The chicken major histocompatibility complex and disease

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Summary
The chicken major histocompatibility complex (MHC), or B complex, consists of several clusters of highly polymorphic genes, some of which are associated with disease resistance. The class I and class II antigens resemble their mammalian counterparts in the encoded protein structure. The class IV region encodes the B blood group antigens, which are readily identified by serological blood-typing. The class III region appears to be divided in chickens, with some elements that are MHC-linked and others that map elsewhere. In addition the Rfp-Y system, which bears a strong similarity to the MHC, maps to the opposite side of the nucleolar organiser region on the same microchromosome as the MHC. Each class of MHC genes is a potential candidate for a role in disease resistance. The MHC genes show associations with response to diseases as diverse as virally induced neoplasia, bacterial, parasitic and auto-immune diseases.

Keywords

Discovery of the chicken major histocompatibility complex

The B complex (or major histocompatibility complex: MHC) of the chicken was first reported by Briles et al. as a highly polymorphic erythrocyte antigen or blood group system (13). The gene locus symbol was assigned as B to indicate that this was the second chicken blood group system to be discovered. Gilmour independently reported the discovery of the same blood group locus (45). Persistence of multiple alleles of the B system, even in small, closed and inbred populations, suggested a role of the B blood group in fitness and a selective advantage of B heterozygosity for survival (12, 45). The discovery by Schierman and Nordskog that the B blood group system is linked to the major histocompatibility complex determined the biological mechanism by which the B system influenced fitness (134). In skin graft experiments using partially inbred birds, grafts between birds of the same B type were accepted while those of different B blood types were rejected, thus the linkage of B with the major skin graft locus was confirmed. Additional evidence that the B system represented the chicken MHC was provided by the identification of B as the locus controlling graft versus host (GVH) splenomegaly (62), GVH-chorioallantoic membrane pocks (135) and the mixed lymphocyte reaction (100).

Unique genetic structure of the chicken major histocompatibility complex region

Pink et al. defined a three-locus model of the chicken MHC (118). In the ensuing two decades, the molecular dissection of the chicken MHC has demonstrated an unanticipated level of complexity of genomic organisation (Fig. 1) (50, 51, 52, 65, 67, 79, 101). Bloom and Bacon assigned the MHC to microchromosome 16 by analysing aneuploid chickens which bore the nucleoli organiser region (NOR) on the extra chromosomes (8, 9). This microchromosome was estimated to be 8 megabase pairs (Mbp), with 6 Mbp of NOR encoding approximately 400 tandemly repeated ribosomal RNA (rRNA) clusters (33, 124).

The genomic organisation of the chicken MHC differs from that of a typical mammalian MHC. The chicken MHC is quite compact, approximately 30 to 100 kilobase (kb) long.
compared to up to 4 Mbp in mammals, and the number of genes in MHC-like multigene families is therefore relatively small (approximately 2 class II β, 1 class II α and 1-2 class I α genes) (63, 71). The few class I α genes located in cosmid cluster I, which are the only genes to encode polymorphic molecules expressed at a high level, represent the classical MHC (the B-F/B-L locus) of the chicken. Other genes, such as the TAP (transporters associated with antigen processing) gene(s) involved in transport of antigenic peptides across the membrane of the endoplasmic reticulum for association with class I molecules, are also located in the classical MHC region. Non-classical (non-class I, non-class II) MHC genes mapping to this region include the 12.3 gene that encodes for a G protein-like molecule (52), the 8.5 gene that encodes a B-G molecule (68), the 21.7 gene that encodes a TAP molecule (J.F. Kaufman and N. Bumstead, unpublished findings), as well as the 17.8 gene that encodes a member of the C-type animal lectin super-family (7).

The distribution of class III genes in the chicken may include non-MHC linked sites. Most genes characteristic of the mammalian class III region have not been identified in the chicken MHC cosmids isolated thus far. Electrophoretic polymorphisms of glyoxalase 1 (GLO) (126) and chicken factor B (78) do not segregate with the B complex. However, a DNA polymorphism, detected by G9a (109), of the class III region of the human MHC has been mapped to the chicken MHC (140), providing evidence that at least some part of the class III region is associated with the chicken MHC.

