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## Supporting Information for "The Molecular Basis of High-Altitude Adaptation in Deer Mice"

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## The Molecular Basis of High-Altitude Adaptation in Deer Mice

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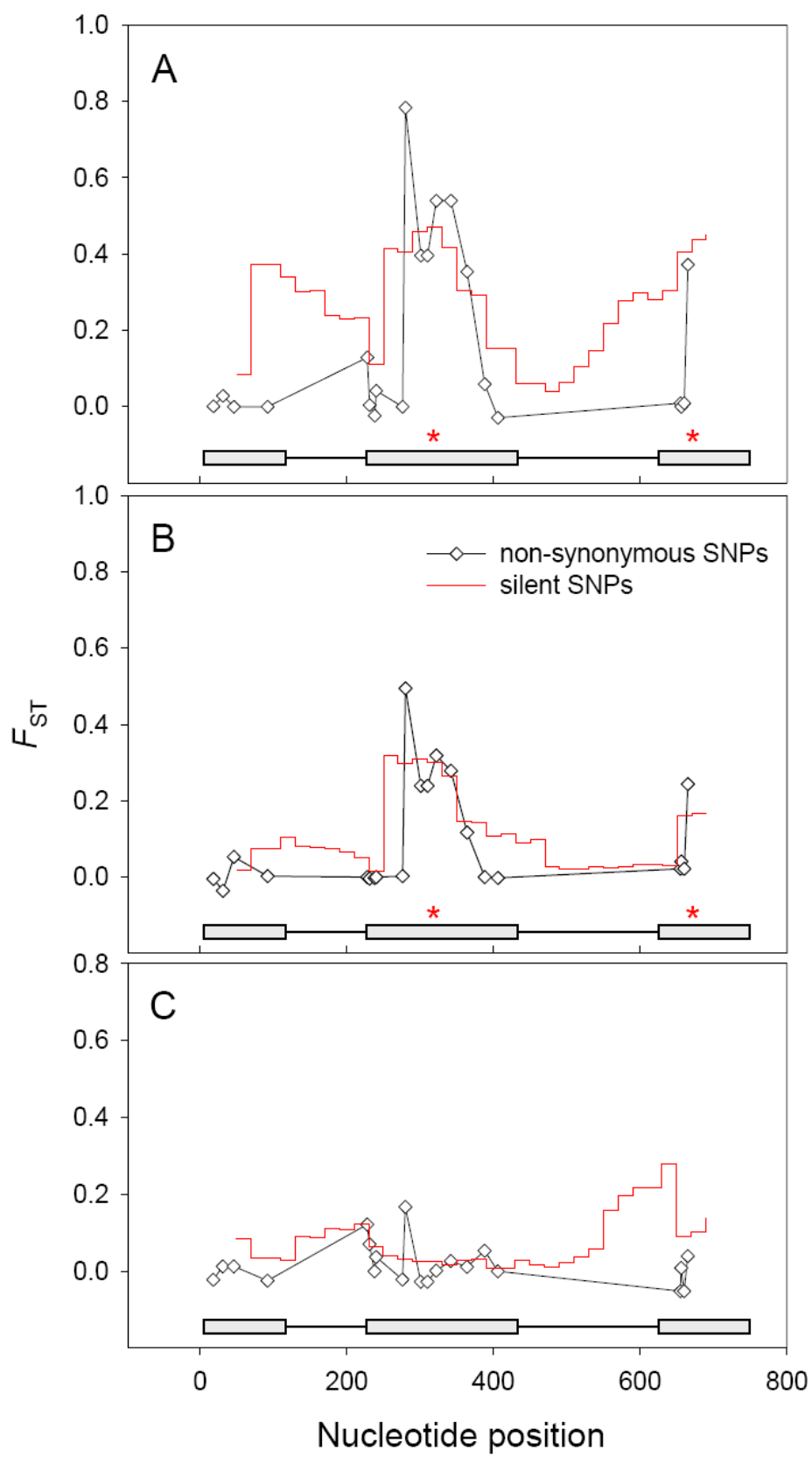
### Figure S1: Variation in Site-Specific Levels of Altitudinal Differentiation across the 5' $\alpha$ -Globin Gene of *P. maniculatus*

(A) Comparison between high- and low-altitude samples (Mt. Evans, Colorado [4,347 m] versus Pawnee County, Kansas [620 m]).

