

NON -TECHNICAL ABSTRACT: (State in layman's terms the application's broad, long-term objectives and specific aims, making reference to the potential public benefits of the project for California.)

Pseudomonas aeruginosa is an opportunistic human pathogen that can cause severe diseases leading to death. *P. aeruginosa* is also a frequent cause of nosocomial infections due to its natural and acquired resistance to many antibiotics. Thus, the pathogen is a serious threat to public health in California and around the world.

A small molecule, cAMP, has been known to be the primary cellular signal utilized by *P. aeruginosa* for the expression of many virulence genes, which is required for the infection and survival of the pathogen inside human hosts. Proteins that sense cAMP are certain to orchestrate such virulence process. At present, only one cAMP-sensing protein is known, and that protein by itself cannot fully explain the known complexity of the cAMP regulatory pathway in *P. aeruginosa* virulence. Here we identify another potential cAMP sensor protein in the genome of *P. aeruginosa* and test its role in virulence, which might bridge the current knowledge gap in the primary virulence pathway of the pathogen. The proposed experiments include the construction of a *P. aeruginosa* mutant lacking the new protein factor and virulence testing of the mutant strain in fruit flies.

The long term goal of this project is to comprehensively understand the primary virulence mechanism of *P. aeruginosa*, and further to develop alternative therapeutic strategies to control the pathogen, which is important due to the diminishing usefulness of antibiotics to this bacterium.