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CANDIDATE GENES APPLICATIONS IN GENETIC IMPROVEMENT PROGRAMS IN CHICKENS

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Abstract: The experimental chicken populations (F_0, F_1, F_2 and F_3) have been constructed all-over the world to be used in gene and quantitative trait loci (QTL) mapping studies in different breeds. The genome-wide QTL are located on seven macro-chromosomes (chromosome 1, 2, 3, 4, 6, 8 and Z) and on one micro-chromosome (chromosome 11) for body weights and gains, on chromosomes 1 and 5 for egg weight, on chromosomes 5 and 7 for number of eggs and on chromosome 1 for age at first egg. The total chromosomal map length for body weight is 1901 *cM* ranging from 25 *cM* on chromosome 11 to 568 *cM* on chromosome 1, while the total chromosomal map length for egg production and egg quality traits was 1949 *cM* ranging from 52 *cM* on chromosome 11 to 542 *cM* on chromosome 1. The majority of molecular markers used nowadays in poultry are microsatellite markers, STRs (short tandem repeats) and SNPs (single nucleated polymorphism). The microsatellites are used as the most widely markers for the analysis of genetic diversity and population structure in poultry. To detect the genetic diversity in poultry, definite number of microsatellite markers covering nine autosomal linkage groups and the sex Z chromosome are considered in genotyping of F_0 grandparents and F_1 and F_2 offspring. Detailed information about selected microsatellites are available at the FAO website (www.dad.fao.org/en/refer/library/guidelin/marker.pdf). Primarily, the chickens' breeds must be characterized on molecular bases in terms of allelic and genotypic frequencies, the effective number of alleles (Ne), the observed (Ho) and expected (He) heterozygosity, Hardy-Weinberg equilibrium (HWE), the polymorphism information content (PIC) and the F-statistics of the reduction in heterozygosity due to inbreeding within each population (F_{IS}). The candidate genes located on 18 chromosomes (number 1, 2, 3, 4, 5, 7, 8, 9, 10, 15, 16, 17, 19, 20, 21, 26, 27 and Z) are associated with growth traits of body weights and gains and feed intakes and conversion in chickens, while the candidate genes located on 11 chromosomes (number 1, 3, 4, 5, 7, 9, 13, 20, 24, 27 and Z) are associated with egg production and egg quality traits. The immune candidate genes located on 15 chromosomes (number 1, 2, 3, 4, 5, 6, 7, 14, 15, 16, 17, 19, 24, 26 and 27) are associated with immune responses against Salmonella in chickens. Recently, genome-wide association studies (GWAS) have been used successfully to identify single nucleotide polymorphisms (SNPs) and candidate genes associated with quantitative traits in chickens since a remarkable range of discoveries from GWASs have been detected in production, reproduction and disease resistance traits. To perform a genetic improvement program for the Arabian breeds of chickens using the molecular applications, the following necessary steps are summarized as: 1) Recording the phenotypic data from full pedigree file to evaluate the birds genetically through estimating the breeding values for chicks, hens and cocks, 2) Determining the list of main equipments required and the main list of chemicals for DNA extraction, 3) Collecting the blood samples from birds and performing DNA extraction, 4) Reporting candidate genes from QTLs data base (http://www.animalgenome.org/QTLdb), 5) Preparing the genotyping files using SNP markers, 6) Applying SNP association test to detect the genes closely associated with economic traits in poultry, 7) Estimating the genomic breeding values (GBV) to be applied in genomic selection, 8) Applying the Genome-Wide Association Study (GWAS) using PLINK software, 9) Applying genomic selection program (GS) using GBV of cocks and hens to be the parents of the next generation.

Keywords: Chickens, Candidate genes, QTL, GWAS, Genomic Breeding Values (GBV)**,** Genomic selection**.**

INTRODUCTION

Using biotechnology techniques are the best way to achieve fast genetic improvement in chickens particularly in indigenous breeds and/or strains in developing countries. Candidate genes as molecular techniques are considered as one of the primary methods to determine the specific genes related to the economic traits in chickens. Quantitative Trait Loci (QTL) could be used to identify these specific genes or their chromosomal regions. This approach has enabled opportunities to enhance genetic improvement programs in chickens by direct selection based on genes or genomic regions that affect economic traits through marker-assisted selection (MAS). In chickens, selection programs through quantitative genetics are time consuming in case of lowly heritable traits. The identification and utilization of QTL provide more potentiality for rapid genetic improvement in selection programs, especially for traits that are difficult to be improved with traditional selection (Ikeobi *et al.*, 2002). Nassar *et al.* (2013, 2015) detected Cholecystokinin type A receptor gene (CCKAR) that had specific effects on growth traits and fat deposition using QTL in crosses between New Hampshire and White Leghorn chickens. Khalil *et al.* (2016) reported that QTL detected on chromosomes 1, 2, 3, 4, 6, 8, 11 and Z for body weights and those detected on chromosomes 2, 3, 4, 8 and Z for egg production and egg quality traits were significant.

The genes to be used in selection are regarded as candidate genes that affecting economic traits in chickens and these candidate genes have successful approaches in identifying several DNA markers associated with production and reproductive traits. However, several molecular associations' studies during the decade 2000-2010 have shown the association between candidate genes and growth traits and/or feed conversions in chickens (Amills *et al.*, 2003; Liu and Lamont, 2003; Lei *et al.*, 2005; Qiu *et al.*, 2006; Ye *et al.*, 2006; Cao *et al.*, 2007, Lei *et al.*, 2007; Nie *et al.*, 2008; Leng *et al.* , 2009; Ou *et al.*, 2009; Wei *et al.*, 2009; Zhang *et al.*, 2009; Ahmed, 2010; Fang *et al.*, 2010). In addition, these associations' studies have been confirmed recently during the years of 2011-2021 by other investigators (Uemoto *et al.*, 2011; Niknafs *et al.*, 2012; Rikimaru *et al*, 2012; Cahyadi *et al.*, 2013; Lim *et al.*, 2013; Seo *et al.*, 2013; El Moujahid *et al.*, 2014; Anh *et al.*, 2015; Ashraf and El-Tarabany, 2015; Molee *et al.*, 2016; Kazemi *et al.*, 2018; Zhao *et al.*, 2015; Yi *et al.*, 2018; Jin *et al.*, 2018; Saleh et al, 2020b). Also, the associations between candidate genes and egg production and egg quality traits have been confirmed in chickens (Cui *et al.*, 2006; Li *et al.*, 2009; Xu *et al.*, 2011a,b; Zhu and Jiang, 2014; Ngu *et al.*, 2015; Vu and Ngu 2016; Charoensook *et al.*, 2016; Osman *et al.*, 2017; Nguyen *et al.*, 2018; Azmal *et al.*, 2019; Bhattacharya *et al.*, 2019). In the last two decades, several studies have reported the associations of immune genes with immune response, bacterial burden and antibody titers against Salmonella in chickens (Zhou *et al.*, 2001; Lamont *et al.*, 2002; Kramer *et al.*, 2003; Liu and Lamont, 2003; Malek and Lamont, 2003; Zhou and Lamont, 2003a; Malek *et al.*, 2004; Ahmed, 2010; Cahyadi *et al.*, 2013; Khatab *et al.*, 2017; Saleh et al, 2020b, 2021).

GWAS results have been shown that this GWAS approach could be useful in selection for phenotypic performance using customized gene chips (Moser *et*

Chickens, Candidate genes, QTL, GWAS, Genomic Breeding Values (GBV), Genomic selection.

al., 2009; Xu *et al.,* 2013; Sun *et al.,* 2015; Yuan *et al.,* 2015; Gianola *et al.,* 2016; Psifidi *et al.,* 2016; Fan *et al.,* 2017; Pértille *et al.,* 2017; Azmal *et al.,* 2019; Kudinov *et al.,* 2019; Liu *et al.,* 2019; Qu *et al.,* 2019). The SNP of innate immune genes, such as natural resistance associated macrophage protein 1 (Nramp1; Beaumont *et al.,* 2003), *CD28* and *MD2* genes (Malek *et al.,* 2004) and *TLR4* gene (Li *et al.,* 2010) could be used to enhance *Salmonella Pullorum* resistance in chicken. The expression of *TLR4* and some immune related genes, such as *Gal 1*, *Gal 2*, *IL-8*, *IL-18* and *IFN-*□ could be also used to establish different degrees of correlation against salmonella in chickens (Sadeyen *et al.,* 2006). Ahmed (2010) demonstrated that the novel *IFNG* promoter SNP was associated with antibody kinetics for *Brucella abortus* (BA) in laying hens, suggesting that this cytokine may play a pivotal role in the relationship between immune function and growth. Dehkordi *et al.* (2015) have been performed some studies to detect the gene structure of Salmonella and its ability to resist against antibiotics. Liu *et al.* (2015) suggesting that *MyD88* gene may be one of the major *Salmonella Pullorum* resistant genes in innate immune system in chickens.

Genomic selection using the SNP markers is a powerful new tool for genetic selection (Purcell *et al.,* 2007); this is because: 1) SNPs can be detected by a number of techniques such as PCR-RFLP, 2) SNP can be used for large scale screening of numerous samples in a minimal time, 3) SNP is the most recent contribution to study DNA sequence variation, and 4) SNP represents the most innovative molecular marker in genotyping studies.

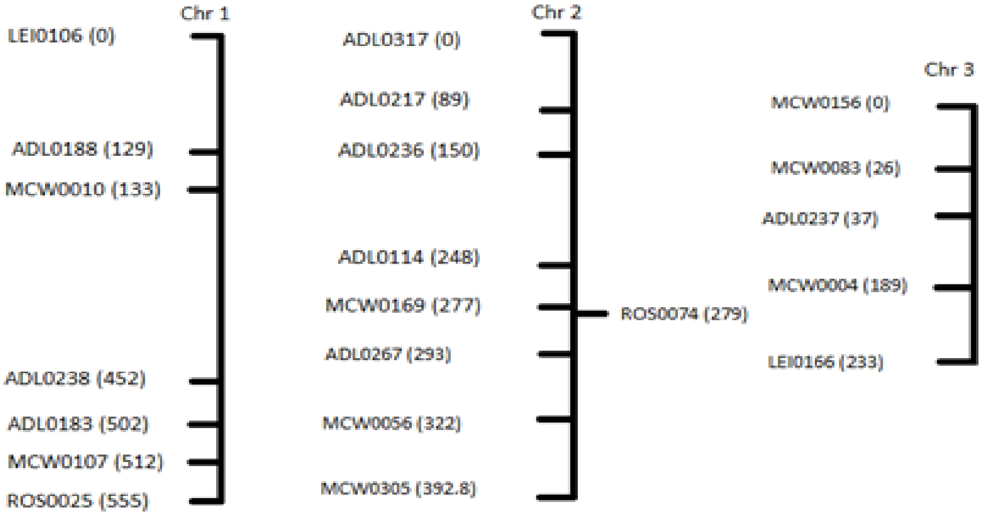
The Objectives

The main objectives of this article are dealing with the following items: 1) To identify the chromosomal QTL mapping and their positions in chicken genome, 2) To apply a fine chromosomal mapping for localizing the QTL affecting economic traits in F_2 population using specific microsatellite markers or SNP's in chickens and possibly to identify the candidate genes associated with economic traits, 3) Determining the molecular markers to be used for evaluating the genetic variability among poultry breeds, 4) Characterizing the candidate genes to be used in genetic improvement programs, 5) Detecting the SNP genotypes and identifying the molecular associations between candidate genes and body weights and gains, feed intakes and conversions, egg production, egg quality, and disease resistance responses, 6) Defining the genetic model for detecting the molecular associations between SNP genotypes of candidate gene and economic traits, 7) Performing genome wide association study (GWAS) in order to detect the potential causative mutations and genomic regions affecting productive and reproductive traits in chickens, 8) Applying genomic selection program based on Genomic Breeding Values (GBV), and 9) Suggesting a genetic improvement program to improve the Arabian' breeds and/or strains of chickens using recent molecular approaches.

