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Unveiling the Patterns and Impact of New Gene Recruitment in Development and Evolution

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Abstract This study explores the critical role of new gene emergence in driving evolutionary innovation and biodiversity. The research reviews various mechanisms of new gene origin, such as gene duplication, de novo gene emergence from noncoding sequences, and the co-option of genomic elements. It focuses on how these genes are recruited into developmental pathways, leading to phenotypic changes and the evolution of complex traits, including brain development and reproductive behaviors. Using comparative genomics, studies of gene regulatory networks (GRNs), and high-throughput sequencing technologies to track gene function, the results show that new genes play a significant role in developmental innovation, adaptive evolution, and environmental adaptation. The study emphasizes the importance of new gene recruitment in understanding the dynamics of genetic networks and its broader implications for evolutionary biology. It suggests improving methods for gene identification and functional characterization, while expanding research to non-model organisms.

Keywords New gene recruitment; Gene duplication; Phenotypic evolution; Gene regulatory networks; Adaptive evolution

1 Introduction

In molecular biology, “recruitment” typically refers to guiding specific molecules or factors to a particular location or complex to perform their function. For example, transcription factors bind to DNA and initiate gene expression by recruiting polymerase and other associated factors. Thus, “new gene recruitment” can be understood as the introduction or integration of new genes into existing biological processes or pathways.

The emergence of new genes is a fundamental driver of evolutionary innovation and diversity. New genes contribute significantly to the adaptive evolution of organisms by introducing novel functions that can lead to phenotypic changes. These genes can originate through various mechanisms, including gene duplication, de novo origination from noncoding sequences, and the co-option of genomic parasites (Andersson et al., 2015). The integration of new genes into existing genetic networks can result in the development of essential functions and the evolution of complex traits, such as brain development and reproductive behaviors (Ranz and Parsch, 2012). The rapid evolution and indispensable roles of new genes underscore their importance in shaping the genetic and phenotypic landscape of species (Ding et al., 2012).

Developmental recruitment refers to the process by which new genes are integrated into the developmental pathways of organisms, often leading to the formation and diversification of novel traits. This process can involve the co-option of conserved genes into new developmental contexts, resulting in the evolution of lineage-specific traits (Xia et al., 2020). The recruitment of genes into the genetic circuitry responsible for butterfly eyespot formation demonstrates how conserved genes can be repurposed to create new morphological features. Similarly, the evolution of C_4 photosynthesis in flowering plants illustrates how preexisting genes can be repeatedly recruited to perform new functions in response to environmental pressures. Understanding the mechanisms and evolutionary history of gene recruitment provides insights into the dynamic nature of genetic networks and their role in developmental innovation.

This study aims to highlight the mechanisms driving genetic and phenotypic diversity by investigating the origin, integration, and functional roles of new genes. This study will explore how new genes integrate into existing

genetic networks, the evolutionary pathways they follow, and their contributions to the development of new traits. We will discuss the significance of these processes in understanding the broader principles of evolutionary biology and developmental genetics, providing valuable insights for ongoing research and future directions in the recruitment of new genes.

2 Origin and Evolution of New Genes

2.1 Gene duplication and divergence

Gene duplication is a well-established mechanism for the creation of new genes. It involves the copying of an existing gene, which can then diverge and acquire new functions. This process is a major source of genetic novelty and has been extensively studied across various species. In Drosophila, tandem gene duplication has generated approximately 80% of nascent duplicates limited to single species, while dispersed duplicates (Fang, 2024), which are more likely to be retained and functional, account for 44.1% of new genes shared by multiple species. Similarly, in yeast and flies, duplicated genes exhibit high turnover rates at the species level but show stability in deeper evolutionary branches, indicating their significant role in long-term evolutionary processes (Montañés et al., 2023).

2.2 Gene fusion and recombination

Gene fusion and recombination are other important mechanisms contributing to the origin of new genes. These processes involve the merging of different genomic sequences to form chimeric genes with novel functions. In the *Drosophila melanogaster* species complex, approximately 30% of new genes have recruited various genomic sequences to form chimeric structures, highlighting the importance of structural innovation in gene fixation (Prabh and Roedelsperger, 2022). Additionally, genomic parasites and messenger RNAs of ancestral genes can be co-opted to form new genes, further expanding the repertoire of genetic diversity (Kaessmann, 2010).

