

SUPPLEMENTAL RESULTS FOR BECKMAN, MARTINS ET AL.

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34 TABLE S1. Pairwise global F_{st} of *M. m. domesticus* populations on northern transect.

	n	≤ 330 m	320–500 m	1300–1900 m	2300–2700 m
≤ 330 m	10	---	---	---	---
320–500 m	10	0.106143	---	---	---
1300–1900 m	9	0.217272	0.204177	---	---
2300–2700 m	10	0.246651	0.241443	0.100608	---
2800–3100 m	10	0.222268	0.222668	0.108947	0.05484

35

36 **TABLE S2. Pairwise global F_{st} of *M. m. domesticus* populations on southern transect.**

	n	≤ 90 m	200–500 m	2500–2900 m	3000–3699 m
≤ 90 m	9	---	---	---	---
200–500 m	6	0.205655	---	---	---
2500–2900 m	12	0.213042	0.146307	---	---
3000–3699 m	10	0.263718	0.277857	0.178009	---
3700–3900 m	8	0.264726	0.279593	0.204191	0.083971

37

38 **TABLE S3. Variant effect predictor results for autosomal SNPs^a.**

	northern transect					southern transect				
	Total	LFMM	LFMM	PBSn1	PBSn1	Total	LFMM	LFMM	PBSn1	PBSn1
		q=0.05	q=0.01	top 1%	top 0.1%		q=0.05	q=0.01	top 1%	top 0.1%
Nonsynon.	9.094	9.16	9.28	10.50	12.60	7.56	10.61***	11.75***	10.51***	10.84
3' or 5' UTR	25.68	26.16	24.22	26.74	22.83	19.65	23.27**	25.28**	24.59***	28.92**
Synonym.	15.35	18.82***	19.76***	18.86***	26.77**	12.24	13.34	11.53	15.45***	15.66
Other	49.88	45.82***	46.74	43.86***	37.8**	60.55	52.77***	51.44***	49.45***	44.58***

39 ^a. Results expressed as percentage of total. Ranks correspond to nonsynonymous variant, 3' or 5' UTR variant,
40 synonymous mutation, and other variants including intronic, intergenic, splice variants, SNPs in flanking regions,
41 noncoding variants. ** p-value ≤ 0.01, *** p-value ≤ 0.001. P values are based on bootstrapping in which the
42 observed number of candidate SNPs were chosen from the total set of SNPs. This was repeated 1000 times, and
43 the variant effect of each SNP was calculated. Observed proportions were then compared to the proportions
44 observed in the bootstrapped data.

TABLE S4. Ancestral vs derived state of major allele at candidate SNPs^a at highest elevation for northern and southern transects.

	<u>LFMM</u>				<u>PBSn1</u>			
	<u>q = 0.05</u>		<u>q = 0.01</u>		<u>top 1%</u>		<u>top 0.1%</u>	
	Ancestral	Derived	Ancestral	Derived	Ancestral	Derived	Ancestral	Derived
north	144	379***	66	186***	145	474***	22	60***
south	145	141	63	62	254	517***	21	62***

^a. Most significant SNP per gene only included. Significant dependence between elevation and ancestral vs derived state indicated by *** ($p \leq 0.001$).

49 **TABLE S5. Ancestral vs derived state of major allele at candidate SNPs^a at highest elevation for northern and**
 50 **southern transects for X chromosome.**

	<u>LFMM $q = 0.05$</u>		<u>PBSn1 top 1%</u>	
	Ancestral	Derived	Ancestral	Derived
North	5	6	1	8**
South	54**	33	4	7

51 ^a. Most significant SNP per gene only included. Significant dependence between elevation and ancestral vs derived
 52 state indicated by ** ($p \leq 0.01$).

TABLE S6. Permutation tests^a for overlap of autosomal unique gene regions from selection scans for northern and southern transects of *M. m. domesticus*.

	Unique regions northern transect	Unique regions southern transect	Overlap	Expected overlap	P-value	Z-score
LFMM q=0.05	624	329	17	15	0.3377	0.5437
LFMM q=0.01	304	134	1	3	0.9520	-1.183
PBSn1 top 5%	2125	2607	655	438	0.0010	12.317
PBSn1 top 1%	586	699	71	32.5	0.0010	7.511
PBSn1 top 0.5%	311	378	22	9.3	0.0010	4.7445
PBSn1 top 0.1%	80	80	0	0.5	1	-0.6891

^a. Restricted to genomic regions sampled on both transects. Significant p-values in **bold**.

56 **TABLE S7. Summary information^a on candidate regions present three or more selection scans^b on northern and**
 57 **southern transects.**