Research conducted by W.E. Briles and M. Miller showed that some class I α and class II β bands on Southern blots do not co-segregate with the serologically defined B complex. This new locus, defined by restriction fragment length polymorphism (RFLP) analysis, was named the Rfp-Y locus (16). The Rfp-Y locus was mapped to cosmid cluster II/IV and III (106), separated from cosmid cluster I by the highly recombinogenic region of the repetitive NOR (108). By in situ hybridisation, both the B and Rfp-Y complexes were mapped to the same microchromosome (42). The Rfp-Y region is thought to be involved in natural killer recognition, based on the involvement of class I and animal C-type lectin (such as the 17.8 gene) molecules (107).

The β2m cDNA clones (the β2m protein being associated with mature class I MHC molecules [115]) were identified by screening with oligonucleotides based on protein sequence. Using these cDNAs as probes, a single β2m gene located outside the MHC was found (69). The β2m gene was located by in situ hybridisation on a non-MHC microchromosome (124).

Genes encoding the MHC class IV, or B-G, erythrocyte alloantigens are closely (approximately 0.05 centiMorgan [cM]) linked to the B-F/B-L region (31, 138). Several groups have isolated cDNA clones corresponding to B-G molecules (37, 47, 64, 65, 68). The B-G genes map to cosmid clusters V and VI. Based on Southern blots using these cDNA clones as
probes, the B-G genes form an extensive multigene family (106). One B-G RFLP corresponds to the 8.5 gene in cosmid cluster I, which encodes a B-G molecule found on B cells (64, 67).

The map of the MHC from CB chicken cosmids provides a good model for an understanding of the chicken MHC (Fig. 1). However, RFLP using class I α, class II β and B-G probes on DNA of other lines have suggested gene expansion and contraction (23, 24, 90, 92, 93, 103, 119, 147, 157). Apparently, there are extra class I α genes in the B21 haplotype, which is known to be associated with Marek’s disease resistance (23, 103).

The use of DNA analysis to provide biochemical characterisation of the existing variation in the MHC is a valuable addition to serological analysis. By using DNA analysis, sub-regions and genotypes for which the production of serological reagents has failed can be examined, MHC chromosomal recombinants can be analysed and newly identified genotypes can be categorised. A standard nomenclature should be defined for DNA polymorphisms of MHC haplotypes, as has been defined for serological analysis (14).

Class I (B-F) and class II (B-L) genes and antigens

Multiple chicken class I α cDNAs, one class I α gene and several chicken β2m cDNAs have been described, as well as class I and β2m proteins from erythrocytes (49, 69, 80, 110, 124, 159). The chicken B-Fαt chain gene is organised similarly to mammalian classical class I genes, with an exon encoding the signal sequence, three exons (α1, α2 and α3) encoding the extracellular domains, an exon encoding the transmembrane (TM) region and three exons encoding the cytoplasmic tail and 3' UT (untranslated region). The β2m gene shows a similar organisation to mammalian β2m genes, with one exon for the signal sequence, another exon for most of the protein, one for the last four amino acids of the protein and part of the 3'UT, and the last exon for the remaining part of 3'UT. Only one class I gene product seems to be expressed at high levels on chicken blood and spleen cells: of the six CB cosmid fragments that hybridised with the class I α cDNA F10, only one (B-FIV of cosmid cluster I) hybridised with an oligonucleotide from the 3’UT (49).

In the initial cloning of the chicken MHC, a chicken MHC class II β pseudogene was isolated by cross-hybridisation with a human class II β cDNA (11) and used to isolate cosmids from a DNA library of a CB (B12) chicken. These cosmids overlapped into four clusters, two of which were later connected by an overlapping lambda genomic DNA clone. Two class II β gene fragments and four class I α genes were identified on cluster I; two class II β gene fragments and two class I α gene fragments and the 17.8 gene were identified on cluster II/IV; and a class II β gene fragment, the 13.8 gene and some rRNA genes were identified on cluster III (49). Researchers later determined that only cluster I corresponds to the serologically defined B complex.

Class II β genes, pseudogenes and cDNAs from several chicken strains have been described (11, 113, 143, 162, 165, 166).

