Supporting Information for "The loci of repeated evolution: a catalog of genetic hotspots of phenotypic variation"

Arnaud Martin[1]* and Virginie Orgogozo[2]

[1]: Department of Ecology and Evolutionary Biology, Cornell University, Corson Hall, 215 Tower Road, Ithaca, NY 14853, USA.

[2]: CNRS UMR7592, Université Paris Diderot, Sorbonne Paris Cité, Institut Jacques Monod, 15 rue Hélène Brion, 75205 Paris cedex 13, France.

*: to whom correspondence should be addressed;

E-mail: heliconiuswing@gmail.com

The Loci of Evolution catalog

This review is accompanied by a catalog of 1008 genetic variants of evolutionary relevance published up to December 2012 (see Supplementary Notes below), deposited in the DRYAD dataset repository (Martin and Orgogozo 2013). This list aims at being used as a bibliographical resource for the exploration of evolutionary genetics literature and for detecting emerging patterns in this fast-evolving field.

The “IL Hotspot” column associates three classes of interlineage hotspots (see Fig. 1D) to each orthologous group. *** (N=357): alleles of orthologous genes for which genotype-to-phenotype association was verified in a cross (Linkage Mapping) for at least two derived alleles. ** (N=254): alleles of orthologous genes where a derived allele was discovered by Linkage Mapping, or where all the entries are associated to Candidate Gene or Association Mapping approaches. * (N=57): putative hotspot genes associated to ambiguous orthology relationships or phenotypic similarities between lineages, shown here for heuristic purposes. Together, the most conservative interlineage hotspot classes (** and ***) span 111 orthologous groups that encompass 60.6% (611/1008) of the alleles in the dataset.

Supplementary Notes

The QTG program: chasing the loci of evolution

The power of geneticists to study variation has dramatically increased over the past two decades. Originally, Quantitative Trait Loci (QTL) mapping studies only aimed at identifying the genetic architecture of phenotypic variation with a sub-chromosomal resolution. Nowadays many studies aim at directly identifying the causative loci that trigger observable changes in phenotypes (Stern and Orgogozo 2008), and a flurry of technical advances in genomics has opened a Golden Age for this research program (Nadeau and Jiggins 2010). Mapping of natural variation on a large scale should provide a global overview of the genetic changes that constitute the molecular basis of phenotypic evolution. This so-called Quantitative Trait Gene (QTG) or Quantitative Trait Nucleotide (QTN) program (Stern and Orgogozo 2008; Rockman 2011) also benefits from the study of domesticated traits, which is informative about the genotype-phenotype map albeit under artificial conditions.

Two approaches for the QTG program

Biologists find the actual genetic variations that matter for evolution using two broad methodologies that have been classically referred to as “forward” (*syn.* “top-down”) and “reverse” (*syn.* “bottom-up”) genetic approaches. Forward genetics moves from a difference in phenotypes to the identification of genetic variants. This includes linkage mapping of quantitative and Mendelian traits segregating in crosses, and association mapping in individuals sampled from populations. In contrast, reverse genetics approaches move from the sequence level to differences in phenotype, and are usually based on *a priori* assumptions on gene function. In reality, most studies locate on a continuum between these two extremes: mapped genetic intervals almost always narrow down to a set of candidate genes, and conversely, candidate gene studies sometimes test *a posteriori* a genetic co-segregation with a phenotype. Thus the distinction is not really operational, but it is important to keep in mind that bottom-up approaches are biased towards known genes and that top-down approaches are limited to comparisons between closely related lineages.

