On *Not* Reading *Signature in the Cell:*

A Response to Francisco Ayala

by Stephen C. Meyer

No doubt it happens all the time. There must be many book reviews written by reviewers who have scarcely cracked the pages of the books they purport to review. But those who decide to write such blind reviews typically make at least some effort to acquire information about the book in question so they can describe its content accurately—if, for no other reason, than to avoid embarrassing themselves. Unfortunately, in his review of my book *Signature in the Cell* (titled ironically, "On *Reading* the Cell's Signature"), eminent evolutionary biologist Francisco Ayala does not appear to have even made a search for the crib notes online. Indeed, from reading his review it appears that he did little more than crack the title page and table of contents—if that. As a result, his review misrepresents the thesis and topic of the book and even misstates its title.

The title of my book is not *Signature* of *the Cell* as Ayala repeatedly refers to it, but *Signature* in *the Cell.*

The thesis of the book is not that "chance, by itself, cannot account for the genetic information found in the genomes of organisms" as he claims, but instead

that intelligent design *can* explain, and does provide the best explanation for (among many contenders, not just chance) the origin of the information necessary to produce the first living cell.

Further, the topic that the book addresses is not the origin of the genomes of organism*s* or the *human* genome as the balance of Professor Ayala's critique seems to imply, but instead the origin of the *first* life and the mystery surrounding the origin of the information necessary to produce it.

Ayala begins his review by attempting to trivialize the argument of *Signature in the Cell*. But he does so by misrepresenting its thesis. According to Ayala, "The keystone argument of *Signature of the Cell* [sic] is that chance, by itself, cannot account for the genetic information found in the genomes of organisms." He notes—as I do in the book—that all evolutionary biologists already accept that conclusion. He asks: "Why, then, spend chapter after chapter and hundreds of pages of elegant prose to argue the point?" But, of course, the book does not spend hundreds of pages arguing that point. In fact, it spends only 55 pages out of 613 explaining why origin-of-life researchers have—since the 1960s—almost universally come to reject the chance hypothesis. It does so, not because the central purpose of the book is to refute the chance hypothesis per se, but for several other reasons intrinsic to the actual thesis of the book.

Signature in the Cell makes a case for the design hypothesis as the *best* explanation for the origin of the biological information necessary to produce the first living organism. In so doing, it self-consciously employs a standard method of historical scientific reasoning, one that Darwin himself affirmed and partly pioneered in the *Origin of Species*. The method, variously described as the method of multiple competing hypotheses or the method of inferring to the best explanation, necessarily requires an examination of the main competing hypotheses that scientists have proposed to explain a given event in the remote past. Following Darwin and his scientific mentor Lyell, historical scientists have understood that *best* explanations typically cite causes that are known from present experience to be capable, indeed uniquely capable, of producing the effect in question.

In the process of using the method of multiple competing hypotheses to develop my case for intelligent design in *Signature in the Cell*, I do examine the chance hypothesis for the origin of life, because it is one of the many competing hypotheses that have been proposed to explain the origin of the first life and the origin of biological information. Naturally, since chance was one of the first hypotheses proposed to explain the origin of life in the wake of the discovery of the information-bearing properties of DNA, I critique it first. Nevertheless, I go on to examine many more recent models for the origin of biological information

including those that rely on physical-chemical necessity (such as current self-organizational models), and those that rely on the interplay between chance and necessity (such as the currently popular RNA world scenario). My discussion of these models takes over 90 pages and four chapters. Did Ayala just miss these chapters?

I should add that my critique of the chance hypothesis provides a foundation for assessing some of these more recent chemical evolutionary theories—theories that Ayala would presumably recognize as contenders among contemporary evolutionary biologists and which rely on chance in combination with other processes. For example, in the currently popular RNA world scenario, self-replicating RNA catalysts are posited to have first arisen as the result of random interactions between the chemical building blocks or subunits of RNA. According to advocates of this view, once such self-replicating RNA molecules had come into existence, then natural selection would have become a factor in the subsequent process of molecular evolution necessary to produce the first cell. In *Signature in the Cell*, however, I show that the amount of sequence-specific information necessary to produce even a supposedly simple self-replicating RNA molecule far exceeds what can be reasonably assumed to have arisen by chance alone. Indeed, my analysis of the probabilities of producing various information-rich bio-molecules is not only relevant to showing that "chance, by itself, cannot account

for" the origin of genetic information, but also to showing why theories that invoke chance in combination with pre-biotic natural selection also fail.

