



**HAL**  
open science

## **Evidence for transmission ratio distortion based on MHC in a sexually monogamous seabird**

Coralie Drack, Maxime Pineaux, Pierrick Blanchard, Léa Ribeiro, Etienne Danchin, Scott A Hatch, Shannon Whelan, Sarah Leclaire

### ► **To cite this version:**

Coralie Drack, Maxime Pineaux, Pierrick Blanchard, Léa Ribeiro, Etienne Danchin, et al.. Evidence for transmission ratio distortion based on MHC in a sexually monogamous seabird. 2025. <hal-05297800>

**HAL Id: hal-05297800**

**<https://hal.science/hal-05297800v1>**

Preprint submitted on 4 Oct 2025

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



HAL Authorization

1 **Evidence for transmission ratio distortion based on MHC in a sexually**  
2 **monogamous seabird**

3 Coralie DRACK<sup>1,\*</sup>, Maxime PINEAUX<sup>1,\*</sup>, Pierrick BLANCHARD<sup>1</sup>, Léa RIBEIRO<sup>1</sup>, Etienne DANCHIN<sup>2,3</sup>, Scott  
4 A HATCH<sup>3</sup>, Shannon WHELAN<sup>3</sup>, Sarah LECLAIRE<sup>1</sup>

5

6 <sup>1</sup>Centre de Recherche sur la Biodiversité et l'Environnement (CRBE, UMR5300), Université de  
7 Toulouse, CNRS, IRD, Toulouse INP, Toulouse, France

8 <sup>2</sup>Centre de Recherches sur la Cognition Animale, Centre de Biologie Intégrative, Université de  
9 Toulouse, CNRS, Toulouse 31400, France

10 <sup>3</sup>Institute for Seabird Research and Conservation, Anchorage, AK 99516, USA

11 \*co-first authors

12 **Abstract**

13

14

## 15 Introduction

16 The genetics of an organism is one of the crucial determinants of its fitness. Sexual selection has  
17 therefore driven the evolution of mechanisms that favor the transmission of good parental genetic  
18 traits to the offspring (Thornhill 1983; Olsson et al. 1996; Firman et al. 2017). Accordingly, numerous  
19 morphological, physiological or behavioral adaptations enable females to bias paternity towards  
20 males carrying good or compatible genes, or males with good genes to outcompete the other males  
21 for mating (Parker 1970; Thornhill 1983; Andersson 1994; Eberhard 1996; Firman et al. 2017).  
22 However, more recent research has suggested that, because each gamete produced by an individual  
23 varies in their genetic pool, selection for genetic traits can not only operate between different  
24 individuals, but also within gametes (Nadeau 2017; Sutter and Immler 2020; Kekäläinen 2022).  
25 Accordingly, a steadily increasing number of genetic studies shows transmission ratio distortion,  
26 which is the preferential (i.e., non-Mendelian) transmission of certain alleles (Huang et al. 2013a;  
27 Friocourt et al. 2023). Mechanisms of transmission ratio distortion include female meiotic drive,  
28 within-ejaculate spermatozoa competition and early embryo lethality (Huang et al. 2013a; Fishman  
29 and McIntosh 2019; Friocourt et al. 2023).

30 The major histocompatibility complex (MHC) has long been proposed as one of the prime  
31 genetic candidates influencing sexual selection (Birkhead and Pizzari 2002; Ziegler et al. 2005; Firman  
32 et al. 2017). The MHC is a group of polymorphic genes that encode for cell-surface proteins that  
33 display antigen peptides to T-cells. The MHC therefore plays critical role in adaptive immunity and  
34 defense against pathogens in vertebrates (Khan et al. 2022). Each MHC molecule can bind a limited  
35 set of antigens (Özer and Lenz 2021), and benefits of single MHC alleles against specific pathogens  
36 have repeatedly been reported (Sepil et al. 2013; Vlček and Štefka 2020; Canal et al. 2024; Ferreira et  
37 al. 2024). As a result, higher MHC diversity (e.g. heterozygosity or divergence) increases the number  
38 of antigens – and thus the number of pathogens - recognized (Pierini and Lenz 2018), and individuals  
39 with higher MHC diversity are thus expected to have increased fitness (Milinski 2006). Although  
40 numerous studies in a range of vertebrate taxa have investigated whether mate choice or between-  
41 ejaculate female cryptic choice favour partners carrying the best or the more compatible MHC alleles  
42 (Kamiya et al. 2014), studies investigating transmission ratio distortion in regard to MHC are rare, and  
43 have yielded mixed results. For instance, while transmission ratio distortion has been detected in  
44 lesser kestrels (*Falco naumanni*), three-spined sticklebacks (*Gasterosteus aculeatus*) and dairy cattle  
45 (Alcaide et al. 2012; Pierini and Lenz 2018; Martin et al. 2022), it received little or no support in Soay  
46 sheep (*Ovis aries*), captive rhesus monkeys (*Macaca mulatta*), and Atlantic salmon (Sterck et al.  
47 2017; Promerová et al. 2017; Huang and Pemberton 2021).

48           Recently, inconsistent findings between studies have been suggested to stem from variations  
49 in the balance between the benefits and costs associated with MHC (Roved et al. 2017; Pineaux et al.  
50 2020; Schubert et al. 2025). For instance, costs associated with higher MHC diversity may relate to  
51 reduced repertoire of T-cell receptors and increased potential for autoimmune disorders (Nowak et  
52 al. 1992; Brown et al. 2024). Within a population, individuals vary on the strength of the immune  
53 response, risks of autoimmune disease, and exposure or susceptibility to each pathogen. For  
54 instance, compared to females, males have increased exposure to parasites, reduced innate  
55 immunity due to elevated testosterone levels, and reduced risks of autoimmune disease (Zuk and  
56 McKean 1996; Rolff 2002; Vincze et al. 2022). Males may thus benefit from higher MHC diversity  
57 more than females (Roved et al. 2017), as observed in great reed warblers (*Acrocephalus*  
58 *arundinaceus*), Alpine chamois (*Rupicapra rupicapra*) and banded mongooses (*Mungos mungos*)  
59 (Schaschl et al. 2012; Roved et al. 2018; Schubert et al. 2025). In addition, given the high intra-locus  
60 polymorphism of the MHC, trade-offs between the transmission of different beneficial MHC alleles  
61 may exist, and may depend on susceptibility or exposure to parasites. While female birds show  
62 higher prevalence of the blood parasite *Haemoproteus* than male birds, they tend to show lower  
63 prevalence of cestodes (Poulin 1996; McCurdy et al. 1998; Valdebenito et al. 2024), suggesting that  
64 males and females may potentially benefit from different MHC alleles. Sex-of-offspring-specific  
65 transmission ratio distortion has been rarely investigated for the MHC (but see Huang and  
66 Pemberton 2021), but it has been shown for other genes in barn owls (*Tyto alba*) (Ducret et al. 2016),  
67 laboratory mice (de la Casa-Esperón et al. 2000) and humans (but see Kasimatis et al. 2021; Lucotte  
68 et al. 2022). Although sex has often been the focus of research investigating variations in MHC  
69 optima within populations, other individual traits may modulate the costs and benefits associated  
70 with MHC. For instance, birth / hatching order, as well as social status and personality (Drent et al.  
71 2003; Ilany et al. 2021), may be associated with variations in immunity and infection risks (Saino et al.  
72 2001; Koolhaas 2008; Habig and Archie 2015). Such variations may lead to intra-locus conflicts that  
73 may be resolved via the evolution of transmission ratio distortion that is specific to the prospective  
74 offspring trait. Interestingly, in laboratory mice, transmission ratio distortion favoring MHC-  
75 heterozygote embryos is detected in virus-infected parents but not in sham-infected parents (Rülicke  
76 et al. 1998).

