Journal of Animal and Veterinary Advances 11 (19): 3499-3505, 2012
ISSN: 1680-5593

Polymorphisms in Exon 2 of *IGF-IR* Gene and Theirs Association with Production Traits in Jinghai Yellow Chicken

[1]Fengping Yang, [2]Chongfu Jin, [2]Guojun Dai, [2]Kaizhou Xie, [3]Yabo Yu and [2]Jinyu Wang
[1]College of Bioscience and Technology, [2]College of Animal Science and Techology,
Yangzhou University, 225009 Yangzhou, China
[3]Jiangsu Jinghai Poultry Group Co., Ltd. 226103 Haimen, China

Abstract: In this study, exon 2 of Insulin-like Growth Factor Receptor type I (*IGF-IR*) gene was studied as a candidate gene associated with production performance in Jinghai Yellow chicken. A pair of primers was designed to screen the Single Nucleotide Polymorphisms (SNPs) using DNA pooling which consisted of DNA from all 200 female chickens and three pairs of primers were then designed to check them individually. The result showed there were three SNPs (G26333A, G26336A and C26639T) in the chicken group, each had three genotypes and was in Hardy-Weinberg equilibrium ($p>0.05$). Correlation analysis showed the G to A transition at 26333 bp was negatively associated with 300 days egg number and body weight at 4 and 16 weeks of age, the G to A transition at 26336 bp was positively associated with body weight at 8 and 12 weeks of age and the C to T transition at 26639 bp was positively associated with body weight at 16 weeks of age. Com-genotype analysis showed that the age at the first egg of chickens with AA/CD/EE was earlier than those with AA/CC/EE and AB/CC/EF ($p<0.05$) and chickens with AB/CC/EE had more 300 days egg number than those with BB/CD/EE ($p<0.05$). AA/CC/EF was an enhancing com-genotype for body weight while AA/CC/EE and AB/CC/EF were the negative ones at 12 and 16 weeks of age. The results suggested a significant association between SNPs of *IGF-IR* gene and production traits and these SNPs could be used as potential genetic markers in future breeding of Jinghai yellow chicken.

Key words: Jinghai Yellow chicken, exon 2 of *IGF-IR* gene, polymorphism, productive traits, China

INTRODUCTION

The Insulin-like Growth Factor system (IGFs) is composed of Ligands (IGF-I, IGF-II), Receptors (IGF-IR, IGF-IIR) and a family of binding Proteins (IGFBPs) (Donovan and Kummar, 2008) with a strong promotion of growth and differentiation. IGF-IR is the main mediator of IGFs among two receptors, expresses after the eight-cell stage (Rappolee *et al*., 1992) and ubiquitously distributes in normal tissues and cells in human body (Coppola *et al*., 1994). It has important functions in immunoloregulation, mitogenic responses, growth of muscle and skeleton (Denley *et al*., 2005) working with Platelet Derived Growth Factor (PDGF), Epidermal Growth Factor (EFG) and Fibroblast Growth Factor (FGF) (Leroith *et al*., 1995; Meyts *et al*., 1994; Baserga *et al*., 1994). Expression of *IGF-IR* gene increases 4-5 fold in Atlantic salmon in May and June, coincided with an increase in bone density (Wargelius *et al*., 2005). IGF-IR-null mutation in mature osteoblasts leads to less bone, decreases periosteal bone formation, impairs stimulatory effects of parathyroid hormone on osteoprogenitor cell proliferation and differentiation in mice (Wang *et al*., 2007). IGF-IR staining of immature mouse declines considerably with age in the proximal femur and distal tibia (hip and ankle) but expression remains high in distal femur and proximal tibia (knee) throughout growth (Serrat *et al*., 2007). IGF-IR is also closely related with the occurrence, development and metastasis of cancer (Burfeind *et al*., 1996; Waksmanski *et al*., 2001; Zhao *et al*., 2004).

