COMPARATIVE STRUCTURAL STUDIES OF TWO LYS49-PLA_2 OF *Bothrops* VENOM COMPLEXED WITH *p*-BROMOPHENACYL BROMIDE (BPB)

MARCHI-SALVADOR D.P.[1], FERNANDES C.A.H.[1], SOARES A.M.[2], FONTES M.R.M.[1]

[1]Depto. de Física e Biofísica, IB-UNESP, Botucatu-SP, Brasil; [2]Depto. de Análises Clínicas, Toxicológicas e Bromatológicas, FCF-USP, Ribeirão Preto-SP, Brasil.

Phospholipases A_2 are responsible for disruption of cell membrane integrity via hydrolysis of its phospholipids. PLA_2s homologues (Lys49PLA_2) are enzymes catalytically inactive, but they maintain myotoxic and cytolytic activities. The alkylation of His48 residue by the *p*-bromophenacyl bromide (BPB) reduced these toxics effects. We report the structural determination of two complexes chemically modified by BPB: BthTX-I-BPB (from *B. jararacussu* venom) and PrTX-I-BPB (from *B. pirajai* venom) by X-ray diffraction experiments. There is a BPB bound for all H48 residues located in the region corresponding to the catalytic domain of Asp49-PLA_2s. In the comparative analyses between these complexes and their native structures, the presence of BPB does not result in significant structural differences in the calcium binding loop, hydrophobic channel and the catalytic domain regions. However, it shows different position of residues of C-terminus, mainly in the Lys122 residue involved with the myotoxic activity. This change can be the explanation of the reduction in the toxics activities in these complexes and might add insights into the mechanisms of Lys49-PLA_2s.

Financial support: FAPESP, FUNDUNESP, CNPq and LNLS.