77           Here, we investigated transmission ratio distortion of MHC-IIB alleles in the black-legged  
78 kittiwake (*Rissa tridactyla*), a genetically monogamous seabird, with no extra-pair copulation  
79 (Helfenstein et al. 2004). In this species, female chicks, especially when hatched in second position  
80 (two eggs is the typical clutch size in the studied population of kittiwakes), suffer from low MHC-IIB  
81 diversity in term of reduced growth rate, tick clearance and survival (Pineaux et al. 2020). Therefore,

82 we tested whether, in contrast to other sex\*hatching-order chicks, female late-hatched chicks had  
83 higher MHC-IIB diversity than expected under random association of gametes. In the studied  
84 population of kittiwakes, higher MHC-IIB diversity of the offspring is related to both the MHC-IIB  
85 dissimilarity between parents (Pineaux et al. 2022) and the MHC-IIB diversity of each parent (sup mat  
86 S1). Therefore, to determine which mechanism may potentially favor increased MHC-IIB diversity, we  
87 also tested whether chicks preferentially carried more MHC-IIB dissimilar maternal and paternal  
88 haplotypes than expected under random association of gametes, and whether they preferentially  
89 inherited the more MHC-IIB diverse paternal or maternal haplotype, in each sex\*hatching-order  
90 category of chicks. In addition, in this population of kittiwakes, one specific MHC-IIB variant (i.e., the  
91 supertype “SUP6”; a supertype being a cluster of functionally similar MHC-IIB alleles) has recently  
92 been shown to confer protection against a sexually-transmitted bacterial infection and to be  
93 associated with increased fitness in breeding females, but not in breeding males (Ribeiro et al. 2025).  
94 We therefore expected non-random transmission of alleles favoring the transmission of SUP6  
95 especially in female offspring. We therefore tested for non-random transmission of SUP6 in each  
96 sex\*hatching-order category of chicks and tested whether this potential preferential transmission  
97 was due to the male or female parent.

98

## 99 **Materials and methods**

### 100 *Study site*

101 The study was carried out in 2006-2023 in a population of black-legged kittiwakes nesting on an  
102 abandoned U.S. Air Force radar tower on Middleton Island (59°26'N, 146°20'W), Gulf of Alaska.  
103 Artificial nest sites created on the upper walls were observed from inside the tower through sliding  
104 one-way windows (Gill et al. 2002). This enabled us to easily capture and monitor breeders. Birds  
105 were individually identified using color and metal bands, and were sexed based on molecular  
106 methods (Merkling et al. 2012) or sex-specific behaviors (copulation and courtship feeding; Jodice et  
107 al. 2000). Nest sites were checked twice daily (9:00 and 18:00) to record laying, hatching and death  
108 events. All eggs were marked with nontoxic waterproof ink within 12h of laying. We focused on  
109 chicks hatched in 2006, 2009-2013, 2016-2018 and 2022-2023, because these chicks were blood  
110 sampled at hatching (in contrast to ca. 25 days-old in the other years), thereby avoiding our results to  
111 be potentially due to post-hatching selection mechanisms (e.g., differential mortality of the chicks  
112 after hatching). We excluded chicks sired by parents that were involved in experiments during the  
113 pre-laying or incubation period, such as food supplementation or use of anti-copulatory devices (Gill  
114 et al. 2002; White et al. 2008). In this population, most females lay two eggs, that hatch in the order

115 of oviposition (hereafter, first- and second-laid eggs are named A- and B-eggs respectively), and one-  
116 egg and three-egg clutches are rare. Because we were interested in potential variations in  
117 transmission ratio distortion according to hatching order, we focused on chicks of two-egg clutches.  
118 In hatchlings, blood was collected by puncturing the metatarsal vein with a 25-gauge needle and  
119 collecting a drop of blood in a heparinized capillary tube. In adults, blood was collected with a 25-  
120 gauge needle and a 1ml syringe from the brachial vein. We collected also tissues of 49 unhatched  
121 embryos which died in the egg at a late stage of incubation. Although these samples can be unique to  
122 test whether transmission ratio distortion is due to late embryo mortality, the low sample size did  
123 not allow us to test specifically for this effect. Chicks and embryos were sexed based on molecular  
124 methods (Merkling et al. 2012).

125

### 126 *MHC analyses*

127 Adult and chick DNA were extracted from blood samples using the Qiagen blood and tissue DNA  
128 extraction kit and the standard protocol. The DNA samples were used to amplify 258 bp fragments  
129 (including primers) of the exon 2 of the black-legged kittiwake MHC class-IIB. MHC-IIB shows usually  
130 stronger signal of positive selection than MHC-IIA (Dearborn et al. 2022). In addition, the second  
131 exon of the MHC IIB gene is often used to characterize the variability of MHC II genes, because it  
132 contains the antigen-binding domain. We used the MHC class-IIB specific primers (forward: 5'  
133 GCACGAGCAGGGTATTTCCA or 5' GCAYGAGCAGGGTATTTCCA and reverse: 5'  
134 GTTCTGCCACACTCACC) (Leclaire et al. 2014), which amplify at least three MHC class-IIB loci.  
135 Samples were sequenced with an Illumina MiSeq platform, using the 2 × 300 bp protocol (Fasteris SA,  
136 Plan-les-Ouates, Switzerland; see (Pineaux et al. 2020, 2023), for a detailed sequencing protocol).  
137 Amplicon sequences were analyzed with ampliSAS, a three-step pipeline that consists of read  
138 demultiplexing, unique sequence clustering, and erroneous sequence filtering (Sebastian et al. 2016).  
139 In AmpliSas, we used the parameters from Pineaux et al. (2023).

140 The MHC haplotype reconstruction for each individual was performed based on the allelic  
141 segregation within families as described in Gaigher et al. (2016). No recombination was detected  
142 between the different MHC-IIB loci. This is in line with the two MHC IIB loci of the reference genome  
143 of the black-legged kittiwake being situated close to each other (i.e., 4870 bp apart; **Sup mat S2**;  
144 Genbank : GCA\_028500815.1) (Sozzoni et al. 2023). Our MHC-IIB dataset includes the individual  
145 which the NCBI reference genomes originated from. Our haplotype reconstruction of this individual  
146 was in line with the maternal and paternal haplotypes published at NCBI (GCF\_028500815.1 and  
147 GCA\_028500815.1). We excluded all families in which the parental or offspring haplotypes could not

148 be reconstructed. The final dataset includes 1016 chicks, corresponding to 652 clutches sired by 428  
149 different pairs (n = 269 female A-chicks, 232 females B-chicks, 259 male A-chicks, 244 male B-chicks,  
150 and eight A-chicks and four B-chicks of unknown sex). Among these chicks, we detected 86 different  
151 haplotypes. Using sequencing coverage as in Gaigher et al. (2016), we found copy number variation.  
152 Most haplotypes had two genes, but 20 % of the haplotypes had one gene (n = 17 haplotypes), while  
153 6 % of the haplotypes had three genes (n = 5 haplotypes).

154 To estimate MHC-IIb diversity and dissimilarity, we focused on the amino acid sequences of  
155 the peptide binding region (Leclaire et al. 2014). As in Pineaux et al. (2023), we estimated MHC-IIb  
156 diversity using two indices: the number of functional alleles and the degree of functional diversity (or  
157 divergence) of alleles across all MHC-IIb loci. We described the chemical binding properties of each  
158 amino acid in the PBR with Sandberg's five physicochemical descriptors (z-descriptors) (Sandberg et  
159 al. 1998). This Sandberg's matrix was used to construct a UPGMA dendrogram of alleles (function  
160 hclust in R), which represents clusters of functionally similar MHC-IIb sequences. The dendrogram  
161 was used as a reference to calculate the functional MHC-IIb diversity of an individual as the minimum  
162 total length of all the branches required to span its MHC-IIb alleles (function treedive in package  
163 vegan) (Petchey and Gaston 2006). The functional diversity and the number of functional alleles were  
164 correlated ( $r = 0.86$ ,  $P < 0.0001$ ). We estimated MHCIIb dissimilarity between the paternal and  
165 maternal haplotypes using also two indices: the functional dissimilarity and the allelic dissimilarity.  
166 The functional dissimilarity was estimated using the tree distance (treedist function in the vegan  
167 package) (Oksanen et al. 2013), which is found by combining sequences in a common dendrogram  
168 and calculating how much of the sum of the branch length is shared and how much is unique. Allelic  
169 dissimilarity was based on a pure shared/non-shared allele basis and was calculated as  $100 \times (1 - (\text{the}$   
170  $\text{number of shared alleles}/\text{the total number of alleles}))$ . 74% of the chicks had maternal and paternal  
171 haplotypes that shared no alleles, and only 4% of the chicks had similar maternal and paternal  
172 haplotypes.

173 The MHC-IIb supertype called SUP6 was defined as in Ribeiro et al. (2025). Briefly, we  
174 performed K-means clustering procedures on the Sandberg's matrix by using the *find.cluster* function  
175 in the *adegenet* R package. The optimal number of clusters was defined by comparing the Bayesian  
176 Information Criterion (BIC) values of different clustering solutions. We detected 16 superotypes. SUP6  
177 comprises nine MHC-IIb alleles, corresponding to three unique amino acid sequences of the PBR.  
178 SUP6 is found in 38 different haplotypes, and is carried by 20% of the chicks.