In chicken, *IGF-IR* gene locates on chromosome 10, consists of 21 exons and codes for 1363 amino acid residues. Mature IGF-IR is composed of two α and two β chains held together by disulfide bonds (Bhaumick *et al*., 1981; Chernausek *et al*., 1981; Massague and Czech, 1982), its 1333 amino acid residues was found 85% homology with that of human (Matsumura *et al*., 1996). At present, researchers do their best to find certain correlation between gene and production performance of livestock to offer some useful ways for molecular-assistant breeding. Lei *et al*. (2006) considered the mutation in exon 3 of *IGF-IR* gene was significantly correlated with growth and slaughter traits in chicken; Gao *et al*. (2009) draw conclusions that C919G mutation in

Corresponding Author: Jinyu Wang, College of Animal Science and Techology, Yangzhou University, 225009 Yangzhou, China

exon 4 of *IGF-IR* gene significantly affected 5 weeks body weight ($p<0.05$) and T2761C in exon 13 significantly affected metatarsus circle, metatarsus and ungual ratio ($p<0.01$) and was also correlated with metatarsus, ungual weight and femur weight ($p<0.05$). A significant effect of a SNP genotype was found on 10 weeks body weight ($p<0.01$), 4-10 and 6-10 weeks average daily gain ($p<0.05$) in Japanese quail (Moe *et al*., 2007).

Jinghai yellow chicken is the first chicken breed after the enactment of the new Animal Husbandry Law of the People's Republic of China in 2006. It is a high quality, small meat chicken breed and is widely accepted in Jiangsu Province. In the present study, researchers analyzed the polymorphisms of exon 2 of *IGF-IR* gene in female Jinghai yellow chicken, explored the association between its SNPs and production performances aiming to enrich the characteristic of *IGF-IR* gene in Jinghai Yellow chicken and to find more useful molecular breeding methods for this new breed.

MATERIALS AND METHODS

Chicken populations: A total of 200 female Jinghai Yellow chickens belonging to generation eight, bred in Jiangsu Jinghai Poultry Group Co., Ltd. were sampled. Growth traits (including hatch weight and body weight at 4, 8, 12, 16 weeks of age) and reproductive traits (including age at first egg, beginning-laying-weight, primary egg weight and 300 days egg number) of each individual were noted. Blood samples were obtained from the wing vein with sodium heparin as an anticoagulant and then stored at -20°C. Genomic DNA was extracted from the whole blood using the phenol-chloroform method. DNA concentrations were quantified spectrophotometrically.

Primers design and PCR amplification: Based on DNA sequence of IGF-IR (GenBank Accession No. NC_006097), a pair of Primers (P) was designed with Primer Premier 5.0 Software. Using pool DNA as template, the PCR amplification was to screen out SNPs in exon 2 of *IGF-IR* gene. The DNA pooling was constructed by fully mixed 200 DNA samples, each was 5 μL. According to the sequencing result, three pairs of primers, P2 for RFLP and the other two for SSCP were designed to detect the SNPs in each chicken (Table 1).

PCR was performed in a total volume of 20 μL which included 2.0 μL 10×buffer, 2.2 μL Mg^{2+} (20 mmol L^{-1}), 0.8 μL dNTPs (2.5 mmol L^{-1}), 1.0 L each primer (10 μmol L^{-1}), 1.0 μL template DNA (100 mg L^{-1}), 0.2 μL Taq DNA polymerase (2U μL) and 11.8 μL ddH_2O. Amplification conditions were all as follows: denaturation at 95°C for 6 min followed by 30 cycles of 95°C for 30 sec, 58-62°C for 30 sec, 72°C for 30 ec and a final extension at 72°C for 10 min. PCR products were verified by electrophoresis on 1% agarose gel in 0.5×TBE and stained with gold view.

For SSCP analysis, 2.5 μL of amplified product was mixed with 7.5 μL denaturing buffer (95% formamide, 0.5% bromophenol blue, 0.5% xylene cyanole FF and 10 mmol L^{-1} EDTA (pH 8.0), heated for 6 min at 95°C then immediately chilled on ice for 5 min. Electrophoresis was performed on 10% non-denaturing polyacrylamide gel at 250 V for 10-15 h at 16°C, SSCP patterns on the gels were visualized by silver staining (Xu *et al*., 2002).

