Title, Times New Roman 14 Font Bold.
Example: *Burkholderia pseudomallei* Antimicrobial Resistance Mechanisms

Names, Times New Roman 12 Font Bold, Italics.
Example:
Apichai Tuanyok[1] and Herbert P. Schweizer[1,2]

Affiliation(s), Times New Roman 12 Font, Italics.
Example:
Emerging Pathogens Institute[1], Center for Therapeutic Innovation[1,2], University of Florida, USA

Text and Key Words, Times New Roman, 12 Font. Maximum 500 words.

Example: *Burkholderia pseudomallei* (*Bp*) is the etiologic agent of melioidosis. Therapeutic options for this disease are limited because of *Bp*'s intrinsic and acquired antimicrobial resistance. While this had been recognized for some time, the underlying mechanisms remained largely undefined at the onset of this work. The aims of our studies were to define and characterize resistance mechanisms to clinically significant antibiotics in clinical and environmental isolates and to generate and characterize antibiotic resistant mutants in a defined strain background. This information provides the basis for establishing means to monitor antibiotic resistance in naturally occurring or maliciously engineered *Bp* strains. Our studies established that efflux mediated by members of the resistance nodulation cell division (RND) family is the dominant resistance mechanism in naturally occurring *Bp* isolates. Efflux affects all clinically significant antibiotics, including trimethoprim, sulfamethoxazole and doxycycline, but not β-lactam antibiotics. We characterized three RND efflux pumps, AmrAB-OprA, BpeAB-OprB and BpeEF-OprC. AmrAB-OprA had previously been shown as being responsible for *Bp*'s intrinsic aminoglycoside and macrolide resistance. We demonstrated that rare aminoglycoside-susceptibility in *Bp* isolates is either due to deletion of AmrAB-OprA or mutations preventing its expression. While BpeAB-OprB is a multidrug efflux pump, its clinical significance is unclear because of the low level resistance its provides and resistance due to expression of this pump has never been demonstrated outside of the laboratory. BpeEF-OprC is clinically most significant as it is responsible for the widespread trimethoprim resistance in Australian and Thai isolates. Its expression also causes resistance to trimethoprim-sulfamethoxazole in a smaller number of clinical strains. We showed that regulation of BpeEF-OprC expression is complex and governed by at least two LysR-type regulators, BpeT and BpeS. Resistance to β-lactam antibiotics used to treat melioidosis, including ceftazidime and amoxicillin-clavulanic acid, is mediated by mutations affecting expression and structure of chromosomally-encoded PenA β-lactamase. We demonstrated that PenA is unique in that it is a twin arginine transporter-exported, membrane-associated lipoprotein. Deletion of the penicillin binding protein 3 target via large genomic deletions was established as novel ceftazidime resistance mechanism in slow-growing ceftazidime resistant clinical Thai isolates.

Key Words: Melioidosis therapy, antibiotics, resistance, efflux pump, β-lactamase

Note: Please indicate student and/or postdoc presenter by underlined name.