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Epigenetics again: will it cause a revolution in evolution?

Readers will know that from time to time (e.g., [here](#) and [here](#)) I weigh in on the persistent and loud claim that epigenetic inheritance (that is, the transmission from parent to offspring of traits that are not coded for in the DNA) will have huge effects on the current paradigm of neo-Darwinian evolution. There’s a segment of the evolution community who sees this form of nonstandard inheritance as a revolution in our field. That’s because, perhaps, some *environmental* modifications of an organism—changes induced by climate, diet, or the like—might become inherited, forming a type of “Lamarckian” inheritance. (Lamarck [1744-1829] was a French zoologist who proposed that evolution occurred by the inheritance of acquired traits.)

Now it’s unlikely that, say, a change in diet or habits alone will cause changes in an organism that can be passed on to its offspring. Athletes don’t tend to produce muscular children, nor amputees legless ones. But there is one type of “acquired” trait that can be inherited, at least for a few generations: the attachment of methyl groups to DNA. Certain components of the DNA, most particularly the cytosine residues (“C”s: one of the four DNA bases), have a tendency to be **methylated**: a one-carbon methyl group attaches itself to the 5 position of the ring in that DNA base. Those changes, which can have important effects on gene regulation, can themselves be coded for in the DNA (that is, there is some gene which gives instructions for another gene to become methylated). But some methylations seem to occur spontaneously, without any genetic instruction, and these are in effect environmentally induced changes that can be inherited from parent to offspring. It is those changes that many evolutionists point to as the “nongenetic” inheritance that could revolutionize our view of evolution.

Whether such changes can indeed be important material for evolution is

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the subject of a new paper in *Nature* by Becker et al. The authors examined DNA methylation in the plant *Arabidopsis thaliana*, a small (and largely self pollinated) plant known as the “Drosophila of plants” because its ease of culture and short generation time (six weeks from one generation to the next!) makes it suitable for breeding experiments.

The point of the experiment was to start with a single homogeneous inbred line of the plant and then subculture it into ten lines, all of which were genetically identical at the start of the experiment. Each of the ten lines was then propagated for thirty generations through inbreeding, and then subjected to DNA sequencing. That DNA sequencing detects which bases are methylated, and then the methylation patterns of each line could be compared to see two things: 1) how much the initially identical lines differed in methylation patterns after 30 generations; that is, how much the environment had created different methylation patterns in the different lines; and 2) how “heritable” those changes were among generations. That could be seen by comparing the generation-30 lines with some generation-3 lines that were ancestral. If stable methylation patterns arose in the different lines that could be transmitted over 27 generations, that means that, at least in the short term, acquired changes in the DNA could be inherited.

Here are the important findings:

- The lines rapidly accumulated differences in methylation patterns of DNA, and some of these could be stably inherited over at least 27 generations (they had only two lines to do this 27-generation comparison, so the results are tentative). But many changes also disappear over time, and thus are not stably inherited.
- Despite this high mutation rate, the number of methylated sites does not accumulate linearly with time. The authors consider this their most important finding because it indicates “that many [epigenetic changes] are not stably inherited over the long term.”
- The “mutation rate” to methylation changes of cytosine bases was very high: roughly a thousand times higher than the “real”

mutation rate at which one DNA base changes to another (the latter are what has been considered the main heritable basis of evolutionary change).

- Methylation occurred at certain “privileged” regions of the genome: in the coding parts of genes (“exons”) rather than noncoding parts, and in regions closer to “transposable elements” (bits of the DNA known to jump around in the genome).
- Methylation could affect gene expression. Analyzing the three genes with the highest differences in expression levels among lines, the authors found that the less-methylated genes were expressed more strongly. Methylation tends to reduce gene expression, then, but of course reduced gene expression can also be of evolutionary significance.
- The authors don’t know how this differential methylation of DNA bases occurs, though they hypothesize that “siRNAs” (small interfering RNA molecules, which affect gene expression themselves) play a role.

What’s the upshot? First, that environmental changes in DNA *not* mediated by genes did occur: the different sublines of the plant, though genetically identical, accumulated different methylation patterns in their DNA. These environmental “mutations” occur very rapidly and some of them are inherited over several generations. Some of them could affect gene expression, too. Putting it all together, the experiment shows that it’s theoretically possible for environmental influences to produce inherited changes that could affect evolutionarily important traits (in this case the level of gene expression). In other words, it’s possible for evolution to occur in a Lamarckian way.

Does this, then vindicate Lamarckian inheritance and presage a revolution in evolution? I don’t think that’s likely. As I’ve written before, every evolutionarily important change that has shown to be inherited, and has been mapped to specific positions in the genome, shows that *real* genetic mutations—not methylated changes in DNA bases—are

responsible. While it's possible that some adaptations or evolutionary changes could rest on epigenetic modifications not involving substitutions of one DNA base for another or an interruption of DNA sequences by the interposition of other sequences, we haven't yet found any.

At the end of the paper, the authors raise another problem with touting these environmental changes as important sources of evolution change: the modifications don't appear stable in the long term, and so couldn't be the basis of adaptations that arise and are stable over thousands or millions of years:

Perhaps our most important finding is that the number of epimutations does not increase linearly with time, indicating that many are not stably inherited over the long term. In addition to DMPs [differentially methylated positions] and DMRs [differentially methylated regions] that arose apparently independently in several strains, we even discovered a DMR that had become demethylated after 31 generations, but was re-methylated in the following generation. This suggests that DNA methylation in specific regions of the genome can fluctuate over relatively short timescales. Such sites can be considered as going through recurrent cycles of forward and reverse epimutation, which is very different from what is found at the level of the genome sequence, where reverse mutations are exceedingly rare. Importantly, reversion rates directly determine the ability of any type of allele to be subject to Darwinian selection. This needs to be taken into account when considering the potential of epialleles as a factor in evolution.

Translation: These epigenetic changes in the DNA aren't all that stable, folks, so we need to be really careful before touting them as important aspects of evolution.

My conclusion: Though the results are intriguing—especially the observation of a high rate of epigenetic “mutation”—there's still no

reason to see this type of heritable change as presaging the overturning or drastic revision of the current neo-Darwinian view of evolution.

Becker, C. et al. 2011. Spontaneous epigenetic variation in the *Arabidopsis thaliana* methylome. Nature, in press. Published online, doi:10.1038/nature10555

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Were the ten lines exposed to very different environments? If not, why would one expect that methylation changes would be stable? In other words, if the specific methylations didn't have an opportunity to confer selective advantage to a line, we shouldn't necessarily expect them to persist in a line, should we?

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