

Selection of both habitat and genes in specialized and endangered caribou

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Abstract

Genetic mechanisms determining habitat selection and specialization of individuals within species have been hypothesized, but not tested at the appropriate individual level in nature. In this work, we analyzed habitat selection for 139 GPS-collared caribou belonging to three declining ecotypes sampled throughout Northwestern Canada. We used Resource Selection Functions (RSFs) comparing resources at used and available locations. We found that the three caribou ecotypes differed in their use of habitat suggesting specialization. On expected grounds, we also found differences in habitat selection between summer and winter, but also, originally, among the individuals within an ecotype. We next obtained Single Nucleotide Polymorphisms (SNPs) for the same caribou individuals, we detected those associated to

habitat selection, and then identified genes linked to these SNPs. These genes had functions related in other organisms to habitat and dietary specializations, and climatic adaptations. We therefore suggest that individual variation in habitat selection was based on genotypic variation in the SNPs of individual caribou, indicating that genetic forces underlie habitat and diet selection in the species. We also suggest that the associations between habitat and genes that we detected may lead to lack of resilience in the species, thus contributing to caribou endangerment. Our work emphasizes that similar mechanisms may exist for other specialized, endangered species.

Introduction

Habitat selection is the process whereby animals use a non-random set of available habitats, i.e. they select the habitat they use most (Morris, 2003). Habitat selection may be performed by individual organisms and, like other characteristics comprising an ecological type, should have a substantial effect on evolutionary processes (Holt, 1987), and may be genetically determined. Models of natural selection in heterogeneous environments become much more powerful if individuals with different genotypes are able to select the habitat in which they are most fit (Jones, 1980). If genotypes differ in their fitnesses in the available habitats and if organisms practice habitat selection, so that they choose to occupy those habitats where most fit, then genetic polymorphisms can be maintained (Taylor, 1976). Genetic mechanisms determining habitat selection and specialization have therefore been hypothesized, but not tested at the appropriate individual level in nature, and never in an endangered mammal (Jaenike & Holt 1991).

For many species, habitat selection has been convincingly determined by examining habitat features of used locations collected with telemetry and tracking devices (Manly et al., 2002). A well-established approach is conducting Resource Selection Functions (RSF) analyses, which compare resources used (GPS-telemetry locations) by an animal with those deemed to be available (random points; Boyce & McDonald, 2003). Habitat selection can be examined at different scales that reflect different biological aspects of studied animals (Johnson, 1980). For example, examining individual-level selection within seasonal ranges, as we did in this study, gives valuable insights on foraging (Hebblewhite & Merrill, 2009).

Patterns in habitat selection should be interpreted with respect to other ecological traits and genetic forces (Skulason & Smith, 1995). For example, habitat selection and diet may co-vary, as animals will disproportionally use areas where high quality food items are available (Manly et al., 2002). Most varying attributes of an organism may have a genetic basis. Thus, habitat selection may be maintained by selection of genes that determine habitat preferences (Savolainen et al., 2013). Nonetheless, association studies analyzing the obvious link between the two types of selection (i.e. of habitat and of genes) are yet to be conducted. Investigating the genetic component of habitat selection can shed light on ecological specialization, which can describe how stringently animals select for specific habitats (Futuyma & Moreno, 1988; Devictor et al., 2010), and could have consequential conservation implications. The stringency of the choice might depend on the existence and strength of genetic mechanisms associated to habitat selection (Hoffmann & Sgro, 2011; Chase et al., 2020). Ultimately, organisms that are habitat specialized may be less resilient to environmental change, and therefore more likely to become endangered, if habitat selection is also reinforced by genetic determination (Futuyma & Moreno, 1988).

However, investigations of the genetic component of habitat selection are challenging. Hoban et al. (2016) claimed that “low-resolution environmental data” may reduce the

accuracy of genetic association studies, even if the “selective environment” is known.

Accuracy of associations might be best achieved if the selective environment is determined at a correct biological scale. Typically, association studies determine the correlation of individual or pooled genotypes with environmental variables surveyed and averaged for population ranges (Edelaar & Bolnick, 2019), which could paradoxically also include areas, such as refugia, where organisms survive under unfavorable and not-selected-for conditions (Stewart et al., 2010). Therefore, such population ranges (if taken as a whole) may not represent fairly all environmental conditions under which species evolved, and could provide biased results in gene association studies. There is no easy solution to addressing such biases. Alternatively to averaged population ranges approaches, individual genomic data could be correlated to habitat selection by individual animals, as in this study. While some individual may live in refugia only, some others may have home ranges including pristine environments in various proportions, and their preference for each available type of habitat could be assessed. Therefore, our study responds to previous recommendations to utilize higher resolution environmental data, to accurately assess selection of the environment, and then to examine whether correlations occur with given genes.

Caribou (a conspecific of Reindeer, *Rangifer tarandus*) in Canada are among the many wild ungulate species that are in dramatic decline worldwide (Vors & Boyce, 2009; Di Marco et al., 2014), and are composed of distinct ecological types (ecotypes), some of which are of “special concern”, threatened, endangered or at risk of extirpation (COSEWIC, 2011; Festa-Bianchet et al., 2011; Hebblewhite et al., 2017). Past studies investigating caribou habitat selection indicated a preference for pristine environments (i.e. not human-disturbed), but with each ecotype selecting for different habitats (Geist, 1998; Bergerud et al., 2007; Hummel & Ray, 2008; COSEWIC, 2011). Caribou decline is mainly the consequence of habitat alterations that decrease availability of preferred habitat for this specialized species

(Vors & Boyce, 2009; Hebblewhite, 2017; Leech et al., 2017; Palm et al., 2020). Thus, there is an urgent need to understand the processes shaping caribou's ecological specialization, including habitat selection and selection of associated genes, as genetic determination might augment this species' sensitivity.

In this work, we assessed habitat selection for GPS-collared caribou sampled throughout Northwestern Canada (Fig. 1). We then obtained Single Nucleotide Polymorphisms (SNPs) for those same individuals and determined the genetic associations to habitat selection factors. We also identified genes associated to habitat selection-SNPs, and their gene function. Overall, we employed a multidisciplinary approach to investigate the association between genes and habitat selection in an endangered habitat specialist, and explored its applicability to other species in which genetic traits may also influence ecologically important behaviors and limit resilience to changing habitats.

Methods

Sampling and molecular analyses

We obtained blood and tissue samples from 284 caribou from animals captured and sampled during monitoring activities across Northwestern Canada from 2004-2016. Sampled caribou were from 24 herds which belong to Barren-ground (*R. t. groenlandicus*) and Woodland (*R. t. caribou*) subspecies, with Woodland further divided into three ecotypes (Northern Mountain; Central Mountain and Boreal ecotypes) (Fig. 1). Research was conducted under permits of Governments of British Columbia, Alberta, Northwest Territories, and Yukon, Parks Canada, and University of Montana, and of Calgary (Life & Environmental Sciences Animal Care Committee, LESACC, ACC Study #AC16-0195).

The Barren-ground caribou we sampled were from an area north of the treeline consisting of semi-arid low-Arctic tundra (Bliss 1988). Our Boreal caribou were from the boreal coniferous forest, where annual rainfall is relatively higher (Elliot-Fisk, 1988). Finally, the study's Northern Mountain and Central Mountain caribou came from montane, subalpine and alpine ecoregions in Yukon and British Columbia (and also transboundary with the Northwest Territories), which are characterized by long winters and short, dry summers (Gubili et al., 2017).

We followed Ali et al. (2016) to extract DNA and check its quality and to prepare restriction site associated DNA sequencing (RADseq) libraries. We therefore barcoded each individual sample with unique tags, which allowed us to run 96 samples into a single genomic library. The genomic libraries were then sequenced with paired-end 2x100nt reads on an Illumina HiSeq 2500 at Princeton University (full details on sampling and molecular analyses in Supporting Information).

