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What Is the Role of Genome Duplication in the Evolution of Complexity and Diversity?

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Gene and genome duplications provide a source of genetic material for mutation, drift, and selection to act upon, making new evolutionary opportunities possible. As a result, many have argued that genome duplication is a dominant factor in the evolution of complexity and diversity. However, a clear correlation between a genome duplication event and increased complexity and diversity is not apparent, and there are inconsistencies in the patterns of diversity invoked to support this claim. Interestingly, several estimates of genome duplication events in vertebrates are preceded by multiple extinct lineages, resulting in preduplication gaps in extant taxa. Here we argue that gen(om)e duplication could contribute to reduced risk of extinction via functional redundancy, mutational robustness, increased rates of evolution, and adaptation. The timeline for these processes to unfold would not predict immediate increases in species diversity after the duplication event. Rather, reduced probabilities of extinction would predict a latent period between a genome duplication and its effect on species diversity or complexity. In this paper, we will develop the idea that genome duplication could contribute to species diversity through reduced probability of extinction.

Introduction

In the last century, gene and genome duplication has been recognized as a prominent factor in the evolution of eukaryotes (Ohno 1970; Otto and Whitton 2000; reviewed in Taylor and Raes 2004). Over 50 years ago it was noted that without a mechanism for increasing its genetic material, our primordial common ancestor would have needed to possess all the genetic components responsible for the diversity of species observed (Metz 1947). While individual gene duplication is common, whole-genome duplications also are thought to have been a significant factor in vertebrate evolution, and the primary source of gene duplicates in plants (Wendel 2000). The most obvious contribution of gene duplication to evolution is providing new genetic material for mutation, drift, and selection to act upon, making new evolutionary opportunities possible (Zhang 2003). As a logical extension of this argument, many authors have drawn a correlation between gen(om)e duplication and the evolution of complexity and diversity (reviewed in Otto and Whitton 2000; Donoghue and Purnell 2005). This sets up the prediction that there is a significant increase in species diversity after a genome duplication event. However, there are inconsistencies between this hypothesis and observed patterns of diversity (Donoghue and Purnell 2005), and the evolutionary significance of gene and genome duplication is likely not fully characterized (Wagner, Amemiya, and Ruddle 2003).

Genome Duplication Is a Common Evolutionary Phenomenon

Genome duplication is both an ancient and ongoing process in yeast, plants, and animals. It was recently confirmed that the yeast genus, *Saccharomyces*, experienced an ancient whole-genome duplication (Kellis, Birren, and Lander 2004), and genome duplication is ubiquitous in plants (D. E. Soltis and P. S. Soltis 1999). Multiple episodes of genome duplication have occurred during the diversification of angiosperms including ancient polyploidization events and a multitude of independent duplications in various lineages (Ku et al. 2000; Vision, Brown, and Tanksley 2000; Bowers et al. 2003; Blanc and Wolfe 2004*a*; Soltis 2005). While not as common as in plants, hundreds of genome duplication events have occurred in independent lineages in metazoans as well. In chordate evolution, whole-genome duplications have occurred coincident with the origin of vertebrates, gnathostomes, and teleosts (Holland et al. 1994; Meyer and Schartl 1999; Postlethwait et al. 2000; Hoegg et al. 2004; Prohaska and Stadler 2004; Crow et al. 2005).

Conflict in the Putative Correlation Between Genome Duplication and the Evolution of Complexity and Diversity

Have these genome duplications been accompanied by dramatic jumps in species richness? A causal link between any specific genome duplication event and increased species diversity remains elusive (Otto and Whitton 2000; Wendel 2000; Donoghue and Purnell 2005). In plants, an ancient whole-genome duplication event occurred before the divergence of *Arabidopsis* and other dicots (Ku et al. 2000; Bowers et al. 2003), putatively before the radiation of core eudicots—the most diverse group of angiosperms. However, extensive genomic expansion and contraction in plants due to frequent gen(om)e duplications, and subsequent gene loss, obscures the signature of individual duplication events (Blanc and Wolfe 2004*a*) and therefore makes detection of correlations between specific events and increased diversity difficult. Alternatively, there is evidence from a well-studied gene family, the MADS-box genes, indicating that extensive gene duplication, and subsequent modification in various lineages, has resulted in diversified

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protein functions (Irish and Litt 2005) and is associated with the development of new floral morphologies in angiosperms (Irish 2003).

