

**REVISITING THE QUINONES: FROM THEIR REPRESENTATION AT THE SCALE OF THE INDIVIDUAL CELL TO THEIR MOLECULAR ANCESTRY.** A-L Ducluzeau<sup>1</sup> and R.E Collins<sup>1</sup>, <sup>1</sup>Institute of Marine Science - University of Alaska Fairbanks. (aducuzeau@alaska.edu - recollins@alaska.edu)

Conservation of energy via the proton motive force (pmf) relies on the use of lipophilic redox active molecules, *i.e.* membrane electron carriers, to create charge separation across the cell membrane. Through the entire tree of life, quinones are the only compounds known so far to hold this function with the only exception of methanophenazine, which is found in one order of Archaea.

When the chemiosmotic coupling principle was proposed in 1966 by H. Mitchell, it was seen as too complex of a process to figure among the metabolic repertoire of the Last Universal Common Ancestor (LUCA). In the meantime, microbiologists bringing to light a plethora of new pmf-based metabolisms considered them at first as a collection of disparate and unrelated bioenergetic systems. Hence, the simple but energy-inefficient fermentation was considered the primordial way for life to maintain high levels of ATP. However, over the past couple of decades, the fermentation-first paradigm gradually lost ground with (i) the acknowledgement of a basic enzymatic construction kit which allowed the unification of our conception of the different pmf-based electron-transport chains and (ii) the increasing number of phylogenies pointing towards the ancestry of these enzymatical building blocks (1). Along with the renewal of our vision of LUCA bioenergetics, the Wood-Ljungdahl pathway (acetogenesis and methanogenesis) has been the favored candidate for the first way life harvested free energy. This assumption is based on the capability of this metabolism to combine the reduction of CO<sub>2</sub> into organic compounds with the generation of a chemiosmotic potential upon substrates (H<sub>2</sub> and CO<sub>2</sub>) that were likely abundant on Earth during the archaean eon (2). However, this hypothesis was challenged in 2009 when NO was proposed as a better oxidant for primitive bioenergetic systems, which therefore would have been respiratory-type electron transport chains (3). In an interesting way, this view implies that cofactors like hemes and quinones might have been operating in LUCA. This idea brought us to consider the quinones as an area of great interest for the improvement of our understanding of early life.

First, we aimed to address the lack of basic knowledge about the quinones at the scale of the individual cell. Through HPLC-MS and spectroscopy, we compared the quinone and lipid contents of various types of prokaryotic membranes. Our results indicated that the quinone pool is a numerically important component of the membrane. Therefore we propose an update of the “Fluid Mosaic” model. This result, together with pre-

viously observed structural changes of the methanophenazine pool, led us also to consider that the quinone pool might be involved in the maintenance of membrane fluidity. We are currently exploring this idea by culturing and analyzing psychrophiles isolated from sea ice and sea water community enrichments grown at different temperatures.

From an evolutionary perspective the quinones have been barely studied so far. This might be explained by the fact that the « genealogy » of this family of molecules cannot be inferred directly. Indeed, as secondary metabolites, the assessment of quinone ancestry necessitates phylogenetic reconstructions of their multiple biosynthetic pathways representing dozens of enzymes. The few reports published in that regard focused on the hydrosoluble moiety of the electron carriers and turned out to not be in favor of the pre-LUCA existence (4-6). We tackled this question with the other moiety of the molecules, *i.e.* the isoprenyl side-chain, which requires only two enzymes for its biosynthesis : the polyprenyl diphosphate synthases. In prokaryotes, we conducted a phylogenomic survey of these proteins and their phylogenetic reconstructions. In an unexpected way this work provided us a hypothesis for the molecular origin of the membrane of Archaea. But more importantly, unlike the previously reported investigations, our results support the existence of liposoluble electron shuttle in LUCA and from there, also support the hypothesis of a respiratory-based metabolism as a primordial bioenergetical system. [1] Baymann F. et al. (2003) *Philos Trans R Soc Lond B.*, 358, 267-274 [2] Martin W. and Russell M. (2007) *Philos Trans R Soc Lond B.*, 362, 1887-1925. [3] Ducluzeau A-L. et al. (2009) *TIBS*, 34, 9-15. [4] Gross J. et al. (2008) *BMC Evol Biol.*, 8,117. [5] Zhi XY et al. (2014) *Genome Biol Evol.*, 6, 149-160. [6] Sousa F.L et al. (2013) *Philos Trans R Soc Lond B.*, 368, 1622.