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**Bordetella adenylate cyclase toxin induces calcium infflux into CD11b$^{+}$ cells through non voltage-sensitive L-type-like calcium channels.**

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Adenylate cyclase toxin (ACT), a 200 kDa protein, is an essential virulence factor for Bordetella pertussis, the bacterium that causes whooping cough. ACT is a member of the pore-forming RTX (repeats-in-toxin) family of proteins that share a characteristic calcium-binding motif of Gly- and Asp-rich nonapeptide repeats and a marked cytolytic or cytotoxic activity. In addition, ACT exhibits a distinctive feature: it has an N-terminal calmodulin-dependent adenylate cyclase domain. Translocation of this domain into the host cytoplasm results in uncontrolled production of cAMP, and it has classically been assumed that this surge in cAMP is the basis for the toxin-mediated killing. Several members of the RTX family of toxins, including ACT, have been shown to induce intracellular calcium increases through different mechanisms. In the case of ACT, it has been proposed that translocation of the catalytic domain participates itself in the formation of a novel type of membrane path for calcium ions. ACT has also been reported to rise [Ca2+]i in non-immune cells, such as pancreatic beta-cells and myocytes that do not contain the integrin receptor, through L-type calcium channels. We show here that ACT stimulates a raft-mediated calcium influx, through its cAMP production activity, that activates PKA, which in turn activates non voltage-sensitive calcium channels with L-type properties. We also show that this ACT-induced calcium influx does not correlate with the toxin-induced cytotoxicity.

Keywords: adenylate cylcase toxin, calcium, cd11b, cAMP