

CORRESPONDENCE

Neo-Darwinism is just fine

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Denis Noble argues ‘that the Modern Synthesis (neo-Darwinist) theory of evolution requires either extension or replacement’ (Noble, 2015a) and a Correction amended his quotation from a *Nature* 2010 editorial (Noble, 2015b). That Correction helps us appreciate the potential problems when citing pre-print editions, but Noble implies that this *Nature* 2010 editorial and its two inclusive essays by Francis Collins and Craig Venter support his call for either an extension or replacement of neo-Darwinist theory. Quite the contrary, those essays do not support his position. Moreover, his position is mistaken because he omits a critical factor incorporated within neo-Darwinist theory. When this omission is considered, I conclude that neo-Darwinism is just fine.

First, as to the Collins and Venter essays, they simply lament the poor understanding of genetic regulation at the time the human genome project was announced, and which led to over zealous promises. They do not suggest we have learned something since those ‘heady days’ that calls into question neo-Darwinian principles (with the arguable exception of information transfer from RNA to DNA represented by endogenous retrotransposons, which was unappreciated by Collins and Venter at the time). In fact, Collins encourages projects like ENCODE and the NIH’s Roadmap Epigenomics Program because they ‘continue to define the “parts list” of the human genome’ (Collins, 2010). Venter writes, ‘Establishing the complete set of genetic information that we received from each parent is crucial to understanding the links between heritability, gene function, regulatory sequences and our predisposition to disease’ (Venter, 2010). Metaphors such as ‘parts list’ and phrases like ‘the complete set of genetic information’ could very well have been penned by a classic neo-Darwinist.

Besides mistakenly claiming that Collins and Venter support him, Noble omits the fact that neo-Darwinian principles accommodate discoveries whereby some genetic regulatory mechanisms (epigenetic processes) are sometimes ‘tuned’ to the organism’s external environment. This neo-Darwinian adaptation confers some flexibility in the face of changing environments, which is extremely important to relatively immobile species such as plants but less important for mammals, whose complex brains provide great flexibility in the face of environmental change. However [and adopting Noble’s (2008) metaphor from his book, *The Music of Life*], that music is inaudible unless the receiving instrument (the inherited ‘book of life’) has coded for the auditory characteristics of a particular tune. That receiving instrument is exactly what Venter meant by ‘the complete set of genetic information that we received from each parent’ (Venter, 2010).

Thus, Noble’s omission is this: external factors only influence gene expression via epigenetic mechanisms if the inherited DNA sequence is ‘permissive’, or specially tuned to respond to that signal (Yuan, 2012; Heyn, 2014). That is a critical omission, which effectively misrepresents neo-Darwinism.

Noble’s omission seems to spring from overplaying observations of transgenerational epigenetic inheritance, wherein ‘the sins of the

fathers are visited upon the sons’ (Hughes, 2014). Recent observations reveal multiple generations sharing the parent’s environmentally induced phenotype, even in the absence of the original factor (Nilsson and Skinner, 2015). Various ‘epigenetic-inducing molecules’ (so to speak) are inherited in egg or sperm (e.g. miRNAs, piRNAs, modified histones etc.). Neo-Darwinian theory has never denied their existence as inherited factors, and new research suggests that they may have a causal role in inheritance of the parent’s environmentally acquired trait. However, no matter how those suspected (and speculative) molecules came to be present in the zygote, or how long they might persist in future generations, the inherited DNA sequence must still be ‘permissive’ in order for those molecules to reach their functional potential. They are functionless without a neo-Darwinist, naturally selected and inherited DNA sequence. This is still the case even if those inherited molecules escape important processes designed to protect against inheritance of acquired traits (e.g. mammalian erasure of DNA methylation).

Thus, the inherited DNA sequence is still the ultimate source of this newly discovered form of inheritance, which means neo-Darwinian language and metaphors like ‘the book of life’ and ‘blueprint’ are still apt and Lamarck is still wrong. This remains true even when the relationship between genotype, epigenetic state and phenotype cannot be modeled in a linear fashion. Neo-Darwinism has never contradicted dynamic systems concepts.