2.3 De novo gene birth

De novo gene birth is the process by which new genes evolve from previously non-genic sequences. This mechanism has gained increasing attention as a significant source of genetic innovation. Studies have shown that de novo genes can arise from noncoding DNA and gradually integrate into cellular networks, although their prevalence and functional significance are still under investigation (Moyers and Zhang, 2016). In mammals, comparative genomics has identified thousands of new transcriptional events in humans and chimpanzees, some of which show evidence of protein translation and natural selection, suggesting their potential functionality. In yeasts, de novo genes preferentially emerge in GC-rich intergenic regions and recombination hotspots, indicating that meiotic recombination may facilitate their origination (Vakirlis et al., 2018).

The evolutionary dynamics of de novo genes differ from those of duplicated genes. De novo candidates are typically shorter, show less expression, and are overrepresented on sex chromosomes. They also exhibit higher attrition rates and weaker evolutionary constraints, reflecting their rapid turnover and evolutionary lability (Prabh and Roedelsperger, 2022). Despite these differences, both de novo and duplicated genes share similarities in their initial evolutionary phases, such as low sequence constraints and high turnover rates.

3 Patterns of Developmental Recruitment of New Genes

3.1 Spatiotemporal expression patterns

Spatiotemporal expression patterns are crucial for understanding how new genes are recruited during development. These patterns refer to the specific times and locations where genes are expressed, which can significantly influence developmental processes. The study of transcription factors has shown that they regulate gene expression in specific spatiotemporal domains, leading to robust developmental outcomes despite environmental and genetic variations. Additionally, the formation of spatiotemporal patterns is essential in various biological phenomena, such as embryogenesis and neural network formation, where gene regulatory networks (GRNs) play a pivotal role (Roy et al., 2022). The integration of spatial and temporal datasets, as demonstrated in the sea anemone *Nematostella vectensis*, further highlights the importance of these patterns in identifying potential gene interactions and regulatory networks (Abdol et al., 2017).

3.2 Integration into gene regulatory networks

The integration of new genes into existing gene regulatory networks (GRNs) is a fundamental aspect of their recruitment during development. GRNs consist of interactions between developmental control genes, cis-regulatory modules, and differentiation genes, which collectively generate refined patterns of gene expression (Fernandez-Valverde et al., 2018). The flexibility of GRNs over time allows for the cooption of individual genes, facilitating the evolution of novel traits. For example, the recruitment of the engrailed gene in the fly *Samoaia leonensis* to generate a new wing pattern (Figure 1) illustrates how GRN flexibility and the functional time windows of individual genes enable their independent recruitment during evolution (Dufour et al., 2020). Moreover, the integration of omic networks, such as transcriptome, proteome, and phosphoproteome data, enhances the predictive power of GRNs, as seen in the developmental atlas of maize.

