Evolutionary Ecology (2021) 35:513–535
https://doi.org/10.1007/s10682-021-10108-x

ORIGINAL PAPER

Association between sexually selected traits and allelic distance in two unlinked MHC II loci in white-tailed deer (*Odocoileus virginianus*)

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Received: 13 August 2020 / Accepted: 20 February 2021 / Published online: 18 March 2021

Abstract
Body size and secondary sexual characteristics are drivers of male reproductive success among polygynous species. A gene complex found to be associated with morphology in several species is the major histocompatibility complex (MHC). However, while several studies have found that greater MHC diversity is associated with larger body size and secondary sexual characteristics, other studies have demonstrated that maximal MHC diversity is not always optimal for the individual's fitness. This study tested if MHC diversity, measured as pairwise allelic distances at each of two unlinked MHC II loci (exon 2 for the classical antigen-binding protein *MHC-DRB* and exon 2 for the accessory protein *MHC-DOB*), was associated with body size (male and female) or antler size in a semi-wild enclosed population of white-tailed deer (*Odocoileus virginianus*). After accounting for the effect of age on body and antler size, we used residual analysis to assess whether MHC allelic distances explained any of the remaining variation in body and antler size. While we found no associations between physical characteristics and *MHC-DRB*, we found that both male body and antler size were associated with *MHC-DOB* nucleotide allelic distances. Specifically, we found a quadratic relationship between *MHC-DOB* and male body size, where body size peaked at moderate *MHC-DOB* nucleotide allelic distance. However, we found a positive linear association between *MHC-DOB* nucleotide allelic distances and antler size. Neither *MHC-DRB* nor *MHC-DOB* influenced female body size, even though the average allelic distances of males and females were not significantly different. Our results suggest that *MHC-DOB*, or a gene genetically linked to this locus, may influence male morphological characteristics in white-tailed deer.

Keywords Major histocompatibility complex · White-tailed deer · Sexual selection · Morphology · Secondary sexual characteristics

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Introduction

Polygyny, where males breed with more than one female, is a common breeding strategy, especially among terrestrial Artiodactyla (Geist 1974; Jarman 1974; Ralls 1977; Bubenik 1985; Clutton-Brock 1989; Weckerly 1998; Loison et al. 1999). In polygynous species, male competition is high, as only a few males may monopolize breeding access, and fights are common and ensure that the strongest males are able to pass on their genetics (Clutton-Brock and Huchard 2013). Males must therefore invest energy into body size and other physical traits that positively influence reproductive success, such as teeth, horns, and antlers (West-Eberhard 1979; Clutton-Brock and Huchard 2013). Although a polygynous breeding strategy can grant successful males increased reproductive success, such a strategy is very costly. These costs are especially apparent with seasonal breeders, where males may cease feeding altogether during the breeding season (Thompson et al. 1973; Clutton-Brock and Huchard 2013). Male white-tailed deer (*Odocoileus virginianus*), for example, may lose up to 30% of their body mass during the breeding season (Hewitt 2011). Unlike the strong selection for large ornamentation (e.g., antlers) found among polygynous males, no such selection exists for females, as costly morphological investments are unnecessary for females to attract mates (Ditchkoff 2011). Instead, female reproductive success is determined by her ability to bear and raise offspring to reproductive age (Strassmann and Gillespie 2002).

Body and ornamentation size can be influenced by an individual's genetics. A gene complex of particular interest with respect to its association with morphology is the major histocompatibility complex (MHC; Bennett 1975; Gill and Kunz 1979; von Schantz et al. 1996, 1997; Ditchkoff et al. 2001; Fernandez-de-Mera et al. 2009; Brambilla et al. 2015, 2018). These genes do not influence morphology directly, but instead code for proteins that are essential for the immune system to distinguish self from foreign pathogens by binding to peptide fragments (i.e., antigens) and displaying these on the surfaces of cells where they are monitored by T-cell lymphocytes (Hedrick 1994; Schook and Lamont 1996; Janeway et al. 2001; Kamiya et al. 2014). If the antigen is recognized by the body as 'self,' the T-cells will not destroy the cell. If the antigen is foreign, however, the T-cells will cause cellular destruction or initiation of a systemic immune response to clear foreign particles (Janeway et al. 2001). While gene products from MHC type I genes primarily display endogenous antigens on nucleated cells, MHC type II genes produce proteins that display exogenous antigens on immune cells such as dendritic cells and macrophages (Janeway et al. 2001). There are classical (ex. DR, DQ) and non-classical (ex. DO, DM) MHC type II genes, whose proteins serve different immunological roles. Non-classical MHC genes produce accessory proteins that are used for properly loading antigens onto classical MHC gene products, which then display these antigens at the immune cell's surface (Poluektov et al. 2013; Mellins and Stern 2014). While classical MHC genes are highly polymorphic, non-classical MHC genes are more conserved (Janeway et al. 2001; Denzin 2013).

Due to their vital role in determining the immune system's effectiveness, MHC genes may influence resources available for an individual's growth, development, and reproduction. Several studies have examined the association between the MHC and morphology. For example, spur length of male pheasants (*Phasianus colchicus*), which correlates to male viability and female mate choice, is highly influenced by male MHC genotype characteristics (von Schantz et al. 1996, 1997). This relationship between an individual's MHC genotype and morphology may be linked to the improved immune system associated with MHC heterozygosity (von Schantz et al. 1996; Sauermann et al. 2001; Olsson et al. 2005).

Specifically, the heterozygote advantage hypothesis states that individuals with greater MHC heterogeneity are able to fight off a greater diversity of pathogens (Hughes and Nei 1992; Sommer 2005). Under this hypothesis, heterozygotes should be healthier, better able to attain larger size of sexually selected traits, and consequently achieve greater reproductive success (Hughes and Nei 1989; Takahata and Nei 1990).

However, costs of increased MHC diversity exist that may define optimal levels of MHC heterozygosity for an individual (Demas and Nelson 2011). High individual MHC heterozygosity is associated with increased deletion of T-cell lineages, which results in reduced T-cell repertoire diversity, and therefore a less effective immune response (Vidovic and Matzinger 1988; Vidovic 1989; Nikolich-Zugich et al. 2004). A reduced T-cell repertoire can also lead to limited regulatory T-cell diversity. These immune cells are responsible for controlling the intensity of an immune response (Graham et al. 2005), and reduced regulatory T-cell diversity can make an individual more prone to immunopathology and autoimmune disease (Milner et al. 2007; Ferreira et al. 2009). Increased MHC heterozygosity may also increase an individual's chances of having an MHC allele that predisposes the carrier to several autoimmune diseases, such as multiple sclerosis, lupus, diabetes, and Crohn's disease in humans (Fernando et al. 2008). Similarly, certain MHC alleles may predispose the carrier to contracting some infectious diseases (McClelland et al. 2003). Additionally, immune responses can be physiologically costly and divert resources away from growth (Klasing et al. 1987; Fair et al. 1999; Bonato et al. 2009) and reproduction (Ilmonen et al. 2000, 2007; Bonneaud et al. 2003, 2004; Hanssen 2006; Cai et al. 2009; Bascunan-Garcia et al. 2010). Thus, as MHC heterozygous individuals typically mount a stronger immunological response than homozygotes (Doherty and Zinkernagel 1975), individuals with greater MHC heterozygosity may suffer greater physiological costs that could reduce their overall fitness (Ilmonen et al. 2007). Lastly, maximum MHC heterozygosity may negatively influence T-cell activation by reducing the concentration of specific peptide-MHC complexes on the cells' surfaces (van den Berg and Rand 2003; Woelfing et al. 2009). All of these costs of increased MHC diversity may ultimately reduce those resources that individuals can devote to developing and building sexually selected morphological characteristics. Given the known trade-offs associated with increased MHC diversity, maximizing MHC diversity may not be the optimal strategy.

