

The genomics of adaptation

Jacek Radwan and Wieslaw Babik

Proc. R. Soc. B 2012 **279**, doi: 10.1098/rspb.2012.2322 first published online 24 October 2012

References

[This article cites 63 articles, 22 of which can be accessed free](#)

<http://rsob.royalsocietypublishing.org/content/279/1749/5024.full.html#ref-list-1>

[Article cited in:](#)

<http://rsob.royalsocietypublishing.org/content/279/1749/5024.full.html#related-urls>

Subject collections

Articles on similar topics can be found in the following collections

[evolution](#) (1371 articles)

[genetics](#) (49 articles)

[genomics](#) (25 articles)

Email alerting service

Receive free email alerts when new articles cite this article - sign up in the box at the top right-hand corner of the article or click [here](#)

*Introduction***The genomics of adaptation****Jacek Radwan^{1,*} and Wiesław Babik²**¹*Institute of Environmental Biology, Faculty of Biology, Adam Mickiewicz University,
Umultowska 89, 61-614 Poznań, Poland*²*Institute of Environmental Sciences, Jagiellonian University, Gronostajowa 7, 30-387 Kraków, Poland*

The amount and nature of genetic variation available to natural selection affect the rate, course and outcome of evolution. Consequently, the study of the genetic basis of adaptive evolutionary change has occupied biologists for decades, but progress has been hampered by the lack of resolution and the absence of a genome-level perspective. Technological advances in recent years should now allow us to answer many long-standing questions about the nature of adaptation. The data gathered so far are beginning to challenge some widespread views of the way in which natural selection operates at the genomic level. Papers in this Special Feature of Proceedings of the Royal Society B illustrate various aspects of the broad field of adaptation genomics. This introductory article sets up a context and, on the basis of a few selected examples, discusses how genomic data can advance our understanding of the process of adaptation.

Keywords: adaptation; genomics; natural selection**1. INTRODUCTION**

Evolution via natural selection is possible owing to heritable variation in phenotypic traits [1]. The amount and nature of genetic variation available to natural selection may affect the rate, course and outcome of evolution. Consequently, the question ‘What is the genetic basis of adaptive evolutionary change?’ has intrigued biologists for decades [2]. This general query consists of several empirically tractable and interconnected questions of fundamental importance for our understanding of evolutionary processes. One key question is whether adaptation occurs through the rapid fixation of new mutations or draws from standing genetic variation. If the latter is true, what are the mechanisms generating and maintaining adaptively relevant standing variation? The answer may differ for different organisms and traits, depending on the number of genes affecting the trait and the distribution of their fitness effects; this variability emphasizes the need to understand the genetic architecture of adaptive traits [3]. Genetic architecture involves not only the number of genes and the distribution of fitness effects, but also the interactions between alleles at various loci (epistasis), the degree to which variation in a particular gene affects multiple traits (pleiotropy), and the form (if any) of interactions between a genotype and environment. For example, epistasis may affect the chances that beneficial alleles will spread [4,5] and pleiotropy may constrain adaptive evolution [6]. A related and as yet unresolved controversy has long surrounded the relative importance of protein-coding versus *cis*-regulatory adaptive changes. Arguments in favour of both alternatives have been advanced, and the

data that have been collected are still insufficient to provide quantitative answers [7–10].

While questions regarding the genetic basis of adaptive change may only be reliably answered using good-quality data, researchers, until recently, had been constrained by the lack of a genomic perspective. Enormous progress in high-throughput DNA sequencing technologies over the last few years has enabled researchers to sequence genomes at the population scale, thus providing unbiased, genome-wide records of evolutionary changes [11,12]. These advances have at last brought a truly genomic perspective to the study of adaptive evolutionary change. We hope that this Special Feature, which brings together several papers dealing with various aspects of adaptation genomics, will give the reader a taste of the most recent developments in the field. The few articles in this Special Feature certainly cannot cover all the genomic approaches used in the study of adaptation, nor could we do so in our introductory article. Rather, we briefly discuss a few examples that illustrate how genomic data can advance our understanding of the process of adaptation and refer interested readers to a number of excellent recent review articles summarizing specific topics.