1.The chromosomal QTL mapping and their positions in chicken genome:

QTL mapping was the perfect approach to identify genes related to complex traits at genome-wide level. The chicken genome consists of 38 pairs of autosomal chromosomes and sex Z and W chromosomes. The chromosomes can be classified into two size groups, nine macro-chromosomes and 30 micro- Recent development of statistical methods and comprehensive linkage maps of the chicken genome has provided tools for mapping loci affecting quantitative traits (Mackay *et al.*, 2009). In the last 15 years, several experimental chicken populations (F_0, F_1, F_2 and F_3) have been constructed from different breeds for use in gene and QTL mapping studies (Jacobsson, 2005; Liu *et al.*, 2008; Bulut *et al.*, 2013; Abdel A'al *et al.*, 2016,2017). However, several studies have been investigated to detect the chromosomal regions affecting phenotypic performance of many growth and egg production traits in different chicken breeds (Tatsuda and Fujinaka 2001; Sewalem *et al.*, 2002; Li *et al.*, 2003; Sasaki *et al.*, 2004; Siwek *et al.*, 2004; Nones *et al.*, 2006; Nassar *et al.*, 2013; Abdel A'al *et al.*, 2016,2017). In chromosomes (Bloom *et al.*, 1993).

Germany, Goraga et al. (2012) reported highly significant QTL region on chromosome 4 for egg production traits, on chromosomes 1, 5 and 9 for egg weight, on chromosomes 5 and 7 for number of eggs, on chromosome 1 for age at first egg. In Egypt, the chromosomal map to be used for detecting growth and egg traits in F_2 population is presented in Figure 1 as cited by Abdel A'al *et al.* (2016) who reported a total of 19 significant genome QTL located on seven macro-chromosomes (chromosome1, 2, 3, 4, 6, 8 and Z) and one micro-chromosome (chromosome 11) affecting growth traits, on chromosomes 1 and 5 for egg weight, on chromosomes 5 and 7 for number of eggs, on chromosome 1 for age at first egg.



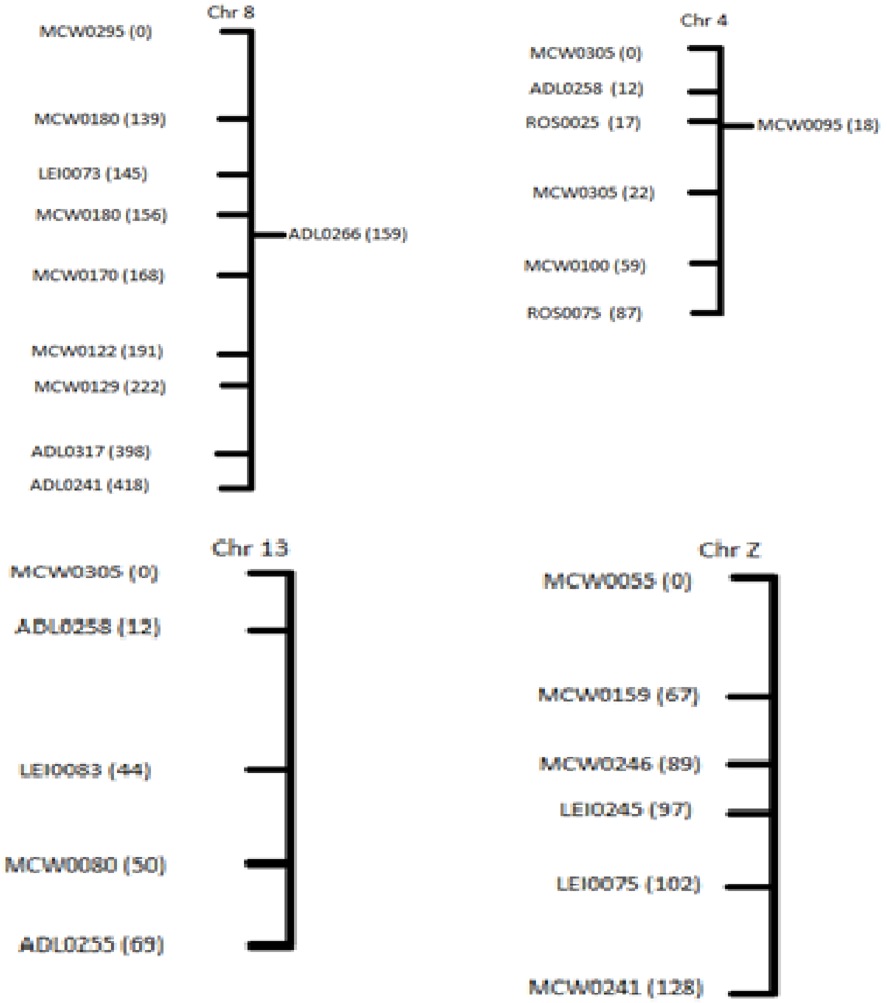


Figure (1): QTL mappings in chickens, including positions and names of the markers as cited by the Egyptian study (Abdel A’al *et al.*, 2016&2017).

For QTL mapping and their positions detected for growth and egg production and egg quality traits, Abdel A’al *et al.* (2016, 2017) have been illustrated the chromosomal group, number of informative microsatellite markers and chromosomal map length (*cM*) for the whole genome scan of growth traits in F_2 cross (Table 1). This study has reported that: 1) The total chromosomal map length for body weights was 1901 *cM* ranging from 25 *cM* on chromosome 11 to 568 *cM* on chromosome 1, with marker spacing ranging from 7.8 *cM* on chromosome 8 to 24.3 *cM* on chromosome 1, 2) The total chromosomal map length for egg production and egg quality traits was 1949 *cM* ranging from 52 *cM* on chromosome 11 to 542 *cM* on chromosome 1, with marker spacing ranging from 15.3 *cM* on chromosome 4 to 71.5 *cM* on chromosome 6.

Table (1): Chromosome group, number of microsatellite markers and map length (cM), that was used for a whole genome scan of growth and egg traits in F_2 cross

Chromosome	Number of microsatellite markers		Chromosome map length (*cM*)		Average marker spacing by the chromosome (*cM*)	
	Growth	Egg	Growth	Egg	Growth	Egg
1	10	9	568	542	24.3	60.2
2	8	8	298	401	18.7	50.1
3	2	6	273	144	11.6	24
4	7	4	198	286	17.6	15.3
6	4	3	111	123	10.4	71.5
8	3	2	97	88	7.8	44
9	1	2	123	112	20.1	56
11	5	3	25	52	8.3	17.3
13	2	2	71	69	14.5	34.5
Z	5	6	137	132	11.5	22
Total	47	45	1901	1949		

Source: Abdel A'al *et al.* (2016, 2017)

1. Identifying the molecular markers to be used for evaluating the genetic variability among chickens' breeds:

Molecular markers can be used to evaluate genetic variability, either within or among individuals, families, and populations. Genetic markers provide information as bioinformatics indicators about polymorphism in allelic frequency at a given locus. In the last two decades, DNA sequencing, and PCR technique have helped in increasing the application of molecular markers (Weigend, 2004) and the majority of molecular markers could involve microsatellite markers, STRs (short tandem repeats) and SNPs (single nucleated polymorphism). Among all types of the molecular markers, the microsatellites are used as the most widely markers for the analysis of genetic diversity and population structure in poultry (Erhardt and Weimann, 2007). Nowadays, DNA molecular marker techniques are widely applied in the fields of germplasm identification, phylogenetic tree, and genetic structural analysis (Yang *et al.*, 2013). Accordingly, the microsatellite has been used to develop the markers from genes and they have been referred as genic molecular markers (GMMs) or functional markers (FMs). Definite number of microsatellite markers covering nine autosomal chromosomal groups and the sex Z chromosome are considered in genotyping F_0 grandparents and F_1 and F_2 offspring. These markers were selected based on the degree of polymorphism and the genome coverage recommended in the molecular genetic characterization of animal genetic resources (FAO, 2011). However, the detailed information about selected microsatellites are available at the FAO website (www.dad.fao.org/en/refer/library/guidelin/marker.pdf). The assessment of markers was based on their positions on the consensus map. A target for marker spacing of 10 *cM* was used to test markers across the genome (http://www.ncbi.nlm.nih.gov/mapview and http://www.thearkdb.org).

Kumar *et al.* (2007) examined the genetic relationships among the indigenous chickens' populations in India using 10 genotyped SNP markers of the Myostatin gene *(GDF-8)* by PCR-RFLP. Another application of SNPs in chickens was applied by Twito *et al.* (2007) who used 25 SNPs for different genes and chromosomes to examine the genetic relationships among 20 chicken populations using the STRUCTURE software program and they compared the SNP results with the analysis using microsatellites and concluded that: 1) Microsatellites provide high clustering success due to high polymorphic nature, 2) SNPs provide broader genome coverage and reliable estimates of genetic relatedness in the genome, and 3) SNP considered to be an efficient and cost-effective genetic tool.

2. Characterizing the genetic diversity of candidate genes to be used in improvement programs in chickens' breeds:

The candidate genes in local chickens' breeds must be characterized in terms of the following genetic diversity parameters:

1) Calculating the allelic and genotypic frequencies.

2) Calculating the effective number of alleles *(Ne)*, the observed (*Ho*) and expected (*He*) heterozygosity for candidate genes using GENALEX software, version 6.5 (Peakall and Smouse, 2012).

3) Estimating Hardy-Weinberg equilibrium (HWE) within each population using GENEPOP program (Raymond, 1995 ; http://genepop.curtin.edu.au/) and performing the Chi-square test for each genetic group studied.

4) Calculating the polymorphism information content (PIC) using CERVUS software, version 3 (Kalinowski *et al.*, 2007):

5) Calculating the F-statistics of the reduction in heterozygosity due to inbreeding within each population (F_{IS}) using GENEPOP software, version 3.4 **(Raymond, 1995 ;** http://genepop.curtin.edu.au/).