Several class II α cDNAs have also been isolated (70). Kaufman et al. identified the major class II α cDNA by using degenerate oligonucleotide polymerase chain reaction (PCR) based on the protein sequence. Using this cDNA as a probe, the gene was found to co-segregate with neither the B complex nor the Rfp-Y locus in the F2 family described by Bries, but was located about 5 cm away from the B complex in the Compton reference family (70). The α chain cDNAs have an α1 domain, an α2 immunoglobulin (Ig)-like domain, a transmembrane domain and a short cytoplasmic tail. The sequences and analysis of the B-L antigen (48) demonstrate the B-L to be a typical class II MHC molecule.

The chicken MHC class II β genes are organised similarly to those of mammals, with an exon encoding the signal sequence, a polymorphic β1 PRB domain, a non-polymorphic β2 Ig-like domain, a transmembrane domain and two cytoplasmic exons, the last including the 3'UT. Based on sequences of several haplotypes, there seem to be three isotypes of class II β genes. The two class II β genes (B-LBI and II) in cluster I are closely related and highly expressed. The two genes located on cosmid cluster II/IV (Rfp-LIII and V) and the gene on cosmid cluster III (B-LBIV) are quite different from the cluster I genes, but are virtually identical to each other and are poorly expressed. Other class II β sequences (named B-LBVI) form a third group.

The chicken MHC has many features which contrast with those of mammals. The genes are very rich in guanine + cytosine (G+C) compared to the mammalian counterparts, and this is particularly true for some promoters, exons and introns. The promoters for class I α, class I β, and β2m genes have G+C-rich regions near the transcription initiation site instead of the typical mammalian TATA boxes, and also have X and Y boxes, which are expected for class II β - but not class I α or β2m - genes. The promoters of class I α and β2m also contain interferon response elements (IRE). The sequence differences may lead to important functional differences between chicken and mammalian MHC genetic regulatory elements.

Understanding the functional activity of chicken MHC regulatory elements will be important for the modulation of gene expression levels and, thereby, MHC function. The conserved IRE in the chicken MHC class I promoter region has been shown to induce gene expression (164). Chen et al.
characterised a functional chicken MHC class II gene promoter as a 0.7 kb chicken DNA fragment that contains a functional promoter, but may require additional enhancer(s) outside this immediate 5' upstream region for efficient initiation of transcription (25, 26). Deletion analysis of this DNA fragment revealed a short fragment in the 3' end that was crucial for the promoter function, and negative regulatory elements located further upstream. Surprisingly, the conserved MHC class II X and Y boxes did not have a significant influence on promoter activity when transfected in a macrophage cell line. Recent studies show protein-DNA binding of the Y box with nuclear extracts of lymphocyte, but not macrophage, cell lines (Y. Chen, S. Carpenter and S.J. Lamont, unpublished findings). The involvement of interferon, ETS-related proteins and other factors involved in the regulation of this promoter were suggested by sequence analysis. Glucocorticoids decreased interferon-induced gene expression (26).

Class IV (B-G) genes and antigens

The MHC class IV (B-G) molecules were initially studied because of their extensive serological polymorphism, which could contribute to the active search for correlated functional variation in biological traits. The availability of alloantibodies to B-G antigens on erythrocytes enabled the discovery of the chicken MHC. B-G proteins, cDNAs and genes have been examined (67, 68, 104, 105). In addition, the whole B-G region and a B-G gene expressed on B cells are linked to cosmid cluster I. There are multiple B-G molecules present on erythrocytes, and very similar molecules are present on thrombocytes, lymphocytes, and on stromal cells of the caecal tonsil, bursa, thymus and the epithelial cells of the small intestine (65, 77, 105, 128). The erythrocyte-surface B-G molecules are generally disulphide-linked dimers (66, 77, 102, 118, 127). These B-G chains vary significantly in size (35 to 55 kiloDaltons [kDa]) depending on the length of the cytoplasmic tails. The B-G molecules on stromal cells in the bursa, thymus, caecal tonsil and on small intestine epithelial cells are larger than the erythrocyte B-G molecules (65, 77, 127, 128).

While the true functions of B-G molecules are not yet known, their structure suggests that these are typical adhesion molecules, with the extracellular region involved in interactions with other cells or with the environment and the cytoplasmic tail involved in signal transduction. The polymorphism may help the molecules respond to a wide range of stimulating molecules. The B-G molecules exhibit specific immune phenomena (including an 'adjuvant effect', which initiates a rapid and strong antibody response) and the presence of natural antibodies (55, 67, 97, 129, 136).

