

Structure Conservation of the Carboxylesterase Substrate Binding Pocket in Dipteran Disease Vectors

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INTRODUCTION: *Aedes aegypti* is closely associated to humans and, therefore, it is the main vector of viruses in Brazil, such as dengue, yellow fever and, more recently, chikungunya and zika. Besides, mosquitoes from the *Anopheles* genus transmit the *Plasmodium sp.*, which causes malaria, one the most important neglected disease in the world. The long exposition to insecticides can yield resistant population due to the strong selective pressure. Indeed, detoxifying enzymes, such as carboxylesterases (CCE), might be responsible for disabling insecticide molecules. This family is highly diversified in arthropods, however, its tertiary fold is conserved as well as the catalytic site. The molecular structure of the *Lucilia cuprina* est-E3 allowed the modeling of mosquitoes homologous in order to better understand the diversity of these enzymes. **OBJECTIVES:** Access the structural conservation of the substrate binding pocket (SBP) of dipteran detox CCEs. **MATERIAL AND METHODS:** Sequences were aligned using PRALINE software and maximum likelihood tree was calculated using RAxML software with 500 bootstrap replicates. Catalytic triad and SBP residues were identified using CD-search. Comparative modeling used Modeller v9.14. Model quality was evaluated using ERRAT and PROCES. Model optimization was performed on 3Drefine webserver and PyMOL was used to model visualization and RMSD calculations. **RESULTS AND DISCUSSION:** Twenty-seven sequences were successfully modelled, whereas four were from *A. aegypti*, five from *A. gambiae*, five from *Culex quinquefasciatus* and thirteen from *Drosophila melanogaster*. Comparative analysis between the tertiary structures of these orthologous shown that the SBP was highly conserved in sequences grouped in the clade labeled detox1. In contrast, orthologous from clades detox2 and 3 only showed conservation within paralogous that evolved recently. **CONCLUSION:** CCEs from the clade detox1 might share the same function among mosquitoes and flies, while the substrate preference may have been diversified in detox2 and detox3 clades.

Keywords: *Aedes aegypti*, vectors of infectious diseases, carboxylesterase structure, insecticide resistance.

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