Systems Biology Research Symposium
Oral Presentation Session

Grand Ballroom
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7:00-8:30pm

Yeast Functional Genomic Approaches Provide New Insights Into How Human Bacterial Pathogens Cause Disease

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The vast array of strategies that bacterial pathogens utilize to survive within hosts and ultimately cause disease is staggering. Many gram-negative pathogens encode specialized secretion systems that can deliver on the order of tens of effector proteins (effectors) into host cells. Each pathogen delivers its own unique set of effectors. The identification and characterization of these proteins is often challenging and is a major limitation in furthering our understanding of how these pathogens cause disease. For example, pathogens that no longer express individual effectors often do not exhibit phenotypes presumably due to functional redundancy. Similarly, most of the effectors lack homology with proteins of known function and do not exhibit a detectable phenotype when expressed in mammalian cells. To address these limitations, we have developed the yeast *Saccharomyces cerevisiae* as a model system to study effectors. The underlying premise of this work being that many effectors likely target cellular processes conserved from yeast to mammals. Remarkably, we have found that when expressed in yeast almost half of the effector proteins but hardly any of >1,000 bacterial housekeeping proteins inhibit growth. These observations strongly suggesting that growth inhibition is a sensitive and specific reporter of secreted effector proteins. We have exploited this growth inhibition in yeast functional genomic and chemical genetic screens in order to identify conserved host cell processes targeted by the virulence proteins. And have developed a novel yeast-based visualization assay to monitor binary protein interactions. Together, these multi-pronged functional genomic approaches have led into insights into both the identification and characterization of bacterial virulence proteins in pathogenesis.