In vertebrates, a major focus in understanding the evolution of complexity and diversity has been elucidating the causes and effects of increasing Hox cluster number and conservation throughout chordate phylogeny. It is widely accepted that Hox gene cluster duplication is the result of whole-genome duplications before the origins of vertebrates, gnathostomes, and teleost fishes (Meyer and Schartl 1999). However, a tight correlation between Hox cluster duplication and the evolution of complexity and diversity is not apparent. First, invertebrates exhibit a greater variety of body plans and far greater species diversity than any vertebrate group, yet exhibit, at most, a single Hox cluster (Carroll 1995). Sarcopterygians exhibit greater complexity and diversity than cartilaginous fishes, yet both groups exhibit the same number of Hox clusters (Robinson-Rechavi, Boussau, and Laudet 2004).

One of the most popular examples of a putative correlation between genome duplication and increased diversity is the proposal that increased genomic complexity of rayfinned fishes, due to multiple rounds of genome duplication, has contributed to their evolutionary success and diversity (Meyer and Schartl 1999; Zhou, Cheng, and Tiersch 2001). Recently it has been shown that the "fish-specific" Hox cluster duplication is specific to teleosts (Crow et al. 2005), and this whole-genome duplication is supported by numerous studies of other paralogous genes (e.g., Hoegg et al. 2004). Teleosts are the most diverse group of vertebrates—comprising half of all vertebrate species (over 23,000 species, Nelson 1994). By all accounts, teleosts are considered a highly successful and diverse group. However, the most basal teleost group, the Osteoglossomorpha, is not characterized by an explosion in species richness (217 species, Nelson 1994), and the majority of species richness associated with teleosts is sequestered in two groups, the Ostariophysi (6,508 species) and the Perciformes (9,293 species), which originated long after the genome duplication at the root of teleosts. Although it should be noted that several independent genome duplications have been discovered in lineages within the Ostariophysi (Le Comber and Smith 2004). Teleosts belong to a group of fishes called actinopterygians, and indeed, basal actinopterygians, including bichirs, sturgeons and paddlefish, gars, and bowfin, are relatively species poor. Together they comprise less than 1% of extant actinopterygians. Therefore, there appears to be an increase in species diversity in teleosts. However, Donoghue and Purnell (2005) have argued that extinct basal actinopterygian lineages harbor diversity that has not been considered in hypotheses regarding genome duplication and diversity, and that increased body plan complexity is not associated with teleosts when extinct forms are considered. Therefore, paleontological data provide no support for a close correlation between genome duplications and increased complexity or species diversity (Donoghue and Purnell 2005). This observation is troubling. Therefore, we propose a hypothesis that is consistent with observations of diversity and complexity with respect to genome duplications, which has not previously been suggested.

Genome Duplication May Play a Role in Escaping Extinction

A potential explanation for the lack of a tight correlation between genome duplication and increased diversification is that the former is an event and the latter is a process. While it is likely that genome duplication contributes to opportunities for adaptation, adaptation requires ecological necessity. Novel gene functions must evolve in response to changing environmental or ecological pressures, but the origination of beneficial mutations may not occur on the same timescale as changes in external factors. Therefore, in the face of changing environmental and ecological conditions, lineages must first, or simultaneously, escape extinction. Remarkably, estimates of several genome duplication events in vertebrate history are preceded by multiple extinct lineages, resulting in preduplication gaps in extant taxa (fig. 1, adapted from Donoghue and Purnell 2005). Donoghue and Purnell (2005) argue that preduplication extinct lineages were relatively diverse and hence there is no postduplication increase in diversity, however, the authors did not consider a correlation between genome duplication and reduced extinction risk.

We reanalyzed the data used in Donoghue and Purnell (2005, from Patterson 1993) to evaluate whether the probability of extinction is reduced in postduplication teleost lineages. This analysis requires a shift in the analysis of dependent factors to investigate a correlation between genome duplication and reduced extinction rates rather than increased diversity. We used number of families as a conservative proxy for diversity, and added data for crown-group teleosts from Patterson (1993), which included both extinct and extant lineages. The total and extinct number of families in preduplication and postduplication lineages were converted to extinction rates using conservative time estimates for the origin of actinopterygian and teleost lineages. Using these data, we calculated the fraction of the surviving families as an estimate of the probability of survival, Ps, and then used the age of the clade to estimate the rate of extinction, assuming an exponential death model:

$$Ps = \mathrm{e}^{-\lambda T}$$

$$\lambda = \frac{-\ln Ps}{T}.$$

The time used in these equations assumes that all the lineages arose at the same time, which they did not, therefore we use times resulting in a conservative estimate of the extinction rate relative to our hypothesis that the rate of extinction before the duplication is higher than after.

