

ABSTRACT

Significant associations of the mitochondrial transcription factor A promoter polymorphisms with marbling and subcutaneous fat depth in Wagyu x Limousin F2 crosses

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Mitochondrial transcription factor A (TFAM), a nucleus-encoded protein, regulates the initiation of transcription and replication of mitochondrial DNA (mtDNA). Decreased expression of nuclear-encoded mitochondrial genes has been associated with onset of obesity in mice. Therefore, we hypothesized genetic variants in TFAM gene influence mitochondrial biogenesis consequently affecting body fat deposition and energy metabolism. In the present study, both cDNA (2259 bp) and genomic DNA (16,666 bp) sequences were generated for the bovine TFAM gene using a combination of in silico cloning with targeted region PCR amplification. Alignment of both cDNA and genomic sequences led to the determination of genomic organization and characterization of the promoter region of the bovine TFAM gene. Two closely linked A/C and C/T single nucleotide polymorphisms (SNPs) were found in the bovine TFAM promoter and then genotyped on 237 Wagyu x Limousin F(2) animals with recorded phenotypes for marbling and subcutaneous fat depth (SFD). Statistical analysis demonstrated that both SNPs and their haplotypes were associated with marbling ($P=0.0153$ for A/C, $P=0.0026$ for C/T, and $P=0.0004$ for haplotype) and SFD ($P=0.0200$ for A/C, $P=0.0039$ for C/T, and $P=0.0029$ for haplotype), respectively. A search for transcriptional regulatory elements using MatInspector indicated that both SNPs lead to a gain/loss of six putative-binding sites for transcription factors relevant to fat deposition and energy metabolism. Our results suggest for the first time that TFAM gene plays an important role in lipid metabolism and may be a strong candidate gene for obesity in mammals.

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