RADseq analysis and SNPs finding

We retained individuals with a minimum of 500,000 reads (Heppenheimer et al., 2018), which were mapped to the reference *Bos taurus* genome (UMD3.1- Elisk et al., 2009) using *Stampy* v1.0.20 – see details on RAD-seq analysis and SNPs finding in Supporting Information, Methods S2. Our pick of the *Bos taurus* genome was motivated by its quality and established use in the literature for cervids (see for example Powell et al., 2016), like caribou. The taurine genome has been successfully used for association studies for over a decade, with numerous works conducted on other Artiodactyls also including cervids (Haines et al., 2019). In addition, Ba et al. (2020) evaluated that the quality of newly published deer genomes may not be comparable to that of the taurine genome, and questioned the premature use of deer genomes as reference. Furthermore, we conducted Gene Ontology analyses using

categories described for *Bos Taurus* (as well as for other Mammals and Vertebrates), making our choice of the taurine genome appropriate.

After this filtering step, we retained 190 individuals, which were used for SNPs discovery. Also following Heppenheimer et al. (2018), we then used *SAMtools* v1.5 to remove reads with low mapping quality ($\text{MAPQ} < 60$) and *Stacks* 2.0 to identify SNPs. We then retained SNPs that had a minor allele frequency greater than 0.05 and a mean coverage $> 3x$. As a result, we discovered 31,080 reference-dependent SNPs. SNPs were further filtered for linkage disequilibrium (LD - Purcell et al., 2007), thus obtaining a final dataset including 29,443 SNPs.

Assessment of habitat selection

Data collection, screening, and seasonal range analyses

Female caribou were radio-collared by government staff or contractors during 2004-2016.

The collaring of females was decided by respective programs as this sex was considered the first monitoring priority for conservation. Females are also ideal to define seasonal movements in caribou (Bergerud et al., 2007; McDevitt et al., 2009). We standardized telemetry data to obtain, for every animal, a daily location (randomly chosen). We defined summer (1 April - 31 October) and winter (1 November - 31 March) seasons following Johnson et al. (2015) and DeCesare et al. (2012). For subsequent analyses, we only included the animals that had at least 30 locations per season—i.e. a viable minimum sample size (Girard et al., 2002). After these screening procedures, the data set contained 75,223 locations from 139 unique individuals. The final dataset with caribou that were both genotyped and also collared therefore included individuals from 19 herds: 54 individuals from three herds of the Barren-ground subspecies, and 85 individuals from 16 herds belonging to two different

ecotypes of Woodland subspecies (Boreal, $n_{\text{herds}}=7$, $n_{\text{individuals}}=18$; Northern Mountain, $n_{\text{herds}}=9$, $n_{\text{individuals}}=67$; Central Mountain not collared and only used for genotyping).

For each animal's season, we estimated utilization distributions (UD) using the *kernelUD* function (reference bandwidth used) within the *adehabitHR* package (Calenge 2006) in R version 3.5. We then derived the 95% fixed-kernel isopleth (DeCesare et al., 2012). Finally, we obtained “used” and “available” locations within seasonal ranges to be compared in habitat selection analyses (Manly et al., 2002). In this study, “used” points were the telemetry locations, while “available” locations were 10 times more randomly picked points within the 95% kernels (Gustine & Parker, 2008).

Choice of resource variables for habitat selection analyses

We analyzed selection of caribou for variables that were topographic (elevation, slope, aspect, and distance to water [distances to rivers, lakes, and water-saturated soils]), climatic (Index of snow cover during October and November), and vegetative (land cover type and normalized difference vegetation index [NDVI] during July and August). We also analyzed selection for anthropogenic disturbance, including forest loss and distances to linear features (e.g. roads and trails). Overall, we used the above variables only (i.e. a parsimonious set), because found to be important predictors of caribou occurrence in previous ecological research (see for example DeCesare et al., 2012, and also the rationale in Supporting Information).

Variables were obtained following methodologies described in Cavedon et al. (2019). However, snow cover and the normalized difference vegetation index (NDVI) were identically assessed for October and November and for July and August (respectively), but using average of values for the caribou monitoring years. Finally, all habitat covariates were associated to each caribou location point, random or used, with ArcGIS 10 and screened for

collinearity using the Spearman correlation test (correlation values in Supporting Information).

Habitat selection analyses with Resource Selection Functions

We used RSFs to assess habitat selection by conducting logistic regressions that compare resources used and available (Manly et al., 2002). Habitat selection can vary between ecotypes, herds, and individuals (and seasons) (McDevitt et al., 2009; DeCesare et al., 2012). Our focus was on individuals, since our aim was to associate variation in habitat selection to variation in individual genotypes. However, to account for ecotype variation, we also ran habitat selection models at the ecotype level, which allowed us to choose variables to be used in individual analyses. We therefore ran univariate logistic regressions for winter and summer seasons for each ecotype (Barren-ground, Northern Mountain, and Boreal) with the *glmer* function within the *lme4* package in R 3.5. Herd's belonging was used as a random effect to represent possible differences between populations, due to unaccounted for factors and variables (Gillies et al., 2006). Continuous variables were standardized to range from -1 to 1 and, for the categorical variable "land cover", the reference class was LC12 ("grassland-lichen-moss" expected to be moderately selected). A p value < 0.05 was used to infer the statistical significance of the β regression coefficients (using a Wald's test). For further, multivariate analyses, we only used variables that were not collinear ($|r| > 0.7$) as well as significantly selected or avoided in univariate analyses.

We subsequently ran RSFs at the individual level in a multivariate logistic regression framework with the *glm* function in R 3.5. When the p value for a specific β was ≥ 0.05 , the value of β was manually changed to zero, as this value indicates that a resource is used in proportion to its availability (indifferent choice of an animal for a specific resource - Leclerc et al., 2016). Our study assessed selection of resources present within individual ranges each season. Individuals could perhaps vary in habitat selection between years, especially if

available resources change. Every time β was obtained for multiple years for the same individual, an average β was calculated. This averaging approach was designed to best capture a permanent signal of individual selection or avoidance, perhaps correlated to genetics (i.e. also a permanent trait), rather than a pattern of variation during an animal's lifetime.

Association study between SNPs and habitat selection factors

To identify caribou genetic clusters, we ran population structure analyses as explained in Supporting Information (Method S3). We also ran a univariate mixed model, with the software package *Gemma* (Zhou et al., 2014), to examine the dependence of habitat selection factors upon each single SNP (an association study). Following guidelines by Zhou et al. (2014), we accounted for population stratification. We used *Gemma* with the LD-filtered SNPs to calculate relatedness of individuals. Relatedness matrixes measure a weighted covariance of genotypes, averaged over all SNPs across the genome, between each pair of individuals. We incorporated the matrix, as covariate, in the model. We then used Wald's test to determine significance of analyses, where a SNP was considered as associated with a factor' Beta coefficients when the Bonferroni adjusted p value was below 0.05. We did not have pedigree information for our caribou, as it is common in ecological studies conducted on wild animals. However, in association studies like ours, it is still possible to calculate the proportion of variance in phenotypes explained (Proportion of Phenotypic Variance Explained, PVE) by available genotypes, or SNP heritability (Zhu & Zhou 2020). We therefore calculated PVE values for SNPs that we found associated (Shim et al., 2015).

Gene Ontology

We annotated all SNPs as genic (intron or exon), within a promoter (i.e. within 2 Kb of transcription start site), or intergenic using an in-house python script. For genic SNPs, we

inferred gene functions and gene ontology (GO) functional categories (biological process, cellular component and molecular function) of those associated to habitat selection factors using *Ensembl BioMart* (Kinsella et al., 2011). Then, we tested these habitat-associated SNPs for significant enrichment of GO categories using *Gprofiler* (Raudvere et al., 2019). We used our genic SNPs as the reference set, and evaluated significance of enrichment of the habitat-associated SNPs using a false discovery rate (FDR) Benjamini–Hochberg threshold of 5%.

