9.10: Paralogous genes and gene families

As noted previously genome dynamics play a critical role in facilitating evolutionary change, particularly in the context of multicellular organisms. When a region of DNA is duplicated, the genes in the duplicated region may come to be regulated differently, and they can be mutated in various ways while the other copy of the gene continues to carry out the gene’s original function. This provides a permissive context in which mutations can alter what might have been a gene product’s off-target or as it is sometime called, promiscuous activities. While typically much less efficient than the gene product’s primary role, they can have physiologically significant effects.

The two versions of a duplicated gene are said to be paralogs of each other. In any gene duplication event, the two duplicated genes can have a number of fates. For example, both genes could be conserved, providing added protection against mutational inactivation. The presence of two copies of a gene often leads to an increase the amount of gene product generated, which may provide a selective advantage. For example, in the course of cancer treatment gene duplication (a form of copy number variation) can be selected for because increased copies of genes may encode gene products involved in the detoxification of, or resistance to an anti-cancer drug. It is possible that both genes retain their original functions, but are expressed at different levels and at different times in different cell types. One gene’s activity may be lost through mutation, in which case we are back to where we started. Alternatively, one gene can evolve to carry out a new, but important functional role, so that conservative selection acts to preserve both versions of the gene.

Such gene duplication processes can generate families of evolutionarily related genes. In the analysis of gene families, we make a distinction between genes that are orthologs of each other and those that are paralogs. Orthologous (or homologous) genes are found in different organisms, but are derived from a single common ancestral gene present in the common ancestor of those organisms. Paralogous genes are genes present in a particular organism that are related to each other through a gene duplication event. A particular paralog in one organism can be orthologous to a gene in another organism, or it could have arisen independently in an ancestor, through a gene duplication event.
Detailed comparisons of nucleotide sequences can distinguish between the two. The further in the past that a gene duplication event is thought to occur, the more mutational noise can obscure the relationship between the duplicated genes. Remember, when looking at DNA there are only four possible bases at each position. A mutation can change a base from A to G, and a second mutation from G back to A. If this occurs, we cannot be completely sure as to the number of mutations that separate two genes, since it could be 0, 2 or a greater number. We can only generate estimates of probable relationships. Since many multigene families appear to have their origins in organisms that lived hundreds of millions of years ago, the older the common ancestor, the more obscure the relationship can be. The exceptions involve genes that are extremely highly conserved, which basically means that their sequences are constrained by the sequence of their gene product. In this case most mutations produce a lethal or highly disadvantageous phenotype, meaning that the cell or organism with that mutation dies or fails to reproduce. These genes evolve very slowly. In contrast, gene/gene products with less rigid constraints (and this includes most genes/gene products) evolve much more rapidly, which can make determining the relationships between genes found in distantly related organisms more tentative and speculative. Also, while functional similarities are often seen as evidence for evolutionary homology, it is worth considering the possibility, particularly in highly divergent genes and gene products, of convergent evolution. As with wings, the number of ways to carry out a particular molecular level function may be limited.

Questions to answer & to ponder

- Using a diagram, consider the effects of flipping a chromosomal region around (180°) on gene expression.
- Consider the effects of such rearrangements on chromosome pairing during meiosis.
- How does sexual reproduction increase the genetic diversity within a population?
- Speculate on what selective factors might favor sexual over asexual reproduction (and visa versa).
- Provide an explanation for the persistence of duplicated genes. What forces would act to remove them?
- What type of event would lead to total genome duplication?
- Why are some genes often lost after genome duplication?

References


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