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TRABALHOS CIENTÍFICOS

AREA TEMÁTICA: BIOTECNOLOGIA

823-1 - MOLECULAR MODELING OF δ-ENDOTOXINS FROM BACILLUS THURINGIENSIS

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Resumo:

Bacillus thuringiensis (Bt) is a Gram-positive entomotoxic bacterium widely used to control crop pests and disease vectors. Since the introduction of transgenic plants expressing Bt genes, it has been demonstrated that Bt-crops constitute an important tool in the increase of productivity and in the decrease of the use of chemical pesticides. Its success comes from the production of the δ-endotoxins (Cry). These toxins share a molecular mechanism of similar action or, at least, some common aspects. Activity of Cry proteins is due to N- or C-terminal cleavages, binding to at least one membrane receptor (e.g. cadherins) and conformational changes. The aim of this work was to study structural aspects of Cry1Aa, Cry1Ab, Cry1Ac, Cry3Aa, Cry8Ea1, Cry8Ka1, Cry8Ka5 and Cry1Ia12 δ-endotoxins, using homology modeling, molecular dynamics (MD) and molecular docking. Eight Cry toxins and two cadherins (CAD) were modeled. Four toxins (Cry1Aa, Cry1Ac, Cry3Aa and Cry8Ea1) were used to construct eight systems (whole Cry toxins and α-1 removed proteins (Δα1)). Cry8Ka1, Cry8Ka5, Cry1Ia12 and their three variants were compared to analyze the contributions of each mutation. The cadherins and Cry1Ab and Cry1Ac were used on docking calculations. The Cry1A residues with high flexibility are the same identified as recognition/binding sites (apex of domain II and domain-II/IIIinterface) or to play a role on its dynamic. The data show that the global and local flexibilities of Cry toxins studied was increased by helix α-1withdrawal (Δα1) and it is closely related with the mode of action. This effect propagates on the surface and not only on the N-termini suggesting a complex process of conformational transition. Regarding Cry1Ac, the absence of helix α-1 triggers structural changes on loop2, which is related to binding GPI-receptors. Some Cry8Ka5 and Cry1Ia12 mutations are in the neighborhood of receptor-binding sites and this fact may imply alterations on binding affinity. It was possible to obtain a map of Cry/CAD interface by docking studies. Therefore, this work was able to obtain molecular level insights into the Cry activation mechanism and its interaction with CAD.

Palavras-chave:

Cry Proteins, Molecular Dynamics, 3D Structure, Toxin/Receptor Interaction

Apoio:

Embrapa, CNPq e Capes