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Genomic Analysis Reveals Strong Signatures of Selection in Guangxi Three-Yellow Chicken in China

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ABSTRACT

Much like other indigenous domesticated animals, Guangxi Three-yellow chickens (GX-TYC) in China have experienced strong selective pressure, and show specific phenotypic changes in physiology, morphology and behavior. To identify genomic footprints or selection signatures left by artificial selection during domestication of GX-TYC, the whole genomes of 12 GX-TYC hens were sequenced to executed selective sweep analyses and gene functional enrichment analysis (Gene Ontology and Kyoto Encyclopedia of Genes and Genome pathways). A total of 10.13 million single nucleotide polymorphisms and 842,236 insertion/deletion polymorphisms (Indels) were found. Forty-six windows showed a Z score of heterozygosity (ZHp) lower than -5, which potentially were considered to be positively selected regions. Gene annotation identified 55 genes in these regions. Selection signatures were found mainly on the SSC5, SSC8, SSC23 and SSCZ. GO and KEGG analyses revealed that these genes were related to growth, immune responses as well as carbohydrate, lipid and amino acid metabolisms. In addition, two genes, fructose-1,6-bisphosphatase 1 and fructose-1,6-bisphosphatase 2 were enriched into four signaling pathways, three of which are involved in carbohydrate metabolism and insulin signaling. SHC3, FANCC and PTCH1, in combination with FB1 and FBP2, were clustered together in a region of chromosome Z, and thus might have been selected together. The results have uncovered some genetic footprints of chicken domestication, providing not only an important resource for further improvements of fowl breeding, but also a useful framework for future studies on the genetics of domestic chickens as well as on the phenotypic variations and certain diseases of chickens.

Key words: Chicken; Selective sweeps; Single nucleotide polymorphism; Whole genome resequencing

INTRODUCTION

Three-yellow chicken (TYC) is internationally well known for its desirable meat quality including juiciness, flavor and tenderness. They were named for their yellow feather, yellow beak and yellow feet. Three-yellow chicken is not a particular species, but rather is a collective name for those chicken breeds with these three yellow traits, including Huxu, Qingyuan, Xinghua, Huaixiang, Wenchang and Yangshan chickens in the Guangdong province, Pudong chicken in Shanghai, Xiaoshan chicken in the Zhejiang province, etc. (Zheng et al.1989). Guangxi three-yellow chicken (GX-TYC), a breed that has been intensively selected both naturally and artificially, is mainly distributed in Yulin, Beiliu, Bobai, Cenxi counties or cities in the Guangxi province as a typical traditional breed locally. Because of its aforementioned meat quality, GX-TYC has been widely used in the development of many special lines of yellow-feather broilers in China (Wei et al. 2019). For future breeding efforts to develop better breeds for the broiler industry, a better understanding of the GX-TYC domestication and identify genetic components obtained from various selections that are likely the consequence of GX-TYC domestication are needed. For these purposes, the whole genome sequencing approach to explore favorable alleles, candidate mutations or single nucleotide polymorphisms (SNPs), and insertions/deletions (Indel) of TX-TYC were used, and the resulting data were reported herein.

MATERIALS AND METHODS

Ethical approval

All animal procedures used in this study were carried out in accordance with the Guide for Care and Use of Laboratory Animals (8th edition, released by the National

Research Council, USA) and were approved by the Institutional Animal Care and Use Committee (IACUC) of Guangxi Institute of Animal Science.

Sequencing of the Guangxi Three-yellow chicken genome

Twelve GX-TYC hens raised at Chunmao Farming Co. Ltd. of Guangxi, China, were used in this study. Blood samples were collected from the wing vein using standard venipuncture. Genomic DNA was isolated from the blood samples with a bloodGen Mini Kit (Cwbiotech., China), and it was assessed for purity and quality using NanoDrop and gel electrophoresis. A pair-end library with insert sizes varying from 250 to 300 base-pairs (bp) was constructed and sequenced with the Illumina Hiseq 2000/2500 platform by BerryGenomics Biotechnology Co., Ltd., Beijing, China. Raw reads contained some interference information, including the adapter, low quality paired reads and unidentified nucleotides. Clean reads were obtained by removing this interference information (Li et al., 2010), and were mapped onto the chicken reference genome (*Gallus gallus*, Galgal 14.78) using the BWA software (Li and Durbin, 2009).

Single nucleotide polymorphisms and insertion/deletion polymorphisms Calling

After the alignment, SNP and InDel calling using a Bayesian approach implemented in the package SAMtools were performed. The 'mpileup' command was used to identify SNPs and InDels with the parameters as '-m 2 -F 0.002 -d 1000'. The identified SNPs were filtered with more stringent parameters, i.e., coverage depth ≥ 4, and Root Mean Square (RMS) mapping quality ≥ 20, to obtain high quality SNPs, which were annotated using the Ensembl gene sets (http://www.ensembl.org/biomart/). The SNPs and InDels in gene regions were annotated using the ANNOVAR annotation tool (Wang et al., 2010).

Selective sweep analysis

Selective sweep screen was performed with the sequenced DNA pools. Allele counts at each SNP position were used to detect signatures of selection in 200-Kb sliding windows with a step size of 50% overlapping for the genome sequences of GX-TYC. At each detected SNP position, the sums of major and minor alleles (n_{MAJ} and n_{MIN}) were determined, and then the corresponding heterozygosity score were calculated using the following formula: $Hp=2\sum n_{MAJ}\sum n_{MIN}/ (\sum n_{MAJ}+\sum n_{MIN})^2$. Individual Hp was then Z-transformed to a standard normal distribution as follows: $ZHp=(Hp-\mu Hp)/\sigma Hp$. A threshold of ZHp≤-5 was set for putative selective sweeps because windows below it ended the distribution (Rubin et al., 2012).

Analysis of functional enrichment

Functional enrichment analysis of Gene Ontology (GO), as well as Kyoto Encyclopedia of Genes and Genome (KEGG) pathways were performed using "Benjamini-corrected modified Fisher's exact test" in the DAVID web server (Huang et al., 2009). Genes were mapped onto their respective human orthologs. *P* values that indicated the significance of the overlap between various gene sets were corrected with Benjamini-Hochberg false discovery rate (FDR). Only were terms with a *P* value less than 0.05 considered significant, and were listed. The GO categories "biological processes", "molecular function" and "cellular component" were used in these analyses.

RESULTS AND DISCUSSION

Data production and short read alignment

Sequencing of the GX-TYC genome generated a total of 35.85 Gbs of paired-end DNA sequences, of which 35.58 (99.25%) Gbs of high quality paired-end reads were mapped onto the chicken reference genome assembly (*Gallus_gallus*, Galgal 4.78) with 33.66-fold sequence depth using Burrows-Wheeler-Alignment tool (BWA). Several categories of genetic variation, including SNPs and Indels were identified between the uniquely mapped reads and the reference genome.

Single nucleotide polymorphisms and insertion/deletion polymorphisms Identification

Mapping the sequencing reads to the reference genome revealed about 0.13 million SNPs, which exceeded the findings reported in the literature (Wong et al., 2004; Fan et al., 2013). A total of 4,332,562 (43%) SNPs located in genic regions, of which 125,732 were coding ones that leaded to 37,045 nonsynonymous nucleotide substitutions (291 stop gains, 47 stop losses and 36,707 being non-synonymous) detected in a total of 5,839 genes (Figure 1 and supplementary table 1). Identification of 842,236 small Indel polymorphisms ranging from 1 to 50 bps in length (Supplementary table 2) was done, which tended to be detected with a greater frequency than their longer counterparts. About 43% of the Indels were in genic regions, similar to the distribution of SNPs, of which 1613 located in coding sequences (Figure 1).

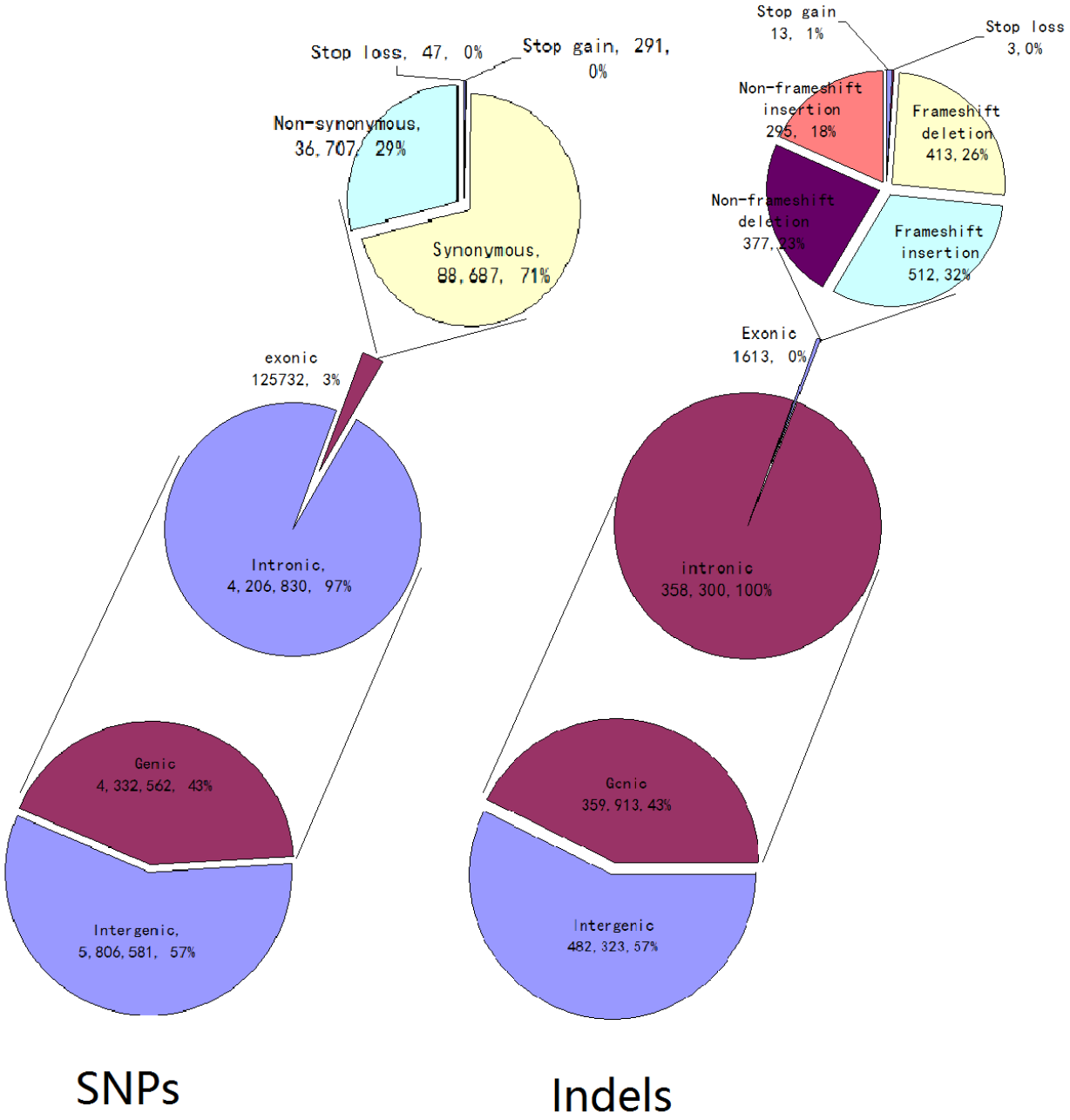

Figure 1. Annotation and distribution of single nucleotide polymorphisms and insertion/deletion polymorphisms