The MHC region of the white-tailed deer (*Odocoileus virginianus*), a polygynous ruminant, has been examined by several studies. Two MHC genes have been characterized in this system, the classical *MHC-DRB* and the non-classical *MHC-DOB*. Currently, 30 unique *MHC-DRB* exon 2 alleles and 11 *MHC-DOB* alleles have been documented for this species (Van Den Bussche et al. 1999, 2002; Ivy-Israel et al. 2020). Ivy-Israel et al. (2020) also found no significant linkage disequilibrium between *MHC-DRB* and *MHC-DOB* loci, suggesting that these loci are not closely linked and likely occupy two different MHC II subregions on the same chromosome—possibly separated by an inversion (Band et al. 1998)—that are able to evolve independently from one another. Since 2001, when Ditchkoff et al. found a positive association between *MHC-DRB* diversity and both body mass and antler size in male white-tailed deer, 15 additional *MHC-DRB* exon 2 alleles have been identified. Therefore, in this study we examined if an association exists between morphology and *MHC-DRB* allelic distance of both males and females in a previously unstudied white-tailed deer population using next-generation sequencing. We also included *MHC-DOB* in our analyses as no studies to date have assessed the role of this MHC locus on vertebrate morphology. Based on previous findings and what is known about *MHC-DRB* and *MHC-DOB* in other species, we hypothesized that *MHC-DRB* allelic distance would influences male morphology but not female morphology, as females should not invest resources

towards costly sexually selected traits (Ditchkoff 2011). Since *MHC-DOB* is a conservative MHC II locus that is not closely linked to *MHC-DRB*, we further hypothesized that there would be no association between *MHC-DOB* and morphology in both male and female white-tailed deer.

Methods

Study area

This study took place at the Auburn Captive Facility (ACF) located north of Camp Hill, Alabama, USA. The facility was part of the Piedmont Agricultural Experiment Station, which was owned by Auburn University. Deer sampled during the study were enclosed in a 174-hectare area surrounded by a 2.6-m-high fence, which was constructed in October 2007. The deer present within the ACF during the study included the original deer that inhabited this area during fence installation in 2007 and their subsequent offspring. The population size and effective population size of the adult, founding population (initial population) were 71 and 64.8, respectively. Effective population size was calculated as $N_e = 4N_mN_f / (N_m + N_f)$, where N_m is the number of breeding males ($n = 25$) and N_f is the number of breeding females ($n = 46$) in the population (Wright 1938). Subsequent to fencing the area, deer were neither introduced nor hunted within the ACF. Instead, population size was mainly regulated via natural mortalities and planned releases of deer outside the facility (Newbolt et al. 2017). Population size varied annually between 70 and 120 deer (Newbolt et al. 2017). Deer had access to supplemental feed in the form of food plots, corn feeders, and ad libitum protein feeders. A creek and its tributaries were present on the property, which provided a reliable water source year-round.

Animal handling

Adult white-tailed deer (≥ 6 months of age) were captured over 12 trapping seasons (October–July each year) from 2007 to 2018 via chemical immobilization. A tranquilizer mixture was administered into the deer's hindquarter muscle with the use of a cartridge fired dart gun (Pneu-Dart model 193) and 0.22 caliber blanks. The mixture was prepared by adding 4 cc of xylaxine (100 mg/ml; Lloyd Laboratories, Shenandoah, IA) to a 5 mL vial of Telazol® (100 mg/ml; Fort Dodge Animal Health, Fort Dodge, IA; Miller et al. 2003). We then added 2 cc of this tranquilizer mixture into a telemetry dart (2.0 cc, type C, Pneu-Dart Inc., Williamsport, PA) containing a radio transmitter (Advanced Telemetry Systems, Inc., Isanti, MN). The transmitter enabled us to locate the sedated deer via radio telemetry as the dart stayed attached to the deer's hindquarter after impact (Kilpatrick et al. 1996). Sedation was reversed by injecting Tolazine (100 mg/ml; Lloyd Laboratories) into the shoulder and hindquarter muscles once data collection was complete (Miller et al. 2004). Additionally, newborn fawns were sampled in the summer of 2010 using Vaginal Implant Transmitters (Neuman et al. 2016). These methods were approved by the Auburn University Institutional Animal Care and Use Committee (2008-1417, 2008-1421, 2010-1785, 2011-1971, 2013-2372, 2014-2521, 2016-2964, and 2016-2985) and in compliance with the American Society of Mammalogists' guidelines (Sikes and Gannon 2011).

All darted deer received a unique 3-digit identification number at initial capture, which was displayed on ear tags. For each individual, we recorded sex, age (tooth replacement

and wear aging technique; Severinghaus 1949), and several body measurements (total body length, hind foot length, chest circumference; Ditchkoff et al. 2001; Newbolt et al. 2017). We also took several antler measurements for males (beam and tine lengths, antler beam circumference, inside spread) to calculate their annual gross Boone and Crocket score (a combined score consisting of the lengths of all tines, main beams, circumferences of the main beams between successive antler points, and inside spread; Nesbitt et al. 2009; Strickland et al. 2013). Lastly, a 1-cm^2 notch of tissue was removed from their ear for genetic analysis. This tissue sample was then stored in a − 80 °C freezer until DNA analysis could be performed in the laboratory.

To estimate abundance and age structure of our white-tailed deer population, images of marked and unmarked deer were collected using infrared-triggered cameras at both feeders and randomly selected sites baited with corn for 14 days every February. These images were then used to calculate deer abundance using mark-recapture methods (Overton 1969; Jacobson et al. 1997). We supplemented these data with field observations and capture/mortality records to determine final population demographic estimates.

Genetic analysis

Ivy-Israel et al. (2020) used the ear tissue samples collected from the ACF population to sequence the *MHC-DRB* exon 2 (n = 373) and *MHC-DOB* exon 2 (n = 380) amplicons on the Illumina MiSeq platform (Genbank accession numbers: MK952679-MK952701). The characterization of these alleles in the focal population was described in detail by Ivy-Israel et al. (2020), and in brief here. While Ivy-Israel et al. (2020) only targeted exon 2 for *MHC-DRB* (250 bp), the *MHC-DOB* amplicon contained exon 2 plus noncoding regions around it. We used the extended *MHC-DOB* sequence (360 bp) when analyzing nucleotide sequences and *MHC-DOB* exon 2 (270 bp) for the amino acid sequences.

For each individual, the pairwise genetic distance between the alleles at a locus (*MHC-DRB* and *MHC-DOB*) was calculated as the number of differences at either the nucleotide level (DRB_nuc and DOB_nuc, respectively) or the amino acid level (DRB_aa and DOB_aa, respectively). We used nucleotide and amino acid distances between the two alleles at a locus as proxies for MHC diversity/heterozygosity. Once sequenced, distance matrices were generated via Geneious (v11.1.5).

