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# Mega Protein: Cryo-EM structural determination a 8 MDa molluscan hemocyanin with substantial biomedic impact

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With the ability to provide high resolution structural information of large and dynamic protein complexes, the single-particle cryo-electron microscopy (cryo-EM) turned possible study of proteins that were almost impossible to analyze with previous methods, due to its huge size and flexibility. So through collaborative efforts between research groups from Chile and Brazil, a synergistic approach to determine the cryo-EM structure of the hemocyanin from *Concholepas concholepas* (CCH), a marine organism endemic to the southern Pacific coasts, became possible. Hemocyanins are megadalton-sized oligomers that participate in oxygen transport in multiple invertebrate organisms, used as natural, non-toxic, and nonspecific immunostimulants with critical biomedical and clinical applications; thus, understanding the precise molecular mechanisms of hemocyanins is essential for future targeted improvement. So far, the most well-studied hemocyanin from a structural and immunological standpoint is KLH, from *Megathura crenulate*, that had its functional units revealed through the combination of cryo-EM and X-ray crystallography, displaying highly symmetric homodecameric rings featuring extensively glycosylated regions. However, regardless of their similarities, marine hemocyanins present a significant degree of structural diversity among them, especially concerning glycosylation patterns, which might explain their unequal efficiency in generating appropriate adjuvant effects on immunological oriented therapies. The CCH has shown promising biomedical applications, with a higher stability and solubility when compared with homologs. (1) Nevertheless, despite the unique biomedical potential of CCH, its structure and even its amino acid sequence remain unknown. With two distinct polypeptide chains forming heterodimeric rings, each subunit presents eight copper globular oxygen-binding domains, termed functional units (FU), and up to 3 or 4 glycosylation sites. Thus, a 3,2 Å Cryo-EM map was built allowing the construction of the whole 8 MDa protein structure with all its FU and glycosylations.

**Palavras-chave:** Cryo-EM. Protein. Hemocyanin.

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### Referências:

1 REYES, D. *et al.* Tumour celllysate-loaded dendritic cell vaccine induces biochemical and memory immune response in castration-resistant prostate cancer patients. **British Journal of Cancer**, v. 109, n. 6, p. 1488-1497, 2013.