Seminario de Química Orgánica

Miércoles 21 de abril de 2021, 13 hs

AULA VIRTUAL DQO: **qo.aula04 - Acceso:** https://zoom.us/my/qo.aula04 **- Clave:** exactas20

Biogenesis of copper sites in heme-copper oxidases: An NMR-based approach

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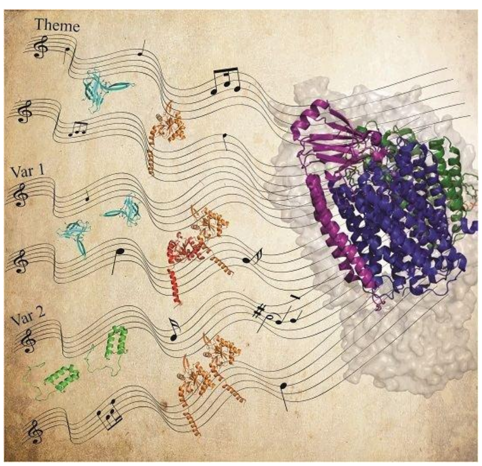
Copper is an essential cofactor of cytochrome c oxidase (COX), the terminal oxidase of the respiratory chain in most aerobic organisms. COX I and COX II are the two copper-containing subunits harboring the Cu_B and Cu_A sites, respectively, conserved in heme-copper oxidases. Assembly of the oxidase is a complex process involving the synthesis and folding of the individual subunits and the incorporation of the metal cofactors. The redox properties of these metal ions make them essential but also toxic when their levels are not adequately regulated. For example, copper and iron ions are responsible for the formation of toxic hydroxyl radicals due to the Fenton reaction process. Another source of toxicity of copper ions resides in its ability to bind different ligands with high affinity. Thus, copper levels in the cells are tightly regulated, and the storage, transport and delivery to the final destination takes place by a complicate network of protein-protein interactions.



These interactions are transient in nature, thus forming relatively labile complexes. Thus, NMR is a suitable technique that enables the study of the copper transfer processes.

Sco proteins belong to a family of proteins related to thioredoxins that contain two redox-active cysteine residues, and a histidine involved in copper binding. These proteins have been shown to be essential in the assembly of the Cu_A site, from subunit COX II. However, their role and the number of essential Sco orthologs differ among organisms. Indeed, the can act as Thiol-Oxidoreductases and/or copper chaperones in Cu_A assembly.

We have studied the molecular mechanisms of insertion of the copper in bacteria, plants and mammals. These proteins, despite being highly conserved, are able to show promiscuous functions with an impressive chemical versatility, fulfilling different roles in distinct organisms.

References

1. Morgada *et al.*, *Chem.Comm.*, 56, 1223-1226 (2020).
2. Soma *et al.*, *Cell Reports*, **29**, 4114-4126.e5 (2019).
3. Llases *et al.*, *FEBS J.*, 287, 749-762 (2019).
4. Morgada *et al.*, *Proc.Natl.Acad.Sci USA*, **112**, 11771-6 (2015).
5. Morgada *et al.*, *Angew.Chemie*, **10,** 6188-92 (2014).
6. Zaballa *et al. Proc.Natl.Acad.Sci USA*, **109**, 9254-9 (2012)
7. Abriata *et al.*, *Nature Chem.Biol.*, **4**, 599-601 (2008).