Preduplication, actinopterygian lineages include 59 families. Four of these include extant taxa. Therefore, the probability of survival in preduplication actinopterygian lineages is $5/59 = 0.0678$. The deepest node in this paraphyletic group is 450 Myr, which gives a rate estimate of

$$\lambda_{\mathrm{est}} = \frac{-\ln 0.0847}{450} = 0.00548.$$

This is an underestimate of the true rate (i.e., $\lambda > \lambda_{\mathrm{est}}$) because most of the lineages actually arose after 450 Myr.

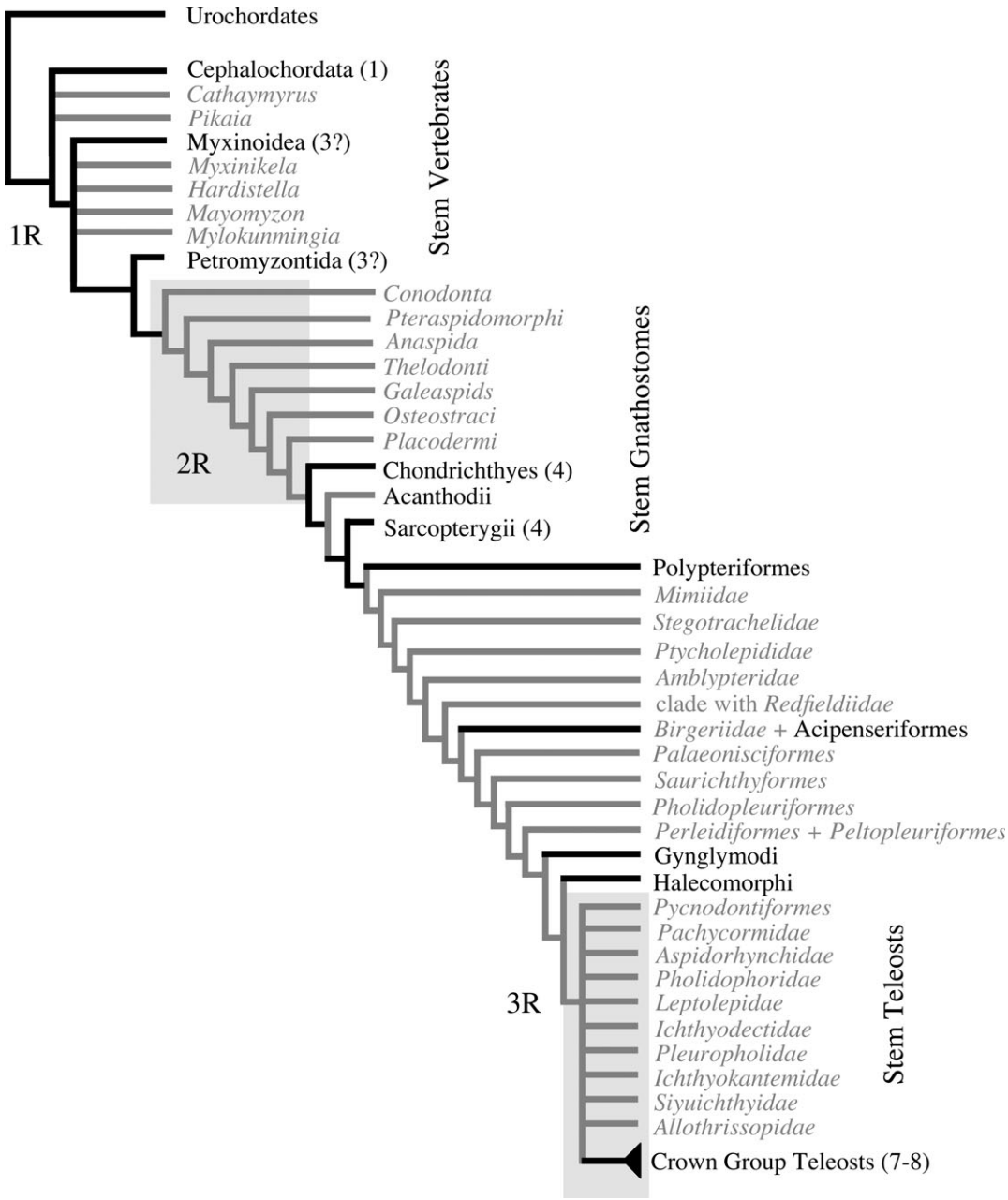

FIG. 1.—Adapted from Donoghue and Purnell (2005). Hypothesis of relationships among living (black lines) and extinct (gray lines) vertebrate lineages. Shaded areas indicate possible lineages where the "2R" and "3R" genome duplications are estimated to have occurred. The number of extinct and extant families follow Patterson (1993). Number of families include all taxa originating in the Paleozoic to the Cenozoic. Nonteleost actinopterygians include totally 59 families, four of which include extant taxa. Stem teleosts and crown teleosts include 324 families, 255 of which include extant taxa.

The total number of families classified as teleosts including stem groups is 324, with 255 surviving. Because there is no way to assess whether extinct stem-teleost lineages shared the genome duplication exhibited by crown-group teleosts, we included extinct stem-group lineages in the duplicated group to ensure a conservative estimate of postduplication extinction rates. Although studies on the molecular evolution of *HoxA11* and *HoxB5* estimate that the duplication occurred within a relatively short time period (3.4–5 Myr) before the teleost radiation (Crow et al. 2005). The root of the crown group is estimated at 220 Myr, but the extinct stem teleosts originated before that. Using the date of the crown group and including the extinct stem lineages bias the estimate toward larger extinction rates, but the fact that the crown-group lineages arose later than 220 MYA biases the estimate toward a lower extinction rate. We assume that these two biases cancel to some extent. The probability of survival in this inclusive teleost clade is 255/324 = 0.787, which leads to a rate estimate of

$$\lambda = \frac{-\ln 0.787}{220} = 0.00108.$$

Comparing these two rates leads to an extinction rate in preteleost actinopterygians at least 5 times higher than in teleosts.

There are two additional methodological challenges in this analysis that should be considered. First, diversity and extinction rates are likely to be underestimated due to incomplete taxonomic representation and preservation bias in the fossil record. However, the fact that the teleosts are more recent should favor the discovery of extinct lineages compared to the more ancient nonteleost actinopterygians. This bias is conservative with respect to our hypothesis. Second, the occurrence of mass extinctions is a confounding factor because the prominent genome duplications that occurred