(B) Comparison between high- and low-altitude samples (Mt. Evans versus Yuma County, Colorado [1,158 m]).

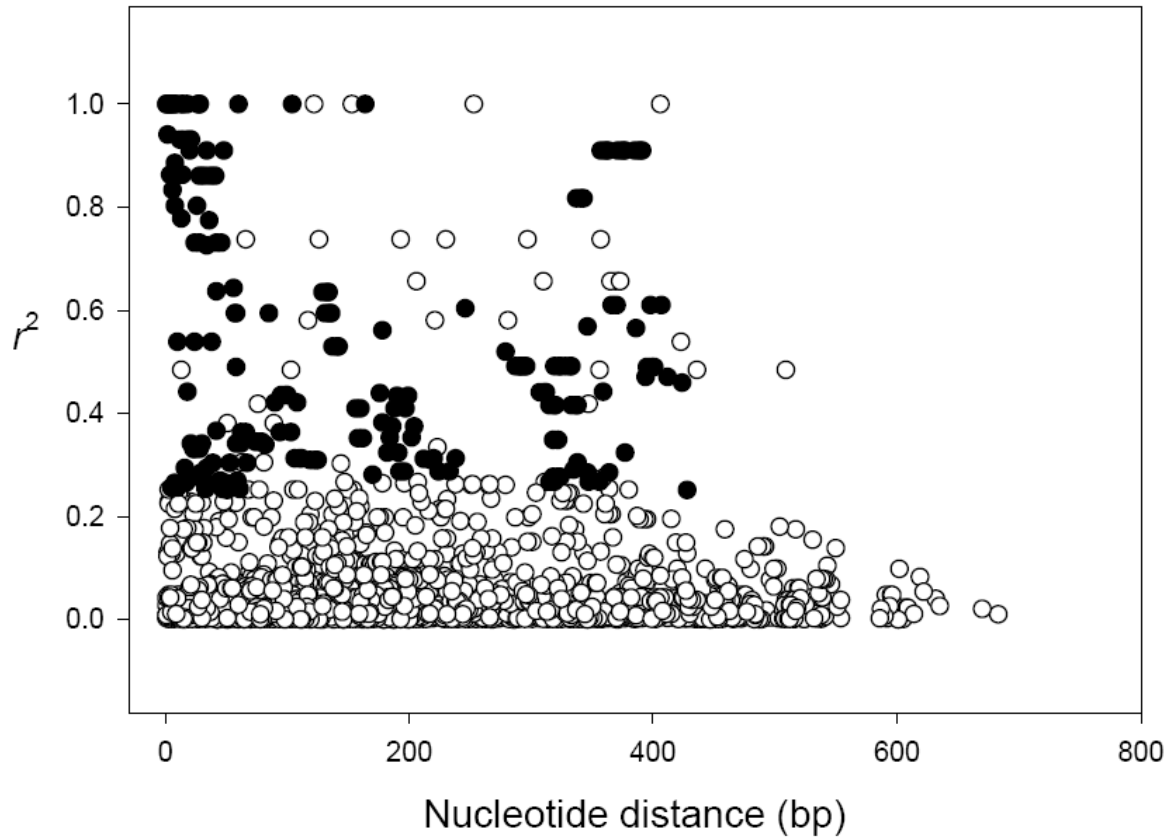
(C) Comparison between the two low-altitude localities (Pawnee County versus Yuma County).

Open diamonds denote  $F_{ST}$  values for nonsynonymous nucleotide polymorphisms ( $n = 21$  sites). The red line represents a sliding-window plot of variation in site-specific  $F_{ST}$  values for synonymous and noncoding nucleotide polymorphisms across the gene. Red asterisks mark the mid-point of 100-bp windows containing one or more replacement polymorphisms that exhibited higher-than-expected  $F_{ST}$  values.



## Figure S2: Relationship between Pairwise Linkage Disequilibrium and Distance in bp

Filled symbols denote 201 pairwise associations that were significant by a Fisher's exact test after Bonferroni correction



## Accession Numbers

The GenBank (<http://www.ncbi.nlm.nih.gov/Genbank>) accession numbers for all sequences discussed in this paper are [EF369525–EF370032](#).