The chicken major histocompatibility complex and immune response

Regulation of cellular communication in the immune response is a critical function of the chicken MHC (34). The MHC cell-surface proteins distinguish 'self' from 'nonself'. This allows immune reaction to occur against foreign antigens of a virtually infinite variety while simultaneously preserving the self-integrity of the organism. The MHC cell-surface molecules interact with both the foreign antigen and with complementary structure of other immune cells, thereby generating an immune response that is specific for the inducing antigen.

Cells of the immune system must share at least one MHC haplotype to communicate effectively; this phenomenon is known as MHC restriction. The MHC restriction may function at the level of interactions between mature cells in the immune response or at immune cell differentiation (149, 151, 152). The T/B-cell co-operation necessary for antibody production and for the generation of germinal centres in the spleen requires identity at the MHC (146). The interaction of antigen-presenting cells and T cells, evaluated by the in vitro proliferation of T cells in response to specific antigen in the presence of antigen-presenting cells, is also MHC-restricted. The B-F/B-L antigens are the restriction elements for all of these cellular interaction phenomena (150, 153).

The cytotoxic reactions of T cells with some virus-infected and/or transformed cells are MHC-restricted (99, 132). An antigen-restricted class II-positive T cell with cytotoxic properties was identified as the effector cell responsible for the MHC-restricted cell-mediated cytotoxicity (158). Cytotoxic cells which are MHC- and virus-restricted may be an important immune surveillance mechanism for preventing the proliferation of virally induced tumours (137).

The MHC has widespread effects on genetic control of immuno-responsiveness, either due to its role as a restriction element or through specific MHC-linked immune response genes. Antibody production against a variety of antigens, such as immune response to synthetic polypeptides, is linked to the chicken MHC (6, 54, 112). Antibody titres to several soluble antigens (e.g., bovine serum albumin: BSA), to viral antigens (3) and to cellular antigens (e.g., Salmonella Pullorum bacterin, sheep erythrocytes) (98, 111) are also associated with the chicken MHC. Total serum IgG levels are also under genetic control by the B complex (123).

Genetic control of immuno-responsiveness linked to the chicken MHC has also been shown in assays of cell-mediated immunity. The delayed wattle reaction is commonly used as a measure of cell-mediated immunity in the chicken (76). Both polyclonal activators of T cells, such as phytohaemagglutinin
(144), and specific inducers, such as *Staphylococcus aureus* (an important pathogen of poultry) (28), show cell-mediated immune responses associated with the B complex.

Complement proteins are extremely important in the immune reaction as a means to destroy invading pathogens. The levels of total serum haemolytic complement and the activity and recruitment to the peritoneal cavity of macrophages varied among B-congenic lines, which differ from each other only in the microchromosome (or a fraction of it) which bears the MHC (121, 122). Chicken B-congenic lines were also used to demonstrate MHC associations with cell-surface CD4 (cluster of differentiation antigen 4) and CD8 lymphocyte percentages and ratios (56).

The MHC has been studied in chicken lines selected for various traits of immunoresponsiveness, for example, in experiments to measure long-term selection for antibody response to sheep red blood cells. Correlated changes of MHC allelic frequencies with the antibody selection occurred (39, 117). Although MHC genotype explains part of the variation in antibody levels, the background genome also had a substantial effect (40, 116). After divergent selection for early antibody response to *Escherichia coli* vaccination in meat-type chicken lines, differences in the frequency of MHC class IV RFLP bands were present (148). Although the MHC class IV differences did not persist to large measure in the F2 generation, RFLP bands of class I and TAP2 clones were associated with the antibody response (21). In Leghorn lines selected divergently for an index of immunocompetence traits (antibodies, cell-mediated response and reticuloendothelial activity) (27), differences occurred in MHC genotype frequencies identified both by serology (73) and by DNA analysis of class II (N. Lakshmanan and S.J. Lamont, unpublished findings), and class IV (S. Weigend and S.J. Lamont, unpublished findings). Many diverse facets of the immune response, therefore, are partly under MHC genetic control.

