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Dissociation of a dimeric PLA2 with a micellar substrate analog.

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Susana A Sánchez, Yan Chen, Joachim D Müller, Enrico Gratton, and Theodore L Hazlett.

Dissociation of a dimeric PLA2 with a micellar substrate analog.

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Abstract

The venom phospholipases A2 (PLA2) are soluble, small molecular weight enzymes that hydrolyze the sn2-acyl ester bond of phospholipids. The PLA2 from *C. atrox* venom has been shown to exist as a homodimer in solution, and early reports had suggested that the dimer was the active form. Later studies indicated that the monomer was the active unit and structural data has supported this view. In this study, we use fluorescence correlation spectroscopy (FCS) on a fluorescein-labeled PLA2 to examine this issue. The state of the PLA2 monomer-dimer equilibrium was measured above and below the CMC of dodecylphosphocholine (C12-PN), micellar substrate analog by FCS and intrinsic fluorescence. We have interpreted that data in terms of three PLA2-lipid forms: (1) PLA2 dimers free in solution minimally bound with C12-PN monomers, (2) an intermediate condition where two loosely interacting PLA2 monomers are contained in a co-micelle of protein and C12-PN and (3) complete dissociation of PLA2 into subunits and/or distribution among C12-PN micelles. Our data indicate that PLA2 is dissociated and distributed by micellar C12-PN. In light of the high activity of PLA2s against micellar substrates, our results strongly support the monomer hypothesis for PLA2 action. Financial support: NIH RR03155, Amer. Heart Assoc.-IL 97-CGS-07/G10.