On the abundance of zinc in the evolutionarily old protein domains

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A recent paper in PNAS (1) analyzed the evolution of metalloproteins and confirmed our earlier observation on the abundance of Zn-binding proteins among the most widespread – and evolutionarily oldest – protein folds (2). As that observation appeared to contradict the extremely low ($<10^{-12}$ M) estimates of Zn levels in the primeval anoxic ocean (3), we had suggested that the first cells developed in continental Zn-rich environments (2, 4). Specifically, we proposed that hydrothermal precipitates of zinc sulfide (ZnS), similar to those seen about modern deep-sea vents, catalyzed abiogenic photosynthesis of organic compounds under the solar light (2, 4). This led to the release of Zn ions, yielding a Zn-rich milieu. In the course of evolution, cells have maintained the initial metal homeostasis and preserved high levels of Zn in the cytoplasm (2).

Dupont and coworkers (1) offer two alternative explanations to reconcile the abundance of ancient, ubiquitous Zn-binding protein domains with the extremely low Zn levels in the anoxic ocean. First, they suggest cambialism, i.e. "using a different metal in what are modern day Zn metalloenzymes"; these metals were supposedly replaced by Zn when its levels started to rise with the oxygenation of the ocean (1). However, the increase in the ocean Zn content is said to occur 0.8-0.5 Gy ago (1), i.e. long after the separation of the major phylogenetic lineages. Thus, the cambialism hypothesis implies the unlikely scenario where the incorporation of Zn into the plethora of ubiquitous enzymes, which are now unambiguously Zn-dependent, took place independently in multiple lineages. The specific suggestion of Dupont and coworkers that modern Zn fingers initially bound cobalt (1) does not sound credible. Cobalt-dependent enzymes, with few exceptions, rely on vitamin B12 as the cobalt-binding cofactor because amino acid residues are poor ligands for Co (3). The concentration of Co in the ancient ocean (estimated at 10^{-9} M) (3) was too low to allow its direct recruitment by amino acid ligands of the first life forms.

Secondly, Dupont and colleagues suggest that "while the concentration of uncomplexed Zn was likely very low, aqueous Zn-S species were certainly present and microbial Zn acquisition might have proceeded through a ligand production and scavenging strategy similar to that employed for Fe acquisition in the modern world" (1). The abundance of aqueous ZnS species in the anoxic ocean is unlikely, since it contained $>10^{-6}$ M of Fe^{2+} (3), so that Zn could be present only as a minor impurity in the aqueous FeS clusters (5). Besides, the efficient metal-scavenging machinery of modern bacteria, as argued elsewhere (2), must have been absent at the stage of the first cells.

Finally, the “cambialism” and “scavenging” explanations contradict each other: if the first cells were able to efficiently scavenge and accumulate Zn ions, there would be no reason to substitute Zn for other metals in the course of evolution. In summary, we believe that emergence of the first cells in terrestrial metal-enriched habitats still provides the most plausible explanation for the abundance of Zn in the evolutionarily old protein folds.

References

1. Dupont CL, Butcher A, Valas RE, Bourne PE, & Caetano-Anolles G (2010) History of biological metal utilization inferred through phylogenomic analysis of protein structures. *Proc Natl Acad Sci USA* 107:10567-10572.
2. Mulkidjanian AY & Galperin MY (2009) On the origin of life in the zinc world. 2. Validation of the hypothesis on the photosynthesizing zinc sulfide edifices as cradles of life on Earth. *Biol Direct* 4:27.
3. Williams RJP & Frausto da Silva JJR (2006) *The Chemistry of Evolution: The Development of our Ecosystem* (Elsevier, Amsterdam).
4. Mulkidjanian AY (2009) On the origin of life in the zinc world: 1. Photosynthesizing, porous edifices built of hydrothermally precipitated zinc sulfide as cradles of life on Earth. *Biol Direct* 4:26.
5. Luther GW & Rickard DT (2005) Metal sulfide cluster complexes and their biogeochemical importance in the environment. *J Nanopart. Res.* 7:389-407.