in the stem lineages of vertebrates, gnathostomes, and teleost fishes are estimated to have occurred within relatively short time frames of the Ordovician mass extinction (approximately 450 MYA) and the Permian mass extinction (approximately 248 MYA). Therefore, alleviation from risk of extinction is difficult to attribute solely to genome duplication in this geological context. However, it is important to consider that mass extinctions may have been a driving force in shaping survivorship probabilities associated with genome duplication. In fact, relatively few lineages would necessarily have to escape extinction to later produce the diversity observed in the major vertebrate lineages. Gen(om)e duplication provides a period of genetic redundancy that confers robustness against deleterious mutations, relaxed constraint, and genetic opportunities for adaptation. We propose that these phenomena could contribute to reduced risk of extinction via functional redundancy, increased rates of evolution, directional selection, and adaptation. These processes are measurable and have been shown to be associated with gen(om)e duplications.

The following model has been proposed in which genome duplication is associated with increased evolvability, which in turn contributes to reduced probabilities of extinction and, eventually, potential for diversification (Crow et al. 2005). Gen(om)e duplication initially provides the genetic redundancy necessary to confer robustness against deleterious mutations (Gu et al. 2003; Conant and Wagner 2004), while opening a window of relaxed constraint (Wagner, Amemiya, and Ruddle 2003) and increased rates of evolution (Seoighe, Johnston, and Shields 2003; Fried, Prohaska, and Stadler 2004; Crow et al. 2005; Wagner et al. 2005). This may provide the opportunity for genetic variability to accrue at a higher rate than before the duplication and with fewer deleterious side effects, which would be necessary for directional selection, adaptation, and functional innovation to occur. The timeline necessary for these evolutionary processes to unfold and contribute to species diversity or innovative gene functions would not predict immediate explosive radiations or jumps in phenotypic complexity. Rather, various degrees of latency associated with the evolution of species diversity would be expected, depending on a mosaic of random processes and external forces imposed on diverging lineages. Here we review evidence drawn from yeast, plants, and vertebrates, which is organized by processes related to (1) diploidization and (2) selection. Diploidization is the process by which duplicated genes are lost, rearranged, or changed. This sets the stage for adaptive evolution and diversification via increased rates of evolution and positive selection on some genes. Patterns of differential loss of duplicate paralogs could further contribute to opportunities for reproductive isolation and species diversity (Lynch and Conery 2000; Lynch and Force 2000).