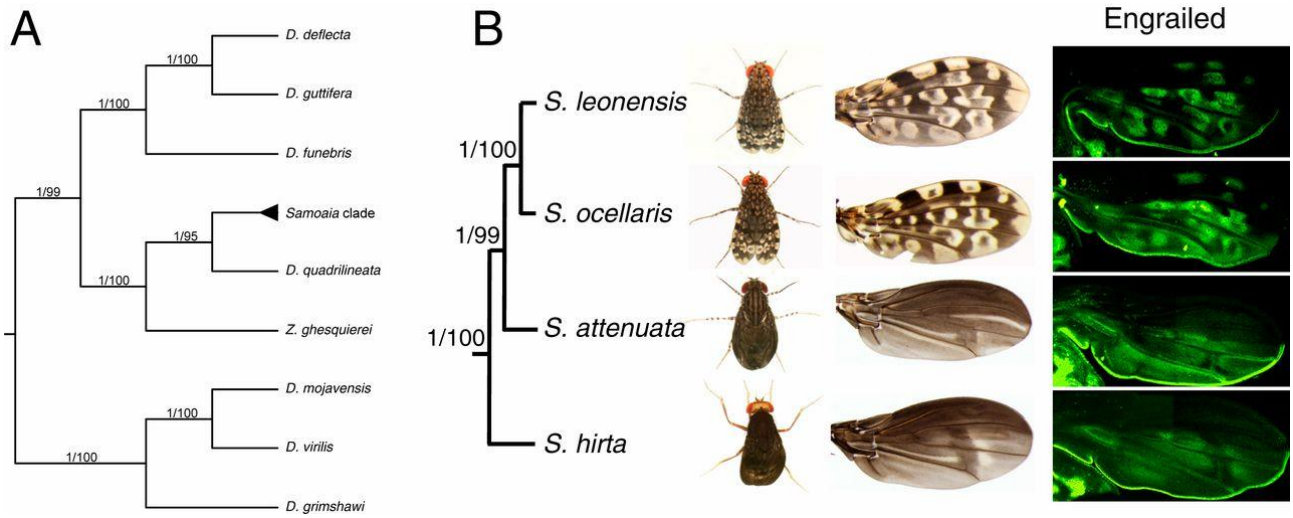

Figure 1 Cooption of engrailed underlies wing pigmentation pattern in the genus Samoaia (Adopted from Dufour et al., 2020)

Image caption: (A) Phylogenetic reconstruction shows that the genus Samoaia is monophyletic and belongs to the Drosophilidae. (B) The black wing species represent the earliest-diverging lineages within the genus Samoaia. (C) The expression domain of the protein En prefigures the localization of the white spots in adult wings in *S. leonensis* and *S. ocellaris*. For each wing, two overlapping high-magnification clichés were acquired and manually stitched to cover the whole wing (Adopted from Dufour et al., 2020)

3.3 Patterns across different organisms

The recruitment of new genes and their integration into developmental processes can vary significantly across different organisms. Comparative studies across species, such as those involving Drosophila, reveal that despite changes in regulatory DNA sequences, developmental programs can be conserved over millions of years (Wunderlich et al., 2018). This conservation allows for the detection of subtle phenotypic differences and the development of computational models linking regulatory DNA sequences to expression patterns. The study of vertebrate species has shown that changes in cis-regulatory elements can lead to morphological novelties, as exemplified by the regulation of the sonic hedgehog (*Shh*) gene (Amano, 2020). These findings underscore the importance of understanding the evolutionary origins of novel gene expression patterns and the mechanisms by which new enhancers arise, such as the co-option of latent activities of existing regulatory sequences.

4 Biological Implications of New Gene Recruitment

4.1 Role in functional innovation

New gene recruitment plays a crucial role in functional innovation by providing raw material for the evolution of novel traits and functions. The emergence of new genes through various mechanisms, such as gene duplication, de novo gene birth, and co-option of genomic parasites, has been shown to significantly impact the evolution of cellular, physiological, morphological, behavioral, and reproductive traits. For instance, the recruitment of conserved developmental genes has been linked to the formation and diversification of novel traits, such as the eyespots on butterfly wings, which involve the co-option of multiple transcription regulators (Shirai et al., 2012). Additionally, the flexibility of gene regulatory networks (GRNs) allows for the independent recruitment of single

genes, facilitating the evolution of new morphological features, such as the novel wing patterns in flies (Dufour et al., 2020). These examples highlight the importance of new gene recruitment in driving functional innovation and contributing to the adaptive evolutionary novelties observed in various organisms.

4.2 Impact on developmental regulation

The recruitment of new genes can have profound effects on developmental regulation, often leading to the evolution of essential functions in development. Studies on Drosophila have revealed that recently evolved new genes can quickly acquire essential roles in viability during development, challenging the conventional view that the genetic basis of development is highly conserved (Xia et al., 2020). In vertebrates, new genes have been found to originate and be recruited for functions in embryonic development, particularly after the midblastula transition, indicating their importance in early developmental stages (Xu et al., 2018). The evolution of floral homeotic gene function in angiosperms also exemplifies how gene duplication and sequence divergence have allowed the recruitment of *MADS-box* genes to new developmental pathways, contributing to the specification of floral organ identities and other developmental processes (Kulkarni et al., 2020). These findings underscore the significant impact of new gene recruitment on developmental regulation and the evolution of complex developmental traits.

4.3 Role in environmental adaptation

New gene recruitment is a key factor in environmental adaptation, enabling organisms to respond to changing environmental conditions. Gene duplication, in particular, has been shown to increase phenotypic plasticity and enhance the transcriptional response to environmental stresses, as observed in Saccharomyces cerevisiae (Mattenberger et al., 2016). The variation in transcription factor-binding sites (TFBSs) within a species also reflects adaptation to different environments, with changes in promoter regions and coding sequences indicating functional innovation and positive selection. The co-option of genes involved in germ line functions for neural roles suggests that the molecular and biochemical properties of these genes make them well-suited for adaptation to diverse cellular contexts (Kulkarni et al., 2020). These examples illustrate how new gene recruitment contributes to environmental adaptation by providing the genetic flexibility needed to cope with and thrive in varying environmental conditions.