2. A GENOMIC PERSPECTIVE ON ADAPTATION: A FEW EXAMPLES**(a) *Loci of adaptation***

There has been a long debate regarding the properties of genes underlying adaptive changes (see [13] for a review and historical perspective). The influential infinitesimal model proposed by Fisher assumes that adaptation occurs via mutations of very small effects arising in a very large number of genes. In the late 1980s and throughout the 1990s, this view was seemingly challenged by reports suggesting that quantitative trait loci (QTL) of large effects may be common [14–16]. Genomic resources should, in

* Author for correspondence (j.w.radwan@gmail.com).

One contribution to a Special Feature ‘Genomics of adaptation’.

principle, now allow us to replace anonymous marker-based QTLs with quantitative trait nucleotides (QTNs), the nucleotide substitutions associated with variation in quantitative traits. However, large-scale genome-wide association studies in humans have detected surprisingly few QTNs (reviewed in [17]), and those that have been found account for a very small fraction of variation in complex traits such as blood pressure [18], height [19] or susceptibility to common diseases [20]. Similarly, while many QTLs have been reported for *Drosophila* wing shape [21], the search for QTNs has largely failed, with the best candidate explaining only 1 per cent of variation [22]. One explanation for this apparent incongruence is that QTLs are located in regions of many linked QTNs of small effect [23]. This QTL/QTN inconsistency highlights the usage of genome assembly in inferring the genetic basis of adaptation. If single nucleotide polymorphisms (SNPs) associated with traits of interest cannot be placed onto reference genome sequence, it is impossible to distinguish causality from linkage and to infer effect sizes explained by individual SNPs.

While these new results do not invalidate well-documented cases of adaptation via large-effect genetic variants [24,25], complex quantitative traits, such as body size, longevity, fecundity and length of development, seem to have a highly polygenic basis. Even if common, these genes of very small effect may nonetheless be practically impossible to pinpoint even with huge datasets, a dilemma that emphasizes the need for new alternatives to the QTN approach [17].

(b) Genomics of adaptive change: hard and soft sweeps

The effectiveness of selection depends greatly on effective population size and recombination rate [26,27]; thus it is very probable that the process of adaptation will differ fundamentally in taxonomic groups differing in these parameters. Models of adaptive evolution have traditionally assumed adaptation from de novo mutations [13,28]. Indeed, as reviewed by Burke in this issue [29], such scenarios seem to fit the evolution of microorganisms reasonably well. Whole-genome sequencing in the course of bacterial experimental evolution allows researchers to trace the origin and dynamics of adaptive mutations. Most fixed mutations are beneficial [30,31], and fixations generally occur quickly, although multiple beneficial mutations may compete for fixation [32]. While the rate of adaptation in experimental evolution studies decreases with time, a result that may be linked to widespread negative epistasis [33], the rate of genomic evolution remains surprisingly constant [30].

However, in larger organisms, which typically have smaller effective population sizes, adaptation from standing variation may be commonplace (reviewed in [34]). Soft sweeps [29,35], in which beneficial QTNs occur in variable genetic backgrounds, may explain why clear genomic signatures of the fixation of newly arisen beneficial mutations are often not observed in obvious cases of adaptive evolution [36]. The long-term effective size of the human population seems comparable to those used in experimental evolution studies on non-microbial organisms (reviewed by Burke in this issue [29]), and, as in most human adaptations [37], complete selective

sweeps are rarely observed in such experiments. Burke [29] discusses how the complex genomic landscape of adaptive changes revealed by the genomic analyses of selection experiments may be explained by a combination of soft, incomplete sweeps and subtle changes in allele frequencies that generate dramatic phenotypic changes in highly polygenic complex traits. She also proposes how experimental evolution studies can be modified to allow stringent testing of the effects of population size and recombination on the origins and fates of adaptive alleles.

