

## **A Sco protein among the hypothetical proteins of *Bacillus lehensis* G1: its 3D macromolecular structure and association with cytochrome c oxidase**

### **Abstract**

Background: At least a quarter of any complete genome encodes for hypothetical proteins (HPs) which are largely non-similar to other known, well-characterized proteins. Predicting and solving their structures and functions is imperative to aid understanding of any given organism as a complete biological system. The present study highlights the primary effort to classify and cluster 1202 HPs of *Bacillus lehensis* G1 alkaliphile to serve as a platform to mine and select specific HP(s) to be studied further in greater detail. Results: All HPs of *B. lehensis* G1 were grouped according to their predicted functions based on the presence of functional domains in their sequences. From the metal-binding group of HPs of the cluster, an HP termed Bleg1\_2507 was discovered to contain a thioredoxin (Trx) domain and highly-conserved metal-binding ligands represented by Cys69, Cys73 and His159, similar to all prokaryotic and eukaryotic Sco proteins. The built 3D structure of Bleg1\_2507 showed that it shared the  $\beta\alpha\beta\alpha\beta\beta$  core structure of Trx-like proteins as well as three flanking  $\beta$ -sheets, a 310  $\alpha$ -helix at the N-terminus and a hairpin structure unique to Sco proteins. Docking simulations provided an interesting view of Bleg1\_2507 in association with its putative cytochrome c oxidase subunit II (COXII) redox partner, Bleg1\_2337, where the latter can be seen to hold its partner in an embrace, facilitated by hydrophobic and ionic interactions between the proteins. Although Bleg1\_2507 shares relatively low sequence identity (47%) to Bsco, interestingly, the predicted metal-binding residues of Bleg1\_2507 i.e. Cys-69, Cys-73 and His-159 were located at flexible active loops similar to other Sco proteins across biological taxa. This highlights structural conservation of Sco despite their various functions in prokaryotes and eukaryotes. Conclusions: We propose that HP Bleg1\_2507 is a Sco protein which is able to interact with COXII, its redox partner and therefore, may possess metallochaperone and redox functions similar to other documented bacterial Sco proteins. It is hoped that this scientific effort will help to spur the search for other physiologically relevant proteins among the so-called “orphan” proteins of any given organism.

**Keyword:** Hypothetical proteins; Bleg1\_2507; Sco; Thioredoxin; Copper binding; Redox reaction; Cytochrome c oxidase