

Comment on “A Bacterium That Can Grow by Using Arsenic Instead of Phosphorus”

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Wolfe-Simon *et al.* (*Science Express Research Article*, published online 2 December 2010; 10.1126/science.1197258) reported the discovery of an unusual bacterium, strain GFAJ-1, that can grow in the presence of high concentrations of arsenate. The authors’ contention, however, that this microbe can appreciably vary the elemental composition of its fundamental biomolecules by substituting arsenic for phosphorus appears premature based on the data presented.

Wolfe-Simon *et al.* (*I*) reported that a bacterium isolated from Mono Lake, California, strain GFAJ-1, can substitute arsenic (As) for phosphorus (P) to sustain its growth. Although their data clearly indicate that GFAJ-1 can survive and grow in the presence of high arsenate concentrations (by itself, an exciting result), and thereby incorporate some As into cellular constituents, their evidence for arsenate-dependent growth is weak.

Key evidence that Wolfe-Simon *et al.* presented to support their claim is of a negative form, namely the observed lack of growth of GFAJ-1 on medium lacking added arsenate or phosphate [see figure 1A in (*I*)]. In addition, much of the positive evidence in favor of arsenic incorporation into biomolecules seems insufficient or difficult to interpret with confidence. First, figure 2A in (*I*) shows an agarose gel loaded with genomic DNA extracted from GFAJ-1 grown in the +As/−P and −As/+P conditions. The DNA is of different sizes, however, for the two samples shown. The −As/+P, but not the +As/−P DNA, is partly degraded, which is the reverse of expectation (2). Second, high-resolution secondary ion mass spectrometry analysis of the excised genomic bands [figure 2, B to D in (*I*)] show that the As:carbon (C) ratio of the +As/−P DNA is only twice that of the −As/+P DNA. In table S2 of (*I*), the As:C ratio of the +As/−P DNA is only 1/64th that of the P:C ratio of the −As/+P DNA, which is difficult to reconcile with the assertion that As substitutes for P in this organism. Also in table S2, the excised DNA values are close to the blank agarose values, confounding interpretation. Third, the bulk cellular P/C ratio for cells grown in +As/−P media actually overlaps the lower end of the range observed for cells grown in −As/+P [figure S2 in (*I*)].

Thus, cells grown in +As/−P media have, apparently, sufficient phosphate to support growth. The +As/−P cells also exhibit only an approximately 4-fold higher As/C ratio than the −As/+P cells. Finally, the extended x-ray absorption fine structure data shown in figure 3A in (*I*) seem simply to indicate that the bulk of cellular As is in the form of arsenate (and possibly its mono- or di- or triesters).

Does GFAJ-1 incorporate As into its macromolecules? According to the radioactive [⁷³As]-arsenate data shown in table 2 in (*I*), it apparently does, to some small extent. Perhaps this result is not so surprising for an organism that somehow manages to detoxify high, normally poisonous arsenate concentrations. Have arsenate esters replaced phosphate esters to any appreciable extent, for example, in adenosine triphosphate, DNA, RNA, vitamins, phosphoproteins, or phospholipids? The data presented by Wolfe-Simon *et al.* seem to suggest not, nor do the authors provide any compelling arguments for how GFAJ-1 avoids deleterious hydrolysis of arsenate esters (2). In particular, their proposal that critical arsenate ester-containing biomolecules are protected from hydrolysis by sequestration in the observed (putatively poly-β-hydroxybutyrate-rich) vacuole-like regions, or in other (unspecified) intracellular regions, implicitly invokes unprecedented mechanisms both for maintaining and for carrying out key metabolic processes in the presence of such a sequestration.

Given both the data inconsistencies and the required unprecedented mechanisms outlined here, the authors’ assertion that arsenic can appreciably substitute for phosphorus in biomolecules of GFAJ-1 seems at best speculative based on the current data.

References

1. F. Wolfe-Simon *et al.*, *Science*, 2 December 2010 (10.1126/science.1197258).
2. F. H. Westheimer, *Science* **235**, 1173 (1987).

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