(c) Parallel evolution

If genetic variation in certain traits is maintained by some form of balancing selection, or many polymorphisms exhibit conditional neutrality, repeated adaptation from standing genetic variation may result in parallel evolution. The genetic basis of parallel adaptations has intrigued researchers for years because its understanding may help answer questions about repeatability of evolution [38].

It appears that multiple outcomes are possible: identical polymorphisms repeatedly recruited from standing variation [39], independent adaptive mutations in a single gene or changes in various genes involved in particular pathways [25,31,34,40]. Conte *et al.* (this issue [41]) provide the first systematic assessment of the probability of the same gene being used by convergent or parallel evolutionary processes. The numbers are surprisingly high, with probability estimates of gene reuse ranging from 0.32 (based on genome-wide linkage studies) to 0.55 (based on candidate gene data). Rough calculations based on these estimates indicate that the effective number of genes available to adaptive evolution in such cases may typically be as small as two or three. Possible reasons for this low number may be the limited availability of adaptive mutations or effect sizes and mutation rates favouring repeated gene use. Apart from the recruitment of genes from standing genetic variation, which may increase the probability of gene reuse in closely related populations or taxa, other factors that limit the effective number of genes available for adaptation require further study. The study of Conte *et al.* [41] also highlights the usage of the genome-wide approach compared with the candidate-locus approach, as the latter appears to bias estimates upwards.

(d) Evolution of genomes

The architecture of the genome itself may be shaped by the action of natural selection or its relative inefficiency [26,42]. The excess DNA that appears in the genome as a consequence of the activity of selfish DNA elements such as introns or transposons is considered slightly deleterious (mutational-hazard hypothesis). In very large populations of microorganisms, selection effectively removes this excess DNA, whereas organisms with smaller effective population sizes accumulate excess DNA because drift overcomes weak purifying selection. Empirical evidence derived from genomic studies seems to support the mutational-hazard hypothesis ([43] but see [44,45]). The other side of the coin is, however, the possibility that extra DNA, which may be initially slightly deleterious but that persists owing to the inefficiency of selection, could then be recruited to serve as the basis for new adaptations [43].

Gene duplications have long been considered a major source of evolutionary novelty, since new functions can evolve by modification of one of the duplicated copies while the original function can be retained by the other copy [46]. The question remains as to how the duplicated copy is initially maintained. The traditional view that the duplication event is initially neutral has been challenged by Kondrashov *et al.* [47], who argued that duplication is likely to affect the dosage of the gene product. Kondrashov (this issue [48]) reviews the available evidence and concludes that, especially under stressful conditions, the higher level of expression resulting from gene duplication is indeed often beneficial. He encourages researchers to look for evidence of gene duplication when scrutinizing genomes for adaptation to stress.

(e) *Genomics of speciation*

The process of speciation, which is responsible for generating biodiversity, has an inherent genomic component. Speciation may be viewed from the genomic perspective as the gradual development of reproductive isolation across the genome [49–51]. Recent interest in the process of selection-driven ecological speciation, which may occur in spite of gene flow, has spurred interest in assessing the number, size and extent of clustering of genomic regions subject to disruptive selection [52].

New, genome-wide data may modify previous views and contribute to an understanding of the mechanisms responsible for the maintenance of such regions of genomic differentiation [53–55]. The study by Nosil *et al.* (this issue [56]) emphasizes that, even in a seemingly simple case of parallel ecological speciation and despite clear phenotypic parallels, genomic patterns of divergence between replicate pairs of incipient species may be surprisingly complex, with multiple factors affecting genomic divergence.

