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no other notable global correlations. These effects may be important locally, but they do not represent a dominant global pattern. Additionally, we have not evaluated the possible effects of 3D slab morphology on trench-parallel flow in the wedge (e.g., *26*) or beneath the slab (*14*, *27*). Such flow is likely important locally and may serve to strengthen or otherwise modulate the trench-parallel flow induced by trench migration.

Our model essentially requires a thin decoupling zone between the downgoing slab and the subslab mantle, because we observe no detectable anisotropic signal from slab-entrained flow. [Cascadia represents an exception (*8*) to this rule; this may be a consequence of the very young age of the subducting lithosphere or the region's complicated subduction history and slab morphology.] This decoupling zone appears to be universal, in that slab-entrained flow is not generally detected even for subduction zones with a nearly stationary trench, and may be a consequence of the entrainment of a thin layer of buoyant asthenosphere (*28*). The inferred subslab flow field also requires a partial barrier to mantle flow beneath the slab, as proposed by (*14*), as well as an effective barrier to horizontal flow in the trench-normal direction (*29*), so that mantle material is forced to escape laterally in response to the motion of the trench. The barrier to entrained flow beneath the slab provides a constraint on mass transfer between the upper and lower mantle, which in turn has major implications for mantle evolution and dynamics. Finally, the existence of trench-parallel flow in the mantle wedge as a common (although not ubiquitous) phenomenon implies that along-strike transport of mantle material is important for many arcs, with consequences for magma genesis, volatile transport, and thermal structure.

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Supporting Online Material

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A Localized Negative Genetic Correlation Constrains Microevolution of Coat Color in Wild Sheep

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The evolutionary changes that occur over a small number of generations in natural populations often run counter to what is expected on the basis of the heritability of traits and the selective forces acting upon them. In Soay sheep, dark coat color is associated with large size, which is heritable and positively correlated with fitness, yet the frequency of dark sheep has decreased. This unexpected microevolutionary trend is explained by genetic linkage between the causal mutation underlying the color polymorphism and quantitative trait loci with antagonistic effects on size and fitness. As a consequence, homozygous dark sheep are large, but have reduced fitness relative to phenotypically indistinguishable dark heterozygotes and light sheep. This result demonstrates the importance of understanding the genetic basis of fitness variation when making predictions about the microevolutionary consequences of selection.

Evolutionary theory states that directional selection on a heritable trait should result in evolutionary change (*1*). Analyses of long-term data sets from wild vertebrate populations reveal directional selection on heritable traits, yet many studies report no microevolutionary change (stasis) or, in some cases, responses in the opposite direction to that predicted (*2*). Explaining such discrepancies is a major challenge in evolutionary biology (*2*). The absence of a predicted microevolutionary response may be due to constraints imposed by genetic correlations between the phenotype of interest and other fitness-related traits (*3*). If this is true, then the loci affecting the focal trait should be colocalized in the genome with genes for other fitness-related traits, either because the same genes affect both traits (pleiotropy) or because genetic correlations arise between tightly linked genes (linkage disequilibrium). However, empirical evidence for colocalized antagonistically acting quantitative trait loci (QTLs) that constrain microevolutionary change is currently lacking.

In the free-living Soay sheep of St Kilda, Scotland, coat color is either dark brown or light tawny (Fig. 1) (*4*); the two phenotypes have been documented for at least 90 years (*5*, *6*). Variation in coat color is controlled by a single autosomal locus at which the dark allele is dominant to the light allele (*6*). The light phenotype is determined by homozygosity of a single recessive amino acid–changing G→T transversion at coding position 869 in the *tyrosinase-related protein 1* (*TYRP1*) gene (*7*).

Coat color in Soay sheep is related to fitness because of an association with body size: Dark sheep are larger than light sheep (*8*). Body size is heritable throughout life (*9*, *10*) and is positively correlated with survival (*11*) and reproductive success (*12*). Moreover, a genetic response to selection for increased size has been detected (*9*). If the association between coat color and body

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size has a genetic basis, then dark sheep should be favored by selection because of their size advantage relative to light sheep. However, a 20-year time series of phenotypic data shows a significant decrease in the frequency of dark sheep (linear regression, slope of −0.38%/year, $R^2 = 0.326$, $P = 0.009$; Fig. 2A).

