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Intracellular Invasion of *Orientia tsutsugamushi* through the Interaction with Fibronectin

Nam-Hyuk Cho*, Jung-Hee Lee, Se-Yoon Kim, Sun-Young Bang, Myung-Sik Choi, and Ik-Sang Kim

Department of Microbiology and Immunology, Seoul National University College of Medicine, Seoul 110-799

Orientia tsutsugamushi, a causative agent of scrub typhus, is an obligate intracellular bacterium. The cellular invasion mechanism of the pathogen is poorly characterized. Here, we have identified a bacterial invasin which interact with fibronectin (Fn) to enhance the intracellular invasion of *O. tsutsugamushi*. *O. tsutsugamushi* can bind to immobilized Fn *in vitro* and exogenous Fn stimulates bacterial invasion into mammalian host cells. Bacterial invasion in the presence of Fn was abrogated by the addition of RGD peptides or by an anti- $\alpha 5\beta 1$ integrin antibody. Through a ligand immunoblot and GST pull-down assay, a 56 kDa type specific antigen (TSA56) was identified as the bacterial ligand responsible for the interaction with Fn. The antigenic domain III and the adjacent C-terminal region (amino acid 243~349) of TSA56 interact with Fn. Furthermore, we have found that the enhanced invasion of the pathogen was abrogated by the addition of purified recombinant peptides derived from TSA56.