Gene	Position	North			South			Combined		Summary of function
		LFMM	PBS _{n1}	Pi _{diff}	LFMM	PBS _{n1}	Pi _{diff}	LFMM	Tissue ^a	
PPP1R42	1:9968624	-	X	-	X**	X**	-	-	MS	Cytoskeleton binding activity
CHRNA2	1:87190607	X	-	-	X**	X	-	X	MS, N	Neurotransmitter binding activity at neuromuscular junction
RBM44	1:91145089	X	X	-	-	X**	-	-	GU	Homodimerization; impacts male germ cell morphology
TRAF3IP1	1:91494647	X**	X	-	-	X	-	X	I, ED	Cytoskeleton binding and signal receptor binding; Impacts organ development and interferon-beta production
CNTNAP5B	1:99772765	-	X	X	X**	X	X	-	N	Cell adhesion
ITIH5	2:10153571	X	X**	X	-	X	-	X	-	Component of collagen-containing extracellular matrix
KIF5C	2:49619298	-	X	-	X**	X	-	-	N	Motor neuron axon guidance; Apolipoprotein receptor binding activity
CDH4	2:179442431	X**	X	-	-	X	-	-	N, R	Cell adhesion; Neuron generation
HADH	3:131233419	-	X	-	X	X	-	X	MET	Positive regulation of cold-induced thermogenesis; Protein-protein interaction with Itga2
CSMD2	4:127987857	X**	X	-	X	-	-	-	N	
KDM1A	4:136550540	X	X	-	-	X	-	-	C	Chromatin binding activity; Involved in primitive erythrocyte differentiation
PERM1	4:156215868	-	X	-	X	X**	-	-	MS	Regulation of transcription
PRKAG2	5:24862744	-	X	-	X	X	-	X	C, MET	Lipid metabolism and signal transduction Apelin signaling pathway
TGFBR3	5:107106570	X**	X	-	-	X	-	-	C	Angiogenesis; blood vessel and heart development; Protein-protein interaction with Tgfr2
CTTNBP2	6:18366478	X	X	-	-	X	-	-	N	Cytoskeleton organization in glutamatergic synapse
CTU1	7:43672016	X	X	-	-	X	-	X	-	tRNA binding activity; localized at mitochondrion
KNDC1	7:139894696	X	-	-	X	X**	-	X	N	Dendrite morphogenesis
B4GALNT4	7:141061104	X	X	-	-	X	-	X	-	Transferase activity associated with Golgi apparatus
PKP3	7:141078229	X	X	-	-	X**	-	X	S	Keratinization, null allele impacts hair follicle
MUC5AC	7:141788972	X	X	-	-	X	-	X	O, R	Maintenance of lens transparency
COG2	8:124520767	X**	X**	X	X	-	-	X	GU	Golgi organization and transport
SRGAP1	10:121780991	X**	X	-	X	X	-	-	N	Signal transduction and cell migration

SH3PXD2B	11:32347820	X	X	-	X**	X	-	X	C, MS	Essential to organ development and osteoblast fate; null allele
									N, O	mutants have severe skeletal and cardiac defects
ANKFN1	11:89390092	-	X	X	X**	X**	-	X	B	Involved in behavioral fear response, balance, locomotion.
DHX58	11:100694884	X	X	-	-	X**	-	-	I, N	Involved in innate immune response and response to virus
STAT5B	11:100780731	-	X	-	X	X	-	-	ED, I	Involved in organ development, cell surface receptor signaling pathway and lymphocyte activation
CCDC103	11:102881224	-	X	-	X**	X	-	-	-	Critical in determinization of left/right symmetry
SYT16	12:73997624	X	X	X	-	X	-	X	N	Integral component of membrane; involved in exocytosis
DNAH11	12:117877982	X**	X	-	-	X	-	X	-	Critical in determinization of left/right symmetry
NALCN	14:123276634	X	-	-	X	X	-	X	N	Cation transmembrane transport; Regulation of resting membrane potential
ITGBL1	14:123659971	X**	-	-	X**	X	-	X	C, MS	Involved in cell adhesion, cell-matrix adhesion
									N	Integrin-mediated signaling pathway Colocalizes with Mmp2
FGF14	14:123977907	X**	X	-	X	X	-	X	C, N, R	Growth factor activity that includes heparin binding activity; Involved in cardiac conduction and muscle contraction
COL22A1	15:71795795	X**	X	X	X	X	-	-	C, N	Component of extracellular matrix organization, Key to collagen formation and angiogenesis
MROH5	15:73786936	X	X	-	X	X	-	-	-	---
MYOM1	17:71003332	X	-	-	X	X**	-	X	MS	Involved in muscle contraction, exhibits homodimerization
PPP1R21	17:88530124	X**	X	-	-	X	-	X	N	Impacts early embryo development
STON1	17:88597615	X**	X	-	X	X	-	X	GU	Involved in cell adhesion, cellular signaling and cell migration
GTF2A1L	17:88668660	X**	X	-	-	X	-	X	ED	Transcription factor active in early embryo
LHCGR	17:88716481	X**	X**	-	-	X	-	X	ED	Hormone receptor activity; impacts reproductive system
PUM3	19:27388698	X**	X**	-	-	X	-	X	-	Regulation of translation through mRNA binding
ENO4	19:58943425	X**	X	-	-	X	-	X	GU	Involved in cilium organization; impacts sperm motility

^a. N: Nervous system, MS: musculoskeletal, I: immune, R: respiratory, MET: metabolism, C: cardiovascular, GU:

geniurinary, ED: Embryo development, O: ocular, B: BEHAVIOR, S: SKIN

^b X indicates significance value of $q \leq 0.05$ for LFMM, top 1% for *PBSn1* and top 1 percent for π_{diff} . ** indicates a

significance value of $q \leq 0.01$ for LFMM or the top 0.1% of *PBSn1* values.

62 TABLE S8. Permutation test^a results for autosomal SNP overlap.

	Unique SNPs	Unique SNPs	overlap	Expected	P-value	Z-score
	northern transect	southern transect		overlap		
LFMM q=0.05	1787	944	1	123	1	-3.9759
LFMM q=0.01	809	400	0	24	1	-1.5541
PBSn1 top 5%	6034	8451	598	4033	1	-26.3044
PBSn1 top 1%	1171	1688	38	157.4	1	-4.576
PBSn1 top 0.5%	564	841	10	38.5	0.996	-2.0611
PBSn1 top 0.1%	124	156	0	1.5	1	-0.6919

63 ^a. Restricted to genomic regions sampled on both transects.

