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Detection and Utility of Genetic Variation in Chinese Local Chicken Breeds

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Abstract

China has a wide variety of indigenous chicken breeds. Most of these local chicken varieties have valuable genetic features. These resources could provide valuable breeding material for the poultry industry in China and even for the rest of the world. Assessment of genetic differences of these important chicken genetic resources is an important prerequisite to establish efficient conservation and utilization. Up to now, several types of genetic variations have been identified across genomes, and the area of genetic variation in the chicken genome seems to be a rapidly growing research topic in China. These research data can also provide additional evidence for our understanding of chicken genome variation, developing molecular markers, and elucidating the association between genetic variations and phenotypes in the future. This chapter reviews the research progress of molecular genetic variation in Chinese native chicken breeds in recent years.

Keywords: SNP, INDEL, CNV, Chinese native chicken breeds

1. Introduction

In China, with its long history of animal husbandry and diversified geographical conditions, there is a wealth of chicken genetic resources with more than 107 different indigenous chicken breeds. However, many Chinese native breeds are characterized by slow growth, late maturity, and low production performance. At present, the majority of these chickens are maintained in small populations. Due to underutilization and a lack of protective measures, many favorable alleles have been lost. Most of these breeds have unique meat and/or egg qualities, disease resistant, and other useful characteristics. For example, in recent years, blue-shelled layers and

black-bone chickens have gained popularity, and their eggs generate greater profit as the consumption demand diversifies. Xichuan black-bone chicken (XC), Yunyang black-bone chicken (YY), and Silkie fowl (SY) are well-known black-bone chicken breeds, and XC and Lushi chicken (LS) are popular blue-eggshell chicken breeds in China [1]. Such indigenous breeds may contain genes and alleles pertinent to the adaptation to particular environments and local breeding goals and needs to maintain genetic resources permitting adaptation to unforeseen breeding requirements in the future and a source of research materials [2]. Therefore, a study on the genetic diversity of Chinese chicken breeds has important significance for protecting and using local breeds and resources.

As a result, identifying genetic determinants of economically important traits is one of the main focuses of chicken genetic studies, which requires a comprehensive knowledge of DNA sequence variations as well as the development of numerous informative genetic markers. The near-complete chicken genome has made it possible to systematically study genetic variations. Genetic variation takes many forms and ranges from large microscopically visible chromosome anomalies to single-nucleotide changes. Up to now, several types of genetic variations have been identified across genomes. Genetic variation can be divided into different forms according to the size and type of genomic variation underpinning genetic change. Small-scale sequence variation (<1 Kbp) includes base-pair substitution and insertion and deletion. Large-scale structural variation (>1 Kbp) can be either copy number variation (loss or gain) or chromosomal rearrangement (translocation, inversion, or segmental acquired uniparental disomy) [3]—namely, single-nucleotide polymorphism (SNP), insertion and deletion (INDEL), and copy number variations (CNV).

SNP is a variation in a single nucleotide that occurs at a specific position in the genome, where each variation is present to some appreciable degree within a population (e.g., >1%). For example, at a specific base position in the genome, the C nucleotide may appear in most individuals, but in a minority of individuals, the position is occupied by a T. This means that there is an SNP at this specific position, and the two possible nucleotide variations—C or T—are said to be alleles for this position [4].

INDEL is a molecular biology term for an insertion or deletion of bases in the genome of an organism. It is classified among small genetic variations, measuring from 1 to 10,000 base pairs in length [5]. A microindel is defined as an INDEL that results in a net change of 1–50 nucleotides [6]. In domestic animals, INDELs are also found to be responsible for a number of traits and diseases, such as double-muscle trait [7] in cattle and immotile short-tail sperm defect in pig [8]. In chicken, INDELs of 9–15 bp in PMEL17 gene are causative mutations for plumage color (dominant white, dun, and smoky) [9], and an INDEL mutation in the growth hormone receptor (GHR) gene causes sex-linked dwarfism [10]. With the rapid advance of sequencing technology, considerable progress has been made in INDEL discovery in chicken genome. Three chicken breeds were partially sequenced by capillary sequencing and 2.8 million SNPs were identified by aligning the resultant reads to the reference genome, and about 10% of these variations are actually INDELs [11]. The segregating short indels in unique sequence of the chicken genome are on average 5% as common as SNPs [12]. Recently, genome-wide INDELs in 12 Chinese diverse chickens were detected by next-generation

sequencing (NGS) and their potential influence on gene functions were examined [13]. The transcriptomic SNPs and INDELs in Chinese Gushi chickens were detected by Ribo-Zero RNA-Seq technology [14].