For RFLP, restriction digests were performed in a 20 μL reaction including 10 μL amplified product, 2.0 μL 10×buffer, 7.6 μL ddH_2O and 0.4 μL Alu I. Reactions were incubated in 37°C through a night and digested products were separated on 10% polyacrylamide gel. DNA bands were stained with silver. PCR products of homozygous/heterozygous individuals of different genotypes were purified with a DNA Fragment Quick Purification/Recover kit. The purified PCR products were sequenced in both directions, completed by Shanghai Invitrogen Biotechnology Co.

Statistical analysis: Hardy-Weinberg equilibrium was tested for each SNP using the χ^2-test. The General Linear Model (GLM) was established to analyze the genotype effects of exon 2 in *IGF-IR* gene on body weight and reproductive traits. The model was used as:

$$y_{ij} = \mu + G_i + e$$

Where:

y_{ij} = Value of production traits
μ = Mean value
G_i = The fixed effect of each SNP
e = The residual error

Table 1: Primers designed to amplify exon 2 of *IGF-IR* gene in Jinghai yellow chickens

Primers	Primer sequence (5'-3')	Position in NC_006097	Annealing Temp. (°C)	Length (bp)
P	F:CCATGGGAATAGCCTACGTG R:ACAGAGAGCACAGCTCCTCA	26114-26774	60	661
P1	F:AACGCCTGGAGAACTGTACG R:AGTCAGTTATGACGGTCAGCTT	26246-26355	58	111
P2	F: AACGCCTGGAGAACTGTACG R:ATCGCTGAGGCTTTCCAAG	26246-26402	62	155
P3	F:GGCCATACGGATTGAGAAGA R:ATGGAGGTCTTCTCGCACAA	26523-26696	58	174

Differences among genotypes or com-genotypes were analyzed using SPSS 16.0 Software. For all companions, differences were considered to be statistically significant if $p<0.05$.

RESULTS

Sequencing result of the amplification product of DNA pooling: Checking the sequence of amplification product of DNA pooling, double peaks were found in three positions (26333, 26336 and 26639 bp) (Fig. 1) which signified that there would be three SNPs possibly. And further analysis showed there would be a change of Alu I endonuclease locus at 26336 bp.

PCR amplification, SSCP and RFLP analysis: The PCR products amplified by three pairs of primers were ideal and each all displayed polymorphisms. For primer P1, three genotypes were detected and were named AA, AB and BB, respectively (Fig. 2) for primer P3, three genotypes, EE, EF and FF were observed also (Fig. 3). For primer P2, the amplified 155 bp fragment, digested with Alu I, yielded products of 90 and 65 bp for the C allele and 155 bp for the D allele and three genotypes (CC, CD and DD) were detected (Fig. 4).

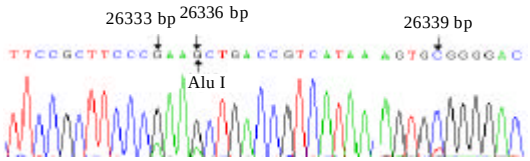

Fig. 1: Sequence alignment of amplification of DNA pooling

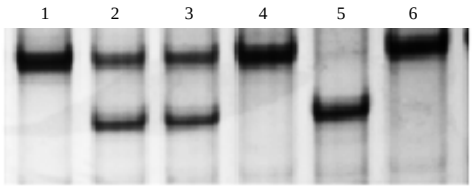

Fig. 2: SSCP analysis of PCR amplification using primer P1 Lanes 1, 4 and 6: AA genotype; Lanes 2, 3: AB genotype; Lane 5: BB genotype

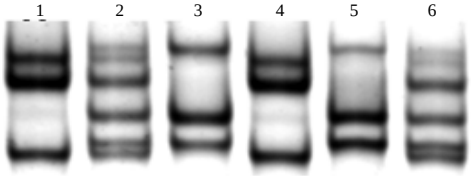

Fig. 3: SSCP analysis of PCR amplification using primer P3 Lanes 1 and 4: FF genotype; Lanes 2, 6: EF genotype; Lane 3, 5: EE genotype

Sequence analysis: PCR products of AA and BB were cloned and sequenced and a synonymous mutation, G to A was found at the position of 26333 bp between them (Fig. 5). In the similarly way, G to A at 26336 bp between CC and DD (Fig. 6) and C to T at 26639 bp between EE and FF (Fig. 7) were revealed and the two were also synonymous base mutation.

