«Review»

The Avian MHC-Antigen System

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Introduction

The avian Major Histocompatibility Complex (MHC) is the only gene locus with a proved industrial significance and is the key to the commercial success of the poultry-farming. Nevertheless it is not completely understood although during the last decades considerable progress has been made.

Most of the immunologically related phenomena or functions which are known for H-2 alleles are now known for the chicken MHC. These include the determination of serologically detectable antigens, histocompatibility antigens, immune responses, serum proteins, resistance to virus-induced malignancy and cell-cell interactions. The finding that all these immunological functions are grouped together in close linkage disequilibrium in species as diverse as chickens, mice and humans, as well as the striking homologies among MHC antigens of these species strongly favours the view that MHCs evolved and persisted in association with some functional advantages to the species.

One might ask the question "why study the avian MHC ?" The answer to this question is that basic studies on the avian MHC have given important clues to be functional advantage of MHC polymorphism as well as the survival value for the species of certain MHC alleles. The herpes virus causing Marek's disease is an important agent of natural selection in chicken and one MHC haplotype is strongly associated with resistance to this contagious lymphoma in several unrelated populations of chickens, including the progenitor of the species. Other MHC haplotypes of the birds are associated with long life span and general fitness, or with high adult mortality.

What do we know about avian MHC and where is the dividing line between the inherited and acquired MHC-regulated antigens ?

The chromosome region which is now known to contain the avian MHC locus, is discovered first in 1947 by using alloimmune hemagglutination reagents and the locus was identified as "D". Later the locus symbol was changed to "B" with the aim to symbolize the second blood group system, stated in the University of Wisconsin (Briles *et al.*, 1950). The discovery of histocompatible, connected with the immune response,

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genes in mammals (Benacerraf and McDevitt, 1972), and the demonstration of associated with the immune response alleles in the B-locus of chickens led to the necessity of an information about the possibility of a haplotype homology among the examined genetic lines in the different laboratories (Guenther *et al.*, 1974 ; Benedict *et al.*, 1975). After recombination inside of the B-complex it was shown that the erythrocyte alloantigenic determinants are coded separately by two subloci - B-F (which codes for histocompatible determinants on erythrocytes and leukocytes) and B-G (which codes for determinants only on erythrocytes - Hala *et al.*, 1976 ; Pink *et al.*, 1977b). Each of the haplotypes represents a chromosome fragment controlling the *specificity* of at least two separate erythrocyte antigens. It can be expected the presence of "exchangeable" subsegments between casual haplotypes (Pink *et al.*, 1977b). Recombinants sharing B-F or B-G segments with their annalogical "parent" haplotypes are stated in genetically typified parents possessing partly paired combinations of 7 haplotypes (Hala *et al.*, 1976 ; Briles and Briles, 1977).

Loci of I st class : The B-F locus and its products have typical class I structures. Sera with B-F-antibodies can suppress completely the GVH-splenomegaly caused after injection of embryos with foreign B-haplotype. This suppression is not observed either after anti-B-G-, or after anti-B-L-antibodies. The inhibiting effect can be eliminated after preincubation with appropriate erythrocytes.

Loci of IInd class : The primary biochemical identification of "Ia"-like molecules, estimated by the B-L-locus (Ziegler and Pink, 1976) was subsequently confirmed also by Simonsen (1980). While the first two antigens (class I + 11) are glycoproteins with affinity to ConA and Lens ciliaris-lectins, the B-L-antigens can bind to ricin as well and show many other properties (Crone *et al.*, 1981 ; Kvist *et al.*, 1978).

The cellular appearance of the "Ia"-like antigens in chickens is examined by Ewert and Cooper (1978) who could find them on Ig⁺-lymphocytes, bursal cells and plasmocytes.

Ontogenetically the "Ia"-antigens are found first in the bursa of Fabricius on the 10th day after hatching. They are not observed on T-cells, renal cells, embryonal liver cells, fibroblasts and spermatosoids.

Loci of III rd class : Until now a separate locus for the complement system in the B-complex has not been found. The C3-system in the chicken can not be easily activated by experimental conditions and it was supposed that either the chicken C2 or C4 are missing and/or can not substitute the mammalian C2 and C4 in the mixed complement system.