3. Molecular associations between candidate genes and growth and feeding traits in chickens:

The genetic associations' studies cited in literature have been investigated to clarify the relationship between candidate genes and growth and feeding traits in chickens. In this concept, there are several genes located on 18 chromosomes (number 1, 2, 3, 4, 5, 7, 8, 9, 10, 15, 16, 17, 19, 20, 21, 26, 27 and Z) to be associated with growth and/or feed intakes and conversion in chickens (Table 2). Regarding SNP genotypes for candidate genes and their associations with economic traits in chickens, chicks with TT genotype of *Pit-1* gene had significantly heavier body weight than those of CT and CC genotypes, while AA genotype had heavier body weight and favorable feed conversion than those of AT and TT genotypes.

Zhou *et al.* (2005) found significant associations ($P<0.05$) between *IGF1-*SNP and average daily gains in F_2

generation of hybrids (Leghorn×broiler and Fayoumi×broiler). Also, the *IGF-1* gene is associated with growth in chickens as reported by others (Seo *et al.*, 2001; Kita *et al.*, 2005; Li *et al.*, 2009). Nie *et al.* (2005) found that SNP had significant associations with almost growth traits in F_2 cross of White Recessive Rock Xinghua Chinese chicken. Ahmed (2010) found that body weight at 12 weeks of age was associated with *IFNG* SNP in Fayoumi chickens. Gouda and Essawy (2010) reported significant effects of *IGF-I* gene on growth traits of Egyptian chicken breeds. Ashraf and El-Tarabany (2015) found that SNP of Bone morphogenetic protein receptor 1B gene (BMPR-1B) was associated significantly with body weight at 2nd to 8th weeks of age ($P=0.01$). Lim *et al.* (2013) found that the SNP of Inducible nitric oxide synthase gene (*INOS*) had a significant association with body weight at 270 days of age ($p<0.05$) in both Korean Native Black and Rhode Island Red chickens. El-Moujahid *et al.* (2014) reported that four SNPs of leptin receptor gene (LEPR) were significantly associated with body weight at 49 and 70 day of age ($P < 0.05$) and feed intake ($P < 0.05$) in yellow N202 strain, and feed conversion ($P <0.01$) in yellow N301 strain. Zhao *et al.* (2015) detected the association between *IGFBP-2* gene and body weight in Jinghai Yellow, Arbor Acre, Youxi and Bian chickens. Molee *et al.* (2016) identified seven SNPs of Major Histocompatibility Complex class II gene (C125T, A126T, C209G, C242T, A243T, C244T and A254T) and recorded significant associations between all SNPs and body weights. Kazemi *et al.* (2018) reported significant associations between *IL-2* gene at promoter region and body weight at 8 weeks of age in Mazandaran native fowls ($P\leq0.05$). Yi *et al.* (2018) found that SNP of Cholecystokinin type A receptor gene *(CCKAR)* was associated with feed intake ($P < 0.01$) and significantly associated with daily gain traits ($P < 0.05$) in Chinese local chicken Ianlu Black pure-line N416. Jin *et al.* (2018) reported that SNP of Pituitary-specific transcription factor-1 gene (*Pit-1*) was associated significantly with feed intake, feed conversion and body weight at 70 days of age ($p<0.05$).

Chickens, Candidate genes, QTL, GWAS, Genomic Breeding Values (GBV), Genomic selection.

Table (2): Candidate genes associated with body weights and gains and/or feed intakes and conversions as cited in literature.

Candidate gene associated with both body weights and gains and/or feed intakes and conversions	**Chromosome number**	**Reference**
Pituitary-specific transcription factor-1 ***(Pit-1),*** Inhibitor of apoptosis protein-1 **(*IAP1*)**, Chicken-B-cell marker **(*CHB6*)**, Insulin-like growth factor 1 ***(IGF1)***,	1	Amills *et al.* (2003), Liu and Lamont, (2003), Ye *et al.* (2006), Cao *et al.* (2007), Nie *et al.* (2008) , Wei *et al.* (2009), Ahmed (2010), Jin *et al.* (2018)
Insulin-like growth factor *(IGF2),* Insulin-like growth factor binding, protein 1 and 3 *(IGFBP),* Protein of toll like receptor 4 *(TLR4*)	2	Amills *et al.* (2003), Ye *et al.* (2006), Ou *et al.* (2009), Zhao *et al.* (2015)
Ornithine decarboxylase *(ODC),* Gallinacins 2 to 5 *(Gal 2 to Gal 5)*	3	Ye *et al.* (2006), Uemoto *et al.* (2011), Cahyadi *et al.* (2013), Saleh et al (2020b)
Cholecystokinin type A receptor *(CCKAR),* Interleukin-2 (*IL-2),* Tumor necrosis factor-related apoptosis-inducing ligand (*TRAIL),* Bone morphogenetic protein receptor 1B (BMPR-1B)	4	Ye *et al.* (2006), Niknafs *et al.* (2012), Rikimaru *et al.* (2012), Ashraf and El-Tarabany (2015), Kazemi *et al.* (2018), Yi *et al.* (2018)
Calpain 3, Transforming growth factor-*β*3 (*TGF-β3),* Insulin *(INS)*	5	Qiu *et al.* (2006), Ye *et al.* (2006), Lei *et al.* (2007), Zhang *et al.* (2009)
Insulin-like growth factor binding protein-2 *(IGFBP-2)*	7	Lei *et al.* (2005), Leng *et al.* (2009)
Leptin receptor gene (*LEPR*)	8	El Moujahid *et al.* (2014)
Growth hormone secretagogue receptor (GHSR)	9	Fang *et al.* (2010)
Insulin-like growth factor 1 receptor (IGFR1)	10	Lei *et al.* (2008)
Macrophage migration inhibitory factor (*MIF)*	15	Ye *et al.* (2006)
Major histocompatibility complex *MHC Class II*	16	Ye *et al.* (2006), Molee *et al.* (2016)
Toll-like receptor 4 (*TLR4*)	17	Lim *et al.* (2013)
Inducible nitric oxide synthase (*INOS*), Caspase-1 (*CASP1)*	19	Liu and Lamont (2003), Ye *et al.* (2006), Lim *et al.* (2013)
Bone morphogenetic protein-7 (*BMP7*)	20	Ye *et al.* (2006)
PR domain containing 16 *(PRDM16)*	21	Cahyadi *et al.* (2013)
Thyroid-stimulating hormone beta subunit(*TSH*-β)	26	Lei *et al.* (2007), Seo *et al.* (2013)
Growth hormone (GH and *GH1)*	27	Nie *et al.* (2005), Anh *et al.*(2015)
Growth hormone receptor (GHR)	Z	Lei *et al.* (2007)

4. Molecular associations between candidate genes and egg production and quality traits in chickens:

The molecular associations' studies given in Table 3 illustrated that there are several candidate genes located on chromosome 1, 3, 4, 5, 7, 9, 13, 20, 24, 27 and Z associated with egg production and egg quality traits in chickens (Table 3). Many studies have been confirmed recently the associations between candidate genes and egg production and egg quality traits in poultry (e.g. Osman *et al.*, 2017; Nguyen *et al.*, 2018; Azmal *et al.*, 2019; Bhattacharya *et al.*, 2019). These molecular associations' studies cited in Table 3 could be outlined as follows:

1) Genes located on chromosome 1: Insulin -like Growth Factor I *(IGF-I)* (Li *et al.*, 2009; Ngu *et al.*, 2015), Melatonin Receptor 1B *(MTNR1B)* (Li *et al.*, 2013), Matrix metallopeptidase 13 (Yuan *et al.*, 2016),

2) Genes located on chromosome 2: Neuropeptide Y *(NPY)* (Xu *et al.*, 2011b; Nguyen *et al.*, 2015), Gonadotropin releasing hormone I *(GnRHI)* (Bhattacharya *et al.*, 2019), Prolactin *(PRL)* (Cui *et al.*, 2006; Kulibaba 2015; Osman *et al.*, 2017; Nguyen *et al.*, 2018), Vasoactive intestinal peptide receptor- 1 *(VIPR1)* (Xu *et al.*, 2011b; Nguyen *et al.*, 2018),

3) Genes located on chromosome 3: Vasoactive intestinal peptide *(VIP)* (Zhou *et al.*, 2010; Nguyen *et al.*, 2018), Follicle-stimulating hormone receptor *(FSHR)* (Li *et al.*, 2011),

4) Genes located on chromosome 4: Melatonin Receptor 1A and 1C *(MTNR1A)* and *(MTNR1C)* (Li *et al.*, 2013), Gonadotropin releasing hormone II *(GnRHII)* (Bhattacharya *et al.*, 2019),

5) Genes located on chromosome 5: gremlin *(GREM1)* and *(GREM2) (Tyasi et al.*, 2018),

6) Genes located on chromosome 7: Inhibin α *(INHA)* (Cui et al., 2019),

7) Genes located on chromosome 9: Ovocalyxin-32 Fulton *et al.* (2012),

8) Genes located on chromosome 13: Growth Differentiation Factor 9 Gene (GDF9) (Liu *et al.*, 2018), Dopamine receptor D1 *(DRD1)* (Tempfli *et al.*, 2015), Rap guanine nucleotide exchange factor 6 *(RAPGEF6)* (Azmal *et al.*, 2019),

9) Genes located on chromosome 20: Matrix metalloproteinases *(MMP9)* (Zhu and Jiang, 2014),

10) Genes located on chromosome 24: Dopamine D2 Receptor *(DRD2)* (Xu *et al.*, 2011a; 2011b; Ngu *et al.*, 2015),

11) Genes located on chromosome 27: Growth hormone *(GH)* (Su *et al.*, 2014; Kulibaba, 2015; Vu and Ngu 2016), Single transducers and activators of transcriptions 5B *(STAT5B)* (Charoensook *et al.*, 2016)

12) Genes located on chromosome Z: Prolactin receptor gene *(PRLR)* (Kulibaba, 2015), growth hormone receptor (Kulibaba, 2015).

