Review of: "Non-Darwinian Molecular Biology"

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Invited Commentary on “Non-Darwinian Molecular Biology,” Alexander F. Palazzo* and Nevraj S. Kejiou, Front. Genet., 16 February 2022 | https://doi.org/10.3389/fgene.2022.831068 peerreview@reach.qeios.com

When I first saw the title of this review article, I was interested to write a commentary because I thought the review would highlight many of the exciting new topics in evolutionary genomics and molecular biology. When I read the article, however, I was disappointed to find that Drs. Palazzo and Kejiou denigrated important contemporary research and preferred an out-of-date view of evolution producing “messy” genomes as well as embracing the long discredited notion of “junk DNA.

Molecular Biology and genomics have made it possible to study evolutionary processes with unprecedented precision and revealed the major roles played by important molecular agents, such as transposable elements and (protein) noncoding DNA and RNA sequences. The authors have chosen to ignore the growing body of evidence revealing how these unexpected players in genome evolution have contributed to the origins of adaptive innovations and new taxa, especially in the most complex eukaryotes. Their concluding summary makes this retrograde point of view quite clear:

“Most molecular biologists use an antiquated model of how evolution shapes biological processes leading them to an unrealistic hyper-adaptationalist view. A prime example of this is the interpretation of the ENCODE project results. Ultimately, this ultra-Darwinian mindset perpetuates the notion that the genome, and life itself, is like a Swiss watch—ornate, and complicated, with every part hand crafted for a specific purpose. This view is completely compatible with the idea that genome is pure information. However, this view is based on ignorance of developments in molecular evolution. It also ignores principles of biochemistry, that predict suboptimal reactions and widespread promiscuity. A more modern view of the eukaryotic cell, shaped by drift-dominated evolution, is a messy junk-filled entity, full

of Rube-Goldberg contraptions that were hobbled together by non-adaptive forces. With this new vantage point, certain aspects of eukaryotic biology become clarified, including the evolution of complexity."

Palazzo and Kejiou's concept of non-Darwinian evolution is to downplay Darwin's focus on the importance of adaptive novelty as reflecting "an unrealistic hyper-adaptationalist view," and they choose research on noncoding RNA functionalities stimulated by the ENCODE (Encyclopedia of DNA Elements) project as the chief example of what they characterize as a mistaken "hyper-adaptationalist" focus, disregarding the fact that noncoding RNA research is currently one of the hottest topics in molecular cell biology and genetics (see below on PubMed results). Instead, they prefer to focus on a notion of genomic and cellular "sloppiness" predicted by neutral evolution theories and molecular buffering processes.

Molecular Biology, and more particularly the field of genomics, are indeed Non-Darwinian for a very good reason. But it is not the anti-adaptationist argument of this review. Non-Darwinian evolutionary theory arises because molecular genetics and genomics have provided us with new ways of thinking about genome content, genome functioning, and evolutionary genome change. Protein-coding DNA constitutes less than 2% of our own genomes (de Koning et al., 2011), and an early comparative genome analysis found that noncoding DNA content in a genome is a more accurate predictor of organismal complexity than protein-coding content (Liu et al., 2013).

Readers should consider how thinking about the basic biology and genetic principles underpinning evolution studies have changed in recent years when deciding what parts of the scientific literature to follow:

1. What Palazzo and Kejiou label as "messiness" is considered by disciplines such as Evo-Devo to reflect robust redundancy and complexity that ensure the exceptional reliability of inherited characteristics under varying conditions (Keane et al., 2014; Kim et al., 2014; Oliveira et al., 2014; Payne & Wagner, 2014; Plata & Vitkup, 2014; Ruz et al., 2014; Zheng & Triesch, 2014; Cui et al., 2015; Jung et al., 2015; Araujo & Liotta, 2018; diCenzo et al., 2018; Osterwalder et al., 2018).

2. Instead of discrete phenotypic traits defined by independently evolving genetic units, we now recognize that cellular and organismal properties result from integrated adaptive systems that depend on expression of coordinated genomic networks (e.g. animal body plan development) (Li et al., 2020; Nishihara, 2020; Panni et al., 2020; Chu et al., 2021; Dandage et al., 2021; Duran et al., 2021; Etxebeste, 2021; Hagolani et al., 2021; Mottes et al., 2021; Sharma et al., 2021).

3. Genome network evolution has been found to involve the ability of transposable

elements to spread appropriate expression signals to multiple different genetic loci and so integrate them into coordinated systems (Jacques et al., 2013; Johnson, 2017; Trizzino et al., 2017; Morata et al., 2018; Rishishwar et al., 2018; Sundaram & Wang, 2018; Trizzino et al., 2018; Fawcett & Innan, 2019; Baud et al., 2020; Moschetti et al., 2020; Nishihara, 2020; Qiu & K hler, 2020; Voronova et al., 2020; Almojil et al., 2021; Nicolau et al., 2021; Senft & Macfarlan, 2021; Zhang et al., 2021) (https://shapiro.bsd.uchicago.edu/Distributed_genome_network_innovation_attributed_to_mobile_DNA_elements.html).

4. Many aspects of cell and organismal function have been documented by genetic analysis to require the presence of noncoding RNAs, which act as enzymes, sensors, and polyvalent aggregation centers for assembling multimolecular complexes in both the nucleus and cytoplasm. (Johnson & Guigo, 2014; Wang et al., 2016; Andergassen & Rinn, 2021; Borkiewicz et al., 2021; Oo et al., 2021; Statello et al., 2021) (Quinodoz & Guttman, 2014; Chujo et al., 2016; Chishima et al., 2018; Mattick, 2018; Salviano-Silva et al., 2018; Daneshvar et al., 2020). The functional diversity of noncoding RNAs is beginning to rival that of proteins, and these versatile molecules carry out some very high level and taxonomically restricted regulatory functions (https://shapiro.bsd.uchicago.edu/Regulatory_Functions_Reported_for_Long_Noncoding_lncRNA_molecules.html).

The fact is that so-called “junk DNA” elements (transposons, retrotransposons, repeats, noncoding sequences) are the genome components that change most during evolutionary transitions, and all have been well-documented to help generate major adaptive novelties.The importance of noncoding, transposable and repetitive DNA elements and of their RNA transcripts as research subjects is reflected in their publication numbers. Here are the numbers I found with different PubMed search entries:

noncoding RNA - 257,261 results
long noncoding RNA - 38,262 results
transposable element - 29,836 results
repetitive DNA - 32,783 results
noncoding DNA - 22,441 results
chromosome structure - 116,574 results
genome network - 84,415 results
neutral evolution - 16,971 results

While these numbers provide only a rough estimate of the research being done on a topic, it is clear that many molecular biologists and molecular evolutionists are producing discoveries and publishing their findings at a significant clip. To me, having studied and practiced molecular genetics, it would seem to be a poor choice to follow the advice of Palazzo and Kejiou and ignore all of this exciting and revelatory research.

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