**Table S1: Amino Acid Variation in the  $\alpha$ -Globin Genes of High- and Low-Altitude Deer Mice**

Amino acid replacement polymorphisms in deer mice where the derived variant is present at a frequency of >0.100 in the high-altitude sample.

Nucleotide site	Codon change	Amino acid replacement <sup>1</sup>	Frequency of derived variant at high-altitude	$F_{ST}$		
				High vs. Low (Mt. Evans vs. Pawnee Co.)	High vs. Low (Mt. Evans vs. Yuma Co.)	Low vs. Low (Yuma Co. vs. Pawnee Co.)
5' $\alpha$ -globin						
18	GAA→GAC	5(A3)Glu→Asp	0.933	0.001	-0.005	-0.022
280	CAC→CCC	50(CD15)His→Pro	0.833	0.784**	0.494**	0.167
322	GAC→GGC	64(E13)Asp→Gly	0.933	0.540**	0.318**	0.002
342	GGC→AGC	71(EF1)Gly→Ser	0.933	0.540**	0.278**	0.027
364	GGT→GCT	78(EF8)Gly→Ala	1.000	0.354	0.117	0.011
665	GAG→GAT	116(GH4)Glu→Asp	0.553	0.373*	0.244*	0.039
3' $\alpha$ -globin						
7	CTC→TTC	2(NA2)Leu→Phe	0.115	0.127	-0.005	0.089
	GTC→TTC	2(NA2)Val→Phe				
18	GAG→GAC	5(A3)Glu→Asp	0.231	-0.035	0.057	-0.019
37	ACT→GCT	12(A10)Thr→Ala	0.115	0.013	0.081	-0.042
59	GGC→GAC	19(AB1)Gly→Asp	0.160	0.013	-0.042	-0.011
282	GGC→AGC	51(CD16)Gly→Ser	0.115	-0.031	0.246*	0.124
364	GGT→GCT	78(EF8)Gly→Ala	0.307	0.109	0.260*	0.027
393	GCT→ACT	88(F9)Ala→Thr	0.154	0.077	0.024	-0.020
634	CTG→CAG	105(G12)Leu→Gln	0.696	0.270	0.540**	0.063

<sup>1</sup>For each polymorphism, the derived variant is shown on the right (e.g., for 'Leu→Phe', Leu is ancestral and Phe is derived).

\* $P < 0.05$ , \*\* $P < 0.001$  under a neutral model of population structure (see *Materials and Methods*).

**Table S2: Additional Information on Sequenced Loci:** Primer sequences for nuclear loci in *P. maniculatus*.

Locus	Sequenced gene region	Length (bp)	Primers	
5' $\alpha$ -globin	Exons 1-3, introns 1-2	743	D-1518	5' CTTGCTCTGCAGCGCACC 3'
			D-2387R	5' CAAAGACCAAGAGGTACAG 3'
3' $\alpha$ -globin	Exons 1-3, introns 1-2	743	KEP107	5' GGCCATGGTATGTCTCTAACTCC 3'
			KEP97	5' CGTTAACACACTTCCTTGGGTC 3'
$\beta$ -globin	Exons 1-3, introns 1-2	1140	BETA_PM_F1	5' GTAGAGCAGGATCAGTTGC 3'
			BETA_PM_R1	5' ACTGACCTTTGAGCACAGAC 3'
$\beta$ -fibrinogen	Intron 7	614	BFIB-R1	5' ATTCACAACGGCATGTTCTTCAG 3'
			BFIB-R2	5' AANGKCCACCCCAGTAGTATCTG 3'
Vimentin	Intron 8	785	VIM-E8 F1	5' AGAACACTCCTGATTAAGACG 3'
			VIM-E9 R1	5' GCATCACGATGACCTTGAATAA 3'
LCAT	Exons 3-6, introns 3-5	456	LCAT-F2	5' CTGGTACAGAATCTGGTTAAC 3'
			LCAT-R5	5' TAAGACATCCTAATGGTGCTG 3'
RAG1	Exon 1	1183	S77	5' TCCATGCTTCCCTACTGACCTG 3'
			S71	5' TGGCTTCTGGTTATGGAGTGGA 3'
AP5	Exons 2-3, intron 2	385	AP5120-F1	5' AATGCCCCATTCCACACAGC 3'
			AP5 564-R1	5' GCAGAGACGTTGCCAAGGTG 3'