Potential independent signatures of selection in guangxi three-yellow chicken

Domestic animals were excellent models for genetic studies of phenotypic evolution (Andersson, 2001). They evolved genetic adaptations to new environments and were subjected to long-term artificial selections (Rubin et al., 2010). As a result of this process, marks in the proximity of genes influencing breed-defining traits were reduced levels of variability, and showed specific selection signature, including high population differentiation, greatly reduced variation, temporary increase in linkage disequilibrium, skewed allele frequency, and long-ranged haplotype homozygosity (Kaplan et al., 1989; Fay and Wu 2000; Kim and Stephan 2002; Kim and Nielsen 2004; Pollinger et al., 2005; Smith and Haigh, 2007). Selective sweep drew much attention, and a number of statistical tests, mostly based on summed statistics such as the tests by Lewontin and Krakauer (1973), Li et al. (1985), Tajima

(1989), McDonald and Kreitman (1991), Fu and Li (1993), Fu (1997), Fay and Wu (2000) and Sabeti et al. (2002). Recently, the commonly used method was H-based heterozygosity of SNPs and Fst-based genetic diversification (Rubin et al., 2012). To accurately detect the genomic footprints left by selection in the GX-TYC, a selective sweep screen was performed by searching for genomic regions with high degrees of fixation. The pooled heterozygosity Hp was calculated, in sliding 200-Kb windows crossing the chromosomes from sequence reads that correspond to the most and least frequently observed alleles at all SNP positions. The distribution of observed Hp values and the Z transformations of Hp and ZHp were marked in the Figure 2. The putative sweeps on those reaching a ZHp score of -5 or less were mainly described, as they are in the lower end of the distribution. In the genome-wide screen, only about 0.45% of windows (n=46) showed a Z score of heterozygosity (ZHp) lower than -5 (Figure 2 and supplementary table 3). Striking selection signatures were mainly found on the SSC5, SSC8 and SSCZ regions (Figure 2), while some windows that did not reach the significance threshold may have contributed significantly to chicken domestication. The strongest signature of selection (ZHp = -17.158) was observed at 2.20 to 2.24 Mbs on the chromosome 5, which included two genes, for instance SLC6A5 (Solute Carrier family 6, member 5) and NELL1 (neural EGFL like 1). The SLC6A5 gene encodes a sodium- and chloride-dependent glycine neurotransmitter transporter, which is an important glycoprotein for scavenging extracellular glycine in glycine-mediated neurotransmission. Mutation in this gene can cause hyperekplexia. The neural EGFL like (NELL) gene encoded a cytoplasmic protein that contained epidermal growth factor (EGF) -like repeats. The protein may be involved in cell growth regulation and differentiation in a variety of tissues, including heart muscle, skeletal muscle and blood vessels, and may promote osteoblast cell differentiation and terminal mineralization (Bokui et al., 2008). The NELL1 gene was identified in a selective sweep in broilers (Elferink et al., 2012). The biological functions of NELL1 may be related to the selection on the muskuloskeletal integrity in modern broiler chickens. Bone integrity was likely to be co-selected with growth rate and meat yield, as the skeleton of modern broilers needed to support a heavier weight (Zhou et al., 2007). The second convincing signature of selection (ZHp = -14.043) occurred on the sex chromosome Z that harbored the death-associated Protein Kinase 1 (DAPK1), cathepsin L2 (CTSL2), fructose-1,6-bisphosphatase 2 (FBP2) and fructose-1,6-bisphosphatase 1 (FBP1). Death-associated Protein Kinase 1 gene is a calmodulin-dependent serine-threonine kinase involved in a variety of cell signaling pathways that regulate cell survival, apoptosis and autophagy. Cathepsin L2, a lysosomal cysteine proteinase, has been shown to be particularly powerful in degrading myofibrillar components in post-mortem autolysis. In fish muscles, CTSL2 exhibits heat-stability on 50 to 60℃, and can degrade surimi protein during the manufacturing of silver carp surimi products (Li et al., 2008). fructose-1,6-bisphosphatase 1 that acts as a rate-limiting enzyme in gluconeogenesis, catalyzes the hydrolysis of fructose 1,6-bisphosphate to fructose 6-phosphate, and inorganic phosphate in the presence of divalent cations, and mediates in gluconeogenesis and carbohydrate biosynthesis. fructose-1,6-bisphosphatase deficiency is associated with hypoglycemia and metabolic acidosis. FBP1 and FBP2 are two important paralogs. Although there is a strong selective signature on chromosome 8, it was impossible to annotated any genes on it.

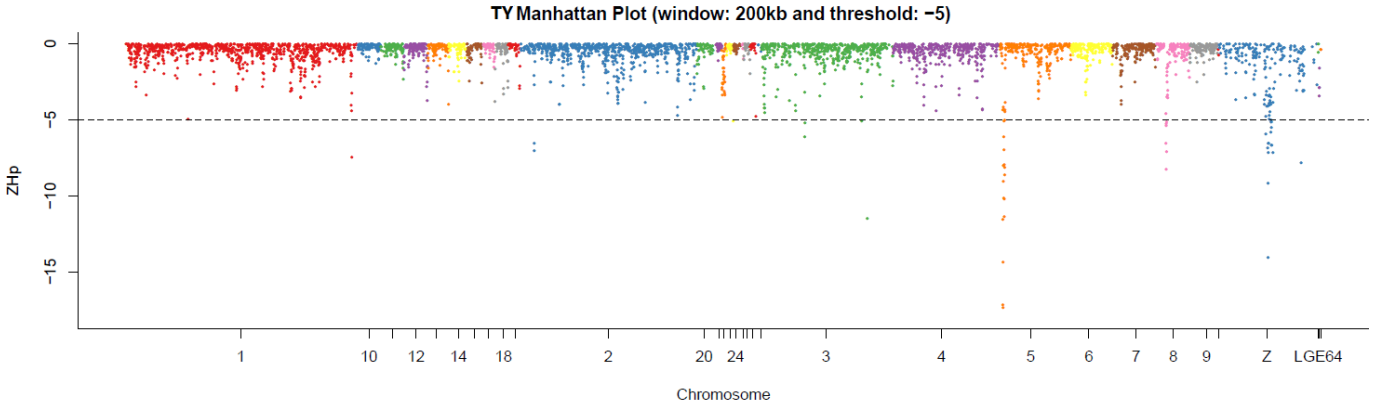

Figure 2. Genome-wide Z score of heterozygosity (ZHp) distribution. The Y axis is ZHp and the X axis shows positions of windows along each chromosome. Dotted lines indicate the thresholds with ZHp = -5.

Gene Ontology and Kyoto Encyclopedia of Genes and Genome pathways analyses

A total of 55 genes were identified in the regions that were considered to be positively selected (Supplementary table 3). Analysis of gene enrichment within this set of genes showed that, in biological-process (BP), significant enrichment for genes was primarily concentrated on the acid and anion transport, the hexos and monosaccharide metabolisms, the mesonephric development, and the defense response, whereas in cellular-component (CC) enrichment was potentially in cell periphery, plasma membrane and interleukin-28 receptor complex. In molecular-function (MF), enrichment was mainly concentrated on several sugar phosphatase activities and on rRNA (cytosine) methyltransferase activity (Figure 3 and Supplementary table 4). As gene enrichment analysis may yield high false-positive rates (Pavlidis et al., 2012), additional functional and physiological experiments were needed to verify the contribution of these genes to these processes. KEGG analysis identified eight pathways retaining a statistical significance (P<0.05), i.e. Hedehog signaling pathway (3 genes, P=0.0017), pentose phosphate pathway (2 genes, P=0.0059), fructose and mannose metabolism (2 genes, P=0.012), valine, leucine and isoleucine degradation (2 genes, P=0.020), insulin signaling pathway (3 genes, P=0.022), Fanconi anemia pathway (2 genes, P=0.026), glycolysis/gluconeogenesis (2 genes, P=0.028), as well as synthesis and degradation of ketone bodies (1 gene, P=0.049) (Figure 4, table 1 and Supplementary table 5). Most of these pathways were related to carbohydrate, lipid and amino acid metabolisms, while some were involved in processing genetic information and environmental information (Table 1).

