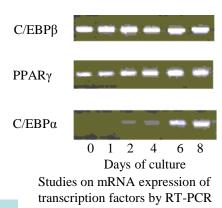
# NUTRITION FOR HIGH QUALITY BEEF PRODUCTION

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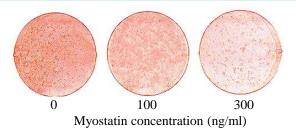
Beef marbling consists of a large amount of fat deposited in the skeletal muscle. High marbling is the distinct characteristic of beef in Japan and is preferred by Japanese consumers. Intramuscular adipogenesis is induced by feeding high-energy diets for long periods. Adipogenesis results from adipocyte differentiation. Therefore, intramuscular adipocyte differentiation significantly affects the formation of beef marbling. However, its regulating mechanisms have not been clarified. We are making studies on the mechanisms of intramuscular adipocyte differentiation and nutritional manipulation of adipocyte differentiation.

## Bovine preadipocytes derived from adipose tissue

Preadipocyte cell lines sequentially express several transcription factors such as C/EBPs and PPAR $\gamma$  after induction of differentiation and these factors act cooperatively in this process. The adipose tissue—derived bovine preadipocytes, however, express C/EBP $\beta$  and PPAR $\gamma$  before induction of differentiation. The bovine preadipocytes reach more advanced stage of differentiation than preadipocyte cell lines.



# **Bovine adipocyte differentiation and paracrine factors**



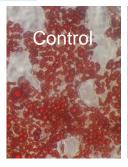
The red color shows accumulated fat.

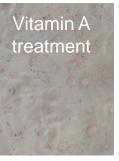
Myostatin suppressed adipocyte differentiation.

Members of the TGF- $\beta$  family potently regulate cell growth and differentiation in a cell type-dependent manner. Myostatin and activin, members of the TGF- $\beta$  family inhibited differentiation of preadipocytes, whereas BMP, another member of the TGF- $\beta$  family, stimulated the differentiation. Currently, the mechanism on regulation of adipocyte differentiation by the TGF- $\beta$  family is explored.

# Nutritional manipulation of adipocyte differentiation

Japanese farmers give their beef cattle a vitamin A-deficient feed to improve beef marbling. This resulted in an increased incidence of blindness and muscular edema in the beef cattle. We found that vitamin A suppressed bovine adipocyte differentiation, and developed a new feeding strategy for improving beef marbling without the induction of vitamin A-deficient syndrome, i.e., feeding a low-vitamin A diet just during the early fattening period when the number of adipocytes increases in the muscle. Furthermore, we clarified that vitamin C and zinc stimulated bovine adipocyte differentiation. Now, we are trying to find other substances affecting adipocyte differentiation.





The red color shows fat droplets.

Vitamin A suppressed adipocyte differentiation.

## **Keywords**

Beef cattle, Fattening, Beef marbling, Cell culture, Adipocyte differentiation, Vitamin, Mineral, Paracrine factor, Muscle, Animal nutrition, Molecular biology

### **Recent Publications**

#### 2012

**Regulatory responses to excess zinc ingestion in growing rats.** Fujimura T, Matsui T, Funaba M. British Journal of Nutrition in press.

Mg and Ca deficiencies additively increase the Zn concentrations and metallothionein expression in the rat liver. Kotani M, Kim H-K, Ishizaki N, Funaba M, Matsui T. British Journal of Nutrition in press.

Magnesium absorption from mineral water decreases with increasing quantities of magnesium per serving in rats. Nakamura E, Tai H, Uozumi Y, Nakagawa K, Matsui T. (2012) Nutrition Research 32(1):59-65.

The in vitro digestibility and absorption of magnesium in some edible seaweeds. Nakamura E, Yokota H, Matsui T. Journal of the Science of Food and Agriculture in press.

Microphthalmia-associated transcription factor is required for mature myotube formation. Ooishi R, Shirai M, Funaba M, Murakami M. (2012) Biochimica et Biophysica Acta 1820(2):76-83.

#### 2011

Magnesium deficiency up-regulates Myodexpression in rat skeletal muscle and C2C12 myogenic cells. Furutani Y, Matsui T, Funaba M. (2011) Cellular Biochemistry and Function 29(7):577-581.

Role of endogenous TGF-β family in myogenic differentiation of C2C12 cells. Furutani Y, Umemoto T, Murakami M, Matsui T, Funaba M. (2011) Journal of Cellular Biochemistry 112(2):614-624.

**Activin in glucose metabolism.** Hashimoto O, Funaba M. (2011) Vitamins and Hormones 85:217-234.

**Hepcidin expression in the liver of rats fed a magnesium-deficient diet.** Ishizaki N, Kotani M, Funaba M, Matsui T. British Journal of Nutrition 106(8):1169-1172.

Effect of magnesium deficiency on various mineral concentrations in rat liver. Kim KH, Ishizaki N, Iguchi E, Funaba M, Matsui T. Biological Trace Element Research 144(1-3):865-871.

