THE SOUTHWESTERN NATURALIST 50(1):57–64 MARCH 2005

MHC-DRB EVOLUTION PROVIDES INSIGHT INTO PARASITE RESISTANCE IN WHITE-TAILED DEER

STEPHEN S. DITCHKOFF,* STEVEN R. HOOFER, ROBERT L. LOCHMILLER, RONALD E. MASTERS, AND RONALD A. VAN DEN BUSSCHE

Department of Zoology, Oklahoma State University, Stillwater, OK 74078 (SSD, SRH, RLL, RAVDB)
Department of Forestry, Oklahoma State University, Stillwater, OK 74078 (REM)
Present address for SSD: School of Forestry and Wildlife Sciences, Auburn University, AL 36849
Present address for SRH: Department of Biological Sciences, Texas Tech University, Lubbock, TX 79409
Present address for REM: Tall Timbers Research Station, Tallahassee, FL 32312-0918
**Correspondent: ditchss@auburn.edu*

ABSTRACT—The major histocompatibility complex (MHC) is a gene complex closely linked to the vertebrate immune system due to its importance in antigen recognition and immune response to pathogens. As a result, the MHC has been considered a basis for genetic quality because of the devastating impact that parasites and disease can have on fitness. To improve our understanding of the MHC and parasite resistance in free-ranging species, we gathered data on genetics and parasite loads of white-tailed deer (*Odocoileus virginianus*) to determine whether the *DRB* region of the MHC contains alleles that are associated with abundance, intensity, and prevalence of parasites. Mean abundance and intensity of abomasal nematodes were strongly associated with phylogenetic groupings of *Odvi-DRB* alleles. Infection of ectoparasitic ticks was strongly associated with *Odvi-DRB* alleles but had a positive association with alleles from a different evolutionary lineage than abomasal nematodes. Our data suggest that allelic composition of the *Mhc-DRB* of white-tailed deer in southeastern Oklahoma might represent a genetic trade-off. Deer with alleles from the same *Mhc-DRB* evolutionary clade had strong resistance to one class of parasite, either abomasal nematodes or ectoparasitic ticks, whereas deer with alleles from both lineages tended to have moderate resistance to both pathogens, although weaker.

RESUMEN—El compuesto mayor de histocompatibilidad (MHC) es un complejo del gene cercanamente ligado al sistema de inmunidad en vertebrados debido a su importancia en el reconocimiento de antígenos y a la respuesta inmunológica a los patógeno. Consecuentemente, el MHC se ha considerado una base para la calidad genética debido al impacto devastador que los parásitos y enfermedades pueden tener en el estado físico. Para mejorar nuestro entendimineto del MHC y de la resistencia del parásito en un rango-libre de especies recogimos datos sobre la genética y carga parasitaria de los venados de cola blanca (*Odocoileus virginianus*) y así poder determinar si la región de *DRB* del MHC contiene alelos que se asocien con la abundancia, intensidad, y predominio de parásitos. La abundancia y la intensidad promedio de nematodos abomasales se encontraron fuertemente asociadas a agrupaciones filogenéticas de los alelos *Odvi-DRB*. La infección de ectoparásitos (garrapatas) se encontró fuertemente asociada a los alelos de *Odvi-DRB* pero tenía una asociación positiva con alelos de un linaje evolutivo distinto a los nematodos abomasales. Nuestros datos sugieren que la composición alelica del *Mhc-DRB* en los venados de cola blanca en el sudeste de Oklahoma puede representar una compensación genética. Los venados con alelos de la misma evolución cladistica de *Mhc-DRB* tenían fuerte resistencia a una clase de parásito, ya sea a los nematodos abomasales o a ectoparásitos (garrapatas), mientras que los venados con los alelos de ambos linajes tendieron a tener resistencia moderada a ambos patógenos, aunque la resistencia fue más débil.

The major histocompatibility complex (MHC) is widely recognized as being closely linked to the vertebrate immune system due to its role in antigen recognition and immune response to pathogens (Klein, 1986). Molecules produced by the MHC bind to foreign antigens and are then recognized by T-cells. This recognition leads to T-cell activation, multipli-

cation, and ultimately lysis of the infected cell or antibody formation through an immune response (Klein, 1986; Falk et al., 1991).

