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Burkholderia pseudomallei inhibits autophagy to benefit its intracellular survival in lung epithelial cells by suppressing ATG10

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Burkholderia pseudomallei is a notorious pathogen of human meloidosis, which is classically characterized by pneumonia and multiple abscesses with a high mortality and relapse rate. Autophagy as one of the earliest defense responses encountered by intracellular pathogens is a process that engulfs and delivers intracellular bacteria for lysosomal degradation. Recent studies indicate that *B. pseudomallei* can survive inside mammalian cell lines owning to its ability to evade autophagy in an active behavior. However, the associated mechanisms remain to be established. In our study, in order to reveal the underlying mechanisms, levels of mRNA and miRNAs in human lung epithelial A549 cells during *B. pseudomallei* infection were measured using microarray assay. We showed that ATG10, an important regulator of autophagy, was down-regulated during *B. pseudomallei* infection in A549 cells. Furthermore, overexpression of ATG10 promoted to eliminate intracellular *B. pseudomallei* by enhancing the process of autophagy. As a potential mechanistic explanation for this observation, we demonstrated that three novel miRNAs, MIR4458, MIR4667-5p and MIR4668-5p, bound to the 3'-untranslated region of ATG10, by different time course and spatial manner. Up regulation of these miRNAs reduced the level of ATG10 and inhibited autophagy, leading to increased numbers of intracellular *B. pseudomallei*. These results suggest that infection with *B. pseudomallei* up-regulates miRNAs to reduce expression of protein required for autophagy and autophagy response in lung epithelial cells.

Biography

Qian Li is a currently a PhD student in Third Military Medical University, majoring in Microbiology. Currently, she is studying in Dan Luo's lab of Cornell University, as a "jointly-supervised" PhD student, centering on applying DNA nanotechnology in point-of-care pathogen detection.

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