179

180 *Statistical analyses*

181 In the first analyses, we investigated whether offspring had higher MHC-IIB diversity than  
182 expected under random association of gametes. Then we investigated whether the MHC-IIB  
183 dissimilarity between the paternal and maternal haplotypes was higher than expected, and whether  
184 chicks inherited more frequently the more diverse maternal or paternal haplotype than expected. In  
185 this latter analysis, we tested inheritance from the father and the mother separately. Next, we  
186 examined whether the frequency of SUP6 was over-represented in comparison with random  
187 association of gametes. In this analysis, we excluded chicks whose none of the parents had SUP6 (n =  
188 300 chicks excluded). We also excluded chicks sired by at least one SUP6-homozygous parents  
189 because the probability to carry SUP6 of the simulated offspring (probability = 1) would not differ  
190 from the real data (n = 150 chicks excluded). We also investigated whether the transmission ratio  
191 distortion of SUP6 was mainly due to paternal or maternal transmission by testing whether paternal  
192 or maternal inheritance of SUP6 was different from random expectation. In these latter analyses, we  
193 focused on chicks whose the father or the mother, respectively, was heterozygous for SUP6.

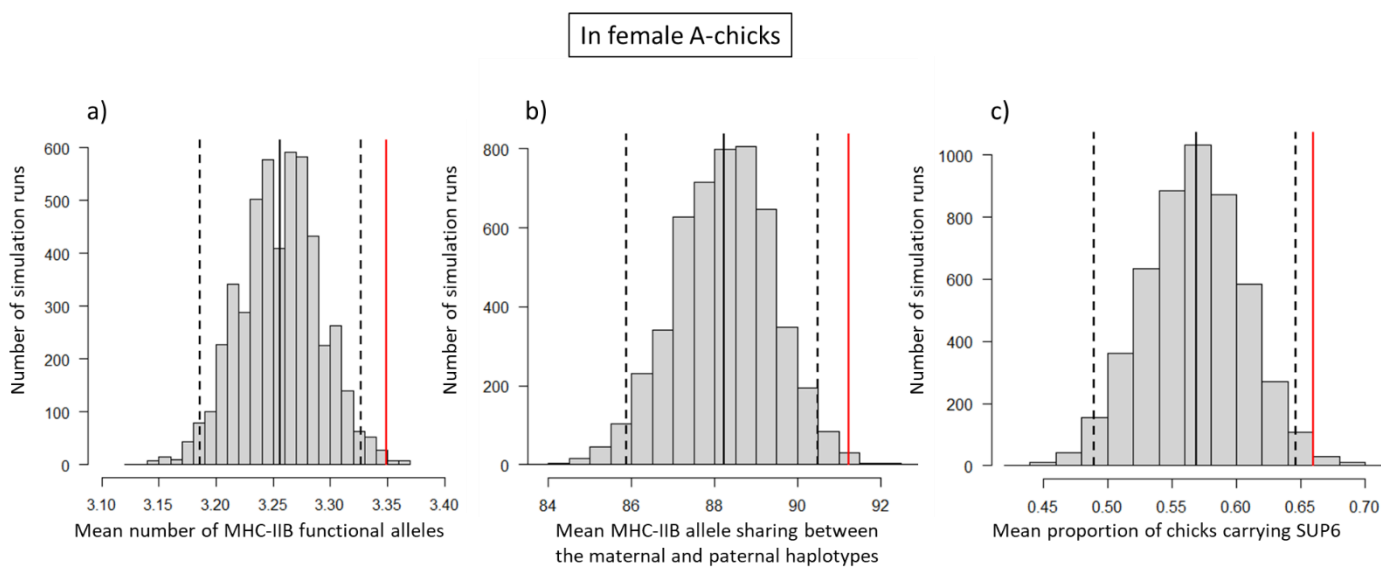
194 In all these analyses, we used Monte Carlo simulations as in Huang and Pemberton (2021).  
195 For each offspring of the dataset, we randomly chose one of the two haplotypes of each of its  
196 parents to create a simulated diplotype. We carried out 5000 simulation runs. Then, we compared  
197 the mean value of the MHC-IIB diplotypes of the real offspring (e.g., mean MHC-IIB diversity, mean  
198 MHC-IIB dissimilarity or mean SUP6 frequency) with the 2.5% and 97.5% tails of the distribution of  
199 the values of the 5000 simulation runs. We carried analyses within the four “sex – hatching order”  
200 categories separately (i.e., female A-chicks, female B-chicks, male A-chicks and male B-chicks). In all  
201 analyses, we excluded offspring sired by two homozygous parents, because the diplotype of the  
202 simulated offspring would not differ from the real data (n = 2 chicks excluded). No offspring were  
203 sired by heterozygous parents with identical MHC-IIB genotype.

204 To determine whether transmission ratio distortion translated into variations in MHC-IIB  
205 diversity or SUP6 frequency between the different sex\*hatching-order categories of chicks, we tested  
206 whether MHC-IIB functional diversity, the number of MHC-IIB functional alleles or SUP6 frequency  
207 varied with sex, hatching order and their two-way interaction. We used linear mixed models with the  
208 *lmer* function in the R package *lme4* when testing functional diversity, cumulative link mixed models  
209 with the *clmm* function in the R package *ordinal* when testing the number of alleles, and generalized  
210 linear mixed models with a binomial distribution of error with the *glmer* function in the R package  
211 *lme4* when testing SUP6 frequency. In all models, we included hatching year and pair identity as  
212 random factors. For these analyses, we also included hatchlings sired by parents that were not  
213 genotyped at MHC-IIB (n = 1270 chicks in total).

214

## 215 Results

216 Female A-chicks had higher MHC-IIb diversity than expected under random association of gametes  
217 (allele number:  $P = 0.010$ , Fig. 1a, and functional divergence:  $P = 0.036$ ;  $n = 269$  chicks). Their two  
218 haplotypes were more dissimilar at MHC-IIb than expected (allele sharing:  $P = 0.008$ , Fig. 1b, and  
219 functional dissimilarity:  $P = 0.029$ ;  $n = 269$  chicks). They did not preferentially inherit the more  
220 diverse haplotype of their father or their mother (functional divergence:  $P = 0.42$ ,  $n = 126$  chicks, and  
221  $P = 0.87$ ,  $n = 157$  chicks, respectively). Female A-chicks had a higher probability to carry SUP6 than  
222 expected under random association of gametes ( $P = 0.016$ ,  $n = 147$  chicks; Fig. 1c).



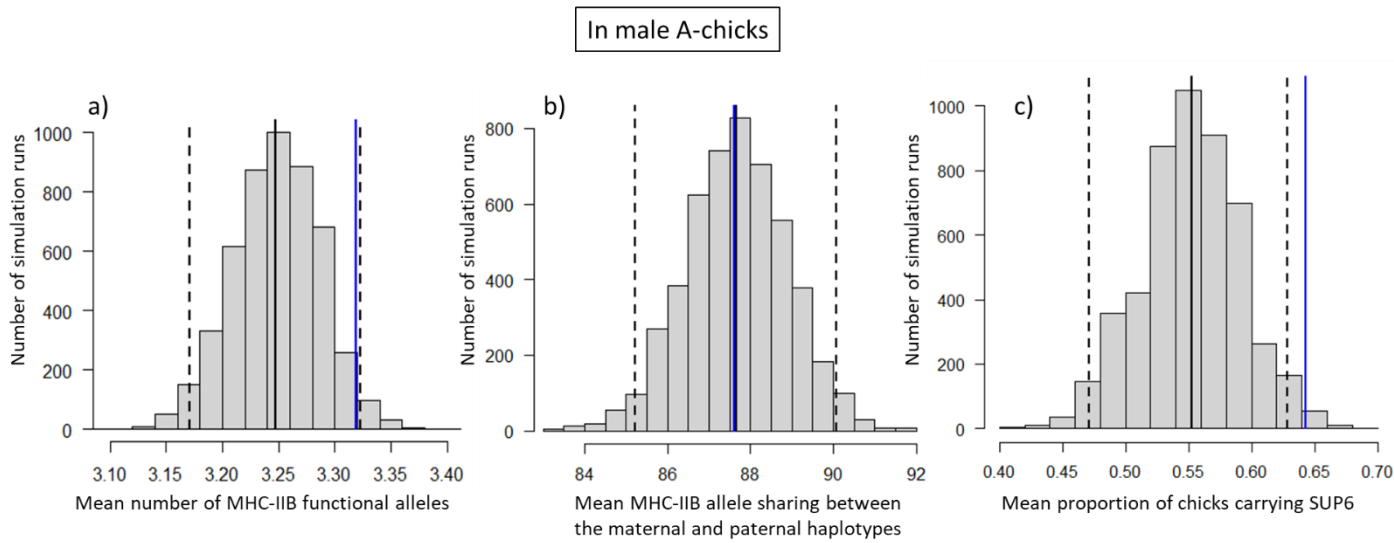
223

224 **Figure 1:** For female A-chicks, (a) mean number of MHC-IIb alleles (i.e., MHC-IIb diversity), (b) mean MHC-IIb  
225 allele sharing (i.e., MHC-IIb dissimilarity) between the two haplotypes, and (c) mean proportion of chicks  
226 carrying the MHC-IIb supertype SUP6. Histograms represent the means of each simulation runs ( $n = 5000$  runs).  
227 The black line represents the mean of the simulated distribution, and the black dashed lines represent the 2.5%  
228 and 97.5% quantiles of the simulated distribution. The red line is the observed mean.