Results

Seasonal habitat selection varied between caribou individuals, but with characteristic ecotype patterns

We used Resource Selection Functions and determined that caribou selected or avoided a total of thirteen habitat variables: they used them non-randomly within individual seasonal ranges. Coefficients of habitat selection for caribou individuals varied across caribou ecotypes and seasons (Fig. 2). Six habitat selection variables were topographic: slope, elevation, aspect, distance from rivers, distance from lakes and distance from water-saturated soils. Two variables were vegetative: land cover that represents plant associations, and normalized difference vegetation index (NDVI) that represents plant productivity. One habitat selection variable was climatic: the snow cover index, which indicates the proportion of an area covered by snow. Finally, four habitat selection variables represented human infrastructure: distance from roads, distance from petroleum wells, distance from hiking trails, and distance from soil works (i.e. excavated areas, such as mines; full description of variables used in habitat selection analyses in Supporting Information, Table S1).

Variation of habitat selection caribou individuals

Habitat selection varied among caribou individuals even when they belonged to the same ecotype (for example, elevation; Fig. 3) and herd, and the same individual could also select different habitats in winter and summer (Fig. 4). We found that variables for which patterns of selection varied the most between individuals were the ones representing anthropic disturbances (mean and variance of seasonal regression coefficients indicated in Supporting Information). For example, the coefficient of selection calculated in the summer for soil works averaged across all individuals was -0.53 (indicating avoidance), with a variance of 38.05. Resources for which patterns of selection varied the least among individuals were topographic. For instance, the mean summer coefficient of selection for elevation was 0.48 with a variance of just 0.69.

Summer habitat selection patterns by caribou ecotypes

We found evidence that two topographic variables and one representing anthropogenic disturbance were consistently selected or avoided by all ecotypes during the summer. All ecotypes selected areas located at higher elevation (demonstrated by positive and significant selection coefficients; summer regression coefficients for caribou ecotypes in Table S5, Supporting Information) and farther from lakes, but avoided areas closer to soil works. On the other hand, the other topographic variables were differentially selected by caribou ecotypes. We found that Barren-ground and Boreal caribou ecotypes selected for or avoided steeper areas, respectively. Furthermore, both Barren-ground and Boreal caribou selected for areas closer to water-saturated soils (i.e. wetlands). Finally, Barren-ground caribou selected for areas closer to rivers, which were avoided by Northern Mountain and Boreal caribou.

All climatic and vegetative resources were also differentially selected across caribou ecotypes. Barren-ground and Northern Mountain caribou selected for areas covered by snow, but the Boreal ecotype neither selected nor avoided them. Furthermore, Barren-ground

caribou selected for areas with higher plant productivity (NDVI), which were avoided by Boreal and Northern Mountain caribou. Finally, Barren-ground caribou selected for land cover class 2 (LC2, “Sub-polar taiga needleleaf forest”); instead, Northern Mountain and Boreal caribou selected for class LC11 (“Sub-polar or polar shrubland-lichen-moss”) and class LC14 (“Wetland”), respectively. Three out of four variables representing anthropogenic disturbance were also differentially selected for by caribou ecotypes (whereas soil works were always avoided, as explained above). Barren-ground and Northern Mountain caribou avoided areas closer to petroleum wells and hiking trails. Boreal and Northern Mountain caribou avoided and selected for areas closer to roads, respectively.

Winter habitat selection patterns by caribou ecotypes

Caribou belonging to all ecotypes consistently selected for areas within their individual winter range that had more snow and were closer to water-saturated soils (for example, wetlands) (winter regression coefficients for caribou ecotypes in Table S6, Supporting Information). On the other hand, four topographic variables were differentially selected. Northern Mountain and Boreal caribou selected flatter areas. Furthermore, only Barren-ground and Northern Mountain caribou selected for areas located at higher elevation. Barren-ground caribou also selected for areas closer to lakes, which were instead avoided by Northern Mountain caribou. Finally, Barren-ground and Northern Mountain caribou selected and avoided areas closer to rivers, respectively.

All vegetative resources were differentially selected by caribou ecotypes. Barren-ground caribou selected for land cover classes LC2 and LC13 (“Sub-polar” and “Polar barren-lichen-moss”), LC14 (“Wetland”), and LC16 (“Barren Lands”). On the other hand, Boreal caribou selected for LC1 (“Temperate or sub-polar needleleaf forest”) and LC14. Three variables representing anthropogenic disturbance were also differentially selected by

caribou ecotypes. Only Barren-ground caribou selected for areas closer to soil works and to hiking trails. Finally, Northern Mountain caribou avoided areas closer to roads (Fig. 5).

Habitat selection genes in caribou ecotypes

We confirmed a main North-South separation of caribou genetic clusters corresponding to the currently recognized subspecies (full details of population structure findings in Results S1, Supporting Information). We conducted association studies between the thirteen habitat selection factors detected above and our set of SNPs. As for all association studies, associations could be influenced by the demographic history of individuals; we therefore corrected for neutral genetic structure by employing a relatedness matrix, as covariate, in the mixed models used to detect associations. After this step, we detected a total of 1,337 SNPs associated ($p < 0.05$ after Bonferroni correction) (Data file S3). Of these, 1,143 SNPs were associated with a single factor while 194 loci had associations to multiple factors (example, to both elevation and proximity to rivers). The habitat selection factor associated with the highest number of SNPs ($n=291$) was LC11, which corresponds to summer selection of “Sub-polar or polar shrubland-lichen-moss”. The next highest number of associated SNPs ($n=156$) was detected for LC6, which corresponds to winter selection of “Mixed Forest”. From pairwise F_{ST} estimates calculated across all SNPs (rare alleles excluded), we found that Boreal caribou were distinguishable from Barren-ground or Mountain caribou, and these differences were more noticeable when habitat selection-associated SNPs only were used (Fig. 6).

Out of the habitat selection-associated SNPs, 520 were located in 493 genes (i.e. multiple SNPs were sometimes located in the same gene) and annotated as introns (464), exons (43) or within a promoter (13). Gene Ontology analyses of genes associated to habitat selection showed significant enrichment ($FDR \leq 0.05$) in numerous GO categories ($n=112$). Enriched

categories revealed a possible expression of genes regulating important dietary, metabolic, and sensory processes within the Biological Process domain, and other processes within the Cellular Component or Molecular Function domains (Fig. 7).

The genes harboring SNPs that were associated to habitat selection in this study were known to regulate nutrition and thermoregulation/metabolism processes in the conspecific reindeer, and in other ungulates or mammals (Table 1). The Proportion of Phenotypic Variance Explained (PVE) by a single associated SNP had a mean value of 0.24 (+0.09 SD). Eleven of these caribou genes were involved in nutrition, with three in taste perception in particular. Ten genes we detected have an important role in thermoregulation, with four playing an important role in metabolism and fat production in particular. In addition, seven of the habitat selection-associated genes detected in this study were known to regulate for light sensitivity and biorhythm.

Discussion

Genomic associations to habitat selection suggest ecological specialization in endangered caribou

In our study, we confirmed habitat selection factors that are ecologically important for caribou and demonstrate this species' reliance on pristine environments (i.e. not human-disturbed), including elevation, snow cover, the vegetation index NDVI, plant associations, and distance to human infrastructure (Apps et al., 2001, DeCesare et al., 2012; Nobert et al., 2016; DeMars & Boutin, 2018). Furthermore, our work indicated that habitat selection predictably varied between winter and summer, likely concurrent with seasonal variation in resource availability (DeCesare et al., 2012; Hornseth & Rempel, 2016). Our approach involved determining habitat preferences of caribou individuals, while statistically accounting for ecotype belonging. The habitat factors available and selected for were consistently

determined within individual ranges. The study therefore documented both varying habitat preferences of individuals and differences between ecotypes. Our results originally revealed that resources were not consistently selected or avoided across caribou groups, supporting ecological specialization of distinct ecotypes, which was predicted in the literature (Jones et al., 2007; Vors & Boyce, 2009; Pond et al., 2016; Hebblewhite, 2017; Palm et al., 2020), also including a study of maladaptation after translocation between different ecotypes (Leech et al., 2017).