A specific example brings this closer to home for most readers. The expression of many human genotypes is altered in the presence of prenatal stress, and the developing offspring’s HPA axis is changed from the typical state via epigenetic processes. This results in hyper-vigilance (among other atypical phenotypes). This is a perfect example of a neo-Darwinian adaptation. Importantly, however, some (perhaps, most) genotypes are not responsive to that set of environmental cues; that is, the ‘stress music’ sometimes falls on deaf ears because those inherited genotypes are not tuned to that particular signal. There are many such ‘protective’ (and ‘susceptibility’) genotypes, which neo-Darwinian language and principles comfortably accommodate (Belsky et al., 2007).

I close by thanking Denis Noble for giving us information that, when correcting for the critical omission noted above, helps explain how new and exciting discoveries fit within the existing language and principles of the Modern Synthesis (neo-Darwinist) theory. Biology textbooks do not need revision, but rather routine updates to incorporate new discoveries, primarily in gene control and regulation. Thus, neo-Darwinism is just fine.

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10.1242/jeb.125088

Central tenets of neo-Darwinism broken. Response to ‘Neo-Darwinism is just fine’

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This correspondence on my article (Noble, 2015) is very welcome since it accepts the main point I made in relation to epigenetics and evolution. Williams and I therefore agree that ‘recent observations reveal multiple generations sharing the parent’s environmentally induced phenotype, even in the absence of the original factor’. Where we disagree is whether this is incompatible with neo-Darwinism.

Those who formulated neo-Darwinism would not have accepted this. The central basis of the theory was established by Weismann (1892) in postulating the existence of the Weismann barrier that would make inheritance of environmentally induced variation impossible: ‘when these deviations only affect the soma, they give rise to temporary non-hereditary variations; but when they occur in the germ-plasm, they are transmitted to the next generation and cause corresponding hereditary variations in the body’. As Dawkins expressed it, genes are ‘sealed off from the outside world’ (Dawkins, 1976). Mayr (1982) and many other neo-Darwinists concur: ‘All of the directions, controls and constraints of the developmental machinery are laid down in the blueprint of the DNA genotype as instructions or potentialities’.

If we accept that environmentally induced phenotypes can be inherited, as recent observations abundantly show (Tollefsbol, 2014), then we have broken the Weismann barrier, because the germline is no longer isolated from the environment and the organism’s response to it. We have also automatically broken the other neo-Darwinian assumption of random variation because phenotype changes can then guide inheritable variation. The honest response to this situation is to say that the central tenets of neo-Darwinism are no longer valid. We then return to a modern version of Darwinism. Darwin accepted the inheritance of acquired characteristics and formulated a hypothesis in his 1868 book *The Variation of Animals and Plants under Domestication*, his pangenesis theory of gemmules, which turns out to be not so far

removed from what we have now found. His gemmules can be viewed as our inheritable epigenetic changes.

If, as the commentator seems to imply, we make neo-Darwinism so flexible as an idea that it can accept even those findings that the originators intended to be excluded by the theory it is then incumbent on modern neo-Darwinists to specify what would now falsify the theory. If nothing can do this then it is not a scientific theory.

Concerning Collins and Venter, I did not quote or refer to either of them in my article. I quoted an earlier version of the *Nature* Editorial, with which I entirely concur: ‘They began to see DNA as the “book of life”, which could be read like an instruction manual. It now seems that the genome might be less like a list of parts and more like the weather system, full of complicated feedbacks and interdependencies’. This is the reason why the gene-centric approach has failed to deliver its promises on health care (Joyner and Prendergast, 2014). The references to Collins and Venter are in a revised editorial, not in my article.

It is impossible to reply to all the points made. Further details are in the recording of a session on evolutionary biology at EB2015 (https://www.youtube.com/watch?v=A_q_bOWc8i0).

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10.1242/jeb.125526