229

230 Male A-chicks tended to have higher MHC-IIb diversity than expected under random  
231 association of gametes when considering the number of alleles ( $P = 0.053$ ,  $n = 257$  chicks; Fig. 2a),  
232 but not when considering functional divergence ( $P = 0.13$ ,  $n = 257$  chicks). In contrast to female A-  
233 chicks, their two haplotypes were not more dissimilar at MHC-IIb than expected (allele sharing:  $P =$   
234  $0.96$ , Fig. 2b, and functional dissimilarity:  $P = 0.72$ ;  $n = 257$  chicks). Male A-chicks did not  
235 preferentially inherit the more diverse haplotype either from their father or from their mother  
236 (functional divergence:  $P = 0.63$ ,  $n = 147$  chicks, and  $P = 0.057$ ,  $n = 141$  chicks, respectively). Similar to

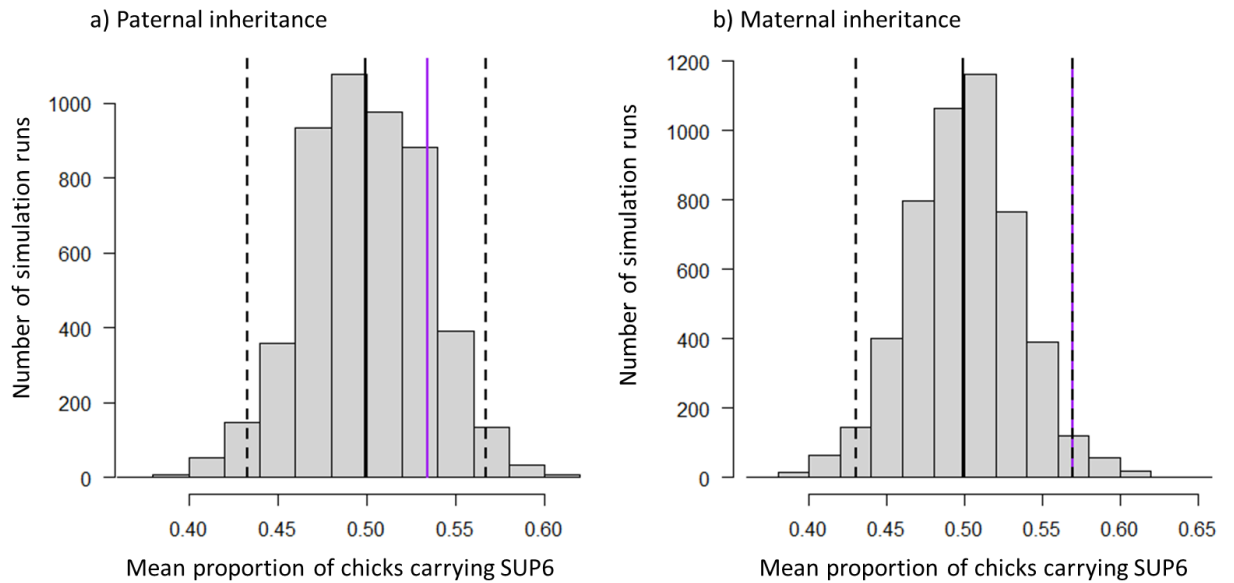
237 female A-chicks, male A-chicks had a higher probability to carry SUP6 than expected under random  
238 association of gametes ( $P = 0.008$ ;  $n = 140$  chicks; Fig. 2c).



239 **Figure 2:** a) Mean number of MHC-IIb alleles (i.e., MHC-IIb diversity) in male A-chicks, b) mean MHC-IIb allele  
240 sharing (i.e., MHC dissimilarity) between the paternal and maternal haplotypes of male A-chicks, and c) mean  
241 proportion of male A-chicks carrying the MHC-IIb supertype SUP6. Histograms represent the result of  
242 simulations. The black line represents the mean of the simulated distribution, and the black dashed lines  
243 represent the 2.5% and 97.5% quantiles of the simulated distribution. The blue line is the observed mean.  
244

245

246 Because both male and female A-chicks showed positive transmission ratio distortion for  
247 SUP6 ( $P = 0.0016$ ,  $n = 292$  A-chicks, when pooling the two sexes), we tested whether this observed  
248 distortion stemmed from maternal or parental inheritance by pooling male and female A-chicks  
249 together, thereby increasing the sample size. We found that the transmission ratio distortion of SUP6  
250 was driven by maternal inheritance ( $P = 0.040$ ;  $n = 193$  chicks; Fig. 3), rather than paternal  
251 inheritance ( $P = 0.28$ ;  $n = 217$  chicks; Fig. 3).

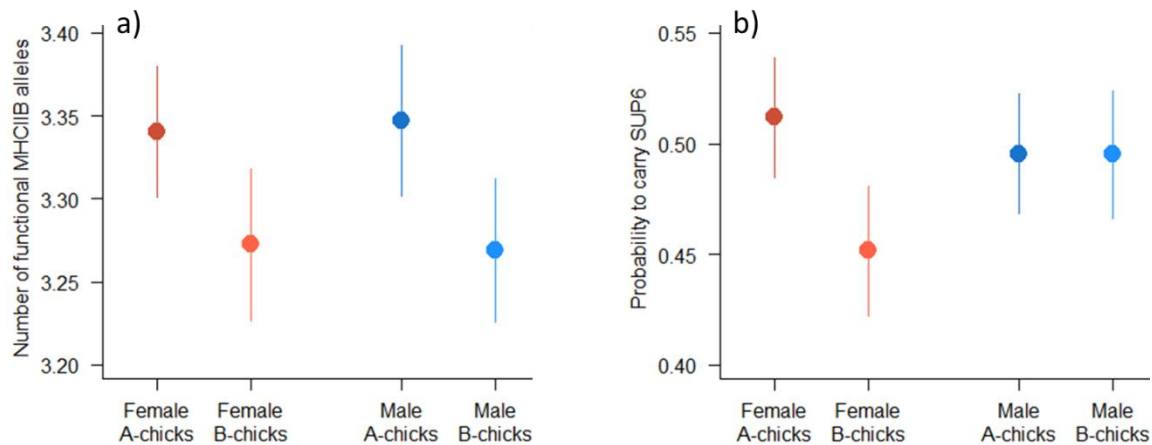


252

253 **Figure 3:** Mean proportion of A-chicks carrying SUP6 a) transmitted by the father and b) transmitted by the  
 254 mother, when considering in a) chicks whose father carried SUP6 and b) chicks whose mother carried SUP6.  
 255 Histograms represent the result of simulations. The black line represents the mean of the simulated  
 256 distribution, and the black dashed lines represent the 2.5% and 97.5% quantiles of the simulated distribution.  
 257 The purple line is the observed mean.

258 Neither female, nor male B-chicks had higher MHC-IIB diversity than expected under random  
 259 association of gametes (functional diversity:  $P = 0.93$  and  $P = 0.91$ , and number of MHC-IIB functional  
 260 alleles:  $P = 0.62$  and  $P = 0.80$ , Fig. S3, in female and male B-chicks respectively;  $n = 232$  female B-  
 261 chicks and  $n = 244$  male B-chicks). They did not have higher probability to carry SUP6 than expected  
 262 (females:  $P = 0.11$ ,  $n = 139$  and males:  $P = 0.43$ ,  $n = 134$  chicks; Fig. S3).

