

◀ Review ▶

Genetic Mapping of Quantitative Trait Loci for Egg Production and Egg Quality Traits in Chickens: a Review

Tatsuhiko Goto^{1,2,4} and Masaaki Tsudzuki^{2,3}

¹Genetics, Ecology and Evolution, School of Life Sciences, University of Nottingham, University Park, Nottingham NG7 2RD, UK

²Japanese Avian Bioresource Project Research Center, Hiroshima University, Higashi-Hiroshima, Hiroshima 739-8528, Japan

³Graduate School of Biosphere Science, Hiroshima University, Higashi-Hiroshima, Hiroshima 739-8528, Japan

⁴Present address: Department of Life Science and Agriculture, Obihiro University of Agriculture and Veterinary Medicine, Inada-cho, Obihiro, Hokkaido 080-8555, Japan

Chickens display a wide spectrum of phenotypic variations in quantitative traits such as egg-related traits. Quantitative trait locus (QTL) analysis is a statistical method used to understand the relationship between phenotypic (trait measurements) and genotypic data (molecular markers). We have performed QTL analyses for egg-related traits using an original resource population based on the Japanese Large Game (Oh-Shamo) and the White Leghorn breeds of chickens. In this article, we summarize the results of our extensive QTL analyses for 11 and 66 traits for egg production and egg quality, respectively. We reveal that at least 30 QTL regions on 17 different chromosomes affect phenotypic variation in egg-related traits. Each locus had an age-specific effect on traits, and a variety in effects was also apparent, such as additive, dominance, and epistatic-interaction effects. Although genome-wide association study (GWAS) is suitable for gene-level resolution mapping of GWAS loci with additive effects, QTL mapping studies enable us to comprehensively understand genetic control, such as chromosomal regions, genetic contribution to phenotypic variance, mode of inheritance, and age-specificity of both common and rare alleles. QTL analyses also describe the relationship between genotypes and phenotypes in experimental populations. Accumulation of QTL information, including GWAS loci, is also useful for studies of population genomics approached without phenotypic data in order to validate the identified genomic signatures of positive selection. The combination of QTL studies and next-generation sequencing techniques with uncharacterized genetic resources will enhance current understanding of the relationship between genotypes and phenotypes in livestock animals.

Key words: chickens, egg production trait, egg quality trait, epistasis, genotype-phenotype relationship, quantitative trait loci

J. Poult. Sci., 54: 1-12, 2017

Introduction

Animals show phenotypic variation in a large number of traits (Darwin, 1868). In chickens, phenotypic variation is also seen not only in traits with Mendelian inheritance such as plumage color, but also in quantitative traits such as egg-related traits. Presently, chickens that display high egg production abilities have been developed by intensive artificial selection in the egg layer industry. In fact, the breeding

strategy of the layer industry has resulted in the current high performance commercial chickens that are used for egg production worldwide. Although significant genetic changes must occur through selective breeding, the relationship between genotypes and phenotypes is not well characterized. Quantitative trait locus (QTL) analysis (Lander and Botstein, 1989; Haley and Knott, 1992) is a statistical method used to understand the relationship between phenotypic (trait measurements) and genotypic data (molecular markers) (Miles and Wayne, 2008). In egg-production and egg-quality traits of chickens, over 890 QTLs have been reported to date and listed in the Animal QTLdb (Hu *et al.*, 2016). These studies have been conducted using several types of F₂ and/or back-cross populations based on breeds such as White Leghorn, Rhode Island Red, Cornish, and White Plymouth Rock (*e.g.*, Tuiskula-Haavisto *et al.*, 2002, 2011; Sasaki *et al.*, 2004; Hansen *et al.*, 2005). Accumulation of QTL information

Received: September 20, 2016, Accepted: October 24, 2016

Released Online Advance Publication: November 25, 2016

Correspondence: Dr. Tatsuhiko Goto, Genetics, Ecology and Evolution, School of Life Sciences, University of Nottingham, University Park, Nottingham NG7 2RD, UK. (E-mail: tatsuhiko-goto@hotmail.co.jp) and Dr. Masaaki Tsudzuki, Graduate School of Biosphere Science, Hiroshima University, Higashi-Hiroshima, Hiroshima 739-8528, Japan.

(E-mail: tsudzuki@hiroshima-u.ac.jp)

will contribute toward a holistic understanding of the relationship between genotypes and phenotypes.

Genetic analysis using original resource populations is advantageous to understand how phenotypic variation of quantitative traits is influenced by common and rare alleles in the experimental populations. It is well known that genome-wide association study (GWAS) enables GWAS loci to be specified at gene-level resolution (Ozaki *et al.*, 2002). However, GWAS usually focuses on common variants only, because genetic markers (single nucleotide polymorphisms; SNPs) that show minor allele frequencies, lower than 0.05, are generally excluded from the analysis. For QTL analysis with a segregating population, both common and rare alleles can be analyzed experimentally. In addition, QTL analysis can estimate chromosomal regions, genetic contribution to the phenotypic variance, and effects (additive, dominance, and epistatic-interaction effects) of loci in the population. These parameters are essential to understand the genotype-phenotype relationship in heterogeneous populations such as livestock animals.