We considered two competing hypotheses to explain this disparity; first, that the correlation between coat color and body size is a consequence of environmentally induced, rather than genetic, covariance between traits. In this case, selection on body size would not result in a parallel response for coat color. Alternatively, if there is a genetic association between coat color and size, the failure of dark sheep to increase in frequency may indicate a negative genetic correlation between body size and other fitness-related loci in the vicinity of *TYRP1*. Under this scenario, dark sheep are larger but less fit than light sheep. Other explanations for the discrepancy can be dismissed. For example, selection cannot favor light sheep on the basis of cryptic coloration (*13*), because predators have never existed on St Kilda (*4*). Similarly, light sheep are not favored by sexual selection because there is no evidence for assortative mating with respect to either coat color [$\chi^2_{(1)} = 0.32$, $P = 0.570$] or *TYRP1* genotype [$\chi^2_{(4)} = 1.53$, $P = 0.822$] on the basis of 559 phenotyped and genotyped parent/offspring trios.

To test our hypotheses, we genotyped the *TYRP1* mutation in 2509 sheep living between 1985 and 2005 and integrated these data with estimates of body size and individual lifetime fitness. We used a linear mixed model (LMM) (the so-called animal model) (*14*) that accounts for shared additive genetic effects on phenotype among relatives, in addition to the effects of non-genetic factors and environmental variation on the covariance between traits (*15*). In all analyses, we present estimates of the mean and standard error (SE) of the differences in trait value between *TYRP1* genotypes and between dark and light sheep, rather than the population means for each genotype and phenotype, because we are primarily interested in these contrasts.

We identified a strong genetic association between *TYRP1* and birth weight [LMM, $F_{(2,1623.1)} = 8.96$, $P = 0.0001$, $n = 1757$ sheep; Fig. 3A and table S1]; sheep with genotypes GG and GT (dark coats) were heavier at birth than sheep with genotype TT (light coats) by an average of 132.3 (±37.4) g and 111.3 (±28.5) g, respectively. Dark homozygotes (GG) were largest but not significantly larger than dark heterozygotes (GT) (mean difference 21.0 ± 32.0 g). Overall, dark sheep were an average of 122.4 (±24.0) g heavier at birth than light sheep [LMM, $F_{(1,2201.5)} = 26.03$, $P < 0.0001$, $n = 2370$]; this difference is similar to that between males and females (129.9 ± 23.8 g). The general pattern of larger size in sheep carrying the *TYRP1* G allele was also present in lambs [LMM, $F_{(2,800.8)} = 4.39$, $P = 0.014$, $n = 1087$; Fig. 3B] and adults [LMM, $F_{(2,369.8)} = 3.86$, $P = 0.023$, $n = 1367$; Fig. 3D] but was non-significant in yearlings [LMM, $F_{(2,316)} = 0.40$, $P = 0.672$, $n = 556$; Fig. 3C], presumably due to a lack of power associated with the relatively small sample size in that intermediate age class (table S1).

Our results suggest that the *TYRP1* G allele (dominant for dark color) is associated with partial dominance for body size. We determined whether this was due to genetic linkage by applying a transmission disequilibrium test (TDT) (*16*) to a set of birth weight records from 492 fully phenotyped and genotyped parent/offspring trios (*15*). This revealed linkage between *TYRP1* and birth weight [LMM, within-families coefficient (b_{TD}), $F_{(1,421)} = 4.60$, $P = 0.034$] and discounted a spurious association arising from recent admixture or the nonrandom spatial distribution of sheep in the study area (*17*, *18*) [LMM, between-families coefficient (b_{PD}), $F_{(1,377.6)} = 1.48$, $P =$

Fig. 1. Dark (left) and light (right) coat color morphs in Soay sheep. [Photograph: J. M. Pemberton]