Loci of IV th class : The B-G locus should be placed in its own class - with or without a mammalian homologue. The biochemistry of its gene products is less well defined than the B-F and B-L products. Pink *et al.* (1977b) have described two chains with molecular weights of 42 and 31 kDa and supposed that the smaller chain arose from the bigger chain through a proteolytic disintegration. The B-G locus appearance on definite cells was completely different from those of the B-F- and B-L-antigens. The B-G-antigens are present in both embryonic and mature erythrocytes.

Loci of Vth class : In this class are genes which mediate the main inherited properties

and which are under endocrine control. Briles and Alien (1961) have observed the relationship between B-blood group locus and reproduction/vitality in poultry farms. They noted significant differences in these parameters among the B-locus heterozygotes.

Our present knowledge about the structure of the avian B-complex is based on the split of genetic recombinations into two regions (Hala *et al.*, 1976) - the region with the two loci B-F and B-L and the B-G region.

Hartmanova and Hala (1976) have shown that the humoral immune response develops earlier against B-antigens on avian erythrocytes than against A-blood group antigens and the tolerance to A-antigens is induced more rapidly than to B-antigens (Schulmannova *et al.*, 1978). Thymectomy prolonged the survival of the A-incompatible, but not of the B-incompatible ⁵¹Cr-labelled erythrocytes while the bursectomy extended the survival of both cell types (Hala *et al.*, 1980). This specific answer against B-antigens could be referred to the presence of "natural" B-antibodies in normal chickens, which means that they are sensitized somehow to B-antigens (Longenecker and Mossman, 1980).

Berjonneau and Brogen (1983) stated, that avian serum contains B-L antigen which is immuno-chemically closely related to the membrane associated antigen, but not identical with it. Pevzner *et al.* (1978) has first demonstrated the presence of Ir-gene in the chicken, which can be separated by recombination of serologically defined MHC-alloantigens. These authors estimated two alleles of the Ir-GAT-locus - Ir-GA-Lo and Ir-GAT-Hi. The possible crossing over can separate the B-G-region (which encodes for alloantigens only on erythrocytes) from the B-F and B-L regions. Since no recombinations between B-L- and B-F-regions have been observed, it can not be decided which of the functions belong only to the B-L-, and which to the B-F-region. For example the alloaggressive (AA) locus of Simonsen (Simonsen *et al.*, 1977), who estimated the GVH-potential, could be a part or identical to the B-F locus, because anti-T-lymphocyte antibodies (inhibiting the GVH- reaction) could be adsorbed by erythrocytes. The results have shown that the B-L-region can contain more than one locus coding for B-L-antigens. The investigations on the B-complex led to the results of Pink and Rijnbeek (1983) who stated that the surface of avian thymocytes and bursal cells possess 4 groups of antigen receptors. Kornfeld *et al.* (1983) compared the surface antigen determinants on avian normal and leukemic (Mc29, AMV and E-26) hemopoietic cells and explained the transition of the normal (inherited) determinants to acquired.

Historical view : Schierman and Nordskog (1965) demonstrated avian lymphocyte antigens by the help of B- and C-blood group antisera. Now we know that the B-blood group system is estimated by the MHC (Pazderka *et al.*, 1975 a). The A-antigen system was demonstrated by A-blood group antisera (Wong *et al.*, 1972). The lymphocyte antigens of the Th-1- and Bu-1-systems were discovered by the use of two pairs of antisera - one, cytotoxic to the lymphoid thymus cells (Donnelly *et al.*, 1975) and the second - cytotoxic to the bursal lymphocytes (Gilmour *et al.*, 1976). The Ly-4 system was revealed by antisera which inhibit the GVH-splenomegaly of the peripheral blood lymphocytes (Fredericksen *et al.*, 1975).

The first three lymphocyte alloantigens (B-, C- and A) are reported primarily as erythrocyte antigen systems. Pace *et al.* (1978) stated that the thymus membrane fraction has three specific antigens - T₁, T₂ and T₃. T₁ and T₂ are bound to the membrane, but do not lay on its external surface. A common (BT) antigen was discovered in the fractions from bursal and thymus cell membranes.

The avian MHC, called now B-complex, is described by Briles *et al.* (1950) as "blood group locus", renamed later as "B-locus". After 10 years it was stated that this locus plays a role in the GVH-reactions (Schierman and Nordskog, 1961), in the stimulation of the T-cells in MLC (Jaffe and McDermid, 1962). Simonsen (1980) showed that the MHC-antigens on the erythrocytes can provoke the GVH-reactions, while other antigens (belonging to the same haplotype) are independent. The biochemical analysis of the B-complex antigens was started by Ziegler and Pink (1975, 1976) who assumed the existence of two classes of molecules which correspond to the similar classes I- and II- gene products in mammals. In 1976 Hala *et al.* described the RI-haplotype (cock Nr.744) which is a recombinant between the MHCs of the inbred lines CC and CB. They offered the 3-locus model of the avian MHC (Hala, 1977).

