Online Proceedings

POSTER SESSION 2

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Exploiting the Antimicrobial Properties of a Type VI Effector-Immunity Pair

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The export of signals is a vital aspect of bacterial communication with its environment and it was recently found that Gram-negative bacteria can send signals directly to neighboring bacteria via the type VI secretion system (T6SS). The bacterial T6SS translocates antibacterial toxins into neighboring bacterial cells and provides a means for bacteria to compete in their environment. Bacteria can also target their own cells with the T6SS but are protected against self-intoxication by cognate immunity proteins that inactivate their partner toxins. For example, one T6-exported toxin found in Pseudomonas aeruginosa, Tse1, degrades the cell wall of the recipient cell. The cell wall provides structural support for bacteria, and degradation of this protective layer by Tse1 causes the target cell to lyse. P. aeruginosa is immune to this toxicity, however, because an immunity protein, Tsi1, in the cell wall layer of P. aeruginosa binds and inhibits T6-exported Tse1. Our lab has found that Tse1 and Tsi1 are members of a large superfamily of type VI amidase effector-immunity widely found in Gram-negative bacteria, suggesting that these T6 toxin-immunity pairs may play a major role in influencing the structure of polymicrobial communities in general. Because of the large influence the T6SS can have on polymicrobial environments, I predict the T6-toxin-immunity system could also be utilized as an antimicrobial strategy. My aim is to engineer a novel Tse1–Tsi1 toxin–immunity pair that escapes rescue by immunity proteins in naturally occurring bacteria, thus giving the engineered P. aeruginosa strain the ability to outcompete the natural wild-type strain. To do this I will use a structure-based approach in conjunction with a genetic directed evolution strategy to identify and mutate Tse1 and Tsi1 residues that play an important role in Tsi1–Tse1 recognition and inhibition.