The gradualist perception of the speciation process, where parts of the genome may be exchanged between species at various stages of their diversification, encompasses not only the genetic basis of local adaptation and reproductive isolation, but also the exchange of adaptive alleles between species [57–59]. Genomic data now allow a comprehensive assessment of the extent of adaptive introgression, as illustrated by recent work on a species complex in which Mullerian mimicry occurs [60].

3. PROSPECTS

As the articles in this Special Feature testify, this is an exciting time for the field of adaptation genomics. Long-standing questions can now be addressed at a scale and level of precision that we could have hardly imagined a decade ago, with new approaches providing some definite answers while also often revealing the limitations of our current thinking about adaptation genomics. This situation is well illustrated by studies of human evolutionary history: it was anticipated that extensive genomic and financial resources would help provide a detailed understanding of the molecular basis of numerous human adaptations and diseases. The picture emerging from several years of intense research is, however, somewhat sobering [20,36,61,62]. Candidate loci as well as genomic scans have resulted in some spectacular discoveries, including signals of independent incomplete sweeps at

lactase promoters in Europe and Africa [63,64] or genes underlying adaptation to high altitude [65]. Many scans for recent positive selection have been performed that have identified large portions of the genome as targets. However, most of the findings from individual studies have not been replicated and relatively few unequivocal targets of positive selection have been discovered in the human genome [61]. These findings contrast with the overwhelming evidence for recent adaptive phenotypic evolution in our species [36]. Adaptations have obviously been occurring, but they have not taken the form of classical selective sweeps [37]. The accumulating empirical evidence has led to renewed interest in population genetics models of adaptation from standing genetic variation, including soft sweeps [35], as well as an appreciation of the highly polygenic nature of most adaptations in humans [66].

Furthermore, genomic approaches offer completely new possibilities in the study of adaptation. For example, it has become feasible to infer selection and identify its phenotypic targets from genomic patterns of variation observed under various environmental conditions, which may be termed the ‘reverse ecology of adaptation’. The traditional genetics of adaptation linked observed phenotypic divergence to underlying genetic variation. The phenotypic traits associated with adaptation are not always easy to identify, especially in microorganisms. High-throughput sequencing technologies now allow an examination of whole-genome patterns of genetic diversity within and between populations and the identification of those genes that show signatures of recent positive selection and/or divergent adaptation between populations. For example, Ellison *et al.* [67] sequenced transcriptomes of 48 *Neurospora crassa* isolates and, on the basis of detected SNPs, identified two thus-far cryptic, recently diverged populations. Further high-resolution scans for divergent chromosomal regions identified areas that were enriched with genes involved in responses to low temperature. Indeed, experiments designed on the basis of these results showed that the cryptic populations differed in fitness at low temperatures. This study demonstrates that by scanning genomes from multiple populations, researchers may not only be able to identify genes responsible for local adaptation, but also learn about the adaptive phenotypes and selective pressures acting on them.

As evident from the reviews contained in this Special Feature, existing data already offer important insights into the genomic basis of adaptation, but generalization will require more genome-wide studies, ideally including a diverse range of taxa. For example, Kondrashov’s review [48] indicates that both data from additional study systems and progress in the genomic analysis of copy number variation are required to fully assess the role of gene duplications in adaptation. There are also areas of study, as argued in the papers by Nosil *et al.* [56] and Conte *et al.* [41], in which there are still simply too few data available from which to draw generalizations. In these areas, additional genomic information from suitable systems may speed progress in addressing questions of speciation genomics or the genomic nature of parallel adaptation. Carefully designed experimental evolution studies using new model systems, such as sexually reproducing microbes, may overcome the limitations of traditional approaches and allow a careful dissection of the process

of adaptive evolution, as suggested by Burke [29]. Finally, the sequencing of the genomes of many non-model organisms will allow the precise inference of natural selection's action on genomic regions, which is thus far only available for humans and a few model organisms.