The data and its biases

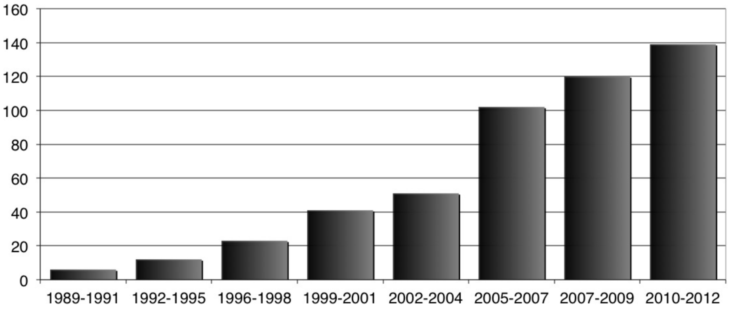
The derivation of meaningful insights from the QTG program has lagged behind, and the swarm of data incites most reviews on the topic to focus on limited subsets of the literature. The need to summarize and classify such information is growing, as a panoramic view of the literature may not only allow the detection of general principles, but may also help us to identify knowledge gaps and define future axes of investigation. Here we synthesized research on the Loci of Evolution into a list of genes and alleles that have been reported to cause phenotypic variation between individuals at the micro- and macro-evolutionary time scales (Martin and Orgogozo 2013).

This updated catalog builds on a previous list of 395 mutations (Stern and Orgogozo 2008), and has now expanded to 1008 entries. To identify relevant studies, we used multiple search methods. We screened every issue of the major journals in evolutionary genetics for the last five years (update from (Stern and Orgogozo 2008), performed countless keyword searches on online search tools, and paid particular attention to citations in primary research articles as well as in review papers.

The list comprises findings from: 1) Linkage Mapping – (top-down) studies that verify genotype-phenotype co-segregation in crosses; 2) Association Mapping – (top-down) genome-wide association studies (GWAS) between between heterogeneous individuals from naturally reproducing populations (these are here limited to variants tightly linked to well-supported candidate genes). 3) Candidate Gene – (bottom-up) studies that, with various arguments, suggest a causal relationship between genotype and phenotype without co-segregation tests.

Importantly, we excluded candidate gene studies that lack evidence of sequence-level change, and for instance, the proposed link between *BMP4* and the microevolution of beak shape in Darwin's finches (Campas et al. 2010) was ignored here, as its differential expression between beak morphs could be due to mutations in upstream regulator genes. To take experimental biases into account, we assigned to each evolutionary change one category among these three, that best reflects the type of evidence associating a given allele to a phenotypic effect.

We attempted to compile a comprehensive list of linkage mapping studies that identified genetic loci responsible for phenotypic evolution (**Supplementary Figure 1**) as these studies are initially blind in terms of genotype inferences and avoid spurious effects of gene re-discovery due to ascertainment biases. In contrast, the Candidate Gene and Association Mapping categories are still largely incomplete. With a few exceptions, "Candidate gene" studies that identified causal but fixed sequence differences between distant species have not been included. This is not only because compiling the relevant articles would require a unreasonable effort, but also because focusing on microevolutionary time scales avoids the confounding effect of cumulative changes over long times of divergence (see Stern 2000 for a discussion of "evolutionarily-relevant mutations"). We also note that the "Candidate Gene" category also reflects strong ascertainment biases inherent to this approach, as illustrated by the fact that *MC1R* alleles make a sixth of all entries in this category (70/413=16.9%). The "Association Mapping" category was purely the product of cherry picking, but we kept it for comparative and heuristic purposes. It consists of 101 well-supported variants isolated from genome-wide association studies, among which 55 entries concern human studies, 18 were found in domesticated species (mostly in dog), and 18 relate to experimental evolution studies (mostly in yeast). The catalog is thus primarily based on top-down studies, with about half (494/1008) of entries belonging to the "Linkage Mapping" category. It is also inherently biased towards large-effect QTLs, the low hanging fruits of phenotypic variation (Rockman 2011), and towards shallow phylogenetic levels, because linkage mapping is not feasible in species that do not hybridize.



Supplementary Figure 1. Progress in the discovery of Loci of Evolution by Linkage Mapping. The vertical axis represents numbers of alleles in the main category of the dataset ("Linkage Mapping", 49% of entries in the list).