64 **TABLE S9. Permutation tests^a for overlap of unique gene regions on X chromosome from selection scans for**
 65 **northern and southern *M. m. domesticus*.**

	Unique regions northern transect	Unique regions southern transect	Overlap	Expected overlap	P-value	Z-score
LFMM q=0.05	13	97	2	2.59	0.77	-0.42
PBSn1 top 1%	9	14	0	0.30	1	-0.57

66 ^a. Restricted to genomic regions sampled on both transects.

67 **TABLE S10. Permutation tests^a for overlap SNPs on X chromosome from selection scans for northern and**
 68 **southern *M. m. domesticus*.**

	Unique regions northern transect	Unique regions southern transect	Overlap	Expected overlap	P-value	Z-score
LFMM q=0.05	13	100	0	2.56	1	-1.71
PBSn1 top 1%	10	14	0	0.31	1	-0.56

69 ^a. Restricted to genomic regions sampled on both transects.

70 Supplemental Figures.

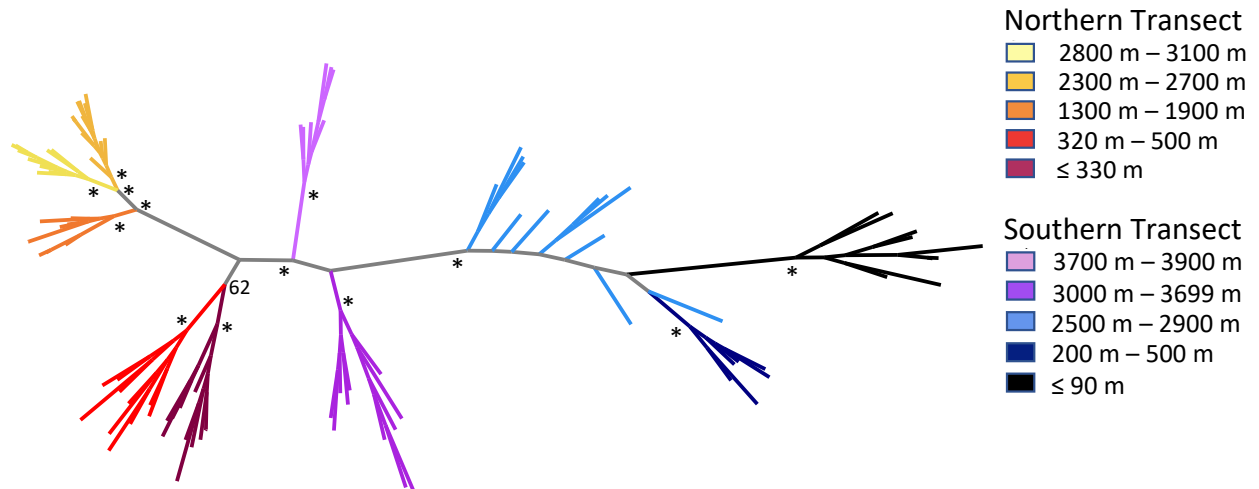


Figure S1. Unrooted maximum likelihood tree of South American *M. m. domesticus*. Phylogeny was estimated with 96 individuals and 63,513 SNPs pruned for linkage disequilibrium. Bootstrap support indicated at key nodes; * indicates bootstrap support of ≥ 96 .

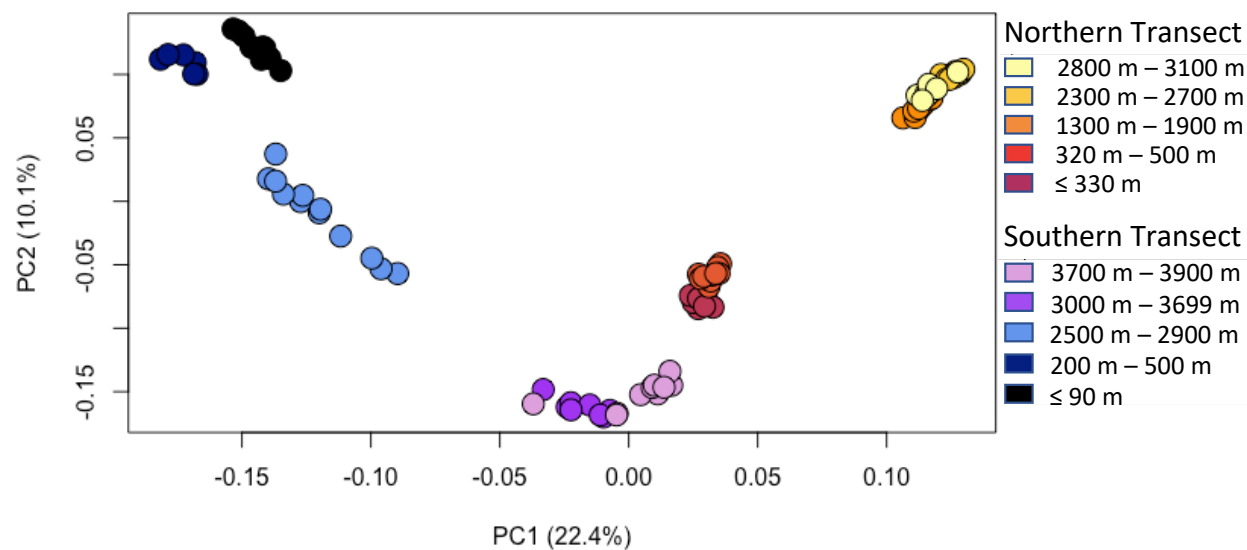


Figure S2. Principal component analysis of northern and southern transects individuals. Principal component analysis was conducted with 380,272 SNPs and 96 house mice. Samples are colored by elevation and transect; see legend on right.