Diploidization and Genome Reorganization

Several mechanisms contribute to the evolutionary fate of duplicated genes, such as genome reorganization, gene loss, epigenetic gene silencing, and neofunctionalization (Song et al. 1995; Walsh 1995; Force et al. 1999; Hughes 1999; Lynch and Conery 2000; Wendel 2000; Prince and Pickett 2002). Genome reorganization can occur quite rapidly after polyploidization in some lineages (e.g., within five generations in *Brassica*, Song et al. 1995; Gale and Devos 1998) but varies in different lineages (reviewed in Lawton-Rauh 2003). One potential consequence of genome reorganization is that a duplicated gene may immediately differentiate from its parental copy by being placed under the influence of new *cis*-regulatory elements (Lynch and Katju 2004). Gene loss after duplication is significant and resulted in the loss of 88% of paralogous genes in the yeast *Saccharomyces cerevisiae* (Kellis, Birren, and Lander 2004). The seven Hox clusters of zebrafish and fugu have only a few more Hox genes than humans or mice, 51 and 39, respectively (Wagner, Amemiya, and Ruddle 2003), and the pattern of loss is variable. In fact, the majority of duplicate genes are expected to be lost due to mutational decay (i.e., pseudogenization), but remarkably, a greater proportion of genes are retained than would be predicted, in a variety of taxa (reviewed in Otto and Whitton 2000), and genes exhibiting functional divergence tend to be preferentially retained. For example, in yeast the retained paralogs which exhibited increased substitution rates were predominantly kinases and regulatory proteins (Kellis, Birren, and Lander 2004). In *Arabidopsis*, duplicated kinases are preferentially retained, while copies of DNA repair enzymes are preferentially lost (Blanc and Wolfe 2004*b*). These data suggest that preferentially retained paralogs tend to exhibit a variety of functions. And, these aspects of genome reorganization imply an active role of selection in shaping the fate of duplicated genes.

Increased Rates of Evolution and Selection on Duplicated Genes

Genome duplication is often followed by increased rates of evolution and directional selection on some genes (Lynch and Conery 2000; Malaga-Trillo and Meyer 2001; Kondrashov et al. 2002; Conant and Wagner 2003; Fares et al. 2003; Seoighe, Johnston, and Shields 2003; Crow et al. 2005; Wagner et al. 2005). Relatively quickly thereafter lineages diverge, which then continue to exhibit increased rates of evolution compared to nonduplicated lineages, as demonstrated in the teleost-specific Hox cluster duplication (Crow et al. 2005). This corresponds to a postduplication "window of evolvability" due to relaxed constraint that has been previously postulated (Wagner, Amemiya, and Ruddle 2003) and is supported by the pattern and frequency of transposable elements in vertebrate and invertebrate Hox clusters (Fried, Prohaska, and Stadler 2004). Finally, positive Darwinian selection on duplicated genes can be responsible for functional divergence and innovation (Ohno 1970; Tanaka and Nei

1989; Zhang, Rosenberg, and Nei 1998; Duda and Palumbi 1999; Hughes et al. 2000; Zhang, Dyer, and Rosenberg 2000; Merritt and Quattro 2001; J. Z. Zhang, Y. P. Zhang, and Rosenberg 2002).

How Is Genome Duplication Related to Extinction?

Three by-products of gen(om)e duplication could contribute to decreased probabilities of extinction: mutational robustness, increased genetic variation, and increased tolerance to environmental conditions. In yeast, mutations to one copy of a duplicated gene had a reduced probability of lethal effect compared to single-copy genes, and gene silencing had an increased probability of weak or no effect in yeast (Gu et al. 2003) and *Caenorhabditis elegans* (Conant and Wagner 2004).

Factors that contribute to increased genetic variation will reduce the probability of extinction and mediate the effects of changing environmental and ecological factors. Because genome duplication is much more common in plants than in animals, there are more data that bear on factors directly related to genetic variation and reduced probability of extinction. We know that genome duplication is often followed by rapid genomic rearrangements, variable patterns of gene loss, and decay of synteny (Song et al. 1995; Wendel 2000; Bowers et al. 2003). These factors contribute to increased genetic variation which may allow stronger responses to various selection pressures, thereby providing more opportunities for survival in changing environments (Soltis 2005).

