Review Article

GENETICS, GENOMICS AND BREEDING FOR DISEASE RESISTANCE IN POULTRY

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ABSTRACT

The diseases in poultry cause huge losses in the form of mortality in acute infections or as substandard performance due to chronic illness. Biosecurity and vaccination are considered as two important primary strategies for disease prevention in poultry. On the other hand, breeding for disease resistance is an alternate strategy to combat the damages of diseases. Although, attempts were initiated to develop disease resistant poultry by breeding almost a century before, this branch of science renewed the interest among scientists because of catastrophic emerging and re-emerging diseases like Avian influenza. It has proven over a period of time that poultry exhibits genetic resistance to viral diseases like avian leukosis complex, Marek's disease, avian influenza and Newcastle disease, bacterial disease like salmonellosis and may parasitic infestations. The key genes responsible for resistance to specific diseases have also been demonstrated. The breeding attempts for developing disease resistant poultry has yielded positive results with varying degree of success. The advent of sophisticated molecular methods like genomic selection using high-density SNP chips, RNA-seq technique and identification of key marker genes and transgenesis could complement the conventional breeding methods to a larger extent in developing disease resistant poultry.

Keywords: Breeding, disease resistance, heritability, poultry, selection

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INTRODUCTION

The chicken genetic maps for morphological and physiological traits have been built over many years since almost the beginning of twentieth century (Bitgood and Somes, 1990). However, our knowledge of chicken genome changed enormously at present especially due to the advent of the analytic procedures to analyze large numbers of partial cDNA sequences (Abdrakhmanov *et al*., 2000) and now, culminated most recently in description of chicken genome sequence data (Hillier *et al*., 2004). These were the milestones in our understanding about developmental biology of aves and the evolution of vertebrates. These developments have immense applications

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in breeding of poultry for various economic traits.

A unique characteristic of avian genomes is the large variability in the size of their chromosomes. Chicken, one of the most important avian species have 39 pairs of chromosomes; of which, 5 are macro-chromosomes, 5 are intermediate, 28 are micro-chromosomes and one is sex (Z and W) chromosome (ICGS, 2004). The chicken genome comprises of approximately 1.2 billion base pairs of DNA only in 39 pairs of chromosomes, including a pair of sex chromosomes ZZ for males and ZW for females (Masabanda *et al*., 2004). Despite the fact that the DNA content of chicken genome is nearly 40 per cent of a typical mammalian genome, it has almost same number of genes to that of mammalian counterparts (Carre *et al*., 2006). This could be possible with the reduced intergenic spaces and reduced repetitive sequence content in chicken genome. However, blocks of conserved sequences have been preserved during the course of evolution of aves which spanned over 500 million years.

The diseases in poultry have severe economic impact with their involvement towards expenditures on disease prevention and treatment apart from losses due to reduced production (Biggs, 1982). Bacterial diseases not only cause significant human food safety problems by exposing the public to contaminated meat and eggs, but also reduce the production efficiency of human due to pathogenic bacterial burden (Klasing and Korver, 1997). Furthermore, there are negative consumer reactions to antibiotic usage in food animals and the potential introduction of antibiotic resistant bacteria into the food chain (Hedman *et al*., 2020).

Genetic resistance in livestock has kindled a lot of interest in terms of industrial and academic viewpoints (Pal and Chakravarty, 2020). Breeding for disease resistance can be a powerful tool to ward off diseases as a long-term strategy. Roberts and Card in (1935) first attempted to breed for developing disease resistant poultry. This science has progressed well during the recent decades. Molecular breeding for developing resistant animals by introducing the genomic marker responsible for disease resistance or immunocompetence has taken momentum. Also, the recent understanding of molecular biology unveils scopes of application of targeted genome editing in animal breeding for disease resistance (Islam *et al*., 2020).

In this review, the recent advances in our understanding about genetic and genomic control of diseases in the poultry are discussed. This information could further promote the research in the area of breeding poultry for disease resistance.

Elements of disease resistance in chicken genome

The sequencing of chicken genome (Hillier *et al*., 2004) and development of single-nucleotide polymorphism (SNP) map (Wong *et al.,* 2004) has opened up new possibilities to understand the impact of genetic variation on immune response, health and host response to

pathogens in poultry. This, in turn, will enable more informed and effective use of genetic enhancement strategies as means to protect avian health through genetic selection for improved immune responsiveness (Islam *et al*., 2020) and production of specific pathogen-resistant transgenic lines of birds (Lyall *et al*., 2011).