Because of the potential effects of the MHC on body condition and fitness, it has been examined in a wide array of species, including mammals (Trowsdale, 1995), birds (Edwards and Potts, 1996), fishes (Dixon et al., 1995), reptiles (Grossberger and Parham, 1992), and amphibians (Radtkey et al., 1996). However, most of our knowledge of the MHC in free-ranging species has been limited to genetic organization, number of genes, and allelic diversity. In addition to functioning in immune response, several life-history traits seem to be influenced by genetic variation at MHC loci. For example, lifespan, mate selection, testicular volume, testosterone levels, egg and milk production, and spontaneous abortion have been associated with MHC-linked loci (Finch and Rose, 1995; von Schantz et al., 1996). These observations have led some (Finch and Rose, 1995) to refer to the MHC as a ''life-history gene complex'' that directly influences fitness, as has been proposed in a model for its involvement in demography of animal populations (Lochmiller, 1996).

The importance of the MHC to the life history of vertebrate species becomes apparent when examining the potential impact that parasites can have on fitness. Parasites can negatively influence fitness in vertebrate hosts by competing for resources (e.g., energy and nutrients), transmitting diseases that place further demands on the host, and causing secondary infection. Resources that would normally be used for maintenance, growth, or reproduction are lost or must be redirected to mount an immune response. Individuals that possess MHC characteristics enabling them to mount a rapid, effective response to parasitic assault might benefit from increased resources available for growth or reproduction (Lochmiller and Deerenberg, 2000) and reduced risk of predation (Lochmiller, 1996).

We have long recognized intraspecific variation in parasite resistance, and recently, relationships between allelic variation of the MHC and parasite-disease resistance have been documented (Blackwell, 1996; Lessard et al., 1996; Outteridge et al., 1996). Furthermore, evidence suggests that heterozygotes at the MHC might have resistance to a greater number of pathogens and exhibit greater fitness than homozygotes (Penn et al., 2002). These factors, because of their implications, have resulted in an abundance of studies on the MHC, and domestic ungulates have begun to receive considerable attention because of their economic importance. Work with Soay sheep (*Ovis aries*) has suggested that allelic variation of the MHC at locus *DRB* is associated positively with juvenile survival and resistance to intestinal nematodes (Paterson et al., 1998). Alleles that were associated with high parasite loads also were associated with low survivorship, suggesting that MHC-based resistance to parasites might be a good measure of individual quality. Similarly, in an effort to isolate alleles responsible for resistance to abomasal helminths, it was found that the *DRB* locus was important in parasite resistance in sheep, and certain alleles were associated with lower fecal egg counts than other more common alleles (Schwaiger et al., 1995). Results from these studies suggest that resistance to intestinal helminths in ungulates might be associated with allelic variation at *Mhc-DRB*.

While our understanding of the MHC is improving with each new study, we are far from having a complete understanding of the function and importance of this gene complex. In this study, we investigated the role of the MHC in parasite resistance in a free-ranging population of white-tailed deer (*Odocoileus virginianus*) by estimating densities of abomasal nematodes and ectoparasitic ticks from hunter-harvested deer and determining allelic composition of the *Mhc-DRB* exon 2. We chose to study the *Mhc-DRB* because it is highly variable, is involved in immune defense against macroparasites, and has been the most widely studied MHC locus in Artiodactyla (Mikko and Andersson, 1995; Swarbick et al., 1995; Mikko et al., 1997; Van Den Bussche et al., 1999). We examined exon 2 of the *Mhc-DRB* locus because it codes for the peptide binding region of MHC molecules (Klein, 1986).

METHODS—*Study Area*—We collected data from 150 adult, male white-tailed deer that were harvested by hunters during October and November 1995 and 1996 at the McAlester Army Ammunition Plant in southeastern Oklahoma (34°49′N, 95°55′W). The 18,212-ha facility had been managed under objectives of Quality Deer Management since 1989 (Ditch-

koff et al., 1997), resulting in a mature herd, where estimates suggested that >50% of the males in the population were ≥3.5 y old (Ditchkoff et al., 2000). Density of deer on the area was about 13 deer/km^2 and the buck : doe ratio was approximately 1:2.2.

Parasite Collection—Immediately following harvest, deer were field-dressed and the abomasum removed, tied at both ends with string to avoid loss of contents, and frozen. Deer were aged by tooth wear and replacement (Severinghaus, 1949). Abomasal contents were removed, diluted with water to 1,000 mL, and a 50-mL aliquot examined (Prestwood et al., 1973). Total nematodes in the abomasum were calculated by multiplying number of nematodes in the 50-mL aliquot by 20. Nematodes were identified based upon structure of spicules and gubernacula (Kubat et al., 1980). Ectoparasitic ticks (mainly *Amblyomma americanum* and *Ixodes scapularis*) were counted on the sternum of each deer prior to field-dressing using a 2.5-cm × 12.5-cm template (Sams et al., 1996), and the count was used as an index of the degree of ectoparasite infestation.