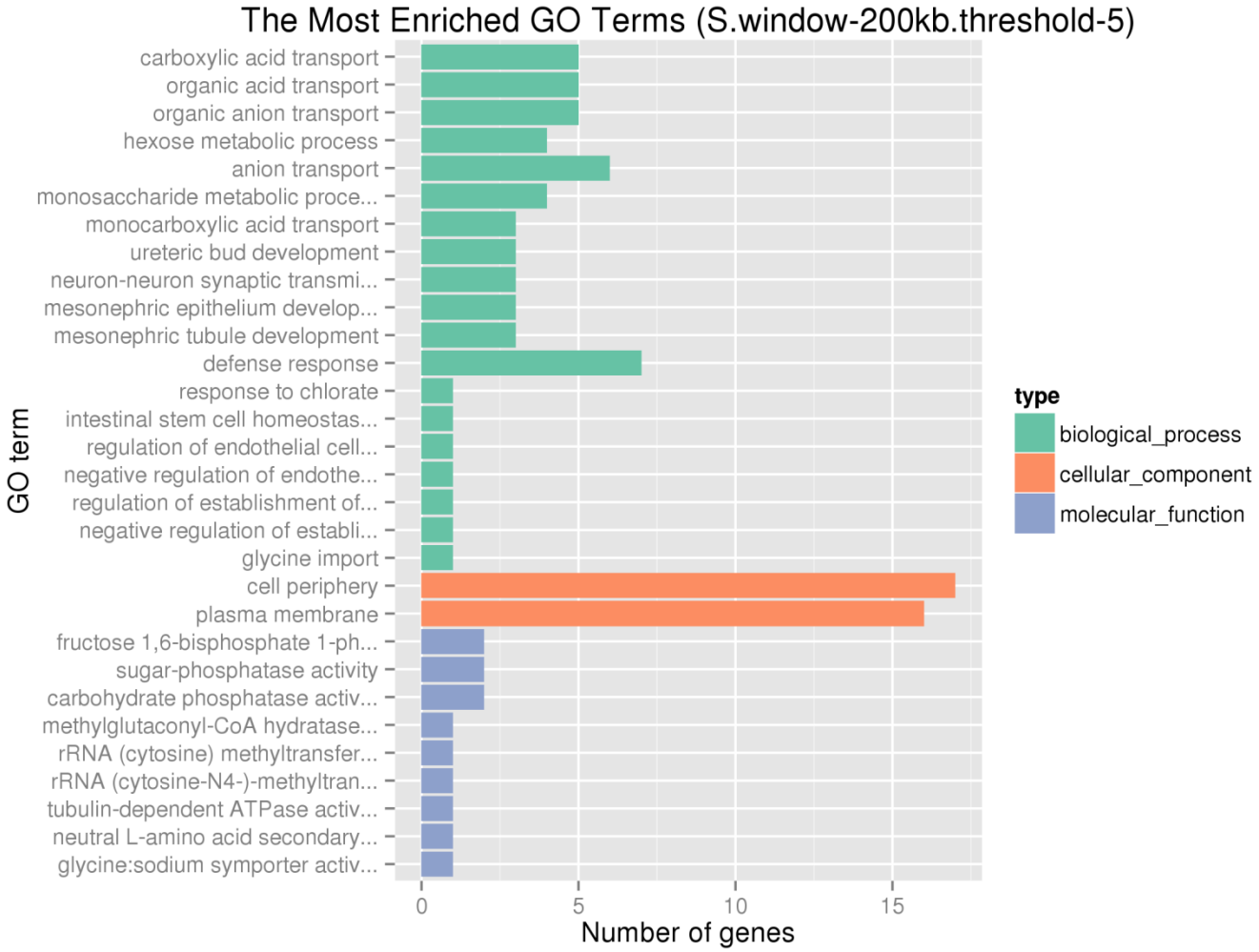

Figure 3. The most enriched gene ontology terms within significant selection of genes on Guangxi Three-yellow chicken of the present study.

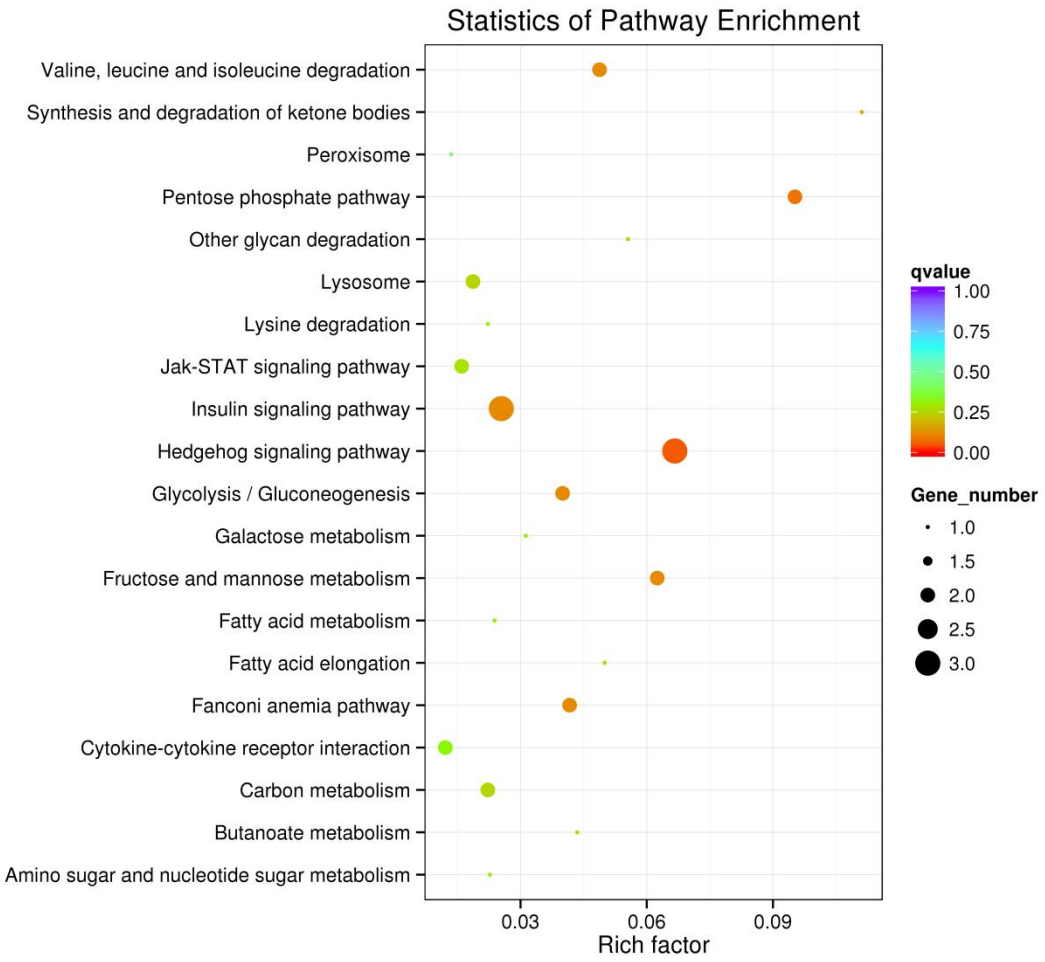

Figure 4. The 20 most enriched Kyoto Encyclopedia of Genes and Genome pathways within significant selection of genes on Guangxi three-yellow chicken in the present study.

Table 1. Results of Kyoto encyclopedia of genes and genome pathways analysis

ID	KEGG Term	Gene	P-Value
Environmental information processing			
Gga 04340	Hedgehog signaling pathway	GAS1, Novel, PTCH1	1.78E-03
Carbohydrate metabolism			
Gga 00030	Pentose phosphate pathway	FBP1, FBP2	5.90E-03
Gga 00051	Fructose and mannose metabolism	FBP1, FBP2	1.26E-02
Gga 00010	Glycolysis / Gluconeogenesis	FBP1, FBP2	2.82E-02
Amino acid metabolism			
Gga 00280	Valine, leucine and isoleucine degradation	HMGCL, AUH	1.97E-02
Organismal systems-Endocrine systems			
Gga 04910	Insulin signaling pathway	FBP1, FBP2, SHC2	2.29E-02
Genetic information processing			
Gga 03460	Fanconi anemia pathway	FANCF, FANCC	2.62E-02
Lipid metabolism			
Gga 00072	Synthesis and degradation of ketone bodies	HMGCL	4.93E-02

Three genes, i.e. the growth arrest-specific gene-1 (GAS1), Novel and protein patched homolog-1 (PTCH1), were enriched on the Hedgehog (Hh) signaling pathway that has many roles in development, cell proliferation, tissue patterning and stem cell maintenance. As a putative tumor suppressor gene (Del et al., 1992; Del et al., 1994; Atsumi et al., 2014), Growth arrest-specific 1(GAS1) inhibits cell replication by blocking the entry into the S

phase of the cell cycle (Del et al., 1992). Protein patched homolog 1 (PTCH1) was a member of the patched gene family, and was the receptor for sonic hedgehog (SHH), which was a secreted molecule implicated in the formation of embryonic structures, and in tumorigenesis (Carpenter et al., 1998). PTCH1 prevented cells from growing and dividing in the absence of SHH, thus it was considered as a tumor suppressor (Villavicencio et al., 2000), although it stoped suppressing cell proliferation in the presence of SHH.Fanconi anemia group F (FANCF) and Fanconi anemia group C (FANCC) belonged to the Fanconi anemia (FA) family, which contained of 22 genes whose protein products form a complex to participate in the efficient repair of damaged DNA (Nepal et al., 2017; Nalepa and Clapp, 2018; Tsui and Crismani, 2019). FANCF stabilized the FANCC/FANCE sub complex and the FANCA/FANCG subcomplex, and locked the whole FA core complex in a conformation that was essential for DNA repair (Leveille et al., 2004), suggesting its important role in maintaining the cell's genomic integrity (Medhurst et al., 2001). FANCF-deficient mice found with no germ cells in the seminiferous tubules, and no or almost no primordial follicles in the ovaries (Bakker et al., 2012). As a mitochondrial enzyme, 3-Hydroxymethyl-3-Methylglutaryl-CoA Lyase（HMGCL） was involved in the valine, leucine and isoleucine degradation and synthesis as well as in the degradation of ketone bodies. When glucose is not available, such as during fasting, ketones are the compounds used for energy by certain organs and tissues, particularly the brain. In human, HMGCL deficiency, often as an autosomal recessive mitochondrial disease (Lin et al., 2009), usually presented with acute episodes of vomiting, hypotonia, hypoketotic, hypoglycemia metabolic acidosis and hyperammonemia in infancy. In the valine, leucine and isoleucine degradation pathways, 3-methylglutaconyl-CoA hydratase (AUH) was another selected gene encoding a bifunctional mitochondrial protein that had both RNA-binding and hydratase activities. The protein can catalyze the transformation of 3-methylglutaconyl-CoA to 3-hydroxy-3-methyl-glutaryl-CoA, and binds AU-rich elements found in the 3'-untranslated regions of rapidly decaying mRNAs. Decreased levels of AUH also leaded to a slower cell growth. Reduced or elevated levels of AUH can lead to defects in mitochondrial translation, ultimately leading to changes in decreased RNA stability as well as in the mitochondrial morphology, biogenesis and respiratory function (Mack et al., 2006). FBP1 and FBP2 were enriched in pentose phosphate pathway, in fructose and mannose metabolism, in glycolysis/gluconeogenesis, and in insulin signaling pathway that regulates carbohydrate metabolism and endocrine systems. The pentose phosphate pathway is a glucose metabolism process that produces reduced Nicotinamide Adenine Dinucleotide Phosphate and pentoses, which is an essential part of histidine and purine/pyrimidine biosynthesis nucleotides. Glycolysis/gluconeogenesis is the process of converting glucose to pyruvate and producing small amounts of ATP (energy) and NADH (reducing power). FBPs ultimately control the rate of gluconeogenesis, whereas the insulin signaling pathway is responsible for regulation of glucose and lipid metabolism, besides many other functions such as regulation of cell proliferation in response to mitogens. Src homology 2 domain containing-transforming protein 2 (SHC2), as a substrate of insulin receptor, can activate the RAS/MAPK pathway independently of IRS-1 (Taha and Klip, 1999; Ferguson et al., 2014). Of the ten genes enriched in the aforementioned pathways, FBP1, FBP2, SHC3, FANCC and PTCH1 were located on the 41.2 to 43.3 region of chromosome Z, which might be integrally chained due to selected certain particular genes, with FBP1 and FBP2 being the most likely objectives and the others likely being jointly selected. Within the selective sweeps in all of the domestic chickens in the present and other studies (Rubin et al., 2010), some of the genes were also found to be associated with domestication traits in chickens and other farmed animals, which reinforced their important roles in chicken domestication. For instance, BCDO2 was found to be associated with the yellow skin (Eriksson et al., 2008). However, this gene in GX-TYC was not detected. ESRP2 is associated with chicken abdominal fat contents (Zhang et al., 2012), and NELL1 was identified in a selective sweep in the broilers (Elferink et al., 2012). In the present study, NELL1 gene was found to undergo a strong selection in GX-TYC, which verified GX-TYC as a broiler, thus conforming to the long-term breeding purpose of GX-TYC and confirming that the present approach and the resulting data were reliable.