The chicken genome sequence data revealed many facts about genetic resistance in chicken. This include discovery of cytokines like IL 4 that involve in the T Helper 2 (Th2) cell response (Smith *et al*., 2004). It was previously suggested that typical Th2 response cannot be elicited by chicken (Staeheli *et al*., 2001). Further, the interleukin receptors for IL10 and IL13 were also identified in chicken. The chicken genome sequence revealed the presence of cytokines, chemokines and their receptors (Hillier *et al.,* 2004) and even genes like IL3, IL7, IL9, IL26, CSMF, LIF and Cathelicidin, which were considered to be mammalian-specific earlier. However, many orthologs to human chemokines like CCL2, 7, 8, 11, 15, 18, 23, 24, and 26; CXCL1–7, 9, 10, and 11 and chemokine receptors like CCR1, CCR3, CCR10, CXCR3, and CXCR6 are absent in chicken genome (Hillier *et al.,* 2004).

Chicken B locus

The major histocompatibility complex (MHC) in chicken genome was first discovered as a blood group locus and was also termed the B complex (Briles *et al.,* 1950). Schierman and Nordskog (1961) demonstrated that the B blood group locus in chickens is linked to genes controlling histocompatibility. The MHC encodes for three classes of proteins named B-F, B-L, and B-G (Kaufman and Lamont, 1996). At the molecular level, the chicken MHC has unique features that will enhance its value as a marker for disease resistance. The class I and II genes overlap, therefore forming extremely tight linkage; introns are relatively small (10% of the size of most mammalian MHC); additional genes, including ones with homology to mammalian genes involved in lymphocyte activation and TAP2 (transporter associated with antigen processing) have been identified in the chicken MHC (Kaufman and Lamont, 1996).

Kaufman *et al.* (1999) described the sequence in a region that is responsible for rapid allograft rejection in chickens. This is a region of 92 kb size of B locus that houses only 19 genes. The chicken MHC is nearly 20 times smaller than that of mammals. Interestingly, the genes in MHC of the birds have counterparts in the human MHC. This minimal essential MHC of birds conserved over 200 million years of divergence between birds and mammals. However, the MHC genes in birds are organized differently compared to mammals; wherein, class III region genes are located outside the class II and I regions. The presence of putative natural killer receptor gene(s) is unprecedented and might explain the importance of the B locus in the response to the Herpes virus responsible for Marek's disease. Further, some regions in the chicken B-locus are highly polymorphic within (Singh *et al*., 2007) and between (Singh *et al*., 2005) different poultry species.

There have been strong associations reported between the MHC B-locus with occurrence of viral, bacterial and parasitic pathogens with B21 haplotype possibly conferring partial protection of between 60% and 30%, while B12 found to be responsible for high susceptibility (Hunt *et al*., 2010).

Genetic resistance to specific diseases

The genetics of a bird is reported to have a profound impact on its ability to resist diseases (Deist *et al*., 2017). However, because of the need in molecular genetics for controlled disease challenges to study marker associations, the number of studies conducted to date is limited, especially for genome-wide scans. From the limited studies conducted so far, there is evidence for genetic control of poultry diseases caused by a wide range of pathogens, including viruses (Elleder *et al.,* 2004), bacteria (Lamont and Hasenstein, 2005) and parasites (Gul *et al*., 2022).