The list includes cases of domesticated, intraspecific and interspecific variation identified with reasonable confidence at a genic or sub-genic level in pluricellular organisms (plants and animals), as well as in yeasts. Repartition of traits into the broad categories "Physiology", "Morphology" and "Behavior" was assigned based on common sense (Stern and Orgogozo 2008), but inevitably contains some ambiguous cases (*e.g.* the effects of the *Myostatin* locus on muscular mass could equally be considered morphological or physiological). Studies of artificial selection (domestication; experimental evolution) were treated separately from natural cases. The "Taxonomic level: Domesticated" category includes examples that relate to adaptation to laboratory conditions (*e.g.* McGrath et al. 2011) but deleterious mutants obtained in the laboratory were excluded because they are actively maintained for research rather than from commercial use by breeders. However this later statement is not always easy to verify: for instance, it is not clear if the pea strains studied by Gregor Mendel should be considered as mutants or cultivars, but the recent mapping studies of pea color phenotypes were included here (Hellens et al. 2010; Moreau et al. 2012). Thus, the boundary between mutants and *bona fide* selected phenotypes can be blurry. We also included gene variants that underlie traits considered syndromic in human and mice but maintained by breeders in other species, such as mutations underlying dwarfism in dogs (Parker et al. 2009), or predispositions to deafness linked to equine coat color phenotypes (Hauswirth et al. 2012).

Supplementary Tables

	Animals	Plants	Yeasts	total
Intraspecific	343	113	22	**478**
Interspecific	92	16	2	**110**
Intergeneric or higher	44	0	1	**45**
Domesticated	138	195	20	**353**
Experimental	5	0	17	**22**
total	**622**	**324**	**62**	**1008**

Supplementary Table 1. Number of Loci of Evolution according to their taxon level. The Loci of Evolution catalog (Martin and Orgogozo 2013) is enriched in studies of phenotypic variation between sibling populations, strains and closely-related species. Studies of artificial selection (domestication; experimental evolution) are treated separately from natural cases.

Locus	Mutation	Homoplastic lineages	Variation	Xenobiotic
Ace-1	Gly119Ser	5 (insects)	Intraspecific	Insecticides (organophosphorus)
ERG3	Trp205Stop	4 (yeast lines)	Experimental	Fungicide (nystatin)
ERG6	Gln44Stop	3 (yeast lines)	Experimental	Fungicide (nystatin)
	Gly127Arg	4 (yeast lines)		
	Tyr223Stop	4 (yeast lines)		
Esterase E3	Gly137Asp	3 (flies)	Intraspecific	Insecticides (diazinon)
	Trp251Leu/Ser	2 (blowflies)		Insecticides (malathion)
Na,K-ATPase α	Asn122His	5 (insects)	Interspecific	Host plant toxins (cardenolides)
	Glu111Val	3 (insects)		
	Glu111Leu	3 (insects)		
	Iso315Val	2 (insects)		
	Thr797Ala	2 (insects)		
Nav1.4 channel	Glu945Asp	1 (pufferfish)	Interspecific	Endogenous toxin (tetrodoxin)
	Glu945Asp	1 (snake)	Interspecific	Salamander toxin (tetrodoxin)
	Glu945Asp	1 (bivalve mollusk)	Intraspecific	Plankton toxin (saxitoxin)
para (kdr)	Leu1014His	2 (insects)	Intraspecific	Insecticides (pyrethroids)
	Leu1014Phe	11 (insects)		
	Leu1014Ser	2 (mosquitoes)		
	Met918Thr	5 (insects)		
	Thr929Ile	3 (2 moths, 1 louse)		
Rdl	Ala302Gly	3 (insects)	Intraspecific	Insecticides (cyclodienes)
	Ala302Ser	11 (insects)		
Vkorc1	Leu128Ser/Gln	3 (rodents)	Intraspecific	Pesticide (warfarin)
	Tyr139Cys	2 (rodents)		

Supplementary Table 2. Codon-level hotspots of evolution of resistance to xenobiotics. The third column denotes the inferred number of independent apparition of a given mutation (genetic homoplasies). See the Loci of Evolution catalog for references (Martin and Orgogozo 2013).