Table (3): Candidate genes associated with egg production and/or egg quality traits in chickens as cited in literature

Candidate gene associated with egg production and/or egg quality traits	**Chromosome number**	**Reference**
Insulin -like Growth Factor I *(IGF-I)*, Melatonin Receptor 1B *(MTNR1B)*, Matrix metallopeptidase 13 *(MMP13)*	1	Li *et al.* (2009), Li *et al.* (2013), Ngu *et al.* (2015), Yuan *et al.* (2016)
Vasoactive Intestinal Peptide (*VIP)*, Follicle Stimulating Hormone Receptor *(FSHR)*	3	Zhou *et al.* (2010), Li *et al.* (2011), Nguyen *et al.* (2018)
Melatonin Receptor 1A and 1C *(MTNR1A* and *MTNR1C)*, Gonadotropin Releasing Hormone II *(GnRHII)*	4	Li *et al.* (2013), Bhattacharya *et al.* (2019)
Gremlin 1 *(GREM1)* and Gremlin 2 *(GREM2)*	5	Tyasi *et al.* (2018)
Inhibin α *(INHA)*	7	Cui *et al.* (2019)
Ovocalyxin-32	9	Fulton *et al.* (2012)
Growth Differentiation Factor 9 *(GDF9)*, Dopamine receptor D1 *(DRD1)*, Rap Guanine Nucleotide Exchange Factor 6 *(RAPGNEF6)*	13	Tempfli *et al.* (2015), Liu *et al.* (2018), Azmal et al. (2019)
Matrix Metalloproteinases 9 *(MMP9)*	20	Zhu and Jiang (2014)
Dopamine D2 Receptor *(DRD2)*	24	Xu *et al.* (2011a; 2011b)
Growth Hormone *(GH)*, Single Transducers and Activators of Transcriptions 5B *(STAT5B)*	27	Su *et al.* (2014), Kulibaba (2015), Ngu *et al.* (2015), Charoensook *et al.* (2016), Vu and Ngu (2016) ,
Prolactin Receptor *(PRLR)*, Growth Hormone Receptor *(GHR)*	Z	Kulibaba (2015)

5. Molecular associations between candidate genes and immune traits in chickens:

The research conducted on candidate genes associated with immunity traits as cited in literature could be summarized in Table 4. In Iowa State University USA, Malek *et al.* (2004) stated that the SNP of *CD28* gene was associated with both bacterial load and vaccine antibody response ($P < 0.05$), while the SNP of *MD2* gene was associated with the bacterial load ($P < 0.003$). Ghebremicael *et al.* (2008) also in Iowa State University USA, showed that SNP of *MAPKAPK2* and *IL10* genes were strongly associated with Salmonella enteritidis burden ($P < 0.001$) and may be valuable in generating resistant birds by marker-assisted selection. In Malaysia, Tohidi *et al.* (2013) reported that *NRAMP1*, *TGFβ3*, *TGFβ4*, and *TRAIL* genes are potential candidates genes to be used in selection programs for increasing genetic resistance against *Salmonella Enteritidis* burden in native Malaysian chickens. In Egypt, Saleh et al (2020b) stated that the SNP genotypes of gallinacin genes (*GAL 3*, *GAL 4* and *GAL* 5) are significantly associated with the caecal *Salmonella typhimurium* count and antibodies in Fayoumi (F), Rhode Island Red (R) ad their crosses ($p<0.05$).

Table (4): Genes associated with immunity traits in terms of bacterial load and antibody response to Salmonella in chickens as cited in literature

Candidate gene with immunity traits	**Chromosome number**	**Reference**
Dual Specificity tyrosine-(Y), Phosphorylation Regulated Kinase1A (*DYRK1A*), Cluster of Differentiation 28 *(CD28)*, Inhibitor of Apoptosis Protein-1 *(IAP1)*, Interferon-*γ* (*IFN-γ*)	1	Kaiser and Lamont (2002), Liu and Lamont (2003), Malek *et al.* (2004), Sadeyen *et al.* (2006), Ghebremicael *et al.* (2008), Tohidi *et al.* (2013), Kazemi *et al.* (2018)
Myeloid Differentiation Primary Response 88 *(MYD88),* Accessory protein of the toll like receptor 4 *(MD-2*)	2	Malek *et al.* (2004), Liu *et al.* (2015)
Transforming growth factor β4 *(TGF-β4)*, Transforming growth factor β2 *(TGF-β2),* Gallinacins 1 to 13 *(Gal 1 to Gal 13)*	3	Kramer *et al.* (2003), Hasenstein *et al. (*2006), Hasenstein and Lamont (2007), Tohidi *et al.* (2013), Psifidi *et al.* (2016), Muhsinin *et al.* (2017), Saleh et al (2020b)
TNF-related apoptosis-inducing ligand (*TRAIL*), Interleukin 2 *(IL2)*, Interleukin 8 *(IL8)*	4	Kramer *et al.* (2003), Malek and Lamont (2003), Tohidi *et al.* (2013), Kazemi *et al.* (2018)
Tumor necrosis factor-related apoptosis-inducing ligand (*TRAIL),* Transforming growth factor β3 *(TGFβ3)*	5	Kramer *et al.* (2003), Tohidi *et al. (2013)*
Prosaposin *(PSAP)*	6	Kramer *et al.* (2003), Tohidi *et al. (2013)*
Natural resistance-associated protein 1 *(NRAMP1)*	7	Lamont *et al*., 2002, Liu *et al.* (2015), Psifidi *et al.* (2016)
Lipopolysaccharide- induced tumor necrosis α factor (*LITAF*)	14	Malek *et al.* (2004) , Tohidi *et al.* (2013)
Macrophage migration inhibitory factor (*MIF),* Immunoglobulin lambda-like polypeptide 1 *(IgL)*	15	Kramer *et al.* (2003), Malek *et al.* (2004)
Major histocompatibility complex *MHC Class I*	16	Lamont *et al. (*2002), Zhou and Lamont (2003b)
Toll like receptor 4 *(TLR4)*	17	Yunis *et al.* (2002), Malek *et al.* (2004),

		Khatab *et al.* (2017)
Caspase 1 *(CASP1)*, Inducible nitric oxide synthase (*iNOS*)	19	Kramer *et al.* (2003), Tohidi *et al.* (2013)
Interleukin *18 (IL-18)*	*24*	Sadeyen *et al.* (2006), Kazemi *et al.* (2018)
Polymeric immunoglobulin receptor *(PIGR)*, Map kinase activated protein kinase 2 (*MAPKAPK2*), Interleukin 10 *(IL10)*, Ligatin *(LGTN)*	26	Ghebremicael *et al.* (2008)

6. SNP genotypes and their associations with growth, feeding performance, egg production and egg quality, disease resistance responses in chickens:

Regarding growth traits, Seo *et al.* (2013) found a significant association between SNP of TSH- β gene and body weight at day 150 in Cornish chickens where chicks of CC genotype (302 ± 6.3 g) were significantly heavier than that of GG genotype (294 ± 4.5 g) ($p<0.05$). Anh *et al* (2015) reported that genotypes of AG and GG showing similar positive effects on chicken growth, while Zhao *et al.* (2015) reported that chicks of AA genotype of *IGFBP-2* gene had significantly heavier body weight at hatch and 12 weeks of age, than that of AB genotype ($p<0.05$). Jin *et al.* (2018) found that chicks with TT genotype of SNP of *Pit-1* gene had heavier and significant body weight at 70 day than those of CT and CC genotypes ($p<0.05$), while AA genotype had heavier and significant body weight at 70 day and lower feed conversion than those of AT and TT genotypes.

For egg production traits, Xu *et al.* (2011a,b) reported that SNPs genotypes of *VIPR-1* gene were associated significantly ($P<0.001$) with age at first egg, egg number at 300 day and total egg production and hens of genotype CC had lower total egg production compared to TT genotype in Ningdu Sanhuang laying chickens. Li *et al.* (2013) found that two SNPs genotypes of *MTNR1A* and *MTNR1C* genes were significantly associated with egg number at 300 days of age and age at first egg ($P< 0.01$). Kulibaba (2015) stated that chicks with heterozygous genotype AB of *GH* gene in Poltavskaya Glinistaya chickens were characterized by higher egg productivity than chickens with genotype BB. Ngu *et al.* (2015) reported significant associations between genotypes of *IPR-1/TaqI* and *VIPR-1/HhaI* genes and egg numbers at 28-47 weeks of age in Noi chicken of Vietnam ($P<0.05$). Tempfli *et al.* (2015) found that the genotypes of *PRL* and *DRD1* genes were associated significantly with egg production ($P<0.05$). Charoensook *et al.* (2016) showed that genotypes of *STAT5B* gene were significantly associated with egg weight, egg height, shell weight, shell thickness and albumen weight ($p<0.001$) and chicks of genotype GG had better egg quality traits than AA and AG genotypes. Vu and Ngu (2016) found that genotypes of *GH* gene were associated with egg production in Noi chickens. Liu *et al.*

(2018) found that SNP of growth differentiation factor 9 gene was significantly associated with age at first egg and weight at first egg and CC genotype exhibited higher age at first egg and weight at first egg than that of TT genotype. Azmal *et al.* (2019) showed that genotypes of RAPGEF6 gene were significantly associated with egg-laying rate at 60 days in Chinese local Jing Hong layer chickens ($p < 0.0001$).

In terms of immunity and disease-resistance traits, Muhsinin *et al.* (2016) reported that CC genotype of *NMAMP1* gene was significantly lower in *salmonella pullorum* count than TC and TT genotypes in Sentul chickens ($p<0.05$). Khatab *et al.* (2017) reported that Fayoumi as pure Egyptian conserved breed has one genotype (BB) for *TLR4*-exon 2 in resistant and susceptibility compared with Hy-line strain chickens. Saleh et al (2020a,b) found that SNP genotypes of *GAL 3*, *GAL 4* and *GAL* 5 genes were significantly associated with the caecal *Salmonella typhimurium* count and the antibodies produced ($p<0.05$) in Fayoumi (F), Rhode Island Red (R), ½R½F and ½F½R genetic groups.

7. Model for detecting the molecular associations between SNP genotypes of candidate gene and economic traits in chickens:

To detect the molecular associations between the genotypes of candidate gene and economic traits, the effects of SNP genotype on different traits must be estimated using the PEST software (Groeneveld, 2006) and applying the following multi-trait animal model (defined in matrix notation):

$$y = Xb + Z_a u_a + e$$

Where y = vector of observed trait on the bird; b = vector of fixed effects, like sex, genetic group, genotype of candidate gene (three genotypes); X and Z_a = incidence matrices corresponding to the fixed and additive random effects of the bird (u_a), respectively; e = vector of random residual effects.

8. Genome-wide association studies (GWAS) for economic traits in chickens:

Recently, with advances in technologies of next generation sequencing, genome-wide association studies (GWAS) have been used successfully to identify SNPs and candidate genes associated with production, reproduction and disease resistance traits in chickens (Yuan *et al.*, 2015; Fan *et al.*, 2017). One of the essential elements needed in GWAS is the powerful statistical method that can be employed to identify genetic associations. Methods that using model of population structure by estimating the covariance due to genetic correlation between individuals have been reported to perform better in terms of detecting true associations than models that ignore genomic relationship matrix (Gianola *et al.*, 2016).

