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Overview Of Quantitative Traits Loci Associated With Egg Productivity Of Domestic Chickens.

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ABSTRACT

The project is based on the latest achievements in molecular genetics of the chickens which facilitate increasing the egg productivity of domestic selection birds. Today, modern technologies in molecular genetics used DNA markers that help to identify QTL (quantitative traits loci) associated with the egg traits. Moreover, marker assisted selection (MAS) can significantly accelerate the selection process. Identification of numerous single nucleotide polymorphisms (SNP) in animal genomes, progress in high-throughput sequencing, development of computational methods for analyzing SNP data carried out with high-density arrays made possible to use them in genomic mapping of candidate genes. The project proposes to analyze the literature data obtained by GWAS to select QTLs and candidate genes that have effect on egg productivity for creating a system of QTLs responsible for the egg production of laying hens. We summarizes putative QTLs and candidate genes that responsible for performance traits of laying hens, such as egg production, elastic deformation of the eggshell strength, eggshell thickness.

Keywords: QTL (loci of quantitative traits), SNP(single-nucleotide polymorphism), hens, egg quality, egg shell, egg laying rate.

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INTRODUTION

In many countries over the past decades the egg hens crosses obtained by conventional breeding programs significantly improved economic performance of this branch of agriculture. For many decades in conventional chicken crossing programs, most of the economically important traits of the chickens have been selected using phenotype. The fundamental basis for chicken selection is the selection of specific individuals with necessary qualities. In this regard, the egg productivity and, in particular, the egg quality associated with such traits as yolk formation, egg shell thickness, shell strength and egg weight are the primary goal of breeding. Achieving this goal is possible with help of modern molecular genetics. Modern technologies in molecular genetics and availability of DNA markers that help to identify QTL (quantitative traits losi) associated with the egg traits used in marker assisted selection (MAS) can significantly accelerate selection process (1). Population analysis with microsatellite and SNPs markers enable to identify thousands of QTL influencing the exterior, health, physiology and productive traits of the domestic chicken. Although many QTL and some candidate genes have been identified, the application of these results in commercial chicken lines is still not feasible due to low accuracy of QTN mapping. Identification of numerous SNPs in animal genomes, progress in high-throughput sequencing, development of computational methods for analyzing SNPs data obtained with high-density arrays made possible to reveal candidate genes in livestock. The genome-wide association studies (GWAS) have success for detection of the loci affected milk production, fertility and growth in cattle [2] and they arouse interest to high genotyping SNP density platforms to identify nucleotide polymorphisms affecting quantitative traits in the chicken. 60 K SNP Illumina iSelect chicken array developed by USDA Chicken GWMAS Consortium is a new and productive platform for identifying polymorphism in the chicken genome Combination of the traditional phenotypic selection and above mention methods is the most promising scientific approach for identifying the genes of interest. The project proposes to use the literature data obtained by GWAS and our own ROH data to select QTLs and candidate genes that determine egg productivity.

Billions of the eggs are produced annually for people consumption around the world. The poor quality of the eggshell also results in more cracked eggs during the automatic sorting and packaging process in modern industrial egg production [3]. On the other hand, the egg shell is a biologically important structure for the bird embryo development that controlling gas exchange and calcium metabolism. Hatching chickens from eggs with thin eggshells have high fetal mortality due to more water vapor losses during incubation [4]. Moreover, the mass of the egg shell decreases during the aging of the laying hens [5], which prevents the extension of the hen laying cycle. Understanding the genetic control of egg shell quality with the aging process has of great economic and biological importance

