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Minireview

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Minireview

Parasporins 1 and 2: their structure and activity

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Abstract

Parasporins are novel protein toxins preferentially cytotoxic against human cancer cells. They are obtained from parasporal inclusions of *Bacillus thuringiensis* and, accordingly, are considered congeners of the insecticidal Cry toxins. Two types of parasporins have been identified: the three-domain Cry toxin type and the β-pore-forming-toxin (β-PFT) type. Crystal structures of representative members of the two types, PS1Aa1 and PS2Aa1, have been determined and compared with those of well-studied toxins. PS1Aa1 has a typical architecture characteristic of the three-domain insecticidal Cry toxins, though it is cleaved into two polypeptides. It has an extra N-terminal segment found only in the inactive form of the Cry toxins and, hence, it is presumed to act through another mechanism as an activator in the apoptotic signaling pathway rather than a pore-forming toxin. PS2Aa1 shows a remarkable structural similarity to the aerolysin-type β-PFTs, which is much greater than expected from its limited sequence identity to those toxins. This strongly suggests that a pore-forming mechanism similar to that of β-PFTs is involved in the action of this type of parasporin. The structural comparison of PS2Aa1 to other aerolysin-type β-PFTs indicates conserved oligomerization and pore-forming structures in domains 2 and 3, and highly diverse putative receptor binding region structures in domain 1, likely accounting for enhanced cancer cell cytotoxicity as compared to normal control cells. The structural implications for the mechanism of action and cellular specificity of both Cry and β-PFT type parasporins will be