We calculated abundance (average number of parasites of a specific species), intensity (average number of parasites of a specific species, excluding deer that had zero), and prevalence (proportion of deer with a specific species of parasite) of each species of abomasal nematode (Margolis et al., 1982). Abundance was defined as mean number of abomasal nematodes per deer. We determined intensity of infection by calculating mean number of nematodes per deer that had >0 nematodes. Prevalence was the percentage of deer that had >0 nematodes. We calculated tick abundance but did not calculate intensity or prevalence of ticks because prevalence approached 100%.

MHC Typing—Following harvest, approximately 1 g of liver tissue was collected and placed in lysis buffer, and DNA was isolated following standard protocols (Longmire et al., 1997). We conducted polymerase chain reaction (PCR) amplification of *Mhc-DRB* exon 2 using primers LA31 and LA32 (Sigurdardottir et al., 1991). We identified allelic diversity of *Mhc-DRB* exon 2 using a modification of the single-stranded conformation polymorphism (SSCP) analysis (Orita et al., 1989). A complete description of genetic techniques was reported by Van Den Bussche et al. (1999).

Previous methods used to examine associations between parasites and the MHC in ungulates attempted to identify alleles that were associated with low parasite loads (Schwaiger et al., 1995; Paterson et al., 1998). Because little is known about the MHC in white-tailed deer and other cervids, we felt any attempt to associate specific alleles with parasite loads would be premature. Moreover, we detected 15 *Mhc-DRB* alleles in this population (Van Den Bussche et al., 1999), which would limit our ability (e.g., statistical power) to detect associations between parasites and specific alleles. Therefore, we classified alleles into 1 of 2 allelic lineages based upon earlier phylogenetic analyses (Van Den Bussche et al., 1999). Evolution of *Odvi-DRB* usually occurs from point mutations rather than recombination (Van Den Bussche et al., 1999), resulting in lineages containing alleles that are likely similar from a functional standpoint. Using the phylogenetic classification, we were then able to categorize the *Odvi-DRB* profiles of our deer into 3 groups. Deer with both *Odvi-DRB* alleles from lineage 1 were categorized as Type 11, and deer with both alleles from lineage 2 were categorized as Type 22. Deer with alleles from each of the 2 lineages were categorized as Type 12. Sequence divergence between and within lineages was reported by Van Den Bussche et al. (1999). This method of classification has been used previously to assess relationships between *Mhc-DRB* profiles and antler development (Ditchkoff et al., 2001), and similar classification techniques have been used by others (Dorak et al., 1999, 2002) when analyzing MHC data.

Statistics—We compared parasite data between deer with different genetic characteristics (e.g., Types 11, 12, and 22) using generalized linear models (PROC GENMOD; SAS Institute, 1993) with a Poisson distribution and log link (Wilson et al., 1996; Wilson and Grenfell, 1997). Generalized linear models are a broad class of statistics that allow analysis of data sets with a variety of distributions (Agresti, 1996). Because generalized linear models do not assume normality or homogeneity of variance like linear models (e.g., ANOVA), we avoided inherent problems associated with transformations that do not satisfy all assumptions.

RESULTS—We identified 15 *Mhc-DRB* alleles in our population (Table 1) that were classified into 2 evolutionary clades during a previous study (Van Den Bussche et al., 1999). The frequency of deer classified into Type 11, Type 12, and Type 22 *Odvi-DRB* categories were 21.6%, 37.6%, and 40.8%, respectively. These data were not in Hardy-Weinberg equilibrium ($\chi^2_{1,2} = 7.25$; $P = 0.027$).

We identified 6 species of abomasal nematodes, *Haemonchus contortus* Rudolph (25.8 ± 11.0; mean abundance ± *SE*), *Apteragia odocoilei* Dikmans (504.0 ± 35.0), *Apteragia pursglovei* Davidson and Prestwood (3.3 ± 1.5), *Ostertagia dikmansi* Becklund and Walker (148.3 ± 16.7), *Ostertagia mossi* Dikmans (58.4 ± 9.8), and *Ostertagia ostertagia* Stiles (3.0 ± 1.6), but *A. pursglovei* and *O. ostertagia* were each found in ≤5 deer, so statistical analyses on these species

TABLE 1—Categorization of alleles of the *Odvi-DRB* exon 2 found in white-tailed deer from southeastern Oklahoma into evolutionary lineages based upon phylogenetic analysis. Evolutionary groupings were based upon previous phylogenetic analysis (Van Den Bussche et al., 1999).