Locus	TF	Trait	Organism	Allelic series[a]	Variation
CBF	yes	Cold resistance	Wheat	-	Domesticated
			Barley	-	Domesticated
			Arabidopsis	-	Natural
FLC	yes	Flowering time	Turnip	yes	Domesticated
			Cabbage	-	Domesticated
			Arabidopsis	yes	Natural
			Capsella	yes	Natural
FRI	no	Flowering time	Oilseed rape	-	Domesticated
			Arabidopsis	yes	Natural
FT	no	Flowering time	Sunflower	-	Domesticated
			Wheat	-	Domesticated
			Barley	-	Domesticated
			Ryegrass	-	Domesticated
			Arabidopsis	-	Natural
Ghd7/ZmCCT	yes	Flowering time	Teosinte/Maize	yes	Both
			Rice	-	Domesticated
Hd1	yes	Flowering time	Rice	yes	Domesticated
PRR37/Ppd-H1	yes	Flowering time	Barley	-	Domesticated
			Sorghum	yes	
VRN1	yes	Flowering time	Wheat	-	Domesticated
			Ryegrass	-	Natural
			Barley	-	Domesticated
			Wheat	yes	Domesticated
ELF3/EAM8	no	Flowering time[b]	Barley	yes	Domesticated
			Rice	-	Domesticated
			Arabidopsis	yes	Natural
BADH2	no	Fragrance	Rice	yes	Domesticated
			Soybean	-	
GS5	no	Grain quality	Rice	yes	Domesticated
Opaque2	yes	Grain quality	Maize	yes	Domesticated
OsSPL16	no	Grain quality	Rice	yes	Domesticated
qSH1/RPL	yes	Grain shattering	Rice	-	Domesticated
			Brassicacae	-	Natural
Sh1	yes	Grain shattering	Rice	-	Domesticated
			Maize	yes	
			Sorghum	yes	

Continued on next page

Gn1a	no	Grain yield	Rice	yes	Domesticated
GW2	no	Grain yield	Rice	-	Domesticated
			Wheat	-	
TB1/IntC	yes	Grain yield	Teosinte/Maize	yes	Both
			Barley	-	Domesticated
VRS1	yes	Grain yield	Barley	yes	Domesticated
phytochrome B	no	Light sensitivity	Sorghum	-	Domesticated
			Arabidopsis	-	Natural
ALMT	no	Metal tolerance	Rye	-	Domesticated
			Wheat	-	
HMA3	no	Metal tolerance	Rice	-	Domesticated
			Thlaspi	-	Natural
			Arabidopsis	yes	Natural
MATE1	no	Metal tolerance	Sorghum	-	Domesticated
			Maize	-	
An2	yes	Pigmentation	*Petunia*	yes	Both
DFR	no	Pigmentation	Potato	-	Domesticated
			Iochroma	-	Natural
			Morning glory	-	Natural
F3'5'H	no	Pigmentation	Potato	-	Domesticated
			Pea	yes	Domesticated
			Iochroma	-	Natural
			Phlox	-	Natural
			Wild soybean	-	Natural
F3'H	no	Pigmentation	Soybean	yes	Domesticated
			Morning glory	-	Natural
			Petunia	-	Natural
Rc	yes	Pigmentation	Rice	yes	Domesticated
Ruby	yes	Pigmentation	Orange	yes	Domesticated
VvMYBA1-3	yes	Pigmentation	Grapevine	yes	Domesticated
RHT/Dwarf8	yes	Plant stature[b]	Maize	-	Domesticated
			Wheat	yes	
Sd1	no	Plant stature[b]	Rice	yes	Domesticated
TFL1	no	Seasonal growth	Soybean	yes	Domesticated
			Barley	-	Domesticated
			Wild strawberry	-	Natural
Waxy	no	Starch properties	Rice	-	Domesticated
			Barley	-	
			Millet	yes	

Supplementary Table 3. Hotspots of variation in domesticated plants. Disease resistance traits are not included due to unclear orthology relationships between the corresponding loci (see Martin and Orgogozo 2013). Some cases of natural variation are included for comparison. TF: transcription factor; [a]: the allelic series category denotes the detection of multiple derived alleles of the same gene within one species. For instance, three independent mutations in *VRS1* result in six-rowed barley florets, revealing genetic homoplasy in independent selection events on grain yield (Ramsay et al. 2011); [b]: variants at these loci have pleiotropic effects on plant morphology and flowering time. See the Loci of

