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In Silico Structural Analysis of a Putative Class IA Phospholipase A2 from the Brazilian Coral Snake, *Micrurus corallinus*

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INTRODUCTION & AIM

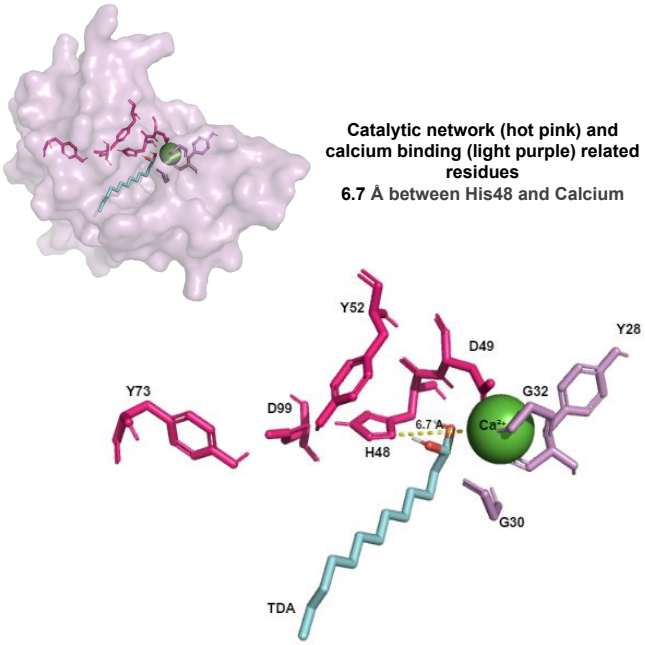
The venom of the coral snake species Micrurus corallinus is highly potent and exerts neurotoxic effects through presynaptic enzymes such as Class IA Phospholipases. However, due to the difficulty in obtaining the venom and the fact that most collected venom is used for antivenom production in Brazil, pharmacological studies of these toxins are scarce. Previous studies had already characterized the primary structure of M. corallinus PLA2. With the advent of tools like AlphaFold2 and recent improvements in tools like CHARMM-GUI, in silico studies of these molecules have become more accessible and accurate.

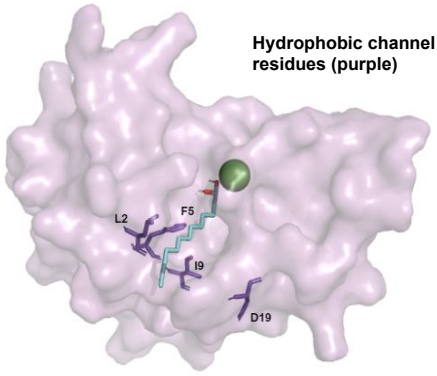
In previous experiments, we conducted in vivo studies with NXH8, a postsynaptic toxin from the same venom. We identified NXH8 as a Three-Finger Toxin (3FTx) with low toxicity. Interestingly, during in vivo neutralisation assays using Varespladib, an inhibitor of phospholipases A2 (PLA2s), we observed a significant increase in animal survival rates. This finding strongly suggests that PLA2 enzymes contribute substantially to the venom's lethality.

This study proposes the in silico characterisation of M. corallinus PLA2, comparing its structure with other characterised elapid PLA2s, evaluating both catalytic and presynaptic toxicity-related residues, and expanding our understanding of its role in venom toxicity.

METHOD

The alignment of primary structures of PLA2s from *Micrurus altirostris* (F5CPF0), *Micrurus nigrocinctus* (P81166), *Naja atra* (P00598), and *Pseudechis australis* (P04056 and P04057) was performed using ClustalW. The three-dimensional structure of *M. corallinus* PLA2 was modeled using AlphaFold2. The interactions of the enzyme with its substrates (phospholipid or tridecanoic acid) were analyzed using the CHARMM-GUI web interface and the PPM 2.0 server. All molecular representations were created using the PyMOL molecular graphics software package.





In this generated images, docking was performed using TDA as the ligand and PLA2 from Micrurus corallinus, obtained through AlphaFold2. The original structure did not include the calcium ion. Calcium was subsequently added to the image based on data from the structure of PLA2 from Naja naja atra (Chinese cobra), PDB 1POA

RESULTS & DISCUSSION

Micrurus corallinus PLA2 presents all residues necessary for catalytic action: CCXXH48D49XC in the active site and GCY28CG30X32GXG in the Ca^{2+} binding loop. Both catalytic mechanisms, the Single-Water Mechanism and the Assisted-Water Mechanism, were evaluated, with the latter being more likely due to the large distance observed between His48 and the Ca^{2+} ion.

CONCLUSION

The results indicate that *M. corallinus* PLA2 possesses all the necessary residues to exert its catalytic effects, supporting the possibility that this toxin is responsible for the presynaptic action observed in *M. corallinus* venom.

FUTURE WORK / REFERENCES