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Evidence from Biochemical Pathways in Favor of Unfinished Evolution rather than Intelligent Design

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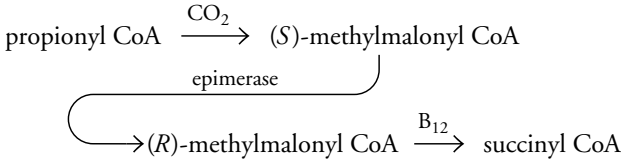
Disagreements among proponents of intelligent design and evolution continue *(1)*. We wish to put forward an argument in favor of imperfect or unfinished evolution based on some metabolic pathways in which it seems that intelligent design would have done better.

In teaching metabolic pathways, every instructor emphasizes the chemical logic of the transformations wherever possible. In cases such as those to be described here, the lecturer is reduced to impotent hand-waving.

Case 1: Unnecessary Inversions (*2*, p 673)

The oxidation of fatty acids with odd numbers of carbon atoms goes through the sequence:



In the epimerase step, the original S configuration at C2 of the methylmalonate moiety is inverted (racemized) to R. Why is this extra step, inversion of configuration at one of the chiral centers of methylmalonyl CoA required? Intelligent design would either have made the diastereomer with the R configuration for the methylmalonyl moiety directly, or would have designed the B_{12}-requiring mutase to accept the diastereomer with (*S*)-methylmalonic acid. The answer from the evolutionary standpoint is that if it works, don't fix it (at least not rapidly).

Case 2: Unnecessary Pathways *(3)*

A somewhat similar stereochemical situation occurs in the biosynthesis of some plant alkaloids where reticuline, with one chiral center, is an intermediate. In a complex metabolic pathway that begins with L-tyrosine, (*S*)-reticuline is first formed and is then inverted to (*R*)-reticuline via an oxidation–reduction reaction. (*S*)-Reticuline is the biosynthetic precursor for berberine, β-narcotine, and so forth. (*R*)-reticuline is required for the formation of thebaine, codeine, morphine, and so forth. Much metabolic manipulation could have been avoided by using (*S*)-reticuline for the biosynthesis of all of these alkaloids.

Case 3: Duplicate Pathways *(4–6)*

In some cases, there are two separate pathways for formation of a metabolite in different organisms. Examples include lysine biosynthesis via the common diaminopimelic acid route and by the less common α-aminoadipic acid route (some fungi, *Euglena*); L-ascorbic acid biosynthesis via D-glucuronic acid (animals) and via L-galactose (plants); and the biosynthesis of phenylalanine and tyrosine by the "classical" route (*E. coli, B. subtilis*) as well as via arogenic acid (*Cyanobacteria, Euglena*). Many other examples could have been cited. An intelligent designer would probably have been content with a single pathway in all cases.

Case 4: Unnecessary Waste (*2*, p 775)

The penultimate step in tryptophan biosynthesis is the condensation of indole with the 3-carbon amino acid, serine. But in the previous step, an adequate 3-carbon fragment was removed as glyceraldehyde 3-phosphate. Indeed, an identical 3-carbon fragment is retained during the biosynthesis of histidine (ref *2*, p 777).

Case 5: Unnecessary Connections (*2*, p 1022)

DNA is double-stranded; one strand runs in the direction 5′ → 3′ and the other runs in the 3′ → 5′ direction. When DNA is replicated, one strand is made continuously in the 5′ → 3′direction, but the other strand is made discontinuously and in pieces (the Okazaki fragments) but also in the 5′ → 3′ direction. The pieces then have to be put together in a complicated way. We would have designed a system using two polymerase activities: the first using deoxyribonucleotide 5′-triphosphates and the second deoxyribonucleotide 3′-triphosphates. Then both strands could be made continuously.

Case 6: Unnecessary Editing *(7)*

Messenger RNA is the intermediate in information transfer between DNA and proteins. Sometimes, messenger RNA has to be "edited" before it conveys the correct message. A pre-messenger RNA that encodes a subunit of a glutamate-sensitive ion channel of mouse neurons contains the codon CAG. This codon specifies glutamine in the protein. This is the wrong amino acid and mutant mice that incorporate glutamine in this position die. In normal mice, an "editing" process uses an enzyme, adenosine deaminase, to convert adenosine to inosine; the sequence CAG is changed to CIG. CIG behaves like the normal codon CGG that codes for the correct amino acid, arginine. Further, it has been possible to create healthy mutant mice that have the CGG codon from the beginning (instead of the normal CAG). The mice are normal and are no longer dependent upon the activity of ad-

enosine deaminase (that can be artificially removed). Would not an intelligent designer have inserted CGG to begin with?

Directed Evolution

Finally, we note that in recent years, "directed evolution" (or in vitro evolution or molecular evolution) has been used to obtain proteins, often enzymes, with modified properties. In brief, this work involves random mutations in DNA followed by a selection process for the best-fitted. Such work has provided new enzymes with altered substrate specificity, specific activity, topology, enantioselectivity, thermal stability, and resistance to organic solvents. There is an extensive literature. To cite two recent papers (2003) in The Proceedings of the National Academy of Sciences, Williams and co-workers modified the stereochemistry of an aldolase *(8)* and Leong and co-workers optimized the expression and specific activity of an interleukin, IL-12 *(9)*. We also cite the classic work of Hartley *(10),* a recent book *(11),* and a short review *(12)*.

Summary

The examples that we have noted argue for the absence of highly intelligent design. They are not intended as a comprehensive collection but as a limited sample of "inefficient" situations in metabolism. Students and instructors can readily unearth more to their own satisfaction. The current success in directed evolution shows that purposeful change, even by human intelligence, is not so difficult.

Acknowledgments

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Literature Cited

1. *Intelligent Design Creationism and Its Critics;* Pennock, R. T., Ed.; MIT Press: Cambridge, MA, 2001.
2. Voet, D.; Voet, J. G. *Biochemistry,* 2nd ed.; Wiley: New York, 1995.
3. Dewick, P. M. *Medicinal Natural Products. A Biosynthetic Approach;* Wiley: Chichester, U.K., 1997; pp 295–321.
4. Metzler, D. E. *Biochemistry;* Academic Press: New York, 1977; p 826.
5. Wheeler, G. L.; Jones, M. A.; Smirnoff, N. *Nature* **1998,** *393,* 365–369.
6. Bentley, R. *Crit. Revs. Biochem. Mol. Biol.* **1990,** *25,* 307–384.
7. Keegan, L. P.; Gallo, A; O'Connell, M. A. *Science* **2000,** *290,* 1707–1709.
8. Williams, G. J.; Domann, S.; Nelson, A.; Berry, A. *Proc. Nat. Acad. Sci. USA* **2003,** *100,* 3143–3148.
9. Leong, S. R.; Chang, J. C.; Ong, R.; Dawes, G.; Stemmer, W. P.; Punnonen, J. *Proc. Nat. Acad. Sci. USA* **2003,** *100,* 1163–1168.
10. Hartley, B. S. *Proc. R. Soc. Lond. B* **1979,** *205,* 443–452.
11. *Directed Molecular Evolution of Proteins;* Brakmann, S., Johnsson, K., Eds.; Wiley-VCH: Weinheim, Germany, 2002.
12. Alexeeva, M.; Carr, R.; Turner, N. J. *Org. Biomol. Chem.* **2003,** *1,* 4133–4137.