The geographic and ecological ranges of polypoid plants have been reported to be larger than those of their diploid relatives, suggesting that polypoidy confers an advantage that can reduce the risk of extinction (Thompson and Lumaret 1992). Specifically, standing genetic variation can be measured as heterozygosity, and it has been shown that polyploid plants have higher heterozygosities and are less likely to incur inbreeding depression (Thompson and Lumaret 1992). Polyploidy in plants increases the potential to invade new niches relative to their diploid progenitors and to persist, and these plants tend to be invasive and weedy (Levin 1983; Thompson and Lumaret 1992). Novel combinations of alleles found in polyploid plants may lead to increased tolerance to wider ranges of environmental conditions (Levin 1983; Thompson and Lumaret 1992). Genome duplication in plants leads to range expansion, resistance to drought, and reduced susceptibility to infestation by pests and fungal diseases (Jackson 1976; Lumaret 1988; Thompson and Lumaret 1992). Larger seed size in polyploid plants leads to accelerated early development which affects the likelihood of establishment of seedlings in resource-limited environments and may result in niche differentiation as a by-product of polyploidization (Otto and Whitton 2000). Furthermore, unstable environments provide polyploid plants the opportunity to exploit their increased genetic variation (Levin 1983; Thompson and Lumaret 1992). Increased number of alleles potentially decreases the deleterious effects of inbreeding depression (Lawton-Rauh 2003), which ultimately reduces the probability of extinction. Without gene duplications, the plasticity of a genome in species adapting to changing environments would be severely limited because no more than two variants could exist at any locus in a diploid individual (Zhang 2003).

Conclusion

Genome duplication is often invoked as a contributing mechanism to adaptation and species diversity. But the relative temporal scales for which these processes unfold are not necessarily the same. While the disparity in temporal scale between a genome duplication event, diploidization, and adaptive evolutionary processes has been noted (Lawton-Rauh 2003), the role of reduced probability of extinction has not previously been considered. We estimate that the probability of extinction was reduced by a factor of at least 5.5 in the lineages following the fish-specific genome duplication. A reduced probability of extinction could explain the lack of close correlation between genome duplication and species diversity and would predict a latent effect on species diversity. Furthermore, a reduced probability of extinction would be consistent with and the preduplication gaps in extant taxa that have been observed in chordates.

Literature Cited

Blanc, G., and K. H. Wolfe. 2004*a*. Widespread paleopolyploidy in model plant species inferred from age distributions of duplicate genes. Plant Cell **16**:1667–1678.

———. 2004*b*. Functional divergence of duplicated genes formed by polyploidy during Arabidopsis evolution. Plant Cell **16**:1679–1691.

Bowers, J. E., B. A. Chapman, J. K. Rong, and A. H. Paterson. 2003. Unravelling angiosperm genome evolution by phylogenetic analysis of chromosomal duplication events. Nature **422**:433–438.

Carroll, S. B. 1995. Homeotic genes and the evolution of arthropods and chordates. Nature **376**:479–485.

Conant, G. C., and A. Wagner. 2003. Asymmetric sequence divergence of duplicate genes. Genome Res. **13**:2052–2058.

———. 2004. Duplicate genes and robustness to transient gene knock-downs in Caenorhabditis elegans. Proc. R. Soc. Lond. B Biol. Sci. **271**:89–96.

Crow, K. D., P. F. Stadler, V. J. Lynch, C. Amemiya, and G. P. Wagner. 2005. The "fish specific" Hox cluster duplication is coincident with the origin of teleosts. Mol. Biol. Evol. **23**:121–136.

Donoghue, P. C. J., and M. A. Purnell. 2005. Gene duplication, extinction, and vertebrate evolution. Trends Ecol. Evol. **20**:312–319.

Duda, T. F., and S. R. Palumbi. 1999. Molecular genetics of ecological diversification: duplication and rapid evolution of toxin genes of the venomous gastropod Conus. Proc. Natl. Acad. Sci. USA **96**:6820–6823.

Fares, M. A., D. Bezemer, A. Moya, and I. Marin. 2003. Selection on coding regions determined Hox7 genes evolution. Mol. Biol. Evol. **20**:2104–2112.

Force, A., M. Lynch, F. B. Pickett, A. Amores, Y. L. Yan, and J. Postlethwait. 1999. Preservation of duplicate genes by complementary, degenerative mutations. Genetics **151**:1531–1545.