In the last decade, a remarkable range of discoveries from GWASs have been detected in chickens. In this concern, Xu *et al.* (2013) reported that chromosome 1 and 4 are the two critical chromosomes influencing growth traits particularly body weight in chickens. Pértille *et al.* (2017) observed that twenty significant SNPs were associated with feed conversion at 35 days and one significant SNP associated with body weight at 35 days of age. Sun *et al*, (2015), Yi *et al.* (2015) and Qu *et al.* (2019) identified candidate genes that provide strong association with egg weight and egg shell traits. GWAS results of Azmal *et al.* (2019) showed that five identified SNPs in chromosome 13 were associated with

Chickens, Candidate genes, QTL, GWAS, Genomic Breeding Values (GBV), Genomic selection.

egg production traits. Kudinov *et al.* (2019) observed significant associations for age at first egg, body weight and egg weight in genotyping of 146 birds in GWASs and reported that there was an association with immune resistance on chromosome 2. Liu *et al.* (2019) found that genes some identified by annotating sixteen genome-wide significant SNPs that can be considered as candidate genes associated with egg numbers.

9. Suggested genetic improvement program to be applied to improve the Arabian chickens using molecular approaches:

Using traditional selection for genetic improvement in poultry will cause slow and low genetic progress and using biotechnology techniques are the best way to achieve fast genetic improvement. The necessary steps to perform a genetic improvement program in the Arabian breeds of chickens using the molecular applications could be summarized as follows:

Chickens, Candidate genes, QTL, GWAS, Genomic Breeding Values (GBV), Genomic selection.

Step No	Procedure and Executable Approach
1.	**Recording the phenotypic data from full pedigree file to evaluate the birds genetically by estimating PBV for chicks, hens and cocks:** Adequate number of birds will be used. Not adequate records must be discarded to ensure a homogenous data set. The pedigreed birds will be used to estimate the breeding value (EBV) for the economic traits in local breeds of chickens using an animal model applying BLUPF90 software **(Misztal et al., 2018)** fitting univariate the following approach: $\mathbf{y = Xb + Za + e}$ where, y= vector of observations, b= vector of fixed effects with an incidence matrix X, a= vector of random bird effects with incidence matrix Z, and e= vector of random residual effects
2.	**Determine the main equipments and chemicals list required for DNA extraction:** The necessary equipments and chemicals are: PCR machine, Real-time PCR, Gel electrophoresis, Gel Documentation System, Vortex, Centrifuge 30000 rpm under cooling, Biosafety cabinet, EDTA, Ethidium Bromide, Magnesium chloride, dNTPs, PCR Master Mix (2X), Sybr green master mix kits, PFU Taq DNA Polymerase, Agarose, Phenol (nucleic acid grade), DNA isolation Kit from animal tissues, Micropipettes set, Eppendorf.
3.	**Collecting the blood samples and performing DNA extraction (Abdel A'al *et al.*, 2016; 2017):** The blood samples will be collected under sterile conditions by jugular vein puncture using 5-ml vacuum tubes of polypropylene containing EDTA. The samples will transfer to the laboratory in iceboxes containing ice packs and stored at -20° C until extract the genomic DNA. Genomic DNA extraction: genomic DNA will extract using a standard phenol-chloroform extraction protocol and ethanol precipitation methods**.**
4.	**Reporting the candidate genes from QTLs data base:** For bovine genome, a list of previously reported QTL for economic traits was obtained from animal QTL data base release 30 **(Hu *et al.*, 2016)** (http://www.animalgenome.org/QTLdb).
5.	**Preparing the genotyping files (Liu *et al.*, 2019) and genotyping the birds:** The birds will be genotyped using SNPs markers.
6.	**Applying SNP association test:** The National Center for Biotechnology Information (NCBI) database will be used to detect the genes closely associated with economic traits in poultry.
7.	**Estimating the genomic breeding values (GBV) to be applied in genomic selection:** The genomic breeding values (GBV) will be estimated as the sum of the effects of dense genetic markers, or haplotypes of these markers, across the entire genome capturing all the quantitative trait loci (QTL) that contribute to

variation in a trait. The QTL effects detected from individual single nucleotide polymorphism (SNP) markers, are first estimated in a large reference population with phenotypic information **(Abdel A'al *et al.*, 2016; 2017)**. In subsequent generations or in related populations, only marker information is required to calculate GBV.

The mixed model will be used to estimate the breeding values and best linear unbiased (GBLUP). These models must include the fixed effects such as sex and SNPs and the random effects for a given quantitative phenotype. The proposed mixed model and its solution are presented as follows **(Lee et al., 2014)**:

$$\mathbf{y = Xb+Zu+e}$$

Where y is the vector of phenotypic values, X and Z are the design matrices; b and u are vectors of fixed and random effects, respectively.

8. Applying the Genome-Wide Association Study (GWAS):

The birds with more than 20% missing marker genotype will excluded from the analysis. A SNP will be removed from the analysis if it had minor allele frequency less than 0.02. Filtration of the marker data was performed with Plink software **(Purcell *et al.*, 2007).** A genome wide association study will performed using linear regression model in the way of regressing the average daily deviations on SNP alleles and will be implemented by Plink software. The PLINK software will be used for analyzing the GWAS using the following model:

$$\mathbf{y = xb+e}$$

Where, y is a vector of each genomic breeding values (GBV) of the genotyped individuals, x is each SNP information and b is coefficient value for x vector.

9. Evaluating the prediction accuracy of EBV vs GBV:

The correlation between traditional predicted breeding values (PBV) using phenotypic data and pedigree) and the genomic breeding values (GBV) using GWAS procedure must be estimated. The reliability of GBV and the correlation between EBV and GBV were used to evaluate the prediction accuracy **(Moser *et al.*, 2009).**

10 Applying genomic selection program (GS) using the genomic breeding values (GBV):

The genomic selection (GS) is a form of marker assisted selection in which genetic markers covering the whole genome are used, i.e. all quantitative trait loci (QTL) for cocks annnd hens are used . This approach has become feasible due to revolution in SNP discovery method like gene sequencing and SNP genotyping on DNA chip. The genomic breeding values (GBV) and their reliabilities for the genotyped birds will be used to select the best cocks and hens based on their GBV to be the parents for the next generation (genomic selection).

Chickens, Candidate genes, QTL, GWAS, Genomic Breeding Values (GBV), Genomic selection.

REFERENCES CITED

Abdel A'al, M.H., Khalil, M.H., Iraqi, M.M. and El-Moghazy, G.M., 2016. Quantitative trait loci affecting growth performance in F2 intercross between Golden Montazah and White Leghorn chickens. In 3rd International Conference on Biotechnology Applications in Agriculture (ICBAA), Benha University, Sharm El-Sheikh, 5-9 April 2016 , Egypt.

Abdel A'al, M.A., Iraqi, M.M., Khalil, M.H., El-Moghazy, G.M. and El-Atrouny, M.M. 2017. Quantitative Trait Loci Associated with Egg Traits in F2 Intercross between Golden Montazah and White Leghorn Chickens. Benha Journal of Applied Sciences. 2 (3):1-10.

Ahmed, A. 2010. Associations of polymorphisms in four immune-related genes with antibody kinetics and body weight in chickens. *Asian-Australasian Journal of Animal Sciences*, 23**,** 1089-1095.

Amills, M., Jimenez, N., Villalba, D., Tor, M., Molina, E., Cubilo, D., Marcos, C., Francesch, A., Sanchez, A. and Estany, J. 2003. Identification of three single nucleotide polymorphisms in the chicken insulin-like growth factor 1 and 2 genes and their associations with growth and feeding traits. *Poultry Science*, 82**,** 1485-1493.

Anh, N. T. L., Kunhareang, S. and Duangjinda, M. 2015. Association of chicken growth hormones and insulin-like growth factor gene polymorphisms with growth performance and carcass traits in Thai broilers. *Asian-Australasian* Journal *of Animal Sciences*, 28**,** 1686-1695.

Ashraf, A. and El-Tarabany, M. S. 2015. Association of single nucleotide polymorphism in bone morphogenetic protein receptor 1B (BMPR-1B) Gene with growth traits in chicken. Kafkas. Univ. Vet. Fak. Derg. 21, 819-824.

Azmal, S. A., Bhuiyan, A. A., Omar, A. I., Ma, S., Sun, C., Han, Z., Zhang, M., Zhao, S. and Li, S. 2019. Novel polymorphisms in RAPGEF6 gene associated with egg-laying rate in Chinese Jing Hong chicken using Genome-Wide SNP Scan. *Genes*, 10, 384-404.

Beaumont, C., Protais, J., Pitel, F., Leveque, G., Malo, D., Lantier, F., Plisson-Petit, F., Colin, P., Protais, M. and Le Roy, P. 2003. Effect of two candidate genes on the Salmonella carrier state in fowl. *Poultry Science*, 82**,** 721-726.

Bhattacharya, T.K., Chatterjee, R.N., Dange, M. and Bhanja, S.K., 2019. Polymorphisms in GnRHI and GnRHII genes and their association with egg production and egg quality traits in chicken. British Poultry Science, 60(3),187-194.

Bloom, S.E., Delaney, M.E. and Muscarella, D.E. 1993. Constant and variable features of avian chromosomes. In: Etches RJ, Gibbins AMV ‹Editors. Manipulation of the avian genome. Boca Raton, FL: CRC Press 39–60.

Brown, S. M. 1999. Snapping Up SNPs. *BioTechniques*, 26**,** 1090-1093.

Bulut, Z., Kurar, E., Ozsensoy, Y., Nizamlioglu, M., Garip, M., Yilmaz, A., Caglayan, T., Dere, S., Kurtoglu, V. andDogan, M. 2013. Determination of chromosomal regions affecting body weight and egg production in Denizli X White

Leghorn F2 populations. Eurasian Journal of Veterinary Sciences, 29, 30-38.

Cahyadi, M., Seo, D., Jin, S., Choi, N., Park, H.-B., Heo, K. N., Kang, B. S., Jo, C. and Lee, J. H. 2013. Association of SNPs in ODC and PRDM16 with body weight traits in Korean Native Chicken. *Korean Journal of Poultry Science,* 40**,** 157-162.

Cao, Z., Wang, S., Wang, Q., Wang, Y. and Li, H. 2007. Association of spot14α gene polymorphisms with body weight in the chicken. *Poultry Science,* 86**,** 1873-1880.

Charoensook, R., Wichasit, N., Pechrkong, T., Incharoen, T. and Numthuam, S. 2016. STAT5B gene polymorphisms are associated with egg production and egg quality traits in laying hens. Asian Journal of Animal and Veterinary Advances, 11 (12): 847-853. DOI: 10.3923/ajava.2016.847.

Cui, J.X., Du, H.L., Liang, Y., Deng, X.M., Li, N. and Zhang, X.Q. 2006. Association of polymorphisms in the promoter region of chicken prolactin with egg production. Poultry Science, 85: 26-31.

Cui, Z., Liu, L., Zhao, X., Ran, J., Wang, Y., Yin, H., Li, D. and Zhu, Q. 2019. Analysis of expression and single nucleotide polymorphisms of INHA gene associated with reproductive traits in chickens. BioMed Research International, 2019, 11 pages. https://doi.org/10.1155/2019/8572837.