(i) Avian leucosis

The *tva* locus located on chromosome 28 that encodes a low-density lipoprotein receptor (LDLR) family protein is found to resist avian leukosis virus subgroup A (ALV-A) (Elleder *et al.,* 2004). Thee *tva* gene is orthologous to the mammalian counterpart *8D6A* which encodes a 282-aa protein expressed mainly in follicular dendritic cells (Elleder *et al*., 2004). It is demonstrated that the cysteine residues of 2 and 3 at the N terminus of the *tva* LDL-A module have a critical role in ALV-A entry (Rai *et al*., 2004). There are seven alleles (*tva, tva*^{r1}, *tva*^{r2}, *tva*^{r3}, *tva*^{r4}, *tva*^{r5}, and *tva*^{r6}) in this locus, mostly arising due to intron 1 deletion. These deletions disrupt mRNA splicing of the *tva* receptor gene and prematurely introduced the TGA stop codon, thereby reducing sensitivity to ALV-A (Reinišová *et al*., 2012). Bids possessing allele *tva* is sensitive to the disease and the alleles *tva*^{r1} and *tva*^{r2} confer resistance; whereas, all the other alleles reduce susceptibility to the disease. The mutation (s7, s8, and K251E) of variable region 3 (vr3) of *tva* locus influence the binding of envelope glycoproteins of ALV-A (but not ALV-K) (Chen *et al*., 2020). The ALV-B, D, and E subgroups share the same *tvb* receptor, which belongs to the tumour necrosis factor receptor family (Adkins *et al*., 2000). The alleles tvb^{s1} and *tvb*^{s3} are sensitive to subgroups ALV-B, D and E; while *tvb*^{r} confers resistance to the host against the entry of ALV-B, D, and E (Mo *et al*., 2022). *tvc* is the receptor of ALV-C, which is similar to mammalian butyrophilins (Elleder *et al*., 2005). The birds having the allele *tvc* are sensitive to the disease caused by ALV-C; while, its allele *tvc*^{r} confers resistance to the invasion of the virus. The receptor of ALV-J is the chicken Na^+/H^+ exchanger 1 (*NHE1*) (Chai and Bates, 2006). The allele *NHE1*$^{\Delta}$ with a base mutation confers resistance to ALV-J, while, the birds having the allele *NHE1* are sensitive to ALV-J infection (Mo *et al*., 2022). Gavora *et al*. (1983) studied the heritability in two populations and found percent heritability range of −1 to 6% in sire and −2 to 12% in dams for ALV resistance.

The CRISPR/Cas9 knock-out ALV receptor locus was demonstrated in tvb and tvj loci (Lee *et al*., 2017). Recently, Koslová *et al*. (2018) have also shown that *tva, tvc* and *tvj*

ALV receptor genes were edited using CRISPR/Cas9 technology resulting in resistance to the respective ALV subgroups. This might be the first step in the development of virus-resistant chickens through gene editing technology.

(ii) Salmonellosis

The influence of genetics on resistance for Salmonellosis has been reported among different lines of White Leghorn (Bumstead and Barrow, 1993). *NRAMP1* and to the tnc locus that is closely associated with *LPS/TLR4* which account for up to 35% of the differences in susceptibility observed between White Leghorn lines (Hu *et al*., 1997). The survival rate of young chicks infected with *S. typhimurium* through intra-muscular route at day-one after hatch was found to be linked with candidate genes *SLC11A1* and *TLR4*. These two genes conferred up to 33% of the differential resistance to infection (Leveque *et al*., 2003). The structural variations in candidate genes like *NRAMP1*, MHC Class 1 and IAP1 (inhibitor of apoptosis 1) were found to be associated with *S. enteritidis* level in the spleen with little role in gastrointestinal tract levels (Lamont *et al*., 2002). The studies in inbred chicken lines revealed that the ability to responds to Salmonella infection is linked with certain MHC class I or class II haplotypes (Liu *et al*., 2002). The association studies of Gallinacin gene (Gal) alleles (*Gal1, Gal2, Gal3, Gal4, Gal5, Gal6, and Gal7*) with *Salmonella enterica serovar enteritidis* (SE) challenge conducted by Lamont and Hasenstein (2005) revealed significant effects of sire allele of *Gal3* and *Gal7* on SE vaccine antibody response. Further, the authors demonstrated moderate association of *Gal2* allele with spleen bacterial load; on the other hand, *Gal3* and *Gal5* alleles with cecum bacterial load. Mariani *et al* (2001) found a novel region determining. Salmonellosis resistance in chickens, termed SAL1 has been mapped to chicken chromosome 5. *SAL1* was found to be involved in bacterial clearance by macrophages. This region comprises of 14 genes, of which CD27-binding protein (Siva) and AKT1. AKT1 inhibits apoptotic processes thereby involved in cellular survival pathways.

The QTLs demonstrated to have influence for the caecal bacterial load and caecal lumen bacterial load by Calenge *et al*. (2009) can be of potential interest for marker-assisted selection in commercial lines. The authors confirmed that two different sets of QTLs and candidate genes had influence on Salmonella infection in both chicks and adult chickens; of which, one was demonstrated to influence for the caecal bacterial load and the other, the caecal lumen bacterial load. These QTLs are mapped on chromosomes 2 and 16 in an experimental chicken line; whereas, in a commercial chicken line the QTLs were mapped on chromosomes 1 and 16. This strengthens the hypothesis of a genetic control of *Salmonella* carrier-state is not differing according to chicken's age.

