can proliferate and differentiate into myoblasts and adipose-like cells. Molecules and Cells 22, 239–245.

Lee EJ, Lee HJ, Kamli MR, Pokharel S, Bhat AR, Lee YH, Choi BH, Chun T, Kang SW, Lee YS, Kim JW, Schnabel RD, Taylor JF and Choi I 2012. Depot-specific gene expression profiles during differentiation and transdifferentiation of bovine muscle satellite cells, and differentiation of preadipocytes. Genomics 100, 195–202.

Lehnert SA, Wang YH, Tan SH and Reverter A 2006. Gene expression-based approaches to beef quality research. Animal Production Science 46, 165–172.

Majka SM, Barak Y and Klemm DJ 2011. Concise review: adipocyte origins: weighing the possibilities. Stem Cells 29, 1034–1040.

May SG, Savell JW, Lunt DK, Wilson JJ, Laurenz JC and Smith SB 1994. Evidence for preadipocyte proliferation during culture of subcutaneous and intramuscular adipose tissues from Angus and Wagyu crossbred steers. Journal of Animal Science 72, 3110–3117.

Muthuraman P 2014. Effect of coculturing on the myogenic and adipogenic marker gene expression. Applied Biochemistry and Biotechnology 173, 571–578.

Oikawa T, Sanehira T, Sato K, Mizoguchi Y, Yamamoto H and Baba M 2000. Genetic parameters for grouth and carcass traits of Japanese Black (Wagyu) cattle. Journal of Animal Science 71, 59–64.

Pena F, Molina A, Aviles C, Juarez M and Horcada A 2013. Marbling in the longissimus thoracis muscle from lean cattle breeds. Computer image analysis of fresh versus stained meat samples. Meat Science 95, 512–519.

Penton CM, Thomas-Ahner JM, Johnson EK, McAllister C and Montanaro F 2013. Muscle side population cells from dystrophic or injured muscle adopt a fibro-adipogenic fate. PLoS One 8, e54553.

Pethick DW, Barendse W, Hocquette JF, Thompson JM and Wang YH 2007. Regulation of marbling and body composition-growth and development, gene markers and nutritional biochemistry. In Energy and protein metabolism and nutrition (ed. I Ortigues-Marty, N Miraux and W Brand-Williams), pp. 75–88. Wageningen Academic Publishers, Wageningen, The Netherlands.

Pethick DW, D'Souza DN, Dunshea FR and Harper GS 2005. Fat metabolism and regional distribution in ruminants and pigs – influences of genetics and nutrition. Recent Advances in Animal Nutrition in Australia 15, 39–45.

Pethick DW, Harper GS and Oddy VH 2004. Growth, development and nutritional manipulation of marbling in cattle: a review. Australian Journal of Experimental Agriculture 44, 705–715.

Reecy JM, Miller SA and Webster M 2003. Recent advances that impact skeletal muscle growth and development research. Journal of Animal Scence 81, E1–E8.

Romao JM, Jin W, Dodson MV, Hausman GJ, Moore SS and Guan LL 2011. MicroRNA regulation in mammalian adipogenesis. Experimental Biology and Medicine. 236, 997–1004.

Ryan KJ, Daniel ZC, Craggs LJ, Parr T and Brameld JM 2013. Dose-dependent effects of vitamin D on transdifferentiation of skeletal muscle cells to adipose cells. Journal of Endocrinology 217, 45–58.

Sadkowski T, Ciecierska A, Majewska A, Oprzadek J, Dasiewicz K, Ollik M, Wicik Z and Motyl T 2014. Transcriptional background of beef marbling-novel genes implicated in intramuscular fat deposition. Meat Science 97, 32–41.

Sainz RD and Hasting E 2000. Simulation of the development of adipose tissue in beef cattle. In Modelling nutrient utilization in farm animals (ed. JP McNamara, J France and DE Beever), pp. 175–182. Cabi, New York, NY, USA.