In Hiroshima University, Japan, Tsudzuki (the last author of this article) and colleagues have constructed a large experimental F₂ resource population in chickens for QTL analysis. The resource population was produced by crossing males of the Japanese Large Game (Oh-Shamo) breed, known for cockfighting, with females of the White Leghorn breeds, and consists of three sub-populations: a population for growth- and meat-related traits (Tsudzuki *et al.*, 2007; Yoshida *et al.*, 2013), a population for growth- and egg-related traits (Goto *et al.*, 2011, 2014a, b), and a population for growth-related traits. Of note, the population for growth- and egg-related traits has 421 F₂ females and well-documented phenotypes that describe a wide range of egg production stages. As a result of QTL analyses, we were able to successfully detect many QTLs affecting egg production traits (Goto *et al.*, 2011), external egg traits (Goto *et al.*, 2014a), and internal egg traits (Goto *et al.*, 2014b) throughout the chicken genome. In this article, we summarized the results of our extensive QTL analyses for egg-related traits with an original resource population created with the Oh-Shamo and White Leghorn breeds of chickens. We will focus on current progress and future prospects toward the main goal of understanding the genetic architecture of quantitative traits in animals.

Resource Population (Fig. 1)

We selected Japanese Large Game (Oh-Shamo) and White Leghorn (CB strain) (Reynaud *et al.*, 1987) as parental breeds for establishing a QTL mapping resource population. It is well known in Japan that the typical cockfighting breed Oh-Shamo yields a large amount of good quality meat (Tsudzuki, 2003), whereas White Leghorn is known as a traditional layer breed and its females are able to produce many white-shelled eggs (Roberts, 1997). In addition, Oh-Shamo chickens display heavier body weights, lower growth rates, longer time to reach sexual maturity (age at the first egg), and less egg production (brownish-shelled) than White

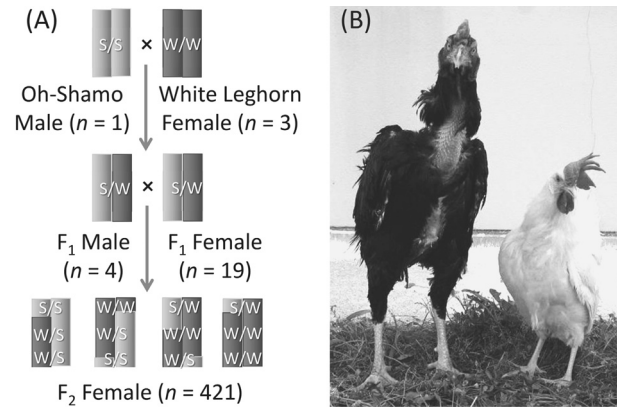


Fig. 1. **Resource population based on the Oh-Shamo and White Leghorn breeds of chickens for QTL mapping.** (A) An Oh-Shamo male was crossed to three White Leghorn females to produce F₁ offspring. F₂ females ($n = 421$) were produced by full-sib mating between four F₁ males and 19 F₁ females. Light and dark gray sections in the chromosomes of the F₂ females indicate the chromosomal fragments derived from the Oh-Shamo and White Leghorn breeds, respectively. S and W indicate the alleles derived from the Oh-Shamo and White Leghorn breeds, respectively. Segregating alleles in the F₂ individuals were confirmed by DNA marker genotyping of individuals in P, F₁, and F₂ generations. (B) An Oh-Shamo male (left) and a White Leghorn female (right). Morphological differences are obvious between the two breeds.

Leghorn chickens. The large phenotypic differences in growth-, meat-, and egg-related traits between the two breeds suggested the existence of significant phenotypic and genotypic variations in the segregating F₂ population. Furthermore, Osman *et al.* (2006) confirmed a large genetic difference between the two breeds. Therefore, it was expected before commencing QTL analyses that polymorphic genetic markers would be found easily throughout the genome, supporting QTL mapping of traits using the generated resource population.

Other resource populations for egg-related traits have been constructed by several research groups to date. Many QTL studies for egg traits have been conducted using resource populations created by crossing various breeds, including White Leghorn × Red Jungle-fowl (Kerje *et al.*, 2003; Wright *et al.*, 2006; Johnsson *et al.*, 2016), Green-legged Partridge (a native Polish breed) × Rhode Island Red (Wardeck *et al.*, 2003), White Leghorn × Rhode Island Red (Tuiskula-Haavisto *et al.*, 2002, 2004; Sasaki *et al.*, 2004; Honkatukia *et al.*, 2005, 2013), White Leghorn × Cornish (Hansen *et al.*, 2005), White Leghorn × White Plymouth Rock (Tuiskula-Haavisto *et al.*, 2011), White Leghorn × New Hampshire (Goraga *et al.*, 2012), layer × broiler (Schreiweis *et al.*, 2006; Podisi *et al.*, 2011), and layer × layer (Honkatukia *et al.*, 2011). The importance of differences in genetic backgrounds for understanding the genetic basis of quantitative traits has been discussed in the fields of

human (Chow *et al.*, 2016) and mouse genetics (Yalcin and Flint, 2012; Goto *et al.*, 2015a; Churchill, 2016). That is, because the effect of a QTL depends on its genetic background, the QTL effect on phenotypic variation can be often validated using segregating genetic material (*e.g.*, an F₂ population), but not using material with a fixed genetic background (*e.g.*, a congenic strain). Moreover, since genetically heterogeneous populations allow us to identify the effect of alleles derived from several strains (Koide *et al.*, 2012), use of these varying genetic resources will enhance our further understanding of the genotype-phenotype relationship.