263 In newly-hatched chicks, the number of functional MHC-IIB alleles varied with hatching order  
 264 ( $LR = 5.18$ ,  $P = 0.023$ ; Fig. 4), but not with sex ( $LR = 0.32$ ,  $P = 0.57$ ; Fig. 4) or their two-way interaction  
 265 ( $LR = 0.01$ ,  $P = 0.91$ ). However, neither the probability to carry SUP6 nor the functional diversity  
 266 varies with hatching order ( $\chi^2 = 1.88$ ,  $P = 0.17$  and  $F_{1,643} = 2.65$ ,  $P = 0.10$ ), sex ( $\chi^2 = 1.28$ ,  $P = 0.25$  and  
 267  $F_{1,1180} = 0.41$ ,  $P = 0.52$ ) or their two-way interaction ( $\chi^2 = 1.45$ ,  $P = 0.23$  and  $F_{1,1100} = 0.06$ ,  $P = 0.81$ ,  
 268 respectively).



269

270 **Figure 4:** a) Mean number of MHC-IIB alleles and b) mean frequency of chicks carrying SUP6, in relation to sex  
 271 and hatching-order. Sample sizes are 338 female A-chicks, 290 female B-chicks, 337 male A-chicks and 305  
 272 male B-chicks.

273

## 274 Discussion

275 We found evidence for non-random transmission of alleles according to MHC-IIB genes in the black-  
 276 legged kittiwake, a genetically monogamous seabird. Female A-chicks had higher MHC-IIB diversity  
 277 and a higher probability to carry MHC-IIB dissimilar haplotypes than expected under random  
 278 association of gametes. In addition, both male and female A-chicks had a higher probability to carry  
 279 the MHC-IIB supertype “SUP6” than expected. In contrast, we did not detect non-random  
 280 transmission of alleles according to MHC-IIB genes in B-chicks.

281 We found that female A-chicks have higher MHC-IIB diversity than expected under random  
 282 transmission of alleles, while the MHC-IIB diversity of male chicks did not differ from random  
 283 expectation (albeit it was close to significance in male A-chicks). This result is in line with the fitness  
 284 benefits associated with higher MHC-IIB diversity detected in female chicks but not male chicks in  
 285 kittiwakes (Pineaux et al. 2020). However, in this latter study, the benefits of MHC-IIB diversity were  
 286 measured at the chick stage only (Pineaux et al. 2020). Benefits observed for juvenile performance  
 287 may not be reflected in lifetime fitness. For instance, in Soay sheep (*Ovis aries*), while MHC diversity  
 288 increases juvenile survival, it is not associated with adult lifespan or lifetime breeding success (Huang  
 289 et al. 2022). Further research investigating the benefits of MHC-IIB diversity over the entire individual  
 290 lifetime are needed to determine whether sexual antagonist selection over MHC-IIB diversity may  
 291 have driven the evolution of sex-specific non-random transmission of MHC-IIB alleles. At the  
 292 proximate level, non-random associations of gametes favouring higher MHC-IIB diversity can be due

293 to preferential transmission of gametes carrying the most MHC-IIB diverse parental haplotype or to  
294 preferential association of MHC-IIB dissimilar paternal and maternal gametes. In the present study,  
295 we did not detect the former mechanism but detected the latter in female A-chicks. Similarly, in  
296 three-spined sticklebacks (*Gasterosteus aculeatus*), haplotype-specific fertilization bias toward  
297 gametes with complementary MHC compatibility has been detected (Lenz et al. 2018). In humans,  
298 spermatozoa have higher survival rate in the reproductive tract fluid of MHC-dissimilar women,  
299 suggesting that molecular interactions between sperm and female's reproductive tract may play an  
300 important role in mediating MHC-IIB disassortative fertilization (Jokiniemi et al. 2020; Magris et al.  
301 2021).

302 We found that A-chicks had higher probability to carry the MHC-IIB supertype "SUP6" than  
303 expected under random association of gametes, while no deviation was detected in B-chicks. In  
304 kittiwakes, SUP6 is associated with higher reproductive performance in females, but not in males  
305 (Ribeiro et al. 2025). Because the transmission of an haplotype may trade-off with the transmission  
306 of other beneficial haplotypes, we expected transmission ratio distortion favoring the transmission of  
307 SUP6 in female offspring but not male offspring. However, we did not detect sex-of-offspring specific  
308 transmission ratio distortion, suggesting no fitness cost of carrying SUP6 in males. In contrast, like  
309 for MHC-IIB diversity in females, we detected a clear hatching-order specific non-random  
310 transmission of gametes. The hatching order of an offspring is known to be associated with  
311 difference in offspring size and the hormones, micronutrients and immunofactors deposited by the  
312 females into eggs, leading to variations in behavior, immunity or physiology (Kozłowski and Ricklefs  
313 2010; Hadfield et al. 2013; Stier et al. 2015; Fortuna et al. 2023). These differences can have long-  
314 term effects on survival or reproductive success of the offspring at adulthood (Song et al. 2019;  
315 Bebbington and Groothuis 2023). In kittiwakes, B-chicks are smaller, have higher androgen levels,  
316 lower corticosterone levels, and recruit earlier than A-chicks in our studied population (Gasparini et  
317 al. 2007; Benowitz-Fredericks et al. 2013; Vincenzi et al. 2013; Young et al. 2017). Therefore, it is  
318 possible that the exposure or immune response to parasites varies with hatching order, even on a  
319 long-term, thereby selecting for different optimum in MHC-IIB diversity and MHC-IIB composition  
320 between A- and B-chicks.

321 In kittiwakes, like in various other bird species (e.g., Dearborn et al. 2016; Gaigher et al. 2016;  
322 Winternitz et al. 2023), copy number variation of MHC-IIB genes is observed. In kittiwakes, while  
323 most haplotypes carry two-gene copies, a few of them carries either one or three gene copies. SUP6  
324 is often found in three gene-copy haplotypes, and 98.6% of the chicks who carried a three-gene-  
325 copies haplotype carried SUP6. The presence of SUP6 is therefore associated with higher MHC-IIB  
326 diversity (mean  $\pm$  SE of allele number and divergence in chicks not carrying vs. carrying SUP6:  $2.88 \pm$

327 0.02 vs  $3.72 \pm 0.03$  alleles and  $5.05 \pm 0.05$  vs.  $5.96 \pm 0.04$ , respectively; Kruskal-Wallis test:  $\chi^2_1 =$   
328 402.19,  $P < 0.0001$  and  $\chi^2_1 = 165.76$ ,  $P < 0.0001$ , respectively;  $n = 1136$  chicks) (Ribeiro et al. 2025).  
329 The transmission ratio distortion of SUP6 may therefore be one of the mechanisms favoring higher  
330 MHC-IIB diversity in A-chicks, and might be at the origin of the slight, albeit non-significant, higher  
331 MHC-IIB diversity than expected in male A-chicks.

332 Numerous proximal mechanisms for transmission ratio distortion of alleles have been  
333 suggested (Huang et al. 2013b; Friocourt et al. 2023). They include female meiotic drive, competition  
334 between male or female gametes, and zygote mortality. In the present study, non-random  
335 transmission of SUP6 was detected when SUP6 is inherited from the mother, not from the father.  
336 This result suggests that the observed non-random transmission of SUP6 is not driven by differential  
337 mortality at the embryo stage, or competition among sperm cells based on SUP6. Instead, it may be  
338 due to female meiotic drive, which is the transmission advantage of a certain genetic element during  
339 meiosis (Sandler and Novitski 1957; Srinivasa and Zanders 2020; Knief et al. 2020). It may also be due  
340 to differential atresia of follicles based on SUP6 carried by the oocytes. In mammals, MHC genes are  
341 expressed in the immature oocyte (Doyle et al. 2009), and may thus play a role in the protection from  
342 pathogenic organisms and the modulation of premature ovarian failure. The mechanism driving the  
343 hatching-order specific non-random transmission of SUP6 is also not known. The environment of the  
344 female reproductive tract is likely to vary between the A- and B-eggs, which might therefore  
345 potentially modulate transmission ratio distortion mechanisms. In mice, post-copulatory selection for  
346 MHC heterozygosity has also been shown to be influenced by an external factor, a viral infection  
347 (Rülicke et al. 1998). Clearly, further studies are required to clarify the molecular mechanisms  
348 responsible of the transmission ratio distortion of SUP6 in A-chicks.