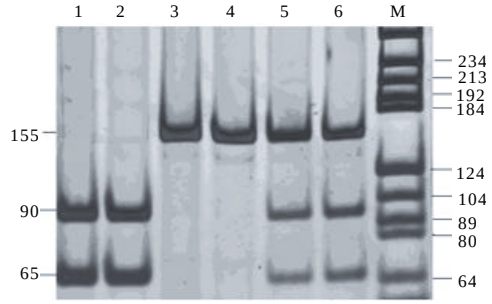

Fig. 4: RFLP analysis of PCR amplification using primer P2 Lanes 1and 1, 2: CC genotype; Lanes 3, 4: DD genotype; Lane 5, 6: CD genotype; M: DNA marker pBR322

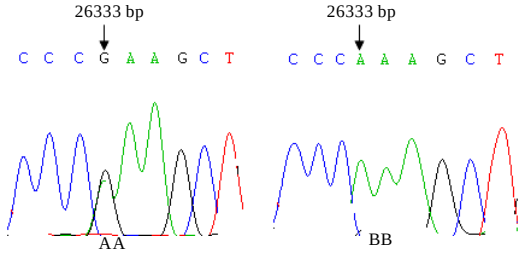

Fig. 5: Sequence alignment of AA and AB of primer P1

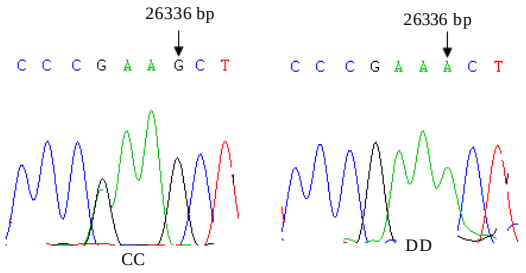

Fig. 6: Sequence alignment of CC and DD of primer P2

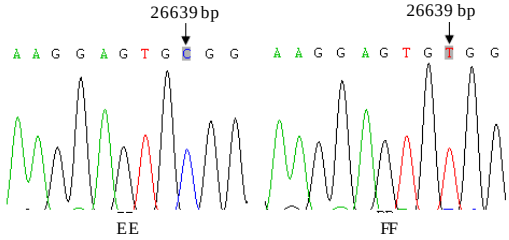

Fig. 7: Sequence alignment of EE and FF of primer P3

Genotype and allele frequencies in Jinghai Yellow chicken group: Frequencies of genotypes and alleles are shown in Table 2. In three SNP loci, A, C and E were the dominant alleles in this chicken group with frequencies of 0.855, 0.755 and 0.870, respectively and AA, CC and EE were the dominant genotypes with frequencies of 0.745, 0.555 and 0.765. The χ^2-test showed that the observed genotypic values of three SNPs were not statistically different from the expected values, based on the Hardy-Weinberg equilibrium.

Table 2: Genotype and allele frequency of three SNPs in Jinghai Yellow chicken

Primers	--------Genotype frequency---------			--Allele frequency--		χ^2
P1	AA:0.745	AB:0.220	BB:0.035	A:0.855	B:0.145	2.541
P2	CC:0.555	CD:0.400	DD:0.045	C:0.755	D:0.245	0.988
P3	EE:0.765	EF:0.210	FF:0.025	E:0.870	F:0.130	1.026

Association of genotypes with production performances: Chickens with AA and AB genotypes had significantly higher 300 days egg number and body weight at 4 weeks than those with BB genotypes ($p<0.05$) (Table 3). Chickens with AA had higher body weight at 16 weeks than those with BB ($p<0.05$). Chickens with DD had higher body weight at 8 weeks than those with CC ($p<0.05$) and they also had higher body weight at 12 weeks than those with CC and CD ($p<0.05$). For primer P3, chickens with EE and EF had higher body weight at 16 weeks than those with FF ($p<0.05$).