Egg-related Traits (Fig. 2)

In our study, a large number of eggs were collected over the course of a year and analyzed for many traits (Goto *et al.*, 2011, 2014a, b). Egg traits are classified into three categories: egg production traits, external egg traits, and internal egg traits (Roberts, 2004). Egg production traits include the age at the first egg (AFE) and the egg production rates (EPRs). AFE is defined as the age of hens when they produce an egg for the first time, and is therefore an indicator of sexual maturity, the timing of which is quite important for chicken industry. We recorded the AFE for all hens in our resource population. EPRs are defined as the number of eggs laid per day. We calculated the EPR for 22- to 62-week old hens at every four weeks, which created a total of 10 individual traits for EPR, referred to as EPR1 (22–26 weeks of age) up to EPR10 (58–62 weeks of age). In total, we collected data for 11 egg production traits, *i.e.*, AFE and 10 EPRs (Goto *et al.*, 2011).

In addition, data for 11 kinds of external and internal egg traits were collected at three different egg production stages, namely early (E- first egg), middle (M- 300 days old), and late (L- 400 days old) stages. At the E stage, we collected 10 eggs following the first egg. At the M and L stages, we collected eggs laid during a two-week period from 300- and 400- day-old hens, respectively. External egg traits included egg weight (EW), lengths of the long and short axes of the egg (LLA and LSA, respectively), eggshell strength (SS), eggshell weight (SW), eggshell thickness of the narrow end, blunt end, and equator of the egg (STN, STB, and STE, respectively), and lightness, redness, and yellowness of the eggshell color (SCL, SCR, and SCY, respectively). Internal egg traits included albumen weight (AW), albumen height (AH), lengths of the long and short axes of the thick albumen (LTA and STA, respectively), yolk weight (YW), yolk height (YH), lengths of the long and short axes of the yolk (YL and YS, respectively), and lightness, redness, and yellowness of the yolk color (YCL, YCR, and YCY, respectively). We used 3–10 eggs per hen to analyze each egg quality trait. Mean values of the traits were calculated and treated as individual phenotypic values. In total, we collected data for 33 external and 33 internal egg traits through the E, M, and L egg production stages (Goto *et al.*, 2014a, b).

As described above, our study included analysis of a large amount of phenotypic data (24 kinds of traits; 77 traits in total), including two kinds of egg production traits (AFE and EPRs; 11 traits) in 22- to 62-week-old hens and 22 kinds of egg quality traits (EW, LLA, LSA, SS, SW, STN, STB, STE, SCL, SCR, SCY, AW, AH, LTA, STA, YW, YH, YL, YS, YCL, YCR, and YCY) during three different egg production

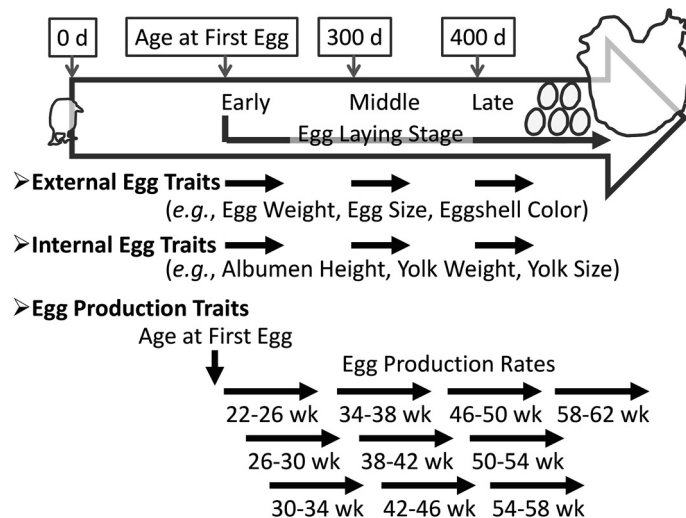


Fig. 2. **Illustration of the egg laying stage and egg-related traits investigated.** Chickens were reared over the course of a year from hatching. Eggs were inspected for external and internal traits at early (first egg age), middle (300-days-old), and late (400-days-old) egg laying stages. Egg production rates were calculated every four weeks for 22- to 62-week-old.

stages (66 traits in total). Conversely, other studies analyzed 1–2 types of egg production traits and 1–10 kinds of egg quality traits (Tuiskula-Haavisto *et al.*, 2002, 2004, 2011; Kerje *et al.*, 2003; Wardeck *et al.*, 2003; Sasaki *et al.*, 2004; Honkatukia *et al.*, 2005, 2011, 2013; Hansen *et al.*, 2005; Wright *et al.*, 2006; Schreiweis *et al.*, 2006; Goraga *et al.*, 2012; Podisi *et al.*, 2011; Johnsson *et al.*, 2016). A notable feature of our QTL studies is the large number of phenotypic traits that were characterized. In addition, a comparable study in which many kinds of egg quality traits are measured at more than three different stages of egg production does not exist. Our study facilitates a thorough understanding of age-specific genetic control of egg-related traits (Goto *et al.*, 2014a, b).