Statistical analysis

Data processing

Ruminants that form tending bonds, such as white-tailed deer, display great sexual-size dimorphism (Weckerly 1998). We therefore analyzed female and male body size separately. As male fawns did not have antlers, we excluded this age group from our antler size analyses. We therefore analyzed three separate dependent variables: male body size (n = 366), male antler size (n = 313), and female body size (n = 183).

The average age of adult males (≥ 6 months) present in the population was calculated for each sampling season to account for observed changes in population demographics (Newbolt et al. 2017). Average annual male age is highly correlated with other demographic parameters (i.e., deer density and adult sex ratio; Newbolt et al. 2017), which are known to be associated with body size via resulting competition for mates, resources, and mating costs (Emlen and Oring 1977; Kokko and Rankin 2006; Dreiss et al. 2010). We therefore

included the average annual male age in several a priori non-linear models to also account for these population demographic parameters along with individual age (see section on 'Nonlinear age models' below). Since standardization improves the convergence of complicated linear models, we standardized average annual male age, individual age, body size, antler size, *MHC-DRB* nucleotide distance, *MHC-DRB* amino acid distance, *MHC-DOB* nucleotide distance, and *MHC-DOB* amino acid distance prior to analysis (i.e., subtracted mean and divided by standard deviation).

All analyses were conducted in R (v3.6.0; R Core Team, 2019). We performed a principal component analysis (PCA) of the 3 standardized body measurements to generate a single term (first principal component) for annual body size (princomp function) as described by Newbolt et al. (2017). Gross Boone and Crocket antler scores were used to represent an individual's annual antler size. Collinearity was assessed for all independent variables by calculating variance inflation factors (VIFs). We only found collinearity between the nucleotide and amino acid sequences for *MHC-DRB* exon 2 [VIF scores for DRB_nuc and DRB_aa: 37.96 and 37.84 (male body size dataset); 38.98 and 38.74 (antler size dataset); 32.81 and 32.86 (female body size dataset)], as all other independent variables had VIF scores < 1.40 among the three datasets.

Allelic distance comparison for males and females

We examined whether *MHC-DRB* or *MHC-DOB* allelic frequencies differed between the males (n = 156) and females (n = 134) in our population. We also assessed if the average nucleotide and/or amino acid distances for *MHC-DRB* and *MHC-DOB* differed between the sexes via unpaired t-tests (lm function).

Nonlinear age models

We accounted for the strong effect of age on body and antler size using non-linear models (nls function). Mammalian growth is typically asymptotic, thereby making sigmoid growth functions more realistic (Leberg et al. 1989). Popular growth models include the Von Bertalanffy asymptotic growth, Logistic, and Gompertz models (Zullinger et al. 1984; Lesage et al. 2001; Canaza-Cayo et al. 2015; Thalmann et al. 2015; Table 1). There are three growth curve parameters for each of these curves: A, the asymptotic mature body size or antler size; B, the parameter that influences the proportion of asymptotic size achieved at birth; and k, the parameter that influences the maturation rate or how fast individuals approach maximum size. The Von Bertalanffy growth model (VBGM) for body length data is often cubed for weight data. As we were using principal component scores for body size, we considered both the regular VBGM and the cubed VBGM in our set of a priori models. We also considered variations of these models by incorporating average annual buck age (α; capture changes in population demographics over time) into the non-linear model's term for the proportion of asymptotic size achieved at birth (M), the asymptote (N), the growth rate (Z), or a combination of these terms (Table 1). A total of 32 a priori non-linear models were generated for male body size, male antler size, and female body size each.

The Akaike's Information Criterion adjusted for sample size (AIC_c; package bbmle; Bolker 2017) was used to select our most competitive non-linear models for the male body size, male antler size, and female body size datasets. We closely examined all models that were within 2 AICc units of the top-supported model to assess the presence of uninformative parameters (Arnold 2010). If uninformative variables were identified in our growth

Table 1 a priori growth models used to account for the effect of age on body and antler size, where y_{ij} is the observed principal component score for body size of individual i (i = 1,…,n) at measurement time j (j = 1,…,n_i) for animal i, t_{ij} is the age of animal i (years) at time j, and ε_{ij} is the random residual term. There are three growth curve parameters: A, the asymptotic mature body size (asymptote); B, the proportion of asymptotic body size attained at birth (size proportion); and k, the maturation rate or how fast individuals approach adult weight (growth rate). We considered variations of the original growth models by incorporating average annual buck age (α) into the non-linear model's term for the proportion of asymptotic size achieved at birth (M), the asymptote (N), the growth rate (Z), or a combination of these terms

Model	Formula	References
Von Bertalanffy (length)	$y_{ij} = A_i\left(1 - B_i e^{-k_i t_{ij}}\right) + \varepsilon_{ij}$	Von Bertalanffy (1938)
With average annual buck age in size proportion	$y_{ij} = A_i\left[1 - (B_i + M_i\alpha_j)e^{-k_i t_{ij}}\right] + \varepsilon_{ij}$	
With average annual buck age in asymptote	$y_{ij} = (A_i + N_i\alpha_j)\left(1 - B_i e^{-k_i t_{ij}}\right) + \varepsilon_{ij}$	
With average annual buck age in growth rate	$y_{ij} = A_i\left(1 - B_i e^{-(k_i + Z_i\alpha_j)t_{ij}}\right) + \varepsilon_{ij}$	
With average annual buck age in size proportion and asymptote	$y_{ij} = (A_i + N_i\alpha_j)\left[1 - (B_i + M_i\alpha_j)e^{-k_i t_{ij}}\right] + \varepsilon_{ij}$	
With average annual buck age in size proportion and growth rate	$y_{ij} = A_i\left[1 - (B_i + M_i\alpha_j)e^{-(k_i + Z_i\alpha_j)t_{ij}}\right] + \varepsilon_{ij}$	
With average annual buck age in asymptote and growth rate	$y_{ij} = (A_i + N_i\alpha_j)\left(1 - B_i e^{-(k_i + Z_i\alpha_j)t_{ij}}\right) + \varepsilon_{ij}$	
With average annual buck age in size proportion, asymptote and growth rate	$y_{ij} = (A_i + N_i\alpha_j)\left[1 - (B_i + M_i\alpha_j)e^{-(k_i + Z_i\alpha_j)t_{ij}}\right] + \varepsilon_{ij}$	
Von Bertalanffy (weight)	$y_{ij} = A_i\left(1 - B_i e^{-k_i t_{ij}}\right)^3 + \varepsilon_{ij}$	Von Bertalanffy (1957)
With average annual buck age in size proportion	$y_{ij} = A_i\left[1 - B_i(B_i + M_i\alpha_j)e^{-k_i t_{ij}}\right]^3 + \varepsilon_{ij}$	
With average annual buck age in asymptote	$y_{ij} = (A_i + N_i\alpha_j)\left(1 - B_i e^{-k_i t_{ij}}\right)^3 + \varepsilon_{ij}$	
With average annual buck age in growth rate	$y_{ij} = A_i\left(1 - B_i e^{-(k_i + Z_i\alpha_j)t_{ij}}\right)^3 + \varepsilon_{ij}$	
With average annual buck age in size proportion and asymptote	$y_{ij} = (A_i + N_i\alpha_j)\left[1 - (B_i + M_i\alpha_j)e^{-k_i t_{ij}}\right]^3 + \varepsilon_{ij}$	
With average annual buck age in size proportion and growth rate	$y_{ij} = A_i\left[1 - B_i(B_i + M_i\alpha_j)e^{-(k_i + Z_i\alpha_j)t_{ij}}\right]^3 + \varepsilon_{ij}$	
With average annual buck age in asymptote and growth rate	$y_{ij} = (A_i + N_i\alpha_j)\left(1 - B_i e^{-(k_i + Z_i\alpha_j)t_{ij}}\right)^3 + \varepsilon_{ij}$	
with average annual buck age in size proportion, asymptote and growth rate	$y_{ij} = (A_i + N_i\alpha_j)\left[1 - (B_i + M_i\alpha_j)e^{-(k_i + Z_i\alpha_j)t_{ij}}\right]^3 + \varepsilon_{ij}$	