Association between com-genotypes and production performances: The least square means and SE for body weight and reproductive traits of different com-genotypes in Jinghai yellow chicken are shown in Table 4. For

Table 3: Association of genotypes with production performances in Jinghai Yellow chicken (Mean±SE)

		Genotypes		
Primers	Traits	AA (N = 149)	AB (N = 44)	BB (N = 7)
P1	Age at first egg	140.51±0.85	140.64±1.56	143.14±3.91
	Beginning laying weight	1569.67±15.48	1572.68±28.49	1510.86±71.44
	Primary egg weight	33.05±0.40	32.68±0.74	32.71±1.87
	300 days egg number	95.54±1.73^{a}	96.36±3.18^{a}	77.00±7.96^{b}
	Hatch weight	35.30±0.36	35.75±0.66	37.14±1.65
	Body weight at 4 weeks	193.27±2.10^{a}	186.93±3.86^{a}	168.57±9.67^{b}
	Body weight at 8 weeks	481.83±6.09	471.14±11.21	449.29±28.10
	Body weight at 12 weeks	894.28±10.06	884.71±18.51	820.43±46.40
	Body weight at 16 weeks	1146.26±8.36^{a}	1136.82±15.38^{ab}	1064.14±38.55^{b}
		CC (N = 111)	CD (N = 80)	DD (N = 9)
P2	Age at first egg	142.03±0.97	138.38±1.14	143.44±3.39
	Beginning laying weight	1572.58±17.88	1553.70±21.06	1644.78±62.79
	Primary egg weight	32.98±0.47	32.88±0.55	33.33±1.65
	300 days egg number	94.41±2.03	95.95±2.39	95.44±7.12
	Hatch weight	35.76±0.41	35.08±0.49	35.22±1.45
	Body weight at 4 weeks	189.88±2.47	191.96±2.91	196.44±8.68
	Body weight at 8 weeks	472.28±7.02^{b}	482.08±8.27^{ab}	519.89±24.66^{a}
	Body weight at 12 weeks	884.78±11.54^{b}	884.85±13.59^{b}	991.00±40.52^{a}
	Body weight at 16 weeks	1132.05±9.73	1154.96±11.46	1134.22±34.17
		EE (N = 153)	EF (N = 42)	FF (N = 5)
P3	Age at first egg	140.68±0.84	140.43±1.60	140.80±4.63
	Beginning laying weight	1572.14±15.27	1563.36±29.15	1491.20±84.48
	Primary egg weight	33.28±0.40	32.21±0.75	29.40±2.18
	300 days egg number	95.37±1.73	94.55±3.29	90.40±9.54
	Hatch weight	35.40±0.53	35.79±0.67	34.60±1.95
	Body weight at 4 weeks	191.80±2.10	190.19±4.00	173.80±11.59
	Body weight at 8 weeks	478.52±6.01	482.38±11.48	438.80±33.27
	Body weight at 12 weeks	890.26±9.99	888.88±19.06	875.20±55.24
	Body weight at 16 weeks	1142.16±8.24^{a}	1149.48±15.73^{a}	1046.80±45.60^{b}

Table 4: Association between com-genotypes and production performance in Jinghai Yellow chicken

Com-genotype	Age at first egg	Beginning laying weight	300 days egg number	Body weight at 8 weeks	Body weight at 12 weeks	Body weight at 16 weeks
AA/CC/EE(72)	142.74±9.930^{a}	1564.96±160.210^{abc}	93.68±21.01^{ab}	473.64±74.50	885.12±117.64^{b}	1135.10±101.53^{b}
AA/CC/EF(6)	137.00±15.37^{ab}	1692.50±609.030^{a}	91.33±17.18^{ab}	507.50±34.17	916.33±65.960^{ab}	1227.00±61.040^{a}
AA/CD/EE(57)	137.86±9.473^{b}	1562.04±169.870^{abc}	97.35±22.04^{ab}	484.33±75.36	892.49±113.92^{b}	1154.88±104.11^{ab}
AA/CD/EF(5)	140.00±6.290^{ab}	1415.60±67.2500^{b}	102.20±9.010^{ab}	466.00±18.07	810.60±86.960^{b}	1135.60±105.30^{ab}
AA/DD/EE(9)	143.44±6.860^{ab}	1644.78±217.940^{ac}	95.44±16.13^{ab}	519.89±65.17	991.00±154.60^{a}	1134.22±120.28^{ab}
AB/CC/EE(9)	136.33±11.69^{ab}	1605.11±216.170^{abc}	103.89±17.60^{a}	450.55±83.31	869.44±122.35^{b}	1131.33±105.90^{ab}
AB/CC/EF(19)	143.95±13.60^{a}	1569.58±131.120^{abc}	94.74±30.13^{ab}	475.11±88.42	883.32±152.68^{b}	1113.26±103.12^{b}
AB/CD/EE(3)	146.33±12.42^{ab}	1571.67±149.670^{abc}	94.33±12.58^{ab}	446.67±55.30	813.33±125.83^{b}	1156.67±33.310^{ab}
AB/CD/EF(12)	136.75±8.070^{ab}	1550.50±123.400^{abc}	92.67±13.50^{ab}	488.17±90.73	916.58±145.95^{ab}	1173.83±85.650^{ab}
BB/CC/FF(3)	141.67±4.510^{ab}	1410.67±97.4500^{bc}	91.00±21.52^{ab}	443.00±55.25	861.33±65.040^{ab}	1044.00±83.360^{b}
BB/CD/EE(3)	144.00±9.540^{ab}	1620.33±211.200^{abc}	73.67±27.30^{b}	477.00±28.93	808.00±169.46^{b}	1111.67±162.52^{ab}