CONCLUSION

In summary, herein a whole genome map of Single nucleotide polymorphisms (SNPs), insertion/deletion polymorphisms (InDels) of Guangxi Three-Yellow chicken **(**GX-TYC) were presented and some genetic footprints of its domestication were uncovered. These data provide important resources for further improvements of fowl breeding and for future studies on the molecular mechanisms of chicken phenotypic variations and certain diseases.

DECLARATIONS

Consent to publish

All authors agree to publish this manuscript.

Availability of data and materials

All data have been presented in the manuscript as figures and tables and as the supplementary data. There is no additional data and materials.

Competing interests

All authors claim that there is no completing interest concerned.

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Authors' contributions

YL drafted the manuscript. YL and DJL formulated the concepts. JS, YH, FW and GM analyzed the data and prepared the figures and tables. LZ performed English editing of the manuscript. DJL finalized the manuscript.

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REFERENCES

Andersson L (2001). Genetic dissection of phenotypic diversity in farm animals. Nature Reviews Genetics, 2: 130-138. DOI: http://www.doi.org/10.1038/35052563

Atsumi T, Singh R, Sabharwal L, Bando H, Meng J, Arima Y, Yamada M, Harada M, Jiang JJ, Kamimura D et al. (2014). Inflammation amplifier, a new paradigm in cancer biology. Cancer Research, 74: 8-14. DOI: http://www.doi.org/ 10.1158/0008-5472.CAN-13-2322

Bakker ST, Van de Vrugt HJ, Visser JA, Delzenne-Goette E, Van der Wal A, Berns MA, Van V, Oostra AB, de VS, Kramer P et al. (2012). Fancf-deficient mice are prone to develop ovarian tumours. The Journal of Pathology, 226: 28-39. DOI: https://doi.org/10.1002/path.2992

Bokui N, Otani T, Igarashi K, Kaku J, Oda M, Nagaoka T, Seno M, Tatematsu K, Okajima T, Matsuzaki T, Ting K, Tanizawa K Kuroda S et al. (2008). Involvement of MAPK signaling molecules and Runx2 in the NELL1-induced osteoblastic differentiation. FEBS Letters, 582: 365-371. DOI:https://doi.org/10.1016/j.febslet.2007.12.006

Carpenter D, Stone DM, Brush J, Ryan A, Armanini M, Frantz G, Rosenthal A and de Sauvage FJ (1998). Characterization of two patched receptors for the vertebrate hedgehog protein family. Proceedings of the National Academy of Sciences of the United States of America, 95: 13630-13634. DOI:https://doi.org/10.1073/pnas.95.23.13630.

Del SG, Collavin L, Ruaro ME, Edomi P, Saccone S, Valle GD and Schneider C (1994). Structure, function, and chromosome mapping of the growth-suppressing human homologue of the murine gas1 gene. Proceedings of the National Academy of Sciences of the United States of America, 91: 1848-1852. DOI:https://doi.org/10.1073/pnas.91.5.1848.

Del SG, Ruaro ME, Philipson L and Schneider C (1992). The growth arrest-specific gene, gas1, is involved in growth suppression. Cell, 70: 595-607. DOI:https://doi.org/10.1016/0092-8674(92)90429-g..

Elferink MG, Megens HJ, Vereijken A, Hu X, Crooijmans RP and Groenen MA (2012). Signatures of selection in the genomes of commercial and non-commercial chicken breeds. PLoS One, 7:e32720. DOI:https://doi.org/: 10.1371/journal.pone.0032720

Eriksson J, Larson G, Gunnarsson U, Bed'hom B, Tixier-Boichard M, Stromstedt L, Wright D, Jungerius A, Vereijken A, Randi E et al. (2008). Identification of the yellow skin gene reveals a hybrid origin of the domestic chicken. PLoS Genetics, 4:e1000010. DOI: https://doi.org.10.1371/journal.pgen.1000010..

Fan WL, Ng CS, Chen CF, Lu MY, Chen YH, Liu CJ, Wu SM, Chen CK, Chen JJ, Mao CT et al. (2013). Genome-wide patterns of genetic variation in two domestic chickens. Genome Biology and Evolution, 5:1376-1392. DOI:https://doi.org.10.1093/gbe/evt097.

Fay JC and Wu CI (2000). Hitchhiking under positive Darwinian selection. Genetics, 155:1405-1413. DOI:https://doi.org.10,1002/1098-2272(200007)19:1<81::AID-GEPI6>3.0.CO;2-8.

Ferguson MC, Garland EM, Hedges L, Womack-Nunley B, Hamid R, Phillips JA, III, Shibao CA, Raj SR, Biaggioni I and Robertson D (2014). SHC2 gene copy number in multiple system atrophy (MSA). Clinical Autonomic Research, 24: 25-30. DOI:https://doi.org.10.1007/s10286-013-0216-8.

Fu YX (1997). Statistical tests of neutrality of mutations against population growth, hitchhiking and background selection. Genetics, 147: 915-925. PMID:9335623.

Fu YX and Li WH (1993). Statistical tests of neutrality of mutations. Genetics, 133: 693-709. PMID:8454210.

Huang dW, Sherman BT and Lempicki RA (2009). Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. Nature Protocols, 4: 44-57. DOI:https://doi.org.10.1038/nprot.2008.211.

Kaplan NL, Hudson RR and Langley CH (1989). The "hitchhiking effect" revisited. Genetics, 123: 887-899. DOI:https://doi.org.10.1101/gad.3.12b.2218.

Kim Y and Nielsen R (2004). Linkage disequilibrium as a signature of selective sweeps. Genetics, 167: 1513-1524. DOI:https://doi.org.10.1534/genetics.103.025387.

Kim Y and Stephan W (2002). Detecting a local signature of genetic hitchhiking along a recombining chromosome. Genetics, 160: 765-777. DOI:https://doi.org.10.3410/f.1008369.104907.

Leveille F, Blom E, Medhurst AL, Bier P, Laghmani EH, Johnson M, Rooimans MA, Sobeck A, Waisfisz Q, Arwert F et al. (2004). The Fanconi anemia gene product FANCF is a flexible adaptor protein. the Journal of Biological Chemistry, 279: 39421-39430. DOI:https://doi.org.10.1074/jbc.M407034200.

Lewontin RC and Krakauer J (1973). Distribution of gene frequency as a test of the theory of the selective neutrality of polymorphisms. Genetics, 74:175-195. PMID:4711903.

Li H and Durbin R (2009). Fast and accurate short read alignment with Burrows-Wheeler transform. Bioinformatics, 25: 1754-1760. DOI:https://doi.org.10. 1093/bioinformatics/btp324.

Li S, Zhou X, Zhang N, Liu H and Ma C (2008). Purification and characterisation of cathepsin L2 from dorsal muscle of silver carp (Hypophthalmichthys molitrix). Food Chemistry, 111: 879-886. DOI:https://doi.org.10. 1016/j.foodchem.2008.04.072.

Li WH, Wu CI and Luo CC (1985). A new method for estimating synonymous and nonsynonymous rates of nucleotide substitution considering the relative likelihood of nucleotide and codon changes.

Molecular Biology and Evolution, 2: 150-174. DOI:https://doi.org.10. 1093/oxfordjournals.molbev.a040343.

Lin WD, Wang CH, Lai CC, Tsai Y, Wu JY, Chen CP and Tsai FJ (2009). Molecular analysis of Taiwanese patients with 3-hydroxy-3-methylglutaryl CoA lyase deficiency. Clinica Chimica Acta, 401: 33-36. DOI:https://doi.org.10.1016/j.cca.2008.11.004.

Mack M, Schniegler-Mattox U, Peters V, Hoffmann GF, Liesert M, Buckel W and Zschocke J (2006). Biochemical characterization of human 3-methylglutaconyl-CoA hydratase and its role in leucine metabolism. The FEBS Journal, 273: 2012-2022. DOI:https://doi.org.10. 1111/j.1742-4658.2006.05218.x.

McDonald JH and Kreitman M (1991). Adaptive protein evolution at the Adh locus in Drosophila. Nature, 351: 652-654. DOI:https://doi.org.10.1038/351652a0.

Medhurst AL, Huber PA, Waisfisz Q, de Winter JP and Mathew CG (2001). Direct interactions of the five known Fanconi anaemia proteins suggest a common functional pathway. Human Molecular Genetics, 10: 423-429. DOI:https://doi.org.10.1093/hmg/10.4.423.

Nalepa G and Clapp DW (2018). Fanconi anaemia and cancer: an intricate relationship. Nature Reviews Cancer 18: 168-185. DOI:https://doi.org.10.1038/nrc.2017.116.

Nepal M, Che R, Zhang J, Ma C and Fei P (2017). Fanconi Anemia Signaling and Cancer. Trends in Cancer, 3: 840-856. DOI:https://doi.org.10.1016/j.trecan.2017.10.005.

Pavlidis P, Jensen JD, Stephan W and Stamatakis A (2012). A critical assessment of storytelling: gene ontology categories and the importance of validating genomic scans. Molecular Biology and Evolution, 29: 3237-3248. DOI:https://doi.org.10.1093/molbev/mss136.

Pollinger JP, Bustamante CD, Fledel-Alon A, Schmutz S, Gray MM and Wayne RK (2005). Selective sweep mapping of genes with large phenotypic effects. Genome Research, 15: 1809-1819. DOI:https://doi.org.10.1101/gr.4374505.

Rubin CJ, Megens HJ, Martinez BA, Maqbool K, Sayyab S, Schwochow D, Wang C, Carlborg O, Jern P, Jorgensen CB et. al. (2012). Strong signatures of selection in the domestic pig genome. Proceedings of the National Academy of Sciences of the United States of America, 109: 19529-19536. DOI:https://doi.org.10.1073/pnas.1217149109.

Rubin CJ, Zody MC, Eriksson J, Meadows JR, Sherwood E, Webster MT, Jiang L, Ingman M, Sharpe T, Ka S et al. (2010). Whole-genome resequencing reveals loci under selection during chicken domestication. Nature, 464: 587-591. DOI:https://doi.org.10.1038/nature08832.

Sabeti PC, Reich DE, Higgins JM, Levine HZ, Richter DJ, Schaffner SF, Gabriel SB, Platko JV, Patterson NJ, McDonald GJ et al. (2002). Detecting recent positive selection in the human genome from haplotype structure. Nature, 419: 832-837. DOI:https://doi.org.10.1038/nature01140.

