Cedarburg High School SMART Team

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Coughing up a Cure for Whooping Cough with Pertussis Toxin

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The CDC reported 32,971 cases of pertussis, or whooping cough, in 2014. This respiratory infection mainly affects unvaccinated infants and toddlers, and symptoms include paroxysmal coughing with whooping, vomiting, and pulmonary complications which can lead to death. Pertussis toxin (PT), produced by the pathogenic bacteria *Bordetella pertussis*, causes whooping cough by ADP-ribosylating the G_i protein that inactivates adenylyl cyclase. The inactive ADP-ribosylated G_i protein is unable to interact with G protein-coupled receptors, leading to an increased intracellular concentration of cAMP. Increased concentrations of cAMP can interfere with normal cell signaling, disrupting specific cellular functions. PT is a critical virulence factor for *B. pertussis* that also has potential to create human immunity against pertussis. The Cedarburg SMART Team (Students Modeling A Research Topic) modeled PT using 3-D printing technology to study structure-function relationships. PT contains a total of six subunits, four individual subunits (S1, S2, S3, and S5) and a pair of identical subunits (S4). The A domain consists of the S1 subunit, the catalytic portion of the toxin. Mutations in Glu129 and His35 can reduce ADP-ribosyltransferase activity. Mutations in Arg9, Asp11, and Arg13 also reduce catalytic activity. Trp26 interacts with NAD^+, an important cofactor. The B domain, responsible for binding to cell receptors, contains the remaining subunits. Effective vaccines contain chemically-inactivated PT. However, whole cell pertussis vaccine may cause severe side effects, while acellular pertussis vaccine is not as potent. Non-toxic derivatives of pertussis toxin may be engineered, improving the potency of the acellular vaccine without harmful side effects.