In any case, *Signature in the Cell* does not just make a case *against* materialistic theories for the origin of the information necessary to produce the first life, it also makes a positive case *for* intelligent design by showing that the activity of conscious and rational agents is the only known cause by which large amounts of new functional information arises, at least when starting from purely physical and chemical antecedents.

The closest that Ayala comes in his review to recognizing the central affirmative argument in the book is his rather clumsy attempt to refute the idea of intelligent design by insisting that existence of "nonsensical" or junk sequences in the human genome demonstrates that it did not arise by intelligent design. As he claims explicitly, "according to Meyer, ID provides a more satisfactory explanation of the human genome than evolution does."

Again, I have to wonder whether Professor Ayala even cracked the pages of the book. My book is not about the origin of the *human* genome, nor about human evolution nor even biological evolution generally. It's about chemical evolution, the origin of the first life and the genetic information necessary to produce it. In fact, I explicitly acknowledge in the epilogue that someone could in principle accept my argument for the intelligent design of the first life and also accept the standard neo-Darwinian account of how subsequent forms of life evolved. I don't hold this "front-end loaded" view of design, but my book makes no attempt to refute it or standard accounts of biological evolution. For this reason, it's hard to see how Ayala's attempt to defend biological evolution and refute the particular hypothesis that intelligent design played a discernable role in the origin of the human genome in any way challenges the argument of *Signature in the Cell*.

Even so, it is worth noting that the argument that Ayala makes against intelligent design of the human genome based upon on the presence of "nonsensical" or so-called junk DNA is predicated upon two factually flawed and out-of-date premises. Ayala suggests that no designer worthy of the modifier "intelligent" would have allowed the human genome to be liberally sprinkled with a preponderance of nonsense DNA sequences and that the presence and apparently random distribution of such sequences is more adequately explained as a by-product of the trial and error process of undirected mutation and selection. According to Ayala, the distribution of a particular sequence (the *Alu* sequence), which he asserts contains genetic nonsense, suggests a sloppy, unintelligent editor, not an intelligent designer. As he argues:

> It is as if the editor of *Signature of the Cell* would have inserted between every two pages of Meyer's book, forty additional pages, each containing the same three hundred letters. Likely, Meyer would not think of his editor as being "intelligent." Would a function ever be found for these one million nearly identical *Alu* sequences? It seems most unlikely.

Thus, in essence, Ayala claims that (1) a preponderance of nonsense DNA sequences and (2) the random distribution of these sequences shows that the human genome could not have been intelligently designed. But both of the factual claims upon which Ayala bases this argument are wrong.

First, neither the human genome nor the genomes of other organisms are predominantly populated with junk DNA. As I document in *Signature in the Cell*, the non-protein-coding regions of the genomes (of various organisms) that were long thought to be "junk" or "nonsense" are now known to perform numerous mission-critical functions. Non-protein-coding DNA is neither nonsense nor junk. On page 407 of *Signature in the Cell*, I enumerate ten separate functions that non-protein-coding regions of the genome are now known to play. (References to peer-reviewed scientific publications documenting my claims are there provided). Overall the non-coding regions of the genome function much like an operating system in a computer in that they direct and regulate the timing and expression of the other protein-coding genetic modules.

Further, the *Alu* sequences that Ayala specifically cites as prime examples of widely and randomly distributed nonsense sequences in the human genome are NOT non-functional or "nonsense." Short Interspersed Nuclear Element (SINE) sequences of which *Alu* is one member, perform numerous formatting and regulatory functions in the genomes of all organisms in which they have been found. It is simply factually incorrect for Ayala to claim otherwise.