The chicken major histocompatibility complex and disease resistance

The association of the chicken MHC with resistance to disease has motivated studies of both the basic biology and the practical application of knowledge of the chicken MHC. These studies have been summarised in several recent reviews (2, 43, 72, 83, 84, 85, 87, 142) (Table 1).

<table>
<thead>
<tr>
<th>Type of disease</th>
<th>Disease</th>
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<td>Neoplastic diseases (viral)</td>
<td>Marek's disease neoplasia</td>
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<td></td>
<td>Marek's disease transient paralysis</td>
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<td>Pus' sarcomas</td>
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<td>Lymphoid leucosis</td>
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<tr>
<td>Bacterial diseases</td>
<td><em>Staphylococcus aureus</em></td>
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<td></td>
<td>Fowl cholera (Pasturella multocida)</td>
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<td></td>
<td>Salmonella Enteritidis</td>
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<td>Parasitic diseases (coccidiosis)</td>
<td><em>Eimeria tenella</em></td>
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<td><em>Eimeria acervulina</em></td>
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<td>Autoimmune diseases</td>
<td>Autoimmune thyroiditis</td>
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<td>Vitiligo</td>
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The most intensively investigated association of the MHC with resistance to a specific disease concerns Marek's disease (MD), a herpesvirus-induced lymphoma. The emergence of increasingly virulent strains of MD virus (MDV) ensures continued high levels of interest in the use of genetic resistance approaches to this disease (17). Using MHC recombinants to the B-F/B-L region (15, 60), partial MHC control has been mapped. The MHC is associated with MD-related traits of incidence of tumour formation, mortality and transient paralysis induced by MDV. The haplotype B21 conveys MD resistance to many different genetic backgrounds. Variation in response to MDV by sublines that are identical at the B locus, however, illustrates the influence of non-MHC genes on response to MD (2, 3). An interesting – and currently conflicting – picture is emerging for the role of the *Rfp*-Y region in resistance to MD. Although two studies found no association between *Rfp*-Y variation and resistance to the disease (82, 154), one study found that birds of homozygous Y1 genotype carried more than twice the risk of tumour development than the other pooled genotypes (156). The differences between studies probably result from the specific *Rfp*-Y alleles and background genes used, as well as the MDV strain used for challenge and the recorded disease traits. A recent study which used a genome-wide search for quantitative trait loci has identified several which affect resistance to MD (155). Genetic complementation of MHC alleles with other genes, such as Ir-GAT (141) and the background genome (57), affects susceptibility to Marek's disease. The MHC also influences the response to other virally induced diseases, including Rous' sarcoma virus tumours (137) and avian leukosis (163).

In addition to virally mediated diseases, other categories of disease have also been demonstrated to be associated with the MHC (2, 43). These include fowl cholera (88), obese strain spontaneous autoimmune thyroiditis (125) and coccidiosis (19, 94). MHC congenic lines have played an important role in defining MHC associations for diseases as diverse as...
Marek's disease (4, 133), tumours induced by Rous' sarcoma virus (160) and v-src (145), and Staphylococcus aureus (29). The range and variety of diseases influenced by the chicken MHC is, therefore, extensive.

There is genetic variability for resistance against various diseases in poultry populations, yet selection for fitness and viability is one of the more difficult tasks for breeders who use only conventional genetic selection methods. Avian leukemia and Marek's disease are two successful examples of the application of genetic selection for resistance to specific diseases. Convincing evidence also exists for a genetic component to resistance to Salmonella in chickens. Two groups have examined resistance to Salmonella Enteritidis in several genetic lines and have found variation in the lethal dose 50% in organ contamination and in bacterial burden (18, 20, 53, 120). In recent reports, several natural resistance-associated macrophage protein-1 (Nramp1)-linked markers were examined and two were identified to be associated with splenic bacterial burden three days after intravenous inoculation of Salmonella Enteritidis (46). The possibility that Nramp1 also influences infection by natural routes of exposure and in other lines of chickens remains to be determined. Reports so far present conflicting results regarding the MHC role in resistance to Salmonella, thereby illustrating the need for detailed analysis of this relationship. Recent studies have shown an association of Nramp1 with differential resistance to Salmonella Typhimurium infection (61) and of the MHC with S. Enteritidis infection-induced morbidity and mortality (30). In both studies, the lines examined were derived from backgrounds related to egg-production type stock.

