

## 7 Non-MHC alloantigen genes affecting immunity. W. E. Briles\*, Northern Illinois University, DeKalb, IL 60115.

An alloantigen is a genetically determined cell-surface molecule detected by specific antisera. An identifying letter has been assigned to each genetic locus responsible for the eleven distinct families of alloantigens - *A, C, D, E, H, I, J, K, L, P,* and *R*. The genes of each system segregate independently of the other systems, except that the *A* and *E* are very closely linked (0.5% crossing over). Selection experiments over numerous generations have revealed distinct changes in gene frequency of the *A-E* alloantigens, suggesting immune responses associated with susceptibility to coccidiosis, antibody response to sheep red blood cells (SRBC), regression of Rous sarcomas, and selection for size of the bursa of Fabricius. Immune response effects of the *C* system of alloantigen genes are indicated by distinct gene frequency changes following selection for response to SRBC, selection for size of bursa of Fabricius, differential development of Rous sarcoma tumors, and macrophage nitrite production after LPS stimulation. Immune response effects of the *D* system of

antigens are indicated by data from genetic selection for response to immunization with SRBC, selection for bursa size, and macrophage nitrite production following LPS stimulation. Immune response effects of the *I* system genes are indicated by distinct gene frequency changes in lines selected for bursa size, response to SRBC, selection for egg weight and within family comparisons for macrophage nitrite production. Effects of the *L* system, consisting of only two alleles, are indicated by the gene frequency changes following selection for bursa size, observed fertility effects, and direct comparison of genotypes within families for monocyte phagocytosis, IL-6 production, outcome of Rous sarcomas, and immune responses to SRBC and *Brucella abortus*. Genotypes of the *P* alloantigen system were directly compared within families of fully pedigreed chicks with significant differences for monocyte phagocytosis and macrophage nitrite production. Simultaneous segregation of eight systems in progeny of a single-cross are available to provide critical evaluation of immune response.

**Key Words:** Alloantigen, Genotypes, Haplotype, Immune effect

## Systems for Understanding the Immune System Role in Disease Processes

### 8 Cytokine regulation of local host immune responses to *Eimeria*. H. Lillehoj\*, USDA-ARS, Beltsville, MD.

Parasitic infections usually stimulate a number of immunological defense mechanisms, namely both antibody- and cell-mediated. The particular effect of the response depends upon the specific parasite and stage of infection. Our recent studies on local host immunity to *Eimeria* clearly indicate that intricate and complex interactions of host local cell-mediated immunity and parasites determine the outcome of the host response to coccidiosis. High-throughput gene expression profiling and real-time PCR have been applied to analyze underlying immune mechanisms controlling disease resistance/susceptibility to coccidiosis. The role of various cytokines whose expression increase and decrease in response to coccidia invasion will be discussed.

**Key Words:** Coccidiosis, Gene expression profiling, Cytokines, Local immunity, Chickens

### 9 Immune modulation of the pulmonary hypertensive response to bacterial lipopolysaccharide (LPS, endotoxin) in broilers. R. F. Wideman, Jr.\* and M. E. Chapman, University of Arkansas, Fayetteville AR 72701.

The lungs of broilers are constantly challenged with LPS that can activate leukocytes and trigger thromboxane (Tx)- and serotonin (5HT)-mediated pulmonary vasoconstriction leading to pulmonary hypertension. Among broilers from a single genetic line, some individuals respond to LPS with large increases in pulmonary arterial pressure, whereas others fail to exhibit any response to the same supra-maximal dose of LPS (Wideman et al., 2001; Wang et al., 2002a,b). This extreme variability in the pulmonary hypertensive response to LPS appears to reflect variability in the types or proportions of chemical mediators released by leukocytes. Our research has confirmed that Tx and 5-HT are potent pulmonary vasoconstrictors in broilers, and that broilers hatched and reared together consistently exhibit pulmonary hypertension after i.v. injections of Tx or 5-HT (Wideman et al., 1999; Chapman and Wideman, 2002). Previous in vitro studies conducted using macrophages from different lines of chickens demonstrated innate variability in the LPS-stimulated induction of nitric oxide synthase (iNOS), followed by the onset of an LPS-refractory state (Chang et al., 1996; Hussain and Qureshi, 1997). The NOS enzyme converts arginine to citrulline and nitric oxide (NO). It is known that NO produced by endothelial NOS (eNOS) serves as a key modulator of flow-dependent pulmonary vasodilation (Wideman et al., 1995, 1996), and it is likely that NO generated by iNOS also can function as a vasodilator. Accordingly, it is our hypothesis that broilers exhibit a minimal pulmonary hypertensive response to LPS when their leukocytes innately generate more vasodilator (NO) than vasoconstrictor (Tx, 5-HT) during an LPS challenge. Indeed, inhibiting NOS with L-NAME (and thus inhibiting NO production) modestly increased the baseline pulmonary arterial pressure and dramatically increased the pulmonary hypertensive response to LPS in all broilers evaluated. Innate differences in the effect of LPS on the pulmonary vasculature may parallel genetic differences

in susceptibility of broilers to pulmonary hypertension syndrome (PHS, ascites).

**Key Words:** Ascites, Pulmonary hypertension, Vasoconstriction, Nitric oxide

### 10 Major histocompatibility (*B*) complex control of responses against Rous sarcomas. R. L. Taylor, Jr.\*, Department of Animal and Nutritional Sciences, University of New Hampshire, Durham, NH 03824.

The chicken major histocompatibility (*B*) complex (MHC), affects disease outcome after pathogen infections significantly. One of the best characterized systems of MHC control is the response to the oncogenic retrovirus, Rous sarcoma virus (RSV). Early experiments found that selection altered the tumor growth pattern, either regression or progression. Furthermore, the data suggested genetic control by one or, at best, a few genes. Simultaneous reports defined the essential role of the *B* complex in determining Rous sarcoma outcome. Particular MHC genotypes regressed RSV tumors whereas other MHC genotypes progressed these tumors. Analysis of inbred lines and their crosses, congenic lines as well as noninbred populations has revealed the anti-RSV response of many *B* complex haplotypes. Disparity in tumor growth among lines identical at the MHC but differing in their background genes suggested a contribution of non-MHC genes in the determination of tumor fate. Genetic complementation in tumor growth, characterized by a improved response in heterozygotes, has been demonstrated for both MHC and non-MHC genes. RSV-induced tumor expansion reflects tumor cell proliferation as well as viral replication generating new tumor cells. The *B* complex also controls tumor growth induced by a subviral DNA construct encoding the RSV *v-src* oncogene without other viral sequences. Two other characteristics, immunity to a second tumor induction and metastasis, exhibit MHC control. Genotypes that regressed either RSV or *v-src* DNA primary tumors had enhanced protection against subsequent homologous challenge. In addition, regressor *B* complex genotypes had lower metastatic tumor dissemination to distant sites compared with progressor types. Together, the data indicate that MHC control of RSV-induced tumor fate is strongly defined by the response to a *v-src*-determined function. That function may be a tumor-specific antigen recognized by the immune system. Differential RSV tumor outcomes among various *B* genotypes may include immune influences on viral replication.

**Key Words:** *B* complex, Rous sarcoma virus, *v-src*, oncogene