

The Silence Eclipsing Introns

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1. Abstract

In spite of the deep insight that has been gathered hitherto in Molecular Genetics, a few obscurities are as challenging as they were. Among these, introns, with reference to its functionality, have been debated quite often. And many theories that have emerged following such grappling discussions have given believable explanations but have failed to give a convincing answer eventually. This article attempts to bring a new reason behind the dormancy of introns.

2. Introduction

Intergenic sequences defined as the sequence of nucleotides in a gene that is transcribed but excised before the gene is translated for the reason that it's considered non-coding or nonfunctional, but the mystery masking the evolution of introns continues to be a perplexing, unrequited subject so far and consequently we have simply rendered them as Junk Genes.

In the recent past, two theories have been formulated by Darwinists to explain the evolution of introns:

Intron Early Hypothesis: This theory considers exons as mini-genes. According to this, during the pre-cellular life, exons (the functional sections of a gene) worked as genes do in our day. As organisms evolved from simple to complex, the mini-genes were gathered to make a whole genome; and introns were the meaningless links which held these exons together. It's also advocated that this idea holds for all present genes and genomes. In response to the reasons for the absence of introns in prokaryotes, it (the theory) comments that bacteria lost their introns in latter evolutionary stages. But if the so called mini-genes or the contemporary functional genes (Exons) require the aforementioned functionless pieces or introns for assembly then why did most of the prokaryotes and early eukaryotes lose them as stated and if that be the case how are there functional genes held presently? In fact members of archaeobacteria still possess the discon-

tinuous genetic material with both exons and introns [1-3].

Intron Late Hypothesis: According to this theory introns originated to circumvent the problem of the random distribution of stop codons in random primordial sequences. The theory also talks about a cosmic ancestry. In disagreement to this notion, Noble Prize winner Renaldo Dulbecco says that introns could not have been added late because of the existing likeness between introns in species that diverged a long time ago [4-6].

These two Darwinian conceptions have, hence, not yet led to a concrete consensus about introns.

3. Introns from a New Perception

If one looks at the variation in the occurrence of Introns from the advanced eukaryotes to the primitive eukaryotes right back to the prokaryotes, one interestingly finds that introns are rarer in prokaryotes than eukaryotes. As a matter of fact there is an increase in the number of introns as one climbs up the evolutionary hierarchy [7].

Before the above stated observation is given reasoning, it's important to grasp a few key concepts. In the biological world, the change from the simple to the complex level of organization was never pre-ordained or programmed but was an outcome of the evolutionary stress that acted backstage in order to poise living beings and their framework with the shifting environment, the latter owing to nature's demand for equilibrium and 'survival of the fittest'; whether that is at the cellular level or at the organism level. This evolutionary pressure is nothing but the ultimate force of nature that was responsible for the prebiotic evolution and so on. This natural force comprises of two decisive elements- Mutation and Selection. These two elements have acted whenever modernization or adversity impedes survival. And by doing so, make an organism better and better attuned to the demand. Therefore mutation and selection draw that thin line between success and failure among individuals. So if one tries to

narrow down the aforesaid situation to sets of genes that are exposed to modernization, owing to the evolutionary pressure, some of the genes must not function; for it is a well known fact that the expression of a gene is the ending of an interplay between the inherent codes, that constitute them, and the immediate surrounding environment. After all, why must a gene express if they fail to find an environment favorable enough? And if this is true they are ought to be turned off or kept silent.