In recent years, genomic, transcriptomic, proteomic and structural analyzes of the egg shell have been conducted for better understanding the ultrastructure and mineralization process, contributing to the egg shell quality. Up to date, a total of 62 QTLs associated with egg shell quality have been collected in AnimalQTLdb (http://www.animalgenome.org/cgi-bin/QTLdb/index). Sun et al. [6] performed the first analysis of the GWA with 600 K high density SNP array to identify SNPs associations with the dynamic traits of the egg shell quality such as shell weight and thickness, elastic deformation at 11 time points from the beginning of laying to 72 weeks in the F2 chicken population. According to univariate and multivariate GWA analysis, authors Sun et al.[6] revealed a genomic region spanning from 57.3 to 71.4 M in GGA1 significantly associated with eggshell quality. In total, five missense mutations were detected on GGA1 and one on GGA4 (Table.No.1) They are localized in 6 genes: phosphatidylinositol-4-phosphate-3-kinase, catalytic subunit of type 2 gamma (PIK3C2G), inositol 1,4,5-triphosphate receptor type 2 (ITPR2), RecQ helicase-like (RECQL), subfamily binding ATP cassette C-member 9 (ABCC9) and candidate for susceptibility to cancer 1 (CASC1) on GGA1 and non-SMC subunit G of the condensin I complex (NCAPG) on GGA4 . However, only two SNPs, rs312347405 and rs316607577, located in PIK3C2G and ITPR2, remained significantly associated with the quality of the egg shell after the multivariate analysis of the GWA. Alleles rs312347405 in the PIK3C2G gene associated with the highest phenotypic dispersion of egg shell quality of the above five nucleotide substitutions. The chickens homozygous for GG allele of rs312347405 have eggs with high egg shell strength (ESS), which decreased as the body grew older. The PIK3C2G gene belongs to the family of phosphoinositide-3-kinase (PI3K), contains the lipid kinase catalytic region, and also the C-terminal C2 domain, which acts as the calcium-binding motifs of phospholipid [7]. Previous proteomic studies revealed that a high proportion of lipid-binding proteins was present in a large number of the egg shell matrix, including extracellular protein-binding fatty acids- (ex-FABP), prosaposin and apolipoprotein D. GWAS revealed gene coding the low-density protein receptor protein 8 (LRP8) as a new

candidate of egg matrix protein, significantly associated with the eggshell traits. [8]. Gene PIK3C2G, possesses the C2 domain, acts as a lipid binding motif, is also associated with the formation of the egg shell. PIK3C2G having a C2 region can mediate translocation of proteins to lipid membranes, and also regulates protein-protein interactions in humans and mammals, as well as Interaction of the matrix proteins and calcite form the bioceramic structure of the egg shell [9]. SNP rs316607577 locates in the inositol-1,4,5-triphosphate receptor type 2 (ITPR2) gene (exon 25) was revealed as a positional and functional candidate gene for egg shell quality. The mutation rs316607577 in the ITPR2 gene is a nonconservative substitution of serine for glycine (S1072G), with the glycine-encoding allele associated with a stronger eggshell. The ITPR2 gene is known as a mediator in the endoplasmic reticulum (ER) that triggers the calcium release process by mobilizing Ca2 + from intracellular calcium stores in many cell types [10]. ITPR2 gene was found in the uterine epithelial tissue of the chicken, and expression of ITPR2 gene in the uterus during calcification of the egg shell was significantly higher than in the oviduct and duodenum, which also have active calcium metabolism [11]. ITPR2 gene plays a role in the regulation of intracellular Ca2 + transport in the uterus and contributes to the process of calcification of the eggshell. Due to this role PIK3C2G and ITPR2 genes were first considered as primary candidate genes related to egg shell quality [6].

Table 1: Putative genes associated with egg shell weight(ESW) and egg shell thickness(EST) (Sun et al. BMC Genomics (2015) 16:565)

Tag SNP	Associated Trait	Chromosome	Position	Location	Alleles	SIFTb	Candidate/Nearestgenes
rs14491030	ESW	4	75,486,534	Exon 14 of 21	A/G	0.74	NCAPG
rs316607577	EST	1	67,961,420	Exon 25 of 56	C/T	0.40	ITPR2
rs316447591	EST		67,808,349	3'UTR region	____	____	ITPR2
rs312347405	EST	1	64,287,542	Exon 27 of 32	C/G	0.14	PIK3C2G

bSIFT is a program that predicts whether an amino acid substitution affects protein function. Small values means deleterious amino acid change