Genetic Makers and Linkage Map

We selected and genotyped 147 microsatellite DNA markers on 26 autosomes and the Z chromosome (Goto *et al.*, 2014a). The criteria for selecting markers were set as follows: (i) there are no shared alleles between an Oh-Shamo male and three White Leghorn females which are parental individuals in the F₂ resource population and (ii) markers are distributed throughout the chicken genome as widely as possible. We genotyped microsatellite markers that showed more than two base pairs difference between the two breeds by fluorescence-based DNA-fragment analysis using automated sequencers with samples from three generations (P, F₁, and F₂). Therefore, we can comprehensively trace chromosomal regions in F₂ individuals to their parental breed origins. We annotated each marker in the F₂ individuals indicating whether alleles were homozygous derived from Oh-Shamo or White Leghorn (A and B, respectively) or heterozygous (H). A linkage map was constructed using the Kosambi map function of the Map Manager QTX software (Manly *et al.*, 2001), and marker order was referred to the consensus map 2005 (Schmid *et al.*, 2005) listed in the ArkDB (<http://www.thearkdb.org/arkdb/>). The resulting map covered approximately 68% of the chicken genome with chromosomes 1–15, 17–20, 23–24, 26–28, 32, Z, and linkage group E50C23 (Goto *et al.*, 2014a).

Recently, high-density SNPs genotyping arrays were made available in chickens (Groenen *et al.*, 2011; Kranis *et al.*, 2013). Although efforts are continuing to comprehensively describe the chicken genome, the assembled sequence does not yet cover chromosomes 29–31 and 33–38 (*Gallus_gallus-4.0*; Galgal4, GCA_000002315.2) (Schmid *et al.*, 2015). Using many SNPs, GWASs for egg-related traits have been conducted by several research groups (Abasht *et al.*, 2009; Liu *et al.*, 2011; Wolc *et al.*, 2012, 2014; Yi *et al.*, 2015; Zhang *et al.*, 2015; Liao *et al.*, 2016) resulting in the identification of many GWAS loci at gene-level resolution which are accumulated in the Animal QTLdb (Hu *et al.*, 2016). Further efforts including utilization of SNPs and whole genome sequencing information with several kinds of populations are required to comprehensively understand the genotype-phenotype relationship.

QTL Analysis (Fig. 3)

QTLs are classified into two groups, namely main-effect and epistatic QTLs. Main-effect QTLs affect a trait through individual alleles (three possible genotypes: homozygous with either paternal or maternal alleles, or heterozygous with both parental alleles) at a locus. Epistatic QTLs affect a trait through allele combinations between two loci (nine possible combinations: three genotypes × three genotypes at each locus). Conceptually, it is thought that many QTLs of both types affect phenotypic variation of egg traits. QTL analyses are conducted to identify the mode-of-action, interaction, number, and precise location of the loci (Miles and Wayne, 2008).

In order to detect main-effect QTLs, we performed a simple interval mapping based on multiple regression analysis (Haley and Knott, 1992) using both phenotypic and genotypic data in the F₂ individuals. The analysis enabled us to know the parameter estimates of detected QTLs, including map position, additive effect (half the difference between two homozygotes) and dominance effect (deviation of a heterozygote from the mean of the two homozygotes) (Tsudzuki *et al.*, 2007). After genotypes of marker intervals in the F₂ individuals were imputed every 2-cM step along each chromosome (linkage group) from genotypes of flanking markers and the amount of recombination expected (Haley and Knott, 1992), trait values were regressed onto the additive and dominance scores of each position (Kenney-Hunt *et al.*, 2006). Both additive and dominance effects contribute to understanding the mode of inheritance of the locus. For this, the dominance effect/additive effect (d/a) ratio was calculated and used to determine mode of inheritance, defined as overrecessive ($d/a < -1.5$), recessive ($-1.5 < d/a < -0.5$), additive ($-0.5 < d/a < 0.5$), dominance ($0.5 < d/a < 1.5$), and overdominance ($1.5 < d/a$) (Kenney-Hunt *et al.*, 2006).

Chickens have a ZZ/ZW sex chromosome system, and therefore, female and male birds are hemizygote (ZW) and

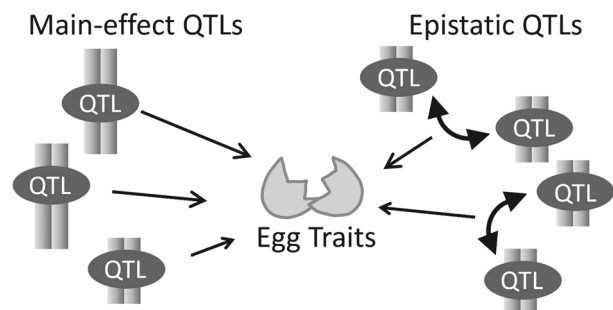


Fig. 3. **Conceptual diagram of the genetic control of quantitative traits.** QTLs are classified into two groups; main-effect QTLs and epistatic QTLs. Main-effect QTLs affect a trait through individual alleles present at a single locus. On the other hand, epistatic QTLs affect a trait through allele combinations between two loci. Conceptually, it is thought that both types of QTLs affect phenotypic variation of egg traits.

homozygote (ZZ), respectively (Smith and Burt, 1998). In our F₂ population, Oh-Shamo male (Z^{OS}Z^{OS}) and White Leghorn females (Z^{WL}W^{WL}) in the parental generation passed their sex chromosomes onto females (Z^{OS}W^{WL}) and males (Z^{OS}Z^{WL}) in the F₁ generation. By crossing F₁ females (Z^{OS}W^{WL}) and F₁ males (Z^{OS}Z^{WL}), 421 F₂ females (Z^{OS}W^{WL} and Z^{WL}W^{WL}) were produced (Goto *et al.*, 2011). Since this manner is similar to that of autosomal loci in a backcross population (F₁ × White Leghorn), the locus mode of inheritance is comparable to that in a backcross population (Rance *et al.*, 1997). Therefore, we used a backcross model (Manly *et al.*, 2001) to search QTLs for the Z chromosome.

