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Science **313**, 761c (2006);
DOI: 10.1126/science.1126765

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Response to Comment on "Gene Regulatory Networks and the Evolution of Animal Body Plans"

Douglas H. Erwin^{1,2*} and Eric H. Davidson³

Contrary to Coyne's assertions, our paper did not advocate a macromutational innovation of phyla but considered the consequences of the introduction of developmental constraints for the evolution of gene regulatory networks based on recent empirical studies of gene regulatory networks.

Most of Coyne's concerns (1) are restatements of long-standing debates over the nature of evolutionary change (2). The comment offers no new data or interpretations but rather comments on issues, such as the nature of phyla, that have a lengthy and disputed history in evolutionary biology and which were not the subject of our paper. Specifically, Coyne seems to reject the role of regulatory genes in evolution. This is refuted by experimental studies of *Drosophila*, butterflies, echinoderms, fish, amniotes, and other organisms. Therefore, Coyne's conflict is not with our review as much as with developmental biology and its implications for evolutionary process.

Contrary to the claims in (1), nowhere in our paper do we suggest that a phylum arose at one step, nor that speciation in the Cambrian did not produce species (what else would be produced?). Rather, we discuss the evolutionary implications of experimental data on the hierarchical structuring of regulatory networks, developed by exhaustive analysis of cis-regulatory interactions between genes and by comparison of these wiring diagrams across taxa. In fact, we specifically note: "Critically, these kernels would have formed through the same processes of evolution as affect the other components, but once formed ... they would have become refractory to subsequent change" (2). Our hypothesis concerns the effects of constructing these regulatory hierarchies. Coyne also states as a certainty that the apparent early occurrence of phyla in the Cambrian is a consequence of subsequent extinction. However, this is but

one of several widely discussed possible explanations for the apparent uniqueness of body plans. As R. C. Lewontin recently noted (3), the cause of these morphologic gaps is certainly one of the most interesting issues facing evolutionary biologists, and the assumption that they reflect either branching order or extinction is just that, an assumption. Furthermore, Foote (4) observed that early maximal morphologic disparity is a robust result of the use of geometric morphometrics to study disparity, independent of any reliance upon higher taxa. These studies confirm that early morphological disparity is a feature of the Cambrian metazoan radiation, whether one analyzes form quantitatively or counts higher taxa. Our theory provides an answer: that regulatory apparatus underlying construction of body plans were early on canalized by the installation of kernels.

Coyne next questions our use of the term phylum, claiming that phyla are simply arbitrary divisions in the tree of life. We suggested that the highly conserved regulatory wirings evolved at a number of points during the early evolution of animals, and no where did we suggest that kernels were unique to phyla. We specifically said that comparative study will reveal that some occur at the level of phyla and some across more inclusive clades that have been called superphyla or pan-bilateria, and we expect that some kernels could be found just within what are described as classes, although in most cases we expect that such class-level regulatory changes lie within what we described as plug-ins and input/output switches. Thus, we claimed no uniqueness about the level of phylum. Further, we noted that the regulatory changes we describe are "imperfectly reflected at different levels of Linnean classification." Here again, Coyne's conflict seems to be with much of modern molecular biology and its explanatory potency rather than with our paper.

Coyne also claims that our suggestion that the levels of the Linnean hierarchy reflect (im-

perfectly) developmental constraints imposed by the structure of regulatory interactions is wrong, but he provides no alternative explanation of the data we presented (2). We quite agree with Coyne that it is extremely unlikely that all differences between orders in all groups of organisms were caused by changes in plug-ins and I/O switches, but we also never claimed that that was the case. We specifically said that the link between the Linnean hierarchy and the hierarchical levels of regulatory evolution was imperfect.

Coyne's final point creates a false dichotomy. Abundant evidence from the Ediacaran-Cambrian fossil record has established the rapidity of morphologic change. Coyne fails to address this pattern and presents as the only "reasonable" view the position that differences between phyla reflect long periods of evolution. As paleontologists have been pointing out for decades, however, this is simply not the pattern that we observe, and for many durably skeletonized groups it is clear that one cannot invoke inadequacies in the fossil record (5, 6). Nowhere in our paper did we reject natural selection, because we support it. Here again, Coyne falsely accuses us of invoking macromutations. As noted previously, we simply suggested that the effect of normal evolutionary process that produced kernels was to "lock in" structures that were extremely refractory to subsequent modification. We neither suggested nor implied that major changes in conserved kernels were responsible for morphologic innovation, because we were specifically addressing the origin of these kernels and their morphologic and evolutionary implications. This is a mechanism for developmental constraint, not macromutation.

Developmental biologists are producing a wealth of data that is highly informative about the mechanisms of morphological change at a genetic and developmental level and about the processes that produce macroevolutionary changes as documented by the fossil record. These studies provide a promising new view into the mechanisms of evolutionary change.

References and Notes

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21 March 2006; accepted 17 July 2006
10.1126/science.1126765