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 (ZH) 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. I

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, Huaxiang, 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 28
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 (nMAJ and nMIN) were determined, and then the corresponding heterozygosity score were calculated using the following formula: \[ H_p = \frac{2 \sum n_{MAJ} \sum n_{MIN} / (\sum n_{MAJ} + \sum n_{MIN})^2}{\text{ }} \] Individual \( H_p \) was then \( Z \)-transformed to a standard normal distribution as follows: \[ \text{ZH}_p = (H_p - \mu H_p) / \sigma H_p \] A threshold of \( \text{ZH}_p \leq -5 \) 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).
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 homozygosiy (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
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 musculoskeletal 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 protease, 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°C, 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.
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. Hedgehog 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 | Hedgehog signaling pathway                | GAS1, Novel, PTCH1       | 1.78E-03  |
| Carbohydrate metabolism | Pentose phosphate pathway                   | FBP1, FBP2               | 5.90E-03  |
|                  | Gga 00030                                     |                          |           |
|                  | Gga 00051                                     | FBP1, FBP2               | 1.26E-02  |
|                  | Gga 00010                                     | FBP1, FBP2               | 2.82E-02  |
| Amino acid metabolism | Valine, leucine and isoleucine degradation | HMGCL, AUH              | 1.97E-02  |
| Organismal systems-Endocrine systems | Insulin signaling pathway                  | FBP1, FBP2, SHC2         | 2.29E-02  |
|                  | Gga 04910                                     |                          |           |
| Genetic information processing | Fanconi anemia pathway             | FANCF, FANCC             | 2.62E-02  |
|                  | Gga 03460                                     |                          |           |
| Lipid metabolism | 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 stopped 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 FANCF/FANCG 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 led 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. ESRR2 is associated with chicken abdominal fat contents (Zhang et al., 2012), and NELL1 was identified in a selective sweep in the broilers (Ellerink 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 competing 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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**Supplementary Data**

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

| Category | Number of SNPs |
|----------|----------------|
| Upstream | 140,563 |
| Stop gain | 291 |
| Stop loss | 47 |
| Exonic | |
| 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 |
| Stop gain | 13 |
| Stop loss | 3 |
| Frameshift deletion | 413 |
| Exonic | |
| 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   |
| ENSGALG000000013311      | -6.9695 | 5     | 3278760 | ANO3   |
| ENSGALG000000013304      | -11.351 | 5     | 3407884 | SLC5A12|
| ENSGALG000000023904      | -11.351 | 5     | 3505528 | FIBIN  |
| ENSGALG000000013297      | -11.351 | 5     | 3530348 | BBOX1  |
| ENSGALG000000012194      | -10.236 | 5     | 3627318 | CCDC34 |
| ENSGALG000000012191      | -8.6053 | 5     | 3651822 | LGR4   |
| ENSGALG000000012170      | -8.6053 | 5     | 3717817 | LIN7B  |
| ENSGALG000000012163      | -8.6053 | 5     | 3757392 | BDNF   |
| ENSGALG000000012162      | -8.6053 | 5     | 3783967 | Novel  |
| ENSGALG000000012160      | -8.137  | 5     | 3878424 | KIF18A |
| ENSGALG000000012153      | -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 |
| Gene Symbol | ENSGALG000000000 | Chromosome | Position | Description |
|-------------|------------------|------------|----------|-------------|
| PNRC2       | ENSGALG00000004122 | 23         | 5565578  |             |
| GRHL3       | ENSGALG00000004249 | 23         | 5643857  |             |
| PITHD1      | ENSGALG00000003986 | 23         | 5536714  |             |
| SRSF10      | ENSGALG00000004133 | 23         | 5572421  |             |
| IFNLR1      | ENSGALG00000004231 | 23         | 5625795  |             |
| IL22RA1     | ENSGALG00000004221 | 23         | 5618293  |             |
| CAP1        | ENSGALG00000003912 | 23         | 5502015  |             |
| GAS1        | ENSGALG000000017658 | -6.8264    | Z        | 40920596    |
| Novel       | ENSGALG000000026583 | -6.8264    | Z        | 40920611    |
| DAPK1       | ENSGALG000000012608 | -14.043    | Z        | 41139762    |