Most varying attributes of an organism, may have genetic correlates (Boyle et al., 2017), also including habitat selection. However, this study documented logical relationships between habitat selection and genetic traits, which were also predicted but never tested and that have conservation implications for this endangered species. Overall, the novel finding of this work was that individual variation in habitat selection was associated to genotypic variation of SNPs, which suggested the existence of genetic forces involved in resource use in relation to resource availability (Hoffmann & Sgro, 2011; Chase et al., 2020), and likely limiting caribou's resilience to environmental change.

Overall, we detected associations between individual genotypes and selection for topographic, climatic and vegetative habitat factors and avoidance of human features, indicating genetic mechanisms involved in caribou foraging behavior. The pristine (not human disturbed) habitats selected for in this study are also known to contain important food sources for caribou, such as lichens (Denryter et al., 2020). We determined selection of both the land cover classes representing plant associations and the plant productivity index NDVI, and the interplay of these two could be interpreted as a surrogate of foraging preferences (Johnson et al., 2004; DeCesare et al., 2012). For instance, the selection for forested areas that we documented in the Boreal and Northern Mountain ecotypes could indicate a preference for arboreal lichens (a dietary preference that is known for the Mountain caribou

of British Columbia; Terry et al., 2000), while Barren-ground caribou's selection for open areas could indicate a preference for terrestrial lichens (Joly et al., 2010). Therefore, the genetic and habitat selection differences that we found between caribou groups were consistent with ecological specialization of the species and evolution of its ecotypes.

The association between individual genotypes and avoidance of human infrastructure that we documented, in addition to indicating a preference for foraging in pristine environments, also suggests that selection forces involved in anti-predator behaviors could simultaneously be at play against human disturbance –i.e. a more recent phenomenon. In this study, caribou avoided a broad range of human infrastructure features, suggesting a preference for pristine environments, which has been previously reported (DeCesare et al., 2012; DeMars & Boutin, 2018). Caribou's preference for such environments was also supported by their selection of high elevation areas, which are known to be the least human-affected in large portions of the study area (Rogala et al., 2011). However, some human infrastructure, such as the linear features that were avoided in our study (example, roads; Fig 5), are also known to increase the travel speed and hunting efficiency of predators (Dickie et al., 2016). Therefore, our study's caribou may have avoided areas with higher predation risk and human disturbance at the same time (DeMars & Boutin, 2018). For these reasons, the genomic signature that we detected in association to avoidance of human infrastructure could be the result of caribou's long-term coevolution with predators (Geist, 1998) or a more recent response to human effects, or both.

Habitat selection genes were involved in dietary specializations and climatic adaptations

The genes associated to habitat selection in this study were involved in nutrition, also consistent with the foraging preferences of this habitat specialist species (Geist, 1998; Denryter et al., 2020). Some associated genes were involved in taste perception in particular. For example, we found *ASIC2*, an important sour-taste receptor gene (Ugawa et al., 2003), as

well as *TRPM5*, which has a key role in the perception of tastes in mammalian species (Xu et al., 2006).

Some of the habitat selection-associated genes in this study are also under selection in other species in response to cold temperatures, indicating specialization to high-latitude habitats. Some genes we identified have an important role in thermoregulation (genes *TRPM2* and *PLCB1*; Lynch et al., 2015; Tan et al., 2016). In particular, *TRPM2* is an important thermo-sensor that allows mammals to regulate their body temperature and survive in cold environments, such as those frequented by caribou (Tan et al., 2016). Furthermore, some of the genes we found (*POR*, *FASN*, and *KCNMA1*) play an important role in metabolism and fat production, both of which are processes essential to mammalian species, like caribou, living at high latitudes (Lin et al., 2019).

Caribou, especially herds living at high latitudes, experience dramatic daylight fluctuations during the year and a marked seasonality in resource availability (Bergerud et al., 2007); the characteristics of the genes we found may help the species to cope with these challenges. Some habitat selection-associated genes identified in this study regulate for light sensitivity and biorhythm in other species (*ADCY1* and *NOS1AP*), which include mammals specialized for high latitudes (Hwang et al., 2013; Lin et al., 2019). Light sensitivity enhances the navigation ability of species frequenting high-latitude environments, which are characterized by the paucity of light during a significant portion of the year. In addition, biorhythm regulation, like the process controlled by the genes of this study, may be necessary to cope with sharp seasonality in resource availability (Lin et al., 2019). Overall, synchronization of the biological clock with external cues, light changes for example, could help caribou, and other animals, prepare for seasonal events, such as migration to reach seasonally productive ranges (Tryland & Kutz, 2018).

Threats to and conservation of ecologically specialized species

Many species are dramatically declining because of habitat alterations caused by anthropic activities (Pereira et al., 2010; Tilman et al., 2017), and species like caribou that, as we detected, are characterized by both gene and habitat selection may be particularly specialized and therefore increasingly threatened. Our results, which indicate that caribou have genes under selection that may have evolved in response to specific habitat and climatic conditions, pose additional layers of consideration for conservation planning, as human-caused habitat alterations and changing climatic conditions are both known to affect caribou (Yannic et al., 2014). The genetic association to the habitat selection factors detected in this study indicates that species may not be as plastic—and as resilient—as we previously thought, since their genomes may be predetermined (or adapted) to cope with historical conditions as opposed to recent, more sudden changes. The declines currently experienced by caribou herds are dramatic (Vors & Boyce, 2009), but may not constitute an isolated example, as other species are also affected by both habitat loss and climate change, particularly at high latitudes where climatic fluctuations are extreme and climatic changes are steep (Post et al., 2009; Garcia et al., 2014). Species may be particularly sensitive when genetically determined to specialize on pristine environments.

Our study investigating the selection of both habitats and associated genes provides knowledge that could be promptly used to benefit caribou, and indicates that a similar conservation science approach could be applied to other ecologically specialized and threatened species. In our study, we found that caribou carry genes that may be involved in foraging in pristine environments. This finding indicates that caribou resources, including food quality and security from human disturbance, could be protected and maintained in the old growth forests, or the remote barren-grounds areas, where the species seems to perform relatively better (Joly et al., 2010; DeCesare et al., 2014). The Government of Canada has

developed a Recovery Strategy for the Woodland Caribou (the subspecies including herds that are “endangered”, “threatened” or of “special concern”), of which the main goal is that of maintaining the species “critical habitat” (Environment Canada, 2014, 2017). These suggestions to focus on selected for habitats are transferable to other species that are similarly threatened due to human-caused habitat loss (Chase et al., 2020), and may be genetically determined habitat specialists. For example, Giant Pandas (*Ailuropoda melanoleuca*) could have all these characteristics (Zhao et al., 2013) and the focus on selected for habitats of current initiatives seems most appropriate (Xu et al., 2017). The recovery actions that are being considered for caribou in Canada include translocations and conservation breeding programs, both requiring moving animals across populations. Our study suggests that these initiatives should account for the associations between genes and habitat selection that we determined, to evaluate the potential occurrence of caribou maladaptation in the receiving environments (Leech et al., 2017).

Overall, determining ecological specialization is fundamental to understanding species adaptability to future changes and resiliency to those changes (Hoffmann & Sgro, 2011). Animals must adapt in response to anthropogenic habitat alterations (Pereira et al., 2010; Tilman et al., 2017); nonetheless, the more specialized they are, the less adaptable they might be (Hoffmann & Sgro, 2011; Guo et al., 2018). Ultimately, assessing the genetic and ecological specialization of species could contribute to detecting and addressing patterns of decline related to both habitat loss and climate change.

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Supporting Information

Supplementary methods (Appendix S1), Results (Appendix S2), tables (Appendix S3), figures (Appendix S4), citations (Appendix S5) and data files (Appendix S6) are available online. The authors are solely responsible for the content and functionality of these materials. Queries (other than absence of the material) should be directed to the corresponding author. Sequencing reads were deposited in the National Center for Biotechnology Information (NCBI), Sequence Read Archive (SRA), under BioProject accession number PRJNA659718. Spatial environmental data are freely available at <https://open.canada.ca>. Raw movement data for caribou is not publicly available as Canadian provincial and federal governments monitor this Species at Risk.

