FUNCTIONAL ANALYSIS OF *BURKHOLDERIA PSEUDOMALLEI* SIGMA N2 AND SIGMA S IN MODULATING MULTINUCLEATED GIANT CELL FORMATION IN MACROPHAGE CELL LINE

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ABSTRACT

A human severe infectious disease with high mortality rate in many Tropical countries, melioidosis, is caused by a highly versatile pathogen *Burkholderia pseudomallei*. The function of the *B. pseudomallei* sigma S (RpoS) transcription factor in survival during stationary growth phase and conditions of oxidative stress is well documented. Beside *rpoS*, bioinformatics analysis of *B. pseudomallei* genome showed the existence of two *rpoN* genes, *rpoN1* and *rpoN2*. To access the function of RpoN , both *rpoN1* and *rpoN2* were inactivated, unfortunately only the *rpoN2* mutant (Δ*rpoN2*) strain was successfully constructed and characterized. It may be due to the potential important role of *rpoN1* in bacteria survival. In this study, by using the mouse macrophage cell line RAW264.7 as a model of infection, the involvement of *B. pseudomallei* RpoS and RpoN2 in invasion, intracellular survival leading to the reduction in Multinucleated Giant Cell (MNGC) formation of RAW264.7 cell line was illustrated. The researcher also demonstrated that MNGC formation in RAW264.7 cell line depended on a certain number of intracellular bacteria (at least 10^4) and that both RpoS and RpoN2 are not directly involved in MNGC formation judging by the same 15% MNGC formation observed in RAW264.7 cells infected with either *B. pseudomallei* wild type MOI 2 or RpoN2 mutant (Δ*rpoN2*) MOI 10 or RpoS mutant (Δ*rpoS*) MOI 100. Moreover, the role of *B. pseudomallei* RpoS and RpoN2 in regulation of Type Three Secretion System *bipB-bipC* gene expression was hypothesized for the first time.

KEY WORDS: *BURKHOLDERIA PSEUDOMALLEI*/ RPOS / RPON2 / MULTINUCLEATED GIANT CELL / INVASION / INTRACELLULAR SURVIVAL.

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