66 QTLs associated with 7 types of egg production, such as the interval between egg laying, the age of the first egg, the number of eggs laid, etc., were identified and 223 QTLs were associated with egg quality such as shell thickness, elastic egg strain, yolk weight, etc. (data cited from Chicken QTLdb, http//www.animalgenome.org/cgibin/QTLdb/GG/index), http //www.animalgenome.org/cgi-bin/QTLdb/GG/index). In addition, by carrying out an associative analysis of markers inside or adjacent to candidate genes, several nucleotide substitutions were identified that affect the quality of the eggs [12, 13]. A significant aspect of the above research is that most of the SNPs revealed in the chicken genome are within known genes, indicating the presence of linkage disequilibrium between SNP markers and causal mutations in or near genes, although the functions and characteristics of these genes have not been studied in detail. The identification of these loci can provide new information about the genetic basis of egg production. Weight of eggs, egg shell strength and egg shell thickness (ESW) are important indicators of egg shell quality. The authors Liu et al. [13] identified several important SNPs affecting the egg shell weight (ESW) at different ages (Table 2). One significant SNP rs13636444 associated to ESW40 revealed in the second intron of GALNT1 gene. In humans, nucleotide mutations of GALNT1 gene can cause ovarian cancer [14]. On the other hand, the wild type of GALNT1 gene can provide normal functions of the human ovary. Characterization of this gene is still not fully understood in chickens, and current research is the first report that the polymorphism of a given gene was related to the quality of the egg.

Another SNP rs14411624 associated with the egg shell weight was located in BLK gene on GGA3 (which can be a new QTL, since it does not coincide with previously reported QTL or candidate genes for ESW) [15]. In this proposed QTL region, there are many known genes, including genes associated with DNA modification, transcription, replication, and RNA translation (NEIL2, GATA4, MCM3 and TRAM2); genes associated with immune functions of the body (IL17, antimicrobial peptide CHP1 and cluster of beta-defensin

gene); gene plays a role in calcium homeostasis (EFHC1). The functions of most of the genes mentioned above are not fully understood in chickens, although they have been extensively studied in humans.

SNP rs14022717 located in the third intron of the ZNF536 gene on GGA11 has a significant association with ESW60 (Table 2). This gene encodes the DNA binding protein with functions of transcriptional repressor [16]. This is the first report in which ZNF536 gene can affect the egg shell weight in chickens. Many QTLs affected the eggshell thickness were detected by previous studies and they were located on GGA1, GGA2, GGA5 and GGA7. Some candidate genes for egg shell thickness have also been identified on GGA2, GGA4, GGA8 and GGA9 [17]. In this study, two associations were found on GGA1 for EST40, rs13978498 which located in the hypothetical locus LOC418918 and the other rs13968878 located in the famous ENOX1 gene (ecto-NOX disulfide-thiol exchanger 1) that is involved in cell defense and growth, promoting cell survival. The region covers these two SNPs from 171.22 MB to 179.35 MB, which may be a new QTL for the egg shell thickness and it locates about 70 MB from the QTL reported by Sasaki et al. [15]. In the study Liu et. al.(36 18), the most significant SNP (GGaluGA315030), associated with egg production, located in intron 12 of the GRB14 gene, which encodes the growth factor of the receptor-binding protein. In humans and mammals, GRB14 gene has high levels of expression in the ovary, liver, kidney, skeletal muscle [18]. It interacts with the insulin receptor (IR) and the insulin-like growth factor receptor (IGFR), and can play an inhibitory role for tyrosine kinase receptor (Tcp) of signaling pathways [19]. It is known that IGF and IGFR genes regulate ovarian function and follicular development of the chickens [20]. Although the function of GRB14 gene in chicken is not defined, it can be included in the IGF system and influence the egg-laying of hens-dryness. Also, significant SNP rs317449530 associated with egg production trait localized in 3'-UTR in the GTF2A1 gene on GGA5. GTF2A1 gene is a common transcription factor and it interacts with the TFIID-promoter complex necessary for the initiation of transcription via RNA polymerase II [21]. It is used as an exact candidate biomarker for detection of human ovarian tumor [22]. SNP GGaluGA092322 in the second intron of the ODZ2 gene has a significant association with the above feature. ODZ2 gene, also known as Teneurin-2, encodes the surface protein of neuronal cells and plays an important role in the development of the nervous system [23]. It was found that Teneurin gene has a significant level of expression in the developing brain of the chickens, and especially in the visual system, including the retina and the optic tectum [24]. In the current study first revealed that Teneurin-2 gene can affect the sexual maturity of the chickens. In addition, some previous studies have shown that light intensity can affect the age at which the first egg is laid down and longer periods of light exposure to the chickens can lead to earlier puberty. Since the light day stimulates egg laying, mainly through the visual and nervous systems, the genes associated with these systems can affect on the puberty of chickens[25].