Allelic lineage 1	Frequency (%)	Allelic lineage 2	Frequency (%)
*Odvi-DRB*01*	1.9	*Odvi-DRB*02*	0.4
*Odvi-DRB*03*	1.9	*Odvi-DRB*05*	32.8
*Odvi-DRB*04*	26.9	*Odvi-DRB*06*	0.8
*Odvi-DRB*09*	0.8	*Odvi-DRB*07*	13.8
*Odvi-DRB*13*	0.8	*Odvi-DRB*08*	1.1
*Odvi-DRB*14*	6.9	*Odvi-DRB*10*	1.9
*Odvi-DRB*15*	0.4	*Odvi-DRB*11*	5.4
		*Odvi-DRB*12*	4.2

were not possible. Mean number of nematode species within the abomasum of each deer was 2.6. Mean abundance of abomasal nematodes (total nematodes of all species) in deer from our study area was 735.7 (*SE* = 52.7) nematodes/deer, with abundance estimates ranging from 20 to 3,200.

Abundance of *H. contortus* was more than 8 times greater ($P < 0.001$) among Type 22 deer than Type 11, and almost 4 times greater ($P < 0.001$) among Type 22 deer than Type 12 deer (Table 2). Type 12 deer had approximately twice ($P < 0.001$) the abundance of *H. contortus* than Type 11 deer. Abundances of *O. mossi* and *O. dikmansi* followed a pattern similar to *H. contortus* and were greater ($P < 0.001$) among Type 22 deer than Types 11 or 12 deer (Table 2). In contrast, Type 11 deer had greater ($P < 0.001$) abundance of *A. odocoilei* than Type 22 deer. There were greater ($P < 0.05$) mean intensities of *H. contortus, O. mossi,* and *O. dikmansi* among Type 22 deer than Type 11 deer, but like abundance, intensity of *A. odocoilei* was greatest in Type 11 deer (Table 2). In general, prevalence of infection with abomasal nematodes followed patterns of abundance and intensity. Mean abundance of ectoparasitic ticks was greater ($P < 0.001$) in Type 11 deer (24.6 ± 4.9, $n = 27$ deer) than Type 22 deer (15.8 ± 2.7, $n = 51$ deer), but not ($P = 0.079$) Type 12 deer (22.5 ± 4.4, $n = 47$ deer). Tick abundance was greater ($P < 0.001$) in Type 12 than Type 22 deer.

TABLE 2—Mean abundance, mean intensity, and prevalence of abomasal parasites of adult, male white-tailed deer from a population in southeastern Oklahoma with different characteristics of the *Odvi-DRB* exon 2.

	Mean abundance						Mean intensity								Prevalence[a]		
	Odvi-DRB 11 ($n = 20$)		*Odvi-DRB* 12 ($n = 31$)		*Odvi-DRB* 22 ($n = 38$)		*Odvi-DRB* 11			*Odvi-DRB* 12			*Odvi-DRB* 22			*Odvi-DRB*		
Parasite	Mean	*SE*	Mean	*SE*	Mean	*SE*	*n*	Mean	*SE*	*n*	Mean	*SE*	*n*	Mean	*SE*	11	12	22
Haemonchus contortus	5.7 a[b]	3.3	12.4 b	5.0	47.2 c	25.1	3	38.2 a	8.1	6	64.2 b	10.0	10	179.3 c	85.0	0.15	0.19	0.26
Apteragia odocoilei	560.9 a	82.8	440.4 b	46.3	526.0 c	58.3	20	560.9 a	82.8	31	440.4 b	46.3	38	526.0 c	58.3	1.00	1.00	1.00
Ostertagia mossi	141.8 a	50.8	128.2 b	19.0	168.2 c	24.4	17	166.8 a	58.9	24	165.6 a	18.4	31	206.2 b	25.3	0.85	0.77	0.82
Ostertagia dikmansi	33.8 a	13.7	40.1 b	10.2	86.3 c	19.3	7	96.5 a	26.5	15	83.0 b	14.3	24	136.7 c	25.5	0.35	0.48	0.63
Total	745.0 a	117.3	609.4 b	59.6	844.7 c	94.4	20	745.0 a	117.3	31	609.4 b	59.6	38	844.7 c	94.4	1.00	1.00	1.00

[a] Sample sizes (n) for prevalence estimates are the same as for mean abundance estimates.

[b] Means in the same row and category (e.g., abundance or intensity) with different letters are different ($P < 0.05$).