Phylogenesis : In recent years a lot of studies have investigated the phylogenetic evolution within the B-complex. For example, Gobel *et al.* (2000) gave evidence for a stepwise evolution of the CD3-family. They showed that TCR/CD3-complex is downregulated by treatment with phorbol ester and demonstrates the integrity of a CD 3- γ -like cytoplasmic internalization motif. The authors have sequenced chicken CD3 cluster and found that it possesses two CD3-proteins playing a role in the $\gamma\delta$ -glycosylation. These data argue for a stepwise CD3-evolution with major differences in the TCR/CD3 structure between mammalian and nonmammalian vertebrates and is the basis for understanding of CD3-phylogenesis and the nature of CD3 $\gamma\delta$ -protein.

Evidence has been given that a ChT₁ on chicken T-cells is a novel antigen on early T-cell progenitors and plays an important role in the early stages of T cell development (Katevuo *et al.*, 1999). A phenotype of prethymic intra-embryonic progenitors, capable of thymic colonization was characterized by Lampisuo *et al.* (1998 b). They studied many cell surface antigens and demonstrated that the early intraembryonic expression of an avian B-cell antigen (chB6) derived from cells in the intra-embryonic areas. The authors made the conclusion that the chicken embryonic B-cell progenitors segregate earlier than the T-cell progenitors. Lampisuo *et al.* (1998 a) also observed that when the bursal cells develop they become mature and ready to migrate - they start to express chL12 -antigen. This antigen is associated with the survival of the bursal cells (*in vitro* and *in vivo*).

Nomenclature : The primary designation of B(MHC) alleles was done by Briles *et al.* (1957). The B-alleles were enumerated like B¹-Bⁿ ; the complex alloantigens - B₁ to B_n and the antisera - anti-B₁ and so on. The lack of unified nomenclature of the avian MHC among the different laboratories led to a classification system proposed by Longenecker and Mosmann (1981). The rules of this system (like the rules of Klein *et al.*, 1979 for the H-2 system) are as follows :

First : The avian MHC-determinants, defined by monoclonal antibodies, differ from the

determinants (defined by alloantibodies) by the prefix “m” and enumeration after it (e.g. one serial number for the identification of the MHC-antigenes, specific for the erythrocytes - B-G ; another serial number for the identification of the MHC-antigenes only on the white blood cells - B-L and a third serial number for the MHC-antigenes on erythrocytes and white blood cells - B-F). The specificities on the white blood cells should be typify as B-L.1, B-L.2 and so on. If the primary test can not distinguish B-F antigen from B-G, the typifying should be B.ml, B.m2 and so on.

Second : There should not be made a parallel expression between the “m”-determinants - e.g. the B.m² - specificity has nothing to do with the original B²-allele.

Third : The m-determinants (defined by more than one monoclonal antibodies) having equal distributing parameters in independent B-haplotypes should be given equal marks. The monoclonal antibodies ED 10 and ED11 discover, for example, one and the same antigenic determinant - B-G²¹. But if there appears a new determinant, it should be given a new number.

Fourth : Hybridomas producing m-antibodies against chicken MHC-antigens should have a code number of the producing laboratory and a serial number of the clone. E.g. the ED-4 is the fourth clone produced and characterized by ED (= Edminton).

Antigens and biological activity : Using monoclonal antibodies against B-G-determinants Longenecker and Mosmann (1980) found that the expression of the B-G antigen is restricted only in the erythroid lineage. The antigen, estimated by the G-region is carried only by the erythrocytes and the only function of this gene is to eliminate the erythrocytes and stimulate the antibody formation against erythrocytes (Hala, 1977). A mammalian analogue of the B-G-region in the avian MHC is not known. The B-G region antigens are highly polymorphic (Pazderka *et al.*, 1975 a) and can not be detected in the chicken serum (Pink *et al.*, 1977 b).

Corbel *et al.* (1992) detected a “new” antigen which is expressed on chicken normal neuronal cells, activated T-lymphocytes and mature CD4+CD8+ thymocytes. The antigen has not been expressed on resting or active proliferating B-cells and could be accepted as a new marker of the T cell activation in birds. While the $\alpha\beta$ -T-cells in mammals can express one of the many variable (V) gene families in the β -locus, the birds have only two β -gene families. Avian V- β 2+T cells are recognized by their T cell receptor 3 (TcR3) and the V- β 1+T cells - by the TcR2 (Cihak *et al.*, 1991).

