**Cryo-EM structure of Homarus americanus α-crustacyanin reveals the astaxanthin molecular tuning in marine invertebrate colouration**

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The study of naturally occurring lipid bioactive compounds and their interactions with proteins has become a critical area of research, particularly in understanding the mechanisms underlying color changes in biological systems. Carotenoproteins are essential in generating vibrant colors through complex interactions between carotenoids and proteins. One key example is the Homarus americanus (American lobster), whose distinctive blue coloration arises from the interaction of the carotenoid pigment astaxanthin (AXT) with the α-crustacyanin (α-CR) protein complex. α-crustacyanins are constituted of multiple copies of the heterodimer β-crustacyanin in which the chromophore, namely the carotenoid astaxanthin (3,3’-dihydroxy-β,β-carotene-4,4’-dione), is associated stoichiometrically 1:1 with the protein subunits (Zagalsky, 1985).

Astaxanthin is a carotenoid that exhibits a characteristic red-orange color, absorbing at 472 nm in its free form. However, when bound to the crustacyanins, it undergoes a bathochromic shift, shifting its absorption maximum from red-orange (λmax = 472 nm) to purple-blue (λmax = 591 nm) to dark-blue (λmax = 632 nm) upon interaction respectively with β-crustacyanin and α-crustacyanin, resulting in the blue hue of the lobster carapace. β-crustacyanin (β-CR) has been extensively studied and structural data provided insight into the molecular basis of the spectral shift to 591 nm, but detailed understanding of α-CR the main complex responsible for the larger shift, has been lacking so far.

Recently, we obtained a high-resolution cryo-EM structure of α-crustacyanin from H. americanus complemented by small angle X-ray scattering and X-ay diffraction, revealing groundbreaking key features behind the molecular mechanisms responsible for the significant bathochromic shift to 631 nm. The cryo-EM structure of H. americanus α-crustacyanin to a resolution of 2.75 Å reveals, besides the expected crustacyanin subunits H1 and H2, the presence of a third protein belonging to the heptatricopeptide repeat protein (HPR) family, which interconnects a variable number of β-Crustacyanin heterodimers and interacts asymmetrically with the two astaxanthin molecules, leading to the observed bathochromic shift to λmax = 631 nm [1].

The study provides not only a successful understanding of the lobster blue coloration but also an exhaustive advance of how protein-carotenoid interaction influences the spectral properties of astaxanthin laying the foundation for the rational design of astaxanthin-based scaffolding compounds. Such compounds hold promise for applications in nanotechnology with the possibility of manipulating the bathochromic shift across the entire visible spectrum.

[1] Cedri et al. *Cryo-EM structure of H. americanus α-crustacyanin and the basis of astaxanthin bathochromic shift for marine invertebrate colouration*. **To be submitted.**