



‘Natural selection merely modified while redundancy created’ – Susumu Ohno’s idea of the evolutionary importance of gene and genome duplications

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Abstract

Susumu Ohno’s influential book *Evolution by gene duplication* dealt with the idea that gene and genome duplication events are the principal forces by which the genetic raw material is provided for increasing complexity during evolution. In 1970, the evidence for this hypothesis consisted mostly of karyotypic information, crude information by today’s standard genetic data, DNA sequences. Nonetheless, although the type of data are outdated, the idea remained current and is still debated today in the age of complete genome sequences. Even more than thirty years after the initial publication more research than ever is being carried out on the evolutionary significance of gene and genome duplications and the contribution of these mechanisms to the advances in genomic and organismal evolution.

The year 2000 marked the 30th anniversary of the publication of Susumu Ohno’s seminal book *Evolution by gene duplication* (Ohno, 1970). Sadly, that year was also the year in which Ohno passed away. His influential book dealt with the idea that gene and genome duplication events are the principal forces by which the genetic raw material is provided for increasing complexity during evolution.

The evidence for this hypothesis, was, certainly by today’s standards, crude, scant and largely circumstantial consisting mostly of comparative measurements of DNA contents, karyotypic information and some data from allozymes. Undeterred by the lack of unequivocal evidence, Ohno postulated that the major advances in evolution such as the transition from single-celled organisms to complex multicellular animals and plants could not simply have been brought about alone through processes such as natural selection based on existing allelic variation at particular genetic loci in populations. He suggested instead that novelty in evolution is most often based on genomic redundancy, as substrate for subsequent divergent nat-

ural selection created initially by gene and entire genome duplications. In a statement that brought his conviction to a point he postulated that “*natural selection merely modified, while redundancy created*”. What he meant was that gene and genome duplications allowed for gene functions of duplicated genes to diversify, take on novel functions, and bring about evolutionary innovation in general. Natural selection would be relegated to the back seat of evolution to only do its conservative job of fine-tuning those duplicates, which had, through duplication, the chance to accumulate a sufficiently large number of “forbidden” mutations to bring about changes in function of these duplicated genes. To be sure, a controversial, almost anti-Darwinian idea, indeed.

One might expect in fast moving scientific disciplines such as molecular biology and evolutionary biology that a 30-year old idea would soon be obsolete and long forgotten. Ohno himself was worried that his book would be outdated even by the time it was published. A quote from the introduction of his book illustrates this nicely: ‘*In this golden age of*

biology, a book faces the danger of becoming obsolete before its publication. It is my belief that in order to avoid early obsolescence, the author, judging on the basis of the scant evidence available, is obliged to anticipate future developments and paint a picture with broad strokes of his brush. This I have done rather freely in this book'. In this attempt, Ohno succeeded brilliantly, far from being obsolete, Ohno's basic tenets of the 1970's remain current and hotly debated still today. Of course, they have been further elaborated on theoretically and tested with much better, now genomic data, during the last 30 years. The collection of papers in this special issue of the Journal of Structural and Functional Genomics are a testament to the viability of these ideas some of which go back to Ohno and some of this contemporaries. To us, this suggests that there must be some important truths and insights that were summarized early on in Ohno's book.

An impression of the importance that the scientific community is placing on studying the evolutionary significance of the decades old ideas of gene and genome duplications can be gleaned also from the number of publications that are devoted to these topics. Figure 1 summarizes this trend for the last 27 years. The graph depicts the results of a search of the ISI Web of Science with the keyword 'gene duplication'. Until about 1990 only about 10–15 publications on the topic of gene duplication were published per year. But in 1991 the number of publications jumped to more than 80 per year and continued to steadily increase until it reached a level of about 200 yearly publications during the last 4–5 years. What happened in 1990/91 that might account for the increased interest in gene and genome duplications?

During this time period important findings were reported on in several areas of inquiry in molecular evolution relating to gene duplications. Some advances of this time seemed to have spawned a lot of interest and activity in research on the evolutionary consequences of gene and genome duplications. An incomplete list of catalytic advances includes: Piatigorsky's pioneering studies on the evolution of novel functions in crystallins (e.g., Piatigorsky and Wistow, 1991), Peter Holland's work on the evolution of Hox clusters in deuterostomes (Holland, 1991), work on the evolution of the immune system by several researchers (reviewed in Ravetch and Kinet, 1991), and also Ohta's (Ohta, 1991) theoretical work on the evolution of genes in multi-gene gene families.