**Activin in humoral immune responses.** Ogawa K, Funaba M. (2011) Vitamins and Hormones 85:235-253.

The effects of TGF-β1 on the expression of type IV collagenases in mouse peritoneal macrophages. Ogawa K, Funaba M, Tsujimoto M. (2011) Molecular Biology Reports 38(2):1451-1456.

Plasma vitamin K concentration in horses supplemented with several vitamin K homologues. Terachi T, Inoue Y, Ashihara N, Kobayashi M, Ando K, Matsui T. Journal of Animal Science 89(4):1056-1061.

Endogenous Bmp4 in myoblasts is required for myotube formation in C2C12 cells. Umemoto T, Furutani Y, Murakami M, Matsui T, Funaba M. (2011) Biochimica et Biophysica Acta 1810(12):1127-1135.

#### 2010

Determination of true absorption and fecal endogenous loss of zinc in goats. Hattori R, Torii S, Funaba M, Matsui T. (2010) Animal Science Journal 81(5):564-568. Regulatory expression of genes related to metastasis by TGF-β and activin A in

Regulatory expression of genes related to metastasis by 1GF-β and activin A in B16 murine melanoma cells. Murakami M, Suzuki M, Nishino Y, Funaba M. (2010) Molecular Biology Reports. 37(3):1279-1286.

**BMP** Inhibition with dorsomorphin limits adipogenic potential of preadipocytes. Suenaga M, Matsui T, Funaba M. (2010) Journal of Veterinary Medical Science 72(3):373-377.

**Nucleotide sequence of canine Smad3.** Sugiyama K, Ooishi R, Nishino Y, Funaba M, Murakami M. (2010) Biochemical Genetics 48(3-4):202-207.

#### 2009

Iron supplementation by intraperitoneal injection eliminates the accumulation of hepatic copper induced by excess calcium in rats. Takasugi S, Matsui T, Yano H. (2009) British Journal of Nutrition 102(2):258-263.

Brewer's yeast efficiently degrades phytate phosphorus in a corn-soybean meal diet during soaking treatment. Chu GM, Ohmori H, Kawashima T, Funaba M, Matsui T. (2009) Animal Science Journal 80(4):433-437.

Investigation for activators of adipocyte differentiation in feed for beef cattle. Kawachi H, Maruakma S, Kamei Y, Kawada T, Matsui T. (2009) Trace Nutrient Research 26:65-69.

Receptor expression modulates the specificity of transforming growth factor-β signaling pathways. Murakami M, Kawachi H, Ogawa K, Nishino Y, Funaba M. (2009) Genes to Cells 14(4):469-482.

Regulation of melanin synthesis by the TGF-β family in B16 melanoma cells. Murakami M, Matsuzaki F, Funaba M. (2009) Molecular Biology Reports. 36(6):1247-1250.

Differential responses to oxidative stress and calcium influx on expression of the transforming growth factor-β family in myoblasts and myotubes. Furutani Y, Murakami M, Funaba M. (2009) Cellular Biochemistry and Function 27(8):578-582. Gene expression of the TGF-β family in rat brain infected with Borna disease virus. Nishino Y, Ooishi R, Kurokawa S, Fujino K, Murakami M, Madarame H, Hashimoto O, Sugiyama K, Funaba M. (2009) Microbes and Infections 11(8-9):737-743. Changes in Borna disease virus genome with adaptation to host. Okayama S, Miura N, Murakami M, Funaba M, Nishino Y. (2009) Microbes and Infections 11(6-7):721-724.

A JNK inhibitor SP600125 induces defective cytokinesis and enlargement in P19 embryonal carcinoma cells. Nakaya K, Ooishi R, Funaba M, Murakami M. (2009) Cellular Biochemistry and Function 27(7):468-472.

#### 2008

Efficacy of a genetically modified yeast phytase on phosphorus bioavailability in a corn-soybean meal based diet for growing pigs. Chu GM, Komori M, Nakayama A, Asanagi M, Yano H, Matsui T. (2008). Animal Science Journal 79(4):466-471. Dietary phytase increases the true absorption and endogenous fecal excretion of zinc in growing pigs given a corn-soybean meal based diet. Chu GM, Komori M, Hattori R, Matsui T. (2008). Animal Science Journal 80(1):46-51.

Magnesium supplementation did not affect the increasing bone zinc concentration in rats given excess calcium as carbonate. Ohata A, Takasugi S, Matsui T. (2008). Biological Trace Element Research 125(2):179-184.

Restraint stress up-regulates expression of zinc transporter Zip14 mRNA in mouse liver. Ohashi T, Matsui T, Chujo M, Nagao M. (2008). Cytotechnology, 57:181-185.

Regulatory expression of Brachyury and Goosecoid in P19 embryonal carcinoma cells. Nakaya K, Murakami M, Funaba M. (2008) Journal of Cellular Biochemistry 105(3): 801-813.

Response of biochemical markers of bone metabolism to exercise intensity in Thoroughbred horses. Inoue Y, Matsui A, Asai Y, Aoki F, Yoshimoto K, Matsui T, Yano H. (2008) Journal of Equine Science 19(4): 83-89.