No haplotype performs optimally in all genetic backgrounds in response to all disease challenges. This is not surprising, given the many different immune mechanisms involved in resistance to each specific disease and the many levels at which genetic control is exerted by the MHC. The repeated association of disease resistance with the MHC, but not with one specific MHC haplotype, suggests an important role for non-MHC genes located within the complex. Specific resistance gene identification and the use of genetic engineering may allow the construction of resistant haplotypes that have not been produced by conventional breeding.

The chicken major histocompatibility complex and production traits

The B complex has been associated with genetic variation in production traits, such as general mortality, for many years (12, 45) (Table II). Economically important traits, such as juvenile and adult mortality, body weight, fertilisation rate, embryonic mortality, hatchability and egg production are influenced by MHC genotype (2, 35, 130). Several independent studies have shown that long-term selection for egg production traits and disease resistance have significantly altered MHC allelic frequencies (44, 81, 89, 139). From these selection studies, $B^2$ and $B^{21}$ appeared to show overall beneficial associations with economic traits in chickens. A variety of other studies have demonstrated MHC associations with particular production traits but no consistency of specific MHC haplotypes or associated traits (1, 41, 74, 75, 131).

<table>
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<tr>
<th>Production traits</th>
<th>Body weight</th>
<th>Juvenile survival</th>
<th>Adult survival</th>
<th>Egg production</th>
<th>Hatchability</th>
<th>Embryonic mortality</th>
<th>Fertilisation rate</th>
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Birds which were aneuploid (trisomic) for the MHC-bearing chromosome were used to map the MHC to microchromosome 16 and to examine the effects of MHC gene dosage on several biological systems. The chicken MHC (B complex) and the NOR were shown to be linked on microchromosome 16 (8, 38). The excess rRNA genes in aneuploid birds appear to be inactivated, but the MHC genes are expressed in a relatively dose-dependent fashion. Aneuploid chickens have both a greater concentration of erythrocyte cell-surface MHC glycoproteins than disomic chickens (9) and an increased amount of B-L antigen on bursal cells (32) and macrophages (95). The dosage of MHC genes also alters primary immune organ development, thus aneuploid chickens have smaller bursae and thymuses and a reduced number of lymphocytes (59). Aneuploid macrophages exhibited a cell-contact-dependent increase in killing tumour target cells (96). The expression of extra MHC copies has important implications for the feasibility of producing chickens by utilisation of natural variation or genetic engineering techniques, with increased copy numbers of the MHC genes to enhance health or production characteristics (10, 83). Because many traits for disease resistance associated with the MHC are dominant traits (43), an individual with extra MHC gene copies may be resistant to a greater variety of diseases.
Applications of knowledge of the major histocompatibility complex in the poultry industry

Knowledge of the chicken MHC and the impact of this complex on the avian immune system is now at a sufficient level for manipulation of the MHC to be used to integrate immune systems management into poultry production systems (36). Industrial use of MHC information in chickens occurs in two main areas. The first use is for pedigree confirmation. As a result of the enormous number of eggs and chicks that may be handled simultaneously at a hatchery and the practice of separating hens from progeny, even a very small percentage of pedigree errors could result in large numbers of incorrectly pedigreed chicks. Line-specific genetic markers can be used to assure purity of lines. Blood group antigens, including the B blood group, are excellent candidates for use as genetic markers because such antigens are highly polymorphic and are quickly and cheaply identifiable from a small blood sample.

Another contemporary application of MHC information is as a means of altering MHC allelic frequencies selectively to improve correlated traits (primarily disease resistance and vaccine response). Marek's disease vaccination efficacy in commercial genetic backgrounds has been associated with the MHC alleles (5). Beneficial MHC alleles can be increased in frequency or fixed within a grandparent line. The extreme polymorphism of the MHC (over 50 allelic forms in Leghorns, more in meat-type birds) gives many options for choice of specific B alleles in grandparent lines and various heterozygous combinations at the commercial crossbred level. The interaction of MHC alleles with the background genome, however, is an important practical consideration.

