Obligatory intracellular bacterium exploits evolutionarily conserved host signaling pathway to survive

In order to survive, obligately intracellular pathogens exploit host cellular signaling pathways and other cellular processes via molecular interactions between pathogen - secreted “effectors” and host target proteins to reprogram host cell functions. However, the molecular mechanisms and pathways targeted are not well defined, nor are the complex pathogen-host interactions involved.

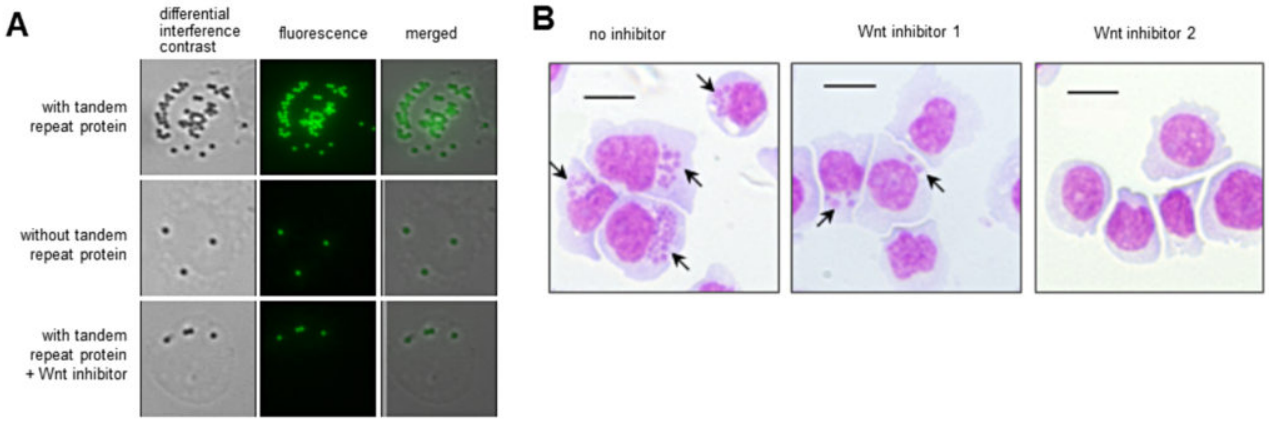

Fig. 1. *E. chaffeensis* tandem repeat proteins stimulate Wnt activation leading to (A) internalization and (B) prolonged survival in macrophages. Wnt pathway inhibitors reduce both Ehrlichia internalization and survival after entry. (A) TRP-coated beads are internalized by the cell. After Wnt pathway inhibitor treatment, the internalization is largely reduced. (B) Stained cells collected after 3 days of Ehrlichia infection demonstrate decreased number of infected cells and bacteria following treatment with Wnt pathway inhibitors. The arrows show bacteria. Bars, 10 um.

Ehrlichia chaffeensis is an obligately intracellular bacterium responsible for the emerging tick-transmitted life-threatening zoonosis, human monocytotropic ehrlichiosis. In this study, we demonstrate that *E. chaffeensis* activates the host Wnt signaling pathway to enter and survive in the host cell. Molecularly defined *E. chaffeensis* effectors, known as tandem repeat proteins, interact with a cell surface receptor to mediate the invasion and survival through activation and modulation of canonical and noncanonical Wnt signaling. After *E. chaffeensis* infection, host Wnt signaling is significantly stimulated and the expression of many Wnt signaling genes is altered. Inhibition of Wnt pathway components and regulators results in decreased survival of the bacteria.

This study highlights the ability of pathogens utilize evolutionarily conserved host signaling pathways to survive and identifies specific pathogen effectors necessary for exploitation of these pathways.

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Publication

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