Smith JM and Haigh J (2007). The hitch-hiking effect of a favourable gene. Genetical Research, 89: 391-403. DOI:https://doi.org.10.1017/S0016672308009579.

Taha C and Klip A (1999). The insulin signaling pathway. The Journal of Membrane Biology, 169: 1-12. DOI:https://doi.org.10.1007/pl00005896.

Tajima F (1989). Statistical method for testing the neutral mutation hypothesis by DNA polymorphism. Genetics, 123:585-595. PMID:2513255.

Tsui V and Crismani W (2019). The Fanconi Anemia Pathway and Fertility. Trends in Genetics, 35: 199-214. DOI:https://doi.org.10.1016/j.tig.2018.12.007.

Villavicencio EH, Walterhouse DO and Iannaccone PM (2000). The sonic hedgehog-patched-gli pathway in human development and disease. American Journal of Human Genetics, 67: 1047-1054. DOI:https://doi.org.10.1016/S0002-9297(07)62934-6.

Wang K, Li M and Hakonarson H (2010). ANNOVAR: functional annotation of genetic variants from high-throughput sequencing data. Nucleic Acids Research, 38: e164. DOI:https://doi.org.10.1093/nar/gkq603.

Wei FY, Wu Q, Deng JX, Yang FJ, Chen X, Chen JP and Zhu CS (2019). The breeding and industrialization of San yellow chicken in Guangxi. Poultry Husbandry and Disease Control, 5: 10-25. Available at: https://kns.cnki.net/KCMS/detail/detail.aspx?dbcode=CJFQ&dbname=CJFDLAST2020&filename=YQYF201905004&v=MDg4NDR1eFlTN0RoMVQzcVRyV00xRnJDVVI3cWZZT1JwRnlqbFZyckFQRHpTYUxHNEg5ak1xbzlGWUlSOGVYMUw=.

Wong GK, Liu B, Wang J, Zhang Y, Yang X, Zhang Z, Meng Q, Zhou J, Li D, Zhang J et al. (2004). A genetic variation map for chicken with 2.8 million single-nucleotide polymorphisms. Nature, 432: 717-722. DOI:https://doi.org.10.1038/nature03156.

Zhang H, Hu X, Wang Z, Zhang Y, Wang S, Wang N, Ma L, Leng L, Wang S, Wang Q et. al. (2012). Selection signature analysis implicates the PC1/PCSK1 region for chicken abdominal fat content. PLoS One, 7: e40736. DOI:https://doi.org.10.1371/journal.pone.0040736.

Zheng PL, Zhang ZG, Chen XH, Tu YR, Cheng ST, Xu ZY,Chen LF, Zhang SY, Li G, Yu DX et. al. (1989). Poultry Breeds in China.

Zhou H, Deeb N, Evock-Clover CM, Mitchell AD, Ashwell CM and Lamont SJ (2007). Genome-wide linkage analysis to identify chromosomal regions affecting phenotypic traits in the chicken. III. Skeletal integrity. Poultry Science, 86: 255-266. DOI:https://doi.org/10.1093/ps/86.2.255.

Supplementary Data

Supplementary Table 1. Summary and annotation of single nucleotide polymorphisms in Guangxi three-yellow chickens

Category		Number of SNPs
Upstream		140,563
Exonic	Stop gain	291
	Stop loss	47
	Synonymous	88,687
	Non-synonymous	36,707
	Unknowns	0
Intronic		3,938,603
Splicing		387
Downstream		122,273
Upstream/downstream		5,004
Intergenic		5,806,581
Total		10,139,143

Supplementary Table 2. Summary and annotation of Indels in Guangxi three-yellow chickens

Category		Number of Indels
Upstream		10632
Exonic	Stop gain	13
	Stop loss	3
	Frameshift deletion	413
	Frameshift insertion	512
	Non-frameshift deletion	377
	Non-frameshift insertion	295
Intronic		335096
Splicing		175
Downstream		11948
Upstream/Downstream		418
Intergenic		482323
Insertion		380249
Deletion		461987
Het Rate (%)		0.643
Total		842236

Supplementary Table 3. Detail information of single nucleotide polymorphisms loci with ZHp ≤ -5

Ensembl Gene ID	ZHp	CHROM	Start	Gene
ENSGALG00000003958	-11.572	5	2129860	PRMT3
ENSGALG00000003908	-17.158	5	2204843	SLC6A5
ENSGALG00000003777	-17.158	5	2243366	NELL1
ENSGALG00000003748	-9.0503	5	2760128	ANO5
ENSGALG00000003660	-10.144	5	2946165	FANCF
ENSGALG00000003655	-10.144	5	2976276	GAS2
ENSGALG00000003648	-6.1477	5	3060193	SVIP
ENSGALG00000013311	-6.9695	5	3278760	ANO3
ENSGALG00000013304	-11.351	5	3407884	SLC5A12
ENSGALG00000023904	-11.351	5	3505528	FIBIN
ENSGALG00000013297	-11.351	5	3530348	BBOX1
ENSGALG00000012194	-10.236	5	3627318	CCDC34
ENSGALG00000012191	-8.6053	5	3651822	LGR4
ENSGALG00000012170	-8.6053	5	3717817	LIN7B
ENSGALG00000012163	-8.6053	5	3757392	BDNF
ENSGALG00000012162	-8.6053	5	3783967	Novel
ENSGALG00000012160	-8.137	5	3878424	KIF18A
ENSGALG00000012153	-5.0344	5	3921314	METTL15
ENSGALG00000004112		23	5552378	FUCA1
ENSGALG00000004120		23	5558027	CNR2
ENSGALG00000003971		23	5518731	TCEB3
ENSGALG00000004002		23	5540404	LYPLA2
ENSGALG00000004047		23	5545884	GALE
ENSGALG00000003936	-5.0735	23	5514567	PPT1
ENSGALG00000004268		23	5696766	NIPAL3
ENSGALG00000004155		23	5586447	MYOM3
ENSGALG00000003879		23	5493121	MFSD2A
ENSGALG00000004141		23	5581470	LBFABP
ENSGALG00000004057		23	5548630	HMGCL

ENSGALG00000004122		23	5565578	PNRC2
ENSGALG00000004249		23	5643857	GRHL3
ENSGALG00000003986		23	5536714	PITHD1
ENSGALG00000004133		23	5572421	SRSF10
ENSGALG00000004231		23	5625795	IFNLR1
ENSGALG00000004221		23	5618293	IL22RA1
ENSGALG00000003912		23	5502015	CAP1
ENSGALG00000017658	-6.8264	Z	40920596	GAS1
ENSGALG00000026583	-6.8264	Z	40920611	Novel
ENSGALG00000012608	-14.043	Z	41139762	DAPK1
ENSGALG00000012610	-14.043	Z	41267496	CTSL2
ENSGALG00000012612	-14.043	Z	41282076	FBP2
ENSGALG00000012613	-14.043	Z	41306732	FBP1
ENSGALG00000012615	-7.1684	Z	41350384	C9orf3
ENSGALG00000012618	-7.1684	Z	41521328	FANCC
ENSGALG00000012620	-6.5791	Z	41632373	PTCH1
ENSGALG00000010683	-5.8349	Z	43300329	S1PR3
ENSGALG00000010688	-5.8349	Z	43311888	SHC3
ENSGALG00000010694	-5.8349	Z	43414992	SECISBP2
ENSGALG00000010697	-5.8349	Z	43446316	SEMA4D
ENSGALG00000005323	-5.1417	Z	43855798	DIRAS2
ENSGALG00000015216	-5.1608	Z	43939409	SYK
ENSGALG00000015213	-5.1608	Z	43980705	TPPP2
ENSGALG00000021843	-6.6507	Z	44067508	AUH
ENSGALG00000015209	-6.683	Z	44205924	NFIL3
ENSGALG00000000151	-7.1704	Z	45148296	ADAMTS19

Supplementary Table 4. Gene functional enrichment analysis of genes significant selection in Guangxi three-yellow chickens

GO_accession	Term_type	Description	N	P Value
GO:0042132	MF	fructose 1,6-bisphosphate 1-phosphatase activity	2	9.74E-06
GO:0046942	BP	carboxylic acid transport	5	1.72E-04
GO:0015849	BP	organic acid transport	5	1.77E-04
GO:0050308	MF	sugar-phosphatase activity	2	4.43E-04
GO:0019203	MF	carbohydrate phosphatase activity	2	5.40E-04
GO:0015711	BP	organic anion transport	5	6.52E-04
GO:0019318	BP	hexose metabolic process	4	7.37E-04
GO:0071944	CC	cell periphery	17	7.53E-04
GO:0006820	BP	anion transport	6	8.51E-04
GO:0005996	BP	monosaccharide metabolic process	4	1.12E-03
GO:0005886	CC	plasma membrane	16	1.48E-03
GO:0015718	BP	monocarboxylic acid transport	3	2.05E-03
GO:0001657	BP	ureteric bud development	3	2.60E-03
GO:0007270	BP	neuron-neuron synaptic transmission	3	2.65E-03
GO:0072163	BP	mesonephric epithelium development	3	2.69E-03
GO:0072164	BP	mesonephric tubule development	3	2.69E-03
GO:0006952	BP	defense response	7	2.71E-03
GO:0004490	MF	methylglutaconyl-CoA hydratase activity	1	3.15E-03
GO:0010157	BP	response to chlorate	1	3.15E-03
GO:0016434	MF	rRNA (cytosine) methyltransferase activity	1	3.15E-03
GO:0036335	BP	intestinal stem cell homeostasis	1	3.15E-03
GO:0071424	MF	rRNA (cytosine-N4-)-methyltransferase activity	1	3.15E-03
GO:0070463	MF	tubulin-dependent ATPase activity	1	3.15E-03
GO:1901550	BP	regulation of endothelial cell development	1	3.15E-03
GO:1901551	BP	negative regulation of endothelial cell development	1	3.15E-03
GO:1903140	BP	regulation of establishment of endothelial barrier	1	3.15E-03
GO:1903141	BP	negative regulation of establishment of endothelial barrier	1	3.15E-03
GO:0005294	MF	neutral L-amino acid secondary active transmembrane transporter activity	1	3.15E-03
GO:0015375	MF	glycine:sodium symporter activity	1	3.15E-03
GO:0036233	BP	glycine import	1	3.15E-03
GO:1990379	BP	lipid transport across blood brain barrier	1	3.20E-03
GO:0001823	BP	mesonephros development	3	3.21E-03
GO:0046854	BP	phosphatidylinositol phosphorylation	2	3.51E-03
GO:0032002	CC	interleukin-28 receptor complex	1	3.54E-03
GO:0046834	BP	lipid phosphorylation	2	4.02E-03
GO:0050747	BP	positive regulation of lipoprotein metabolic process	1	4.18E-03
GO:1903061	BP	positive regulation of protein lipidation	1	4.18E-03
GO:0006836	BP	neurotransmitter transport	3	4.30E-03
GO:0005548	MF	phospholipid transporter activity	2	4.53E-03
GO:0003978	MF	UDP-glucose 4-epimerase activity	1	4.53E-03
GO:0005169	MF	neurotrophin TRKB receptor binding	1	5.14E-03
GO:0061193	BP	taste bud development	1	5.14E-03