349 We found that newly-hatched A-chicks had higher MHC-IIB diversity than newly-hatched B-  
350 chicks. This difference is likely the result of the ratio transmission distortion favoring higher MHC-IIB  
351 diversity in A-chicks observed in the present study. This result contrasts however with the results of  
352 Pineaux et al. (2020), which detected no differences in MHC-IIB diversity between A- and B-chicks at  
353 hatching. The difference between the two studies is due to the inclusion in Pineaux et al. (2020) of  
354 the chick cohorts sampled after hatching (sup mat), and in which chicks may therefore have gone  
355 through post-hatching selection processes, e.g., mortality of B-chicks with low MHC-IIB diversity  
356 (Pineaux et al. 2020). In contrast, while we also detected transmission ratio distortion for SUP6 in A-  
357 chicks, we did not find newly-hatched A-chicks to carry SUP6 more frequently than newly-hatched B-  
358 chicks. First, SUP6 is carried by ca. half of the parents only (i.e., 44% of the mothers and 50% of the  
359 fathers). Selection process favoring transmission of SUP6 can therefore possibly occur only in half of  
360 the chicks, which may result in an apparent low effect size when considering all chicks.

361 In conclusion, we detected evidence for transmission ratio distortion based on MHC-IIB in a  
362 genetically monogamous species. Our results are consistent with the other reproductive strategies  
363 based on MHC-IIB dissimilarity between mates detected in the species, namely mate choice and sex-  
364 allocation (Pineaux et al. 2022; Thel et al. 2025). They add thus evidence to the significant role of  
365 MHC-IIB in sexual selection in kittiwakes. In addition, while post-copulatory selection has been  
366 suggested to be the consequence of females copulating with different males during a single  
367 reproductive cycle, and has therefore been studied intensively in polygamous species (Firman et al.  
368 2017), our results suggest that post-copulatory selection may provide a great evolutionary advantage  
369 in genetically monogamous species also (Otto et al. 2015; Kekäläinen 2022). Finally, the hatching-  
370 order specific transmission ratio distortion detected in the present study shows that, in contrast to  
371 suggested (Song et al. 2019), the hatching position of an offspring may influence its genetic traits.  
372 This may explain some of the hatching-order effects detected in kittiwakes and other species  
373 (Massemin et al. 2002; Cam et al. 2003; Dey et al. 2014; Song et al. 2019), and paves the road for  
374 further studies investigating its generality, as well as the driving evolutionary and proximal processes.

375

## 376 **Acknowledgements**

377 We are grateful to all the Middleton fieldworkers who collected data for this study, and the  
378 undergraduate students who helped with lab work. The experiment was conducted under the  
379 approval of the U.S. Geological Survey Alaska Science Center, the University of Alaska Institutional  
380 Animal Care and Use Committees, in accordance with United States laws and under permits from the  
381 U.S. Fish and Wildlife Service and the State of Alaska. Fieldwork was supported by a grant from the  
382 Institut Polaire Français Paul-Emile Victor (IPEV “Programme 1162”) to S.L. and E.D, and a research  
383 grant from the Fondation Fyssen to S.L. This work was supported by the French Laboratory of  
384 Excellence Project “TULIP” (ANR-10-LABX-41; ANR-11-IDEX-0002-02).

385

## 386 **References**

- 387 Alcaide M, Rodríguez A, Negro JJ, Serrano D (2012) Male transmission ratio distortion supports MHC-  
388 linked cryptic female choice in the lesser kestrel (Aves: Falconidae). *Behav Ecol Sociobiol*  
389 66:1467–1473
- 390 Andersson M (1994) *Sexual selection*. Princeton University Press, Princeton

391 Bebbington K, Groothuis TGG (2023) Position in the laying order has sex-specific consequences for  
392 reproductive success in adult black-headed gulls. *J Evol Biol* 36:925–934.  
393 <https://doi.org/10.1111/jeb.14184>

394 Benowitz-Fredericks ZM, Kitaysky AS, Welcker J, Hatch SA (2013) Effects of food availability on yolk  
395 androgen deposition in the black-legged kittiwake (*Rissa tridactyla*), a seabird with  
396 facultative brood reduction. *PLoS ONE* 8:e62949

397 Birkhead TR, Pizzari T (2002) Postcopulatory sexual selection. *Nat Rev Genet* 3:262–273.  
398 <https://doi.org/10.1038/nrg774>

399 Brown AJ, White J, Shaw L, et al (2024) MHC heterozygosity limits T cell receptor variability in CD4 T  
400 cells. *Sci Immunol* 9:eado5295. <https://doi.org/10.1126/sciimmunol.ado5295>

401 Cam E, Monnat J, Hines JE (2003) Long-term fitness consequences of early conditions in the  
402 kittiwake. *J Anim Ecol* 72:411–424. <https://doi.org/10.1046/j.1365-2656.2003.00708.x>

403 Canal D, Roved J, Lara A, et al (2024) MHC Class II Supertypes Affect Survival and Lifetime  
404 Reproductive Success in a Migratory Songbird. *Mol Ecol* 33:e17554.  
405 <https://doi.org/10.1111/mec.17554>

406 de la Casa-Esperón E, de Villena FP-M, Verner AE, et al (2000) Sex-of-Offspring-Specific Transmission  
407 Ratio Distortion on Mouse Chromosome X. *Genetics* 154:343–350.  
408 <https://doi.org/10.1093/genetics/154.1.343>

409 Dearborn DC, Gager AB, McArthur AG, et al (2016) Gene duplication and divergence produce  
410 divergent MHC genotypes without disassortative mating. *Mol Ecol* 25:4355–4367.  
411 <https://doi.org/10.1111/mec.13747>

412 Dearborn DC, Warren S, Hailer F (2022) Meta-analysis of major histocompatibility complex (MHC)  
413 class IIA reveals polymorphism and positive selection in many vertebrate species. *Mol Ecol*  
414 31:6390–6406. <https://doi.org/10.1111/mec.16726>

415 Dey CJ, O’connor C, Quinn JS (2014) Hatching order affects offspring growth, survival and adult  
416 dominance in the joint-laying Pukeko *Porphyrio melanotus melanotus*. *Ibis* 156:658–667.  
417 <https://doi.org/10.1111/ibi.12158>

418 Doyle J, Ellis SA, O’Gorman GM, et al (2009) Classical and non-classical Major Histocompatibility  
419 Complex class I gene expression in in vitro derived bovine embryos. *J Reprod Immunol*  
420 82:48–56. <https://doi.org/10.1016/j.jri.2009.06.125>

421 Drent PJ, Oers K van, Noordwijk AJ van (2003) Realized heritability of personalities in the great tit  
422 (*Parus major*). *Proc R Soc Lond B Biol Sci* 270:45–51. <https://doi.org/10.1098/rspb.2002.2168>

423 Ducret V, Gaigher A, Simon C, et al (2016) Sex-specific allelic transmission bias suggests sexual  
424 conflict at 1R. *Mol Ecol* 25:4551–4563. <https://doi.org/10.1111/mec.13781>

425 Eberhard W (1996) *Female control: sexual selection by cryptic female choice*. Princeton University  
426 Press

427 Ferreira D, San-Jose LM, Roulin A, et al (2024) Limited associations between MHC diversity and  
428 reproductive success in a bird species with biparental care. *Ecol Evol* 14:e10950.  
429 <https://doi.org/10.1002/ece3.10950>

