Hydrogen and the Evolution of Respiration

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Introduction: Hydrogen (H_2) has likely served as a key point of interface between the geosphere and the biosphere since the earliest stages of life on Earth [1]. The interaction between water and crustal rocks, in particular those with high ferrous iron contents such as peridotites, can lead to the formation of H_2. The production of H_2 through such reactions is known as serpentinization, a process that was likely widespread on the early Earth and which has been hypothesized to have played a central role in sustaining early forms of H_2-dependent life.

The widespread distribution of H_2 metabolism among genetically- and physiologically-diverse organisms [2] is indicative of both its central place in biochemistry and is consistent with its ancient origin. Two families of hydrogenase, [FeFe]- and [NiFe]-enzymes, which contain active sites of iron (Fe) or iron-nickel (Fe-Ni) metalloclusters, respectively, are principally responsible for H_2 metabolism in modern biology. [FeFe]-hydrogenases are present in a limited number of strict anaerobic bacteria and a few unicellular eukaryotes but not in archaea. In contrast [NiFe]-hydrogenase are widely distributed in both the archaeal and bacterial domains but are absent in eukaryotes. This suggests that [NiFe]-hydrogenase rather than [FeFe]-hydrogenases are likely to have supported H_2-dependent metabolisms early in life's history.

Results: Here we report recent insights into the evolutionary history of [NiFe]-hydrogenase and related paralogs that were obtained from a comprehensive phylogenetic analysis. In particular, we report a characterization of the physiology of organisms reliant on [NiFe]-hydrogenase in their metabolism in the context of the evolutionary history of [NiFe]-hydrogenase to reveal new insights into the physiological role of ancestral [NiFe]-hydrogenase enzymes and their role in the evolution of complex respiratory processes. Key findings include *i)* the ancestral [NiFe]-hydrogenase likely functioned in the oxidation of H_2 during methanogenesis, *ii*) the ancestral enzyme likely coupled with ferredoxin, iii) the ancestral enzyme underwent a series of gene duplications and gene recruitments that resulted in enzymes capable of coupling with a variety of redox partners including flavins and cytochromes and *iv*) these duplication events most likely took place in an ancestor of hydrogenotrophic methanogens [3, 4]. Finally, new data will be presented on the evoluitonary history of an ancient class of [NiFe]-hydrogenases (termed Group 4) that are likely to represent the most primitive respiratory complexes. These energy conserving enzymes function to couple the oxidation of ferredoxin and reduction of protons to the generation of sodium ion gradient. Group 4 enzymes represent the evolutionary precursor to several subunits that comprise the NADH input domain (NADH dehydrogenase) present in Complex I. This key evolutionary transition would have propelled the diversification of life by allowing it to exploit electron acceptors such as nitrate, polysulfide, nitric oxide, arsenate and oxygen through coupling of quinone oxidation by other respiratory membrane oxidoreductase complexes.

Conclusions: The results of this phylogenetic-based study provide new support for the importance of H_2 in the evolution of early life. Moreover, these results help to explain how H_2 has been integrated into such a wide array of metabolisms alluding to its role in driving the diversification of early life. Finally, these results provide new perspective on the role of H_2 in the evolution of complex respiratory pathways present in nearly all aerobes including higher eukaryotes.

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