The different letter of superscripts indicated the significant difference ($p<0.05$)

reproductive traits, chickens with AA/CD/EE had first egg significantly earlier than those with AA/CC/EE and AB/CC/EF ($p<0.05$). Chickens with AA/CC/EF and AA/DD/EE had higher beginning-laying-weight than those with AA/CD/EF and chickens with AA/CC/EF had higher beginning-laying-weight than those with BB/CC/FF. Chickens with AB/CC/EE had higher 300 days egg number than those with BB/CD/EE. For body weight, the differences between all com-genotypes were not significant at hatch day 4 and 8 weeks ($p>0.05$). Chickens with AA/DD/EE had the highest body weight at 12 weeks, significantly higher than those with AA/CC/EE, AA/CD/EE, AA/CD/EF, AB/CC/EE, AB/CC/EF, AB/CD/EE and BB/CD/EE. Chickens with AA/CC/EF had higher body weight at 16 weeks than those with AA/CC/EE, AB/CC/EF, BB/CC/FF.

DISCUSSION

PCR-SSCP was an ease and economic experimental technique for detecting SNPs combined with the direct sequencing of DNA pooling, it made the screening even faster and more correct. In this study, researchers found three SNPs in exon 2 of *IGF-IR* gene through this method. The screening result showed there was mere 3 bp interval between two mutation loci (26333 and 26336 bp) which would bring some difficulties to further detect if only through PCR-SSCP. So, when designed primer P1, researchers made the base of 26336 bp in the primer P1 then the SNP at 26333 bp was detected by SSCP easily. The base mutation at 26336 bp was detected by RFLP making use of the loss of Alu I endonuclease site. At last, three SNPs were all checked out successfully, fully avoiding omission and erroneous judgment because of the direct sequencing of DNA pooling. Population analysis showed the three SNPs were all in Hardy-Weinberg equilibrium which meant the three SNPs were not affected by breeding selection or re-achieved equilibrium state through eight generations breeding.

IGF-IR gene is the member of the transmembrane tyrosine kinase receptor family plays a mitogen role in promoting cell proliferation (Coppola *et al*., 1994). In *IGF-IR* gene deficient mouse fibroblast, EFG and PDGF did not stimulate DNA synthesis and cell proliferation, but these defects could be corrected by high expression of *IGF-IR* gene (Coppola *et al*., 1994; DeAngelis *et al*., 1995). Mice lacking functional IGF-1Rs were born weighing less than half the normal weight and die soonthere after (Liu *et al*., 1993).

As the only receptor of IGF-I and IGF-II in birds, IGF-IR plays an important role for IGFs' biological functions and *IGF-IR* gene was studied as an important candidate gene with growth and development for poultry (Armstrong and Hogg, 1992; Gao *et al*., 2009). In this study, G to A transition at 26333 bp had significant effect on reproductive traits in Jinghai yellow chicken. Chickens with BB genotype had less 300 days egg number than those with AA and AB (short of 18.54 and 19.36, respectively) which showed A was a reproductive enhancer gene and B was a leaky one. Body weight of chickens with BB was 24.70 and 18.36 g less than that of AA and AB, respectively at 4 week and it also significantly less than those with AA (<82.12 g) at 16 week which verified that B was a leaky gene for body weight. For primer P2, body weight of chickens with DD was 47.61 and 106.22 g higher than those with CC which meant the G to A transition at 26336 bp was positively associated with body weight at 8 and 12 weeks. Analysis of primer P3 showed F was a leaky gene for body weight at 16 week.