DISCUSSION—We detected significant relationships between abundance and intensity of abomasal nematodes, and allelic composition at *Odvi-DRB* exon 2. Individuals with both alleles from allelic lineage 1 (Type 11) had lower infection levels of *H. contortus* than Type 22 deer, while Type 12 deer had intermediate levels of infection. Similar trends were found with *A. odocoilei, O. mossi,* and *O. dikmansi.* These data suggest that alleles of *Odvi-DRB* are codominant, a common trait among MHC loci. Codominant alleles in the MHC theoretically double the number of pathogens against which a host can mount an immune response. Because of codominance, heterozygosity at MHC loci could increase recognition of and response to foreign pathogens, thereby decreasing susceptibility to disease, and potentially increasing lifetime fitness (Apanius et al., 1997). Similar relationships were found when examining associations between resistance of sheep to intestinal nematodes and characteristics of the *Mhc-DRB* (Paterson et al., 1998). They noted that some *Mhc-DRB* characteristics, through suppression of parasite infestations, could lead to increased probability of survival.

Because *H. contortus* is probably the most pathogenic abomasal nematode of white-tailed deer in North America (Prestwood and Kellogg, 1971; Prestwood et al., 1973), we expect that selection pressures on the MHC by this species would be greater than pressures exerted by less pathogenic species, such as *A. odocoilei, O. mossi,* and *O. dikmansi.* Severe infection with *H. contortus* can result in lesions, blood loss, and sometimes death (Prestwood and Pursglove, 1981); however, we did not encounter severe infestations in our study. *Apteragia odocoilei, O. mossi,* and *O. dikmansi,* while common in deer, rarely promote clinical symptoms or serious debilitation in their host (Prestwood and Pursglove, 1981). Although not as strong, we detected relationships similar to those found with *H. contortus* between these parasitic species and *Odvi-DRB.* These results suggest that either different alleles in the same evolutionary lineage are associated with these abomasal nematodes, or the same alleles can respond to all 4 species of nematode. Activation of immune response to suppress *H. contortus* infections has been shown previously to suppress other species of intestinal strongyles (Stewart, 1953; Stewart, 1955).

Whereas individuals with alleles from lineage 1 of *Odvi-DRB* had fewer abomasal nematodes, these same individuals had a greater abundance of ectoparasitic ticks. Ticks are the most important ectoparasite of deer in North America and occur throughout most of their range (Strickland et al., 1981). Although not usually associated with mortality in adult deer, their impact on neonates in this region can indirectly increase risk of mortality (Logan, 1972; Sams et al., 1996). Severe infestations can induce blood loss, secondary infection, and disease transmission and can result in anemia, weight loss, or death (Stewart, 1955). Our understanding of the MHC and its functionality (e.g., peptide binding characteristics) suggests that parasites as different as abomasal nematodes and ticks would be associated with, at the very least, different alleles. Therefore, we do not find it surprising that these parasites were associated with different allelic lineages. Furthermore, this discovery suggests that there might be an immune tradeoff with regard to allelic composition at this locus, because both abomasal nematodes and ticks are prevalent parasites in Oklahoma deer (Sams et al., 1996; Sams et al., 1998) and at times can adversely affect deer populations, as described earlier. Considerable diversity has been documented between allelic lineages of *Odvi-DRB* (Van Den Bussche et al., 1999), which could be explained by the need for immune defenses for multiple pathogens.

Hughes and Nei (1988) argued that what is expected under the overdominant selection model is that while one MHC allele is associated with resistance to one pathogen, another MHC allele is associated with resistance to another. The calculated selective advantage of heterozygotes over homozygotes (Edwards and Hedrick, 1998) of 0.122 coupled with the deficiency of *Odvi-DRB* exon 2 homozygotes (Van Den Bussche et al., 2002) is interpreted as suggesting that allelic diversity at the *Odvi-DRB* exon-2 locus is being maintained by some form of heterozygote advantage and that different allelic clades are associated with different pathogens. This suggests that there should be an advantage for deer that have alleles from both clades of *Odvi-DRB* alleles because of resistance to a greater diversity of pathogens. Ultimately, decreased parasitism because of these genetic characteristics could lead to greater fitness

through increased attractiveness to mates, social status, resource acquisition, and survival (Prestwood and Pursglove, 1981; Borgia and Collis, 1989). This has been found in adult, male deer, where individuals with alleles from both evolutionary clades of *Mhc-DRB* had greater antler development and body size than deer with alleles from the same evolutionary lineage (Ditchkoff et al., 2001).

