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Dimeric Lys49-Phospholipases A2: Which Is The Correct Biological Assembly?

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Short Abstract: Several myotoxic-phospholipases A2-like have been extensively structurally and biochemically characterized and, a dimer conformation has been considered as the biological assembly. We propose an alternative dimer conformation based on small angle X-ray scattering, crystal structures of complexes with ligands, interface analysis and energy minimization.

Long Abstract:

Dimeric Lys49-Phospholipases A2: Which Is The Correct Biological Assembly?

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Phospholipases A2 are components of Bothrops venoms responsible for disruption of cell membrane integrity via hydrolysis of its phospholipids. Several myotoxic phospholipases A2-like, which lack the catalytic activity upon phospholipids due to the D49K mutation, have been extensively structurally and biochemically characterized. The oligomeric conformation has been addressed as an important role to the development of their pharmacological activities. Based on the crystallographic and spectroscopic data, a dimer conformation formed mainly by polar contacts between the beta-wing and N-terminal helice, which exposes the hydrophobic channel or interfacial face, has been considered as the biological assembly. However, two recent Lys49-PLA2s structures suggested an alternative dimeric conformation as the correct assembly. In order to study this discrepancy, we revised the crystal lattice of seven Lys49-PLA2s and the presence of the alternative dimer was a common feature of all lattices analyzed. In this alternative conformation, the dimeric interface consists of non-polar contacts between the interfacial faces connecting the nominal active site which gives stability and high solubility of this protein in water. Regarding that these protein are very stable and water soluble, we proposed an alternative dimer conformation whose interface consists of non-polar contacts between the interfacial faces connecting the nominal active sites. This hypothesis, which explains the hydrodynamic behavior of Lys49-phospholipases A2-like, is based on small angle X-ray scattering, crystal structures of complexes with ligands, interface analysis and energy minimization.