Com-genotypes analysis showed that the age at the first egg of chickens with AA/CD/EE was the earliest, 5 and 6 days earlier than those with AA/CC/EE and AB/CC/EF, respectively which meant AA/CD/EE could be an advantage com-genotype for improving the age at first egg. Chickens with AA/CC/EE had 30 eggs more than those with BB/CC/EE at 300 days which indicated that the AA/CC/EE was beneficial to the improvement of 300 days egg number in Jinghai Yellow chicken. Chickens with AA/CC/EF had more 98.509-183.000 g body weight than any other at 12 weeks which meant AA/CC/EF could be the most advantageous com-genotype for body weight at this age. Meanwhile AA/CC/EF was a favorable com-genotype for body weight at 16 weeks. Chickens with AA/CC/EE and AB/CC/EF had low body weight at 12 and 16 weeks.

CONCLUSION

Jinghai Yellow chicken was a high quality, small meat chicken breed, its growth curve turning point was about 11.13 week (Yang *et al*., 2007) and the selling time of its breeding objective was about 16 weeks age. Researchers detected three SNPs in exon 2 of *IGF-IR* gene in female Jinghai yellow chicken and the result showed these mutations had some effects on production performances especially on the body weight at 12 and 16 week, the time for its selling. Further study involving larger sample size and male chickens will be needed to confirm the association between these SNPs and production performances in Jinghai yellow chicken and/or in other chicken breeds.

ACKNOWLEDGEMENTS

This research was founded by National Broiler Industrial and Technology System (No.nycytx-42-G1-05). The researchers gratefully acknowledge the members of Jinghai Poultry Group Corporation in Jiangsu Province for providing experimental animals.

REFERENCES

Armstrong, D.G. and C.O. Hogg, 1992. The expression of a putative insulin-like growth factor-I receptor gene in the liver of the developing chick. Mol. Endocrinol., 8: 193-201.

Baserga, R., C. Sell, P. Porcu and M. Rubini, 1994. The role of the IGF-I receptor in the growth and transformation of mammalian cells. Cell Prolif., 27: 63-71.

Bhaumick, B., R.M. Bala and M.D. Hollenberg, 1981. Somatomedin receptor of human placenta: solubilization, photolabeling, partial purification and comparison with insulin receptor. Proc. Natl. Acad Sci., 78: 4279-4283.

Burfeind, P., C.L. Chernicky and F. Rininsland, 1996. Antisense RNA to the type 1 insulin-like growth and prevents invasion by rat prostate cancer cells *in vivo*. Proc. Natl. Acad Sci. USA, 93: 7263-7268.

Chernausek, S.D., S, Jacobs and J.J. Van Wyk, 1981. Structural similarities between human receptors for somatomedin C and insulin: Analysis by affinity labeling. Biochemistry, 20: 7345-7350.

Coppola, D., A. Ferber, M. Miura, C. Sell, C. D'Ambrosio, R. Rubin and R. Baserga, 1994. A functional insulin-like growth factor I receptor is required for the mitogenic and transforming activities of the epidermal growth factor receptor. Mol. Cell. Biol., 14: 4588-4595.

DeAngelis, T., A. Ferber and R. Baserga, 1995. Insulin-like growth factor 1 receptor is required for the mitogenic and transforming activities of platelet derived growth factor receptor J. Cell. Physiol., 164: 214-221.

Denley, A., L.J. Cosgrove, G.W. Booker, J.C. Wallace and B.E. Forbes, 2005. Molecular interactions of the IGF system. Cytokine Growth Factor Rev., 16: 421-439.

Donovan, E.A. and S. Kummar, 2008. Role of insulin-like growth factor-1R system in colorectal carcinogenesis. Crit. Rev. Oncol. Hematol., 66: 91-98.