Iron supplementation by intraperitoneal injection eliminates the accumulation of hepatic copper induced by excess calcium in rats. Takasugi S, Matsui T, Yano H. (2008) British Journal of Nutrition 13(1):1-6.

Cellular regulation of bovine intramuscular adipose tissue development and composition. Smith SB, H Kawachi, CB Choi, CW Choi, G Wu, and JE Sawyer. (2008) Journal of Animal Science 87:E72-E82.

#### 2007

The effect of vitamin C supplementation on plasma concentration and urinary excretion of vitamin C in cattle. Padilla L, Matsui T, Ikeda S, Kitagawa M, Yano H. (2007). Journal of Animal Science 85(12):3367-3370.

Magnesium deficiency stimulated mRNA expression of tumor necrosis factor-α in skeletal muscle of rats. Matsui T, Kobayashi H, Hirai S, Kawachi H, Yano H. (2007). Nutrition Research 27(1):66-68.

Lipogenesisand stearoyl-CoAdesaturasegene expression and enzyme activity in adipose tissue of short-and long-fed Angus and Wagyusteers fed corn-or hay-based diets. Chung KY, Lunt DK, Kawachi H, Yano H, Smith SB. (2007). Journal of Animal Science 85(2):380-387.

Excess calcium Increases bone zinc concentration without affecting zinc absorption in rats. Takasugi S, Matsui T, Ohmori H, Yano H. (2007). Biological Trace Element Research 166(3):311-320.

Nitric oxide suppresses preadipocytedifferentiation in 3T3-L1 culture. Kawachi H, Moriya N, Korai T, Tanaka S-y, Watanabe M, Matsui T, Kawada T, Yano H. (2007). Molecular Cellular Biochemistry 300(1-2):61-67.

Molecular cloning and expression of bovine (BosTaurus) leptin receptor isoform mRNAs. Kawachi H, Yang SH, Hamano A, Matsui T, Smith SB, Yano H. (2007). Comparative Biochemistry and Physiology 148(2):167-173.

Relationship between plasma vitamin C and serum diagnostic biochemical markers in lactating cows. Padilla L, Matsui T, ShibanoK-i, KatamotoH, Yano H. (2007). Journal of Veterinary Medical Science 69(9):909-913.

**Myostatin inhibits differentiation of bovine preadipocyte.** Hirai S, Matsumoto H, Hino N, Kawachi H, Matsui T, Yano H. (2007). Domestic Animal Endocrinology 32(1):1-14.

Urinary excretion of purine derivatives and plasma allantoin level in sheep and goats during fasting. Fujihara T, Shem MN, Matsui T. (2007). Animal Science Journal 78(2): 129-134.

#### 2006

Changes in serum biochemical markers of bone cell activity in growing Thoroughbred horses. Inoue Y, Asai Y, Ohmori H, Fujii H, Matsui T, Yano H. (2006). Asian-Australasian Journal of Animal Science 19(11):1632-1637.

Heat stress decreases plasma vitamin C concentration in lactating cows. Padilla L, Matsui T, Kamiya Y, Kamiya M, Tanaka M, Yano H. (2006). Livestock Science 101(1-3): 300-304.

The effect of exogenous purine supply on the endogenous excretion of purine derivatives in the urine of growing lambs. Fujihara T, Shem MN, Matsui T. (2006). Animal Science Journal. 77(6): 582-586.

#### 2005

Plasma vitamin C concentration is not related to the incidence of ketosis in dairy cows during the early lactation period. Padilla L, Shibano K, Inoue J, Matsui T, Yano H. (2005). Journal of Veterinary Medical Science 67(9): 883-886.

Activin A inhibits differentiation of 3T3-L1 preadipocyte. Hirai S, Yamanaka M, Kawachi H, Matsui T, Yano H. (2005). Molecular and Cellular Endocrinology 232(1-2): 21-26.

**Effect of exercise on iron metabolism in horses.** Inoue Y, Matsui A, Asai Y, Aoki F, Matsui T, Yano H. (2005). Biological Trace Element Research 107(1): 33-42.

#### 2004

Red yeast rice extracts suppress adipogenesis by down-regulating adipogenic transcription factors and gene expression in 3T3-L1 cells. Jeon T, Hwang SG, Hirai S, Matsui T, Yano H, Kawada T, Lim BO, Park DK (2004). Life Sciences 75(26): 3195-3203.

PCR detection of bovine mitochondrial DNA derived from meat and bone meal in feed. Toyoda A, Nakajo M, Kawachi H, Matsui T, Yano H (2004). Journal of Food Protection. 67(12): 2829–2832.

Effects of protein deficiency on the mRNA levels of insulin-like growth factors and myostatin in skeletal muscle of weaned lambs. Hirai S, Kawachi H, Matsui T, Yano H (2004). Animal Science Journal. 75(3): 207-212.

**Expression of agouti gene in bovine adipocytes.** Sumida T, Hino N, Kawachi H, Matsui T, Yano H (2004). Animal Science Journal 75 (1):49-51.