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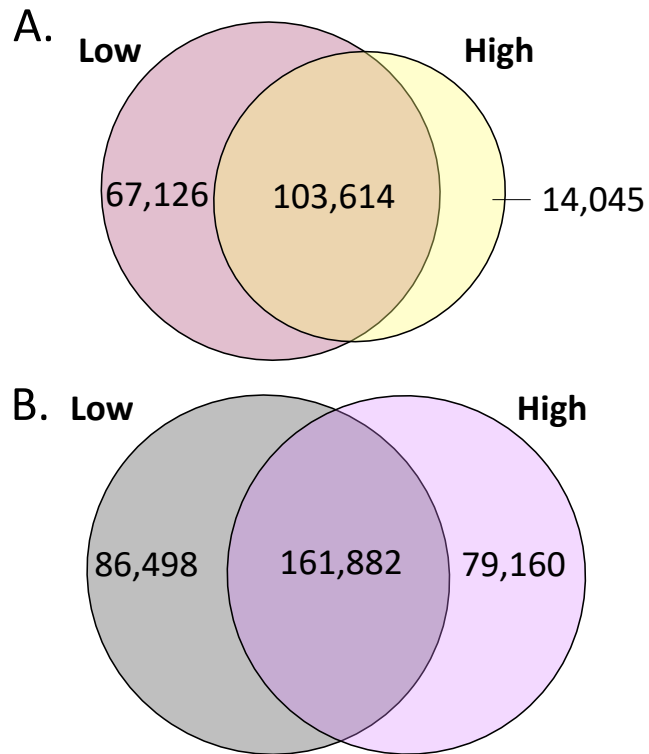


Figure S3. Shared and unique variable sites for high and low populations. A. northern transect. B. southern transect. Sites in overlap were variable in both high and low populations.

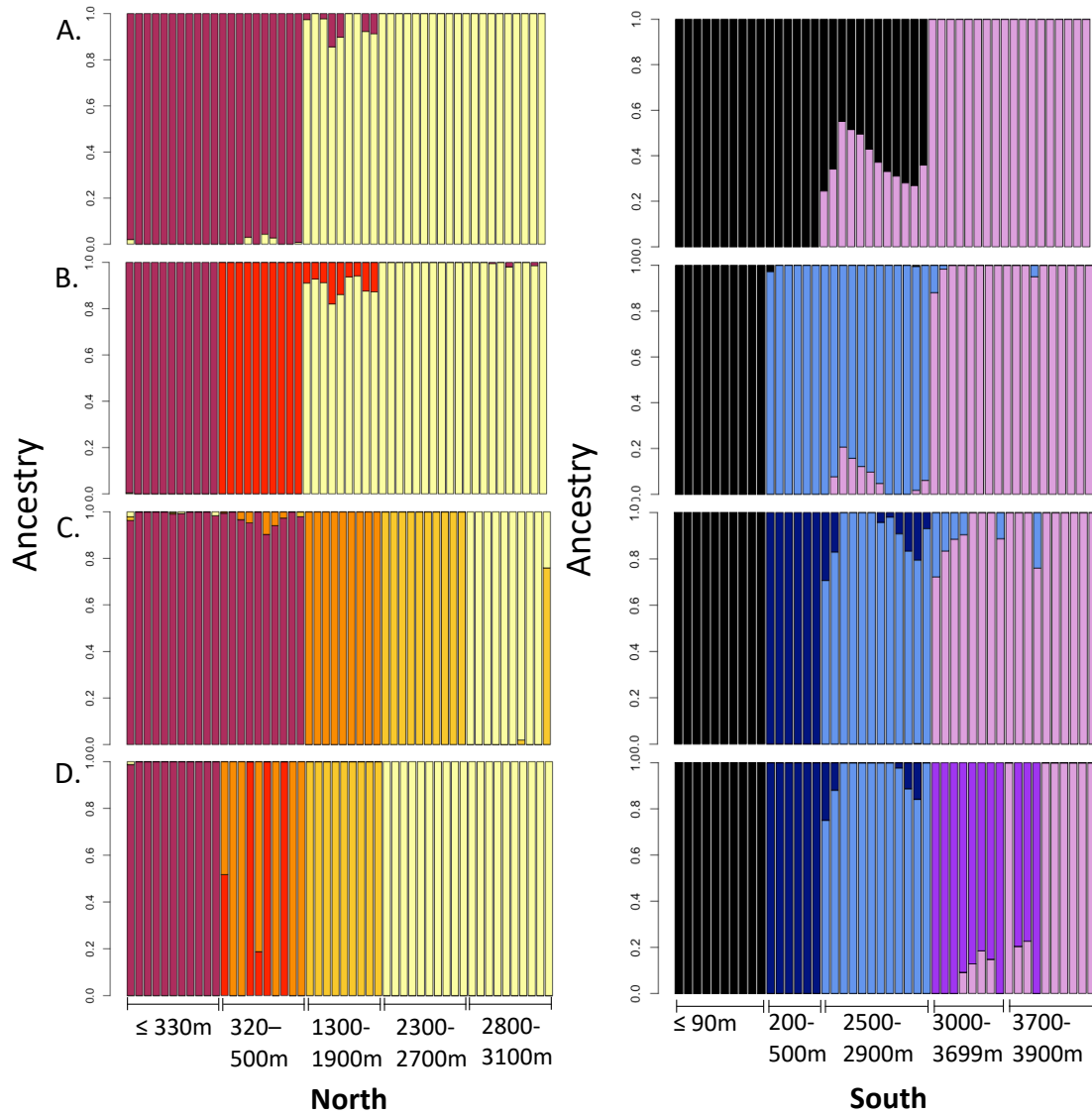


Figure S4. Admixture analyses *M. m. domesticus*. Individuals from northern (left) and southern (right) transects at **A.** K =2, **B.** K=3, **C.** K=4, and **D.** K=5; elevation of capture indicated at bottom of graphs. Colors ordered by elevation, as in Fig. 2.