Scraggs E, Zanella R, Wojtowicz A, Taylor JF, Gaskins CT, Reeves JJ, de Avila JM and Neibergs HL 2014. Estimation of inbreeding and effective population size of full-blood Wagyu cattle registered with the American Wagyu Cattle Association. Journal of Animal Breeding and Genetics 131, 3–10.

Shirouchi B, Albrecht E, Nuernberg G, Maak S, Olavanh S, Nakamura Y, Sato M, Gotoh T and Nuernberg K 2014. Fatty acid profiles and adipogenic gene expression of various fat depots in Japanese Black and Holstein steers. Meat Science 96, 157–164.

Singh NK, Chae HS, Hwang IH, Yoo YM, Ahn CN, Lee SH, Lee HJ, Park HJ and Chung HY 2007. Transdifferentiation of porcine satellite cells to adipoblasts with ciglitizone. Journal of Animal Science 85, 1126–1135.

Sul HS 2009. Minireview: Pref-1: role in adipogenesis and mesenchymal cell fate. Molecular Endocrinology 23, 1717–1725.

Taylor-Jones JM, McGehee RE, Rando TA, Lecka-Czernik B, Lipschitz DA and Peterson CA 2002. Activation of an adipogenic program in adult myoblasts with age. Mechanisms of Ageing and Development 123, 649–661.

Teboul L, Gaillard D, Staccini L, Inadera H, Amri EZ and Grimaldi PA 1995. Thiazolidinediones and fatty acids convert myogenic cells into adipose-like cells. Journal of Biological Chemistry 270, 28183–28187.

Wang YH, Bower NI, Reverter A, Tan SH, De Jager N, Wang R, McWilliam SM, Cafe LM, Greenwood PL and Lehnert SA 2009. Gene expression patterns during intramuscular fat development in cattle. Journal of Animal Science 87, 119–130.

Wang YH, Byrne KA, Reverter A, Harper GS, Taniguchi M, McWilliam SM, Mannen H, Oyama K and Lehnert SA 2005. Transcriptional profiling of skeletal muscle tissue from two breeds of cattle. Mammalian Genome 16, 201–210.

Wei S, Fu X, Liang X, Zhu M, Jiang Z, Parish SM, Dodson MV, Zan L and Du M 2015. Enhanced mitogenesis in stromal vascular cells derived from subcutaneous adipose tissue of Wagyu compared with those of Angus cattle. Journal of Animal Science 93, 1015–1024.

Wertz AE, Berger LL, Walker PM, Faulkner DB, McKeith FK and Rodriguez-Zas SL 2002. Early-weaning and postweaning nutritional management affect feedlot performance, carcass merit, and the relationship of 12th-rib fat, marbling score, and feed efficiency among Angus and Wagyu heifers. Journal of Animal Science 80, 28–37.

Yamada T, Higuchi M and Nakanishi N 2014. Fat depot-specific differences in pref-1 gene expression and adipocyte cellularity between Wagyu and Holstein cattle. Biochemical and Biophysical Research Communications 445, 310–313.

Yamada T, Kawakami SI and Nakanishi N 2007. Effects of fattening periods on the expression of adipogenic transcription factors in Wagyu beef cattle. Meat Science 76, 289–294.

Yamada T, Kawakami SI and Nakanishi N 2009. Expression of adipogenic transcription factors in adipose tissue of fattening Wagyu and Holstein steers. Meat Science 81, 86–92.

Yang A, Larsen TW, Powell VH and Tume RK 1999. A comparison of fat composition of Japanese and long-term grain-fed Australian steers. Meat Science 51, 1–9.

Zuk PA, Zhu M, Ashjian P, De Ugarte DA, Huang JI, Mizuno H, Alfonso ZC, Fraser JK, Benhaim P and Hedrick MH 2002. Human adipose tissue is a source of multipotent stem cells. Molecular Biology of the Cell 13, 4279–4295.