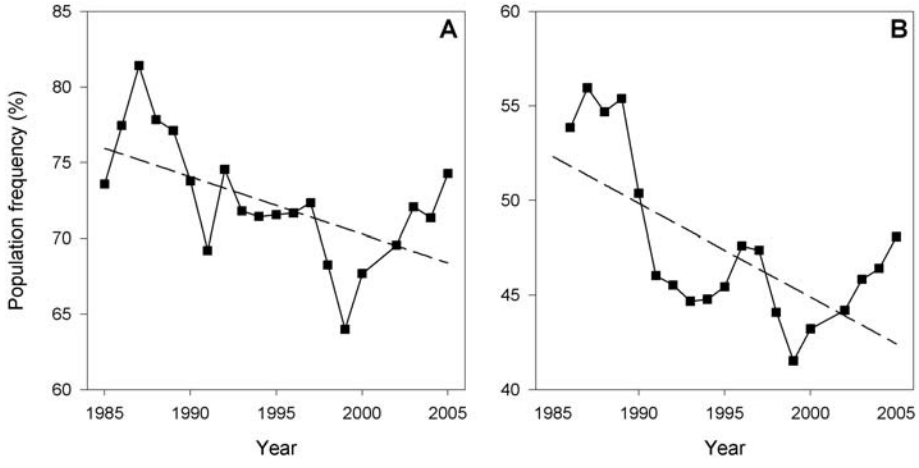

Fig. 2. Estimated frequency of (**A**) dark sheep and (**B**) the *TYRP1* G allele (dominant for dark color) in the Village Bay study population from 1985 to 2005. Frequency estimates are from August of each year. Linear regression lines are fitted and show a significant decline in the frequency of both dark sheep (slope of −0.38%/year, $R^2 = 0.326$, $P = 0.009$) and the *TYRP1* G allele (slope of −0.49% /year, $R^2 = 0.390$, $P = 0.004$).

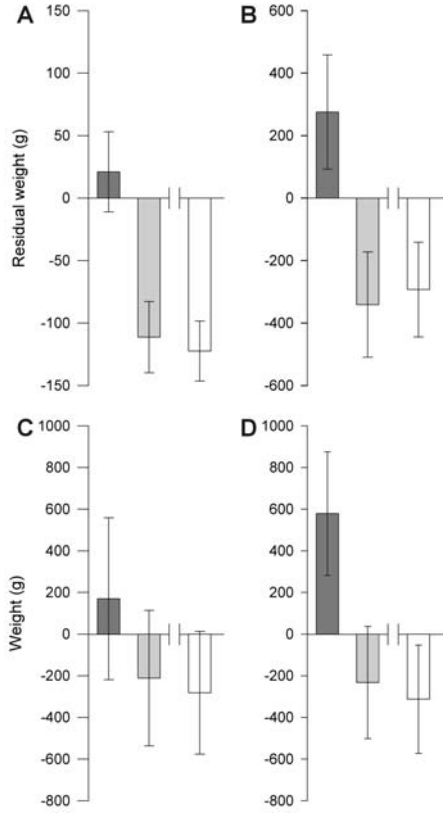

Fig. 3. Bar plots showing the mean (±SE) weight differential of homozygous (GG) dark sheep (dark gray bars) and homozygous (TT) light sheep (light gray bars), in each case relative to heterozygous (GT) dark sheep, and of light sheep (white bars) relative to dark sheep at (**A**) birth, and in (**B**) lambs, (**C**) yearlings, and (**D**) adults.

0.225]. We can therefore reject the hypothesis that the correlation between coat color and body size arises purely from environmental effects. Consequently, because body size is positively correlated with fitness (*11*, *12*) and the *TYRP1* G allele is associated with large size, the failure of dark sheep to increase in frequency may be due to microevolutionary constraints imposed by other genetic factors in the vicinity of *TYRP1*.

We characterized the genetic relationship between coat color and lifetime fitness with the delifing approach, which estimates an individual's contribution to annual population growth, $p_{t(i)}$, through survival and reproduction (*19*). De-lifed fitness is standardized by the population mean in each year, correcting for annual environmental variation, which can affect fitness (*4*). Our analyses were based on the lifetime sum of $p_{t(i)}$ from all sheep for which complete life histories were available (*15*). We identified a significant genetic association between *TYRP1* and lifetime $p_{t(i)}$ [LMM, $F_{(2,1336)} = 4.03$, $P = 0.020$, $n = 1355$] and showed, using a TDT, that this is due to genetic linkage [LMM, $F_{(1,427)} = 6.87$, $P = 0.010$, $n = 492$]. Intriguingly, the relationship between coat color and fitness is inconsistent with that between dark coat color and large body size (Fig. 4 and table S2). Homozygous dark sheep (GG) exhibited a fitness disadvantage relative to phenotypically identical heterozygous dark sheep (GT) (i.e., a cryptic difference), but there was no evidence for differential fitness between heterozygous dark sheep and light sheep (TT). At a phenotypic level, the average fitness of dark sheep (genotypes GG and GT combined) was indistinguishable from that of light sheep, and thus there was no evidence for selection on coat color itself [LMM, $F_{(1,2117.8)} = 1.70$, $P = 0.192$, $n = 2334$].