Evolution catalog for references (Martin and Orgogozo 2013). **Note:** color variation relates in particular to modulations of anthocyanin pigment biosynthesis through changes within clusters of transcription factors of the MYB R2R3 and bHLH families, and we refer to the Loci of Evolution catalog and to previous reviews on the topic for a more comprehensive overview (Allan et al. 2008; Streisfeld and Rausher 2011; Martin and Orgogozo 2013). In a nutshell, variations in fruit, flower and plant coloration repeatedly map in both cultivated and wild species to genes encoding transcription factors of the MYB R2R3 and bHLH families (Martin and Orgogozo 2013). Independent episodes of duplication and polyploidization complicate the orthology/paralogy relationships between these factors, somewhat confusing the inference of parallelism between species (Cooley et al. 2011) but this difficulty disappears at the intraspecific level. For instance, two independent transposable element insertions in the promoter of the MYB gene *Ruby* are each responsible for the temperature-dependent coloration of Sicilian and Asian varieties of blood oranges (Butelli et al. 2012). We refer to the Loci of Evolution catalog and to previous reviews on the topic for a more comprehensive overview (Allan et al. 2008; Streisfeld and Rausher 2011; Martin and Orgogozo 2013).

Locus	Trait	Organism	Allelic series*	Variation
ABCG2	Milk production	Cattle	-	Domesticated
		Sheep	-	
Agouti/ASIP	Pigmentation	**many**	yes	Both
BCO2	Milk and fat color	Cattle	-	Domesticated
		Sheep	-	
BMP15	Fertility	Sheep	yes	Domesticated
EDNRB	Pigmentation	Horse	-	Domesticated
		Quail	-	
FGF5	Hair type	Cat	yes	Domesticated
		Dog	-	
FGFR1a	Scale loss	Carp	yes	Domesticated
HMGA2	Growth (body)	Dog	-	Domesticated
	Growth (body)	Human	-	Natural
	Growth (ears, skin)	Pig	-	Domesticated
KIT	Pigmentation	Cattle	yes	Domesticated
		Horse	yes	
		Pig	-	
KITLG	Pigmentation	Human	-	Natural
		Stickleback	-	
KRT71	Hair type	Dog	-	Domesticated
		Cat	yes	
MC1R	Pigmentation	**many**	yes	Both
MITF	Pigmentation	Cattle	-	Domesticated
		Dog	-	
		Horse	yes	
		Quail	-	
MLPH	Pigmentation	Cat	-	Domesticated
		Dog	-	
		Quail	-	
Myostatin/GDF8	Meat yield	Cattle	yes	Domesticated
	Meat yield	Pig	-	
	Meat yield	Sheep	yes	
	Racing performance	Horse	-	
	Racing performance	Dog	-	
OCA2	Pigmentation	Human	yes	Natural
		Cavefish	yes	
PMEL17	Pigmentation	Chicken	yes	Domesticated
PPAR-Delta	Growth (body)	Human	-	Natural
	Growth (ears, skin)	Pig	-	Domesticated
SLC45A2/MATP	Pigmentation	Chicken	-	Domesticated
		Horse	-	Domesticated
		Quail	-	Domesticated
		Human	-	Natural
TYR	Pigmentation	Cat	yes	Domesticated
		Human	-	Natural
TYRP	Pigmentation	**many**	yes	Both
Taqpep	Coat color pattern	Cat	yes	Both
		Cheetah	-	Natural

Supplementary Table 4. Hotspots of variation in domesticated animals
Asterisk: the allelic series category denotes the detection of multiple derived alleles of the same gene within one species. For instance, three independent mutations in *PMEL17* underlie strain-defining plumage color phenotypes in chickens (Kerje et al. 2004); the *KITLG* and *OCA2* loci are included here as hotspots of natural variation for comparison with other vertebrate pigmentation hotspots. See the Loci of Evolution catalog for references (Martin and Orgogozo 2013). **Note:** domesticated variation in pigmentation has been particularly well studied. Among 139 known alleles underlying vertebrate color variations, 67 relate to cases of domestication and the remaining 72 relate to natural cases, including in human. Most cloned genes that are associated to pigmentation variation are regulators of melanin synthesis in melanocytes. The melanocortin

receptor MC1R and its secreted antagonist Agouti/ASIP, which act as master switches for the synthesis of dark eumelanin, are well-established hotspots that contribute to 88 alleles out of 139 in the list of vertebrate pigmentation loci, and we refer to the Loci of Evolution catalog and previous review articles for a comprehensive overview of the topic (Manceau et al. 2010; Kronforst et al. 2012; Martin and Orgogozo 2013).