Dehkordi, M. S., Doosti, A. and Arshi, A. 2015. Deletion of Salmonella enterica serovar typhimurium sipC gene. *Asian Pacific Journal of Tropical Biomedicine,* 5**,** 987-991.

El Moujahid, E. M., Chen, S., Jin, S., Lu, Y., Zhang, D., Ji, C. and Yang, N. 2014. Association of leptin receptor gene polymorphisms with growth and feed efficiency in meat-type chickens. *Poultry Science,* 93**,** 1910-1915.

Erhardt, G. and Weimann, C. 2007. Use of molecular markers for evaluation of genetic diversity and in animal production. Arch. Latinoam. *Production Animal*. 15, 63-66.

FAO. 2011. Molecular genetic characterization of animal genetic resources. FAO Animal Production and Health Guidelines. No. 9. Rome.

Fan, Q., Wu, P., Dai, G., Zhang, G., Zhang, T., Xue, Q., Shi, H. and Wang, J. 2017. Identification of 19 loci for reproductive traits in a local Chinese chicken by genome-wide study. Genetics and Molecular Research, 16 (1): gmr16019431.

Fang, M., Nie, Q., Luo, C., Zhang, D. and Zhang, X. 2010. Associations of GHSR gene polymorphisms with chicken growth and carcass traits. *Molecular Biology Reports,* 37**,** 423-428.

Fulton, J.E., Soller, M., Lund, A.R., Arango, J. and Lipkin, E., 2012. Variation in the ovocalyxin-32 gene in commercial egg-laying chickens and its relationship with egg production and egg quality traits. *Animal Genetics*, *43*, 102-113.

Ghebremicael, S., Hasenstein, J. and Lamont, S. 2008. Association of interleukin-10 cluster genes and Salmonella response in the chicken. *Poultry Science,* 87**,** 22-26.

Gianola, D., Fariello, M. I., Naya, H. and Schön, C.C. 2016. Genome-wide association studies with a genomic relationship matrix: a case study with wheat and arabidopsis. G3: Genes, Genomes, Genetics, 6, 3241-3256.

Goraga, Z., Nassar, M. and Brockmann, G. 2012. Quantitative trait loci segregating in crosses between New Hampshire and White Leghorn chicken lines: I. egg production traits. Animal Genetics, 43, 183-189.

Gouda, E. M. and Essawy, G. S. 2010. Polymorphism of insulin-like growth factor I gene among chicken breeds in Egypt. *Zeitschrift für Naturforschung C,* 65**,** 284-288.

Groeneveld, E. 2006. PEST User´s Manual. *Institute of Animal Husbandry and Animal Behaviour, FAL, Germany*.

Harini, N. M., Duryadi, S., Sri, S. and Cece, S. 2013. Polymorphisms of Insuline-like growth factor-I (IGF-1) and pituitary positive transcription factor-1 (Pit-I) genes and their effect on growth traits in indonesian native chickens. Proceeding of the International Conference on 4th Green Technology Faculty of Science and Technology, January 2013, State Islamic University of Malang, Indonesia.

Hasenstein, J.R. and Lamont, S.J . 2007 .Chicken gallinacin gene cluster associated with Salmonella response in advanced intercross line .Avian. Dis ‹(2007) 51 ‹.pp567-561 .

Hasenstein ‹J.R .Zhang, G . and Lamont S.J .2006 . Analyses of five gallinacin genes and the Salmonella enterica serovar enteritidis response in poultry .Infect. Immun ‹(2006) 74 ‹. pp.3380-3375 .

Hu, J., Bumstead, N., Barrow, P., Sebastiani, G., Olien, L., Morgan, K. and Malo, D. 1997. Resistance to salmonellosis in the chicken is linked to NRAMP1 and TNC. *Genome Research,* 7**,** 693-704.

Hu, Z.L., Park, C.A., Reecy, J.M., 2016. Developmental progress and current status of the Animal QTLdb. Nucleic Acids Res. 44, 827-833.

Ikeobi, C., Woolliams, J., Morrice, D., Law, A., Windsor, D., Burt, D. and Hocking, P. 2002. Quantitative trait loci affecting fatness in the chicken. Animal Genetics, 33, 428-435.

Iraqi, M. M., Hanafi, M., El-Moghazy, G. M., El-Kotait, A. and A'al, M. A. 2011. Estimation of crossbreeding effects for growth and immunological traits in a crossbreeding experiment involving two local strains of chickens. *Livestock Research for Rural Development,* 23, *Article #82..*

Jacobsson, L., Park, H., Wahlberg, P., Fredriksson, R., Perez-Enciso, M., Siegel, P., and Andersson, L. 2005. Many QTLs with minor additive effects are associated with a large difference in growth between two selection lines in chickens. *Genetical Research, 86*(2): 115-125.

Jin, S., He, T., Yang, L., Tong, Y., Chen, X. and Geng, Z. 2018. Association of polymorphisms in Pit-1 gene with growth and feed efficiency in meat-type chickens. *Asian-Australasian Journal of Animal Sciences,* 31**,** 1685-1690.

Kaiser, M. and Lamont, S. 2002. Microsatellites linked to Salmonella enterica Serovar Enteritidis burden in spleen and cecal content of young F1 broiler-cross chicks. *Poultry Science,* 81**,** 657-663.

Kalinowski, S. T., Taper, M. L. and Marshall, T. C. 2007. Revising how the computer program CERVUS accommodates genotyping error increases success in paternity assignment. *Molecular Ecology,* 16**,** 1099-1106.

Kazemi, H., Najafi, M., Ghasemian, E., Rahimi-Mianji, G. and Pirsaraei, Z. A. 2018. Polymorphism detection of promoter region of IFN-γ and IL-2 genes and their association with productive traits in Mazandaran native breeder fowls. *Journal of Genetics,* 97**,** 843-851.

Khalil, M.H., Iraqi, M.M., El-Moghazy, G.M. and Abdel A'al, M.H. 2016. QTL and chromosomal mapping for growth and egg performance in chickens: Applications and emphasis of results in Egypt. In 3rd International Conference on Biotechnology Applications in Agriculture (ICBAA), Benha University, Sharm El-Sheikh, 5-9 April 2016 , Egypt.

Khatab, Shymaa A., Hemeda, S.A., El-Nahas, Abeer F. and Abd El Naby, Walaa S.H. 2017. Polymorphisms of TLR4 gene and its association with genetic resistance to salmonella enteritidis infection in Fayoumi breed and Hy-line strain in Egypt. *Alexandria Journal for Veterinary Sciences,* 55, 1-9.

Kita, K., Nagao, K. and Okumura, J. 2005. Nutritional and tissue specificity of IGF-I and IGFBP-2 gene expression in growing chickens-a review. *Asian-Australasian Journal of Animal Sciences,* 18**,** 747-754.

Kramer, J., Malek, M. and Lamont, S. 2003. Association of twelve candidate gene polymorphisms and response to challenge with Salmonella enteritidis in poultry. *Animal Genetics,* 34**,** 339-348.

Kudinov, A. A., Dementieva, N. V., Mitrofanova, O. V., Stanishevskaya, O. I., Fedorova, E. S., Larkina, T. A., Mishina, A. I., Plemyashov, K. V., Griffin, D. K. and Romanov, M. N. 2019. Genome-wide association studies targeting the yield of extraembryonic fluid and production traits in Russian White chickens. BMC Genomics, 20, 270-282.

Kulibaba, R.A. 2015. Polymorphism of growth hormone, growth hormone receptor, prolactin and prolactin receptor genes in connection with egg production in poltava clay chicken. Agricultaral Biology, 50(2):198-207.

Kumar, S., Dilbaghi, N., Ahlawat, S., Bina, M., Tantia, M. and Vijh, R. 2007. Genetic relationship among chicken populations of India based on SNP markers of Myostatin gene (GDF 8). *International Journal of Poultry Science* 9**,** 684-688.

Lamont, S., Kaiser, M. and Liu, W. 2002. Candidate genes for resistance to Salmonella enteritidis colonization in chickens as detected in a novel genetic cross. *Veterinary Immunology and Immunopathology,* 87**,** 423-428.

Lander, E. S. 1996. The new genomics: global views of biology. *Science,* 274**,** 536-539.

Lee, W., Tonelli, M. & Markley, J. L. 2014. NMRFAM-SPARKY: enhanced software for biomolecular NMR spectroscopy. *Bioinformatics,* 31**,** 1325-1327.

Lei, M., Nie, Q., Peng, X., Zhang, D. and Zhang, X. 2005. Single nucleotide polymorphisms of the chicken insulin-like factor binding protein 2 gene associated with chicken growth and carcass traits. *Poultry Science,* 84**,** 1191-1198.

Lei, M., Luo, C., Peng, X., Fang, M., Nie, Q., Zhang, D., Yang, G. and Zhang, X. 2007. Polymorphism of growth-correlated genes associated with fatness and muscle fiber traits in chickens. *Poultry Science,* 86**,** 835-842.

Lei, M., Peng, X., Zhou, M., Luo, C., Nie, Q. and Zhang, X. 2008. Polymorphisms of the IGF1R gene and their genetic effects on chicken early growth and carcass traits. *BMC Genetics,* 9**,** 70-79.

Leng, L., Wang, S., Li, Z., Wang, Q. And Li, H. 2009. A polymorphism in the 3′-flanking region of insulin-like growth factor binding protein 2 gene associated with abdominal fat in chickens. *Poultry Science,* 88**,** 938-942.

Li, D.Y., Zhang, L., Smith, D.G., Xu, H.L., Liu, Y.P., Zhao, X.L., Wang, Y. and Zhu, Q., 2013. Genetic effects of melatonin receptor genes on chicken reproductive traits. Czech J. Anim. Sci. 58(2), 58-64 **.**

Li, G., Sun, D.X., Yu, Y., Liu, W.J., Tang, S.Q., Zhang, Y., Wang, Y.C., Zhang, S.L., Zhang, Y., 2011. Genetic effect of the follicle-stimulating hormone receptor gene on reproductive traits in Beijing You chickens. *Poultry Science.* 90, 2487–2492.https://doi.org/10.3382/ps.2010-01327.

Li, H., Deeb, N., Zhou, H., Mitchell, A., Ashwell, C. and Lamont, S. J. 2003. Chicken quantitative trait loci for growth and body composition associated with transforming growth factor-beta genes. *Poultry Science,* 82**,** 347-356.

Li, H.F., Zhu, W.Q., Chen, K.W., Wu, X., Tang, Q.P., Gao, Y.S., Song, W.T., Xu, W.J and Xu, H.L. 2009. Polymorphism in NPY and IGF-I genes associate with reproductive traits in Wenchang chicken. African Journal of Biotechnology 8: 4744-4748.

Li, P., Xia, P., Wen, J., Zheng, M., Chen, J., Zhao, J., Jiang, R., Liu, R. and Zhao, G. 2010. Up-regulation of the MyD88-dependent pathway of TLR signaling in spleen and caecum of young chickens infected with Salmonella serovar Pullorum. *Veterinary Microbiology,* 143**,** 346-351.