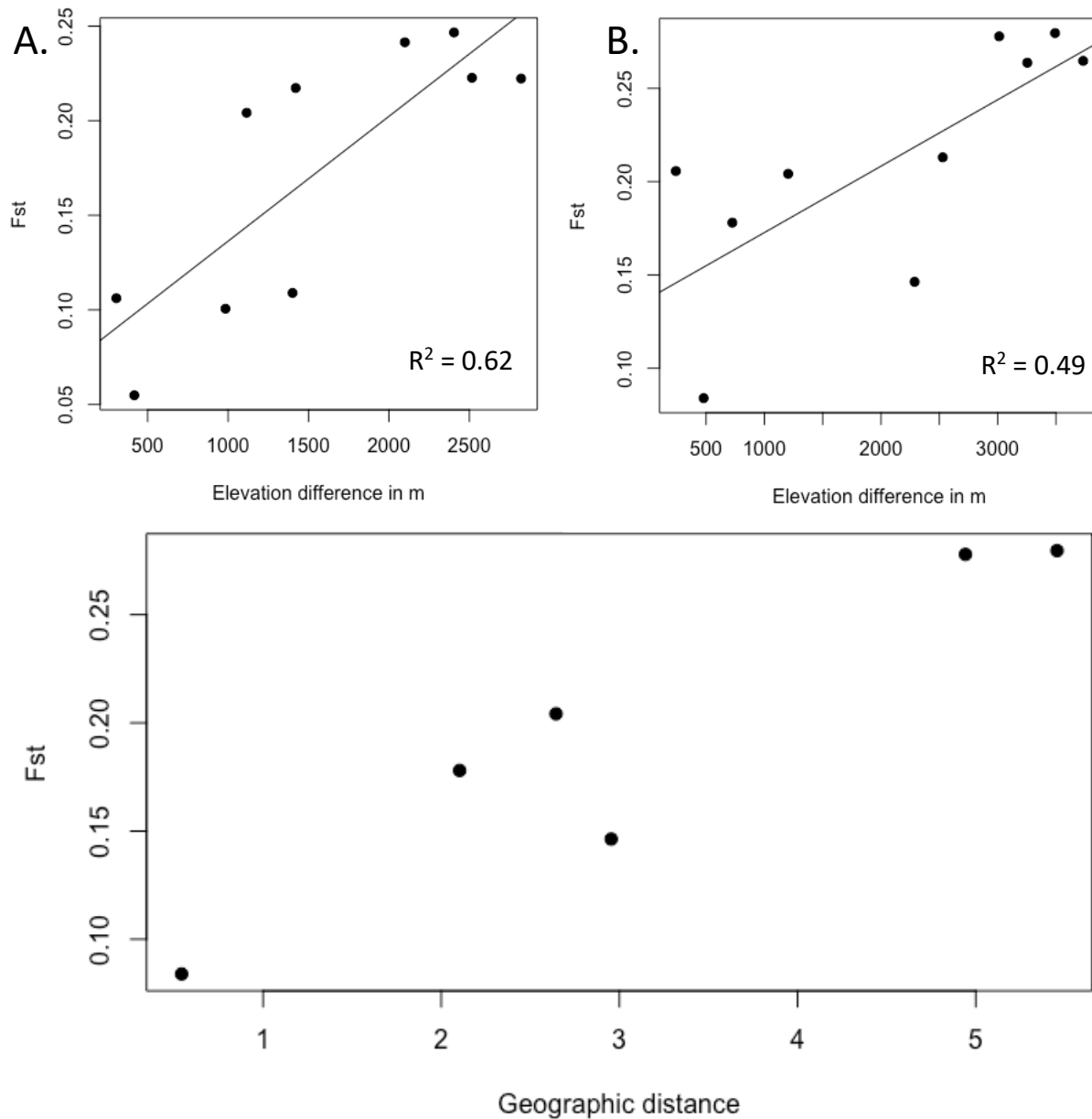


Figure S5. *M. m. domesticus* pairwise genetic differentiation (F_{ST}) across space. (A) Pairwise F_{ST} by difference in elevation (m) for the northern transect. (B) Pairwise F_{ST} by difference in elevation (m) for the southern transect. (C) Pairwise F_{ST} by geographic distance in degrees, only including *M. m. domesticus* populations on the southern transect that were at or above 300 m.