Locus	Trait	Organism	# of lof[a]	gene deletion	nonsense	missense	frameshift[b]	in-frame indel	TE insertion	multiple types	Variation
ABCC2	Insecticide resistance	*Heliothis* moth	1				1				Intraspecific
		Plutella moth	1					1			Intraspecific
		Silkworm	1					1			Intraspecific
ABO	Blood type	Human	4		1	1	2				Intraspecific
		Chimpanzee	2					1		1	Intraspecific
An2	Flower coloration	*Petunia*	6		3		3				Interspecific[c]
Agouti	Pigmentation	Horse (predomestic)	1				1				Intraspecific
		Leopard	1		1						Intraspecific
		Asian Golden Cat	1		1						Intraspecific
BTR1	Insecticide resistance	*Helicoverpa* moth	1		1						Intraspecific
		Heliothis moth	1						1		Intraspecific
		Pectinophora moth	4			1	1	2			Intraspecific
DFR	Flower coloration	*Iochroma*	1			1					Interspecific[c]
		Morning glory	1							1	Interspecific[c]
F3'5'H	Flower coloration	*Iochroma*	1	1							Interspecific[c]
		Wild soybean	1			1					Intraspecific
FLC	Flowering time	*Arabidopsis*	1		1						Intraspecific
		Capsella	1				1				Intraspecific
FRI	Flowering time	*Arabidopsis*	19		5		10	1		3	Intraspecific
G6PD	Malaria resistance	Human	3			3					Intraspecific
HMA3	Tolerance to cadmium	*Arabidopsis*	5		1	4					Intraspecific
MC1R	Pigmentation	Cavefish	2			1	1				Intraspecific
OCA2	Pigmentation	Cavefish	2					1		1	Intraspecific
opsin SWS1	UV-range vision (loss)	*Glaucomys* squirrel	1				1				Intergeneric
		Pteromys squirrel	1					1			Intergeneric
TAS2R38	Gustatory sensation	Human	1			1					Intraspecific
		Chimpanzee	1		1						Intraspecific
Taqpep	Coat color pattern	Black-footed cat	1			1					Interspecific
		Cheetah	1				1				Intraspecific

Supplementary Table 5. Hotspots of evolution linked to coding loss-of-function mutations. Cases of repeated coding loss-of-function variants underlying natural variation. [a]: minimum number of known independent loss-of-function alleles ; [b]: frameshift mutations resulting in a truncated protein ; [c]: loss-of-function variants that have been proposed to drive or reinforce reproductive isolation between phenotypes. See the Loci of Evolution catalog (Martin and Orgogozo 2013) for references and additional examples (*e.g.* MC1R variants).

Supplementary references

Allan, A. C., R. P. Hellens, and W. A. Laing. 2008. MYB transcription factors that colour our fruit. Trends Plant Sci. 13:99-102.

Butelli, E., C. Licciardello, Y. Zhang, J. Liu, S. Mackay, P. Bailey, G. Reforgiato-Recupero, and C. Martin. 2012. Retrotransposons Control Fruit-Specific, Cold-Dependent Accumulation of Anthocyanins in Blood Oranges. Plant Cell 24:1242-1255.

Campas, O., R. Mallarino, A. Herrel, A. Abzhanov, and M. P. Brenner. 2010. Scaling and shear transformations capture beak shape variation in Darwin's finches. Proc. Nat. Acad. Sci. USA 107:3356-3360.

Cooley, A., J. Modliszewski, M. Rommel, and J. Willis. 2011. Gene Duplication in Mimulus Underlies Parallel Floral Evolution via Independent trans-Regulatory Changes. Curr. Biol. 21:700-704.

Hauswirth, R., B. Haase, M. Blatter, S. A. Brooks, D. Burger, C. Drogemuller, V. Gerber, D. Henke, J. Janda, R. Jude, K. G. Magdesian, J. M. Matthews, P.-A. Poncet, V. I. Svansson, T. Tozaki, L. Wilkinson-White, M. C. T. Penedo, S. Rieder, and T. Leeb. 2012. Mutations in *MITF* and *PAX3* cause Splashed White and other white spotting phenotypes in horses. PLoS Genet. 8:e1002653.