In order to detect epistatic QTL, all pairs of marker loci were tested based on a linear regression model with a marker-by-marker interaction term and the assumption that a QTL is at a marker locus (Ishikawa *et al.*, 2005). Both the Map Manager QTX software (Manly *et al.*, 2001) and the *qtl* package (Broman *et al.*, 2003) of R software (<http://www.R-project.org/>) were used to identify both types of QTLs described above. Genome-wide significant thresholds were determined by permutation tests for taking into account multiple testing (Churchill and Doerge, 1994) for autosomes and sex chromosome separately (Broman *et al.*, 2006).

Detected QTLs for Egg-related Traits (Fig. 4)

For egg production traits, main-effect QTLs were detected in three QTL regions, with one located on chromosome 11 and two located on chromosome 1 (Goto *et al.*, 2011). For external egg traits, main-effect QTLs were found in 13 QTL regions, with one located on each of chromosomes 1, 2, 4, 8, 10, 11, 12, and 17, two located on chromosome 5, and three located on the Z chromosome (Goto *et al.*, 2014a). For internal egg traits, main-effect QTLs were discovered in 15 QTL regions, with one located on each of chromosomes 2, 3, 4, 5, 6, 7, 8, 9, 15, and 27, two located on Z chromosome, and three located on chromosome 1 (Goto *et al.*, 2014b).

Epistatic QTLs were detected for egg production and internal egg traits (Goto *et al.*, 2011, 2014b), which are classified into two types. The first epistatic QTL type was those QTLs with both main and interaction effects, shown by dark gray ellipses in Fig. 4. We found this type of loci in four QTL regions, with one located on each of chromosomes 1, 4, 8, and 10. The second epistatic QTL type was those QTLs with an interaction-effect only, shown by dark gray squares in Fig. 4. These interaction effect only loci were found in seven QTL regions, one located on each of chromosomes 7 and 19, two located on chromosome 17, and three located on chromosome 2.

These main and epistatic QTLs accounted for approximately 3–18% of the phenotypic variances (Goto *et al.*, 2011, 2014a, b). However, as described above, differences in genetic backgrounds have a large effect against the expression of quantitative traits (Yalcin and Flint, 2012; Goto *et al.*, 2015a; Chow *et al.*, 2016; Churchill, 2016). The phenotypic variances observed in our F₂ resource population are thought to be changeable under different genetic backgrounds. Thus, the effects of our QTLs should be checked

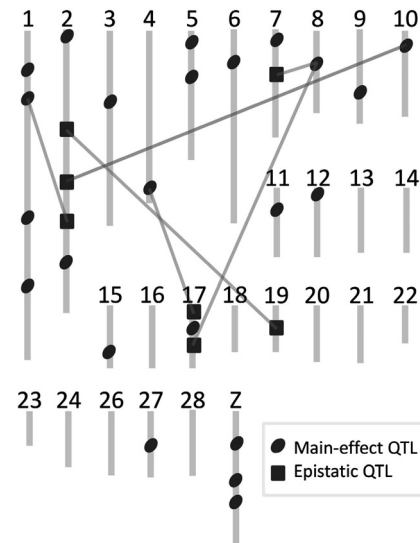


Fig. 4. Genetic network influencing phenotypic variation of egg-related traits found in the QTL studies with a single resource population. QTLs detected in our previous studies (Goto *et al.*, 2011; 2014a; 2014b) are summarized in this figure. Detailed information including QTL position, flanking markers, and mode of inheritance is summarized in Table 1. Light gray vertical lines numbered 1–24, 26–28, and Z (above) indicate chromosomes. Dark gray ellipses and squares indicate QTL regions with main and epistatic effects on egg-related traits, respectively. Light gray lines between loci indicate epistatic interactions. Based on this figure, at least 30 QTL regions on 17 different chromosomes control phenotypic variation of egg-related traits, which clearly indicates a complex genetic basis of quantitative traits.

using different genetic backgrounds prior to applying the QTLs to actual breeding.