5 Case Studies

5.1 Developmental recruitment of new genes in drosophila

Recent research has significantly advanced our understanding of the role of new genes in the development of Drosophila. Contrary to the traditional view that the genetic basis of development is highly conserved, new genes have been shown to rapidly evolve essential functions. For instance, a study involving the knockdown of 702 new genes in *Drosophila melanogaster* revealed a high proportion of these genes to be essential for viability during development, similar to older genes (Xia et al., 2020). This finding underscores the rapid evolution of gene essentiality and highlights the importance of new genes in developmental processes.

The mechanisms behind the origination of new genes in Drosophila have been extensively studied. Tandem gene duplication, de novo gene origination from noncoding sequences, and retroposition are some of the key processes identified. These mechanisms contribute to the formation of new functional genes, with an estimated rate of five to eleven new genes per million years in the *Drosophila melanogaster* subgroup. Additionally, the recruitment of undifferentiated cells has been shown to play a crucial role in the growth of Drosophila wings, further emphasizing the dynamic nature of gene recruitment in development (Figure 2) (Muñoz-Nava et al., 2020).

5.2 New genes in mouse models

Mouse models have been instrumental in studying the recruitment of new genes and their impact on development and disease. The versatility of reverse genetics in mice allows for detailed investigations into gene function and the underlying mechanisms of various biological processes. For example, the mouse model has been pivotal in understanding human physiology and diseases, providing insights that are not easily attainable in other model organisms (Irion and Nüsslein-Volhard, 2022). The use of mouse models has also facilitated the study of gene expression and the evolutionary dynamics of new genes. By examining the rates of protein evolution and the impact of selection on patterns of polymorphism and divergence, researchers have gained a deeper understanding

of how new genes contribute to development and adaptation (Moutinho et al., 2022). These studies highlight the importance of new gene recruitment in shaping the genetic landscape and driving evolutionary change.