Table 1 (continued)

Model	Formula	References
Gompertz	$y_{ij} = A_i e^{-B_i e^{-k_i t_{ij}}} + \varepsilon_{ij}$	Laird (1965)
With average annual buck age in size proportion	$y_{ij} = A_i e^{-(B_i + M_i \alpha_j) e^{-k_i t_{ij}}} + \varepsilon_{ij}$	
With average annual buck age in asymptote with average annual buck age in growth rate	$y_{ij} = (A_i + N_i \alpha_j) e^{-B_i e^{-k_i t_{ij}}} + \varepsilon_{ij}$ $y_{ij} = A_i e^{-B_i e^{-(k_i + Z_i \alpha_j) t_{ij}}} + \varepsilon_{ij}$	
With average annual buck age in size proportion and asymptote With average annual buck age in size proportion and growth rate With average annual buck age in asymptote and growth rate With average annual buck age in size proportion, asymptote and growth rate	$y_{ij} = (A_i + N_i \alpha_j) e^{-(B_i + M_i \alpha_j) e^{-k_i t_{ij}}} + \varepsilon_{ij}$ $y_{ij} = A_i e^{-(B_i + M_i \alpha_j) e^{-(k_i + Z_i \alpha_j) t_{ij}}} + \varepsilon_{ij}$ $y_{ij} = (A_i + N_i \alpha_j) e^{-B_i e^{-(k_i + Z_i \alpha_j) t_{ij}}} + \varepsilon_{ij}$ $y_{ij} = (A_i + N_i \alpha_j) e^{-(B_i + M_i \alpha_j) e^{-(k_i + Z_i \alpha_j) t_{ij}}} + \varepsilon_{ij}$	
Logistic	$y_{ij} = A_i / \left(1 + B_i e^{-k_i t_{ij}}\right) + \varepsilon_{ij}$	Nelder (1961)
With average annual buck age in size proportion	$y_{ij} = A_i / \left[1 + (B_i + M_i \alpha_j) e^{-k_i t_{ij}}\right] + \varepsilon_{ij}$	
With average annual buck age in asymptote With average annual buck age in growth rate	$y_{ij} = (A_i + N_i \alpha_j) / \left(1 + B_i e^{-k_i t_{ij}}\right) + \varepsilon_{ij}$ $y_{ij} = A_i / \left(1 + B_i e^{-(k_i + Z_i \alpha_j) t_{ij}}\right) + \varepsilon_{ij}$	
with average annual buck age in size proportion and asymptote With average annual buck age in size proportion and growth rate With average annual buck age in asymptote and growth rate with average annual buck age in size proportion, asymptote and growth rate	$y_{ij} = (A_i + N_i \alpha_j) / \left[1 + (B_i + M_i \alpha_j) e^{-k_i t_{ij}}\right] + \varepsilon_{ij}$ $y_{ij} = A_i / \left[1 + (B_i + M_i \alpha_j) e^{-(k_i + Z_i \alpha_j) t_{ij}}\right] + \varepsilon_{ij}$ $y_{ij} = (A_i + N_i \alpha_j) / \left(1 + B_i e^{-(k_i + Z_i \alpha_j) t_{ij}}\right) + \varepsilon_{ij}$ $y_{ij} = (A_i + N_i \alpha_j) / \left[1 + (B_i + M_i \alpha_j) e^{-(k_i + Z_i \alpha_j) t_{ij}}\right] + \varepsilon_{ij}$	

curve models, we re-examined model weights for models without these uninformative variables. We examined the need to include a term for autocorrelation (moving average) in our top models via partial-likelihood ratio tests (King 1989) as some individuals were captured multiple times in their lifetime.

Residual analysis with MHC variables

Residuals from our top non-linear models were used in analyses to examine if MHC variables could explain the remaining variation in body and antler size variables after accounting for age. Analyses were performed using linear mixed-effects models with package nlme (lme function; Pinheiro et al. 2018). The support for including non-linear (quadratic) effects for our predictors in our models was evaluated via partial-likelihood ratio tests (King 1989). All models included a random term for individual as some individuals were captured more than once in their lifetime. To aid in model interpretations, we generated estimates of average body/antler size residuals from our statistical models at varying levels of MHC diversity.

Specific MHC alleles

Ivy-Israel et al. (2020) reported that the frequencies of several *MHC-DRB* alleles were changing in the population over time. Specifically, while the DRB*10 allele increased over time, DRB*01 decreased over time in our population. Since morphology can influence an individual's reproductive success (Geist 1966; Clutton-Brock 1988; Rose 1995; Pelabon et al. 1999; McElligott et al. 2001; Mysterud et al. 2004; Johnson et al. 2007), we examined if the allelic frequency trends found for DRB*01 and DRB*10 were driven by differential morphology among individuals with these alleles. We used mixed-effects models (lme function) with residuals from our top non-linear models as the dependent variable and a categorical variable for the frequency of each specific allele in the individual (i.e., 'none,' 'one,' or 'two') as independent variables. A random term for individual was also included in these models.

Results

Allelic distance comparison for males and females

There were no statistically significant differences in MHC allelic distances between males and females for DRB_nuc (difference in standardized distances $\pm$ SE $= 0.150 \pm 0.118$, $p = 0.204$), DRB_aa (difference in standardized distances $\pm$ SE $= 0.095 \pm 0.118$, $p = 0.421$), DOB_nuc (difference in standardized distances $\pm$ SE $= -0.196 \pm 0.118$, $p = 0.097$), or DOB_aa (difference in standardized distances $\pm$ SE $= -0.107 \pm 0.118$, $p = 0.366$). Females had a greater number of unique *MHC-DRB* alleles (19 alleles) compared to males (17 alleles), though the two sexes shared the same most common alleles (DRB*10, DRB*14, DRB*20). While females had a greater range of possible allelic distance values for DOB_nuc, males had more unique extended *MHC-DOB* sequence alleles (11 alleles) than females (10 alleles). DOB*08 was the most common extended *MHC-DOB* allele for both sexes, though the order of remaining allele frequencies differed slightly.