CNV is a type of structural variation: specifically, it is a type of duplication or deletion event that affects a considerable number of base pairs [15]. This variation accounts for roughly 12% of human genomic sequence and each variation may range from about 1 kb (1000 bp) to several megabases in size [16]. Compared with the most frequent polymorphisms of SNPs, CNVs have potentially larger effects by disrupting genes and altering gene dosage, disturbing coding sequences and perturbing long-range gene regulation [17].

Over the past decade, there were quite a few studies that have been done on CNV distribution, function, and role in disease of DNA segments in the human genome. Recently, it has been reported that there is a genome-wide presence of CNVs not only in human beings but also in domestic animals. Previous studies have discovered that CNV was responsible for phenotypic changes in chicken. Examples of phenotypes associated with a CNV in the chicken include late feathering on chromosome Z (GGAZ) [18], pea comb on GGA1 [19], dark brown plumage color on GGA1 [20], and dermal hyperpigmentation on GGA20 [21]. A total of 7.6 million SNPs and 8839 CNVs were identified in the mapped regions; hundreds of shared and divergent structural CNVs were also identified in the genomes of two breeds—Silkie and the Taiwanese native chicken —by Illumina sequencing [22].

Using different technological platforms, substantial progress has been made in identifying DNA sequence variations in chickens. Array comparative genomic hybridization (aCGH) [23], SNP array [24, 25], and next-generation sequencing [26] technologies are efficient and reliable methods for analyzing changes in DNA sequence variations.

2. Association between polymorphisms of candidate gene and economic traits in Chinese chicken breed population

2.1. Association between polymorphisms of candidate gene and economic traits in an F₂ population of Gushi chicken cross Anak chicken

In 2004–2005, Hennan Agricultural University bred an F₂ resource population from Gushi (G) chicken (24 hens and 2 roosters) and Anak (A) broilers (12 hens and 4 roosters). The F₂ population consisted of four cross families (A-roosters mated with G-hens) and three reciprocal families (G-roosters mated with A-hens). To build the F₂ population, nine F₁ females were selected from each of seven families (six unrelated rooster families and one half sib). The 63 F₁ females were mated with 7 F₁ males from 7 families. It included 42 grandparents, 70 F₁ parents, and 860 F₂ chickens. Growth traits including body weight were individually measured every 2 weeks from birth to slaughter, and body size indices including shank girth, chest depth, chest width, breastbone length, breast angle, body slanting length, and pelvis breadth were measured every 4 weeks. At the age of 84 days, 13 carcass traits were measured, such as carcass weight, semi-evisceration weight, evisceration weight, fat bandwidth, skin fat

thickness, abdominal fat weight, breast muscle weight, leg muscle weight, and so on. The meat quality traits, muscle fiber traits, and serum indices were also measured. The measuring methods have been previously described [27].

In the beginning, we mapped quantitative trait loci (QTL) associated with growth traits in this F₂ population by 19 microsatellite markers on chromosomes 8–11, and 13; for 32 growth traits, the QTL significant at the genome-wide level that affected body weight at all ages were identified on chromosome 8. The QTL related to BW at early ages were identified on chromosomes 10 and 11, only one QTL-affected body weight was located on chromosome 13 [28]. And mapped QTL associated with growth traits, carcass traits, and meat quality traits on chromosomes 1–5, 7–11, 13 [in Chinese, not shown].

Then, association study between polymorphisms of 20 candidate genes including PR domain 16 (PRDM16), visfatin, Krüppel-like factor 15 (KLF15), patatin-like phospholipase domain containing 3 (PNPLA3), the paired box 7 (Pax7), pro-melanin concentrating hormone (PMCH), thyroid peroxidase (TPO), Adiponectin Receptor 2 Gene (ADIPOR2), lncRNA-pouBW1 and lncRNA-pouMU1 (new gene found), ankyrin repeat and SOCS box-containing 15 (ASB15) gene, and so on, along with economic traits were done in the F₂ population. Meanwhile, association between SNP of eight microRNAs and production traits were studied in the F₂