REFERENCES

- 1 Darwin, C. 1859 *On the origin of species by means of natural selection, or the preservation of favoured races in the struggle for life*. London, UK: John Murray.
- 2 Lewontin, R. C. 1974 *The genetic basis of evolutionary change*. New York, NY: Columbia University Press.
- 3 Ellegren, H. & Sheldon, B. C. 2008 Genetic basis of fitness differences in natural populations. *Nature* **452**, 169–175. (doi:10.1038/nature06737)
- 4 Phillips, P. C. 2008 Epistasis—the essential role of gene interactions in the structure and evolution of genetic systems. *Nat. Rev. Genet.* **9**, 855–867. (doi:10.1038/nrg2452)
- 5 Ostman, B., Hintze, A. & Adami, C. 2012 Impact of epistasis and pleiotropy on evolutionary adaptation. *Proc. R. Soc. B* **279**, 247–256. (doi:10.1098/rspb.2011.0870)
- 6 Orr, H. A. 2000 Adaptation and the cost of complexity. *Evolution* **54**, 13–20. (doi:10.1111/j.0014-3820.2000.tb00002.x)
- 7 King, M. C. & Wilson, A. C. 1975 Evolution at two levels in humans and chimpanzees. Their macromolecules are so alike that regulatory mutations may account for their biological differences. *Science* **188**, 107–116. (doi:10.1126/science.1090005)
- 8 Hoekstra, H. E. & Coyne, J. A. 2007 The locus of evolution: evo devo and the genetics of adaptation. *Evolution* **61**, 995–1016. (doi:10.1111/j.1558-5646.2007.00105.x)
- 9 Wray, G. A. 2007 The evolutionary significance of *cis*-regulatory mutations. *Nat. Rev. Genet.* **8**, 206–216. (doi:10.1038/nrg2063)
- 10 Razeto-Barry, P. & Maldonado, K. 2011 Adaptive *cis*-regulatory changes may involve few mutations. *Evolution* **65**, 3332–3335. (doi:10.1111/j.1558-5646.2011.01412.x)
- 11 Stapley, J. *et al.* 2010 Adaptation genomics: the next generation. *Trends Ecol. Evol.* **25**, 705–712. (doi:10.1016/j.tree.2010.09.002)
- 12 Metzker, M. L. 2010 Sequencing technologies the next generation. *Nat. Rev. Genet.* **11**, 31–46. (doi:10.1038/nrg2626)
- 13 Orr, H. A. 2005 The genetic theory of adaptation: a brief history. *Nat. Rev. Genet.* **6**, 119–127. (doi:10.1038/nrg1523)
- 14 Tanksley, S. D. 1993 Mapping polygenes. *Annu. Rev. Genet.* **27**, 205–233. (doi:10.1146/annurev.ge.27.120193.001225)
- 15 Kearsley, M. J. & Farquhar, A. G. L. 1998 QTL analysis in plants; where are we now? *Heredity* **80**, 137–142. (doi:10.1046/j.1365-2540.1998.00500.x)
- 16 Mackay, T. F. C. 2001 The genetic architecture of quantitative traits. *Annu. Rev. Genet.* **35**, 303–339. (doi:10.1146/annurev.genet.35.102401.090633)
- 17 Rockman, M. V. 2012 The QTN program and the alleles that matter for evolution: all that's gold does not glitter. *Evolution* **66**, 1–17. (doi:10.1111/j.1558-5646.2011.01486.x)
- 18 Levy, D. *et al.* 2009 Genome-wide association study of blood pressure and hypertension. *Nat. Genet.* **41**, 677–687. (doi:10.1038/ng.384)
- 19 McEvoy, B. P. & Visscher, P. M. 2009 Genetics of human height. *Econ. Hum. Biol.* **7**, 294–306. (doi:10.1016/j.ehb.2009.09.005)
- 20 Stranger, B. E., Stahl, E. A. & Raj, T. 2011 Progress and promise of genome-wide association studies for human complex trait genetics. *Genetics* **187**, 367–383. (doi:10.1534/genetics.110.120907)
