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FERREDOXIN MOTIF BOUND TO A Fe_4S_4 GROUP AS A MODEL FOR A PREBIOTIC PROTOFERREDOXIN

Y. Reyes-Medina[1,3], L. Montoya[2,3], and A. Heredia[1]

Earth's ocean has gone through several biogeochemical transformations throughout its four billion years of history and this can be explained by the presence of life (Lenton & Daines 2017). However, it is unknown how the non living material turned into living organisms. This is a key issue since if we knew how life emerged on Earth, we could infer how it could emerge on other planets. Here on Earth, living organisms are made up of a wide variety of proteins, so by figuring out how proteins evolved, we could get a clue about how life started. A starting point can be that in prebiotic Earth there were small peptides that later evolved into complex proteins, however we don't know how these peptides were chemically selected.

Here we're focusing on the ferredoxin enzymes for several reasons. Ferredoxins are oxidoreductases, i.e., the group of enzymes responsible for the redox reactions, crucial and present amongst all living beings. A significant fraction of the oxidoreductases has metals in their active site, and 60% of them have iron. It is of interest within the context of the coevolution of Earth's ocean and life that more than half of these enzymes are ferredoxins, i.e. oxidoreductases linked to iron-sulfur (FeS) clusters. The role of FeS minerals in catalyzing prebiotic reactions has been previously recognized as a potential pathway that led to the formation of simple organic molecules and chemical bond energy necessary for the origin of life (Jelen et al. 2016). The FeS minerals were certainly available during the Archean eon, so it's possible that the peptides from prebiotic Earth took FeS complexes from the environment, therefore giving rise to protoferredoxins (Jelen et al. 2016).

In current ferredoxins, the Fe_4S_4 cluster in the active site is bound to a highly conserved protein fold consisting of a CxxCxxC...C motif or peptide sequence (Jelen et al. 2016). The present project focuses on this motif with the objective of estimating its stability with the internal energy (U, expressed in kcal/mol) as the main reference. The methodology consisted in using different motif sequences to infer which amino acid combination could have worked as a prebiotic protoferredoxin, as well as the FeS dependence.

For the estimation of the stability, we created a sequence base of 97 ferredoxins from the pool of annotated protein sequences *UniProt*. Then, we aligned these sequences to locate the motifs bound to the Fe_4S_4 cluster, and verified them with the available annotations from the *Protein Data Bank* and the PROSITE. The consensus motif sequences were determined with the MEGA software. Currently, we're doing molecular computational experiments, e.g., geometry optimization and molecular dynamics, with the molecular mechanics method (MM+), using the *HyperChem* program to determine whether amino acid identity provides differences in peptide stability regarding alpha/beta configuration.

The consensus peptide sequences we have analyzed so far are: CTGCGTC (the consensus amino acid sequence), CTACATC (a random amino acid sequence), CGSCSGC (a modified amino acid sequence v.1), CAQCRAC (a modified amino acid sequence v.2), and CISCGAC (amino acid sequence belonging to *Clostridium*). Apparently, despite the fact that classical biochemical references have established a link between amino acids to an alpha or beta peptide structure (Lehninger et al. 2008), we didn't detect significant differences among internal energies of the same peptide but with an alpha or beta configuration. Therefore, amino acid composition does not play a relevant role on the peptide structure. Our next objective is to include the iron-sulfur cluster and to use longer peptide sequences.

[1]Instituto de Ciencias Nucleares, Universidad Nacional Autónoma de México, 04510 Ciudad de México, México (yas.rey.med@ciencias.unam.mx).
[2]Facultad de Ciencias Biológicas, Universidad Autónoma del Estado de Morelos, 62209 Morelos, México.
[3]Facultad de Ciencias, Universidad Nacional Autónoma de México, 04510 Ciudad de México, México.

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