Gene name	Gene symbol	Trait(s)	References
PR domain containing 16	PRDM16	Weight gain	[28]
Patatin-like phospholipase domain-containing protein 3	PNPLA3	Carcass	[31]
Pro-melanin-concentrating hormone	PMCH	Meat tenderness	[33]
Thrombopoietin	TPO	Growth and carcass	[34]
Adiponectin Receptor 2	ADIPOR2	Weight	[35]
lncRNA-pouBW1	lncRNA-pouBW1	Weight	[36]
Ankyrin repeat and SOCS box 15	ASB15	Growth and carcass	[37]
Cyclin-dependent kinase inhibitor 2A	CDKN2A	Barring	[39]
Endothelin 3	EDN3	Silky/Silkie	[40]
Sonic hedgehog	SHH	Polydactyly	[41]
Flavin-containing Monooxygenase 3	FMO3	Fishy taint	[42]
miR-1657	miR-1657	Growth and carcass	[49]
Dopamine D2 receptor	DRD2	Egg number	[52]
Vasoactive intestinal peptide receptor-1	VIPR-1	Broodiness	[53]
Growth hormone secretagogue receptor	GHSR	Growth and development	[53]
Growth hormone	GH	Growth and development	[53, 58]
Pituitary-specific transcription factor-1	PIT-1	Growth	[54]
Insulin-like growth factor I receptor	IGF1R	Growth and carcass	[55]

Table 1. SNPs of candidate genes with reported associations for chick traits.

population [27, 29–38]. The SNPs of candidate genes in the F2 population [39–45] are summarized in **Table 1**.

Among these, authors found that allele D (9-bp deletion) of the visfatin gene had a negative effect on skeletal growth, while a 31-bp deletion had a negative effect on chicken growth and carcass traits and positive effect on meat quality traits [29, 32]. The INDELs of candidate genes in chickens [46–48] are summarized in **Table 2**.

2.2. Association between polymorphisms of candidate gene and economic traits in Chinese chicken breeds

In recent years, the SNP mutation of candidate gene in Chinese local chickens was widely studied in China. For example, Xinghua chicken, Ningdu Yellow chicken, Qingyuan partridge chicken, Taihe Silkie Fowls, Kangle yellow chicken, Langshan chicken, Sichuan black-bone chicken, Erlang mountain chicken, Caoke chicken, and Tibetan chicken were used in the experiment to study the relationship between SNPs of prolactin receptor (PRLR), vasoactive intestinal peptide-receptor 1 (VIPR-1), growth hormone secretagogue receptor (GHSR), insulin-like growth factor 1 receptor (IGF1R), prolactin (PRL), pituitary-specific transcription factor (PIT1), growth hormone (GH) gene, and many other genes and chicken reproductive traits, growth traits, and fat traits by some researchers from research institutions and agricultural universities/colleges [49–57]. These studies have laid a good genetic foundation for the development and utilization of Chinese native chicken population. Due to the limitation of this chapter, we are not going into details here.

Gene name	Gene symbol	Trait(s)	References
Premelanosome protein 17	PMEL17	Dominant white	[9]
Growth hormone receptor	GHR	Dwarfism, sex-linked	[11]
Prolactin receptor	PRLR	Early/late feathering	[17]
SRY (sex determining region Y)-box 5	SOX5	Pea-comb phenotype	[18]
SRY (sex determining region Y)-box 10	SOX10	Dark brown	[19]
Visfatin	Vis	Body weight	[29]
Krüppel-like factor 15	KLF15	Growth and carcass	[30]
Paired box 7	PAX7	Growth	[32]
miR-16	miR-16	Body weight	[43]
Tyrosinase	TYR	Recessive white	[44]
Solute carrier family 45, member 2	SLC45A2	Silver Z-linked	[45]
Melanocortin 1 receptor	MC1R	Extended black	[46]
Homeodomain protein 2	MNR2	Rose comb	[47]
Solute carrier organic anion transporter family member 1B3	SLCO1B3	Blue eggshell	[48]

Table 2. INDELs of candidate genes with reported associations for chick traits.

3. Genome-wide association study of production traits in Chinese local chicken

Chicken genomics is likely to have major applications and benefits in comparative genomics, evolutionary biology and systematics, models of development and human disease, and agriculture. Genomic study is required to study genome-wide patterns of DNA variation for dissecting the genetic basis of phenotypic traits. In order to identify genes and chromosome regions associated with body weight, a genome-wide association study using the chicken 60 k SNP panel in a chicken F₂ resource population derived from the crossbreeding between Silkie Fowl and White Plymouth Rock was performed. Results showed that a chicken chromosome 4 (GGA4) region approximately 8.6 Mb in length (71.6–80.2 Mb) had a large number of significant SNP effects for late growth during weeks 7–12. The LIM domain-binding factor 2 (LDB2) gene in this region had the strongest association with body weight for weeks 7–12 and with an average daily gain for weeks 6–12. GGA1 and GGA18 had three SNP effects on body weight with genome-wide significance [58].

