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Random Walking

My Great-Uncle the Giardia

The story of the confrontation between Thomas Huxley and Bishop "Soapy Sam" Wilberforce is one of the best-known anecdotes of the Darwin era. The meeting room at Oxford was packed with up to a thousand people when the Bishop rose to his feet and sneeringly asked Huxley, "I beg to know whether it was through your grandfather or your grandmother that you claim to have descended from a monkey." The accounts vary as to Huxley's response. He was said to have muttered as an aside to his neighbor, "The Lord has delivered him into my hands" (a nice religious touch). Then he thundered at Wilberforce either (a):

> I assert that a man has no reason to be ashamed of having an ape for his grandfather. If there were an ancestor whom I should feel shame in recalling, it would rather be a *man*, a man of restless and versatile intellect who, not content with a success in his own sphere of activity, plunged into scientific questions with which he has no real aquaintance, only to obscure them by an aimless rhetoric, and distract the attention of his hearers from the real point at issue by eloquent digressions and skilled appeals to religious prejudice

or (b): "When I contemplate both you and the grinning chattering creature to which you referred then I would prefer to be descended from an ape than from a bishop." (In short, apes, *si,* bishops, *no.*) So emotionally charged was the moment, that a woman in the audience fainted.

About 125 years later, the exchange would need to be modernized. The Bishop would have to ask: "From which of your grandparents do you claim to descend from the protozoa?", and the reply would be: "Given a choice between you and the industrious eukaryote that spends part of its life in the salivary glands of a mosquito, and part in human erythrocytes, I would prefer to be related to *Plasmodium vivax.* And you keep my family out of this."

We now find ourselves in a corner at the bottom right-hand corner of the evolutionary tree of the eukaryotes, along with mice and horned toads. It is a humbling and salubrious experience. Most of the phylogeny that is now apportioned by ribosomal RNA sequences goes to unicellular organisms. To see the name of the species at the top of the tree as *Euglena gracilis* takes me back to the heady days of 1948, when I first became acquainted with the eminent protozoologist Seymour Hutner, a devotee and sponsor of these unicellular organisms for many decades, then and now, who even used to write Christmas poems about them. (A retaliatory verse that I sent him was quoted in the *New Yorker*: "The reindeer have come from the northern aurora: Nourished by rumen microflora.") Seymour had reported in 1936 that massive growth of *Euglena* depended on an unknown growth factor present in crude casein. He identified the factor in 1948 when he found that 0.01 millimicrograms of vitamin B_{12} per ml of medium was required by *Euglena* for half-maximum growth.

Seymour was at Haskins Laboratories in New York and our group was at nearby Lederle Laboratories. His protozoological garden contained many other inmates, some with finicky food habits. One can now see many of them on phylogenetic trees of the eukaryotes, constructed by comparing rRNA sequences. George Kidder introduced us in 1949 to *Tetrahymena geleii* (now *T. pyriformis*). This was then an obscure organism, but it has achieved fame in recent years because its self-replicating intron was a basis for the discovery of ribozymes and their biochemistry. *T. geleii* needed an unidentified growth factor to which we gave the name "protogen," only to receive an indignant letter from an executive of a baking company that marketed a bread by the same name. We disavowed any competitive intentions and soon gave our substance a different, chemical name. Protogen was eventually isolated and synthesized by our research group; it turned out to be thioctic acid, 1,2-dithiolane-3-valeric acid—the pyruvate oxidation factor (lipoic acid). Another protozoan, *Crithidia fasciculata,* was also sponsored by Hutner. It was distantly related to the trypanosomes and it needed yet another unknown growth factor. We resolved to isolate and identify this substance. We collected urine as a source, and the local chapter of the trade union alleged that we were exploiting its members by placing large bottles (with funnels) in the men's restroom. Again, our group isolated and synthesized the new substance, which we named biopterin. Also in branches of one of the eukaryotic family trees in the publications by De Wachter's group (Hendriks et al. (1988) Eur J Biochem 177:15–20) is *Ochromonas danica,* another organism that is used, like *Euglena,* for the assay of vitamin B_{12}, because of its sensitivity to extremely low levels of this growth factor. Vitamin B_{12} (cobalamin) is synthesized by bacteria, and perhaps protozoa need it because they evolved as their saprophytic neighbors. The molds and yeasts came on the scene, then the green plants (which do not need vitamin B_{12}), then the insects, and then the birds and mammals (which do). Indeed, the need for preformed vitamin B_{12} leads to nutritional deficiency symptoms in human vegetarians if they reject milk and eggs along with meats. Ruminating animals (such as the above-mentioned reindeer) can develop vitamin B_{12} deficiency if they live in cobalt-deficient regions, even though green plants, which do not use vitamin B_{12} and therefore do not need cobalt, can flourish. Several of the vitamins, including B_{12}, are coenzymes with structures related to RNA bases. Because of their chemical configurations, these molecules are postulated as having originated very early in the history of life, during the "RNA world."

The phylogenetic trees of eukaryotes that include protozoa are derived from comparisons of ribosomal RNA sequences, including both 5SrRNA and srRNA. The structures of the trees are being debated, and the conclusions of various authors are conflicting because of large standard errors in the calculations and because protozoa leave no fossils! When all is done, the molecular evolutionary clock must be used for estimations of times of divergence.

Evolution in and before the RNA Era

In a long (eight-page) article in *Nature* (March 10, 1989, pp 217–224), C.F. Joyce examines "the advantages of RNA as the basis for the early evolution of life," also, obstacles to this and how they may have been overcome. The case for an "RNA world" has been presented by various writers, stimulated recently by discovery of ribozymes. Joyce lists seven lines of evidence, including observations that DNA is formed by reduction of RNA, and that thymidylic acid (which he erroneously calls deoxythymidylic acid) is formed by methylation of deoxyuridylic acid. Incidentally, folic acid is well-known as participating in this reaction, blocking of which is used clinically in order to inhibit cell growth. Difficulties with the proposal that "life began with RNA" include the fact that proteins seem far more versatile as catalysts, and that it is unlikely that RNA could "have been produced in significant quantities on the primitive Earth." Joyce discusses the composition of the prebiotic atmosphere, and the possible formation of cyanide and formaldehyde, leading to production of amino acids from HCN and ribose from glycoaldehyde and formaldehyde in the formose reaction. He notes that it is a long way from cyanide and formaldehyde to RNA, but he takes us along possible pathways. He then discusses the origin of self-replication, with references to recent literature, and the transition to an RNA world is reviewed, with questions about catalytic properties of known RNA enzymes, and a plea "to put the evolution of RNA in the context of the chemistry that came before it, and the biology that followed." This review, with 96 references, is recommended for reading.

Thomas H. Jukes