Hellens, R. P., C. Moreau, K. Lin-Wang, K. E. Schwinn, S. J. Thomson, M. W. E. J. Fiers, T. J. Frew, S. R. Murray, J. M. I. Hofer, J. M. E. Jacobs, K. M. Davies, A. C. Allan, A. Bendahmane, C. J. Coyne, G. M. Timmerman-Vaughan, and T. H. N. Ellis. 2010. Identification of Mendel's White Flower Character. PLoS One 5:e13230.

Kerje, S., P. Sharma, U. Gunnarsson, H. Kim, S. Bagchi, R. Fredriksson, K. Schutz, P. Jensen, G. Von Heijne, and R. Okimoto. 2004. The Dominant white, Dun and Smoky color variants in chicken are associated with insertion/deletion polymorphisms in the PMEL17 gene. Genetics 168:1507-1518.

Kronforst, M. R., G. S. Barsh, A. Kopp, J. Mallet, A. Monteiro, S. P. Mullen, M. Protas, E. B. Rosenblum, C. J. Schneider, and H. E. Hoekstra. 2012. Unraveling the thread of nature's tapestry: the genetics of diversity and convergence in animal pigmentation. Pigment Cell Mel. Res. 25:411-433.

Manceau, M., V. S. Domingues, C. R. Linnen, E. B. Rosenblum, and H. E. Hoekstra. 2010. Convergence in pigmentation at multiple levels: mutations, genes and function. Philos. Trans. R. Soc. Lond. B. Biol. Sci. 365:2439-2450.

Martin, A., and V. Orgogozo. 2013. Data from: The loci of repeated evolution: a catalog of genetic hotspots of phenotypic variation. Dryad Digital Repository.

McGrath, P. T., Y. Xu, M. Ailion, J. L. Garrison, R. A. Butcher, and C. I. Bargmann. 2011. Parallel evolution of domesticated Caenorhabditis species targets pheromone receptor genes. Nature 477:321-325.

Moreau, C., M. J. Ambrose, L. Turner, L. Hill, T. H. N. Ellis, and J. M. I. Hofer. 2012. The b Gene of Pea Encodes a Defective Flavonoid 3' 5' Hydroxylase, and Confers Pink Flower Color. Plant Physiol. 159:759-768.

Nadeau, N. J., and C. D. Jiggins. 2010. A golden age for evolutionary genetics? Genomic studies of adaptation in natural populations. Trends Genet. 26:484-492.

Parker, H. G., B. M. VonHoldt, P. Quignon, E. H. Margulies, S. Shao, D. S. Mosher, T. C. Spady, A. G. Elkahloun, M. Cargill, P. G. Jones, C. L. Maslen, G. M. Acland, N. B. Sutter, K. Kuroki, C. D. Bustamante, R. K. Wayne, and E. A. Ostrander. 2009. An Expressed Fgf4 Retrogene Is Associated with Breed-Defining Chondrodysplasia in Domestic Dogs. Science 325:995-998.

Ramsay, L., J. Comadran, A. Druka, D. F. Marshall, W. T. B. Thomas, M. Macaulay, K. MacKenzie, C. Simpson, J. Fuller, N. Bonar, P. M. Hayes, U. Lundqvist, J. D. Franckowiak, T. J. Close, G. J. Muehlbauer, and R. Waugh. 2011. INTERMEDIUM-C, a modifier of lateral spikelet fertility in barley, is an ortholog of the maize domestication gene TEOSINTE BRANCHED 1. Nat. Genet. 43:169-172.

Rockman, M. V. 2011. The QTN program and the alleles that matter for evolution : All that's gold does not glitter. Evolution 66:1-17.

Stern, D. 2000. Evolutionary developmental biology and the problem of variation. Evolution 54:1079-1091.

Stern, D. L., and V. Orgogozo. 2008. The loci of evolution: How predictable is genetic evolution? Evolution 62:2155-2177.

Streisfeld, M. A., and M. D. Rausher. 2011. Population genetics, pleiotropy, and the preferential fixation of mutations during adaptive evolution. Evolution 65:629-642.