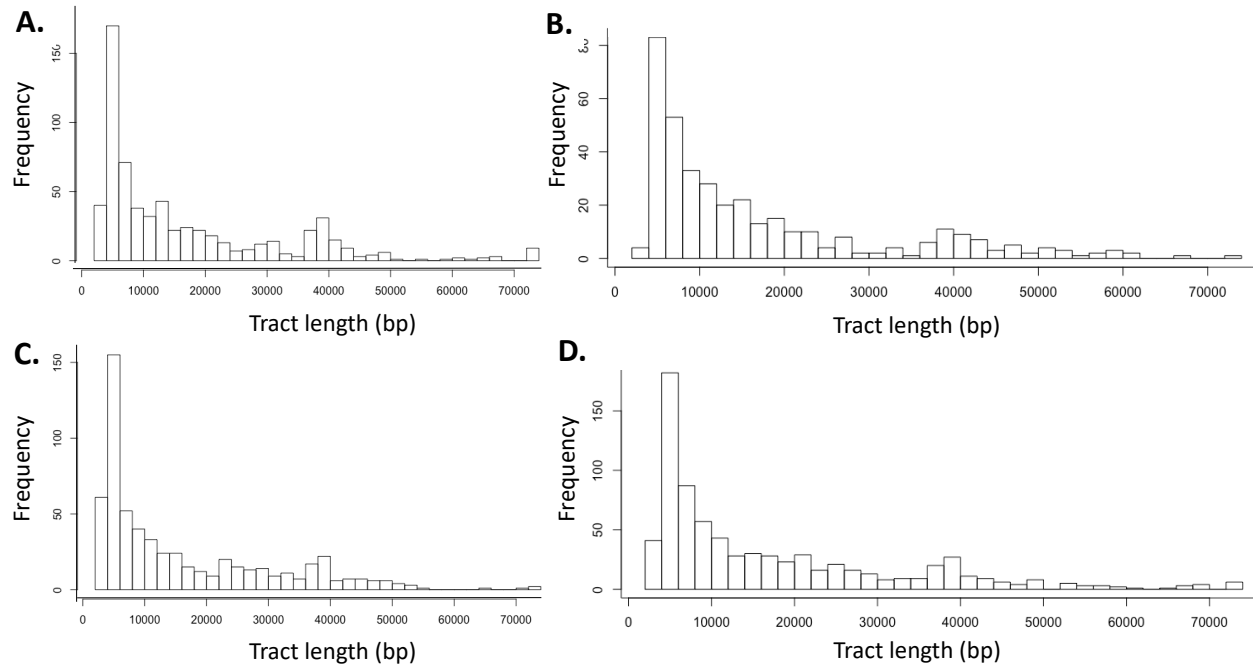


Figure S6. Tract length of consecutive significant SNPs in *M. m. domesticus* selection scans. Histograms of tract lengths shown for **A.** LFMM analysis, $q=0.05$ in northern transect. **B.** LFMM analysis in southern transect. **C.** PBSn1, top 1%, in northern transect. **D.** PBSn1 in southern transect.

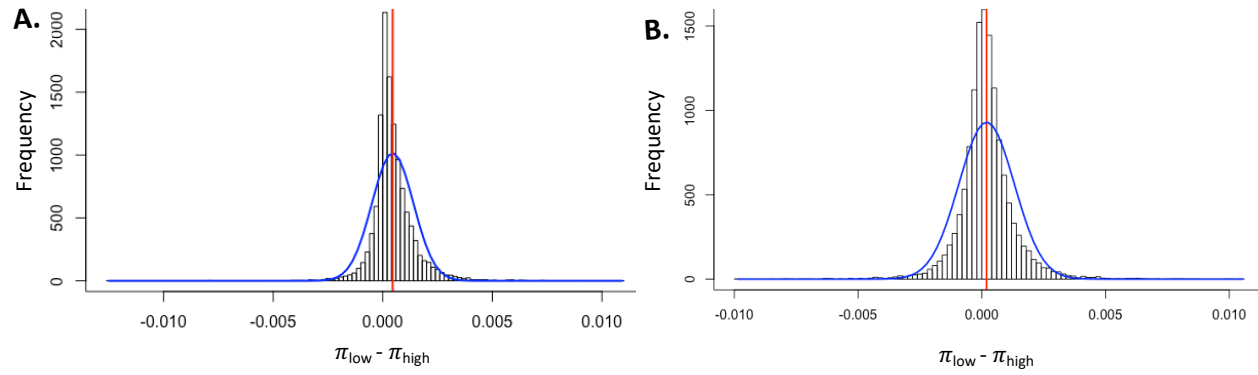
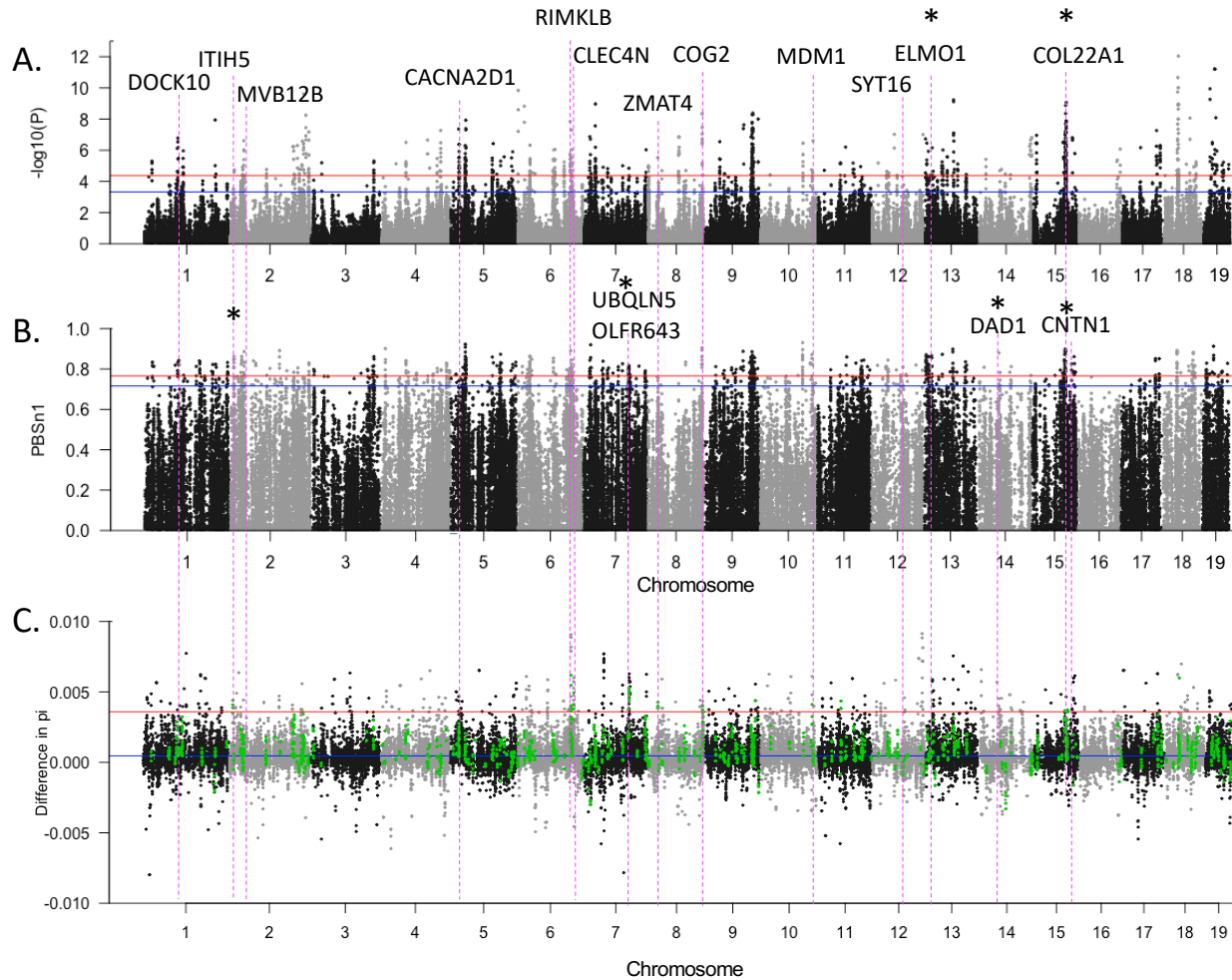