An avian analogue of the mammalian CD45 has been described by Paramithiotis *et al.* (1991). This antigen should be expressed on all leukocytes but not on erythroid cells or their precursors. The B-cells possess a variant of this antigen with higher molecular weight and the thymocytes- with the lower one. The transition from lower to higher molecular weight antigen occurs during the transition of CD4⁻8⁻ to CD4⁺8⁺ cells, before the expression of CD3.

β -2 microglobulin (beta 2m) is another cell surface glycoprotein identified on avian B cells (Pickel *et al.*, 1990). Because of the fact that the expression of this antigen on the avian B-cells is like the mammalian class I-molecules the authors suggested that this CBC-A plays a role in the T- B-cell interactions.

McNagny *et al.* (1997) believed that they found an avian antigen on thrombocytes

and multipotent hematopoietic progenitors (MEP21). They named the gene which codes for this antigen "thrombomucin" because the protein is from the "proteoglycan"-family and is related to the CD34 (in humans). Another avian (chB6) alloantigen on bursal cells has been discovered by Funk *et al.* (1997) with a role in their vitality and adhesion. The mature T-lymphocytes expressing $\alpha\beta$ -T-cell receptors are classified as $CD4^+$ or $CD8^+$ because of the expression of both lymphocyte coreceptors. Zuckermann (1999) showed evidence that there exist double positive lymphocytes (in the secondary lymphoid organs of swine, birds and monkeys) which are from $CD4^+ CD8^+$ dim phenotype. Robertson and Evavold (1999) noted new dual antigen specificity on T-cells (TcRs) after treatment of them with two appropriate peptides. Lampusio *et al.* (1998 a) showed that the ready for migration B-lymphocytes express an antigen (chL12) connected with the cell apoptosis.

A marker (CD57) for the B-cell activation in chicken spleen cells was demonstrated by Mast and Goddeeris (1998). But a small number of T cells in the spleen can also express this antigen. That's why this antigen should be considered as a B-cell activation marker rather than as a marker for bursal B-cells.

The MHC is responsible for the natural resistance of the macroorganism but these mechanisms are still not completely understood. It is known that the Ir-gene plays a role in the antitumor immune response and this response depends on the avian lines. Longenecker *et al.* (1977) and Longenecker and Gallatin (1978) have stated that cell lines from MD lymphoma are rejected quicker in B^{21}/B^{21} chickens than in other haplotype. In similar experiment Calnek *et al.* (1978) showed that the rejection of MHC-compatible lymphomas in B^{21}/B^{21} chickens is a function of T-cells and that the bursectomy increases the effectivity of this rejection. It turned out that the B^{21} -resistance is a dominant property in B^{21} and it is working only if an Ir-gene is involved. Pevzner *et al.* (1979) found that this genetic resistance is in connection with the Ir-GAT-locus of B^1/B^1 recombinant chickens. The B^2 - allele has a role in the continuity of life (Longenecker *et al.*, 1972) and in the resistance to Rous sarcomas (Collins *et al.*, 1977). In common, chickens which are homozygous for the B^{15} -haplotype show low antitumor reaction compared to the B^2 .

Comparison to other animal species and crossreactivity : In the F-region, which controls the GVH-reactions, the MLR (mixed lymphocyte reaction) and the rejection of the skin graft, are identified two antigens (Pink *et al.*, 1977a). One of them, identified as B-L, was discovered on lymphocyte fraction (Ziegler and Pink, 1976) and the second -B-F, on erythrocytes and peripheral lymphocytes. Having the data from the molecular weights it could be supposed that the F-region of the chicken corresponds to the mice class I- antigens and the L-antigens - to the class II-antigens. The B-F antigens are glycoproteins associated with β_2 -microglobulin like polypeptide, while the B-L are glycoproteins too, but not associated with β_2 -microglobulin.

