

## **Structural studies on PlyB, a potential therapeutic for the treatment of pulmonary anthrax.**

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*Bacillus Anthracis* is a category-A bioterrorism agent. Unless treated prophylactically, exposure to weaponized anthrax spores can result in pulmonary anthrax, which has near 100% mortality. While anthrax vaccines are available, these are not in routine use within the general population. Thus, there remains the need to develop new therapeutics for the treatment of pulmonary anthrax infection. Here we describe the structure and function of a novel bacteriophage-derived lysin, PlyB, which displays potent lytic activity against the *B. anthracis*-like strain ATCC 4342. This molecule comprises an N-terminal catalytic domain (PlyB<sub>cat</sub>) and a C-terminal bacterial SH3-like domain, SH3b. It is shown that both domains are required for effective catalytic activity against ATCC 4342. Further, PlyB has comparable specific activity to the phage lysin PlyG, an amidase being developed as a therapeutic against anthrax. In contrast to PlyG, however, the 1.6 Å X-ray crystal structure of PlyB<sub>cat</sub> reveals that the catalytic domain adopts the glycosyl hydrolase (GH)-25, rather than T7 lysozyme-like fold. PlyB therefore represents a new class of anthrax lysin and a new defensive tool in the armament against anthrax-mediated bioterrorism.