New biotechnologies should be incorporated into new industrial applications of MHC manipulation (85, 87). As antigen-binding specificity is critical to effective poultry vaccine design, detailed knowledge of specific MHC types in a population would allow specific choices to optimise the vaccine-host MHC combination or would allow the design of targeted recombinant vaccines (5, 114, 132, 161). The DNA can be examined directly for allelic forms of the MHC genes of each class with the use of specific gene probes. Direct analysis of class I and II genes will avoid the possibility of misclassifying the allelic forms caused by recombinations between the serologically determined class IV genes (B blood group) and the class I and II genes (and additionally the MHC-linked, non-class I, non-class II genes, such as TAP2 and the unique Rfp-Y region). Initial work has begun to address the need for economic technologies capable of defining the genotype of large sample numbers (58). The current understanding of the genetic regulatory elements of the MHC is minimal. The factors controlling gene expression must also be understood to selectively enhance expression. As the allelic diversity of each individual class of MHC genes is defined, the relationships of variation in structural genes and regulatory elements with disease resistance must be determined.

Conclusions

Genetic selection for the MHC is a desirable approach to improving immunoresponsiveness and disease resistance (86, 87, 91). Although the progress per generation may be small, such progress is heritable and therefore the increments are cumulative over time. Understanding MHC-disease associations can allow genetic selection to be performed by marker-assisted selection, rather than by direct challenge of populations with disease agents. This avoids the high costs, labour and animal welfare concerns associated with pathogen challenges. The resulting enhanced immunoresponsiveness conserves natural resources by decreasing the production losses that are due to disease. In addition, both animal welfare and food safety are enhanced by producing genetic stocks which possess greater resistance to disease pathogens.
Complexe majeur d’histocompatibilité chez les volailles et maladie

S.J. Lamont

Résumé
Le complexe majeur d’histocompatibilité chez les volailles (CMH) ou complexe B comporte plusieurs groupes de gènes très polymorphes, dont certains sont associés à la résistance aux maladies. Les antigènes des classes I et II présentent des similitudes avec ceux des mammifères pour ce qui est de la structure protéique codée. La région de la classe IV code pour les antigènes du groupe sanguin B, qui sont facilement identifiés par typage sérologique. La région de la classe III semble être divisée chez les volailles, certains éléments étant liés au CMH et d’autres localisés ailleurs. De plus, le système Rfp-Y, qui présente une grande similitude avec le CMH, apparaît à la cartographie localisé du côté opposé par rapport à la région de l’organisateur nucléolaire sur le même microchromosome que le CMH. Chaque classe de gènes CMH pourrait jouer un rôle dans la résistance aux maladies. Les gènes du CMH présentent des associations avec la réponse à des maladies aussi différentes que les néoplasies d’origine virale, les maladies bactériennes, parasitaires et auto-immunes.

Mots-clés

Enfermedad y complejo mayor de histocompatibilidad en el pollo

S.J. Lamont

Resumen
El complejo mayor de histocompatibilidad (major histocompatibility complex, MHC), o complejo B en el caso del pollo, consiste en varios racimos de genes extremadamente polimórficos, algunos de los cuales están relacionados con la resistencia a la enfermedad. Los antígenos de la clase I y la clase II y se asemejan a sus homólogos mamíferos en cuanto a su estructura proteica codificada. La región de la clase IV codifica a los antígenos determinantes del grupo sanguíneo B, que pueden identificarse fácilmente por tipificación serológica de la sangre. En el pollo, la región de la clase III parece hallarse dividida, con algunos elementos ligados al MHC y otros que aparecen cartográficamente en otros lugares. Además, el sistema Rfp-Y, que presenta una gran similitud con el MHC, aparece cartográficamente en el lado opuesto a la región organizadora nucleolar, en el mismo microcromosoma que el MHC. Todas las clases de genes MHC son susceptibles de desempeñar algún papel en la resistencia a la enfermedad. Los genes del MHC están relacionados con la respuesta a varias enfermedades, desde las neoplasias inducidas por virus hasta las enfermedades de origen bacteriano o parasitario o las enfermedades autoinmunes.

Palabras clave
Bacterias — Complejo mayor de histocompatibilidad — Gallina — Genética — Inmunidad — Parásitos — Resistencia a la enfermedad — Virus.
References