Male body size

Our male body size dataset contained 156 males for a total of 366 entries (Table S1). Ages ranged from 0 to 12.5 years with an average of 3.5 years. The most frequently captured male was measured nine times. Among the males, 21 were homozygous for *MHC-DRB* and 135 were heterozygous for *MHC-DRB* at both the nucleotide and amino acid level. *MHC-DRB* allelic distances ranged from 0 to 46 at the nucleotide level (mean ± SE = 24.6 ± 0.7), and from 0 to 27 for translated *MHC-DRB* amino acid sequences (mean ± SE = 15.7 ± 0.5). While allelic distances were fairly large for the extended *MHC-DOB* nucleotide sequences (33 homozygotes, 123 heterozygotes), the majority of males were homozygous for translated *MHC-DOB* exon 2 sequences (98 homozygotes, 58 heterozygotes). *MHC-DOB* allelic distances ranged from 0 to 4 at the nucleotide level (extended *MHC-DOB* sequence; mean ± SE = 1.62 ± 0.06), and from 0 to 2 at the amino acid level (*MHC-DOB* exon 2; mean ± SE = 0.37 ± 0.03).

Principal component analysis

The first principal component explained 87.90% of the variation in our three body measurements. Each measurement contributed equally to the first principal component: 0.58 (chest), 0.59 (body length), 0.56 (hind foot). Scores ranged from − 7.66 (newborn fawn) to 2.18 (6.5-year-old male).

Nonlinear age model selection

The top model was the regular (i.e., not cubed) VBGM with mean male age in the terms for the proportion of asymptotic size achieved at birth and growth rate (Table S2; Fig. 1a). While the second-best model for male body size did have $\Delta\text{AICc} \leq 2$, the additional parameter (mean age in the asymptote) did not provide a net reduction in AICc and was therefore deemed uninformative (Arnold 2010). When we re-examined model weights for models without uninformative parameters, we found that the new weight for the top model was 1.0. A partial-likelihood ratio test between the top model and the same model with a term for autocorrelation indicated that accounting for autocorrelation in our model significantly improved the fit to the data ($\chi^2 = 23.19$; df = 1; $p < 0.001$).

Residual analysis with MHC variables

The model estimates of male body size residuals tended to increase from − 0.02 (± 0.73; 95% CI) at a small *MHC-DRB* amino acid distance (DRB_aa = 1) to 0.17 (± 0.55; 95% CI) at a large *MHC-DRB* amino acid distance (DRB_aa = 27) for translated *MHC-DRB* sequences, though the relationship was not statistically significant ($p = 0.78$; Table 2). Quadratic effects significantly improved model fit for DOB_nuc according to partial-likelihood ratio test results ($\chi^2 = 4.78$; df = 1; $p = 0.03$). When including all MHC variables and the quadratic effect for DOB_nuc in the model, we found that the residuals for male body size were greater for individuals with a moderate *MHC-DOB* nucelotide distance (DOB_nuc = 2) compared to homozygotes and individuals with greater nucleotide distances (DOB_nuc, $p = 0.06$; DOB_nuc^2, $p = 0.03$). Model estimates of male body

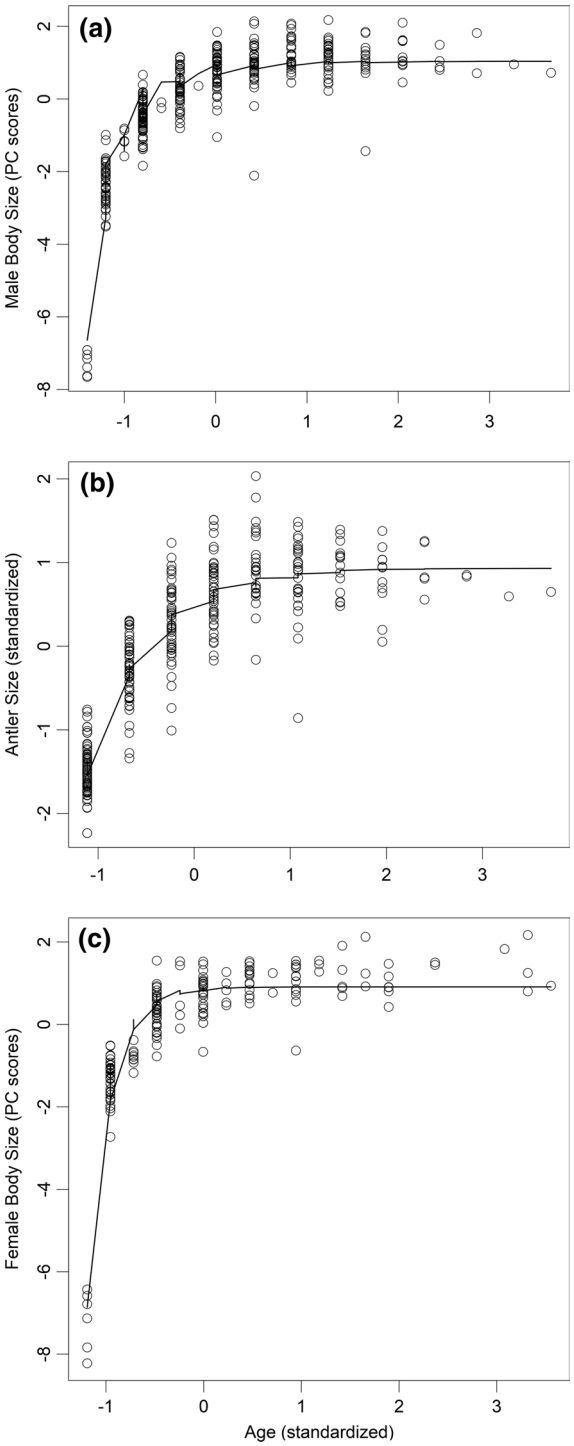

Fig. 1 The Von Bertalanffy (length) model with male mean age in the terms for the proportion of asymptotic size achieved at birth and growth rate was the top model for capturing the relationship between age and (**a**) body size of male white-tailed deer (Table S2), (**b**) antler size of male white-tailed deer (Table S3), and (**c**) body size of female white-tailed deer (Table S6)

Table 2 Residual analysis, using residuals from top growth curve model (Von Bertalanffy with male mean age in the terms for the proportion of asymptotic size achieved at birth and growth rate, Table 1, S2), for examining possible associations between MHC variables and male white-tailed deer body size

Parameter	Value (β)	SE	df	t-value	*p* value
DRB_nuc	−0.038	0.217	206	−0.174	0.862
DRB_aa	0.062	0.217	206	0.285	0.776
DOB_nuc	0.076	0.040	206	1.902	0.059
(DOB_nuc)^2	−0.086	0.039	206	−2.205	0.029
DOB_aa	−0.018	0.041	154	−0.446	0.656

size residuals peaked at 0.10 (±0.10; 95% CI) when DOB_nuc = 2 and then continually decreased to −0.13 (±0.29; 95% CI) at DOB_nuc = 4 (Fig. 2a). However, model estimates of body size residuals were least for homozygous males at −0.19 (±0.16; 95% CI).