GO:0045668	BP	negative regulation of osteoblast differentiation	2	5.15E-03
GO:0061005	BP	cell differentiation involved in kidney development	2	5.53E-03
GO:0051234	BP	establishment of localization	18	5.94E-03
GO:0021997	BP	neural plate axis specification	1	6.29E-03
GO:0097108	MF	hedgehog family protein binding	1	6.29E-03
GO:2001013	BP	epithelial cell proliferation involved in renal tubule morphogenesis	1	6.29E-03
GO:0010693	BP	negative regulation of alkaline phosphatase activity	1	6.29E-03
GO:1900220	BP	semaphorin-plexin signaling pathway involved in bone trabecula morphogenesis	1	6.29E-03
GO:0071226	BP	cellular response to molecule of fungal origin	1	6.29E-03
GO:0004300	MF	enoyl-CoA hydratase activity	1	6.29E-03
GO:0060995	BP	cell-cell signaling involved in kidney development	1	6.29E-03
GO:0061289	BP	Wnt signaling pathway involved in kidney development	1	6.29E-03
GO:0061290	BP	canonical Wnt signaling pathway involved in metanephric kidney development	1	6.29E-03
GO:0072204	BP	cell-cell signaling involved in metanephros development	1	6.29E-03
GO:0045329	BP	carnitine biosynthetic process	1	6.29E-03
GO:0005119	MF	smoothened binding	1	6.31E-03
GO:0005901	CC	caveola	2	6.33E-03
GO:0015908	BP	fatty acid transport	2	6.35E-03
GO:0045121	CC	membrane raft	3	6.51E-03
GO:0072073	BP	kidney epithelium development	3	6.53E-03
GO:0044853	CC	plasma membrane raft	2	6.67E-03
GO:0004560	MF	alpha-L-fucosidase activity	1	6.72E-03
GO:0006004	BP	fucose metabolic process	1	6.72E-03
GO:0015928	MF	fucosidase activity	1	6.72E-03
GO:0015850	BP	organic hydroxy compound transport	3	6.81E-03
GO:0008474	MF	palmitoyl-(protein) hydrolase activity	1	6.91E-03
GO:0098599	MF	palmitoyl hydrolase activity	1	6.91E-03
GO:0007042	BP	lysosomal lumen acidification	1	7.03E-03
GO:1903070	BP	negative regulation of ER-associated ubiquitin-dependent protein catabolic process	1	7.32E-03
GO:1903059	BP	regulation of protein lipidation	1	7.32E-03
GO:0070475	BP	rRNA base methylation	1	7.66E-03
GO:0019388	BP	galactose catabolic process	1	7.67E-03
GO:0016049	BP	cell growth	4	7.89E-03
GO:0004888	MF	transmembrane signaling receptor activity	7	7.92E-03
GO:0046717	BP	acid secretion	2	7.98E-03
GO:0032229	BP	negative regulation of synaptic transmission, GABAergic	1	8.42E-03
GO:0007166	BP	cell surface receptor signaling pathway	13	8.58E-03
GO:0007267	BP	cell-cell signaling	6	8.83E-03
GO:0044425	CC	membrane part	19	8.87E-03
GO:0007611	BP	learning or memory	3	9.03E-03
GO:0060012	BP	synaptic transmission, glycinergic	1	9.42E-03
GO:0008469	MF	histone-arginine N-methyltransferase activity	1	9.42E-03
GO:0019919	BP	peptidyl-arginine methylation, to asymmetrical-dimethyl arginine	1	9.42E-03

GO:0035242	MF	protein-arginine omega-N asymmetric methyltransferase activity	1	9.42E-03
GO:0035247	BP	peptidyl-arginine omega-N-methylation	1	9.42E-03
GO:0045602	BP	negative regulation of endothelial cell differentiation	1	9.42E-03
GO:0097025	CC	MPP7-DLG1-LIN7 complex	1	9.42E-03
GO:0002238	BP	response to molecule of fungal origin	1	9.42E-03
GO:0097016	MF	L27 domain binding	1	9.42E-03
GO:0009957	BP	epidermal cell fate specification	1	9.44E-03
GO:0002351	BP	serotonin production involved in inflammatory response	1	9.48E-03
GO:0002442	BP	serotonin secretion involved in inflammatory response	1	9.48E-03
GO:0002554	BP	serotonin secretion by platelet	1	9.48E-03
GO:0006578	BP	amino-acid betaine biosynthetic process	1	9.49E-03
GO:0045926	BP	negative regulation of growth	3	9.54E-03
GO:0006094	BP	gluconeogenesis	2	9.60E-03
GO:0042806	MF	fucose binding	1	9.87E-03
GO:0042015	MF	interleukin-20 binding	1	9.96E-03
GO:0048549	BP	positive regulation of pinocytosis	1	1.00E-02
GO:0002084	BP	protein depalmitoylation	1	1.00E-02
GO:0098734	BP	macromolecule depalmitoylation	1	1.00E-02
GO:0006810	BP	transport	17	1.01E-02
GO:0035751	BP	regulation of lysosomal lumen pH	1	1.02E-02
GO:0040007	BP	growth	6	1.04E-02
GO:0031324	BP	negative regulation of cellular metabolic process	10	1.04E-02
GO:2000027	BP	regulation of organ morphogenesis	3	1.07E-02
GO:1903069	BP	regulation of ER-associated ubiquitin-dependent protein catabolic process	1	1.09E-02
GO:0090237	BP	regulation of arachidonic acid secretion	1	1.10E-02
GO:0071286	BP	cellular response to magnesium ion	1	1.10E-02
GO:0004419	MF	hydroxymethylglutaryl-CoA lyase activity	1	1.12E-02
GO:0016833	MF	oxo-acid-lyase activity	1	1.12E-02
GO:0019319	BP	hexose biosynthetic process	2	1.14E-02
GO:0032429	BP	regulation of phospholipase A2 activity	1	1.19E-02
GO:0007412	BP	axon target recognition	1	1.21E-02
GO:0008589	BP	regulation of smoothened signaling pathway	2	1.25E-02
GO:0043313	BP	regulation of neutrophil degranulation	1	1.25E-02
GO:1902563	BP	regulation of neutrophil activation	1	1.25E-02
GO:0016273	MF	arginine N-methyltransferase activity	1	1.25E-02
GO:0016274	MF	protein-arginine N-methyltransferase activity	1	1.25E-02
GO:0035246	BP	peptidyl-arginine N-methylation	1	1.25E-02
GO:0005828	CC	kinetochore microtubule	1	1.25E-02
GO:0017128	MF	phospholipid scramblase activity	1	1.25E-02
GO:0061588	BP	calcium activated phospholipid scrambling	1	1.25E-02
GO:0061590	BP	calcium activated phosphatidylcholine scrambling	1	1.25E-02
GO:0061591	BP	calcium activated galactosylceramide scrambling	1	1.25E-02
GO:0030279	BP	negative regulation of ossification	2	1.25E-02
GO:0008170	MF	N-methyltransferase activity	2	1.27E-02

GO:0034969	BP	histone arginine methylation	1	1.29E-02
GO:0050890	BP	cognition	3	1.29E-02
GO:0032009	CC	early phagosome	1	1.30E-02
GO:0001658	BP	branching involved in ureteric bud morphogenesis	2	1.30E-02
GO:0006002	BP	fructose 6-phosphate metabolic process	1	1.31E-02
GO:0046364	BP	monosaccharide biosynthetic process	2	1.31E-02
GO:0004949	MF	cannabinoid receptor activity	1	1.32E-02
GO:0038023	MF	signaling receptor activity	7	1.35E-02
GO:0000835	CC	ER ubiquitin ligase complex	1	1.36E-02
GO:0000836	CC	Hrd1p ubiquitin ligase complex	1	1.36E-02
GO:0005113	MF	patched binding	1	1.37E-02
GO:0015187	MF	glycine transmembrane transporter activity	1	1.38E-02
GO:0048511	BP	rhythmic process	3	1.39E-02
GO:0019320	BP	hexose catabolic process	1	1.39E-02
GO:0046849	BP	bone remodeling	2	1.41E-02
GO:0031982	CC	vesicle	14	1.42E-02
GO:0071345	BP	cellular response to cytokine stimulus	4	1.42E-02
GO:0001649	BP	osteoblast differentiation	3	1.47E-02
GO:0060675	BP	ureteric bud morphogenesis	2	1.53E-02
GO:0007406	BP	negative regulation of neuroblast proliferation	1	1.53E-02
GO:0005319	MF	lipid transporter activity	2	1.54E-02
GO:0015293	MF	symporter activity	2	1.55E-02
GO:0097484	BP	dendrite extension	1	1.56E-02
GO:0032368	BP	regulation of lipid transport	2	1.57E-02
GO:0010692	BP	regulation of alkaline phosphatase activity	1	1.57E-02
GO:0016051	BP	carbohydrate biosynthetic process	3	1.58E-02
GO:0071702	BP	organic substance transport	10	1.58E-02
GO:0030812	BP	negative regulation of nucleotide catabolic process	1	1.59E-02
GO:0045820	BP	negative regulation of glycolytic process	1	1.59E-02
GO:0051195	BP	negative regulation of cofactor metabolic process	1	1.59E-02
GO:0051198	BP	negative regulation of coenzyme metabolic process	1	1.59E-02
GO:0072171	BP	mesonephric tubule morphogenesis	2	1.60E-02
GO:0018216	BP	peptidyl-arginine methylation	1	1.60E-02
GO:0006869	BP	lipid transport	3	1.61E-02
GO:0042159	BP	lipoprotein catabolic process	1	1.63E-02
GO:0048548	BP	regulation of pinocytosis	1	1.64E-02
GO:0015816	BP	glycine transport	1	1.69E-02
GO:0016208	MF	AMP binding	1	1.71E-02
GO:0072203	BP	cell proliferation involved in metanephros development	1	1.71E-02
GO:0045056	BP	transcytosis	1	1.73E-02
GO:0032026	BP	response to magnesium ion	1	1.73E-02
GO:0006811	BP	ion transport	8	1.74E-02
GO:0016139	BP	glycoside catabolic process	1	1.76E-02
GO:0060896	BP	neural plate pattern specification	1	1.77E-02