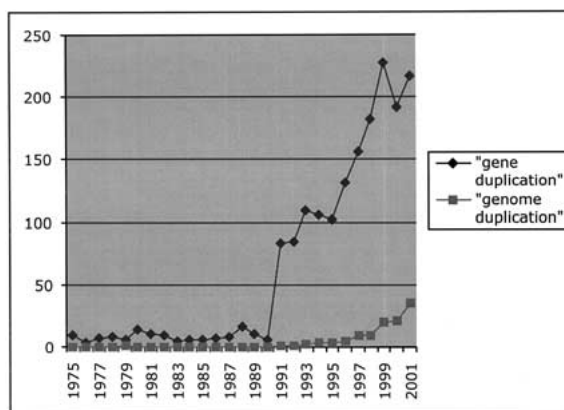


Figure 1. Numbers of publications per year from 1975 to 2001 on "gene" and "genome" duplications as reported by the Institute for Scientific Information (Web of Science).

A survey of the patterns in the literature on genome duplications (Fig. 1) shows a similar trend to that on gene duplications, but only since 1995 did publications on genome duplication really begin to appear in the scientific literature. Also here the comparative genomic and developmental work on Hox gene and Hox cluster evolution, in particular the important work of Frank Ruddle seems to have ignited the research and influenced the thinking of many new researchers (reviewed in Ruddle *et al.*, 1994).

Ohno's tenets were brought forth during a time where the documentation and quantification of genetic variation within populations and between species was largely restricted to scoring allelic variation in enzymes through starch gel electrophoresis and the microscopic inspection of karyotypic differences. Methods to effectively measure genetic variation at the level of the gene and DNA sequencing had still to be invented. Ohno's idea, while expanding on Darwin's principles of evolution by natural selection also clearly relegated natural selection to only second place after duplication in terms of its purported significance in bringing about evolutionary change. That many of Ohno's ideas were brought about at a time when it was not technically possible to test many of them rigorously is rather reminiscent of the situation that Darwin faced when proposing that evolution and natural selection worked by offspring resembling their parents more than the average member of the population. Of course, genetics and inheritance had not been invented in Darwin's time, but it was still at the core of his ideas.

The accumulation of complete genomic sequences during the last years clearly were the main reason for the wide-spread recognition that significant portions of genomes of Eukaryotes consist of duplicated gene loci, that most gene families are large and have complex evolutionary histories, and that these are best explained by the widespread occurrence of tandem gene duplications or even entire genome duplications. *De novo* origins of genes are clearly much rarer events than the duplication and subsequent divergence of previously existing genes, as was already predicted by Ohno.

The 30-year anniversary of the publication of Ohno's book was the impetus for us, together with Hervé Phillippe, to bring together active researchers for a Jacques Monod Conference on 'Gene and genome duplications and the origin of novel gene functions' that took place in Aussois in 2001. We are glad that most of those who were instrumental in shaping the field and who continued to contribute to it also attended the meeting. To this date, the relative importance of gene and genome duplications for evolution remains disputed. Ohno's idea of redundancy continues to be rivaled, as it should be and has been for the last three decades, most strongly by the idea that regulatory evolution is what 'drives' evolution (see recent summaries by Carroll *et al.*, 2001; Davidson, 2001). Thankfully, also adherents to this idea attended the meeting and made themselves heard. Obviously, the two viewpoints on the relative importance of redundancy or regulatory evolution are not mutually exclusive and, as is so often the case, the truth will probably lie somewhere in the middle.

This is the age of genomics. Only since the complete genomes of organisms can be determined became it possible to rigorously test some of the ideas related to Ohno's first bold proposals and as the sampling of complete genome sequences becomes phylogenetically denser will it become possible to better evaluate through what mechanisms of genomic evolution advances and major transitions in evolution are

triggered. Many whose ideas and empirical data advanced the investigation of the evolutionary importance of gene and genome duplication during evolution for the last three decades contributed to this special issue of the Journal of Structural and Functional Genomics. We hope that others still will be attracted to working on this set of questions in the future by reading some of the research that is contained in this set of publications.

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