- 430 Firman RC, Gasparini C, Manier MK, Pizzari T (2017) Postmating Female Control: 20 Years of Cryptic  
431 Female Choice. *Trends Ecol Evol* 32:368. <https://doi.org/10.1016/j.tree.2017.02.010>
- 432 Fishman L, McIntosh M (2019) Standard Deviations: The Biological Bases of Transmission Ratio  
433 Distortion. *Annu Rev Genet* 53:347–372. <https://doi.org/10.1146/annurev-genet-112618-043905>  
434
- 435 Fortuna R, Paquet M, Biard C, et al (2023) Egg components and offspring survival vary with group size  
436 and laying order in a cooperative breeder. *Oecologia* 202:129–142.  
437 <https://doi.org/10.1007/s00442-023-05379-w>
- 438 Friocourt G, Perrin A, Saunders PA, et al (2023) Bypassing Mendel’s First Law: Transmission Ratio  
439 Distortion in Mammals. *Int J Mol Sci* 24:1600. <https://doi.org/10.3390/ijms24021600>
- 440 Gaigher A, Burri R, Gharib WH, et al (2016) Family-assisted inference of the genetic architecture of  
441 major histocompatibility complex variation. *Mol Ecol Resour* 16:1353–1364.  
442 <https://doi.org/10.1111/1755-0998.12537>
- 443 Gasparini J, Boulinier T, Gill VA, et al (2007) Food availability affects the maternal transfer of  
444 androgens and antibodies into eggs of a colonial seabird. *J Evol Biol* 20:874–880
- 445 Gill VA, Hatch SA, Lanctot RB (2002) Sensitivity of breeding parameters to food supply in black-legged  
446 kittiwakes *Rissa tridactyla*. *Ibis* 144:268–283
- 447 Habig B, Archie EA (2015) Social status, immune response and parasitism in males: a meta-analysis.  
448 *Philos Trans R Soc B Biol Sci* 370:20140109. <https://doi.org/10.1098/rstb.2014.0109>
- 449 Hadfield JD, Heap EA, Bayer F, et al (2013) Intraclutch differences in egg characteristics mitigate the  
450 consequences of age-related hierarchies in a wild passerine. *Evolution* 67:2688–2700.  
451 <https://doi.org/10.1111/evo.12143>
- 452 Helfenstein F, Tirard C, Danchin E, Wagner RH (2004) Low frequency of extra-pair paternity and high  
453 frequency of adoption in black-legged kittiwakes. *Condor* 106:149–155.  
454 <https://doi.org/10.1650/7337>
- 455 Huang LO, Labbe A, Infante-Rivard C (2013a) Transmission ratio distortion: review of concept and  
456 implications for genetic association studies. *Hum Genet* 132:245–263.  
457 <https://doi.org/10.1007/s00439-012-1257-0>
- 458 Huang LO, Labbe A, Infante-Rivard C (2013b) Transmission ratio distortion: review of concept and  
459 implications for genetic association studies. *Hum Genet* 132:245–263.  
460 <https://doi.org/10.1007/s00439-012-1257-0>
- 461 Huang W, Dicks KL, Hadfield JD, et al (2022) Contemporary selection on MHC genes in a free-living  
462 ruminant population. *Ecol Lett* 25:828–838. <https://doi.org/10.1111/ele.13957>
- 463 Huang W, Pemberton JM (2021) Within-trio tests provide little support for post-copulatory selection  
464 on major histocompatibility complex haplotypes in a free-living population. *Proc R Soc B*  
465 288:20202862
- 466 Ilany A, Holekamp KE, Akçay E (2021) Rank-dependent social inheritance determines social network  
467 structure in spotted hyenas. *Science* 373:348–352. <https://doi.org/10.1126/science.abc1966>

468 Jodice PGR, Lanctot RB, Gill VA, et al (2000) Sexing adult black-legged kittiwakes by DNA, behavior,  
469 and morphology. *Waterbirds* 23:405–415

470 Jokiniemi A, Kuusipalo L, Ritari J, et al (2020) Gamete-level immunogenetic incompatibility in  
471 humans—towards deeper understanding of fertilization and infertility? *Heredity* 125:281–  
472 289. <https://doi.org/10.1038/s41437-020-0350-8>

473 Kamiya T, O’Dwyer K, Westerdahl H, et al (2014) A quantitative review of MHC-based mating  
474 preference: the role of diversity and dissimilarity. *Mol Ecol* 23:5151–5163

475 Kasimatis KR, Abraham A, Ralph PL, et al (2021) Evaluating human autosomal loci for sexually  
476 antagonistic viability selection in two large biobanks. *Genetics* 217:iyaa015.  
477 <https://doi.org/10.1093/genetics/iyaa015>

478 Kekäläinen J (2022) Cryptic female choice within individual males – A neglected component of the  
479 postmating sexual selection? *J Evol Biol* 35:1407–1413. <https://doi.org/10.1111/jeb.14081>

480 Khan T, Rahman M, Ahmed I, et al (2022) Human leukocyte antigen class II gene diversity tunes  
481 antibody repertoires to common pathogens. *Front Immunol* 13:

482 Knief U, Forstmeier W, Pei Y, et al (2020) A test for meiotic drive in hybrids between Australian and  
483 Timor zebra finches. *Ecol Evol* 10:13464–13475. <https://doi.org/10.1002/ece3.6951>

484 Koolhaas JM (2008) Coping style and immunity in animals: Making sense of individual variation. *Brain  
485 Behav Immun* 22:662–667. <https://doi.org/10.1016/j.bbi.2007.11.006>

486 Kozłowski CP, Ricklefs RE (2010) Egg size and yolk steroids vary across the laying order in cockatiel  
487 clutches: A strategy for reinforcing brood hierarchies? *Gen Comp Endocrinol* 168:460–465.  
488 <https://doi.org/10.1016/j.ygcen.2010.06.006>

489 Leclaire S, van Dongen WF, Voccia S, et al (2014) Preen secretions encode information on MHC  
490 similarity in certain sex-dyads in a monogamous seabird. *Sci Rep* 4:6920

491 Lenz TL, Hafer N, Samonte IE, et al (2018) Cryptic haplotype-specific gamete selection yields offspring  
492 with optimal MHC immune genes. *Evolution* 72:2478–2490

493 Lucotte EA, Albiñana C, Laurent R, et al (2022) Detection of sexually antagonistic transmission  
494 distortions in trio datasets. *Evol Lett* 6:203–216. <https://doi.org/10.1002/evl3.271>

495 Magris M, Jokiniemi A, Kuusipalo L, et al (2021) Structural dissimilarity of partners’ immune genes  
496 increases sperm viability in women’s reproductive tract. *J Evol Biol* 34:1125–1132.  
497 <https://doi.org/10.1111/jeb.13872>

498 Martin AAA, Id-Lahoucine S, Fonseca PAS, et al (2022) Unravelling the genetics of non-random  
499 fertilization associated with gametic incompatibility. *Sci Rep* 12:22314.  
500 <https://doi.org/10.1038/s41598-022-26910-8>

501 Massemin S, Korpimäki E, Pöyri V, Zorn T (2002) Influence of hatching order on growth rate and  
502 resting metabolism of kestrel nestlings. *J Avian Biol* 33:235–244.  
503 <https://doi.org/10.1034/j.1600-048X.2002.330305.x>

- 504 McCurdy DG, Shutler D, Mullie A, Forbes MR (1998) Sex-Biased Parasitism of Avian Hosts: Relations  
505 to Blood Parasite Taxon and Mating System. *Oikos* 82:303–312.  
506 <https://doi.org/10.2307/3546970>
- 507 Merklings T, Leclaire S, Danchin E, et al (2012) Food availability and offspring sex in a monogamous  
508 seabird: insights from an experimental approach. *Behav Ecol* 23:751–758
- 509 Milinski M (2006) The major histocompatibility complex, sexual selection, and mate choice. *Annu Rev*  
510 *Ecol Evol Syst* 37:159–186
- 511 Nadeau JH (2017) Do Gametes Woo? Evidence for Their Nonrandom Union at Fertilization. *Genetics*  
512 207:369–387. <https://doi.org/10.1534/genetics.117.300109>
- 513 Nowak MA, Tarczy-Hornoch K, Austyn JM (1992) The optimal number of major histocompatibility  
514 complex molecules in an individual. *Proc Natl Acad Sci* 89:10896–10899.  
515 <https://doi.org/10.1073/pnas.89.22.10896>
- 516 Oksanen J, Blanchet FG, Kindt R, et al (2013) Package ‘vegan.’ *Community Ecol Package Version 2:*
- 517 Olsson M, Shine R, Madsen T, et al (1996) Sperm selection by females. *Nature* 383:585–585.  
518 <https://doi.org/10.1038/383585a0>
- 519 Otto SP, Scott MF, Immler S (2015) Evolution of haploid selection in predominantly diploid  
520 organisms. *Proc Natl Acad Sci* 112:15952–15957. <https://doi.org/10.1073/pnas.1512004112>
- 521 Özer O, Lenz TL (2021) Unique Pathogen Peptidomes Facilitate Pathogen-Specific Selection and  
522 Specialization of MHC Alleles. *Mol Biol Evol* 38:4376–4387.  
523 <https://doi.org/10.1093/molbev/msab176>
- 524 Parker GA (1970) Sperm competition and its evolutionary consequences in the insects. *Biol Rev*  
525 45:525–567. <https://doi.org/10.1111/j.1469-185X.1970.tb01176.x>
- 526 Petchey OL, Gaston KJ (2006) Functional diversity: back to basics and looking forward. *Ecol Lett*  
527 9:741–758. <https://doi.org/10.1111/j.1461-0248.2006.00924.x>
- 528 Pierini F, Lenz TL (2018) Divergent Allele Advantage at Human MHC Genes: Signatures of Past and  
529 Ongoing Selection. *Mol Biol Evol* 35:2145–2158. <https://doi.org/10.1093/molbev/msy116>
- 530 Pineaux M, Blanchard P, Ribeiro L, et al (2023) A Gull Species Recognizes MHC-II Diversity and  
531 Dissimilarity Using Odor Cues. In: Schaal B, Rekow D, Keller M, Damon F (eds) *Chemical*  
532 *Signals in Vertebrates* 15. Springer International Publishing, Cham, pp 139–151
- 533 Pineaux M, Merklings T, Danchin E, et al (2020) Sex and hatching order modulate the association  
534 between MHC-II diversity and fitness in early-life stages of a wild seabird. *Mol Ecol* 29:3316–  
535 3329
- 536 Pineaux M, Merklings T, Danchin E, et al (2022) MHC-II distance between parents predicts sex  
537 allocation decisions in a genetically monogamous bird. *Behav Ecol* 33:245–251
- 538 Poulin R (1996) Sexual Inequalities in Helminth Infections: A Cost of Being a Male? *Am Nat* 147:287–  
539 295. <https://doi.org/10.1086/285851>