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Table 1

Table 1. Single Nucleotide Polymorphisms (SNPs), Proportion of Phenotypic Variance Explained (PVE) by single associated SNP, and genes associated to habitat selection factors in Northwestern Canada's caribou: type of caribou habitat selection factor, associated number of SNPs and genes, genes of interest (those found associated in other species of mammals) and their expression (processes regulated for and in which species), and references.

Habitat selection factors	SNPs ^a b	Mean (+SD) PVE by SNP	Genes ^a	Genes of interest ^c	Regulating for	In species	Ref. ^d
Aspect	2, 53	0.21 (+0.05)	1, 22	<i>FGF1, SLC27A1, TRPM2</i>	thermoregulation, fat metabolism, oxidative stress response	cow, human, mouse, pig	[1-5]
Elevation	0, 13	0.19 (+0.03)	0, 5	<i>SST</i>	energy metabolism	human	[6-7]
Normalized difference vegetation index (NDVI)	3, 3	0.16 (+0.01)	1, 2	<i>NOTCH2</i>	neuronal activity	reindeer	[8]

Index of snow cover	53, 23	0.20 (+ 0.06)	23, 8	<u>ADAMTSL1</u> , <u>FGF1</u> , <u>SLC24A4</u>	oxidative stress response	human, mouse, sheep	[1-2] [9- 10]
Dist. to water- saturated soils	3, 183	0.22 (+ 0.07)	3, 69	<i>CACNA1C</i> , <i>FGF1</i> , <i>KCNMA1</i> , <i>TRPM2</i> , <i>TRPM5</i>	neuronal activity, oxidative stress response, thermoregulation, taste sensing, body development	goat, horse, human, mouse, pig, reindeer	[1-3] [11-20]
Dist. to lakes	92, 6	0.21 (+ 0.08)	33, 2	<u>ADAMTSL1</u> , <u>FGF1</u> , <u>SLC24A4</u>	thermoregulation, oxidative stress response	human, mouse, sheep	[1-2] [9- 10]
Dist. to rivers	0, 46	0.21 (+ 0.07)	0, 19	<i>NOS1AP</i> , <i>TBX15</i>	neuronal activity, body development	goat, reindeer	[8] [21]
Dist. to roads	63, 34	0.20 (+ 0.04)	25, 16	<u>ALDH1A2</u> , <u>EPHB1</u> , <u>FBN2</u>	energy metabolism, oxidative stress response, body development	cow, human, mouse, reindeer	[15] [22-27]
Dist. to soil works	71, 26	0.20 (+ 0.05)	31, 7	<u>EPHB1</u> , <u>ALDH1A2</u>	energy metabolism, oxidative stress response	human, mouse, reindeer,	[14-15] [22-23]
Dist. to petr. wells	86, 88	0.22 (+ 0.04)	36, 34	<u>ADAMTSL1</u> , <u>SLC24A4</u>	energy metabolism, oxidative stress response	human, sheep	[9-10]
Dist. to trails	77, 3	0.22 (+ 0.08)	30, 1	<u>SLC24A4</u>	oxidative stress response	sheep	[12]
Land Cover (LC) 1 - Temperate or sub- polar needleleaf forest	3, 19	0.29 (+ 0.05)	1, 6	<i>ADCY1</i>	neuronal activity	human, mouse	[28-29]
LC2 - Sub-polar taiga needleleaf forest	0, 19	0.30 (+ 0.06)	0, 4	<i>IGSF5</i>	body development	cow	[30]
LC5 - Temperate or sub-polar broadleaf deciduous forest	0, 17	0.32 (+ 0.07)	0, 7	<i>FGF1</i>	Thermoregulation, oxidative stress response	human, mouse	[1] [2]
LC6 - Mixed Forest	0, 156	0.34 (+ 0.11)	0, 58	<i>KCNMA1</i> , <i>MYO18A</i>	body development, oxidative stress response	horse, human, reindeer	[14-15] [31]
LC8 - Temperate or sub-polar shrubland	2, 20	0.20 (+ 0.03)	2, 10	<u>POR</u>	fat metabolism	reindeer	[8]
LC10 - Temperate or sub-polar grassland	27, 39	0.24 (+ 0.05)	2, 13	<u>FBN2</u>	body development	cow, human, mouse,	[24-27] [32-33]
LC11 - Sub-polar or polar shrubland- lichen-moss	291, 0	0.31 (+ 0.09)	105, 0	<u>ADAMTSL1</u> , <u>FASN</u> , <u>PARP1</u> , <u>REEP1</u> , <u>SLC2A1</u> , <u>THOC2</u> , <u>ARHGEF28</u>	oxidative stress response, fat metabolisms, body development, energy metabolism, neuronal activity	cow, human, pig, polar bear, reindeer, wholly mammoth	[8-9] [34-45]
LC16 - Barren Lands	29, 103	0.24 (+ 0.06)	11, 41	<i>FOXO3</i> , <i>LONP2</i> ,	oxidative stress response, energy metabolism, neuronal activity	cow, human	[46-47]

a Details for each habitat selection-associated SNP are in Supporting Information

b First and second number indicate association with winter and summer habitat selection factors, respectively

c Genes of interest that are underlined are those associated with summer factors (not underlined associated to winter)

d [1] Keeley et al., 2019, [2] Tomaszewski et al., 2015, [3] Lin et al., 2017, [4] Holloway et al., 2011, [5] Zhao et al., 2015, [6] Tremblay et al., 2016, [7] Tostivint et al., 2019, [8] Lin et al., 2019, [9] Bigham 2016, [10] Yang et al 2016, [11] Koppe et al., 2016, [12] Wang et al., 2019, [13] Qanbari et al., 2014, [14] Cardona et al., 2014, [15] Weldenegodguad et al., 2019, [16] Tan et al., 2016, [17] Lynch et al., 2015, [18] McKemy et al., 2002, [19] Talavera et al., 2005, [20] Xu et al., 2006, [21] Wang et al., 2016, [22] Foll et al., 2014, [23] Zhao et al., 2019, [24] Xiao et al., 2017, [25] Hirano et al., 2011, [26] Gupta et al., 2004, [27] Robinson et al., 2000, [28] Wang et al., 2004, [29] Jackson et al., 2009, [30] Alshawi. 2019, [31] Bryan et al., 2017, [32] Asgari et al., 2019, [33] Flori et al., 2019, [34] Raza et al., 2017, [35] Schleinitz et al., 2011, [36] Grzes et al., 2016, [37] Asher et al 2010, [38] Luo et al., 2012, [39] Ruegg et al., 2014, [40] Delmore et al., 2015, [41] Kumar et al., 2018, [42] Kumar et al., 2020, [43] Droppelmann et al., 2013, [44] Smith et al., 2017, [45] Song et al., 2019, [46] Flachsbar et al., 2017, [47] Mészáros et al., 2014 - Full citations in Supporting Information

Figures Legends

Figure 1

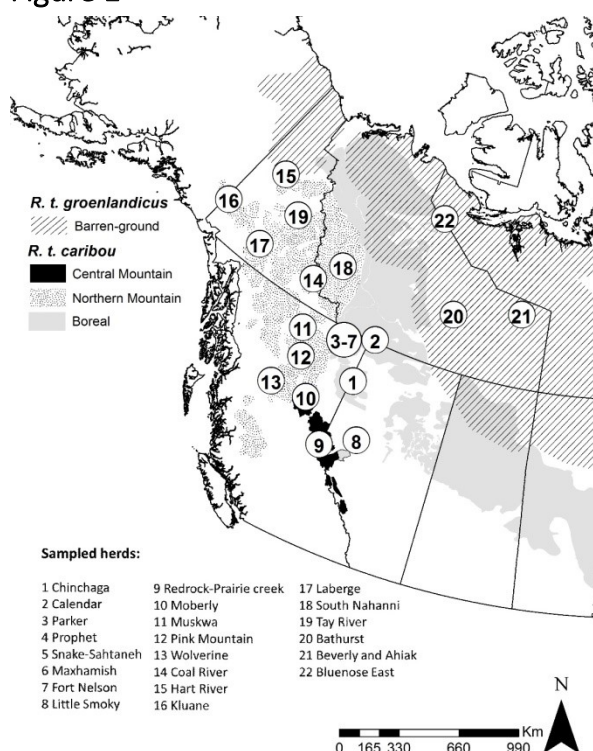


Figure 1. Caribou herds sampled in Northwestern Canada (black numbered circles). Grey-scale polygons show the distribution of subspecies and ecotypes: diagonal black lines represent the threatened Barren-ground subspecies (*R. t. groenlandicus*); black, light gray and black-dots, represent the endangered Central Mountain, threatened Boreal, and Northern Mountain (of “special concern”) ecotypes, respectively, within the Woodland caribou subspecies (*R. t. caribou*). Individuals belonging to all ecotypes were used for SNP genotyping. Radio-

collared individuals, which belonged to Barren-ground, Northern Mountain or Boreal ecotypes, were used in association studies between SNPs and habitat selection factors.

