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COMPARATIVE STUDY OF EXOTOXIN MEDIATED LUNG INFECTION MECHANISMS OF *PSEUDOMONAS AERUGINOSA* AND *BORDETELLA PERTUSSIS*

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Gram negative bacterias such as *Pseudomonas aeruginosa* and *Bordetella pertussis* contribute to respiratory infections in humans by producing potent exotoxins such as Exotoxin A and Pertussis toxin respectively. *Pseudomonas aeruginosa* is a rod-shaped bacteria with a single polar flagellum. A twitching motility is observed due to their pili. They have a unique pigment production and biofilm production in chronic infections and they are commonly found in hospital environments. *Bordetella pertussis* is a small coccobacillus bacteria which is a causative agent of whooping cough. It is non motile aerobic bacteria and an obligate human pathogen of respiratory infections. It cannot survive independently in nature therefore it relies on a continuous chain of human to human transmission. Understanding the mechanisms of the toxin action is a valuable insight into bacterial pathogenesis and is important in developing effective strategies to prevent and treat respiratory infections.

Exotoxin A produced by *Pseudomonas aeruginosa* is an AB type toxin with single-chain protein and three functional domains. The receptor binding domain attaches to the host cells, the translocation domain for cytosolic entry and a catalytic domain for ADP ribosylation of elongation factor 2. Pertussis toxin produced by *B. pertussis* is also an AB_5-type toxin.

Pseudomonas aeruginosa adheres to respiratory epithelial cells via pili and outer membrane protein and establishing lung infection mostly in immunocompromised patients. Exotoxin A, is the major virulence factor causing lung infections by targeting alveolar epithelial cells. It binds to α2-macroglobulin receptor and enter the cell through endocytosis and translocate into cytosol via Golgi apparatus and endoplasmic reticulum through a acidification mediated transport. Then ADP ribosylation of elongation factor 2 happens in the cytosol, catalyzed by domain 3. This alters the protein synthesis and eventually leads to apoptosis of the epithelial cells, disruption of tight junction proteins such as ZO-1 and ZO-2. This epithelial damage allows bacteria to infiltrate lung tissue and cause edema and impaired gas exchange. Clinically this mechanism contributes to acute lung injury, pneumonia and bronchiectasis in patients with underlying pulmonary conditions.

Pertussis toxin is also a key virulence factor in the development of respiratory infections such as whooping cough. A subunit and five B subunits bind to host cell receptors and B subunit specifically binds to glycoprotein receptors on the airway epithelial cell surface and causes endocytosis of the toxin. A subunit translocate into cytosol and catalyze the ADP ribosylation of the inhibitory G protein, therefore it inactivates and prevents inhibition of adenylate cyclase, which leads to sustained elevation of intracellular cyclic AMP (cAMP). This elevation is cAMP alters ion transport and increases mucus secretion therefore it causes impaired removal of bacteria. Elevated cAMP levels also cause phagocytosis and cytokine signaling reducing the effectiveness of the host immune response. These cellular disruptions contribute to inflammation, tissue damage and prolonged colonization in the respiratory tract. Clinically this mechanism contributes to paroxysmal coughing and airway hyperactivity and increased susceptibility to secondary infections such as pneumonia.

In conclusion, the exotoxins produced by *Pseudomonas aeruginosa a*nd *Bordetella pertussis* play an important role in causing lung infections. Exotoxin A attacks the alveolar epithelial cells and block protein synthesis by ADP ribosylation of elongation factor 2. This leads to cell death and cause inflammation and fluid build-up in the lungs, causing pneumonia. On the other hand Pertussis toxin disrupts signaling in immune airway cells and cause sustained elevation in cAMP levels which is responsible for respiratory problems such as whooping cough. These toxins show how Gram-negative bacteria disrupts normal cellular process and cause illness.