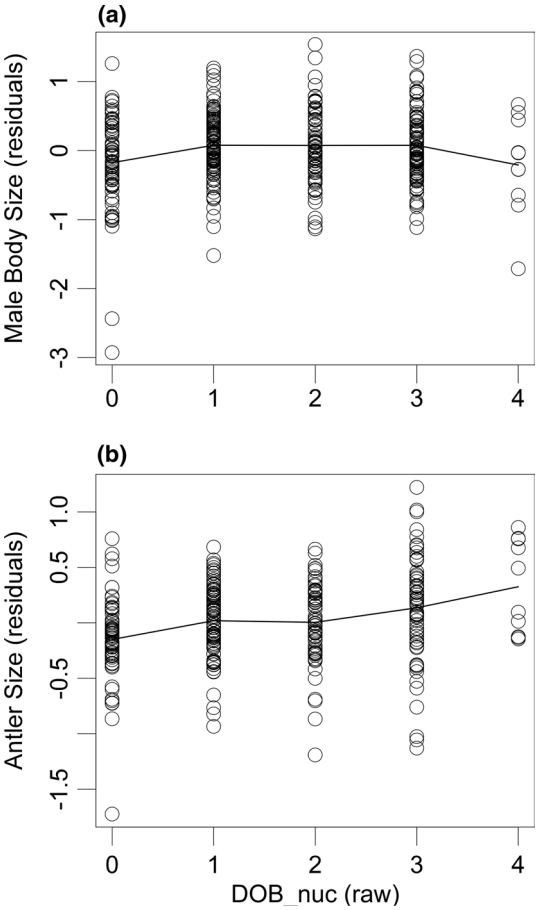

Fig. 2 Relationship between DOB_nuc and the residuals for (**a**) male body size from the model that best explained the effect of age on body size for white-tailed deer (Von Bertalanffy model with male mean age in the terms for the proportion of asymptotic size achieved at birth and growth rate, Table S2), and (**b**) antler size from the model that best explained the effect of age on body size for white-tailed deer (Von Bertalanffy model with male mean age in the terms for the proportion of asymptotic size achieved at birth and growth rate, Table S3). Male body size peaks when DOB_nuc is equal to 2 and then gradually decreases with further increases in DOB_nuc heterozygosity, whereas there is a positive association between antler size and DOB_nuc allelic distance

Antler size

Our antler size dataset contained 124 white-tailed deer for a total of 313 entries (Table S1). Ages ranged from 1.5 to 12.5 years with an average of 4 years, while gross antler scores ranged from 0 (1.5-year-old male) to 168.4 (5.5-year-old male). As with our male body size dataset, the most frequently captured male was measured nine times. Seventeen males were homozygous for *MHC-DRB* and 107 were *MHC-DRB* heterozygotes at both the nucleotide and amino acid level. *MHC-DRB* allelic distances ranged from 0 to 46 at the nucleotide level (mean ± SE = 24.8 ± 1.3) and from 0 to 27 for translated *MHC-DRB* sequences (mean ± SE = 15.8 ± 0.8). As with our male body size dataset, the majority of individuals were homozygous for translated *MHC-DOB* exon 2 (78 homozygotes, 46 heterozygotes) while allelic distances were greater at the extended *MHC-DOB* nucleotide sequences (24 homozygotes, 100 heterozygotes). *MHC-DOB* allelic distances ranged from 0 to 4 at the nucleotide level (extended *MHC-DOB* sequence; mean ± SE = 1.7 ± 0.1) and from 0 to 2 (*MHC-DOB* exon 2; mean ± SE = 0.4 ± 0.05) at the amino acid level.

Nonlinear age model selection

The top model (ΔAICc = 0) for male antler size was the regular (i.e., not cubed) VBGM with mean male age in the terms for the proportion of asymptotic size achieved at birth and growth rate (Table S3; Fig. 1b). However, another competitive model was the regular VBGM without mean age as its ΔAICc ≤ 2 (Arnold 2010). The weights of the top two models were 0.558 and 0.232, respectively, after excluding models with uninformative parameters (Table S3). A partial-likelihood ratio test between the top model and the same model with a term for autocorrelation indicated that accounting for autocorrelation in our model significantly improved the fit to the data ($\chi^2 = 84.86$; df = 1; $p < 0.001$).

Residual analysis with MHC variables

As the top model had more than double the weight of the second-best model, here we report the results of our residual analysis of MHC variables using the top model. No quadratic effects were needed for MHC variables when assessing antler size residuals (DRB_nuc: $\chi^2 = 0.63$, df = 1, $p = 0.43$; DRB_aa: $\chi^2 = 0.11$, df = 1, $p = 0.74$; DOB_nuc: $\chi^2 = 0.01$, df = 1, $p = 0.91$; DOB_aa: $\chi^2 = 0.13$, df = 1, $p = 0.72$). As with male body size, no significant associations were found between antler size residuals and *MHC-DRB* amino acid or nucleotide distances (Table 3). However, the effect size estimates for DRB_nuc were considerable, where model estimates of antler size residuals increased from − 0.31 (± 0.60;

Table 3 Residual analysis, using residuals from top growth curve model (Von Bertalanffy with male mean age in the terms for the proportion of asymptotic size achieved at birth and growth rate, Table 1, S3), for examining possible associations between MHC variables and male white-tailed deer antler size

Parameter	Value (β)	SE	df	t-value	*p* value
DRB_nuc	0.193	0.189	120	1.022	0.309
DRB_aa	− 0.162	0.187	120	− 0.864	0.390
DOB_nuc	0.083	0.034	120	2.447	0.016
DOB_aa	− 0.034	0.033	188	− 1.021	0.309

95% CI) at a small *MHC-DRB* nucleotide distance (DRB_nuc = 2) to 0.29 (± 0.56; 95% CI) at a large *MHC-DRB* nucleotide distance (DRB_nuc = 46; $p = 0.31$). We did find a positive association between DOB_nuc and antler size residuals ($p = 0.02$), where model estimates of antler size residuals increased from − 0.11 (± 0.11; 95% CI) for homozygous males (DOB_nuc = 0) to − 0.04 (± 0.07; 95% CI) at a small *MHC-DOB* nucleotide distance (DOB_nuc = 1) to 0.18 (± 0.15; 95% CI) at a large *MHC-DOB* nucleotide distance (DOB_nuc = 4; Fig. 2b). The residual analysis results were similar when using residuals from the second model (Table S4).

Female body size

Our female body size dataset contained 134 white-tailed deer females for a total of 183 entries (Table S5). Ages ranged from 0 to 10.5 years with an average of 2.5 years. The most frequently captured female was measured four times. Thirteen females were homozygous for *MHC-DRB* and 121 were heterozygous for *MHC-DRB* at both the nucleotide and amino acid level. *MHC-DRB* allelic distances ranged from 0 to 44 at the nucleotide level (mean ± SE = 22.6 ± 3.0) and from 0 to 27 for translated *MHC-DRB* sequences (mean ± SE = 14.9 ± 2.0). Less than a quarter of individuals were homozygous for the extended *MHC-DOB* nucleotide sequences (22 homozygotes, 112 heterozygotes), while the majority of individuals were homozygous for the translated *MHC-DOB* exon 2 sequences (78 homozygotes, 56 heterozygotes). *MHC-DOB* allelic distances ranged from 0 to 5 at the nucleotide level (extended *MHC-DOB* sequence; mean ± SE = 2.1 ± 0.2) and from 0 to 2 at the amino acid level (*MHC-DOB* exon 2; mean ± SE = 0.4 ± 0.1).