Figure S7. Distribution of the difference in nucleotide diversity (π) between high and low populations. Nucleotide diversity difference was calculated in 100 kb non-overlapping windows. The mean of each distribution is shown in red, and the expected normal curve is represented in blue. **A.** northern transect. **B.** southern transect.



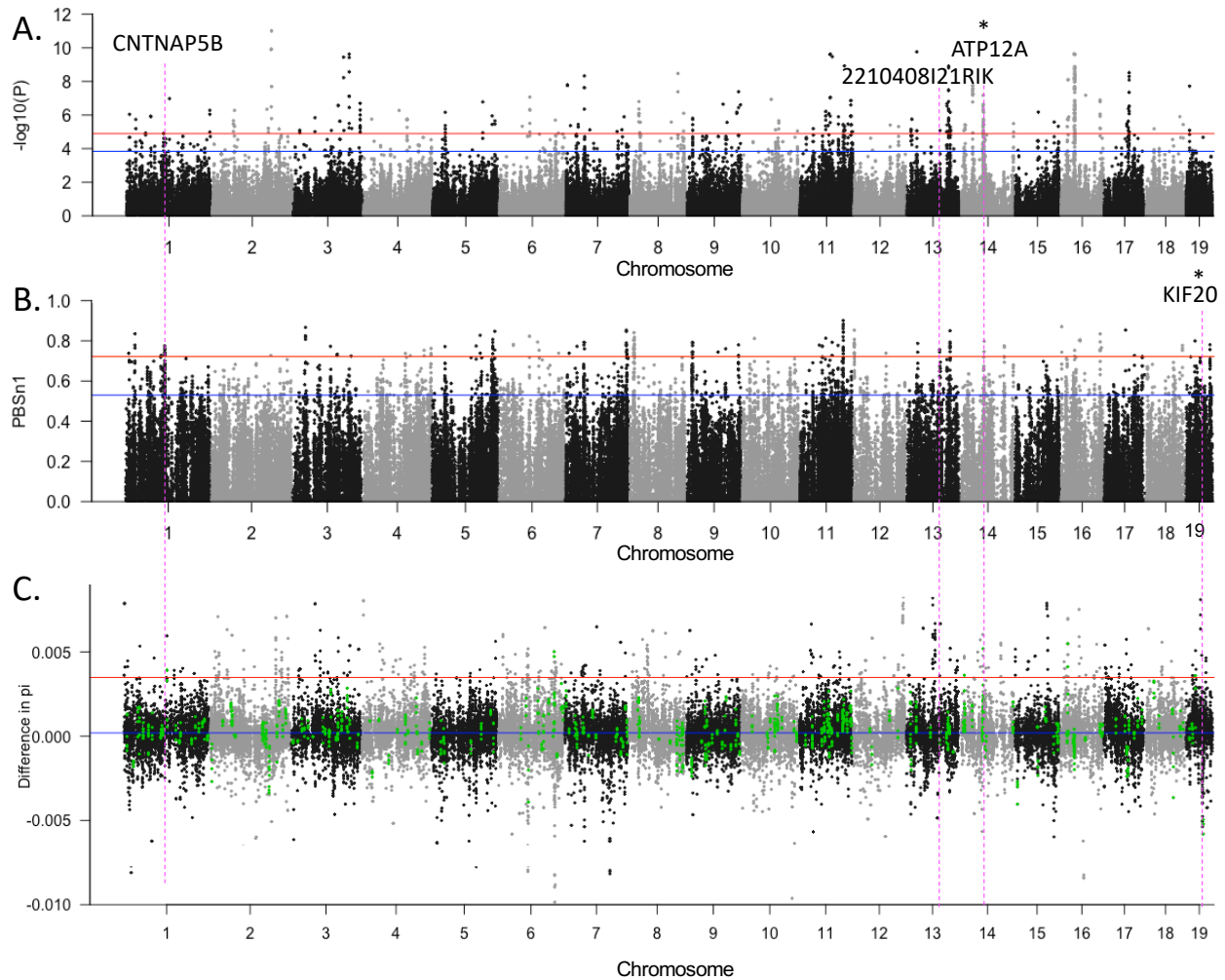


Figure S9. Southern transect *M. m. domesticus* autosomal selection scan results and nucleotide diversity. **A.** LFMM results with elevation ($n=45$; 351,786 SNPs) with $q=0.05$ indicated in blue and $q=0.01$ in red. **B.** PBSn1 results ($n=45$; 176,993 SNPs) with top 1 (blue) and 0.1 (red) percent thresholds shown. **C.