In general, SINEs (and thus *Alu*s) allow genetic information to be retrieved in multiple different ways from the same DNA data files depending on the specific

needs of different cell types or tissues (in different species-specific contexts). In particular, *Alu* sequences perform many taxon-specific lower-level genomic formatting functions such as: (1) providing alternative start sites for promoter modules in gene expression—somewhat like sectoring on a hard drive (Faulkner et al., 2009; Faulkner and Carninci, 2009); (2) suppressing or "silencing" RNA transcription (Trujillo et al., 2006); (3) dynamically partitioning one gene file from another on the chromosome (Lunyak et al., 2007); (4) providing DNA nodes for signal transduction pathways or binding sites for hormone receptors (Jacobsen et al., 2009; Laperriere et al., 2004); (5) encoding RNAs that modulate transcription (Allen et al., 2004; Espinoza et al., 2004; Walters et al., 2009); and (6) encoding or regulating microRNAs (Gu et al., 2009; Lehnert et al., 2009).

In addition to these lower-level genomic formatting functions, SINEs (including *Alu*s) also perform species-specific higher-level genomic formatting functions such as: (1) modulating the chromatin of classes of GC-rich housekeeping and signal transduction genes (Grover et al., 2003, 2004; Oei et al., 2004; see also Eller et al., 2007); (2) "bar coding" particular segments for chromatin looping between promoter and enhancer elements (Ford and Thanos, 2010); (3) augmenting recombination in sequences where *Alu*s occur (Witherspoon et al., 2009); and (4) assisting in the formation of three-dimensional chromosome

territories or “compartments” in the nucleus (Kaplan et al., 1993; see also Pai and Engelke, 2010).

Moreover, *Alu* sequences also specify many species-specific RNA codes. In particular, they provide: (1) signals for alternative RNA splicing (i.e., they generate multiple messenger RNAs from the same type of precursor transcript) (Gal-Mark et al., 2008; Lei and Vorechovsky, 2005; Lev-Maor et al., 2008) and (2) alternative open-reading frames (exons) (Lev-Maor et al., 2007; Lin et al., 2008; Schwartz et al., 2009). *Alu* sequences also (3) specify the retention of select RNAs in the nucleus to silence expression (Chen et al., 2008; Walters et al., 2009); (4) regulate the RNA polymerase II machinery during transcription (Mariner et al., 2008; Yakovchuk et al., 2009; Walters et al., 2009); and (5) provide sites for Adenine-to-Inosine RNA editing, a function that is essential for both human development and species-specific brain development (Walters et al., 2009).

Contrary to Ayala’s claim, *Alu* sequences (and other mammalian SINEs) are not distributed randomly but instead manifest a similar “bar-code” distribution pattern along their chromosomes (Chen and Manuelidis, 1989; Gibbs et al., 2004; Korenberg and Rykowski, 1988). Rather like the distribution of the backslashes, semi-colons and spaces involved in the formatting of software code, the “bar-code” distribution of *Alu* sequences (and other SINEs) reflects a clear functional logic,

not sloppy editing or random mutational insertions. For example, *Alu* sequences are preferentially located in and around protein-coding genes as befits their role in regulating gene expression (Tsirigos and Rigoutsos, 2009). They occur mainly in promoter regions—the start sites for RNA production—and in introns, the segments that break up the protein-coding stretches. Outside of these areas, the numbers of *Alu* sequences sharply decline. Further, we now know that *Alu* sequences are directed to (or spliced into) certain preferential hotspots in the genome by the protein complexes or the "integrative machinery" of the cell's information processing system (Levy et al., 2010). This directed distribution of *Alu* sequences enhances the semantic and syntactical organization of human DNA. It appears to have little to do with the occurrence of random insertional mutations, contrary to the implication of Ayala's "sloppy editor" illustration and argument.

Critics repeatedly claim that the theory of intelligent design is based on religion, not science. But in his response to my book, it is Ayala who relies on a theological argument and who repeatedly misrepresents the scientific literature in a vain attempt to support it. The human genome manifests nonsense sequences and sloppy editing ill-befitting of a deity or any truly *intelligent* designer, he argues. He also sees other aspects of the natural world that he thinks are inconsistent with the existence of a Deity. I'll leave it to theologians to grapple with Ayala's arguments about whether backaches in old age and other forms of generalized human

suffering make the existence of God logically untenable. But on the specific scientific question of the organization of the human genome, I think the evidence is clear. It is Ayala who has been sloppy, and not only in his assessment of the human genome, but also, I must add, in his critique of my book.

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