Principal component analysis

The first principal component explained 93.31% of the variation in our three body measurements. Each measurement contributed equally to the first principal component: 0.58 (chest), 0.58 (body length), 0.57 (hind foot). Scores ranged from − 8.22 (newborn fawn) to 2.17 (9.5-year-old female).

Nonlinear age model selection

The top model (ΔAICc = 0) for female body size was the regular VBGM with mean male age in the terms for the proportion of asymptotic size achieved at birth and growth rate (Table S6; Fig. 1c). The second model had ΔAICc > 2, and the additional parameter did not provide a net reduction in AICc and was therefore deemed uninformative (Arnold 2010). The weight of the top VBG model increased to 0.98 when excluding models with uninformative parameters. A partial-likelihood ratio test between the top model and the same model with a term for autocorrelation indicated that accounting for autocorrelation in our model did not significantly improve the fit to the data ($\chi^2 = 1.47$; df = 1; $p = 0.23$). However, most females were only captured once in their lifetime.

Residual analysis with MHC variables

No quadratic effects were needed for the MHC variables when assessing the residuals for our female body size dataset (DRB_nuc: $\chi^2 = 1.29$, df = 1, $p = 0.26$; DRB_aa: $\chi^2 = 1.25$, df = 1, $p = 0.26$; DOB_nuc: $\chi^2 = 0.01$, df = 1, $p = 0.93$; DOB_aa: $\chi^2 = 2.57$, df = 1, $p = 0.11$).

Unlike male body size, we found no significant association between female body size residuals and the MHC variables (Table 4). Model estimates of female body size residuals only increased from − 0.03 (± 0.94; 95% CI) at a small *MHC-DRB* nucleotide distance (DRB_nuc = 2) to 0.02 (± 0.92; 95% CI) at a large *MHC-DRB* nucleotide distance (DRB_nuc = 44; $p = 0.96$), while model estimates of female body size residuals increased from − 0.02 (± 0.11; 95% CI) at a small *MHC-DOB* nucleotide distance (DOB_nuc = 1) to 0.05 (± 0.26; 95% CI) at a large *MHC-DOB* nucleotide distance (DOB_nuc = 5; $p = 0.70$).

Specific MHC alleles

We found no statistically significant associations between individual alleles and either female body size or male antler size (all $p > 0.05$). For male body size, we found a negative association with DRB*01 ($p = 0.04$) and a positive association with DRB*10 ($p = 0.02$). Specifically, males heterozygous for DRB*01 (n = 51) typically had smaller body sizes (mean male body size residuals ± SE = − 0.17 ± 0.09) compared to males without DRB*01 (n = 308; mean male body size residuals ± SE = 0.06 ± 0.03), and males heterozygous for DRB*10 (n = 128) typically had larger body sizes (mean male body size residuals ± SE = 0.10 ± 0.04) compared to males without DRB*10 (n = 224; mean male body size residuals ± SE = − 0.05 ± 0.04).

Discussion

While previous studies reported an association between *MHC-DRB* diversity and morphology, we did not find similar results. Ditchkoff et al. (2001) found a positive association between *MHC-DRB* diversity and both body mass and antler size in hunter-harvested male white-tailed deer. However, when examining body size, they only found significance for field-dressed body weights and skull length. When analyzing skeletal body measurements, including the body measurements we used here for generating our principal component scores (i.e., body length, chest girth, hind foot length), they also did not find statistical significance. Our results for body size and *MHC-DRB* allelic distances are therefore consistent with Ditchkoff et al. (2001), although we do not have the field-dressed body weights and skull lengths to examine whether a positive association between *MHC-DRB* and body mass would also be found in this study. Antler size, on the other hand, was measured similarly (gross Boone and Crockett scores). Ditchkoff et al. (2001) reported that gross antler scores for heterozygotes were greater than homozygous deer. We found no association between *MHC-DRB* allelic distances (nucleotide and amino acid level) and antler size. This

Table 4 Residual analysis, using residuals from top growth curve model (Von Bertalanffy with male mean age in the terms for the proportion of asymptotic size achieved at birth and growth rate, Table 1, S6), for examining possible associations between MHC variables and female white-tailed deer body size

Parameter	Value (β)	SE	df	t-value	*p* value
DRB_nuc	0.011	0.243	129	0.047	0.963
DRB_aa	− 0.012	0.243	129	− 0.049	0.961
DOB_nuc	0.020	0.051	129	0.389	0.698
DOB_aa	0.007	0.051	129	0.129	0.898

difference in findings may be attributed to our methodological differences. For example, while Ditchkoff et al. (2001) classified individuals as either heterozygotes or homozygotes using the phylogenetic clades determined by Van Den Bussche et al. (1999), we calculated pairwise allelic distances between an individual's *MHC-DRB* alleles based on next generation sequencing (Ivy-Israel et al. 2020). We also included several newly identified *MHC-DRB* alleles in our analyses that were not available in 2001. Standard errors for our *MHC-DRB* variables were quite large, however, which may have also contributed to our lack of significance. Ivy-Israel et al. (2020) reported that the white-tailed deer population sampled in this study was experiencing a heterozygote excess for *MHC-DRB*, and that *MHC-DRB* may be under balancing selection in our population. While the results from Ivy-Israel et al. (2020) suggest that *MHC-DRB* heterozygosity may be selected for in our population, we did not see a significant association between within-individual *MHC-DRB* allelic distance and morphology.

We did find, however, that specific *MHC-DRB* alleles were associated with morphology. Specifically, males that were heterozygous for DRB*01 generally had smaller body size than males without DRB*01, while males heterozygous for DRB*10 had larger body size compared to males without DRB*10. As larger body size is generally associated with greater reproductive success among polygynous males (Clutton-Brock 1988; Pelabon et al. 1999; McElligott et al. 2001; Mysterud et al. 2004; Johnson et al. 2007), these results are consistent with the allele frequency trends reported by Ivy-Israel et al. (2020) for our white-tailed deer population, where DRB*01 had become less frequent in our population over time and DRB*10 had become more frequent in our population over time.

We found a strong association between *MHC-DOB* nucleotide sequences and male body and antler size. Male body size was greatest when the pairwise nucleotide distance between an individual's *MHC-DOB* alleles was at an intermediate level, being equal to 2 from range of 0–4; whereas smaller body sizes were associated with homozygosity and increased pairwise nucleotide distance of *MHC-DOB* alleles. Antler size, on the other hand, had a positive linear association with *MHC-DOB* nucleotide allelic distances, where greater *MHC-DOB* allelic distances were associated with greater antler scores. Both body and antler size are strong determining factors for a male's reproductive success, especially among polygynous species (Geist 1966; Clutton-Brock 1988; Rose 1995; Pelabon et al. 1999; McElligott et al. 2001; Mysterud et al. 2004; Johnson et al. 2007). Indeed, Newbolt et al. (2017), with this same population, found that annual reproductive success of males was positively associated with both male body size and antler size. However, in that study, antler size mainly influenced a male's reproductive success when the population had an older male age structure, possibly due to the increased use of direct intraspecific competition for access to receptive females among males. Newbolt et al. (2017) concluded that body size was a more consistent predictor of reproductive success than antler size in our population as greater body size presented reproductive advantages to both males engaging in direct intraspecific competition for female access and males using alternative tactics, such as sneaking and coursing. Forming tending bonds, regardless of the strategy employed, requires a great amount of endurance for male white-tailed deer, and larger males will have greater energy reserves available for these activities (Hogg 1984; Lindstedt and Boyce 1985). Since larger male body sizes were attained at moderate *MHC-DOB* nucleotide distances, maximum allelic distance at this locus may not be favored in our population. Indeed, Ivy-Israel et al. (2020) found that *MHC-DOB* is under purifying selection in white-tailed deer and reported evidence of a heterozygote deficiency for *MHC-DOB* in our population specifically. Greater *MHC-DOB* allelic distance may be too costly to combine with maintaining a larger body size, as costly immune responses associated with greater MHC diversity can

divert resources away from growth and survival (Klasing et al. 1987; Møller and Saino 1994; Fair et al. 1999; Norris and Evans 2000; Hanssen et al. 2004; Barribeau et al. 2008; Bonato et al. 2009).