- 21 Mezey, J. G., Houle, D. & Nuzhdin, S. V. 2005 Naturally segregating quantitative trait loci affecting wing shape of *Drosophila melanogaster*. *Genetics* **169**, 2101–2113. (doi:10.1534/genetics.104.036988)
- 22 Palsson, A., Dodgson, J., Dworkin, I. & Gibson, G. 2005 Tests for the replication of an association between *Egfr* and natural variation in *Drosophila melanogaster* wing morphology. *BMC Genet.* **6**, 44. (doi:10.1186/1471-2156-6-44)
- 23 Noor, M. A.F., Cunningham, A. L. & Larkin, J. C. 2001 Consequences of recombination rate variation on quantitative trait locus mapping studies: simulations based on the *Drosophila melanogaster* genome. *Genetics* **159**, 581–588.
- 24 Shapiro, M. D., Marks, M. E., Peichel, C. L., Blackman, B. K., Nereng, K. S., Jónsson, B., Schluter, D. & Kingsley, D. M. 2004 Genetic and developmental basis of evolutionary pelvic reduction in threespine sticklebacks. *Nature* **428**, 717–723. (doi:10.1038/nature02415)
- 25 Chan, Y. F. *et al.* 2010 Adaptive evolution of pelvic reduction in sticklebacks by recurrent deletion of a *Pitxl* enhancer. *Science* **327**, 302–305. (doi:10.1126/science.1182213)
- 26 Lynch, M. 2007 *The origins of genome architecture*. Sunderland, MA: Sinauer.
- 27 Charlesworth, B. 2012 The effects of deleterious mutations on evolution at linked sites. *Genetics* **190**, 5–22. (doi:10.1534/genetics.111.134288)
- 28 Orr, H. A. 1998 The population genetics of adaptation: the distribution of factors fixed during adaptive evolution. *Evolution* **52**, 935–949. (doi:10.2307/2411226)
- 29 Burke, M. K. 2012 How does adaptation sweep through the genome? Insights from long-term selection experiments. *Proc. R. Soc. B* **279**, 5029–5038. (doi:10.1098/rspb.2012.0799)
- 30 Barrick, J. E., Yu, D. S., Yoon, S. H., Jeong, H., Oh, T. K., Schneider, D., Lenski, R. E. & Kim, J. F. 2009 Genome evolution and adaptation in a long-term experiment with *Escherichia coli*. *Nature* **461**, 1243–1247. (doi:10.1038/nature08480)
- 31 Tenaillon, O., Rodriguez-Verdugo, A., Gaut, R. L., McDonald, P., Bennett, A. F., Long, A. D. & Gaut, B. S. 2012 The molecular diversity of adaptive convergence. *Science* **335**, 457–461. (doi:10.1126/science.1212986)
- 32 Sniegowski, P. D. & Gerrish, P. J. 2010 Beneficial mutations and the dynamics of adaptation in asexual populations. *Phil. Trans. R. Soc. B* **365**, 1255–1263. (doi:10.1098/rstb.2009.0290)
- 33 Khan, A. I., Dinh, D. M., Schneider, D., Lenski, R. E. & Cooper, T. F. 2012 Negative epistasis between beneficial mutations in an evolving bacterial population. *Science* **332**, 1193–1196. (doi:10.1126/science.1203801)
- 34 Barrett, R. D. H. & Schluter, D. 2008 Adaptation from standing genetic variation. *Trends Ecol. Evol.* **23**, 38–44. (doi:10.1016/j.tree.2007.09.008)
- 35 Hermisson, J. & Pennings, P. S. 2005 Soft sweeps: molecular population genetics of adaptation from standing genetic variation. *Genetics* **169**, 2335–2352. (doi:10.1534/genetics.104.036947)
- 36 Pritchard, J. K., Pickrell, J. K. & Coop, G. 2010 The genetics of human adaptation: hard sweeps, soft sweeps, and polygenic adaptation. *Curr. Biol.* **20**, R208–R215. (doi:10.1016/j.cub.2009.11.055)
- 37 Hernandez, R. D., Kelley, J. L., Elyashiv, E., Melton, S. C., Auton, A., McVean, G., Sella, G. & Przeworski, M. 2011 Classic selective sweeps were rare in recent

