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# Epistatic effect between *ACACA* and *FABP2* gene on abdominal fat traits in broilers

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**Abstract**

Epistasis is generally defined as the interaction between two or more genes or their mRNA or protein products to influence a single trait. Experimental evidence suggested that epistasis could be important in the determination of the genetic architecture of complex traits in domestic animals. Acetyl-coenzyme A carboxylase alpha (ACACA) and fatty acid binding protein 2 (FABP2) are both key factors of lipogenesis and transport. They may play a crucial role in the weight variability of abdominal adipose tissue in the growing chicken. In this study, the polymorphisms of c.2292G>A in *ACACA* and c.-561A>C in *FABP2* were detected among individuals from two broiler lines which were divergently selected for abdominal fat content. Epistasis between the two SNPs on abdominal fat weight (AFW) and abdominal fat percentage (AFP) was analyzed. The additive × additive epistatic components between these two SNPs were found significant or suggestively significant on both AFW and AFP in lean lines of the 9th and 10th generation; whereas, it was not significantly associated with either AFW or AFP in fat lines. At the same time, there were not any other significant epistatic components found in both generations or in both lines. Significant epistatic effects between these two SNPs found only in the lean lines could partly be due to the fact that the abdominal fat traits in these two experimental lines have been greatly modified by strong artificial selection. The results suggested that the epistasis mode may be different between the lean and fat chicken lines. Our results could be helpful in further understanding the genetic interaction between candidate genes contributing to phenotypic variation of abdominal fat content in broilers.

*Keywords*: chicken; fatness; epistasis; *ACACA*; *FABP2*; QTL

## Introduction

Fatness is an important growth trait in chickens, and a large part, about 15%–20% of the broiler body weight is fat, most of which is deposited in adipose tissue (Griffin, 1996; Havenstein et al., 2003). A good understanding in the genetic control of fat deposition in chickens will be a key to genetic enhancement in chicken production performance. Although several selection strategies for leanness in poultry production have been described, it is still laborious and expensive to measure fat deposition (Mallard and Douaire, 1988; Jennen et al., 2004). Molecular marker-assisted selection (MAS) may be required to increase selection efficiency and make further improvements in production performance (Abasht et al., 2006).

Epistasis is generally defined as the interaction between two or more genes or their mRNA or protein products to influence a single trait (Warden et al., 2004). Although a lot of QTLs and SNPs in candidate genes affecting fatness traits in chickens have been identified through various

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methods in previous studies (Abasht et al., 2006, 2007; Koning and Hocking, 2007), it is still unclear how the epistatic interactions contribute to phenotypic variation of fatness traits. Recently, some experimental evidence suggested that epistasis could be important in the determination of the genetic architecture of complex traits (Carlborg et al., 2003, 2006; Estellé et al., 2008). Whole genome QTL analysis is an effective approach in seeking the QTL affecting fatness traits in chickens (Abasht et al., 2006; Lagarrigue et al., 2006; Liu et al., 2007; Le Mignon et al., 2009). However, whole genome QTL analysis accounting for epistasis is not yet widespread due to its high experimental cost. The candidate gene approach may be a good but less costly alternative in epistasis analysis.

Acetyl-coenzyme A carboxylase alpha (ACACA) and fatty acid binding protein 2 (FABP2) are both key factors of lipogenesis and transport (Takai et al., 1988; Hillgartner et al., 1996; Wang et al., 2005). They may play a crucial role in the weight variability of abdominal adipose tissue in the growing chicken. ACACA catalyses the first committed step in the biosynthesis of long-chain fatty acids (FA) by converting acetyl-CoA into malonyl-CoA (Abu-Elheiga et al., 2005; Tong, 2005). Chicken *ACACA* gene, located in chromosome 19, has the similar function as that in mammals (Takai et al., 1988; Hillgartner et al., 1996). A synonymous mutation c.2292G>A was found on exon 19 in this gene in our previous work, which is associated with abdominal fat trait in chicken (Tian et al., 2010). Chicken *FABP2* gene, located in chromosome 4, may function physiologically as a lipid-sensing component of energy homeostasis but no direct role of dietary fatty acid absorption has been suggested (Wang et al., 2005). The pattern of *FABP2* expression and consensus structure strongly suggest functional conservation of the *FABP2* genes between mammals and chicken, which allow *FABP2* gene to be assessed as a candidate gene in chicken QTL detection programs focusing on phenotypes related to lipid metabolism (Wang et al., 2005). A single nucleotide polymorphism c.-561A>C was identified in the 5′ UTR region of *FABP2* gene, 516 bp upstream the initiation site of *FABP2* in our previous work, which is associated with abdominal fat trait in chicken, too (Chu et al., 2008).

The primary objective of the present study was, by carrying out a pairwise epistasis analysis, to estimate the epistatic effects between SNPs in *ACACA* and *FABP2* gene for abdominal fat weight (AFW) and abdominal fat percent (AFP) in the 9th and 10th generation populations from the Northeast Agricultural University broiler lines divergently selected for abdominal fat content (NEAUHLF), which could be helpful in further understanding the genetic interaction between candidate genes.

## Materials and methods

### *Experimental populations*

The NEAUHLF has been selected since 1996 using AFP and plasma very low-density lipoprotein (VLDL) concentration as selection criteria. Abdominal fat traits of the NEAUHLF were recorded at the age of seven weeks. These measurements included body weight (BW) and AFW. AFP was calculated as AFW/BW × 100% at the age of seven weeks. The details of these populations and phenotype measurements were described in Zhang et al. (2008). The genomic DNA was isolated from venous blood samples using a phenol-chloroform method. A total of 958 male birds in the 9th and 10th generation populations in both lines of NEAUHLF were used.

### *Polymorphism analysis*

PCR primers to amplify the *ACACA* exon19 region (5′-TAGGTGGATGGTTGGGCTTGA-3′; 5′-CCCCATCC TCCACCACATG-3′) were designed to amplify a 186 bp fragment by Primer 5.0 (PREMIER Biosoft International, USA) according to chicken genomic DNA sequence in the GenBank database (accession No. NM_205505) and the UCSC Genome Bioinformatics site (http://genome.ucsc.edu). The PCR reaction conditions were 94°C for 7 min, followed by 33 cycles of 94°C for 30 s, 56°C for 30 s, 72°C for 30 s, and an extension at 72°C for 7 min. A synonymous mutation c.2292G>A was found in this fragment. Individuals were genotyped with the following PCR-RFLP method. The PCR product (0.8 μL) was digested using 0.8 U endonuclease-*Mwo* I (TaKaRa Biotechnology Co. Ltd, Dalian, China) at 37°C overnight, then genotyped by electrophoresis.

PCR primers to amplify the 5′ UTR region of *FABP2* gene (5′-ACTTAGCAGCACATCAAC-3′; 5′-CAGTCAC TAACCCATTCAT-3′) were also designed according to chicken genomic DNA sequence in the GenBank database (accession No. AY254202) and the UCSC Genome Bioin-