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The *GGT1* and *IGFBP5* genes are associated with fat deposition traits in the pig (Brief Report)

Die Gene *GGT1* und *IGFBP5* stehen im Zusammenhang mit der Fettablagerung beim Schwein (Brief Report)

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Background

In the earlier comparative linkage mapping of bone-related genes in the pig, the *Gamma glutamyl transferase 1* (*GGT1*) gene was assigned between *SWC6* and *SWR84* on SSC14, and *Insulin-like growth factor binding protein 5* (*IGFBP5*) gene was mapped between *SW120* and *SW936* on SSC15 (ONTERU *et al.* 2008). QTL related to average backfat and 10th rib backfat traits had been reported around these regions (http://www.animalgenome.org/cgi-bin/QTLdb, ROHRER *et al.* 1998, DE KONING *et al.* 2001, MALEK *et al.* 2001). Both genes did not have association with any of body conformation, feet and leg structure traits (FAN *et al.* 2009), but it is worth exploring whether they are associated with fatness. Here we carried out association analyses of the identified SNPs from the genes in two pig populations and investigated the possible effect of them on fat deposition traits.

Procedures

The SNPs c.884-228C>G (dbSNP acc. no. ss86352433) within *GGT1* intron 11 and c.567+79A>C (dbSNP acc. no. ss86352413) within *IGFBP5* intron 2 were detected in the previous study (FAN *et al.* 2009). SNP genotyping was implemented in two different pig populations using a high throughout MassARRAY system (Sequenom Inc, San Diego, CA, USA). Population A consisted of 2 066 commercial sows from Newsham Choice Genetics. The 10th rib and last rib backfat thickness were measured using an ultrasonic imaging approach with a Pie Medical 200 (Classic Medical Supply Inc., Tequesta, FL, USA). The association analyses between the SNPs and traits were performed using the MIXED procedure (SAS 9.0, SAS Institute, Cary, NC, USA), with a statistical model treating genetic line, measurement date and marker genotype as fixed effects, sire as a random effect and body weight as a covariate. Population B, the ISU Berkshire × Yorkshire (B×Y) pig resource family is comprised of 11 F_0, 35 F_1 and 515 F_2 animals. The measurements of four backfat traits including average backfat, backfat at 10th rib, lumbar and last rib points were described by MALEK *et al.* (2001). The association analyses were performed using the MIXED model procedure, including sex, slaughter date and marker genotypes as fixed effects, dam (litter) as a random effect and body weight as a covariate.

Results

The analyzed SNPs showed a high level of polymorphism in both pig populations and had minor allele frequency greater than 0.05. In population A, *GGT1* c.884-228C>G was significantly ($P<0.05$) associated with 10th rib backfat while it was not associated with last rib backfat (Table 1). In the B×Y pig family, c.884-228C>G was very highly significantly ($P<0.001$) associated with all of the four different backfat traits. The allele C was favorably associated with leanness in population A and similarly it was associated with less fatness in the B×Y pig family. *IGFBP5* c.567+79A>C was significantly associated ($P<0.05$) with last rib backfat and suggestively significantly associated ($P<0.1$) with 10th rib backfat in population A. In the B×Y pig family, c.567+79A>C was very highly significantly ($P<0.001$) associated with 10th rib backfat and significantly ($P<0.05$) associated with average backfat, but it was not associated with both lumbar backfat and last rib backfat traits. The allele A was desirable as it was associated with leanness in both populations.

Table 1
Association of the SNPs within *GGT1* and *IGFBP5* genes with backfat traits in two pig populations, respectively

Assoziation der SNPs der Gene GGT1 und IGFBP5 mit der Rückenfettdicke in zwei Schweinepopulationen

Marker	Pop	SSize	Trait	Least Squares Means (SE), cm			P-value
				11	12	22	
GGT1 c.884-228C>G	A	2 066	10th rib backfat	1.39 (0.01)^{a}	1.42 (0.01)^{b}	1.45 (0.02)^{b}	0.02
			Last rib backfat	1.27 (0.01)	1.27 (0.01)	1.29 (0.02)	0.32
	B	515	Average backfat	3.04 (0.06)^{a}	3.31 (0.05)^{b}	3.52 (0.07)^{c}	<0.0001
			10th rib backfat	2.87 (0.07)^{a}	3.14 (0.06)^{b}	3.38 (0.08)	<0.0001
			Lumbar backfat	3.31 (0.08)^{a}	3.58 (0.06)^{b}	3.82 (0.09)^{c}	<0.0001
			Last rib backfat	2.95 (0.06)^{a}	3.18 (0.05)^{b}	3.33 (0.07)^{c}	<0.0001
IGFBP5 c.567+79A>C	A	2 066	10th rib backfat	1.32 (0.06)	1.39 (0.01)	1.42 (0.01)	0.09
			Last rib backfat	1.17 (0.05)^{a}	1.25 (0.01)^{ab}	1.28 (0.01)^{b}	0.03
	B	515	Average backfat	3.26 (0.06)^{a}	3.24 (0.05)^{a}	3.42 (0.07)^{b}	0.02
			10th rib backfat	3.10 (0.07)^{a}	3.06 (0.06)^{a}	3.35 (0.08)^{b}	0.0003
			Lumbar backfat	3.52 (0.07)	3.53 (0.06)	3.67 (0.08)	0.13
			Last rib backfat	3.16 (0.05)^{ab}	3.12 (0.05)^{a}	3.24 (0.07)^{b}	0.14

Pop Population, SSize Sample size, ^{a,b,c}Different superscripts in the same row indicate significant differences between means ($P<0.05$). For SNP GGT1 c.884-228C>G, 1 represents allele C and 2, represents G; for SNP IGFBP5 c.567+79A>C, 1 represents allele A and 2, represents C.

GGT1 is one of potential markers for bone resorption and acts as a pathological bone resorbing factor by stimulating RANK ligand (ASABA *et al.* 2006). Most recently, a genome-wide association study in humans revealed that intronic SNPs within the *GGT1* and *HNF1A* genes were associated with gamma-glutamyl transferase level, which is usually used as indicator of biliary or cholestatic diseases and heavy alcohol consumption (YUAN *et al.* 2008). The genes *GGT1* and *HNF1A* are located on human chromosomes 22q$^{11.23}$ and 12q$^{24.31}$, respectively, but their corresponding porcine genes were mapped between *SWC6* and *SWR84* on SSC14. The *HNF1A* (also known as *TCF1*) gene was associated with the type III form of maturity-onset diabetes of the young people (MODY3) in humans (ELLARD 2000). It is speculated that either the *GGT1* gene has an independent effect on adipose tissue development and deposition, or the possible linkage disequilibrium between these two genes resulted in association of the *GGT1* gene with backfat.

IGFBP5 is one of the members of the insulin-like growth factor binding proteins (IGFBPs) family, and it is primarily expressed in bone tissue and helps to potentiate the action of IGFI on smooth muscle cells, fibroblasts or osteoblasts. The *IGFBP5* gene might be involved in intramuscular fat development in the cattle (WANG *et al.* 2009), and was also associated with serum adiponectin concentrations in humans, which play a crucial role in the modulation of glucose metabolism in insulin-sensitive tissues such as adipose tissue (KALLIO *et al.* 2009). The results from this study suggested that the *IGFBP5* gene is associated with fat deposition in pigs. Further work on causative mutation discovery and function analysis of the *GGT1* and *IGFBP5* genes are needed before they can be recommended for marker assisted selection.

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