Table 2: Genome-wise significant (P <1.51E-06, Bonferroni correction) SNPs for egg production and quality traits (Wenbo Liu et.al., PLoS ONE 6(12)(2011)

Tag SNP	Associated Trait	GGA	Position	P-value	Candidate/Nearestgenes
GGaluGA315030	EN	7	21676854	3.97E-07	GRB14
GGaluGA092322	AFE	13	4796267	1.42E-06	ODZ2
rs13636444	ESW40	2	86114050	5.85E-09	GALNT1
rs14411624	ESW40	3	110095288	1.41E-07	BLK
rs14022717	ESW60	11	9596922	8.62E-07	ZNF536
rs13968878	EST 40	1	171224927	2.81E-08	ENOX1
rs13978498	EST40	1	179350984	9.22 E-07	LOC418918

The egg-laying rate (LR) and age of first egg (AFE) are the two important economic traits in the laying hen poultry husbandry of whose goal is the breeding of chickens with earlier puberty and a high egg-laying rate. Since the heritability of these sex-limited traits is low-to-moderate, DNA marker selection provides more information, since it is directed towards the actual genetic variation. Raising the egg production rate to 500 per 100 weeks is the ultimate goal. However, with the age of the chicken the egg protein becomes thinned, and

the quality of the egg shell deteriorates sharply, in addition, the frequency of abnormal eggs increases, which reduces the number of high-quality eggs. Williams' studies [26] have shown that the production of egg protein positively correlates with the weight of the oviduct, and a larger oviduct reproduces more high-quality eggs. Thus, the bird selection according to the optimal size of the oviduct directly affects the more complete development of embryos and egg production [12]. To date, there is little information on the genetic architecture controlling the mass and length of the oviduct in the late egg-laying period. The aim of the study Shen et. al [27] was to identify the prospective genomic regions and candidate genes associated with the oviduct weight and length using F2 chicken population. The search for significant loci in the Ensembl database show that they are located in remote areas from the nearest known genes. The SNP rs318027552 located on GGA1 in the CKAP2 gene, rs80668034 in the CCKAR gene and rs312570847 in the NCAPG gene on GGA4, rs80715313 in the GORAB gene on GGA8 and rs312614123 in the IGFBP3c gene on GGA2. GGA1 accounted for more than 4% of the phenotypic variance for signs of oviduct weight (OW) and length of oviduct (OL) (Table 3). SNP rs80668034, which was associated with OW, explained 2.48% and 1.97% phenotypic variance for OL and OW traits. The effect of rs80715313 on GGA8 had least phenotypic dispersion for OL. The effect of rs312614123 on GGA2 was 2.05% of the phenotypic OW dispersion. The three main significant SNPs (rs318027552, rs80668034 and rs80715313) were analyzed to compare their effect on the oviduct traits, and on the quality eggs. The results showed that the phenotype of the oviduct and the quality of the eggs differed for the three genotypes, the marker replacement of rs315027552 by GGA1 was also responsible for egg quality. In addition, GG genotype of rs80668034 had a higher OW, albumin weight, and egg shell weight, while CC genotype of rs80715313 had a lower OW and protein height. This study first identified potential genes that associated with oviduct traits [27]. With regard to phenotypic data, the coefficient of variation of OL (13.91%) was lower than that of OW (23.37%). This may be due to the fact that the length of the oviduct is relatively unchanged, while the weight of the oviduct is not constant during the reproductive cycle of the chicken [28]. Closest gene to rs80715313 on GGA8 is GORAB encodes the SCY1-like 1-binding protein 1, which is localized predominantly in the trans-Golgi network, where it performs important functions in the secretory and endocytic pathways [29]. The glandular tissue in the oviduct participates in the secretion of the proteins, ovalbumin and ovotransferrin transferring from the Golgi complex to the plasmalemma using microtubules [30]. They, in combination with the result of the genotypic effect rs80715313, affects the height of albumin. Moreover, the results of human studies have shown that the autosomal recessive mutation GORAB associates with wrinkled skin and osteoporosis [31].