So if the above mentioned conditions are assumed for introns, i.e. If they are regarded as primordial genes that probably thrived in a milieu at that ancient moment in time, any renewing and changing ambiance may well have imposed hardships to their normal functioning. Now the direct environment required by a gene for its expression, can be assumed to be a switch that presides over the activity of a gene. So it can be said that the availability of a product rich environment might lead to the non-functionalization of a gene which is otherwise required for producing enzymes that will catalyze the synthesis of the product. In other words, unless there is a dearth for an enzymatically catalyzed product, nature will not find a reason to keep the responsible genes activated. Something similar would have transpired for introns as a result of which nature would have strengthened its clutches and bent an inescapable pressure accounting for its obvious present day dormancy. The above assumption gathers support from the finding that L-gulono γ -lactone oxidase, an enzyme catalyzing terminal step in ascorbic acid synthesis is absent in the present generations of Homo sapiens. This enzyme is the product of a pseudo gene in humans, i.e. this gene had been silenced long time ago during the evolution of man [8, 9]. And a plausible substantiation that can be drawn from this is, as ascorbic acid (vitamin C) became more and more available in nature, the need to express genes that code for the enzyme L-gulono γ -lactone oxidase was simply unnecessary, eventually silencing the gene in the recent generations. So moreover it's quite possible that introns are also among those silent genes that lost their functions long time ago.

In contrast to the typical organism centered view of evolution, the Selfish Gene Theory or the Gene Selection Theory, as popularized by Richard Dawkins, considers organisms as vehicles driven by genes competing with each other to promote their own survival in the following generations; genes that successfully alter themselves will be passed on, this would ensure the genes perpetuation [10]. Now the idea of gene non-functionalization and the Selfish Gene Theory, put together, fortifies the reasons behind the inactiveness of intronic sequences.

An additional influential evolutionary stimulus imposing quantitative (via gene elongation, dose repetition) and qualitative (via functional divergence, exonization-pseudo-exonization etc.) changes in the genes starting from an ancestral gene was named 'Gene-Duplication'. Now it's known that during gene-duplication there are three outcomes: -

- The resulting duplicate copies may be identical to parent gene.
- Owing to a slight nucleotide substitution, one of the copies may possess a diverged or a novel function.
- A deleterious mutation may occur owing to large number of nucleotide substitution.

Now during gene-duplication, the frequency of non-functionalization in any gene outnumbers a functional divergence in it [11]. And the tilt for this ratio depends on the number of nucleotide substitution in a redundant copy of the duplicated gene and more the number more the probability for a deleterious mutation thereby resulting in a gene transforming to a Pseudogene or a nonfunctional gene. Process of conversion of an exon to a nonfunctional Pseudogene is called Pseudo-exonization. This creates a discontinuous genome rather than a continuous elongated gene as result of gene duplication, referred to as Gene Abridgment. Pseudoxons are created due to a deleterious mutation in one of the exons in a genome [11]. A similar situation may thus be hypothesized to give an explanation for the discrete arrangement of the eukaryote genome as well as the dormancy and uselessness of introns. The continuous stretches of genes that are seen among prokaryotes and early eukaryotes are the ones that have become junk genes in the modern age higher order organisms and that's why given the name Introns. So as these intergenic sequences were found serving no purpose to the evolving organisms in the class structure they could have been no longer accepted along in the Central Dogma, to give rise to functional proteins, and this in turn necessitated a mechanism that could effectively segregate these nonfunctional genetic elements from the exons in consequence evolving, the Mechanism of Splicing, up the hierarchal tree.

An indirect substantiation for the aforesaid notion is the presence of introns in the present-day members of the archaebacterian assemblage [12]. Now Archaebacteria even though coming under the Kingdom Monera diverged from the other Eubacteria long ago and hence show distinction in their characteristics from other prokaryotes.

4. Conclusion

So an incidence of introns in some of the existing generations of primitive microorganisms is a confirmation in itself that introns were neither a singular feature of the eukaryotes (intron early hypothesis) nor a recent assimilation on account of an inexplicable and ambiguous cosmic ancestry (intron late hypothesis). The paradox that a cell puts a huge amount of its energy into the creation of these introns just to discard them later on, continues to question the very underpinning of the contemporary conceptions on introns; Nature for reasons created these sequences, although they are kept silent to our limited knowledge, but evolution chose to keep and conserve it, thereby empowering the very purpose of its prolonging and continued existence. This is the blurring distinction that must be realized.

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