Gao, F.H., L.H. Bian, S.Z. Wang, Q.G. Wang, Z.Q. Tang and H. Li, 2009. Association of chicken IGF1R gene with growth and body composition traits. J. Northeast Agri. Univ., 40: 77-83.

Lei, M.M., Y.B. Tang, M. Zhou, X.B. Shao, X. Peng and X.Q. Zhang, 2006. Analysis on genetic diversities of *IGF1R* gene in chicken. Guangdong Agric. Sci., 11: 132-137.

Leroith, D., H. Werner, D. Beitner-Johnson and A.T. Jr. Roberts, 1995. Molecular and cellular aspects of the insulin-like growth factor I receptor. Endocr. Rev., 16: 143-163.

Liu, J.P., J. Baker, A.S. Perkins, E.J. Robertson and A. Efstratiadis, 1993. Mice carrying null mutations of the genes encoding insulinlike growth factor I (Igf-1) and type 1 IGF receptor (Igfr). Cell, 75: 59-72.

Massague, J. and M.P. Czech, 1982. The subunit structures of two distinct receptors for insulin-like growth factors I and II and their relationship to the insulin receptor. J. Biol. Chem., 257: 5038-5045.

Matsumura, Y., M. Domeki, K. Sugahara, T. Kubo, C.T. Jr. Roberts, D. LeRoith and H. Kato, 1996. Nutritional regulation of insulin-like growth factor-I receptor mRNA levels in growing chickens. Biosci. Biotechnol. Biochem., 60: 979-982.

Meyts, P.D., B. Wallach, C.T. Christoffersen, B. Urso and K. Gronskov *et al*., 1994. The insulin-like growth factor-I receptor structure, ligand-binding mechanism and signal transduction. Horm. Res., 42: 152-169.

Moe, H.H., T. Shimogiri, W. Kamihiraguma, H. Isobe and K. Kawabe *et al*., 2007. Analysis of polymorphisms in the insulin-like growth factor 1 receptor (IGF1R) gene from Japanese quail selected for body weight. Anim. Genet., 38: 659-661.

Rappolee, D.A., K.S. Sturm, O. Behrendtsen, G.A. Schultz, R.A. Pedersen and Z. Werb, 1992. Insulin-like growth factor II acts through an endogenous growth pathway regulated by imprinting in early mouse embryos. Genes Dev., 6: 939-952.

Serrat, M.A., C.O. Lovejoy and D. King, 2007. Age- and site-specific decline in insulin-like growth factor-I receptor expression is correlated with differential growth plate activity in the mouse hindlimb. Anat. Record, 290: 375-381.

Waksmanski, B., J. Dudkiewicz and S. Dabrowski, 2001. Function of insulin-like growth factor (IGF-I) and its binding protein (IGFBP-1) in pathological proliferation of endometrium. Wiadomosci lekarskie, 54: 656-661.

Wang, Y., S. Nishida, B.M. Boudignon, A. Burghardt, H.Z. Elalieh *et al*., 2007. IGF-I Receptor is required for the anabolic actions of parathyroid hormone on bone. J. Bone Miner. Res., 22: 1329-1337.

Wargelius, A., P.G. Fjelldal, S. Benedet, T. Hansen, B.T. Bjornsson and U. Nordgarden, 2005. A peak in gh-receptor expression is associated with growth activation in Atlantic salmon vertebrae, while upregulation of igf-I receptor expression is related to increased bone density. Gen. Comp. Endocrinol., 142: 163-168.

Xu, S., Y. Tao, Z. Yang and J. Chu, 2002. A simple and rapid methods used for silver staining and gel preservation. Hereditas, 24: 335-336.

Yang, Y., J.Y. Wang, L.Y. Wang, J.H. Yu and S.J. Lu, 2007. Analysis of fitting growth model in *Jinghai* yellow chicken. Anim. Husb. Vet. Med., 39: 17-20.

Zhao, H., J. Dupont, S. Yakar, M. Karas and D. LeRoith, 2004. PTEN inhibits cell proliferation and induces apoptosis by downregulating cell surface IGF-IR expression in prostate cancer cells. Oncogene, 23: 786-794.