Thus, GORAB can affect the secretion of albumin proteins during the formation of eggs and it participate in the precipitation of calcium during the formation of the egg shell in the uterus. The most significant SNP rs312614123 associated with OL and located in the IGFBP3 gene on GGA2 that encodes the insulin binding protein as a growth factor of (IGF) 3 [27]. IGFBP3 is one of the proteins that binds IGF, and served as a potent mitotic agent, which is involved in many biological functions, such as protein synthesis, cell differentiation and ovarian development [32]. Cell differentiation in the oviduct during the maturation of the chicken is stimulated by somatotropin and the IGF system. Moreover, it has been found that IGFPB3 associated with early puberty in chicks [33], which presumably can play a vital role in the growth of the oviduct during puberty. Heritability of OL and OW was moderate (0,354 and 0,392 respectively), and the genotypic effect rs318027552 on egg quality showed a constant tendency with the oviduct traits, which means that the selection of these traits will significantly improve the quality of the eggs. Moreover, it was found that the inheritance of OW showed a positive linear correlation with the variance of each chromosome [34]. In genomic analysis, GGA1 explained a 2.91% phenotypic variance after identifying the three leading SNPs as covariates. SNP rs318027552 locates in the genome region explaining the greatest amount of phenotypic variation that suggests that significant SNPs on GGA1 plays a key role in determination of OW. In this study, the association of OL and OW was analyzed for the first time using GWAS. The most significant SNP rs318027552 located at a distance of 88.12 kb from CKAP2 gene (Table 3). Gene CKAP2 encodes the cytoskeleton associated protein 2, which involved in the proliferation and cell survival, and that is necessary to maintain genomic stability [35]. Previous research has shown that the oviduct weight does not remain unchanged during the period of oviposition [36]; Thus, CKAP2 gene can participate in hyperplasia and hypertrophy of the oviduct before the first egg was laid. Locus associated with OW occupies from 74.03 to 76.70 Mb on GGA4.

Yi and Sun et al. [37] reported that this region also associates with egg shell, including yolk, albumin and egg shell weight; the last two of which are produced mainly in magnum and uterus, respectively. Non-synonymic mutation rs80668034 locates downstream from CCKAR gene, which encodes a cholecystokinin type receptor, associated with appetite control. Previous studies have shown that CCKAR gene in chicken is

responsible for a 19% difference in body weight at 12 weeks of age and it associates with signs of growth [38]. Xu studies [39] have shown that CCKAR gene associates with chicken appetite, which affects egg production and feed intake increases after the first egg was laid. In this study, chickens having the genotype GG of rs80668034 had a higher albumin and egg shell weight; so the authors suggest that CCKAR gene plays a role in the use of energy in the oviduct and affects egg production. Another SNP rs312570847 located near the NCAPG gene (encoding the non-SMC subunit G of the condensin I complex), has a pleiotropic effect on chicken body mass [40], the egg weight and the egg shell weight [40, 41] (Table 3). The mutations in NCAPG gene has also effect on cow food intake [42] and body size [43, 44] This study demonstrates that NCAPG can also be associated with OW. In addition, SNPs close to CCKAR and NCAPG genes also showed advisory associations with OL. Thus, CCKAR and NCAPG genes can affect OW by stimulating protein synthesis and egg shell formation during the reproductive season.

Table 3: Contributions of five mutations and genomic regions to oviduct trait. Manman Shen et.al. PLOS ONE 2017

Tag SNP	Associated Trait	Chromosome	Position	Location	Alleles	P-value	Candidate/Nearest genes
rs318027552	OW	1	170318652	U88.12Kb	G/A	2.52E-10	CKAP2
rs80668034	OW	4	74034095	D331.64Kb	A/G	2.24E-07	CCKAR
rs312570847	OW	3	75146457	U1.31Mb	C/T	2.91E-07	NCAPG
rs80715313	OW	3	4917630	D7.34Kb	C/T	5.03E-07	GORAB
rs312614123	OL	1	55157730	D38.59Kb	T/C	3.35E-06	IGFBP3

Another significant SNP rs317510777 was located next to the CLSPN gene on GGA23 (Table 4). It encodes a claspin protein affected monitoring of DNA replication and sensoring of DNA damage in mammals . In addition, claspin expression is significantly high in a cervical cancer cell caused by human papilloma virus [45]. Therefore, it is assumed that GTF2A1 and CLSPN genes associates with the function of the ovary and uterus, They may affect the egg production of the chickens. Significantly associated SNP rs317773842 with egg production traits was located in the 3 'UTR of the FARSB gene on GGA9, which encodes a highly conserved enzyme belonging to the aminoacyl family tRNAsynthetase (ARS) (http://www.genecards.org/cgi-bin/carddisp.pl?gene=FARSB) [46].