The genetic selection for Salmonella resistant chickens was tested as early as the 1930s (Roberts and Card, 1935) and discontinued due to high cost. This was again renewed later due to an outbreak of

Salmonella enteritidis (Calenge *et al*., 2010). Low to medium heritability (0.197, 0.091, and 0.167 in RIR, Beijing You, and Dwarf chicken populations, respectively) was recorded for survival after bacterial challenge; whereas, medium to high (0.32 and 0.16 in DW and RIR respectively) recorded for carrier state by Li *et al*. (2018). The authors concluded that chickens with various genetic background had significantly different *Salmonella* resistant activities and heritabilities.

(iii) Avian influenza

The role of Mx protein in providing resistance to Avian Influenza (AI) virus was studied extensively (Sironi *et al*., 2008; Benfield *et al*., 2008; Alam *et al*., 2022). Many SNP variations of *Myxovirus* resistance gene (*Mx*) gene has been reported to influence the susceptibility to Avian influenza, although contrasting findings were also reported (Sironi *et al*., 2008). Alam *et al*. (2022) reported three genotypes of the Mx gene with homozygous genotypes AA is resistant; while, GG is sensitive. The chickens possessing a particular allele of *Mx* gene with a single-point serine-to-asparagine mutation (AGC to ACC) at 631st position are resistant to avian influenza (Benfield *et al*., 2008). It has been demonstrated by Fulton *et al*. (2014) that the antiviral activity of Mx protein is due to the structural variation of Mx gene in exon 14. Sartika *et al*. (2011) found that slightly better age at first egg and egg weight and body weight of hens at first laying and egg production were observed in susceptible genotype (Mx^-) compared to resistant genotype (Mx^+). Drobik-Czwarno *et al*. (2018) suggested that the candidate gene *NLGN4*, located on chromosome 1 between 126.29 and 126.41 Mb, can confer resistance to H7N3 infection. The authors also found that regions located on chromosomes 9 which overlaps *BCL6* and *ZNF639* genes and a region on chromosome 15 overlapping *MAPK1* gene are also rich in genes with immune system are the potential candidate genes for immune response against AI.

In an attempt to develop Influenza A virus (IAV) resistance chickens, Lyall *et al.* (2011) conducted experiments to introduce cDNA of an RNA hairpin molecule into the chicken genome using a lentiviral system.

(iv) Marek's disease

The control of Marek's disease (MD) through the selection for genetic resistance and breeding is an alternative method other than vaccination to control this disease. The genetic resistance to Marek's disease was first demonstrated long back by Asmundson and Biely (1932). The genetic variability for resistance to MD in chicken has been documented (Flock *et al*., 1975).

The Major Histocompatibility Complex (MHC) class I molecule BF2*2101 from the *B21* haplotype was found to confer disease resistance to the Marek's disease; whereas, *B19* haplotype is generally the most susceptible (Koch *et al*., 2007). Many genes in non-MHC regions namely *GH1, SCYC1, SCA2, IRG1, CD79B, SMOC1*, and *PTPN3* were reported to have influence on infection of oncogenic herpesvirus that cause

Marek's disease (Koch *et al*., 2007). Recently, in a genome-wide chicken genotyping array to investigate genetic structure and genomic signatures across the genome, few more genes like *SIK*, *SOX1, LIG4, SIK1* and *TNFSF13B* contained in ROH region are reported to contribute to immunology and survival for MD (Xu *et al*., 2018). Apart from these genes, Dar *et al*. (2018) in his review listed several other genes namely growth hormone gene, cytokines (IL6 and IL18) and the stem lymphocyte antigen 6 complex, *LY6E* gene. Loci *rs14527240* and *GGaluGA156129* were found to play a role in host resistance/ susceptibility to MD. *Transferrin,* an iron-binding glycoprotein gene in chromosome 9 was also shown to have anti-viral properties against Marek's disease (Giansanti *et al*., 2002)

Based on field data, Von Krosigk *et al*. (1972) estimated a heritability value of 0.10 for MD by contact exposure compared with 0.21 for intraperitoneal injections, and 0.14 for average heritability at 50% mortality in White Leghorn Chickens. Whereas, Friars *et al*. (1972) estimated realized heritability value of 0.67 ± 0.30 for Marek's diseases resistance in female broiler breeders. Similarly, Gavora *et al*. (1974) also estimated a high average heritability value of 0.61 for resistance to Marek's disease among sire families of two Leghorn strains selected for egg production. In cockerels of a brown-egg line, Flock *et al*. (1975) estimated a heritability value of 0.18 at 18 weeks for 50% mortality due to Marek's disease.