A total of 12 different chicken breeds including 7 Chinese indigenous chicken (Beijing You (BY), Dongxiang (DX), Luxigame (LX), Shouguang (SG), Silkie (SK), Tibetan (TB), and Wenchang (WC)) and four commercial breeds (Cornish (CS), Rhode Island Red (RIR), White Leghorn (WL), and White Plymouth Rock (WR)) were selected and the next-generation sequencing methods were applied at an average effective depth of 8.6. Over 1.3 million nonredundant short INDELs (1–49 bp) were obtained. Both the detected number and affected bases were larger for deletions than insertions. Many of them are associated with economically important traits [13].

A total of 78 domestic chickens (36 Tibetan fowls from the Qinghai-Tibet Plateau and 42 domestic fowls from Szechwan Basin) from 17 populations were sequenced to an average of 18-fold coverage for each bird. By combining these data with publicly available genomes of five wild red jungle fowls and eight Xishuangbanna game fowls, a comprehensive comparative genomics analysis of 91 chickens from 17 populations were conducted. Approximately 6.44 million (M) SNPs were identified for each population [59].

In our group, we performed genome re-sequencing identification of genetic mutations in five XC chickens with 229.73 G bp of clean data, and average genome coverage depth of all samples were over 28-fold. The reads were mapped onto the chicken reference genome to 98.73% genome coverage for the five chickens with percentages of Q30 showing >92%. The number of SNPs detected in each chicken varied from 4,998,304 to 5,127,695 in five birds, with an average of 5,062,529 (2,918,565 heterozygous and 247,054 homozygous), 1,593,603 INDELs (693,235 insertions and 900,368 deletions), and 11,437 SVs (7156 insertions and 2418 deletions) were identified in the XC chicken genome. SNPs, Small INDEL and SVs were located in 9732, 2710, and 397 genes, respectively (not public).

All the earlier-mentioned data are vital for population genetics and further studies on chickens, and they serve as a valuable resource for investigating diversifying selection and candidate genes for selective breeding in chickens.

4. Linkage and association study of appearance traits in Chinese local chicken breeds

China Agricultural University's (CAU) chicken resource population was derived using an F₂ design from reciprocal crosses between Silkie and White Plymouth Rock chickens. The Silkie is considerably different from other breeds with its feathers and black skin. The feathering is soft and downy, covering practically the whole body with the exception of the beak. Some Silkies have a crested head and are bearded and muffed. The Silkie has a bluish-black beak, black eyes, fifth toe, small wattles, and very small walnut or cushion combs. The Silkie are known to go broody and lay few eggs. Using this F₂ population, that crest phenotype of Silkie is located on the E22C19W28 linkage group, and that it shows complete association to the HOXC-cluster on this chromosome by linkage analysis and genome-wide association [60]. Other several different appearance traits have been identified and located such as pigmentation [61], rose comb [62], silky [63], Polydactyly [64], muffs, and beards [65] in Chinese Silkie chicken and other breeds.

Dongxiang chicken is from Dongxiang town, Jiangxi province of China. It is characterized by blue eggshell, single comb, and black feather. Lushi chicken is another local breed laying blue-shelled egg from Lushi town, Henan province of China. For a study on blue eggshell, Chinese indigenous blue-shelled chicken breeds and an American blue-shelled breed, Araucana, were selected to use for blue eggshell study—results indicated that the blue eggshell is caused by an Avian endogenous retrovirus elements insertion that promotes the expression of SLCO1B3 gene in the uterus (shell gland) of the oviduct in chicken, and that the insertion site in the blue-shelled chickens from Araucana is different from that in Chinese breeds [66].

In our group, using F₂ resource population of Gushi chicken and Anak broiler, we established the shank color extreme phenotype mixing pool—yellow shank DNA pooling and willow shank DNA pooling and conducted 200× deep sequencing at the 10 Mb interval with Chr. Z 67.1–72.3 Mb as the core region, on the two pools by targeted next-generation sequencing at target region. By SHOREmap and differences observed in mutation sites analysis, we mapped the inhibitor of dermal melanin (Id) gene at the interval for 71.58–72.18 Mb of chromosome Z in chicken, which reduced the interval of inhibitor of dermal melanin gene and laid the foundation for mutation of willow shank in chicken. According to the results of linkage analysis, expression of tissue, and biological information, we conclude that the CDKN2A/B gene was the candidate gene of inhibitor of dermal melanin gene in chicken (not public).

