Open Questions

A homage to *Giardia*

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What are we doing here, where do we come from, and where are we going? Darwin answered many of these questions by proposing that living organisms owe their characters to the successful reproduction of their ancestors. But Darwin's ideas had relatively little impact on our understanding of how organisms reproduce. Like Lamark, Darwin conceived that hereditary traits were collected from different parts of the body and assembled in gametes. This implied that understanding inheritance would depend on knowing first how fertilized eggs give rise to adult organisms — the 'generation' problem — and then how information is collected from adult tissues.

As it turns out, progress in understanding the generation problem has actually stemmed from our prior solution of the inheritance problem. Weissman provided the crucial insight: that reproduction is the exclusive property of individual cells in the germline. This enabled a coherent theory that explains evolution by descent, known as the Neo-Darwinian synthesis, to be constructed from Mendel's notion of particulate genes passed down through the generations *via* the germline. Many people still do not accept the theory, however: apparently 47% of all Americans still believe that man was created in his present form by God within the last 10 000 years. The current neo-Darwinian package says not only that man has a common ancestor with apes but also that all living creatures are descended from a bunch of RNA molecules floating in the primeval soup. Many people's reaction is: "I just don't believe it!"

Does current evolutionary theory miss a crucial ingredient needed to convince the sceptics? One of the reasons for neo-Darwinism's failure to compete with Genesis may be because it fails to provide stories that are comprehensible for laymen but testable for scientists. At present, we have a general theory for genetic change whose Mendelian foundations have been rigorously tested but which makes few testable predictions about the actual course of evolution in mechanistic terms. Our evolutionary stories must explain, for instance, how cells first arose from collections of replicating nucleic acids, as well as the evolution of eukaryotes from prokaryotes, eyes from light-sensitive cells, and consciousness, language and humour from simple nervous systems. If we could provide such stories, in the form of changes within specific sets of genes, then more people might begin to believe us.

We cannot start to tell such stories before we know approximately how genes contribute to biological reproduction. We must understand, for example, how organisms develop from single cells before we can piece together how their mechanisms might have evolved. In other words, solving the generation problem is after all crucial for evolutionary biology. Arguably, recent progress in understanding cellular and developmental mechanisms means that we are almost able to pose sensible questions about the steps by which these mechanisms evolved. As well as biochemical and genetic experiments, gene sequencing has been crucial to this progress.

Sequencing has also revolutionized phylogenetic studies that establish the relatedness of species and allow inferences to be drawn about their common ancestors. Might such information also tell us about the cellular mechanisms of these ancestors? The sequencing of individual genes cannot, but we have just crossed the threshold of genomic sequencing [1], with the determination of the entire genome sequences of *Haemophilus* (a prokaryote) and yeast (a eukaryote). An archaebacterial genome is on its way, and that of the nematode worm *C. elegans* is not far off. Further sequencing and comparisons of genomes may establish which genes were definitely carried by the common ancestors of the major phylogenetic lineages. I am quite sanguine that a story will eventually emerge that can explain the transition from bacteria to man.

Comparing the genomes of yeast or worms with archaebacteria will tell us about the physiological processes of their common ancestor. But because fungi and animals have a relatively recent common ancestor, many attributes common to them but absent from archaebacteria could be concerned with 'recent' developments in the eukaryotic lineage, such as the evolution of meiosis. To learn more about eukaryotes' common ancestor, we need to know about protozoan organisms that descend from the earliest offshoots of the eukaryotic lineage. A good candidate is the archaezoan *Giardia lamblia*, whose common ancestor with yeast and man may have been very ancient [2]; it had apparently not yet acquired mitochondria. A mammalian parasite endemic to many parts of the world and a major cause of infant diarrhoea, *Giardia* has a genome thought to be only a little more complex than that of yeast [3]; at current estimates, sequencing it should cost no more than $5 million. The complete sequence of *Giardia*'s genome is therefore my request for Wolpert's good fairy godmother of science [4]. There seems a reasonable chance that some fairy godmother will actually come up with the goods within the next few years.

References

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