Although these data suggest that *Odvi-DRB* is linked to infection levels of abomasal nematodes and ticks in white-tailed deer, it does not imply that other portions of the MHC are not involved with antigen recognition and immune response to these classes of parasites. Our investigation was limited to a subset ($n = 15$) of alleles at 1 locus (*DRB*) of the MHC. Recent work has resulted in the discovery of 3 new *Odvi-DRB* alleles in white-tailed deer (Van Den Bussche et al., 2002), and more alleles likely exist, considering the high variability of the vertebrate MHC (Edwards and Potts, 1996). Furthermore, this study has proposed a new mechanism to examine MHC-pathogen relationships. Whereas previous studies have reported associations between specific alleles and selected pathogens, we identified associations between groups of alleles from the same evolutionary lineage and selected pathogens. We hypothesize that more than one allele might be associated with some pathogens, particularly those pathogens of high prevalence, such as abomasal nematodes and ectoparasitic ticks among white-tailed deer populations in Oklahoma. MHC alleles from common evolutionary lineages could have enough structural similarity to provide immunologic defense against the same pathogens. Whether this is the case, we can only speculate. But this hypothesis is easily testable by examining how prevalence of MHC alleles from particular evolutionary lineages changes regionally as parasite communities change. We propose that the white-tailed deer is a good model to test this hypothesis because of the wealth of information available regarding parasite communities and life-history of deer, and the information already available on the MHC in this species (Van Den Bussche et al., 1999; Ditchkoff et al., 2001).

We wish to thank E. R. Welch, Jr., D. E. Townsend II, and S. T. Grubbs for collecting data. W. R. Starry, B. J. Farrar, and W. C. Dinkines provided support at our study area. D. M. Leslie, Jr. and T. Bidwell reviewed earlier drafts of the manuscript. This project was funded by the United States Army and the National Science Foundation (BSR-8657043, IBN-9318066). We also thank the Oklahoma Cooperative Fish and Wildlife Research Unit (Oklahoma Department of Wildlife Conservation; Oklahoma State University; Wildlife Management Institute; and United States Geological Survey, Biological Resource Division, cooperating) for logistical support.

Literature Cited

Agresti, A. 1996. An introduction to categorical data analysis. John Wiley and Sons, New York.

Apanius, V., D. Penn, P. R. Slev, L. Ruff, and W. K. Potts. 1997. The nature of selection on the major histocompatibility complex. Critical Reviews in Immunology 17:179–224.

Blackwell, J. M. 1996. Genetic susceptibility to Leishmanial infections: studies in mice and man. Parasitology 112:s67–s74.

Borgia, G., and K. Collis. 1989. Female choice for parasite-free male satin bowerbirds and the evolution of bright male plumage. Behavioral Ecology and Sociobiology 25:445–454.

Ditchkoff, S. S., R. L. Lochmiller, R. E. Masters, S. R. Hoofer, and R. A. Van Den Bussche. 2001. Major-histocompatibility-complex-associated variation in secondary sexual traits of white-tailed deer (*Odocoileus virginianus*): evidence for good-genes advertisement. Evolution 55:616–625.

Ditchkoff, S. S., E. R. Welch, Jr., and R. L. Lochmiller. 2000. Using cast antler characteristics to profile quality of white-tailed deer *Odocoileus virginianus* populations. Wildlife Biology 6:53–58.

Ditchkoff, S. S., E. R. Welch, Jr., W. R. Starry, W. C. Dinkines, R. E. Masters, and R. L. Lochmiller. 1997. Quality deer management at the McAlester Army Ammunition Plant: a unique approach. Proceedings of the Annual Conference of the Southeastern Association of Fish and Wildlife Agencies 51:389–399.

Dixon, B., S. H. M. van Erp, P. N. S. Rodrigues, E. Egberts, and R. J. M. Stet. 1995. Fish major histocompatibility complex genes: an expansion. Developmental and Comparative Immunology 19:109–133.

Dorak, M. T., T. Lawson, H. K. G. Machulla, C. Darke, K. I. Mills, and A. K. Burnett. 1999. Unravelling an HLA-DR association in childhood acute lymphoblastic leukemia. Blood 94:694–700.

Dorak, M. T., T. Lawson, H. K. G. Machulla, K. I. Mills, and A. K. Burnett. 2002. Increased heterozygosity for MHC class II lineages in newborn males. Genes and Immunity 3:263–269.

Edwards, S. V., and P. W. Hedrick. 1998. Evolution

and ecology of MHC molecules: from genomics to sexual selection. Trends in Ecology and Evolution 13:305–311.

EDWARDS, S. V., AND W. K. POTTS. 1996. Polymorphism of genes in the major histocompatibility complex (MHC): implications for conservation genetics of vertebrates. In: T. B. Smith and R. K. Wayne, editors. Molecular genetic approaches in conservation. Oxford University Press, Oxford, England. Pp. 214–237.