Lim, H., Han, J., Oh, J., Lee, H., Jeon, G., Lee, J., Seo, D., Cahyadi, M., Song, K. and Choi, K. 2013. Association of SNPs from iNOS and TLR-4 genes with economic trait in chicken. *Korean Journal of Poultry Science,* 40**,** 83-89.

Liu, Z., Yang, N., Yan, Y., Li, G., Liu, A., Wu, G. and Sun, C. 2019. Genome-wide association analysis of egg production performance in chickens across the whole laying period. BMC Genetics, 20, 67-76.

Liu, L., Cui, Z., Xiao, Q., Zhang, H., Zhao, X., Wang, Y., Yin, H., Li, D. and Zhu, Q. 2018. Polymorphisms in the chicken growth differentiation factor 9 gene associated with reproductive traits. *BioMed Research International,2018* online.

Liu, W. and Lamont, S. 2003. Candidate gene approach: Potentional association of Caspase-1, Inhibitor of Apoptosis Protein-1, and Prosaposin gene polymorphisms with response to Salmonella enteritidis challenge or vaccination in young chicks. *Animal Biotechnology,* 14**,** 61-76.

Liu, X. Q., Wang, F., Jin, J., Zhou, Y.G., Ran, J.S., Feng, Z.Q., Wang, Y. and Liu, Y.P. 2015. MyD88 polymorphisms and association with susceptibility to salmonella pullorum. *BioMed Research International*, 6, 1-7.

Liu, X., Zhang, H., Li, H., Li, N., Zhang, Y., Zhang, Q., Wang, S., Wang, Q. and Wang, H. 2008. Fine-mapping quantitative trait loci for body weight and abdominal fat traits: effects of marker density and sample size. Poultry Science. 87:1314–1319.

Mackay, T.F., Stone, E.A. and Ayroles, J.F. 2009. The genetics of quantitative traits: challenges and prospects. Nature Reviews Genetics, 10, 565-577.

Malek, M. and Lamont, S. J. 2003. Association of INOS, TRAIL, TGF-β2, TGF-β3, and IgL genes with response to Salmonella enteritidis in poultry. *Genetics Selection Evolution*, 35**,** 99-111.

Malek, M., Hasenstein, J. and Lamont, S. 2004. Analysis of chicken TLR4, CD28, MIF, MD-2, and LITAF genes in a Salmonella enteritidis resource population. *Poultry Science*, 83**,** 544-549.

Meng, H., Zhao, J., Li, Z. and Li, H. 2005. Single nucleotide polymorphisms on peroxisome proliferator-activated receptor genes associated with fatness traits in chicken. *Asian-Australasian Journal of Animal Sciences*, 18**,** 1221-1225.

Misztal, I., Tsuruta, S. Lourenco, D.A.L. Masuda, Y. Aguilar, I. Legarra, A. and Vitezica, Z. 2018. Manual for BLUPF90 family of programs. Vol. 2018. Accessed December 17, 2018. http://nce.ads.uga.edu/wiki/lib/exe/fetch.php?media=blupf90_all7.pdf

Molee, A., Kongroi, K., Kuadsantia, P., Poompramun, C. and Likitdecharote, B. 2016. Association between single nucleotide polymorphisms of the major histocompatibility complex class II gene and Newcastle disease virus titre and body weight in Leung Hang Khao chickens. *Asian-Australasian Journal of Animal Sciences*, 29**,** 29-35.

Moser, G., Tier, B., Crump, R. E., Khatkar, M. S. and Raadsma, H. W. 2009. A comparison of five methods to predict genomic breeding values of dairy bulls from genome-wide SNP markers. *Genetics Selection Evolution*, 41**,** 56-72.

Muhsinin, M., Ulupi, N., Gunawan, A., Wibawan, I. and Sumantri, C. 2016. Association of NRAMP1 polymorphisms with immune traits in Indonesian native chickens. *Int. J Poult. Sci.*, 15**,** 401-406.

Muhsinin, M., Ulupi, N., Gunawan, A., Wibawan, I. W. T. and Sumantri, C. 2017. g. 640T> C Polymorphism of the TGF-β2 gene is associated with salmonella pullorum resistance in Indonesian chickens. *Animal Production*, 19**,** 81-92.

Nassar, M., Goraga, Z. and Brockmann, G. 2013. Quantitative trait loci segregating in crosses between New Hampshire and White Leghorn chicken lines: III. Fat deposition and intramuscular fat content. Animal Genetics, 44, 62-68**.**

Nassar, M., Goraga, Z. and Brockmann, G. 2015. Quantitative trait loci segregating in crosses between New Hampshire and White Leghorn chicken lines: IV. Growth performance. Animal Genetics, 46, 441-446.

Ngu, N.T., Xuan, N.H., Vu, C.T., An, N.T., Dung, T.N. and Nhan, N.T.H. 2015. Effects of genetic polymorphisms on egg production in indigenous Noi chicken. Journal of Experimental Biology and Agricultural Sciences. 3(6):487-493.

Nguyen, T.T.B., Duc, N.H., Quy, V.C., Yen, H.T., Loan, T.T., Thuy, D.T.N., Tien, V.T. and Thuy, N.T.D. 2018. Effect of nucleotide polymorphism of candidate genes on egg production traits in native Lien Minh chicken. Livestock Research for Rural Development. Volume 30, Article #103. Retrieved February 1, 2020, from http://www.lrrd.org/lrrd30/6/ntdt30103.html

Nie, Q., Sun, B., Zhang, D., Luo, C., Ishag, N., Lei, M., Yang, G. and Zhang, X. 2005. High diversity of the chicken growth hormone gene and effects on growth and carcass traits. *Journal of Heredity,* 96, 698-703.

Nie, Q., Fang, M., Xie, L., Zhou, M., Liang, Z., Luo, Z., Wang, G., Bi, W., Liang, C. and Zhang, W. 2008. The PIT1 gene polymorphisms were associated with chicken growth traits. *BMC Genetics,* 9**,** 20-27.

Niknafs, S., Nejati-Javaremi, A., Mehrabani-Yeganeh, H. and Fatemi, S. A. 2012. Estimation of genetic parameters for body weight and egg production traits in Mazandaran native chicken. *Tropical Animal Health and Production,* 44**,** 1437-1443.

Nones, K., Ledur, M.C., Ruy, D.C., Baron, E.E., Melo, C.M.R., Moura, A.S.A.M.T., Zanella, E.L., Burt, D.W. and Coutinho, L.L., 2006. Mapping QTLs on chicken chromosome 1 for performance and carcass traits in a broiler x layer cross. Animal Genetics, 37(2): 95-100.

Ou, J., Tang, S., Sun, D. and Zhang, Y. 2009. Polymorphisms of three neuroendocrine-correlated genes associated with growth and reproductive traits in the chicken. *Poultry Science,* 88**,** 722-727.

Ouyang, H., Zhang, H., Li, W., Liang, S., Jebessa, E., Abdalla, B. A. and Nie, Q. 2016. Identification, expression and variation of the GNPDA2 gene, and its association with body weight and fatness traits in chicken. *Peer J,* 4**,** 21-29.

Osman, M. M., Hemeda, S. A., Hassanin, A. A. and Husseiny, W. A. 2017. Polymorphism of prolactin gene and its association with egg production trait in four commercial chicken lines. Journal of the Hellenic Veterinary Medical Society, 68, 391-404.

Park, K. S., Shin, H. D., Park, B. L., Cheong, H. S., Cho, Y. M., Lee, H. K., Lee, J.-Y., Lee, J.-K., Oh, B. and Kimm, K. 2006. Polymorphisms in the leptin receptor (LEPR) putative association with obesity and T2DM. *Journal of Human Genetics,* 51**,** 85-91.

Peakall, R. and Smouse, P. E. 2012. GenAlEx 6.5: genetic analysis in Excel. population genetic software for teaching and research an update. *Bioinformatics,* 28**,** 2537-2539.

Pertille, F., Moreira, G. C. M., Zanella, R., Da Silva Nunes, J. D. R., Boschiero, C., Rovadoscki, G. A., Mourão, G. B., Ledur, M. C. and Coutinho, L. L. 2017. Genome-wide association study for performance traits in chickens using genotype by sequencing approach. Scientific Reports, 7, 41748. doi: 10.1038/srep41748..

Psifidi, A., Banos, G., Matika, O., Desta, T. T., Bettridge, J., Hume, D. A., Dessie, T., Christley, R., Wigley, P. and Hanotte, O. 2016. Genome-wide association studies of immune, disease and production traits in indigenous chicken ecotypes. *Genetics Selection Evolution*, 48**,** 74-90.

Purcell, S., Neale, B., Todd-Brown, K., Thomas, L., Ferreira, M. A., Bender, D., Maller, J., Sklar, P., De Bakker, P. I. and Daly, M. J. 2007. PLINK: a tool set for whole-genome association and population-based linkage analyses. *The American Journal of Human Genetics*, 81**,** 559-575.

Qiu, F., Nie, Q., Luo, C., Zhang, D., Lin, S. and Zhang, X. 2006. Association of single nucleotide polymorphisms of the insulin gene with chicken early growth and fat deposition. *Poultry Science*, 85**,** 980-985.

Qu, L., Shen, M., Guo, J., Wang, X., Dou, T., Hu, Y., Li, Y., Ma, M., Wang, K. and Liu, H. 2019. Identification of potential genomic regions and candidate genes for egg albumen quality by a genome-wide association study. Archives Animal Breeding, 62, 113-123.

Raymond, M. 1995. GENEPOP (version 1.2): population genetics software for exact tests and ecumenicism. *J. Hered.*, 86**,** 248-249.

Rikimaru, K., Komatsu, M., Suzuki, K., Uemoto, Y., Takeda, H. and Takahashi, H. 2012. Association between cholecystokinin type A receptor haplotypes and growth traits in Japanese Hinai-dori crossbred chickens. *Molecular Biology Reports*, 39**,** 4479-4484.

Sadeyen, J.R., Trotereau, J., Protais, J., Beaumont, C., Sellier, N., Salvat, G., Velge, P. and Lalmanach, A.-C. 2006. Salmonella carrier-state in hens: study of host resistance by a gene expression approach. *Microbes and Infection*, 8**,** 1308-1314.

Saleh, M.S. 2019. Using bioinformatics SNP to improve immune genetic response against some pathogens in poultry. M Sc. Thesis In cooperation between Faculty of Agriculture at Moshtohor, Benha University, Egypt and Tempus European Union program 2019.