Genetic linkage between *TYRP1* and both birth weight and lifetime $p_{t(i)}$ can be explained by either pleiotropy or linkage disequilibrium with neighboring QTLs. We consider pleiotropy unlikely for two reasons. First, *TYRP1* has a limited range of expression, in melanocytes and retinal pigment epithelium (*20*). Because there is no evidence of color-associated diseases of the skin or eyes in Soay sheep, it is difficult to envisage how *TYRP1* could directly influence size or fitness. Second, there is no evidence that *TYRP1* has pleiotropic effects on size, survival, or fecundity in mice and humans, despite the characterization of mutations that share a similar molecular basis with the Soay sheep mutation (the loss of a conserved cysteine residue) (*7*) and that have identical effects on pigmentation (*21*). Linkage disequilibrium to body size and fitness QTLs is plausible. Strong linkage disequilibrium extends for a considerable distance in the *TYRP1* region in our study population (supporting online text). The *VLDLR* gene, which in mice is associated with variation in neonatal size (*22*) and is believed to be tightly linked to *TYRP1* on the basis of conserved synteny with cattle (*23*), is a promising candidate gene for the body-size QTL. Similarly, a fitness-associated phenotype named "brown-associated fitness," determined by the *PTPRD* gene in the vicinity of *TYRP1*, has been described in mice (*24*).

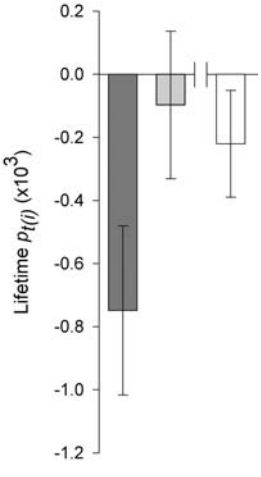

Fig. 4. Bar plots showing the mean (±SE) relative lifetime de-lifed fitness $p_{t(i)}$ of *TYRP1* genotypes and coat color phenotypes, as in Fig. 3.

Our results therefore imply that the relative fitness of *TYRP1* genotypes is determined by linkage to QTLs for both body size and fitness. These QTLs appear to have antagonistic effects because the *TYRP1* G allele (dominant for dark coat color) is associated with large body size (and hence with increased fitness) but also with decreased lifetime $p_{t(i)}$. Thus, despite an overall positive correlation between body size and fitness (*11*, *12*), these traits are negatively correlated in the chromosomal vicinity of *TYRP1*. This is because of linkage disequilibrium between the G allele and both a large body size QTL and a recessive QTL allele with deleterious effects on fitness. Notably, the direct fitness cost associated with G outweighs the expected benefits of being larger, and this will constrain the frequency of dark sheep. Our results actually imply that the light mutation (T) should be increasing in frequency, although genetic drift will also play a role in determining the allelic frequencies.

Our findings are therefore consistent with the observed decrease in the frequency of dark sheep (Fig. 2A). They are also consistent with a 20-year time series of *TYRP1* genotype data (linear regression, slope of −0.49%/year for frequency of the G allele, $R^2 = 0.390$, $P = 0.004$; Fig. 2B). Although sensitive to incomplete sampling in the early years of the study (supporting online material), this genotypic trend is supported by a significant increase in light sheep (and hence the TT genotype) (*7*) that is based on almost perfect sampling (*15*). Thus, the microevolutionary dynamics of coat color are consistent with expectations arising from the presence of a negative genetic correlation between size and fitness in the vicinity of *TYRP1*. This result holds whether the correlation is caused by pleiotropy or by linkage disequilibrium with nearby loci.

This study shows that selection acting on simple Mendelian traits in natural populations can have a complex genetic basis. This has implications for the study of microevolutionary change in natural populations, because fitness variation at the level of the genotype may not be evident in an analysis of selection on phenotype. Consequently, phenotypic studies may wrongly conclude that selection is not acting on genomic regions containing the loci underlying focal traits and may be unable to explain the microevolutionary dynamics of trait variation.

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Supporting Online Material

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References

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