BACILLUS THURINGIENSIS INSECTICIDAL TOXINS INDUCE SHEDDING OF GPI-ANCHORED APN BY ACTIVATION OF PHOSPHATIDYLINOSITOL-SPECIFIC PHOSPHOLIPASE C

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ABSTRACT

Bacillus thuringiensis (Bt) is an aerobic, gram-positive bacterium that is used as a biopesticide. Many Bt strains produce parasporal proteinaceous crystals containing one or more insecticidal crystal proteins referred to as Cry toxins. The Cry toxins bind to the midgut brush border membrane and cause extensive damage to the midgut epithelial cells of susceptible insect larvae. Until recently, it was generally accepted that the pore-forming Cry toxins caused toxic osmotic lysis of the midgut cells by permeabilizing epithelial membranes. However, now it has been proposed that the toxicity of Bt has to do with its perturbation of intracellular signaling pathways.

Previously, we reported that Bt Cry toxins induce massive shedding of a membrane-anchored aminopeptidase N (APN) from midgut epithelial cells into the luminal fluid. In this study, we found that the toxin-induced shedding of APN was inhibited by cyclic AMP and MAPK kinase (MEK) inhibitors PD98059 and U0126, indicating that signal transduction in the MEK/ERK pathway is involved in the regulation of the shedding process. Furthermore, APN released from epithelial cells appears to be generated by the action of a phosphatidylinositol-specific phospholipase C cleavage of the GPI anchor of the membrane-bound APN based upon detection of a cross-reacting determinant (CRD) on the protein shed into the luminal fluid. Because shedding of various cell surface proteins induced by bacterial pathogens has been implicated in promoting their virulence, shedding of APN may promote the cytocidal action of Bt insecticidal proteins