Mutations in the genes encoding ARS gene lead to neurodegeneration in humans [47]. The SNP rs312387499, which has a significant association with egg production was localized in the 18th intron of the KIAA1549 gene on GGA1(Table 4). In humans in many cases of pilocitic astrocytoma this gene was linked to the BRAF oncogene (http://www.genecards.org/cgibin/carddisp.pl?gene=KIAA1549). Function of the FARSB and KIAA1549 genes is unknown in chickens. Based on previous studies in humans presumably they interact with the central nervous system regulating egg production. The putative candidate gene CALM1 for the egg-laying traits on GGA5 involves in the regulation of the production of androstenedione cells and uterine contractility. It is a prototype calcium sensor which directly affects egg production [48]. In a recent study, it was found that CALM1gene has a high level of expression in the ovary of geese [49] and implies that CALM1 may be involved in the process of the chickens oviposition. The age of the first laid egg is an indicator of puberty, which is influenced by several factors such as nutrition, photoperiod, and the genetic potential of the chicken.

The authors Fan et.al [50] identified four SNPs significantly associated with egg production(Table 4). Two rs15602813, rs13628422 were located in the 23.3-23.5 MB region on GGA11. This region overlaps with nearest CBFB gene that encodes the beta subunit of a member of the PEBP2 / CBF transcription factor family. This family regulates the expression of many genes, especially those necessary for hematopoiesis and osteogenesis [51]. Two other SNPs were located at 95.8 MB on GGA1 (rs13905010) and at 31.3 MB (rs15938574) on GGA2 and were proximal to the genes GJA5 and STK31 (serine / threonine kinase 31). STK31 gene encodes a TDRD family proteins that localizes in male germ cells of mice [52]. The STK31 gene plays a decisive role in human cancer. It includes regulating function of the cell cycle; overexpression of STK31 gene, increases cell migration and invasive ability of cancer cells, whereas STK31gene leads to depletion inducing apoptosis. GJA5 encodes a gene that is a member of the connexin family. This gene is a component of gap

junctions consisting of intercellular channel arrays that provide a pathway for the diffusion of low molecular weight compounds between cells [53]. It is play an important role in regulating cell proliferation and differentiation. [54].

Table 4: The information for SNPs significantly associated with egg number (EN)

Tag SNP	Associated Trait	Chromosome	Position	Alleles	P-value	Candidate/Nearest genes	Authors
rs15602813	EN	11	2338929	C/T	1.22E-06	CBFB	Q.C. Fan et.al.Genetics and Molecular Research 16 (1) 2017
rs13628422	EN	11	2350952	G/A	1.40E-06	CBFB	
rs13905010	EN	1	95793916	C/T	1.86E-08	GJA5	
rs15938574	EN	2	31333604	A/G	4.31E-08	20 D STK31	
rs317410777	EN	23	4,191,027	G /A	1.13E-08	CLSPN	Jingwei Yuan et.al. PLOS ONE 2015
rs317449530	EN	5	40,101,576	A/G	4.93E-07	GTF2A1	
rs313187645	EN	5	40,106,943	A/G	4.93E-07	GTF2A1	
rs317773842	EN	9	7,473,958	A/G	3.81E-07	FARSB	
rs312387499	EN	1	56,459,390	G /A	6.50E-07	KIAA1549	
rs14540368	EN	5	43,160,851	G/T	1.82E-07	CALM1	
rs314448799	EN		43,152,230	C/T	5.13E-09	CALM1	

The creation of a system of QTLs affecting the egg production of chickens will be solved by integrating literary with own experimental data. Our strategy for detecting QTLs is based on the presence in the chicken genome of homozygous chromosome regions as signatures of intensive selection of the chickens for egg production. To solve this problem, SNP array technology and methods for detection of extended homozygosity of haplotypes (EHH), such as XP-EHH, hapFLK and XP-CLR will be used. The basis for identifying QTLs affecting egg production will be different breeds of the chickens (fancy, meat, meat-laying and laying crosses). Among the detected EHH regions, only those that either coincide with QTLs from literature sources or include genes potentially involved in egg productivity will be selected. To date, have been published several studies performed by these methods [55, 56].

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