5. Identification and functional characterization of copy number variations in Chinese diverse chicken breeds

A detailed analysis of the copy number variants in locally raised 11 Chinese chicken breeds identified using CGH was presented. The 11 chicken breeds (one male and one female in each breed) used in this study were the Silkie (WJ), Tibet (ZJ), Chahua (CH), Bearded (HX), Jinhu (JH), Anak (AK), Beijing fatty (BY), Langshan (LS), Qingyuan partridge (QY), Shek-Ki (SQ),

and Wenchang (WC) varieties. A total of 833 copy number variants contained within 308 copy-number variant regions were identified. Principal component analysis and agglomerative hierarchical clustering revealed the close relation between the four locally raised chicken breeds, Shek-Ki, Langshan, Qingyuan partridge, and Wenchang [67].

In 2014, we reported a genome-wide analysis of CNVs in five chicken breeds including XC, SK, LS, GS chicken, and one French commercial breed, Houdan chicken (HD) by aCGH. A total of 281 CNVRs across the WUGSC2.1/galGal3 genome sequence was identified, while 216 (76.87%) CNVRs were reported for the first time in our study. A total of 231 genes within the identified CNVRs were retrieved from galGal4 database. Additionally, 83 CNVRs partially or completely overlapped with 143 QTLs, which involved in many important traits including growth traits, carcass traits, meat quality traits, reproductive traits, and disease-related traits. In EDN3 locus, we concluded that there were heterozygote Fmfm and homozygote Fmfm of black skin genotype in XC chicken. Then our results confirmed that this EDN3 locus may be a molecular marker to selection of skin color in poultry production [68].

Two copy number polymorphisms (CNPs) related to different traits in the genome level were identified in chickens by AccuCopy® and CNVplex® analyses. Notably, five white recessive rock (CN = 1, CN = 3) variant individuals and two Xinghua (CN = 3) variant individuals contained a CNP13 (chromosome 5: 10, 500,294–10,675,531), which overlapped with SOX6. The results of Q-PCR and knockdown of the SOX6 suggest that the number of CNVs in the CNP13 is positively associated with the expression level of SOX6 [69].

6. Conclusion

To date, many complete and partial genome-wide scans for genetic variation in Chinese local chicken have been published. Appearance trait is one of important traits due to the old Chinese diet culture, especially in chickens. In this report, analysis of linkage and association has been shown to be effective at identifying appearance traits including black skin, crest, shank color, pigmentation, rose comb, silkie, toe numbers, shank feather, muffs, and breads in Silkie chicken, Xichuan chicken, Lushi chicken, and other Chinese chicken breeds, and molecular marker of these traits have been developed and applied in the breeding programs. On the other hand, many Chinese native breeds are characterized by slow growth, late maturity, and low production performance. In terms of genetic variation and effect for these traits, genome-wide association studies (GWAS) have been deemed successful for identifying statistically associated genetic variants of large effects on complex traits. Past studies have found enrichment of trait-associated SNPs in functionally annotated regions. However, no systematic examination of connections between genomic regions and predictive ability of complex phenotypes has been carried out. Overall, although lot of efforts has been taken and a variety of assays were developed, very few of them are successfully applied in breeding and selection. The reasons are in addition to low heritabilities, the polygenic nature, and the strong environmental influences on these traits. For further research, fine mapping of QTL regions should be extended in order to narrow QTL intervals to reduce the number of positional candidate genes with regard to quantitative trait. A combination of fine mapping and candidate gene

approaches for promising chromosomal regions is a straightforward strategy. At present, whole-genome prediction methods allow predicting complex traits, irrespective of knowledge of their molecular basis. This suggests that whole-genome prediction methods are able to capture signals from the most useful genomic regions. Thus, use of all markers of genome wide seems the way to go, if interest is on prediction of complex traits.

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Conflict of interest

The author has no conflicts of interest to report.

Notes

It should be noted that there has been a large number of studies on genetic variation in Chinese native chicken population, especially on candidate gene for production traits. However, due to limited space, here, we can only introduce some of the main research content.

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