In a selection experiment for developing resistance for MD, Von Krosigk *et al*. (1972) obtained realised genetic response that well agreed with expected response. In another selection programme in two non-inbred White Plymouth Rock (WPR) lines by selecting survivors after heavy exposure to virulent Dutch strain K of MD virus, Maas *et al*. (1981) demonstrated that breeding from survivors for development of resistance to MD is feasible. A high level of resistance to MD was reached within five generations.

(v) Newcastle disease

The association of genetics with innate resistance to Newcastle Disease virus (NDV) was one of the oldest relationships. The divergent genetic selection for antibody response against Newcastle disease vaccination was found to be successful in developing disease resistant populations (Pitcovski *et al*., 1987). The estimated realized family heritability was also very high (0.70) after four generations of selection in chickens which were selected for combined vaccine response of ND and *E. coli*.

The transcriptome analysis between challenged and non-challenged resistant Fayoumi chicken lines revealed that *PPIB* gene may primarily involve in antibody production (Deist *et al*., 2017); whereas, Mpenda *et al*. (2019) demonstrated the association of the polymorphisms in Mx gene promoter on the susceptibility of chicken embryo to the virulent NDV challenge. Del Vesco *et al*. (2020) demonstrated differential expression of *EIF2B5* and *EIF2S3* genes in chicken breeds may indicate their breed difference for resistance to NDV. The gene *EIF2AK2* was found to be the important interferon-inducible

driver gene exhibiting antiviral effects by inhibiting NDV replication through *EIF2* signalling pathway (Deist *et al*., 2017).

Luo *et al*. (2013) concluded that the region near the proximal end of chicken chromosome 1 containing genes *ROBO1* and *ROBO2* are found to have a strong effect on the antibody response to the NDV in chickens. In a recent study in heat stress in Hy-Line Brown layer chickens, Zhou (2023) identified two QTL regions, one containing immune related genes, namely, *CAMK1d* and *CCDC3* on chromosome 1 and their association with viral titer at 2 dpi, and genes *TIRAP*, *ETS1*, and *KIRREL3* and their association with viral titer at 6 dpi and the other containing 30 SNPs spanning in a quantitative trait loci (QTL) on chromosome 24 which were associated with viral titer at 6 dpi.

(vi) Parasites

The genetic resilience in chickens against different parasites has been reviewed by Gul *et al*. (2022). It was found that parasite-specific immune response against *Eimeria* is conferred by myeloid leukemia factor 2 gene in chicken and against Ascaridia is conferred by IFNG in poultry. Further, the MHC haplotypes were found to play roles in protecting the jungle fowl from coccidiosis and domestic chicken from Ascaridiasis. It has been discovered that butyrate, forskolin and lactose compounds together enhance the expression of multiple host defense peptides, increase the survivability by reduce the colonization of *Eimeria maxima* and *Clostridium perfringens* in chickens. Another candidate gene in chromosome 1, namely *zyxin* is found to be associated with increased resistance to coccidiosis in birds. Although seldom reported before, the *zyxin* gene may be a candidate gene potentially associated with avian coccidiosis (Hong *et al*., 2009). Considering the more and more serious infection of coccidiosis, the zyxin gene is promising candidate to play an important role in preventing coccidiosis.

Breeding for disease resistance

Proper biosecurity and vaccination are considered as the primary strategy for disease prevention in poultry flocks. Alternatively, breeding for disease resistance has attracted the interests of scientists in recent times. Disease resistance in a bird is not absolute one; on the other hand, the bird has to defend the invasion of pathogen by interfering its lifecycle (Bishop, 2014). Eliciting an immune response by a bird involves diversion of large amounts of energy from growth and egg production (Rauw, 2012). The birds of disease resistant chicken line need less energy to interact and neutralize the pathogen; thereby, show resilience and continue to grow and produce well in the face of a disease challenge (Bishop, 2014).

