BACTERIAL TOXINS FOR RESEARCH AND INDUSTRY

PRODUCT INFORMATION

ADENYLATE CYCLASE TOXIN
from *Bordetella pertussis*

Adenylate cyclase toxin-hemolysin (ACT, AC-Hly, or CyaA) is an important virulence factor for *Bordetella pertussis*. Adenylate cyclase toxin is a large (178 kDa), 1,706 amino acid, toxin consisting of an amino-terminal adenylate cyclase (AC) domain of 400 residues and a repeat toxin (RTX) moiety of 1,306 residues. Sequences within the RTX domain are responsible for target binding, pore-formation and calcium binding. Also located within this domain are two lysine residues which undergo post-translational modification by acylation (1).

Adenylate cyclase toxin targets sentinel cells of the host's innate immune system. It penetrates a variety of immune cells and, when activated by calmodulin, catalyzes conversion of cellular ATP to cyclic AMP (cAMP), interfering with cell signaling and with the anti-bacterial activity of phagocytes. ACT acts on phagocytes by limiting their ability to produce oxidative burst and kill bacteria through complement or antibodies (2, 3). The entire ACT protein is necessary for adenylate cyclase delivery into cells (4).

In the intoxication process, the Hly portion of the toxin binds to CR3 receptors on target cells ($CD11b^+$) and allows translocation of the ACT enzyme into the cell. Within the target cell, adenylate cyclase rapidly produces extremely high levels of cAMP, disabling the immune cell (5, 6). At a lower efficiency, adenylate cyclase-hemolysin can penetrate cells lacking the CR3 receptor and create cAMP (7). In addition to binding target cells, ACT is able to form small cation-selective pores in cytoplasmic membranes, causing hemolysis in erythrocytes (8).

A non-enzymatic, genetically detoxified ACT toxoid (CyaA-AC^-) has been produced (9). Although the catalytic activity in this toxoid is destroyed, it is still cell invasive and able to induce an immune response to co-administered pertussis antigens (10, 11, 12). This toxoid has been shown to be capable of delivering vaccine antigens into the cytosol of major histocompatibility complex (MHC) class I antigen-presenting cells (13). CyaA-AC^- toxoid has been used as a tool to deliver antigens to T cells in anti-cancer immunotherapeutic vaccines (9, 14, 15).

List Labs provides several variations of the *B. pertussis* Adenylate Cyclase Toxin. Most recently, List Labs has prepared a new formulation of the lyophilized Adenylate Cyclase Toxin, Recombinant, Product #188. Upon request, this product may also be obtained as a liquid (Product #188L). Additionally, samples are available of the genetically detoxified CyaA-AC^- toxoid (Product #198L) and of an especially low endotoxin preparation of Adenylate Cyclase Toxin, Recombinant. Adenylate Cyclase Antigen, Native from *Bordetella pertussis* (Product #189), is also available. Contact List Labs to request any of these products.

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

LIST BIOLOGICAL LABORATORIES, INC.
(408) 866-6363 • (800) 726-3213 • FAX (408) 866-6364
WEBSITE: www.listlabs.com • EMAIL: info@listlabs.com

Ordering Information

Product No.	Description	Size
188	Adenylate Cyclase Toxin, Recombinant	50 µg
188L	Adenylate Cyclase Toxin, Recombinant, Liquid	50 µg
189	Adenylate Cyclase Antigen, Native from *Bordetella pertussis*	50 µg
197L	Adenylate Cyclase, Recombinant, Reduced Endotoxin, Frozen Liquid	50 µg
198L	Adenylate Cyclase Toxoid, Recombinant, Liquid	50 µg
173B	Edema Factor (EF), Recombinant, from *Bacillus anthracis*	0.5 mg

References

1. Sebo P, Osicka R, Masin J (2014) *Expert Review of Vaccines* **13(10)**:1215-1227. Adenylate cyclase toxin-hemolysin relevance for pertussis vaccines. PMID: 25090574