| CTSL2       | ENSGALG000000012610 | -14.043    | Z        | 41267496    |
| FBP2        | ENSGALG000000012612 | -14.043    | Z        | 41282076    |
| FBP1        | ENSGALG000000012613 | -14.043    | Z        | 41306732    |
| C9orf3      | ENSGALG000000012615 | -7.1684    | Z        | 41350384    |
| FANCC       | ENSGALG000000012618 | -7.1684    | Z        | 41521328    |
| PTCH1       | ENSGALG000000012620 | -6.5791    | Z        | 41632373    |
| S1PR3       | ENSGALG000000010683 | -5.8349    | Z        | 43300329    |
| SHC3        | ENSGALG000000010688 | -5.8349    | Z        | 43311888    |
| SECISBP2    | ENSGALG000000010694 | -5.8349    | Z        | 43414992    |
| SEMA4D      | ENSGALG000000010697 | -5.8349    | Z        | 43446316    |
| DIRAS2      | ENSGALG000000005323 | -5.1417    | Z        | 43855798    |
| SYK         | ENSGALG000000015216 | -5.1608    | Z        | 43939409    |
| TPPP2       | ENSGALG000000015213 | -5.1608    | Z        | 43980705    |
| AUH         | ENSGALG000000021843 | -6.6507    | Z        | 44067508    |
| NFI3        | ENSGALG000000015209 | -6.683     | Z        | 44205924    |
| ADAMTS19    | ENSGALG00000000151  | -7.1704    | Z        | 45148296    |
**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:006820    | BP        | anion transport                                  | 6   | 8.51E-04 |
| GO:0005996   | BP        | monosaccharide metabolic process                 | 4   | 1.12E-03 |
| GO:005886    | CC        | plasma membrane                                  | 16  | 1.48E-03 |
| GO:0015718   | BP        | monocarboxylic acid transport                    | 3   | 2.05E-03 |
| GO:001657    | BP        | ureteric bud development                         | 3   | 2.60E-03 |
| GO:007270    | 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:006952    | 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:005294    | 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:006836    | BP        | neurotransmitter transport                       | 3   | 4.30E-03 |
| GO:005548    | MF        | phospholipid transporter activity                | 2   | 4.53E-03 |
| GO:003978    | MF        | UDP-glucose 4-epimerase activity                 | 1   | 4.53E-03 |
| GO:005169    | 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:004300   | 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:0098689  | MF  | palmitoyl hydrolase activity                       | 1  | 6.91E-03 |
| GO:007042   | 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:0048888  | 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:0071666  | 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, glycineric                  | 1  | 9.42E-03 |
| GO:008469   | 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:002554 | 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:200027 | 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:004419 | 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:001658 | BP | branching involved in ureteric bud morphogenesis | 2 | 1.30E-02 |
| GO:006002 | BP | fructose 6-phosphate metabolic process | 1 | 1.31E-02 |
| GO:004364 | BP | monosaccharide biosynthetic process | 2 | 1.31E-02 |
| GO:004949 | 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:0000837 | 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:0046849 | BP | hexose catabolic process | 1 | 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:005319 | 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 | peptidylarginine methylation | 1 | 1.60E-02 |
| GO:0068689 | 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:0016028 | 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:0068811 | 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:0039282 | 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:0039240 | 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:000153  | 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:007269  | 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:009437  | BP | carnitine metabolic process                  | 1 | 2.20E-02 |
| GO:0051010 | MF | microtubule plus-end binding                 | 1 | 2.21E-02 |
| GO:002576  | BP | platelet degranulation                       | 1 | 2.22E-02 |
| GO:008509  | 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:005283  | MF | sodium:amino acid symporter activity         | 1 | 2.49E-02 |
| GO:005229  | MF | intracellular calcium activated chloride channel activity | 1 | 2.50E-02 |
| GO:004896  | MF | cytokine receptor activity                   | 2 | 2.51E-02 |
| GO:006577  | BP | amino-acid betaine metabolic process         | 1 | 2.52E-02 |
| Gene Ontology ID | Category | Description                                                                 | Count | P-value |
|-----------------|----------|------------------------------------------------------------------------------|-------|---------|
| 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:002009       | BP       | morphogenesis of an epithelium                                               | 4     | 2.64E-02|