FALK, K., O. ROTZSCHKE, S. STEVANOVIC, G. JUNG, AND H. G. RAMMENSEE. 1991. Allele-specific motifs revealed by sequencing of self-peptides eluted from MHC molecules. Nature 351:290–296.

FINCH, C. E., AND M. R. ROSE. 1995. Hormones and the physiological architecture of life history evolution. Quarterly Review of Biology 70:1–70.

GROSSBERGER, D., AND P. PARHAM. 1992. Reptilian class I major histocompatibility complex genes reveal conserved elements in class I structure. Immunogenetics 36:166–174.

HUGHES, A. L., AND M. NEI. 1988. Pattern of nucleotide substitution at major histocompatibility complex class I loci reveals overdominant selection. Nature 335:167–170.

KLEIN, J. 1986. Natural history of the major histocompatibility complex. John Wiley and Sons, New York.

KUBAT, G. J., A. A. KOCAN, AND W. R. DAVIDSON. 1980. Identification of abomasal parasites of white-tailed deer. Wildlife Disease Association, Ames, Iowa.

LESSARD, M., D. L. HUTCHINGS, J. L. SPENCER, H. S. LILLEHOJ, AND J. S. GAVORA. 1996. Influence of Mareks-disease virus-strain AC-1 on cellular immunity in birds carrying endogenous viral genes. Avian Diseases 40:645–653.

LOCHMILLER, R. L. 1996. Immunocompetence and animal population regulation. Oikos 76:594–602.

LOCHMILLER, R. L., AND C. DEERENBERG. 2000. Trade-offs in evolutionary immunology: just what is the cost of immunity? Oikos 88:87–98.

LOGAN, T. 1972. Study of white-tailed deer fawn mortality on Cookson Hills Deer Refuge, eastern Oklahoma. Proceedings of the Annual Conference of the Southeastern Association of Game and Fish Commissioners 26:27–39.

LONGMIRE, J. L., M. MALTBIE, AND R. J. BAKER. 1997. Use of ''lysis buffer'' in DNA isolation and its implications for museum collections. Occasional Papers, The Museum, Texas Tech University 163:1–3.

MARGOLIS, L., G. W. ESCH, J. C. HOLMES, A. M. KURIS, AND G. A. SCHAD. 1982. The use of ecological terms in parasitology (report of an ad hoc committee of the American Society of Parasitologists). Journal of Parasitology 68:131–133.

MIKKO, S., AND L. ANDERSSON. 1995. Low major histocompatibility complex class II diversity in European and North American moose. Proceedings of the National Academy of Science, USA 92: 4259–4263.

MIKKO, S., H. A. LEWIN, AND L. ANDERSSON. 1997. A phylogenetic analysis of cattle DRB3 alleles with a deletion of codon 65. Immunogenetics 47:23–29.

ORITA, M., H. IWAHANA, H. KANAZAWA, K. HAYASHI, AND T. SEKIYA. 1989. Detection of polymorphisms of human DNA by gel electrophoresis as single-strand conformation polymorphisms. Proceedings of the National Academy of Science, USA 86: 2766–2770.

OUTTERIDGE, P. M., L. ANDERSSON, P. G. C. DOUCH, R. S. GREEN, P. S. GWAKISA, M. A. HOHENHAUS, AND S. MIKKO. 1996. The PCR typing of MHC-DRB genes in the sheep using primers for an intronic microsatellite: application to nematode parasite resistance. Immunology and Cell Biology 74:330–336.

PATERSON, S., K. WILSON, AND J. M. PEMBERTON. 1998. Major histocompatibility complex variation associated with juvenile survival and parasite resistance in a large unmanaged ungulate population (*Ovis aries* L.). Proceedings of the National Academy of Science, USA 95:3714–3719.

PENN, D. J., K. DAMJANOVICH, AND W. K. POTTS. 2002. MHC heterozygosity confers a selective advantage against multiple-strain infections. Proceedings of the National Academy of Science, USA 99:11260–11264.

PRESTWOOD, A. K., F. A. HAYES, J. H. EVE, AND J. F. SMITH. 1973. Abomasal helminths of white-tailed deer in southeastern United States, Texas, and the Virgin Islands. Journal of the American Veterinary Medical Association 163:556–561.

PRESTWOOD, A. K., AND F. E. KELLOGG. 1971. Naturally occurring Haemonchosis in a white-tailed deer. Journal of Wildlife Diseases 7:133–134.