Saleh, M. S., Iraqi, M.M., Khalil, M.H. Antonio, C. 2018. Molecular analysis of crossbreeding experiment to improve immune genetic response against salmonella in poultry. *4th International Conference on Biotechnology Applications in Agriculture (ICBAA), 4-7 April 2018, Hurghada, Egypt. Benha University, Egypt*

Saleh, M.S., M.M. Iraqi, M.H. Khalil, A. Camarda, 2020. Crossbreeding analyses and polymorphic associations of gallinacin genes with growth traits in chickens. Livestock Science, Volume 240, October 2020, https://doi.org/10.1016/j.livsci.2020.104118

Medhat Saleh, Maher H. Khalil, Mahmoud M. Iraqi, Antonio Camarda, 2020a. Molecular associations of gallinacingenes with immune response against Salmonella typhimurium in chickens.

Livestock Science, https://doi.org/10.1016/j.livsci.2020.104315

M. S. Saleh, M. H. Khalil, M. M. Iraqi and A. Camarda, 2020b. Polymorphic characterisation of gallinacin candidate genes and their molecular associations with growth and immunity traits in chickens. British__Poultry Science, https://doi.org/10.1080/00071668.2020.1847252

Saleh, M. S., Khalil, M. H., Iraqi, M. M., Camarda, A. 2021. Bioinformatics analysis of four Gallinacin genes for immunity traits in chickens. 5th International Conference on Biotechnology Applications in Agriculture (ICBAA), Benha University, 8 April 2021, Egypt (Conference Online), Animal Biotechnology, 37 – 50, https://assjm.journals.ekb.eg/article_183357.html

Sasaki, O., Odawara, S., Takahashi, H., Nirasawa, K., Oyamada, Y., Yamamoto, R., Ishii, K., Nagamine, Y., Takeda, H., Kobayashi, E. and Furukawa, T., 2004. Genetic mapping of quantitative trait loci affecting body weight, egg character and egg production in F2 intercross chickens. Animal Genetics, 35(3): 188-194.

Seo, D., Yun, J., Kang, W., Jeon, G., Hong, K. C. and Ko, Y. 2001. Association of insulin-like growth factor-I (IGF-I) gene polymorphism with serum IGF-I concentration and body weight in Korean Native Ogol chicken. *Asian-Australasian Journal of Animal Sciences*, 14, 915-921.

Seo, J., Oh, J. D., Choi, E. J., Lim, H. K., Seong, J., Song, K. D., Lee, J. H., Lee, H. K., Kong, H. S. and Jeon, G. J. 2013. Effects of SNP in TSH-β Gene of Chicken on Economic Traits. *Korean Journal of Poultry Science*, 40, 115-120.

Sewalem, A., Morrice, D.M., Law, A., Windsor, D., Haley, C.S., Ikeobi, C.O.N., Burt, D.W. And Hocking, P.M. 2002. Mapping of quantitative trait loci for body weight at three, six, and nine weeks of age in a broiler layer cross. Poultry Science, 81, 1775-1781.

Siwek, M., Cornelissen, S. J., Buitenhuis, A. J., Nieuwland, M. G., Bovenhuis, H., Crooijmans, R. P., Groenen, M. A., Parmentier, H. K. and van der Poel, J. J. 2004. Quantitative trait loci for body weight in layers differ from quantitative trait loci specific for antibody responses to sheep red blood cells. Poultry Science, 83:853–859.

Sun, C., Qu, L., Yi, G., Yuan, J., Duan, Z., Shen, M., Qu, L., Xu, G., Wang, K. & Yang, N. 2015. Genome-wide association study revealed a promising region and candidate genes for eggshell quality in an F2 resource population. *BMC Genomics*, 16, 565-579.

Su, Y.J., Shu, J.T., Zhang, M., Zhang, X.Y., Shan, Y.J., Li, G.H., et al. 2014. Association of chicken growth hormone polymorphisms with egg production. The Genetics and Molecular Research Journal, 13(3):4893-4903.

Tatsuda, K. and Fujinaka, K. 2001. Genetic mapping of the QTL affecting body weight in chickens using a F2 family. British Poultry Science, 42(3):333-337.

Tempfli, K., Konrád, S., Kovácsné Gaál, K., Pongrácz, L. and Bali Papp, Á. 2015. Prolactin, dopamine receptor D1 and Spot14αpolymorphisms affect production traits of Hungarian Yellow hens. Livestock Science, 174, 26–30.https://doi.org/10.1016/j.livsci.2015.01.012.

Tohidi, R., Idris, I., Malar Panandam, J. and Hair Bejo, M. 2013. The effects of polymorphisms in 7 candidate genes on resistance to Salmonella Enteritidis in native chickens. *Poultry Science*, 92**,** 900-909.

Tuiskula-Haavisto M., Honkatukia M., Vilkki J., de Koning D.J‹ Schulman N.F. and Maki-Tanila A. 2002. Mapping of quantitative trait loci affecting quality and production traits in egg layers. Poultry Science 81, 919–27.

Tyasi, T. L., Qin, N., Liu, D., Niu, X., Zhu, H. and Xu, R. 2018. The association between novel polymorphisms of gremlin genes and egg-laying performance traits in Chinese village Dagu hens. *Annals of Animal Science*, 18, 361-373.

Twito, T., Weigend, S., Blum, S., Granevitze, Z., Feldman, M., Perl-Treves, R., Lavi, U. and Hillel, J. 2007. Biodiversity of 20 chicken breeds assessed by SNPs located in gene regions. *Cytogenetic and Genome Research*, 117**,** 319-326.

Uemoto, Y., Sato, S., Ohtake, T., Sato, S., Okumura, Y. and Kobayashi, E. 2011. Ornithine decarboxylase gene is a positional candidate gene affecting growth and carcass traits in F2 intercross chickens. *Poultry Science,* 90**,** 35-41.

Vu, C.T. and Ngu, NT. 2016. Single nucleotide polymorphisms in candidate genes associated with egg production traits in native Noi chicken of Vietnam. International Journal of Plant, Animal and Environmental Sciences, 6(1):162-169.

Wei, L., Fangqun, L. and Daquan, L. 2009. IGF-1 Gene polymorphism and weight-related analysis. *Int. J Biol.,* 1**,** 113-118.

Weigend, S. 2004. Overview on the use of molecular markers to characterise genetic diversity in chickens. World's Poultry Congress and Exhibition. In: *Proceedings of XXII World's Poultry Congress*, 8–13 June 2004, 192. Istanbul, Turkey.

Xu, H., Zeng, H., Luo, C., Zhang, D., Wang, Q., Sun, L., Yang, L., Zhou, M., Nie, Q. and Zhang, X. 2011a. Genetic effects of polymorphisms in candidate gens and the QTL region on chicken age at first egg. BMC Genetics 12:33. doi: 10.1186/1471-2156-12-33.

Xu, H., Zeng, H., Zhang, D., Jia, X., Luo, C., Fang, M., Nie, Q. and Zhang, X. 2011b. Polymorphisms associated with egg number at 300 days of age in chickens. Genetics and Molecular Research, 10: 2279-2289.

Xu, Z., Nie, Q. and Zhang, X. 2013. Overview of genomic insights into chicken growth traits based on genome-wide association study and microRNA regulation. Current Genomics, 14, 137-146.

Yang, ZJ., Fu, L., Zhang, GW., Yang, Y., Chen, SY., Wang, J. and Lai, S.J. 2013. Identification and association of SNPs in TBC1D1 gene with growth traits in two rabbit breeds. *Asian-Australasian Journal of Animal Sciences*, 26**,** 1529-1535.

Ye, X., Avendano, S., Dekkers, J. and Lamont, S. 2006. Association of twelve immune-related genes with performance of three broiler lines in two different hygiene environments. *Poultry Science,* 85**,** 1555-1569.

Yi, G., Shen, M., Yuan, J., Sun, C., Duan, Z., Qu, L., Dou, T., Ma, M.,

Lu, J. and Guo, J. 2015. Genome-wide association study dissects genetic architecture underlying longitudinal egg weights in chickens. BMC Genomics, 16, 746-760**.**

Yi, Z., Li, X., Luo, W., Xu, Z., Ji, C., Zhang, Y., Nie, Q., Zhang, D. and Zhang, X. 2018. Feed conversion ratio, residual feed intake and cholecystokinin type A receptor gene polymorphisms are associated with feed intake and average daily gain in a Chinese local chicken population. *Journal of Animal Science and Biotechnology,* 9**,** 50-59.

Yuan, J., Wang, K., Yi, G., Ma, M., Dou, T., Sun, C., Qu, L.-J., Shen, M., Qu, L. and Yang, N. 2015. Genome-wide association studies for feed intake and efficiency in two laying periods of chickens. Genetics Selection Evolution, 47, 82-95.

Yuan, Z., Chen, Y., Chen, Q., Guo, M., Kang, L., Zhu, G. and Jiang, Y., 2016. Characterization of chicken MMP13 expression and genetic effect on egg production traits of its promoter polymorphisms. *G3: Genes, Genomes, Genetics*, *6*(5): 1305-1312.

Yunis, R., Heller, E., Hillel, J. and Cahaner, A. 2002. Microsatellite markers associated with quantitative trait loci controlling antibody response to Escherichia coli and Salmonella enteritidis in young broilers. *Animal Genetics,* 33**,** 407-414.

Zhang, Z.R., Liu, Y.P., Yao, Y.G., Jiang, X.S., Du, H.R. and Zhu, Q. 2009. Identification and association of the single nucleotide polymorphisms in calpain3 (CAPN3) gene with carcass traits in chickens. *BMC Genetics,* 10**,** 10-17.

Zhao, X., Li, M., Xu, S. and Liu, G. 2015. Single nucleotide polymorphisms in IGFBP-2 gene and their associations with body weight traits on Jinghai Yellow chicken. *Brazilian Journal of Poultry Science,* 17**,** 497-502.

Zhou, H. and Lamont, S. 2003a. Associations of six candidate genes with antibody response kinetics in hens. *Poultry Science,* 82**,** 1118-1126.

Zhou, H. and Lamont, S. J. 2003b. Chicken MHC class I and II gene effects on antibody response kinetics in adult chickens. *Immunogenetics,* 55**,** 133-140.

Zhou, H., Buitenhuis, A., Weigend, S. and Lamont, S. 2001. Candidate gene promoter polymorphisms and antibody response kinetics in chickens: interferon-γ, interleukin-2, and immunoglobulin light chain. *Poultry Science,* 80**,** 1679-1689.

Zhou, H., Mitchell, A., Mcmurtry, J., Ashwell, C. And Lamont, S. J. 2005. Insulin-like growth factor-I gene polymorphism associations with growth, body composition, skeleton integrity, and metabolic traits in chickens. *Poultry Science,* 84**,** 212-219.

Zhou, M., Du, Y., Nie, Q., Liang, Y., Luo, C., Zeng, H. and Zhang, X. 2010. Associations between polymorphisms in the chicken VIP gene, egg production and broody traits. British Poulttry Science, 51, 195-203.

Zhu, G. and Jiang, Y. 2014. Polymorphism, genetic and association with egg production traits of chicken matrix metalloproteinases 9 promoter. Asian- Australasian Journal of Animal Sciences, 27(11):1526-1531.