** Difference in nucleotide diversity (π) between populations < 90 m and > 3700 m in sliding 100 kb windows with 25 kb step. SNPs that were significant in LFMM analysis with $q=0.05$ highlighted in green. Purple dashed lines show genes shared in all analyses (3); genes in top 1 percent of values in C that also show an exceptional stretch of significant SNPs in A and B (1, panel A) or just B (1, panel B) are indicated with *.

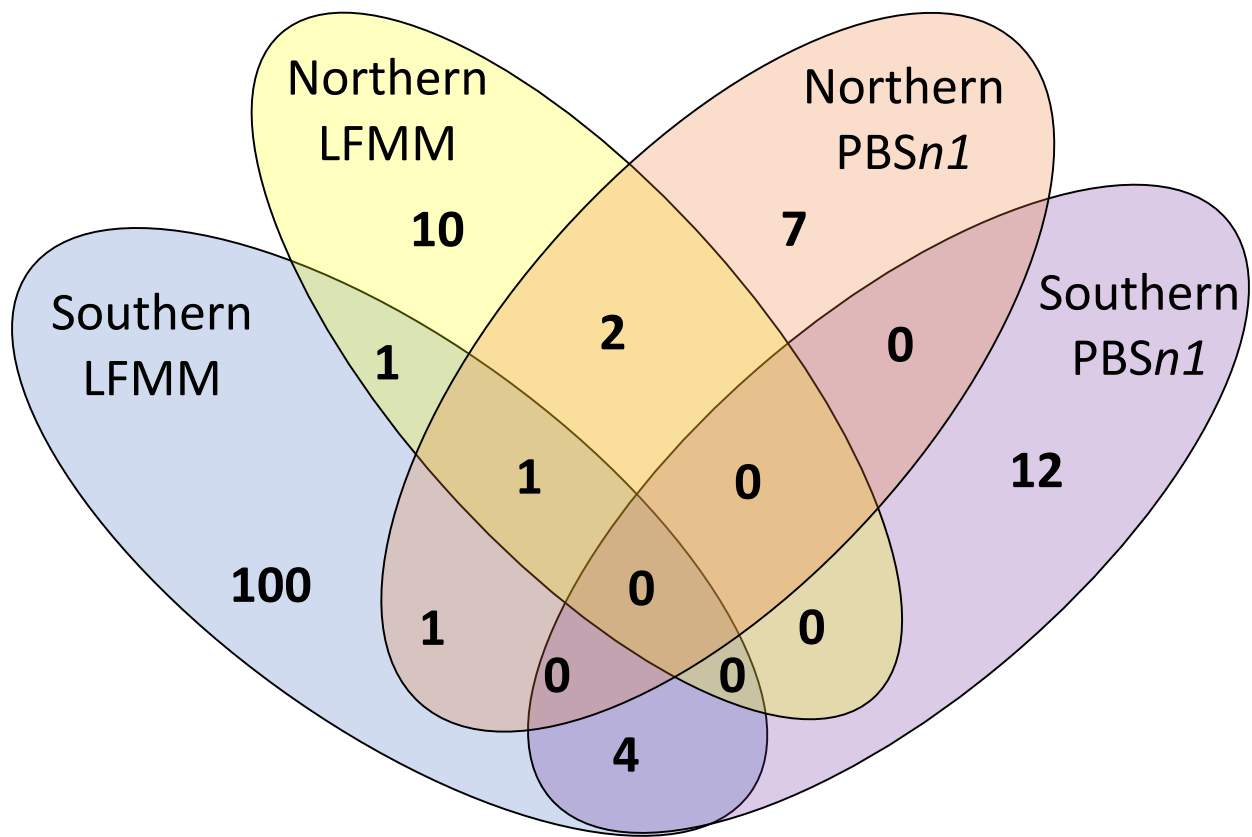


Figure S10. Transect gene overlap of selection scan candidates on X chromosome.
Selection scans with latent factor mixed modeling with $q=0.05$ and top 1 percent of *PBSn1* candidates.