PRESTWOOD, A. K., AND S. R. PURSGLOVE. 1981. Gastrointestinal nematodes. In: W. R. Davidson, V. F. Nettles, and F. E. Kellogg, editors. Diseases and parasites of white-tailed deer. Tall Timbers Research Station, Tallahassee, Florida. Pp. 318–350.

RADTKEY, R. R., B. BECKER, R. D. MILLER, R. RIBLET, AND T. J. CASE. 1996. Variation and evolution of Class I Mhc in sexual and parthenogenetic geckos. Proceedings of the Royal Society of London B 263:1023–1032.

SAMS, M. G., R. L. LOCHMILLER, C. W. QUALLS, JR., AND D. M. LESLIE, JR. 1998. Sensitivity of condition indices to changing density in a white-tailed deer population. Journal of Wildlife Diseases 34: 110–125.

SAMS, M. G., R. L. LOCHMILLER, C. W. QUALLS, JR., D. M. LESLIE, JR., AND M. E. PAYTON. 1996. Physiological correlates of neonatal mortality in an

overpopulated herd of white-tailed deer. Journal of Mammalogy 77:179–190.

SAS INSTITUTE. 1993. SAS/STAT software: the genmod procedure, release 6.09. SAS Institute, Inc, Cary, North Carolina.

SCHWAIGER, F.-W., D. GOSTOMSKI, M. J. STEAR, J. L. DUNCAN, Q. A. MCKELLAR, J. T. EPPLEN, AND J. BUITKAMP. 1995. An ovine *major histocompatibility complex DRB1* allele is associated with low faecal egg counts following natural, predominately *Ostertagia circumcincta* infection. International Journal for Parasitology 25:815–822.

SEVERINGHAUS, C. W. 1949. Tooth development and wear as criteria of age in white-tailed deer. Journal of Wildlife Management 13:195–216.

SIGURDARDOTTIR, S., C. BORSCH, K. GUSTAFSSON, AND L. ANDERSSON. 1991. Cloning and sequence analysis of 14 DRB alleles of the bovine major histocompatibility complex by using the polymerase chain reaction. Animal Genetics 22:199–209.

STEWART, D. F. 1953. Studies of resistance of sheep to infestation with *Haemonchosis contortus* and *Trichostrongylus* spp. and on the immunological reactions of sheep exposed to infestation. V. The nature of the 'self-cure' phenomenon. Australian Journal of Agricultural Research 4:100–117.

STEWART, D. F. 1955. 'Self-cure' in nematode infestations of sheep. Nature 176:1273–1274.

STRICKLAND, R. K., R. R. GERRISH, AND J. S. SMITH. 1981. Arthropods. In: W. R. Davidson, V. F. Nettles, and F. E. Kellogg, editors. Diseases and parasites of white-tailed deer. Tall Timbers Research Station, Tallahassee, Florida. Pp. 363–389.

SWARBICK, P. A., F.-W. SCHWAIGER, J. T. EPPLEN, G. S. BUCHAN, J. F. T. GRIFFIN, AND A. M. CRAWFORD. 1995. Cloning and sequencing of expressed *DRB* genes of the red deer (*Cervus elaphus*) Mhc. Immunogenetics 42:1–9.

TROWSDALE, J. 1995. "Both man and bird and beast:" comparative organization of the MHC genes. Immunogenetics 41:1–17.

VAN DEN BUSSCHE, R. A., S. R. HOOFER, AND R. L. LOCHMILLER. 1999. Characterization of *Mhc-DRB* allelic diversity in white-tailed deer (*Odocoileus virginianus*) provides insight into *Mhc-DRB* allelic evolution within Cervidae. Immunogenetics 49: 429–437.

VAN DEN BUSSCHE, R. A., T. G. ROSS, AND S. R. HOOFER. 2002. Genetic variation at a major histocompatibility locus within and among populations of white-tailed deer (*Odocoileus virginianus*). Journal of Mammalogy 83:31–39.

VON SCHANTZ, T., H. WITTZELL, G. GÖRANSSON, M. GRAHN, AND K. PERSSON. 1996. MHC genotype and male ornamentation: genetic evidence for the Hamilton-Zuk model. Proceedings of the Royal Society of London B 263:265–271.

WILSON, K., AND B. T. GRENFELL. 1997. Generalized linear modelling for parasitologists. Parasitology Today 13:33–38.

WILSON, K., B. T. GRENFELL, AND D. J. SHAW. 1996. Analysis of aggregated parasite distributions: a comparison of methods. Functional Ecology 10: 592–601.

Submitted 8 July 2003. Accepted 15 May 2004.
Associate Editor was Cody W. Edwards.