Fried, C., S. J. Prohaska, and P. F. Stadler. 2004. Exclusion of repetitive DNA elements from gnathostome Hox clusters. J. Exp. Zoolog. B Mol. Dev. Evol. **302**:165–173.

Gale, M. D., and K. M. Devos. 1998. Plant comparative genetics after 10 years. Science **282**:656–659.

Gu, Z., L. M. Steinmetz, X. Gu, C. Scharfe, R. W. Davis, and W. H. Li. 2003. Role of duplicate genes in genetic robustness against null mutations. Nature **421**:63–66.

Hoegg, S., H. Brinkmann, J. S. Taylor, and A. Meyer. 2004. Phylogenetic timing of the fish-specific genome duplication correlates with the diversification of teleost fish. J. Mol. Evol. **59**:190–203.

Holland, P. W., J. Garcia-Fernandez, N. A. Williams, and A. Sidow. 1994. Gene duplications and the origins of vertebrate development. Development (Suppl.):125–133.

Hughes, A. L. 1999. Adaptive evolution of genes and genomes. Oxford University Press, New York.

Hughes, A. L., J. A. Green, J. M. Garbayo, and R. M. Roberts. 2000. Adaptive diversification within a large family of recently duplicated, placentally expressed genes. Proc. Natl. Acad. Sci. USA **97**:3319–3323.

Irish, V. F. 2003. The evolution of floral homeotic gene function. Bioessays **25**:637–646.

Irish, V. F., and A. Litt. 2005. Flower development and evolution: gene duplication, diversification and redeployment. Curr. Opin. Genet. Dev. **15**:454–460.

Jackson, R. C. 1976. Evolution and systematic significance of polyploidy. Annu. Rev. Ecol. Syst. **7**:209–234.

Kellis, M., B. W. Birren, and E. S. Lander. 2004. Proof and evolutionary analysis of ancient genome duplication in the yeast Saccharomyces cerevisiae. Nature **428**:617–624.

Kondrashov, F. A., I. B. Rogozin, Y. I. Wolf, and E. V. Koonin. 2002. Selection in the evolution of gene duplications. Genome Biol. **3**:Research 0008.0001–0008.0009.

Ku, H. M., T. Vision, J. P. Liu, and S. D. Tanksley. 2000. Comparing sequenced segments of the tomato and Arabidopsis genomes: large-scale duplication followed by selective gene loss creates a network of synteny. Proc. Natl. Acad. Sci. USA **97**:9121–9126.

Lawton-Rauh, A. 2003. Evolutionary dynamics of duplicated genes in plants. Mol. Phylogenet. Evol. **29**:396–409.

Le Comber, S. C., and C. Smith. 2004. Polyploidy in fishes: patterns and processes. Biol. J. Linn. Soc. **82**:431–442.

Levin, D. A. 1983. Polyploidy and novelty in flowering plants. Am. Nat. **122**:1–25.

Lumaret, R. 1988. Adaptive strategies and ploidy Levels. Acta Oecol. Oecol. Plant. **9**:83–93.

Lynch, M., and J. S. Conery. 2000. The evolutionary fate and consequences of duplicate genes. Science **290**:1151–1155.

Lynch, M., and A. Force. 2000. The origin of interspecific genomic incompatibility via gene duplication. Am. Nat. **156**: 590–605.

Lynch, M., and V. Katju. 2004. The altered evolutionary trajectories of gene duplicates. Trends Genet. **20**:544–549.

Malaga-Trillo, E., and A. Meyer. 2001. Genome duplication and accelerated evolution of Hox genes and cluster architecture in teleost fishes. Am. Zool. **41**:676–686.

Merritt, T. J., and J. M. Quattro. 2001. Evidence for a period of directional selection following gene duplication in a neurally expressed locus of triosephosphate isomerase. Genetics **159**:689–697.

Metz, C. W. 1947. The American society of naturalists—duplication of chromosome parts as a factor in evolution. Am. Nat. **81**:81–103.

Meyer, A., and M. Schartl. 1999. Gene and genome duplications in vertebrates: the one-to-four (-to-eight in fish) rule and the evolution of novel gene functions. Curr. Opin. Cell Biol. **11**:699–704.

Nelson, J. S. 1994. Fishes of the world. J. Wiley, New York.

Ohno, S. 1970. Evolution by gene duplication. Springer-Verlag, New York.