- human evolution. *Science* **331**, 920–924. (doi:10.1126/science.1198878)
- 38 Stern, D. L. & Orgogozo, V. 2009 Is genetic evolution predictable? *Science* **323**, 746–751. (doi:10.1126/science.1158997)
 - 39 Colosimo, P. F. *et al.* 2005 Widespread parallel evolution in sticklebacks by repeated fixation of ectodysplasin alleles. *Science* **307**, 1928–1933. (doi:10.1126/science.1107239)
 - 40 Elmer, K. R. & Meyer, A. 2011 Adaptation in the age of ecological genomics: insights from parallelism and convergence. *Trends Ecol. Evol.* **26**, 298–306. (doi:10.1016/j.tree.2011.02.008)
 - 41 Conte, G. L., Arnegard, M. E., Peichel, C. L. & Schluter, D. 2012 The probability of genetic parallelism and convergence in natural populations. *Proc. R. Soc. B* **279**, 5039–5047. (doi:10.1098/rspb.2012.2146)
 - 42 Lynch, M. & Conery, J. S. 2003 The origins of genome complexity. *Science* **302**, 1401–1404. (doi:10.1126/science.1089370)
 - 43 Lynch, M., Bobay, L. M., Catania, F., Gout, J. F. & Rho, M. 2011 The repatterning of eukaryotic genomes by random genetic drift. *Annu. Rev. Genom. Hum. Genet.* **12**, 347–366. (doi:10.1146/annurev-genom-082410-101412)
 - 44 Whitney, K. D., Boussau, B., Baack, E. J. & Garland Jr, T. 2011 Drift and genome complexity revisited. *PLoS Genet.* **7**, 1002092. (doi:10.1371/journal.pgen.1002092)
 - 45 Whitney, K. D. & Garland Jr, T. 2010 Did genetic drift drive increases in genome complexity? *PLoS Genet.* **6**, 1001080. (doi:10.1371/journal.pgen.1001080)
 - 46 Ohno, S. 1970 *Evolution by gene duplication*. New York, NY: Springer.
 - 47 Kondrashov, F. A., Rogozin, I. B., Wolf, Y. I. & Koonin, E. V. 2002 Selection in the evolution of gene duplications. *Genome Biol.* **3**, RESEARCH0008. (doi:10.1186/gb-2002-3-2-research0008)
 - 48 Kondrashov, F. A. 2012 Gene duplication as a mechanism of genomic adaptation to a changing environment. *Proc. R. Soc. B* **279**, 5048–5057. (doi:10.1098/rspb.2012.1108)
 - 49 Wu, C. I. 2001 The genic view of the process of speciation. *J. Evol. Biol.* **14**, 851–865. (doi:10.1046/j.1420-9101.2001.00335.x)
 - 50 Wu, C. I. & Ting, C. T. 2004 Genes and speciation. *Nat. Rev. Genet.* **5**, 114–122. (doi:10.1038/nrg1269)
 - 51 Nosil, P., Funk, D. J. & Ortiz-Barrientos, D. 2009 Divergent selection and heterogeneous genomic divergence. *Mol. Ecol.* **18**, 375–402. (doi:10.1111/j.1365-294X.2008.03946.x)
 - 52 Nosil, P. & Feder, J. L. 2012 Genomic divergence during speciation: causes and consequences. *Phil. Trans. R. Soc. B* **367**, 332–342. (doi:10.1098/rstb.2011.0263)
 - 53 Turner, T. L., Hahn, M. W. & Nuzhdin, S. V. 2005 Genomic islands of speciation in *Anopheles gambiae*. *PLoS Biol.* **3**, 1572–1578. (doi:10.1371/journal.pbio.0030285)
