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## **INSECTICIDAL MECHANISMS: Death by cAMP**

The soil bacterium *Bacillus thuringiensis* (Bt) produces insecticidal Cry toxins, which bind to a cadherin-family receptor expressed in the mid-gut epithelium of various insects, thereby triggering cell death. Zhang *et al.*, who previously showed that cell death in response to Cry1AB involved a magnesium-dependent cytotoxic event, used cultured High Five cells (derived from cabbage looper ovarian cells) stably transfected with the BT-R<sub>1</sub> receptor (S5 cells) to investigate the underlying mechanisms. Time-lapse microscopy revealed that S5 cells treated with Cry1AB first showed membrane blebbing and ruffling (within 20 minutes of toxin exposure) and then underwent cell swelling and lysis (within 40 minutes). Although 30 mM raffinose (used as an osmotic protectant) prevented cell swelling, it did not prevent cell death; magnesium chelation with EDTA (ethylenediaminetetraacetic acid) prevented blebbing, swelling, and cell death. Pharmacological analysis indicated that toxin-induced death did not depend on endocytosis, caspases, serine proteases, or cathepsin. Cry1AB stimulated a magnesium- and BT-R<sub>1</sub>-dependent increase in intracellular adenosine 3',5'-monophosphate (cAMP), and a cell-permeable inhibitor of G<sub>αs</sub> reduced Cry1AB toxicity, as did 2',5'-dideoxy-3'-ADP. Moreover, pharmacological inhibition of cAMP-dependent protein kinase (PKA) blocked Cry1AB-dependent morphological changes and cell death. Forskolin and the cAMP analog pCPT-cAMP both enhanced the toxic effects of Cry1AB, although neither was toxic when given alone. The authors conclude that Cry1AB binding to BT-R<sub>1</sub> stimulates a cell death pathway that depends upon activation of a pathway involving adenylyl cyclase and PKA.

X. Zhang, M. Candas, N. B. Griko, R. Taussig, L. A. Bulla Jr., A mechanism of cell death involving an adenylyl cyclase/PKA signaling pathway is induced by the Cry1Ab toxin of *Bacillus thuringiensis*. *Proc. Natl. Acad. Sci. U.S.A.* **103**, 9897-9902 (2006). [\[Abstract\]](#) [\[Full Text\]](#)

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