2. Confer DL and Eaton JW (1982) *Science* **217**:948–950. Phagocyte impotence caused by an invasive bacterial adenylate cyclase. PMID: 6287574

3. Mock M and Ullmann A (1993) *Trends Microbiol* **1**:187–192. Calmodulin-activated bacterial adenylate cyclases as virulence factors. PMID: 8143137

4. Sakamoto H, Bellalou J, Sebo P and Ladant D (1992) *J Biol Chem* **267**:13598–13602. *Bordetella pertussis* adenylate cyclase toxin. Structural and functional independence of the catalytic and hemolytic activities. PMID: 1618862

5. Wolff J, Cook GH, Goldhammer AR, Berkowitz SA (1980) *Proc Natl Acad Sci USA* **77(7)**:3841-4. Calmodulin activates prokaryotic adenylate cyclase. PMID: 6253992

6. Hanski E, Farfel Z (1985) *J Biol Chem* **260(9)**:5526-32. *Bordetella pertussis* invasive adenylate cyclase. Partial resolution and properties of its cellular penetration. PMID: 2859287

7. Vojtova J, Kamanova J, Sebo P (2006) *Curr Opin Microbiol* **9(1)**:69-75. Bordetella adenylate cyclase toxin: a swift saboteur of host defense. PMID: 16406775

8. Szabo G, Gray MC and Hewlett EL (1994) *J Biol Chem* **269**:22496–22499. Adenylate cyclase toxin from *Bordetella pertussis* produces ion conductance across artificial lipid bilayers in a calcium and polarity-dependent manner. PMID: 8077197

9. Simsova M, Sebo P, Leclerc C (2004) *Int J Med Microbiol* **293(7-8)**:571-6. The adenylate cyclase toxin from Bordetella pertussis--a novel promising vehicle for antigen delivery to dendritic cells. PMID: 15149033

10. Macdonald-Fyall J, Xing D, Corbel M, Baillie S, Parton R, Coote J (2004) *Vaccine* **22(31-32)**:4270-81. Adjuvanticity of native and detoxified adenylate cyclase toxin of *Bordetella pertussis* towards co-administered antigens. PMID: 15474718

11. Orr B, Douce G, Baillie S, Parton R, Coote J (2007) *Vaccine* **25(1)**:64-71. Adjuvant effects of adenylate cyclase toxin of *Bordetella pertussis* after intranasal immunisation of mice. PMID: 16916566

12. Cheung GY, Xing D, Prior S, Corbel MJ, Parton R, Coote JG (2006) *Infect Immun* **74(12)**:6797-805. Effect of different forms of adenylate cyclase toxin of *Bordetella pertussis* on protection afforded by an acellular pertussis vaccine in a murine model. PMID: 16982827

13. Osicka R, Osicková A, Basar T, Guemonprez P, Rojas M, Leclerc C, Sebo P (2000) *Infection & Immunity* 68: 247-256. Delivery of CD8(+) T-cell epitopes into major histocompatibility complex class I antigen presentation pathway by Bordetella pertussis adenylate cyclase: delineation of cell invasive structures and permissive insertion sites: PMID: 10603385

14. Dadaglio G, Morel S, Bauche C, Moukrim Z, Lemonnier FA, Van Den Eynde BJ, Ladant D, Leclerc C (2003) *Int Immunol* **15(12)**:1423-30 Recombinant adenylate cyclase toxin of *Bordetella pertussis* induces cytotoxic T lymphocyte responses against HLA*0201-restricted melanoma epitopes. PMID: 14645151

15. Fayolle C, Ladant D, Karimova G, Ullmann A, Leclerc C (1999) *J Immunol* **162(7)**:4157-62. Therapy of murine tumors with recombinant *Bordetella pertussis* adenylate cyclase carrying a cytotoxic T cell epitope. PMID: 10201941