540 Promerová M, Alavioon G, Tusso S, et al (2017) No evidence for MHC class II-based non-random  
541 mating at the gametic haplotype in Atlantic salmon. *Heredity* 118:563–567.  
542 <https://doi.org/10.1038/hdy.2016.129>

543 Ribeiro L, Blanchard P, Manas F, et al (2025) An MHC class II supertype confers resistance to a  
544 sexually transmitted bacterium in females but not in males in a genetically monogamous  
545 seabird. *J Evol Biol* voaf097

546 Rolff J (2002) Bateman’s principle and immunity. *Proc R Soc B Biol Sci* 269:867–872.  
547 <https://doi.org/10.1098/rspb.2002.1959>

548 Roved J, Hansson B, Tarka M, et al (2018) Evidence for sexual conflict over major histocompatibility  
549 complex diversity in a wild songbird. *Proc R Soc B* 285:20180841

550 Roved J, Westerdahl H, Hasselquist D (2017) Sex differences in immune responses: Hormonal effects,  
551 antagonistic selection, and evolutionary consequences. *Horm Behav* 88:95–105

552 Rüllicke T, Chapuisat M, Homberger FR, et al (1998) MHC-genotype of progeny influenced by parental  
553 infection. *Proc R Soc Lond B Biol Sci* 265:711–716. <https://doi.org/10.1098/rspb.1998.0351>

554 Saino N, Incagli M, Martinelli R, et al (2001) Immunity, growth and begging behaviour of nestling Barn  
555 Swallows *Hirundo rustica* in relation to hatching order. *J Avian Biol* 32:263–270.  
556 <https://doi.org/10.1111/j.0908-8857.2001.320309.x>

557 Sandberg M, Eriksson L, Jonsson J, et al (1998) New chemical descriptors relevant for the design of  
558 biologically active peptides. A multivariate characterization of 87 amino acids. *J Med Chem*  
559 41:2481–2491. <https://doi.org/10.1021/jm9700575>

560 Sandler L, Novitski E (1957) Meiotic Drive as an Evolutionary Force. *Am Nat* 91:105–110.  
561 <https://doi.org/10.1086/281969>

562 Schaschl H, Suchentrunk F, Morris DL, et al (2012) Sex-specific selection for MHC variability in Alpine  
563 chamois. *BMC Evol Biol* 12:20

564 Schubert N, Nichols HJ, Mwanguhya F, et al (2025) Sex-Dependent Influence of Major  
565 Histocompatibility Complex Diversity on Fitness in a Social Mammal. *Mol Ecol* 34:e70058.  
566 <https://doi.org/10.1111/mec.70058>

567 Sebastian A, Herdegen M, Migalska M, Radwan J (2016) amplisas: A web server for multilocus  
568 genotyping using next-generation amplicon sequencing data. *Mol Ecol Resour* 16:498–510.  
569 <https://doi.org/10.1111/1755-0998.12453>

570 Sepil I, Lachish S, Hinks AE, Sheldon BC (2013) Mhc supertypes confer both qualitative and  
571 quantitative resistance to avian malaria infections in a wild bird population. *Proc R Soc B Biol*  
572 *Sci* 280:20130134. <https://doi.org/10.1098/rspb.2013.0134>

573 Song Z, Zou Y, Hu C, et al (2019) Silver spoon effects of hatching order in an asynchronous hatching  
574 bird. *Behav Ecol* 30:509–517. <https://doi.org/10.1093/beheco/ary191>

575 Sozzoni M, Ferrer Obiol J, Formenti G, et al (2023) A Chromosome-Level Reference Genome for the  
576 Black-Legged Kittiwake (*Rissa tridactyla*), a Declining Circumpolar Seabird. *Genome Biol Evol*  
577 15:evad153. <https://doi.org/10.1093/gbe/evad153>

578 Srinivasa AN, Zanders SE (2020) Meiotic drive. *Curr Biol* 30:R627–R629.  
579 <https://doi.org/10.1016/j.cub.2020.04.023>

580 Sterck EHM, Bontrop RE, de Groot N, et al (2017) No postcopulatory selection against MHC-  
581 homozygous offspring: Evidence from a pedigreed captive rhesus macaque colony. *Mol Ecol*  
582 26:3785–3793. <https://doi.org/10.1111/mec.14153>

583 Stier A, Massemin S, Zahn S, et al (2015) Starting with a handicap: effects of asynchronous hatching  
584 on growth rate, oxidative stress and telomere dynamics in free-living great tits. *Oecologia*  
585 179:999–1010. <https://doi.org/10.1007/s00442-015-3429-9>

586 Sutter A, Immler S (2020) Within-ejaculate sperm competition. *Philos Trans R Soc B Biol Sci*  
587 375:20200066. <https://doi.org/10.1098/rstb.2020.0066>

588 Thel L, Pineaux M, Ribeiro L, et al (2025) Major histocompatibility complex class IIB disassortative  
589 mate choice in a genetically monogamous seabird. *Proc R Soc B Biol Sci* 292:20251265.  
590 <https://doi.org/10.1098/rspb.2025.1265>

591 Thornhill R (1983) Cryptic Female Choice and Its Implications in the Scorpionfly *Harpobittacus*  
592 *nigriceps*. *Am Nat* 122:765–788. <https://doi.org/10.1086/284170>

593 Valdebenito JO, Jones W, Székely T (2024) Evolutionary drivers of sex-specific parasite prevalence in  
594 wild birds. *Proc R Soc B Biol Sci* 291:20241013. <https://doi.org/10.1098/rspb.2024.1013>

595 Vincenzi S, Hatch S, Mangel M, Kitaysky A (2013) Food availability affects onset of reproduction in a  
596 long-lived seabird. *Proc R Soc B Biol Sci* 280:20130554

597 Vincze O, Vágási CI, Péntes J, et al (2022) Sexual dimorphism in immune function and oxidative  
598 physiology across birds: The role of sexual selection. *Ecol Lett* 25:958–970.  
599 <https://doi.org/10.1111/ele.13973>

600 Vlček J, Štefka J (2020) Association between louse abundance and MHC II supertypes in Galápagos  
601 mockingbirds. *Parasitol Res* 119:1597–1605. <https://doi.org/10.1007/s00436-020-06617-3>

602 White J, Wagner RH, Helfenstein F, et al (2008) Multiple deleterious effects of experimentally aged  
603 sperm in a monogamous bird. *Proc Natl Acad Sci* 105:13947–13952.  
604 <https://doi.org/10.1073/pnas.0803067105>

605 Winternitz J, Chakarov N, Rinaud T, et al (2023) High functional allelic diversity and copy number in  
606 both MHC classes in the common buzzard. *BMC Ecol Evol* 23:24.  
607 <https://doi.org/10.1186/s12862-023-02135-9>

608 Young RC, Welcker J, Barger CP, et al (2017) Effects of developmental conditions on growth, stress  
609 and telomeres in black-legged kittiwake chicks. *Mol Ecol* 26:3572–3584

610 Ziegler A, Kentenich H, Uchanska-Ziegler B (2005) Female choice and the MHC. *Trends Immunol*  
611 26:496–502

612 Zuk M, McKean KA (1996) Sex differences in parasite infections: Patterns and processes. *Int J*  
613 *Parasitol* 26:1009–1024. [https://doi.org/10.1016/S0020-7519\(96\)80001-4](https://doi.org/10.1016/S0020-7519(96)80001-4)

614