GO:0044724	BP	single-organism carbohydrate catabolic process	2	1.77E-02
GO:0038036	MF	sphingosine-1-phosphate receptor activity	1	1.79E-02
GO:0010629	BP	negative regulation of gene expression	7	1.80E-02
GO:0044723	BP	single-organism carbohydrate metabolic process	5	1.89E-02
GO:0001820	BP	serotonin secretion	1	1.92E-02
GO:0033008	BP	positive regulation of mast cell activation involved in immune response	1	1.93E-02
GO:0043306	BP	positive regulation of mast cell degranulation	1	1.93E-02
GO:0032928	BP	regulation of superoxide anion generation	1	1.94E-02
GO:0016052	BP	carbohydrate catabolic process	2	1.95E-02
GO:0038171	BP	cannabinoid signaling pathway	1	1.97E-02
GO:0009892	BP	negative regulation of metabolic process	10	1.97E-02
GO:0072078	BP	nephron tubule morphogenesis	2	1.98E-02
GO:0032940	BP	secretion by cell	5	2.00E-02
GO:0034097	BP	response to cytokine	4	2.01E-02
GO:0017121	BP	phospholipid scrambling	1	2.02E-02
GO:0072088	BP	nephron epithelium morphogenesis	2	2.04E-02
GO:0061333	BP	renal tubule morphogenesis	2	2.09E-02
GO:0000153	CC	cytoplasmic ubiquitin ligase complex	1	2.09E-02
GO:0098542	BP	defense response to other organism	3	2.09E-02
GO:0072028	BP	nephron morphogenesis	2	2.10E-02
GO:0016137	BP	glycoside metabolic process	1	2.11E-02
GO:0046365	BP	monosaccharide catabolic process	1	2.11E-02
GO:0007269	BP	neurotransmitter secretion	2	2.12E-02
GO:0005167	MF	neurotrophin TRK receptor binding	1	2.13E-02
GO:0002281	BP	macrophage activation involved in immune response	1	2.18E-02
GO:0046668	BP	regulation of retinal cell programmed cell death	1	2.19E-02
GO:0009437	BP	carnitine metabolic process	1	2.20E-02
GO:0051010	MF	microtubule plus-end binding	1	2.21E-02
GO:0002576	BP	platelet degranulation	1	2.22E-02
GO:0008509	MF	anion transmembrane transporter activity	3	2.23E-02
GO:0033005	BP	positive regulation of mast cell activation	1	2.24E-02
GO:0017075	MF	syntaxin-1 binding	1	2.25E-02
GO:0072282	BP	metanephric nephron tubule morphogenesis	1	2.26E-02
GO:0001558	BP	regulation of cell growth	3	2.27E-02
GO:0050746	BP	regulation of lipoprotein metabolic process	1	2.28E-02
GO:0016857	MF	racemase and epimerase activity, acting on carbohydrates and derivatives	1	2.28E-02
GO:0010876	BP	lipid localization	3	2.30E-02
GO:0010605	BP	negative regulation of macromolecule metabolic process	9	2.32E-02
GO:0007035	BP	vacuolar acidification	1	2.33E-02
GO:0003376	BP	sphingosine-1-phosphate signaling pathway	1	2.41E-02
GO:0005283	MF	sodium:amino acid symporter activity	1	2.49E-02
GO:0005229	MF	intracellular calcium activated chloride channel activity	1	2.50E-02
GO:0004896	MF	cytokine receptor activity	2	2.51E-02
GO:0006577	BP	amino-acid betaine metabolic process	1	2.52E-02

GO:0018195	BP	peptidyl-arginine modification	1	2.55E-02
GO:0002888	BP	positive regulation of myeloid leukocyte mediated immunity	1	2.56E-02
GO:0031988	CC	membrane-bounded vesicle	13	2.58E-02
GO:0040008	BP	regulation of growth	4	2.62E-02
GO:0002009	BP	morphogenesis of an epithelium	4	2.64E-02
GO:0001656	BP	metanephros development	2	2.65E-02
GO:0015129	MF	lactate transmembrane transporter activity	1	2.67E-02
GO:0015727	BP	lactate transport	1	2.67E-02
GO:0035873	BP	lactate transmembrane transport	1	2.67E-02
GO:0031430	CC	M band	1	2.68E-02
GO:0014047	BP	glutamate secretion	1	2.69E-02
GO:0043090	BP	amino acid import	1	2.71E-02
GO:0043092	BP	L-amino acid import	1	2.71E-02
GO:0090520	BP	sphingolipid mediated signaling pathway	1	2.72E-02
GO:0072080	BP	nephron tubule development	2	2.75E-02
GO:0042157	BP	lipoprotein metabolic process	2	2.77E-02
GO:0002251	BP	organ or tissue specific immune response	1	2.79E-02
GO:0002385	BP	mucosal immune response	1	2.79E-02
GO:0032303	BP	regulation of icosanoid secretion	1	2.81E-02
GO:0060856	BP	establishment of blood-brain barrier	1	2.81E-02
GO:0045978	BP	negative regulation of nucleoside metabolic process	1	2.83E-02
GO:0006837	BP	serotonin transport	1	2.85E-02
GO:0019370	BP	leukotriene biosynthetic process	1	2.86E-02
GO:0048588	BP	developmental cell growth	2	2.86E-02
GO:0045125	MF	bioactive lipid receptor activity	1	2.86E-02
GO:0043302	BP	positive regulation of leukocyte degranulation	1	2.86E-02
GO:0006865	BP	amino acid transport	2	2.87E-02
GO:0072173	BP	metanephric tubule morphogenesis	1	2.88E-02
GO:2000310	BP	regulation of N-methyl-D-aspartate selective glutamate receptor activity	1	2.88E-02
GO:0046666	BP	retinal cell programmed cell death	1	2.90E-02
GO:0001843	BP	neural tube closure	2	2.90E-02
GO:0001822	BP	kidney development	3	2.91E-02
GO:0030856	BP	regulation of epithelial cell differentiation	2	2.92E-02
GO:0005165	MF	neurotrophin receptor binding	1	2.94E-02
GO:0060606	BP	tube closure	2	2.96E-02
GO:0060993	BP	kidney morphogenesis	2	2.99E-02
GO:0061029	BP	eyelid development in camera-type eye	1	2.99E-02
GO:0061326	BP	renal tubule development	2	3.01E-02
GO:0006012	BP	galactose metabolic process	1	3.01E-02
GO:0032269	BP	negative regulation of cellular protein metabolic process	5	3.01E-02
GO:0046903	BP	secretion	5	3.01E-02
GO:0031330	BP	negative regulation of cellular catabolic process	2	3.03E-02
GO:0010875	BP	positive regulation of cholesterol efflux	1	3.06E-02
GO:0043240	CC	Fanconi anaemia nuclear complex	1	3.06E-02

GO:0048589	BP	developmental growth	4	3.08E-02
GO:0008150	BP	biological_process	46	3.09E-02
GO:0008649	MF	rRNA methyltransferase activity	1	3.10E-02
GO:0060831	BP	smoothened signaling pathway involved in dorsal/ventral neural tube patterning	1	3.11E-02
GO:0044459	CC	plasma membrane part	8	3.12E-02
GO:0090330	BP	regulation of platelet aggregation	1	3.12E-02
GO:0040015	BP	negative regulation of multicellular organism growth	1	3.13E-02
GO:0004872	MF	receptor activity	7	3.14E-02
GO:0048672	BP	positive regulation of collateral sprouting	1	3.17E-02
GO:0014020	BP	primary neural tube formation	2	3.19E-02
GO:0002283	BP	neutrophil activation involved in immune response	1	3.19E-02
GO:0043312	BP	neutrophil degranulation	1	3.19E-02
GO:0016021	CC	integral component of membrane	14	3.23E-02
GO:0005416	MF	cation:amino acid symporter activity	1	3.23E-02
GO:0045667	BP	regulation of osteoblast differentiation	2	3.24E-02
GO:0008757	MF	S-adenosylmethionine-dependent methyltransferase activity	2	3.25E-02
GO:0045579	BP	positive regulation of B cell differentiation	1	3.27E-02
GO:1902578	BP	single-organism localization	14	3.28E-02
GO:0042742	BP	defense response to bacterium	2	3.28E-02
GO:0006907	BP	pinocytosis	1	3.32E-02
GO:0060080	BP	regulation of inhibitory postsynaptic membrane potential	1	3.32E-02
GO:0016192	BP	vesicle-mediated transport	6	3.33E-02
GO:0072001	BP	renal system development	3	3.35E-02
GO:0001840	BP	neural plate development	1	3.37E-02
GO:0048025	BP	negative regulation of mRNA splicing, via spliceosome	1	3.38E-02
GO:0061430	BP	bone trabecula morphogenesis	1	3.41E-02
GO:0043524	BP	negative regulation of neuron apoptotic process	2	3.42E-02
GO:0060429	BP	epithelium development	6	3.44E-02
GO:1903307	BP	positive regulation of regulated secretory pathway	1	3.48E-02
GO:0044712	BP	single-organism catabolic process	5	3.48E-02
GO:0048771	BP	tissue remodeling	2	3.49E-02
GO:0006691	BP	leukotriene metabolic process	1	3.49E-02
GO:0043586	BP	tongue development	1	3.51E-02
GO:0030308	BP	negative regulation of cell growth	2	3.52E-02
GO:0072009	BP	nephron epithelium development	2	3.52E-02
GO:0072661	BP	protein targeting to plasma membrane	1	3.56E-02
GO:0048523	BP	negative regulation of cellular process	14	3.58E-02
GO:0090322	BP	regulation of superoxide metabolic process	1	3.59E-02
GO:0046488	BP	phosphatidylinositol metabolic process	2	3.60E-02
GO:0034122	BP	negative regulation of toll-like receptor signaling pathway	1	3.61E-02
GO:0008574	MF	ATP-dependent microtubule motor activity, plus-end-directed	1	3.64E-02
GO:0031224	CC	intrinsic component of membrane	14	3.65E-02
GO:0016500	MF	protein-hormone receptor activity	1	3.67E-02
GO:0032373	BP	positive regulation of sterol transport	1	3.67E-02