Selection of individuals for disease resistance can be classified as (i) direct selection, (ii) indirect selection and (iii) transgenesis (Jie and Liu, 2011).

(i) Direct selection

Three approaches are employed in direct selection, which includes selection based

on pedigree records or individual or family selection for disease resistance. The individual or family selection are not completely accurate because the exposure to the pathogen differs (Jie and Liu, 2011). Cavero *et al*. (2009) observed from breeding for *E. coli* challenge and showed that it was possible to improve colibacillosis resistance in layer chicken without compromising primary traits. Similar results have been reported by Pavlidis *et al*. (2007) for ascites.

(ii) Indirect selection

This method is a widely used one, which is employed based on the reliable resistance related indicator, including genes, pathogen products and biological or immunological responses of the host. Jie and Liu (2011) reviewed the markers like dopamine and immunological parameters, monocytes-macrophages phagocytosis and heterophil/ lymphocyte ratio have been used as markers for selecting antiviral chickens. Genes like *Mx* genes, *NRAMP1* gene, MHC genes have also been used as markers for improving disease resistance. Indirect selection is the popularly used method for breeding poultry for disease resistance. For better genetic improvement, the trait should be highly heritable and accurately measurable, while the influence of environment must be minimum (Jie and Liu, 2011).

(iii) Transgenesis

Transgenesis is the most recent and promising technology to develop disease resistant birds. Transgenic methods like microinjection and viral and cell and sperm mediated gene transfer methods are attempted with varying efficiency and outcome for producing disease resistant poultry (Churchil *et al*., 2011; Jie and Liu, 2011; Churchil and Sharma, 2013). Despite enormous advancement in the research of disease resistant transgenic birds, they are yet to be introduced for commercial farming for disease resistance (Churchil, 2019). The security of transgenic animals is still doubtful. Thoughtful decision making is needed in the biotechnology, industry, scientists, policy-makers, and the public considering ethical, religious, animal and human welfare and food safety issues (Churchil, 2019).

The recent outbreaks of H5Nx viruses across the world highlight the continual threat that avian influenza viruses pose to both poultry and human health. Rapid advances in genomics and gene editing suggest that disease resistant, genetically modified chickens could represent a viable solution to the problem of avian influenza as a novel alternative strategy is to develop chickens that are genetically resistant to infection. Lyall *et al*. (2011) generated transgenic chickens expressing a short-hairpin RNA designed to function as a decoy that inhibits and blocks influenza virus polymerase and hence interferes with virus propagation. Susceptibility to primary challenge with highly pathogenic avian influenza virus and onward transmission dynamics were determined. Although the transgenic birds succumbed to the initial experimental challenge, onward transmission to both transgenic and non-transgenic birds

was prevented.

CONCLUSION

Selective breeding for genetic improvement in economic traits like egg production and growth rate has been practiced for nearly one century. Given the very high prevalence of disease-causing agent in commercial chicken production units, selective breeding for resistance to infectious diseases may represent an attractive alternative approach to biosecurity and vaccination procedures which involve huge amount of money. Genetic resistance to disease for any one individual or line of chickens is the overall outcome of a very complex set of signals and responses with which the chicken and pathogen interact. Many disease specific genes are found to confer resistance in poultry. These marker genes also show associated variations with disease resistance among the individual birds, which can be exploited in selective breeding for genetic improvement on disease resistance. This traditional method is a laborious one that requires the intentional exposure of individuals from elite lines to pathogens and the genetic progresses is rather slow due to indirect selection on overall liveability.

Greater insight as to the genetic basis for natural disease resistance has been gleaned from genome wide association studies (GWAS) using high-density SNP chips comparing birds that survived and succumbed to disease outbreaks. When applied to breeding, the information will provide for the rapid and accurate improvement of commercial lines. With high throughput platforms to determine genotypes, the rate-limiting step is in producing and measuring resource populations. Transcriptome analysis offers powerful solutions in identifying candidate genes in known QTL regions associated with disease resistance in poultry, which can be used as markers in breeding. The advanced genetic technologies like RNA-seq recently become available will be of great utility in future to identify DES which confers disease resistance.

Despite the rapid pace of developments, the detailed understanding of the molecular pathways is yet to be established concisely for almost all the diseases, so that the poultry breeders can use this knowledge to improve their commercial products. The partnership between scientists and breeding companies will hasten this change.

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