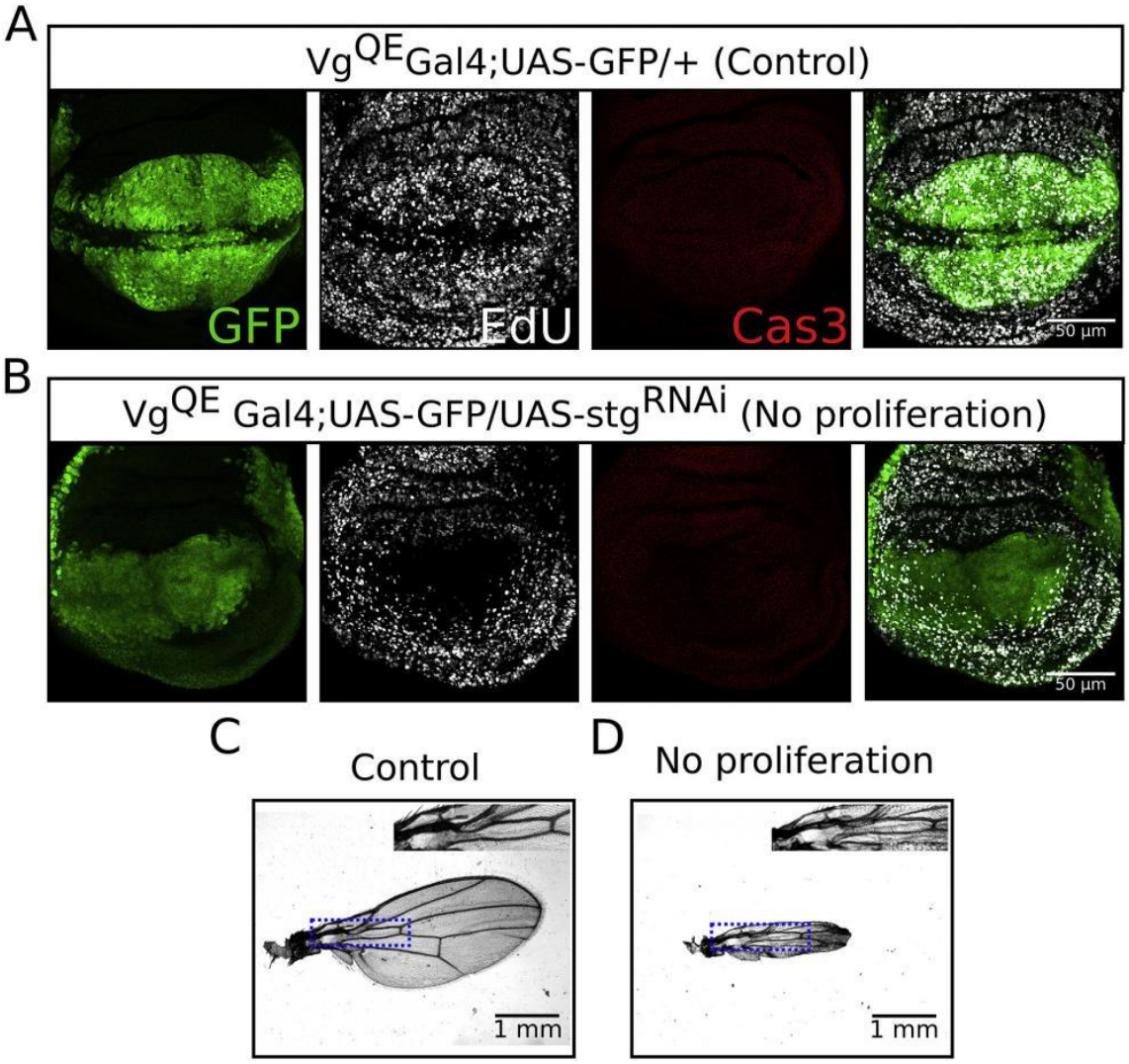

Figure 2 Cell proliferation, recruitment helps with growth, but cannot save the size of adult wings (Adopted from Muñoz-Nava et al., 2020)

5.3 New gene recruitment in *Arabidopsis*

In *Arabidopsis*, the recruitment of new genes has been shown to significantly impact genomic patterns of polymorphism and divergence. Unlike Drosophila, *Arabidopsis* exhibits different patterns of sequence variation, with synonymous divergence being a major predictor of silent polymorphism. This suggests that variation in mutation rates is a key determinant of silent variation in *Arabidopsis* (Slotte et al., 2011).

The adaptive walk model of gene evolution has been supported by studies in *Arabidopsis*. Young genes in *Arabidopsis* tend to evolve faster and experience mutations with stronger fitness effects compared to older genes. This pattern is consistent with the idea that populations evolve by taking larger steps when they are further from their fitness optimum (Jean-Baptiste et al., 2019). These findings provide strong evidence for the role of new gene recruitment in driving adaptation and evolutionary change in *Arabidopsis*.

6 Technological Advances in Studying New Genes

6.1 Genomics and transcriptomics technologies

6.1.1 High-throughput sequencing for gene discovery

High-throughput sequencing (HTS) technologies have revolutionized the field of genomics by enabling the rapid and comprehensive analysis of genetic material. These technologies have facilitated the discovery of new genes

and functional elements across various species. For instance, the sequencing of 12 Drosophila genomes has allowed researchers to identify new protein-coding genes, non-coding RNA genes, and regulatory motifs by analyzing evolutionary signatures. Similarly, HTS has been instrumental in the genomic analysis of viral populations, leading to the discovery of new viruses and a deeper understanding of their genetic diversity (Pérez-Losada et al., 2020). The application of HTS in non-model organisms has also provided significant insights into evolutionary biology, revealing patterns of recombination and the role of population size in adaptive evolution.

6.1.2 Comparative genomics in evolutionary studies

Comparative genomics involves the analysis of genome sequences from multiple species to understand the evolutionary processes shaping genomes. This approach has uncovered the role of natural selection in genome evolution and the functional divergence of protein-coding genes across different lineages (Gouy et al., 2017). Comparative genomics has shown that the ratio of nonsynonymous to synonymous substitutions varies among species, supporting the nearly neutral theory of molecular evolution. Additionally, the study of 12 Drosophila genomes has provided guidelines for comparative studies, highlighting the importance of species divergence and the number of species compared in enhancing discovery power. The integration of comparative genomics with other high-throughput technologies has further expanded our understanding of gene regulatory networks and their evolution (Fernandez-Valverde et al., 2018).

6.2 Proteomics and functional analysis

6.2.1 Mass spectrometry in protein identification

Mass spectrometry (MS) is a powerful tool for the identification and characterization of proteins. It allows for the precise measurement of protein masses and the identification of post-translational modifications. The integration of MS with high-throughput sequencing technologies has enabled the comprehensive analysis of proteomes, providing insights into the functional states of individual cells and the identification of new proteins (Shapiro et al.,2013) This approach has been particularly useful in understanding the functional roles of proteins in various biological processes and their evolutionary significance.