GO:0032376	BP	positive regulation of cholesterol transport	1	3.67E-02
GO:0046943	MF	carboxylic acid transmembrane transporter activity	2	3.78E-02
GO:0072111	BP	cell proliferation involved in kidney development	1	3.78E-02
GO:1900449	BP	regulation of glutamate receptor signaling pathway	1	3.80E-02
GO:0050482	BP	arachidonic acid secretion	1	3.80E-02
GO:1903963	BP	arachidonate transport	1	3.80E-02
GO:0050829	BP	defense response to Gram-negative bacterium	1	3.80E-02
GO:2000191	BP	regulation of fatty acid transport	1	3.82E-02
GO:0045934	BP	negative regulation of nucleobase-containing compound metabolic process	6	3.83E-02
GO:0005342	MF	organic acid transmembrane transporter activity	2	3.85E-02
GO:0090179	BP	planar cell polarity pathway involved in neural tube closure	1	3.85E-02
GO:0001505	BP	regulation of neurotransmitter levels	2	3.85E-02
GO:0050691	BP	regulation of defense response to virus by host	1	3.85E-02
GO:0060627	BP	regulation of vesicle-mediated transport	3	3.85E-02
GO:0006629	BP	lipid metabolic process	6	3.86E-02
GO:0016854	MF	racemase and epimerase activity	1	3.87E-02
GO:0001841	BP	neural tube formation	2	3.87E-02
GO:0045780	BP	positive regulation of bone resorption	1	3.88E-02
GO:0046852	BP	positive regulation of bone remodeling	1	3.88E-02
GO:0051248	BP	negative regulation of protein metabolic process	5	3.91E-02
GO:0072202	BP	cell differentiation involved in metanephros development	1	3.95E-02
GO:0046641	BP	positive regulation of alpha-beta T cell proliferation	1	3.99E-02
GO:0005975	BP	carbohydrate metabolic process	5	4.00E-02
GO:0045601	BP	regulation of endothelial cell differentiation	1	4.01E-02
GO:0051172	BP	negative regulation of nitrogen compound metabolic process	6	4.04E-02
GO:0060628	BP	regulation of ER to Golgi vesicle-mediated transport	1	4.05E-02
GO:0072224	BP	metanephric glomerulus development	1	4.07E-02
GO:0043304	BP	regulation of mast cell degranulation	1	4.11E-02
GO:0090178	BP	regulation of establishment of planar polarity involved in neural tube closure	1	4.15E-02
GO:0031167	BP	rRNA methylation	1	4.18E-02
GO:0007398	BP	ectoderm development	1	4.18E-02
GO:0007224	BP	smoothened signaling pathway	2	4.21E-02
GO:0044765	BP	single-organism transport	13	4.24E-02
GO:0061436	BP	establishment of skin barrier	1	4.24E-02
GO:0007625	BP	grooming behavior	1	4.24E-02
GO:0072330	BP	monocarboxylic acid biosynthetic process	2	4.25E-02
GO:0060037	BP	pharyngeal system development	1	4.25E-02
GO:0031672	CC	A band	1	4.29E-02
GO:0070062	CC	extracellular exosome	11	4.29E-02
GO:1903561	CC	extracellular vesicle	11	4.29E-02
GO:1901215	BP	negative regulation of neuron death	2	4.29E-02
GO:0043931	BP	ossification involved in bone maturation	1	4.30E-02
GO:0070977	BP	bone maturation	1	4.30E-02
GO:0043230	CC	extracellular organelle	11	4.30E-02

GO:0065010	CC	extracellular membrane-bounded organelle	11	4.30E-02
GO:0008158	MF	hedgehog receptor activity	1	4.31E-02
GO:0045087	BP	innate immune response	3	4.38E-02
GO:0033006	BP	regulation of mast cell activation involved in immune response	1	4.42E-02
GO:0051649	BP	establishment of localization in cell	9	4.42E-02
GO:0031579	BP	membrane raft organization	1	4.45E-02
GO:0000154	BP	rRNA modification	1	4.48E-02
GO:0090177	BP	establishment of planar polarity involved in neural tube closure	1	4.51E-02
GO:0033561	BP	regulation of water loss via skin	1	4.54E-02
GO:0033119	BP	negative regulation of RNA splicing	1	4.55E-02
GO:0008514	MF	organic anion transmembrane transporter activity	2	4.56E-02
GO:0006006	BP	glucose metabolic process	2	4.56E-02
GO:0009895	BP	negative regulation of catabolic process	2	4.57E-02
GO:0015095	MF	magnesium ion transmembrane transporter activity	1	4.57E-02
GO:0004871	MF	signal transducer activity	7	4.58E-02
GO:0003854	MF	3-beta-hydroxy-delta5-steroid dehydrogenase activity	1	4.62E-02
GO:0072006	BP	nephron development	2	4.62E-02
GO:2000647	BP	negative regulation of stem cell proliferation	1	4.67E-02
GO:0001655	BP	urogenital system development	3	4.67E-02
GO:0051181	BP	cofactor transport	1	4.70E-02
GO:0060562	BP	epithelial tube morphogenesis	3	4.70E-02
GO:0007623	BP	circadian rhythm	2	4.71E-02
GO:0015693	BP	magnesium ion transport	1	4.73E-02
GO:2000178	BP	negative regulation of neural precursor cell proliferation	1	4.75E-02
GO:0016358	BP	dendrite development	2	4.76E-02
GO:0010874	BP	regulation of cholesterol efflux	1	4.78E-02
GO:0034105	BP	positive regulation of tissue remodeling	1	4.79E-02
GO:0042249	BP	establishment of planar polarity of embryonic epithelium	1	4.81E-02
GO:0004683	MF	calmodulin-dependent protein kinase activity	1	4.82E-02
GO:0044700	BP	single organism signaling	18	4.85E-02
GO:0048670	BP	regulation of collateral sprouting	1	4.85E-02
GO:0033630	BP	positive regulation of cell adhesion mediated by integrin	1	4.85E-02
GO:0032228	BP	regulation of synaptic transmission, GABAergic	1	4.86E-02
GO:0000184	BP	nuclear-transcribed mRNA catabolic process, nonsense-mediated decay	1	4.87E-02
GO:0002446	BP	neutrophil mediated immunity	1	4.88E-02
GO:0023052	BP	signaling	18	4.90E-02
GO:0042554	BP	superoxide anion generation	1	4.94E-02
GO:0008038	BP	neuron recognition	1	4.95E-02
GO:0009620	BP	response to fungus	1	5.03E-02
GO:0071526	BP	semaphorin-plexin signaling pathway	1	5.05E-02
GO:0005215	MF	transporter activity	7	5.07E-02
GO:0006110	BP	regulation of glycolytic process	1	5.08E-02

N: The enrichment number of genes; MF: molecular function; BP: biological process; CC: cellular component

Supplementary Table 5. KEGG pathway analysis of genes showing significant selection in TY chickens

Term	ID	Input number	Background number	P-Value	Hyperlink
Hedgehog signaling pathway	gga04340	3	45	1.78E-03	http://www.genome.jp/kegg-bin/show_pathway?gga04340/gga:770168%09red/gga:395806%09red
Pentose phosphate pathway	gga00030	2	21	5.90E-03	http://www.genome.jp/kegg-bin/show_pathway?gga00030/gga:395218%09red/gga:395217%09red
Fructose and mannose metabolism	gga00051	2	32	1.26E-02	http://www.genome.jp/kegg-bin/show_pathway?gga00051/gga:395218%09red/gga:395217%09red
Valine, leucine and isoleucine degradation	gga00280	2	41	1.97E-02	http://www.genome.jp/kegg-bin/show_pathway?gga00280/gga:396316%09red/gga:427269%09red
Insulin signaling pathway	gga04910	3	118	2.29E-02	http://www.genome.jp/kegg-bin/show_pathway?gga04910/gga:431265%09red/gga:395218%09red/gga:395217%09red
Fanconi anemia pathway	gga03460	2	48	2.62E-02	http://www.genome.jp/kegg-bin/show_pathway?gga03460/gga:427468%09red/gga:101750641%09red
Glycolysis / Gluconeogenesis	gga00010	2	50	2.82E-02	http://www.genome.jp/kegg-bin/show_pathway?gga00010/gga:395218%09red/gga:395217%09red
Synthesis and degradation of ketone bodies	gga00072	1	9	4.93E-02	http://www.genome.jp/kegg-bin/show_pathway?gga00072/gga:396316%09red
Carbon metabolism	gga01200	2	90	7.84E-02	http://www.genome.jp/kegg-bin/show_pathway?gga01200/gga:395218%09red/gga:395217%09red
Other glycan degradation	gga00511	1	18	9.17E-02	http://www.genome.jp/kegg-bin/show_pathway?gga00511/gga:419687%09red
Fatty acid elongation	gga00062	1	20	1.01E-01	http://www.genome.jp/kegg-bin/show_pathway?gga00062/gga:419681%09red
Lysosome	gga04142	2	107	1.05E-01	http://www.genome.jp/kegg-bin/show_pathway?gga04142/gga:419681%09red/gga:427466%09red
Butanoate metabolism	gga00650	1	23	1.14E-01	http://www.genome.jp/kegg-bin/show_pathway?gga00650/gga:396316%09red
Jak-STAT signaling pathway	gga04630	2	125	1.34E-01	http://www.genome.jp/kegg-bin/show_pathway?gga04630/gga:419692%09red/gga:419694%09red
Galactose metabolism	gga00052	1	32	1.54E-01	http://www.genome.jp/kegg-bin/show_pathway?gga00052/gga:419686%09red
Fatty acid metabolism	gga01212	1	42	1.96E-01	http://www.genome.jp/kegg-bin/show_pathway?gga01212/gga:419681%09red
Amino sugar and nucleotide sugar metabolism	gga00520	1	44	2.04E-01	http://www.genome.jp/kegg-bin/show_pathway?gga00520/gga:419686%09red
Cytokine-cytokine receptor interaction	gga04060	2	165	2.06E-01	http://www.genome.jp/kegg-bin/show_pathway?gga04060/gga:419692%09red/gga:419694%09red
Lysine degradation	gga00310	1	45	2.08E-01	http://www.genome.jp/kegg-bin/show_pathway?gga00310/gga:426932%09red
Peroxisome	gga04146	1	74	3.17E-01	http://www.genome.jp/kegg-bin/show_pathway?gga04146/gga:396316%09red
ErbB signaling pathway	gga04012	1	77	3.27E-01	http://www.genome.jp/kegg-bin/show_pathway?gga04012/gga:431265%09red
Glycerophospholipid metabolism	gga00564	1	86	3.57E-01	http://www.genome.jp/kegg-bin/show_pathway?gga00564/gga:419685%09red
Neuroactive ligand-receptor interaction	gga04080	2	261	3.85E-01	http://www.genome.jp/kegg-bin/show_pathway?gga04080/gga:431264%09red/gga:428232%09red
Spliceosome	gga03040	1	105	4.17E-01	http://www.genome.jp/kegg-bin/show_pathway?gga03040/gga:419689%09red
Metabolic pathways	gga01100	6	1049	4.44E-01	http://www.genome.jp/kegg-bin/show_pathway?gga01100/gga:395217%09red/gga:419681%09red/gga:395218%09red/gga:419686%09red/gga:427269%09red/gga:396316%09red
Phagosome	gga04145	1	127	4.79E-01	http://www.genome.jp/kegg-bin/show_pathway?gga04145/gga:427466%09red
Protein processing in endoplasmic reticulum	gga04141	1	146	5.27E-01	http://www.genome.jp/kegg-bin/show_pathway?gga04141/gga:771022%09red
Focal adhesion	gga04510	1	184	6.11E-01	http://www.genome.jp/kegg-bin/show_pathway?gga04510/gga:431265%09red
MAPK signaling pathway	gga04010	1	214	6.67E-01	http://www.genome.jp/kegg-bin/show_pathway?gga04010/gga:396186%09red