By analysis of the $\gamma\delta$ -T cells in the chicken, Bucy *et al.* (1991) stated that the development of the T cells in birds and man is similar. In both cases the T cells are divided in two subpopulations with different T cell receptors (TcRs) : $\gamma\delta$ - and $\alpha\beta$ -TcRs. This process shows that according to the evolutionary development the T cell differen-

tiation is an old process. Other authors (Li *et al.*, 1999) found a crossreactivity of mouse anti-chicken CD4 and CD8 monoclonal antibodies with turkey leukocytes (and the turkeys belonged to different lines). It turned out that the turkey CD8 α -molecule is polymorphic. In this direction Weigend and Lamont (1999) examined the polymorphism of the avian MHC II and MHC IV by high (H) and low (L) immunocompetence. It was revealed that MHC II has four polymorphic bands but only one of them showed significant difference between L and H. The hybridization with MHC IV probe displayed 26 bands, 18 of which were polymorphic. The differences between the lines were caused by the influence of genetic factors.

The extensive polymorphism of CD8 α in chickens has not been observed in any other species, suggesting that CD8 α and CD8 β have evolved under different selective pressure in the chicken (Luhtala, 1998). The large peripheral blood CD4⁺CD8⁺ T cell population in chickens resembles to that, observed in some human individuals. The inheritance of peripheral blood CD4CD8 $\alpha\alpha$ T cells in the chicken is a unique observation which suggests the presence of a single gene responsible for CD8 α , but not for CD8 β specific expression. CD4, CD8 $\alpha\alpha$ and CD8 $\alpha\beta$ molecules have evolved before the divergence of mammalian and avian branches from their reptilian ancestors.

“New” (acquired) antigens

The chicken 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 resemble their mammalian counterparts in the encoded protein structure. The class IV region encodes for the B blood group antigens and 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-I system which bears strong similarity to the MHC, maps to the opposite side of the nucleolar organizer region on the same microchromosome as the MHC. Lamont (1998) notes that each class of the MHC genes is a potential candidate for a role in disease resistance and that the MHC genes show associations with response to diseases as diverse as virally induced neoplasia, bacterial, parasitic and auto-immune diseases.

After viral infections : The Marek's disease has been investigated by many authors because of its important role in the “natural” selection of the chickens. Hansen *et al.* (1967) have first reported that the B²¹-allele could be responsible for the Marek's disease resistance compared to the allele B¹⁹. Pazderka *et al.* (1975b) demonstrated further that the chicken line “Cole” (chosen by its Marek's disease resistance) is completely homozygous for B²¹, but the line P (which is sensitive) has 3-4 different B-alleles. The genetic influence of the B²¹-allele on the Marek's disease was investigated independently by Longenecker *et al.* (1976, 1977) and Briles *et al.* (1977). They found that several alleles could be categorized according to their ability to evoke resistance to Marek's disease (MD) : the B²¹ gives a complete resistance but B², B⁶ and B¹⁴ - variable resistance (Briles *et al.*, 1980). Chickens with genotype combinations of several other alleles are very sensitive to this infection (B¹, B³, B⁵, B¹³, B¹⁵, B¹⁹ and B²⁷).

Baigent *et al.* (1998) defined the lymphocyte quality and quantity (pp38- lympho-

cytes) of two chicken lines with Marek's disease. They stated that the differential susceptibility of lines 1 (6) and 2 (7) to the development of Marek's disease lymphoma is not attributable to difference in phenotype or location of these pp38-lymphocytes, or time of expression. However susceptibility is associated with greater numbers of pp38-lymphocytes.

After infection of chickens with AMV, Olson and Ewert (1994) have characterized a new antigen - chL5. It was detected on myelocytes, plasma cells, granulocytes, macrophages and activated T cells. But this antigen has very low quantity on cells from young animals. The immature B cells do not possess chL5. The biochemical analysis of Duk *et al.* (2000) showed that leukosis virus erythrocytes possess two specific fractions (dimer and monomer) with properties of glycoporphins. The proportion of O- and N-glycans is greater in them compared to glycoporphin A from human erythrocytes.

