

***Bordetella* Virulence Factors**

Filamentous hemagglutinin (FHA) & Fimbriae 2/3 (Fim)

The initial step in establishing a *Bordetella pertussis* infection is attachment of the bacteria to the epithelial lining of the host respiratory tract. Two *B. pertussis* virulence factors are key in this process, filamentous hemagglutinin (FHA)¹ and fimbriae (Fim).² FHA, which is both surface-associated and secreted by *B. pertussis*, is a multifunctional protein which promotes the attachment of the bacteria through several binding domains. Because FHA is highly immunogenic, it is included in many of the acellular vaccines. Additionally, FHA acts through multiple pathways to modulate the host immune response; an example of this type of activity is induction in macrophages of the secretion of both pro-inflammatory and anti-inflammatory cytokines.^{3,4} Fimbriae are extracellular proteins which, like FHA, participate in the attachment of bacteria to substrates. Based on their recognition by specific antisera, there are two fimbriae serotypes present in *B. pertussis*, fimbriae 2 (Fim 2) and fimbriae 3 (Fim 3).⁵

Both FHA, a large, 220 kDa 8-helical protein, and Fim 2/3 are produced by List Labs. FHA is from the native *Bordetella pertussis* strain 165 and the Fim 2/3 is isolated from cultures of a Pertactin (PRN) negative mutant derived from the *Bordetella pertussis* Wellcome strain 28 expressing a mixture of fimbriae 2 and fimbriae 3. Fimbriae are long structures which serve to tether the bacteria to surfaces. They are composed of subunits which dissociate in SDS producing components with apparent molecular weights of 22,500 and 22,000 Da for Fim 2 and Fim 3, respectively.⁵

Pertactin (PRN) and Lipopolysaccharide (LPS)

Virulence factors located on the surface of *Bordetella pertussis* include pertactin and LPS. PRN is a 69 kDa surface-located protein which, due to its ability to induce protective antibodies, is included in acellular pertussis vaccines. The contribution of this protein to *Bordetella* pathogenesis is under investigation; however, it appears to play a role in overcoming neutrophil-mediated clearance of *Bordetella* during early stages of establishing an infection.⁶ PRN is one of the most polymorphic *B. pertussis* proteins, occurring in the population in more than 13 variations.⁷

B. pertussis LPS has an abbreviated structure, comprised of lipid A and a core oligosaccharide without an O-specific polysaccharide side chain.⁸ In isolated *B. pertussis* LPS, some variants have a trisaccharide in place of the O-chain and some do not. Electrophoresis of this LPS reveals two bands referred to as A and B; the slower migrating band A is composed of the species with the trisaccharide and the faster migrating band B is comprised of lipid A and core oligosaccharide without the trisaccharide.^{9,10} PRN and LPS offered by List Labs are isolated from native cultures of *B. pertussis* strain 165.

Adenylate Cyclase Toxin (ACT) and Adenylate Cyclase Antigen

Adenylate cyclase toxin (ACT) is another important virulence factor secreted by *Bordetella pertussis*. When a lung infection is underway, ACT interacts with tracheal epithelial cells, inserting itself into cytoplasmic membranes, aiding the adhesion of bacteria to the airway lining.¹¹ Host phagocytes responding to the site of infection are disabled by cAMP generated by ACT.¹² Encoded by the *Bordetella pertussis* *cyaA* gene, adenylate cyclase toxin is a single 1706 amino acid polypeptide, with an apparent molecular weight of 220 kDa. The N-terminal of this protein contains an adenylate cyclase domain which binds to host cell calmodulin and catalyzes unregulated conversion of cellular ATP to cAMP.¹³ The C-terminal, receptor binding domain, contains numerous repeat in toxin (RTX) motifs and is responsible for binding to the cellular receptor on the surface of immune cells, translocation into the cell cytosol and creating cation-selective pores in the host cell membrane.

Adenylate cyclase toxin both suppresses and modulates the host immune system contributing to the pathogenesis of *B. pertussis*. This toxin is unusual in its ability to cross mammalian cell membranes and locate within the cytosol.

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As a cell biology tool, adenylate cyclase has been used to deliver immunogenic epitopes to antigen presenting cells (APC).¹⁴ ACT available from List Labs is produced as a recombinant protein in *E. coli* and is appropriate for the study of enzyme mechanism of action or where adenylate cyclase activity is desired.

In addition to the active adenylate cyclase toxin, List Labs provides a much less active version of this material, extracted from the native *B. pertussis* strain 165, called adenylate cyclase antigen. This material is appropriate for studying the interaction of antibodies with this *Bordetella* surface antigen.

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

Ordering Information

Product No.	Description	Size
170	Filamentous Hemagglutinin (FHA) from <i>Bordetella pertussis</i>	50 µg
186	Fimbriae 2/3 from <i>Bordetella pertussis</i>	50 µg
187	Pertactin from <i>Bordetella pertussis</i> (69 kDa Protein)	50 µg
188L	Adenylate Cyclase Toxin, Recombinant	50 µg
400	HPT™ LPS, highly purified from <i>Bordetella pertussis</i> 165	1 mg

Related Products

Pertussis Toxin from *Bordetella pertussis*, in glycerol, Products #179A, #179B

Pertussis Toxin from *Bordetella pertussis*, lyophilized in buffer, Product #180

Pertussis Toxin from *Bordetella pertussis*, lyophilized, salt free, Product #181

Pertussis Toxin Mutant from *Bordetella pertussis*, Product #184

See how others have used List Labs' products on our citations page: <https://www.listlabs.com/citations>

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