論 文 要 旨

Legionella pneumophila infection-mediated regulation of RICTOR via miR-218 in U937 macrophage cells

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Background: Inhalation of aerosolized *Legionella pneumophila*, a Gram-Negative-bacterium, can causesevere pneumonia. During infection, *L. pneumophila* replicates intracellularly in macrophages. The involvement of host microRNAs (miRNAs) in *L. pneumophila* infection is not fully understood.
Methods: The human macrophage-like cell line U937 was infected with *L. pneumophila*. The levels of miRNA and messenger RNA (mRNA) were measured using reverse transcriptase polymerase chain reaction. Release of lactate dehydrogenase was used to evaluate cytotoxicity. The expression of RICTOR and related proteins was examined by western blotting of cell lysates.
Results: *L. pneumophila* infection upregulated the expression of miR-218 and the host genes SLIT2 and SLIT3 in U937 cells. The expression of RICTOR, a component of the mechanistic target of rapamycin complex 2 (mTORC2), decreased during *L. pneumophila* infection. RICTOR protein expression was
inhibited by the overexpression of miR-218, whereas knockdown of miR-218 restored the downregulation of RICTOR by *L. pneumophila*. *L. pneumophila* infection induced the expression of the proinflammatory cytokines IL-6 and TNF-alpha, which was modulated by knockdown of miR-218 or RICTOR.
Conclusions: Our study revealed the involvement of miR-218 in regulating the inflammatory response of macrophages against *L. pneumophila* infection. These findings suggest potential novel roles for miR-218 and RICTOR as therapeutic targets of *L. pneumophila* infection.