BACTERIAL TOXINS FOR RESEARCH AND INDUSTRY

PRODUCT INFORMATION

SIGNAL TRANSDUCTION

Many products from List Biological Laboratories, Inc. may be utilized to affect signal transduction mechanisms in cells. These tools have been useful for determining the involvement of different signal transduction mechanisms in regulating specific processes.

Cholera toxin, pertussis toxin, and adenylate cyclase toxin disrupt cellular control of the concentration of cyclic AMP (cAMP), a major intracellular second messenger. Cholera toxin activates adenylate cyclase by ADP-ribosylation of the regulatory G_s protein.[1] Due to the ubiquitous occurrence of G_{M1} ganglioside receptors on eukaryotic cell membranes, cholera toxin has been used in a wide variety of model systems. Pertussis toxin potentiates cAMP accumulation in cells by ADP-ribosylating the regulatory G_i protein component of adenylate cyclase.[1,2] When treated with pertussis toxin, cells fail to respond to agents that normally block cAMP accumulation. Adenylate cyclase toxin circumvents cAMP regulation in cells. Inside the cell, adenylate cyclase toxin activity is stimulated by endogenous calmodulin in a calcium-dependent manner to produce cAMP from host cell ATP.[3] The resulting cAMP accumulation blocks many cellular response mechanisms that are normally controlled by cAMP concentration.

Exoenzyme C3, as well as toxin A and toxin B from *Clostridium difficile* inactivate the small GTP-binding protein Rho, an important intracellular regulator. The mechanism of the inactivation of Rho by exoenzyme C3 is ADP-ribosylation at asparagine 41. *C. difficile* toxins A and B inactivate not only Rho but also Rac and Cdc42. These toxins work by glucosylation of a threonine; specifically glucosylating at Thr37 for Rho and at Thr35 for Rac and Cdc42. In this manner, these GTPase inactivators shut down signal transduction cascades.[4,5,6] This leads to several downstream events including depolymerization of the cytoskeleton, gene transcription of certain protein kinases, reduction in phosphatidyl-inositol 4,5-bisphosphate concentration and possible loss of cell polarity.

Pasteurella multocida toxin influences another important route of intracellular signaling. It activates the $G_q\alpha$ subunit that stimulates phosphatidyl-inositol-specific phospholipase C-β_1.[7,8] Phospholipase C cleaves phosphatidyl-inositol producing secondary messenger compounds which affect several intracellular events such as the mobilization of calcium pools and protein phosphorylation.[9,10] Another intriguing set of evidence indicates that *Pasteurella multocida* toxin can stimulate Rho kinase directly by a $G_q\alpha$ independent pathway. Some events that are reported to occur downstream in this signal transduction cascade are induction of stress fiber formation and stimulation of focal adhesion assembly through tyrosine phosphorylation of the focal adhesion kinase p125.[11,12]

Many bacterial products activate cell signal transduction pathways that mediate invasion by a pathogen. Filamentous hemagglutinin (FHA) of *Bordetella pertussis* binds an integrin that up-regulates the binding of complement receptor 3 (CR3), another integrin. CR3 binds to a different domain of FHA. Thus, *B. pertussis* could enhance its own binding to a host cell.[13] Another example of host-cell response to bacterial products is the inflammatory reaction created by lipopolysaccharides in intestinal cells. Lipopolysaccharides can activate nuclear factor kappa B through association with toll-like receptors. This subsequently leads to cytokine production (for example, IL-1, IL-6, and IL-8), activation of transcriptional nuclear factors and the activation of some immune cells.[14,15]

These products are intended for research purposes only and are not for use in humans.

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ORDERING INFORMATION

PRODUCT NO.	DESCRIPTION	SIZE
188	Adenylate Cyclase Toxin	50 µg
100B	Cholera Toxin (Azide Free)	1 µg
143	Exoenzyme C3 from *Clostridium botulinum*	50 µg
170	Filamentous Hemagglutinin (FHA)	50 µg
156	*Pasteurella multocida* Toxin	50 µg
180	Pertussis Toxin (Islet-Activating Protein)	50 µg
181	Pertussis Toxin (Salt-free)	50 µg
152A,B,C	Toxin A from *Clostridium difficile*	2,25,100 µg
155A,B,C,D	Toxin B from *Clostridium difficile*	2,20,200,100 µg