Table 1 shows a summary of the positions, age-specificity, and mode of inheritance of QTL regions detected for egg-related traits in our resource population. Since overlapping QTL regions were described across three past studies (Goto *et al.*, 2011, 2014a, b), it seems that at least 30 QTL regions on 17 different chromosomes affect the phenotypic variation in egg-related traits (Table 1 and Fig. 4). Each locus has an age-specific effect on traits and displays various modes of inheritance including overrecessive, recessive, additive, dominance, and overdominance. Eight QTL regions (QTL2, QTL7, QTL11, QTL17, QTL20, QTL21, QTL28, and QTL30) are corresponding to several QTLs (Tuiskula-Haavisto *et al.*, 2002, 2004, 2011; Kerje *et al.*, 2003; Wardeck *et al.*, 2003; Sasaki *et al.*, 2004; Honkatukia *et al.*, 2013; Hansen *et al.*, 2005; Schreiweis *et al.*, 2006) and GWAS loci (Abasht *et al.*, 2009; Liu *et al.*, 2011; Wolc *et al.*, 2014). Especially, QTL7 on chromosome 2, QTL11 on chromosome 4, and QTL17 on chromosome 8 are similar to the GWAS loci in their positions. Comparison of the results from the two analyses may lead to narrower confident

Table 1. Summary of the positions, target traits, expression stages, and mode of inheritance of the QTLs found in our studies

| QTL no. | Chromosome | Markers (position, cM) ¹ | Trait categories ² | Traits ² | Stages of QTL expression ³ | | | d/a ⁴ | References ⁵ | | |
|---------|------------|---|-------------------------------|---------------------|---|-------------------------|---|----------------------|-------------------------------------|-------------------|-----|
| | | | | | E | M | L | | | | |
| QTL1 | 1 | Around <i>ADL0188</i> (133) | egg production | AFE EPR EPR | X X (26-30 weeks of age) X (30-34 weeks of age) | | | -1.1 -1.1 -1.3 | recessive recessive recessive | [1] [1] [1] | |
| QTL2 | 1 | <i>MCW0112</i> (205) - <i>MCW0058</i> (241) | egg production | EPR | X (54-58 weeks of age) | | | 0.7 | dominance | [1] | |
| | | | eggshell color | SCR SCY | X X | X X | | -0.4 -0.2 | additive additive | [2] [2] | |
| | | | albumen height | AH | X | X [†] | | 0.4 | dominance | [3] | |
| | | | yolk color | YCR | | X* | | - | | [3] | |
| QTL3 | 1 | Around <i>MCW0102</i> (441) - <i>ADL0245</i> (459) | albumen height | AH | X* | | | -2.3 | overrecessive | [3] | |
| QTL4 | 1 | <i>GCT0032</i> (518) - <i>MCW0107</i> (565) | yolk color | YCY | | X [†] | | 1.0 | dominance | [3] | |
| QTL5 | 2 | Around <i>LEI0124</i> (0*) | eggshell color | SCY | | X [†] | | 0.7 | dominance | [2] | |
| QTL6 | 2 | Around <i>MCW0062</i> (172) | egg production | EPR | X* | X* (42-46 weeks of age) | | - | | [1] | |
| QTL7 | 2 | Around <i>MCW0027</i> (255) | albumen height | AH | | X* | | - | | [3] | |
| QTL8 | 2 | Around <i>LEI0237</i> (320) | yolk color | YCR | | X* | | - | | [3] | |
| QTL9 | 2 | <i>LEI0070</i> (379) - <i>ADL0146</i> (403) | albumen height | AH | | X [†] | | 13.3 | overdominance | [3] | |
| QTL10 | 3 | <i>MCW0083</i> (51) - <i>ADL0229</i> (111) | yolk color | YCL | X | X | | 0.4 | 1.3 | dominance | [3] |
| QTL11 | 4 | Around <i>MCW00240</i> (201) and <i>ABR0622</i> (234*) | egg production | EPR | X* | X* (30-34 weeks of age) | | - | | [1] | |
| | | | egg weight | EW | X [†] | | | 0.4 | additive | [2] | |
| | | | eggshell color | SCR SCY | X X | | | 1.0 1.0 | dominance dominance | [2] [2] | |
| | | | albumen weight | AW | X | X | | 0.3 | 0.3 | additive | [3] |
| | | | yolk height | YH | X [†] | | | 0.5 | additive | [3] | |
| | | | yolk color | YCL | | X [†] | | 2.1 | overdominance | [3] | |
| | | | | YCY | X | X | | -0.5 | -0.1 | additive | [3] |

Table 1
(continued)