While *MHC-DOB* is not closely linked to *MHC-DRB* in white-tailed deer (Ivy-Israel et al. 2020), it is still in linkage disequilibrium with other MHC II genes in that chromosomal subregion that may be driving the observed association between male morphology and nucleotide sequence diversity at *MHC-DOB*. The TAP1 and TAP2 genes, for example, are part of the MHC II subregion with *MHC-DOB* in cattle (Childers et al. 2005). Numerous studies have identified the role of these genes in diseases such as dengue fever (Soundravally and Hoti 2008), sarcoidosis (Foley et al. 1999), multiple sclerosis (Moins-Teisserenc et al. 1995), and celiac disease (Djilali-Saiah et al. 1994) in humans. Therefore, while our results suggest that *MHC-DOB* may be influencing white-tailed deer morphology, it may simply be serving as a marker for another locus that is genetically linked to *MHC-DOB*. The lack of significance for the translated *MHC-DOB* exon 2 sequences, which represents the functional extracellular domain of the *MHC-DOB* protein (Andersson 1994; NCBI 2009), further suggests that another part of the *MHC-DOB* gene or another locus linked to *MHC-DOB* is driving our results. Future work should therefore take a functional genomic approach to clarify which MHC II locus is truly influencing male morphology.

We did not find a significant association between either *MHC-DRB* or *MHC-DOB* and female body size. Among white-tailed deer, adult females, relative to males, differ little physically from one another. Body size typically plateaus when females reach an age of 2–3 years (Ditchkoff 2011). Therefore, we observed very little variation for body size in our female dataset, which may contribute to our lack of significant findings. The majority of studies that searched for associations between MHC II and morphology focused on males. In fact, the evolution of female morphology and ornaments as a whole are poorly understood, especially for species in which intrasexual competition is most intense among males and where females are responsible for all parental care (i.e., polygynous species; Kokko et al. 2006; Clutton-Brock 2007, 2009). Huchard et al. (2010) did find that certain MHC supertypes are associated with poor body condition and less developed sexual signals (size and shape of sexual swellings) in female baboons (*Papio ursinus*), though they did not find an effect of MHC diversity on the sexual swellings in females. A female's MHC diversity can influence her fecundity (Smith et al. 2010; Grogan 2014). For example, Smith et al. (2010) found that heterozygous European brown hares (*Lepus europaeus*) had greater fecundity compared to homozygotes. Females with larger litters have to invest more nutrients towards lactation (Kounig et al. 1988), which can significantly reduce the female's body mass and condition (Parker et al. 1990; Cook et al. 2004) and subsequent fitness and offspring survival (Allaye Chan 1991; Russell et al. 1998; Thaker and Bilkei 2005). Lactating females also divert more of their resources away from parasite defense (Festa-Bianchet 1989), thereby making them more susceptible to pathogens. Given this, future research on female body size and reproductive trade-offs should also include lactation and/or litter size data, especially since MHC II diversity may particularly influence female size of lactating females by governing their immune responses.

An association between MHC II genes and morphology has been reported for several non-ruminant species, such as pheasants (*Phasianus colchicus*; von Schantz et al. 1996, 1997), common yellowthroats (*Geothlypis trichas*; Dunn et al. 2012), baboons (Huchard et al. 2010), neotropical lesser bulldog bats (*Noctilio albiventris*; Schad et al. 2012), and montane water voles (*Arvicola scherman*; Charbonnel et al. 2010). Ruminants, such as the white-tailed deer, have a unique MHC II organization due to a proposed chromosomal inversion that has split this typically linked region into two subregions (*Bos taurus*,

Andersson et al. 1988; *Ovis aries*, Gao et al. 2010; white-tailed deer, Ivy-Israel et al. 2020). As *MHC-DRB* and *MHC-DOB* occupy different MHC II subregions, these loci are evolving independently in ruminants. The synteny of other mammalian species, however, is relatively well-conserved (Wan et al. 2009). The lack of significant linkage disequilibrium seen in the MHC II region of ruminants can enable us to study these two subregions separately, which may highlight where, and why, these studies found a significant association between MHC II and morphology in these non-ruminant species. The majority of studies examining this association in ruminants were primarily focused on the *MHC-DRB* region, as this locus is known for its extreme variability and polymorphism (Mikko and Andersson 1995; Swarbrick et al. 1995; Mikko et al. 1997; Van Den Bussche 1999, 2002; Ditchkoff et al. 2001, 2005; Fernandez-de-Mera et al. 2009; Brambilla et al. 2015, 2018). More research is therefore needed on the other MHC II subregion (i.e., the one containing *MHC-DOB*) to fully capture which MHC II locus, or perhaps loci, is influencing vertebrate morphology.

In this study we examined the potential association between *MHC-DRB* and *MHC-DOB* heterozygosity and morphology in white-tailed deer. While we found no associations for *MHC-DRB*, we found a strong positive association between *MHC-DOB* nucleotide sequences and antler size and a non-linear relationship between *MHC-DOB* nucleotide sequences and male body size. Our results suggest that *MHC-DOB*, or a gene genetically linked to this locus, may influence male morphological characteristics in white-tailed deer. A broader genome approach is needed to reveal which MHC II locus is actually responsible for this association. Future research should examine whether *MHC-DOB* also influences reproductive success of male white-tailed deer as both body and antler size have been found to determine annual reproductive success (Newbolt et al. 2017). Neither *MHC-DRB* nor *MHC-DOB* influenced female body size, even though the average allelic distances of males and females were not significantly different. Morphology of female white-tailed deer may therefore not be dependent on their MHC diversity, though future studies should include female-specific variables that may better explain the slight variations seen in female body size.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10682-021-10108-x.

Acknowledgements We would like to thank the entire team of volunteers who assisted with data collection, especially V. Jackson for helping with the maintenance of the deer facility. We would also like to thank Code Blue Scents, Moultrie Feeders, EBSCO Industries and Record Rack for their support. All applicable international, national, and/or institutional guidelines for the care and use of animals were followed. All procedures performed in studies involving animals were in accordance with the ethical standards of the institution or practice at which the studies were conducted (Auburn University Institutional Animal Care and Use Committee; 2008-1417, 2008-1421, 2010-1785, 2011-1971, 2013-2372, 2014-2521, 2016-2964, and 2016-2985).

Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

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