Figure 2

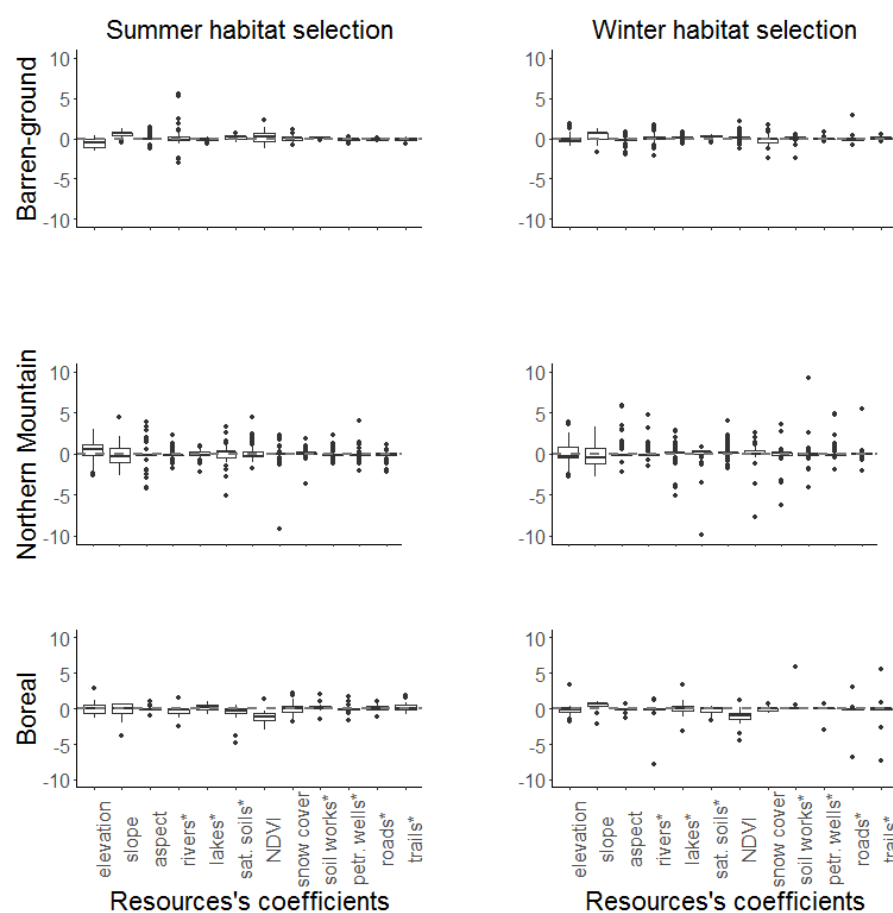


Figure 2. Coefficients of habitat selection determined with resource selection functions (RSFs) for caribou individuals. For each resource, the box shows the 1st and 3rd quartile, and the horizontal line marks the value "0" (indicating no preference). Variables marked with a star are those for which "distance to" was calculated. The type of land cover was also selected, but not shown here as selection was relative to other types (not absolute).

Figure 3

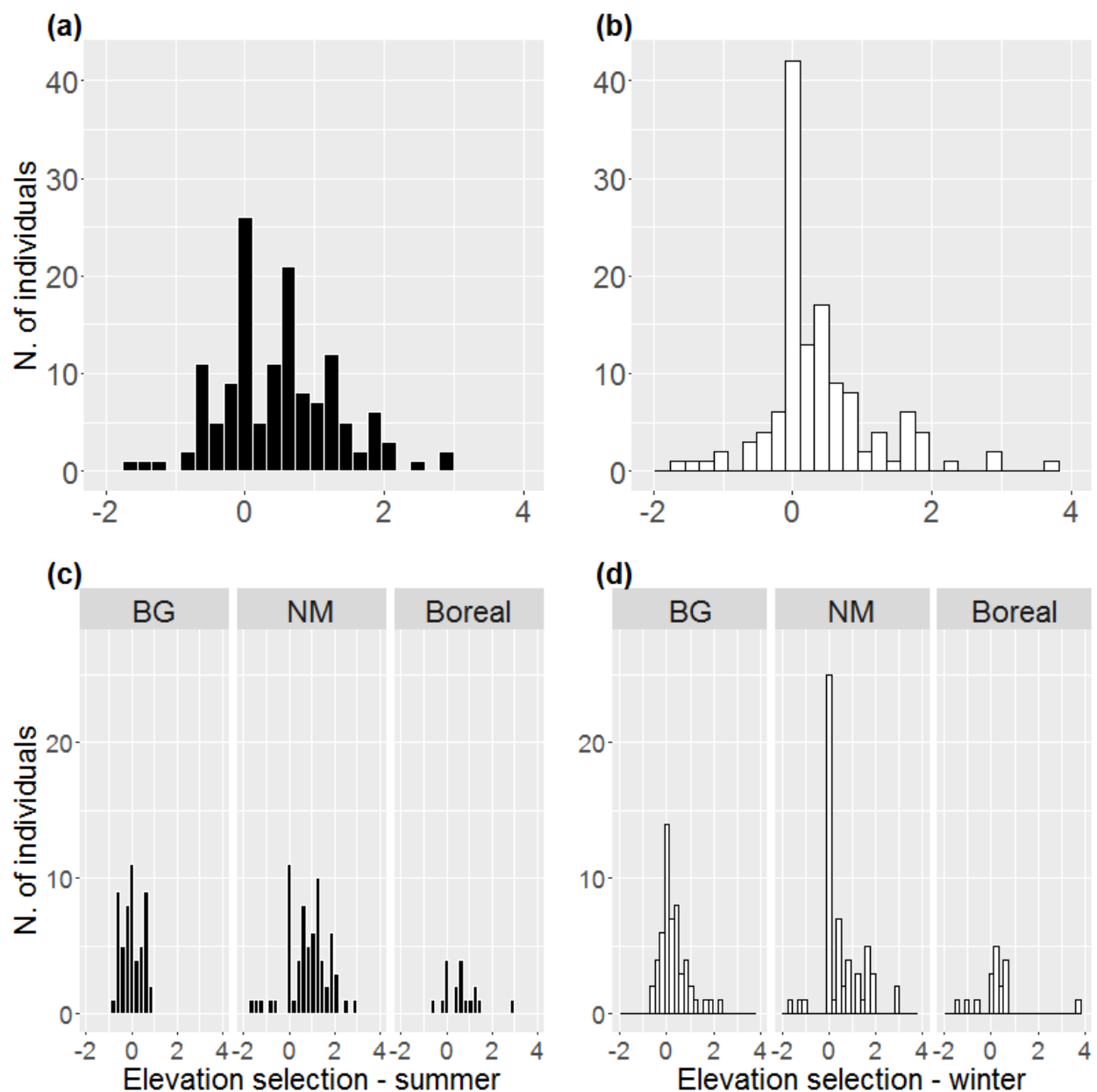


Figure 3. Frequency distribution plots of summer (black) and winter (white) beta coefficients of caribou selection for elevation (positive and negative for higher and lower elevations, respectively; zero if not selected for). Plots (a) and (b) are for all caribou, plots (c) and (d) are by ecotype (BG= Barren-ground; Boreal; NM= Northern Mountain; note that Central Mountain caribou were not collared in this study). Coefficients were obtained for 139 individual caribou with multivariate logistic regression analyses. In addition to elevation (i.e. example in this figure), 12 significant factors were also determined in habitat selection analyses, including slope, aspect, land cover, NDVI, snow cover index, and distances from roads, rivers, trails, lakes, soil works (i.e. excavated areas, such as mines), petroleum wells, and water-saturated soils (full results of seasonal habitat selection for caribou individuals are in Supporting Information).