 - 54 Noor, M. A. F. & Bennett, S. M. 2009 Islands of speciation or mirages in the desert examining the role of restricted recombination in maintaining species. *Heredity* **103**, 439–444. (doi:10.1038/hdy.2009.151)
 - 55 Lawniczak, M. K.N. *et al.* 2010 Widespread divergence between incipient *Anopheles gambiae* species revealed by whole genome sequences. *Science* **330**, 512–514. (doi:10.1126/science.1195755)
 - 56 Nosil, P., Gompert, Z., Farkas, T. E., Comeault, A. A., Feder, J. L., Buerkle, C. A. & Parchman, T. L. 2012 Genomic consequences of multiple speciation processes in a stick insect. *Proc. R. Soc. B* **279**, 5058–5065. (doi:10.1098/rspb.2012.0813)
 - 57 Arnold, M. L. 2004 Transfer and origin of adaptations through natural hybridization: were Anderson and Stebbins right? *Plant Cell* **16**, 562–570. (doi:10.1105/tpc.160370)
 - 58 Castric, V., Bechsgaard, J., Schierup, M. H. & Vekemans, X. 2008 Repeated adaptive introgression at a gene under multiallelic balancing selection. *PLoS Genet.* **4**, e1000168. (doi:10.1371/journal.pgen.1000168)
 - 59 Nadachowska-Brzyska, K., Zielinski, P., Radwan, J. & Babik, W. 2012 Interspecific hybridization increases MHC class II diversity in two sister species of newts. *Mol. Ecol.* **21**, 887–906. (doi:10.1111/j.1365-294X.2011.05347.x)
 - 60 Dasmahapatra, K. K. *et al.* 2012 Butterfly genome reveals promiscuous exchange of mimicry adaptations among species. *Nature* **486**, 94–98. (doi:10.1038/nature11041)
 - 61 Akey, J. M. 2009 Constructing genomic maps of positive selection in humans: where do we go from here? *Genome Res.* **19**, 711–722. (doi:10.1101/gr.086652.108)
 - 62 Gibson, G. 2012 Rare and common variants: twenty arguments. *Nat. Rev. Genet.* **13**, 135–145. (doi:10.1038/nrg3118)
 - 63 Bersaglieri, T., Sabeti, P. C., Patterson, N., Vanderploeg, T., Schaffner, S. F., Drake, J. A., Rhodes, M., Reich, D. E. & Hirschhorn, J. N. 2004 Genetic signatures of strong recent positive selection at the lactase gene. *Am. J. Hum. Genet.* **74**, 1111–1120. (doi:10.1086/421051)
 - 64 Tishkoff, S. A. *et al.* 2007 Convergent adaptation of human lactase persistence in Africa and Europe. *Nat. Genet.* **39**, 31–40. (doi:10.1038/ng1946)
 - 65 Yi, X. *et al.* 2011 Sequencing of 50 human exomes reveals adaptation to high altitude. *Science* **329**, 75–78. (doi:10.1126/science.1190371)
 - 66 Pritchard, J. K. & Di Rienzo, A. 2010 Adaptation—not by sweeps alone. *Nat. Rev. Genet.* **11**, 665–667. (doi:10.1038/nrg2880)
 - 67 Ellison, C. E., Hall, C., Kowbel, D., Welch, J., Brem, R. B., Glass, N. L. & Taylor, J. W. 2011 Population genomics and local adaptation in wild isolates of a model microbial eukaryote. *Proc. Natl Acad. Sci. USA* **108**, 2831–2836. (doi:10.1073/pnas.1014971108)