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.

Toxin A and toxin B from *Clostridium difficile* inactivate the small GTP-binding protein Rho, an important intracellular regulator. *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.

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.[7] 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.[8,9]

These products are intended for research purposes only and are not for use in humans or as diagnostic agents. For further information, please contact List Biological Laboratories, Inc.

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ORDERING INFORMATION

Product No.	Description	Size
188L	Adenylate Cyclase Toxin, Recombinant	50 µg
100B	Cholera Toxin (Azide Free)	1 µg
170	Filamentous Hemagglutinin (FHA) from *Bordetella pertussis*	50 µg
179A,B	Pertussis toxin from *Bordetella pertussis* (in glycerol)	50 µg, 200 µg
180	Pertussis Toxin (Islet-Activating Protein) from *Bordetella pertussis*	50 µg
181	Pertussis Toxin from *Bordetella pertussis* (Salt-free)	50 µg
152C	Toxin A from *Clostridium difficile*	100 µg
155A,B	Toxin B from *Clostridium difficile*	2 ug, 20 µg
155L	Toxin B from *Clostridium difficile*	50 µg

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