In some tumor diseases : Collins *et al.* (1977) have stated that the B²-allele is responsible for the resistance to Rous sarcomas (among its other functions). Subsequently McBride *et al.* (1981) proved that the strain of the sarcoma virus can influence the way of the tumor growth. Brown *et al.* (1984) examined the specificity of the B-genotype response to RSV- induced tumors using 3 different (subgroups) substrains RSV and chickens from two lines. They found that the animals of B²B² and B²B¹⁵ haplotype show stonger answer to the three viruses than the chickens of B¹⁵/B¹⁵ haplotype. Schierman *et al.* (1977) gave evidences for MHC crossover of genes which control alloantigens on erythrocytes ; and genes which control the rejection of Rous sarcomas. They named the locus R-RS-1 and the allelic gene - r-RS-1. Bacon *et al.* (1979) discovered that in B²/B⁵- chickens the B² is connected not only with the resistance to Rous sarcomas and MD, but to erythroblastosis and lymphoid leukosis as well. The authors supposed that the Ir-genes can influence the tumor development and/or that the B² -haplotypes contain regulator genes directing the progression or regression of the tumors. Shami *et al.* (1999) using the epitope spreading examined the antitumor cytotoxic T-cells(CTL) responses. They made a conclusion that CTL-mediated tumor cell destruction *in vivo* favours cross-presentation of additional epitopes with consequent activation of complementary tumor-reactive lymphocytes. It was even concluded that the epitope spreading in that context has obvious important implications for the design of antigen-specific antitumor immunotherapies.

In parasitic diseases : After an avian coccidiosis Lillehoy and Lillehoy (2000) have examined the T- and B-cells and found that the T-cells have the most pronounced protective effect and possess CD8 and $\gamma\delta$ -surface antigens (which are phenotype markers of the cytotoxic T cells). The T cell function became stronger after application of γ -IFN and IL-2.

Experimental models : The contemporary experimentation is developed not only on the macroorganism (*in vivo*), but much more *in vitro* -on cellular and subcellular level. Hemendinger *et al.* (1995) *e.g.* tried to influence the expression of MHC-antigens by increasing/decreasing of the MHC-chromosomes for the T-cell receptors on chicken cells (embryonal and posthatched) and to estimate their role after that. They stated that after an increased MHC-chromosome dosages the T cell differentiation is shifted in

different directions.

After an infection of chickens with bronchitis virus (IBV) Seo *et al.* (2000) transferred lymphocytes from them to healthy exemplars that were infected after that with the IBV as well. The authors observed that most of the recipients were protected by this passive transfer from the infection. This protection is even more complete when the lymphocytes were of gd-T- or CD8-classes (but not CD4). Karaca *et al.* (1999) followed the effect of MHC on the kinetics of primary and secondary T-cell dependent (SRBC) and T-cell independent (Bruc. abortus - BA) antigens in 8 genetic groups of chickens. They found a positive correlation between the coefficients of BA and SRBC secondary responses. This led to the suggestion that the rate of decline in the secondary response is similar between the T cell dependent and T cell independent responses. This study indicated also complex interactions between specific MHC alleles and non-MHC background.

Personal observations

Our examinations on the antigens which appeared after a virus action and tumor development (by the myelocytomathosis virus, strain 31 - Mc3 1) in turkeys showed (Wesselinova, 1994) that the emergence of a new acquired antigen is a glycoprotein with specific amino acid structure -high levels of Gly and Ala (Wesselinova, 1995) and very low molecular weight - 14 kDas. On the other hand the appearance of this antigen depends on the age of the turkeys - animals can not develop the disease (or tumors) after infection in age over 14 days (age resistance). As it was mentioned above, similar examinations have been done with Mc29, AMV and E26, and the results we got were again evidence for the inheritance of many processes.

Is there any connection between MHC-regulated avian resistance and the higher body temperature of birds ? (personal considerations)

I came to the idea that something should be done in explaining this question. We have noticed that turkeys bred by favorable ambient temperature up to 14 days after hatching became resistant to Mc31 virus strain and those which had not -became sensitive (unpublished data). Zhou (2000) commented that the high ambient temperature increases the risk of some diseases in chickens, but it concerns only mature birds. The body and the ambient temperature of the birds are somehow in vice versa correlation -young (not matured birds) need higher temperature for their development and the mature do not need this high ambient temperature and seem even more resistant. The question why the birds possess an increased resistance to infections and do not suffer from multifarious diseases like the mammals remains open. I am far from saying that their raised body temperature is only responsible for this, but I am almost sure that the combination between genetic inheritance and the high body temperature contributes to this peculiarity. There is a lot more to be done in this field.

Conclusion

Most of the immunologically related phenomena of functions which are known for

H-2 alleles (in mice) are now known for the chicken MHC. These include the determination of serologically detectable antigens, histocompatibility antigens, immune responses, serum proteins, resistance to virus-induced malignancy and cell-cell interactions. The findings of all these immunological functions grouped together in close linkage disequilibrium in species as different as chickens, mice and humans, as well as the striking homologies between MHC-antigens of these species strongly favours the view that MHC's evolved and persisted in association with some functional advantages to the species.

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