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Reply to Garg and Martin: The mechanism works

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Garg and Martin formulated two problems (1) regarding our recent modelling paper (2) demonstrating how prudent predation and farming by a phagotrophic host could lead to endosymbiotic establishment and how it might have had a role in the origin of mitochondria.

We see three main problematic items in their criticism. They concern (*i*) the issue of phagotrophy without (or prior to) mitochondria, (*ii*) the question of alternative bet hedging strategies, and (*iii*) the status of eukaryogenesis as an idiosyncratic megaevolutionary transition. We discuss these in turn.

First, “the physiological benefit of evolving phagocytosis ... is only realized in the presence of mitochondria” – not so, as the free-living amitochondriate protists testify. These organisms make a living of predation without mitochondria (and hydrogenosomes or mitosomes) (3). The question, whether the evolutionary path needs an energetic boost, allegedly transiently bumping up the genome size of the evolving lineage may be up to a hundred dozen genes (4), is another matter, but this suggestion remains highly controversial (5, 6).

Second, there are alternative strategies to hedge your bets. This is certainly true: the actual path taken is bound to be historically contingent. Certainly, there are examples in the living world that farming can work, so this idea is as good as any other. More importantly, while glycogen is synthesized by the cell at its energetic and material expense, a reproducing endosymbiont grows autonomously (there is some energetic cost to the host cell due to necessary extra nutrient transport through its membrane). As we wrote: "If the farm autonomously grows within the host, allocation becomes a neutral trait" (2). Nevertheless, we plan to undertake a directed modelling study of the competitive advantages of the two rival strategies involved.

Third, because of its profound uniqueness, there must have been some idiosyncratic component to eukaryogenesis. Garg and Martin identify this step with the critical endosymbiotic syntrophy (c.f. (7)) – early phagocytosis with the concomitant cellular reorganization (8) is another possible, unique series of events. Martin et al. (9) present numerous arguments against early phagotrophy, but we do not consider any of them decisive—detailed elaboration of this point warrants in-depth examination. Here we just call attention to the fact that the a stimulating scenario for the emergence of *minimal* phagocytosis (10) has escaped the authors‘ scrutiny.

All existing consistent scenarios for eukaryogenesis involve difficult (“improbable”), yet possible steps. The jury is out on the question whether any of them was actual. Besides, the mechanism we have modelled might well be a not uncommon factor behind endosymbioses.

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