Figure 4

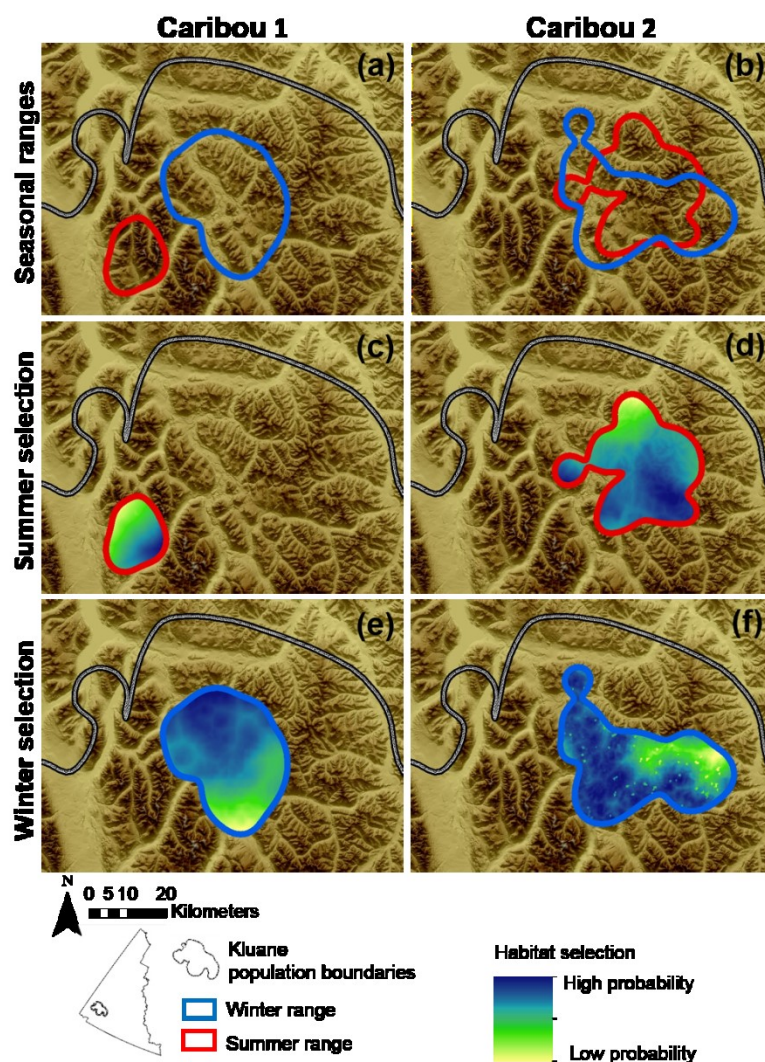


Figure 4. Seasonal ranges (Panels (a) and (b)) and habitat selection within ranges (summer in panels (c) and (d), winter in panels (e) and (f)) for two individuals (caribou 1 and caribou 2) from the same herd and ecotype (Northern Mountain). Selection was studied in a multivariate logistic regression framework, which compared resources of used and available locations within each individual's seasonal range. Cold and warm colors in maps indicate areas with high or low probability of use, respectively, assessed for the whole herd's range. In this study, similar analyses were conducted for 139 individuals.

Figure 5

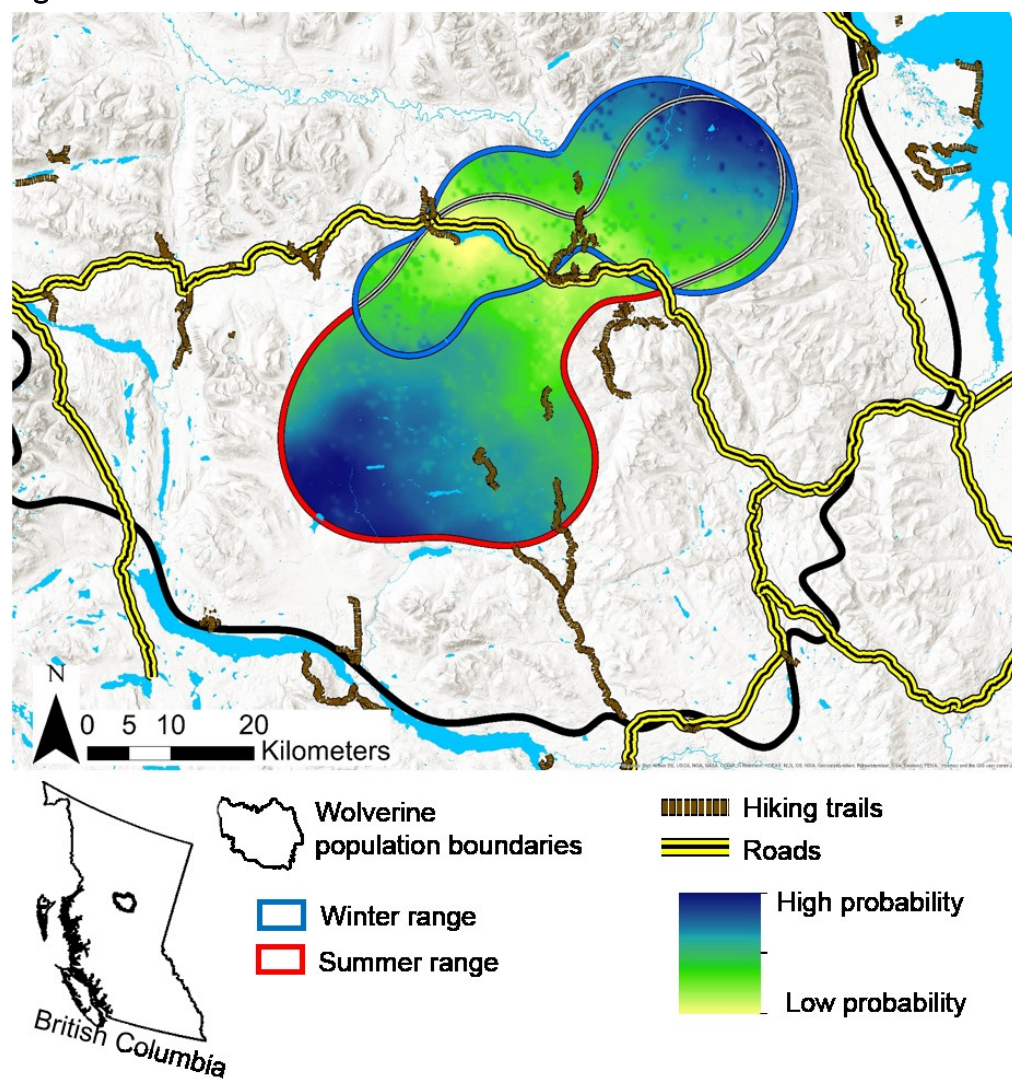


Figure 5. Habitat selection for an individual caribou from the Wolverine herd. Winter selection values are superimposed on summer selection values, as the seasonal ranges overlapped partially. Cold and warm colors indicate areas with high or low probability of use (example, areas avoided around trails or roads), respectively.