| | | | | | | | | | | |
|-------|----|--|--------------------|-----|------------------------|---|----------------|------|---------------|-----|
| QTL12 | 5 | <i>MCW0038</i> (71) - <i>MCW0214</i> (88) | eggshell thickness | STN | X [†] | X | X | 1.5 | dominance | [2] |
| QTL13 | 5 | <i>MCW0223</i> (123) - <i>ADL0233</i> (151) | eggshell color | SCL | | X | X | 0.0 | additive | [2] |
| | | | | SCR | X | X | X | -0.4 | additive | [2] |
| | | | | SCY | X | X | X | -0.2 | additive | [2] |
| | | | albumen height | AH | X | | | 3.1 | overdominance | [3] |
| QTL14 | 6 | <i>LEI0092</i> (59) - <i>LEI0196</i> (110) | albumen height | AH | X [†] | | | 0.9 | dominance | [3] |
| QTL15 | 7 | <i>MCW0120</i> (44) - <i>ABR0397</i> (50*) | yolk height | YH | X | | | 1.3 | dominance | [3] |
| QTL16 | 7 | Around <i>LEI0158</i> (122) | egg production | AFE | X* | | | - | | [1] |
| QTL17 | 8 | Around <i>MCW0305</i> (15) and <i>MCW0095</i> (26) | egg production | AFE | X* | | | - | | [1] |
| | | | egg weight | EW | X | X | X | -1.9 | overrecessive | [2] |
| | | | eggshell thickness | STN | | X | X | -7.0 | overrecessive | [2] |
| | | | | STB | | X | X | -2.0 | overrecessive | [2] |
| | | | | STE | | X | X | -0.2 | additive | [2] |
| | | | albumen weight | AW | X | X | X [†] | -3.2 | overrecessive | [3] |
| | | | albumen size | LTA | X | X | X | -1.7 | recessive | [3] |
| | | | | STA | X | X | X | -2.0 | recessive | [3] |
| | | | yolk weight | YW | X | X | X | -1.8 | recessive | [3] |
| | | | yolk height | YH | X | X | X | -2.2 | recessive | [3] |
| | | | yolk size | YL | X | X | X | -1.4 | recessive | [3] |
| | | | | YS | X | X | X, X* | -1.7 | recessive | [3] |
| | | | yolk color | YCL | X | | | 0.1 | additive | [3] |
| | | | | YCY | X | | | 0.4 | additive | [3] |
| QTL18 | 9 | Around <i>ABR0526</i> (79*) | albumen height | AH | X [†] | X | X | 0.8 | dominance | [3] |
| | | | yolk color | YCL | | | X [†] | 0.7 | dominance | [3] |
| QTL19 | 10 | <i>ADL0272</i> (44) - Around <i>ADL0106</i> (88) | egg size | LSE | X [†] | | | 0.4 | additive | [2] |
| | | | albumen height | AH | | | X* | - | | [3] |
| QTL20 | 11 | <i>ADL0210</i> (54) - <i>MCW0066</i> (69) | egg production | EPR | X (30-34 weeks of age) | | | 1.3 | dominance | [1] |
| | | | eggshell color | SCY | | X | | 0.6 | dominance | [2] |

Table 1
(continued)

| | | | | | | | | |
|-------|----|------------------------------|----------------------------------|------------|-------------------------|-------------|-----------------------|------------|
| QTL21 | 12 | Around <i>ADL0372</i> (0) | egg size | LLE LSE | X X | -0.1 0.2 | additive additive | [2] [2] |
| QTL22 | 15 | Around <i>MCW0211</i> (49) | eggshell strength yolk height | SS YH | X [†] | 1.2 -0.1 | dominance additive | [2] [3] |
| QTL23 | 17 | Around <i>ADL0293</i> (26) | eggshell thickness | STN | X | 1.5 | dominance | [2] |
| QTL24 | 17 | Around <i>ABR0530</i> (0*) | egg production | STE | X | 0.4 | additive | [2] |
| QTL25 | 17 | Around <i>ABR0387</i> (55*) | eggshell weight | EPR | X* (30-34 weeks of age) | - | additive | [1] |
| QTL26 | 19 | Around <i>ABR0180</i> (24*) | eggshell weight | SW | X [†] | -0.4 | additive | [2] |
| QTL27 | 27 | Around <i>MCW0328</i> (47) | yolk size | YS | X* | - | additive | [3] |
| QTL28 | Z | Around <i>ADL0273</i> (73) | egg production | EPR | X* (42-46 weeks of age) | - | additive | [1] |
| QTL29 | Z | Around <i>MCW0154</i> (95) | albumen size | STA | X | 0.2 | additive | [3] |
| QTL30 | Z | Around <i>ABR0119</i> (135*) | yolk color | YCL | X [†] | 0.5 | additive | [3] |
| | | | albumen height | AH | X | - | additive | [3] |
| | | | yolk height | YH | X | - | additive | [3] |
| | | | eggshell strength | SS | X | - | additive | [2] |
| | | | egg size | LLE | X | - | additive | [2] |
| | | | eggshell weight | LSE | X | - | additive | [2] |
| | | | eggshell thickness | SW | X | - | additive | [2] |
| | | | | STN | X | - | additive | [2] |
| | | | | STB | X | - | additive | [2] |
| | | | | STE | X | - | additive | [2] |
| | | | yolk weight | YW | X | - | additive | [3] |

¹ Markers close to QTL and their reference positions in the consensus map 2005 (<http://www.thearkdb.org/arkdb/>). * indicates approximate position because the marker has no reference map position.

² Traits were classified into 14 categories, i.e. egg production (AFE and EPR), egg weight (EW), egg size (LLE and LSE), eggshell weight (SW), eggshell thickness (STN, STB, and STE), eggshell strength (SS), and eggshell color (SCL, SCR, and SCV), albumen weight (AW), albumen height (AH), albumen size (LTA and STA), yolk weight (YW), yolk height (YH), yolk size (YL and YS), and yolk color (YCL, YCR, and YCY). Trait abbreviations were shown in main text of the section of egg-related traits.

³ X indicates the stage when the QTL was detected for egg-related traits. For AFE and external and internal egg traits, E=early stage (first 10 eggs), M=middle stage (during two weeks from 300 days of age), L=late stage (during two weeks from 400 days of age). For EPR, stage was shown in parentheses. * Epistatic QTL. [†] QTL at the suggestive level.

⁴ Significant QTL by a two-QTL model (Broman and Sen, 2009).