Otto, S. P., and J. Whitton. 2000. Polyploid incidence and evolution. Annu. Rev. Genet. **34**:401–437.

Patterson, C. 1993. Osteichichthyes: Teleostei. Pp. 621–656 *in* M. J. Benton, ed. The fossil record 2. Chapman & Hall, London.

Postlethwait, J. H., I. G. Woods, P. Ngo-Hazelett, Y. L. Yan, P. D. Kelly, F. Chu, H. Huang, A. Hill-Force, and W. S. Talbot. 2000. Zebrafish comparative genomics and the origins of vertebrate chromosomes. Genome Res. **10**:1890–1902.

Prince, V. E., and F. B. Pickett. 2002. Splitting pairs: the diverging fates of duplicated genes. Nat. Rev. Genet. **3**:827–837.

Prohaska, S. J., and P. F. Stadler. 2004. The duplication of the Hox gene clusters in teleost fishes. Theory Biosci. **123**:89–110.

Robinson-Rechavi, M., B. Boussau, and V. Laudet. 2004. Phylogenetic dating and characterization of gene duplications in vertebrates: the cartilaginous fish reference. Mol. Biol. Evol. **21**:580–586.

Seoighe, C., C. R. Johnston, and D. C. Shields. 2003. Significantly different patterns of amino acid replacement after gene duplication as compared to after speciation. Mol. Biol. Evol. **20**:484–490.

Soltis, D. E., and P. S. Soltis. 1999. Polyploidy: recurrent formation and genome evolution. Trends Ecol. Evol. **14**:348–352.

Soltis, P. S. 2005. Ancient and recent polyploidy in angiosperms. New Phytol. **166**:5–8.

Song, K. M., P. Lu, K. L. Tang, and T. C. Osborn. 1995. Rapid genome change in synthetic polyploids of Brassica and its implications for polyploid evolution. Proc. Natl. Acad. Sci. USA **92**:7719–7723.

Tanaka, T., and M. Nei. 1989. Positive Darwinian selection observed at the variable-region genes of immunoglobulins. Mol. Biol. Evol. **6**:447–459.

Taylor, J. S., and J. Raes. 2004. Duplication and divergence: the evolution of new genes and old ideas. Annu. Rev. Genet. **38**:615–643.

Thompson, J. D., and R. Lumaret. 1992. The evolutionary dynamics of polyploid plants—origins, establishment and persistence. Trends Ecol. Evol. **7**:302–307.

Vision, T. J., D. G. Brown, and S. D. Tanksley. 2000. The origins of genomic duplications in Arabidopsis. Science **290**:2114–2117.

Wagner, G. P., C. Amemiya, and F. Ruddle. 2003. Hox cluster duplications and the opportunity for evolutionary novelties. Proc. Natl. Acad. Sci. USA **100**:14603–14606.

Wagner, G. P., K. Takahashi, V. Lynch, S. J. Prohaska, C. Fried, P. F. Stadler, and C. Amemiya. 2005. Molecular evolution of duplicated ray finned fish HoxA clusters: increased synonymous substitution rate and asymmetrical co-divergence of coding and non-coding sequences. J. Mol. Evol. **60**:665–676.

Walsh, J. B. 1995. How often do duplicated genes evolve new functions. Genetics **139**:421–428.

Wendel, J. F. 2000. Genome evolution in polyploids. Plant Mol. Biol. **42**:225–249.

Zhang, J. Z. 2003. Evolution by gene duplication: an update. Trends Ecol. Evol. **18**:292–298.

Zhang, J. Z., K. D. Dyer, and H. F. Rosenberg. 2000. Evolution of the rodent eosinophil-associated RNase gene family by rapid gene sorting and positive selection. Proc. Natl. Acad. Sci. USA **97**:4701–4706.

Zhang, J. Z., H. F. Rosenberg, and M. Nei. 1998. Positive Darwinian selection after gene duplication in primate ribonuclease genes. Proc. Natl. Acad. Sci. USA **95**:3708–3713.

Zhang, J. Z., Y. P. Zhang, and H. F. Rosenberg. 2002. Adaptive evolution of a duplicated pancreatic ribonuclease gene in a leaf-eating monkey. Nat. Genet. **30**:411–415.

Zhou, R. J., H. H. Cheng, and T. R. Tiersch. 2001. Differential genome duplication and fish diversity. Rev. Fish Biol. Fish. **11**:331–337.

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