Figure 6

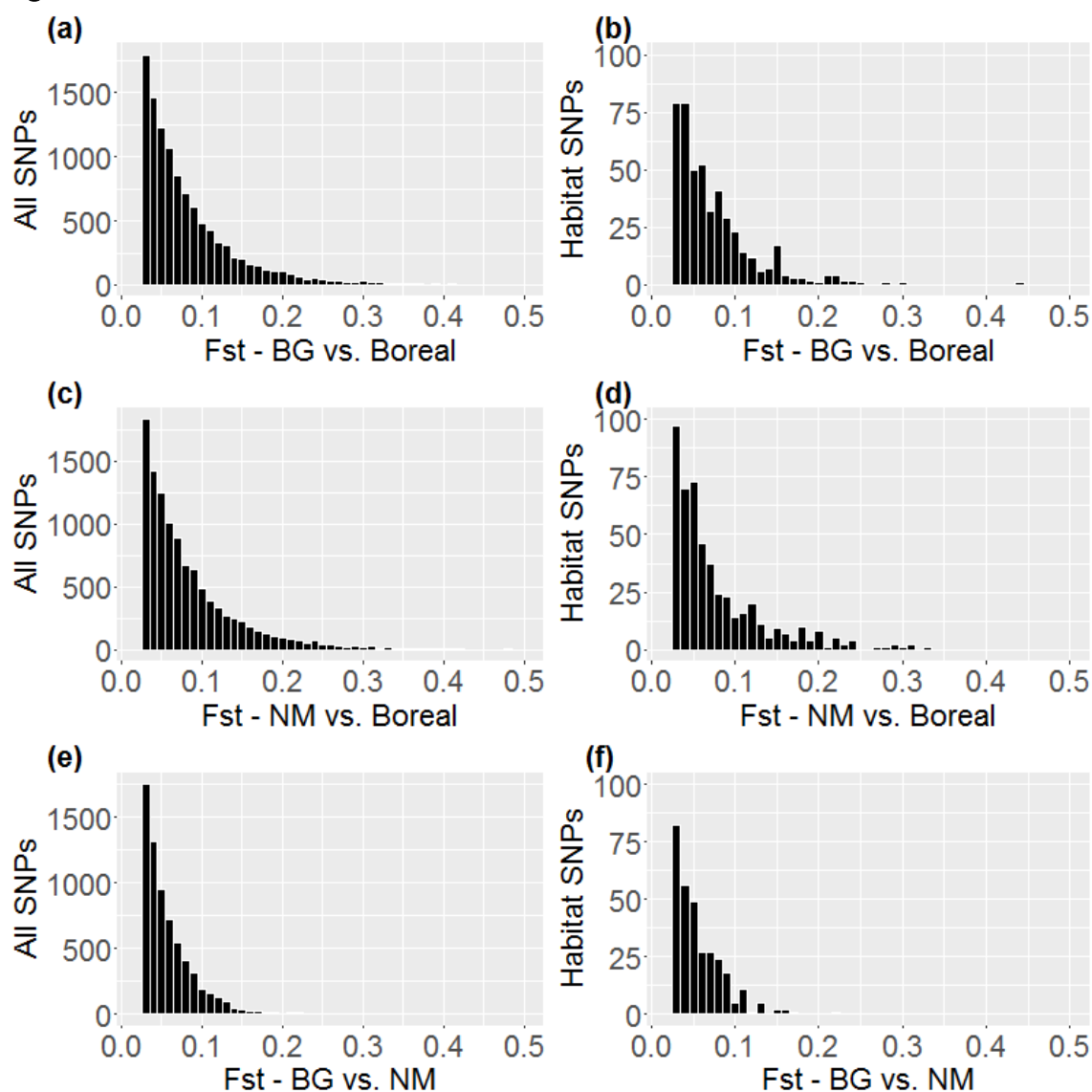


Figure 6. Frequency distribution plots of pairwise genetic distances (assessed using the F_{ST} index) between caribou ecotypes. Plots (a), (c), and (e) are calculated across all SNPs (rare alleles excluded, see Methods). Plots (b), (d), and (f) are calculated across habitat selection-associated SNPs only. F_{ST} ranging from <0.02 are not represented. Labels of ecotypes are: BG= Barren-ground; NM= Northern Mountain; and Boreal.

Figure 7

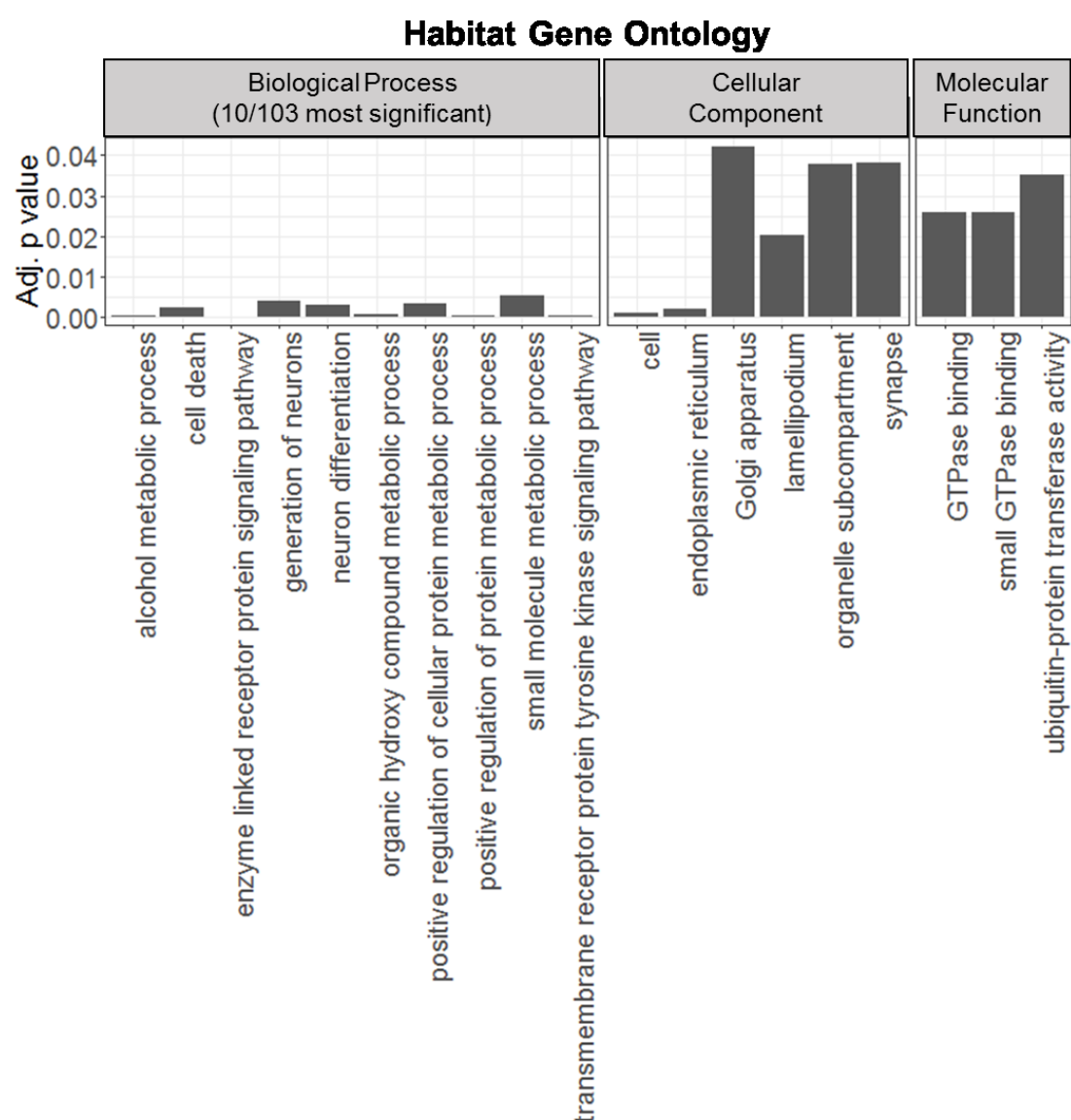


Figure 7. Gene Ontology plots of most significant genes harboring SNPs associated to habitat selection factors. Bar plots represent the top most significantly enriched (FDR Benjamini–Hochberg threshold of 5%) Gene Ontology categories within the Biological Process, Cellular Component, and Molecular Function domains. For the Biological Process domain, the most significant 10 out of 103 significantly enriched categories are shown (i.e. over-represented categories of genes). For Cellular Component and Molecular Function domains, all significant categories are shown. Gene Ontology for all habitat selection-associated SNPs are in Supporting Information.