| GO:001656       | BP       | metanephrin 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:0015196      | 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:002385       | 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       | metanephrin 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:006012       | 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 anemia 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:004459   | 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   | 3.29E-02 |
| GO:0060080  | BP   | regulation of inhibitory postsynaptic membrane potential | 1   | 3.29E-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:0016224  | 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 | GO:0032376 | BP | positive regulation of cholesterol transport | 1 | 3.67E-02 |
| GO:0049643 | MF | GO:0049643 | MF | carboxylic acid transmembrane transporter activity | 2 | 3.78E-02 |
| GO:0072111 | BP | GO:0072111 | BP | cell proliferation involved in kidney development | 1 | 3.78E-02 |
| GO:1900449 | BP | GO:1900449 | BP | regulation of glutamate receptor signaling pathway | 1 | 3.80E-02 |
| GO:0050482 | BP | GO:0050482 | BP | arachidonic acid secretion | 1 | 3.80E-02 |
| GO:1903963 | BP | GO:1903963 | BP | arachidonate transport | 1 | 3.80E-02 |
| GO:0050829 | BP | GO:0050829 | BP | defense response to Gram-negative bacterium | 1 | 3.80E-02 |
| GO:2000191 | BP | GO:2000191 | BP | regulation of fatty acid transport | 1 | 3.82E-02 |
| GO:0045934 | BP | GO:0045934 | BP | negative regulation of nucleobase-containing compound metabolic process | 6 | 3.83E-02 |
| GO:0005342 | MF | GO:0005342 | MF | organic acid transmembrane transporter activity | 2 | 3.85E-02 |
| GO:0050691 | BP | GO:0050691 | BP | regulation of defense response to virus by host | 1 | 3.85E-02 |
| GO:0006629 | BP | GO:0006629 | BP | regulation of vesicle-mediated transport | 3 | 3.85E-02 |
| GO:0016854 | MF | GO:0016854 | MF | racemase and epimerase activity | 1 | 3.87E-02 |
| GO:0001841 | BP | GO:0001841 | BP | neural tube formation | 2 | 3.87E-02 |
| GO:0045780 | BP | GO:0045780 | BP | positive regulation of bone resorption | 1 | 3.88E-02 |
| GO:0046852 | BP | GO:0046852 | BP | positive regulation of bone remodeling | 1 | 3.88E-02 |
| GO:0051248 | BP | GO:0051248 | BP | negative regulation of protein metabolic process | 5 | 3.91E-02 |
| GO:0072202 | BP | GO:0072202 | BP | cell differentiation involved in metanephros development | 1 | 3.95E-02 |
| GO:0046641 | BP | GO:0046641 | BP | positive regulation of alpha-beta T cell proliferation | 1 | 3.99E-02 |
| GO:0060627 | BP | GO:0060627 | BP | regulation of endothelial cell differentiation | 1 | 3.99E-02 |
| GO:0005975 | BP | GO:0005975 | BP | carbohydrate metabolic process | 5 | 4.00E-02 |
| GO:0001505 | BP | GO:0001505 | BP | regulation of neurotransmitter levels | 2 | 4.01E-02 |
| GO:0051172 | BP | GO:0051172 | BP | regulation of mast cell degranulation | 1 | 4.11E-02 |
| GO:0057398 | BP | GO:0057398 | BP | ectoderm development | 1 | 4.18E-02 |
| GO:0007224 | BP | GO:0007224 | BP | smoothened signaling pathway | 2 | 4.21E-02 |
| GO:0044765 | BP | GO:0044765 | BP | single-organism transport | 13 | 4.24E-02 |
| GO:0060037 | BP | GO:0060037 | BP | establishment of skin barrier | 1 | 4.24E-02 |
| GO:0072330 | BP | GO:0072330 | BP | monocarboxylic acid biosynthetic process | 2 | 4.25E-02 |
| GO:0050829 | BP | GO:0050829 | BP | arachidonic acid secretion | 3 | 4.25E-02 |
| GO:0031672 | CC | GO:0031672 | CC | extracellular exosome | 11 | 4.29E-02 |
| GO:0070062 | CC | GO:0070062 | CC | extracellular exosome | 11 | 4.29E-02 |
| GO:003230 | CC | GO:003230 | 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:0008514 | MF  | organic anion transmembrane transporter activity | 2 | 4.51E-02 |
| GO:0006006 | BP  | glucose metabolic process | 2 | 4.51E-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:0033630 | BP  | positive regulation of cell adhesion mediated by integrin | 1 | 4.79E-02 |
| GO:0042497 | BP  | establishment of planar polarity of embryonic epithelium | 1 | 4.81E-02 |
| GO:0046833 | 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 cholesterol efflux | 1 | 4.70E-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:009620 | BP  | response to fungus | 1 | 5.03E-02 |
| GO:0032228 | BP  | regulation of synaptic transmission, GABAergic | 1 | 4.86E-02 |
| GO:0001843 | BP  | nuclear-transcribed mRNA catabolic process, nonsense-mediated decay | 1 | 4.87E-02 |
| GO:0002446 | BP  | neutrophil mediated immunity | 1 | 4.88E-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                      | gga00300 | 2            | 21                | 5.90E-03  | http://www.genome.jp/kegg-bin/show_pathway?gga00300/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 glycans 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 |

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