The degree of dominance calculated by the dominance effect of the QTL/the additive effect of the QTL. In the case of multiple QTLs detected in the region, the minimum and maximum values are indicated. The most likely mode of inheritance was estimated as overrecessive ($d/a < -1.5$), recessive ($-1.5 < d/a < -0.5$), additive ($-0.5 < d/a < 0.5$), dominance ($0.5 < d/a < 1.5$), and overdominance ($1.5 < d/a$) at each locus. - indicates main-effect QTL on the Z chromosome and/or epistatic QTL detected.

⁴ [1] Goto *et al.*, 2011, [2] Goto *et al.*, 2014a, [3] Goto *et al.*, 2014b.

intervals of the QTL positions. Moreover, a number of QTL regions affect egg production and external and internal egg quality traits, *e.g.*, QTL2 on chromosome 1, QTL11 on chromosome 4, and QTL17 on chromosome 8, where pleiotropic genes and/or multiples of closely linked genes are likely located. These regions, in particular QTL17 on chromosome 8 which showed the highest LOD scores, require further detailed analysis not only in the present resource population but also in other populations for a deeper understanding of the genotype-phenotype relationship.

As shown in Fig. 4, the complex genetic architecture of egg-related traits has been revealed using an experimental resource population based on the Oh-Shamo and White Leghorn breeds. Since the QTL regions found in the present study have relatively wide confidential intervals, it is likely difficult to identify the specific genes in each region. However, it seems advantageous that many loci showing variation in modes of inheritance were found. For understanding the genetic basis of quantitative traits, characterization of each kind of genetic effect described above is likely essential. Therefore, it is important to conduct not only studies at gene-level resolution such as GWAS (focusing on the additive effect) but also QTL mapping studies (focusing on additive, dominance, and epistatic-interaction effects). In addition, since phenotypic variation of quantitative traits differs with age, long-term studies focused on egg-related traits are required in future. Further efforts are necessary to understand the genotype-phenotype relationship in animals using several kinds of genetic resources and next-generation techniques such as whole genome sequencing.

Concluding Remarks

In this review article, we summarized the results of our genetic mapping studies for egg-related traits in chickens. Our original resource population created using an indigenous Japanese breed, Oh-Shamo, enabled us to reveal a large number of QTLs that contribute to phenotypic variations, and which have additive, dominance, and epistatic-interaction effects and age-specific natures. This holistic view of the genetic control of quantitative traits will prove useful for understanding the relationship between genotypes and phenotypes in livestock animals.

To date, layers and broilers created by commercial breeders have been studied intensively to understand the relationship between genotypes and phenotypes. Recent intensive artificial selection has in fact led to significant results for the production of eggs and meat, producing new lines that are strikingly different from other domestic chickens. Although these commercial resources are absolutely important, further chicken resources also offer a large potential (Tixier-Boichard *et al.*, 2009). Classical breeds of chickens maintained worldwide show a wide variety of phenotypes (Roberts, 1997) as do many indigenous breeds of chickens in Japan (Tsudzuki, 2003). For example, it has been revealed that egg characteristics of the Japanese Extremely Long Tail (Onagadori) breed are apparently different from those of the White Leghorn breed (Goto *et al.*, 2015b).

This example is only the tip of an iceberg, demonstrating that unexploited genetic resources should be thoroughly investigated in the future. In addition, free-range scavenging village chickens (Dessie *et al.*, 2011; Leroy *et al.* 2012; Desta *et al.*, 2013) also offer large potential to understand the genetic control of phenotypic diversity. Since village chickens possess a richness of accumulated recombination and a number of adaptive characteristics for extreme environments such as high temperature, they provide a useful genetic resource for high-resolution genetic mapping (Wragg *et al.*, 2012; Megens and Groenen, 2012).

Efforts are continuing to comprehensively describe the chicken genome (Schmid *et al.*, 2015). Recently, population genomics studies, which search for genetic signatures of selection in the genome (Akey, 2009), have been conducted using high density SNPs genotyping and whole genome sequencing techniques in the livestock genome (*e.g.*, Rubin *et al.*, 2010; Elferink *et al.*, 2012; Fan *et al.*, 2013; Qanbari *et al.*, 2015). This population genomics approach has allowed gene-level resolution mapping of loci that have been positively selected for, without any phenotypic information (Qanbari *et al.*, 2014). In fact, this approach can reveal a number of interesting findings, including genes that affect adaptation to local environments such as high altitude (Wang *et al.*, 2015). Most studies analyzed whether genetic signatures of selection were co-localized with QTLs listed in the Animal QTLdb (Hu *et al.*, 2016), in order to validate the signals of positive selection (*e.g.*, Zhang *et al.*, 2012; Gholami *et al.*, 2015). Since QTL mapping studies reveal more direct evidence of the relationships between certain phenotypes and DNA regions in resource populations, the integration of QTL information into the Animal QTLdb (Hu *et al.* 2016) will also be useful for researchers in the field. Using next-generation technologies and unexploited genetic resources, further efforts are required to uncover the genotype-phenotype relationship of livestock animals.

Acknowledgments

We thank the Japan Poultry Science Association for the award for promotion of scientific studies on Poultry Science for QTL mapping studies on chickens to TG. We really appreciate scientific colleagues related to the works. We thank Dr. L. M. Liao for English language editing.

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