6.2.2 Functional characterization of new proteins

The functional characterization of new proteins involves determining their roles in cellular processes and their contributions to phenotypic traits. Advances in high-throughput sequencing and proteomics have facilitated the identification of gene regulatory networks and the interactions between genes that govern cell differentiation and development (Fernandez-Valverde et al., 2018). For example, the analysis of gene networks has revealed the polygenic basis of adaptation to high-altitude in human populations, highlighting the importance of multiple genetic components in the evolution of complex traits. These findings underscore the significance of functional characterization in understanding the evolutionary dynamics of new genes and their impact on development.

6.3 CRISPR technologies for studying new genes

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technologies have emerged as powerful tools for genome editing and the study of gene function. By enabling precise modifications of the genome, CRISPR allows researchers to investigate the roles of specific genes in development and evolution. The application of CRISPR in functional genomics has provided new opportunities for the systematic analysis of gene regulatory networks and the identification of key regulatory elements (Zhang, 2024). This technology has the potential to revolutionize our understanding of gene function and the mechanisms underlying evolutionary change.

7 Conclusion

The study of new gene recruitment in development and evolution has unveiled several critical insights. New genes significantly contribute to phenotypic evolution and are often integrated into rapidly evolving pathways such as spermatogenesis, immune response, and brain development. The integration of new genes into gene-gene interaction (GGI) networks follows a gradual process, starting from peripheral positions and eventually becoming central hubs with essential functions. Functional shifts, where genes acquire new roles, are pivotal in generating

evolutionary novelties, particularly in developmental pathways. In Drosophila, new genes have rapidly evolved essential functions, challenging the traditional view of conserved genetic bases in development. The modular and hierarchical recruitment of protein domains has also been highlighted as a key mechanism in the evolution of protein functions. RNA-based gene duplication has emerged as a significant source of new functional genes, particularly in mammalian genomes. The birth of new genes through various mechanisms, including gene duplication and retroposition, has been a major driver of adaptive evolutionary innovations. The recruitment of genes into complex traits, such as C_4 photosynthesis, often shows a bias towards certain gene lineages, indicating that some genes are more predisposed to new functions. The temporal flexibility of gene regulatory networks (GRNs) allows for the independent recruitment of genes, facilitating the evolution of novel traits. Finally, the burst of retroposition in primates has led to the emergence of new human genes, particularly those involved in spermatogenesis.

Despite the progress in understanding new gene recruitment, several challenges remain. One major challenge is the accurate inference of gene ages and the annotation of their protein-coding potential. Different methods yield varying results, and there is a need for more reliable and consistent approaches. Another challenge is the functional characterization of new genes, particularly distinguishing between true functional genes and pseudogenes. This requires comprehensive experimental validation, which is often resource-intensive. The integration of new genes into existing GGI networks and their gradual acquisition of essential functions also pose challenges in terms of understanding the underlying mechanisms and evolutionary pressures. Additionally, the study of functional shifts and the co-option of genes in developmental pathways requires a detailed understanding of the historical sequence of events and the selective pressures involved. The rapid evolution of new genes in model organisms like Drosophila raises questions about the generalizability of these findings to other species. The modular and hierarchical nature of protein domain recruitment adds another layer of complexity to the functional characterization of new genes. Finally, the study of RNA-based gene duplication and retroposition requires advanced genomic and transcriptomic analyses to uncover the full extent of their contributions to new gene functions.

Future research should focus on developing more accurate and reliable methods for inferring gene ages and annotating protein-coding potential. Integrating multiple approaches and validating results through experimental data will be crucial. There is also a need for comprehensive functional characterization of new genes, including high-throughput experimental validation and detailed phenotypic analyses. Understanding the mechanisms of new gene integration into GGI networks and their evolutionary significance will require advanced computational models and network analyses. Research should also explore the historical sequence of co-option and duplication events to better understand functional shifts in developmental pathways. Expanding studies to a broader range of species will help determine the generalizability of findings from model organisms. Investigating the modular and hierarchical recruitment of protein domains will provide deeper insights into the evolution of protein functions. Finally, future studies should leverage advanced genomic and transcriptomic technologies to uncover the full extent of RNA-based gene duplication and retroposition in generating new functional genes.

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Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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