Poster Presentation

MS53.P35

InIC of L. monocytogenes Binds Human Tuba for Bacterial Cell-Cell Spreading

L. Polle^{2,3}, L. Rigano⁴, K. Ireton⁴, <u>W. Schubert^{1, 2}</u>

¹University of Pretoria, Department of Biochemistry, Pretoria, South Africa, ²University of the Western Cape, Department of Biotechnology, Cape Town, South Africa, ³Helmholtz-Centre for Infection Research, Braunschweig, Germany, ⁴University of Otago, Department of Microbiology and Immunology, Dunedin, New Zealand

The human pathogen Listeria monocytogenes is able to directly spread to neighboring cells of host tissues, a process recently linked to the virulence factor InIC. InIC targets the sixth SH3 domain (SH3-6) of human Tuba, disrupting its physiological interaction with the cytoskeletal protein N-WASP. The resulting loss of cortical actin tension proposedly slackens the junctional membrane allowing protrusion formation by motile Listeria. Complexes of Tuba SH3-6 with physiological partners N-WASP and Mena reveal equivalent binding modes but distinct affinities. The interaction surface of the infection complex InIC/Tuba SH3-6 is centered on phenylalanine146 of InIC stacking upon asparagine1569 of Tuba. Replacing Phe146 by alanine largely abrogates molecular affinity and in vivo mimics deletion of inIC. Collectively, our findings indicate that InIC hijacks Tuba through its LRR domain, blocking the peptide binding groove to prevent recruitment of its physiological partners.

[1] Rajbanian T, Gavicherla B, Heisig M, Müller-Altrock S, Goebel W, Gray-Owen SD, Ireton K (2009) Nature Cell Biology 10, 1212-8, [2] Polle L, Rigano LA, Julian R, Ireton K, Schubert W-D (2014) Structure 22, 304-314., [3] Ireton K, Rigano LA, Polle L, Schubert W-D (2014) Frontiers in Microbiology (in press).



Keywords: Bacterial Pathogenesis, Protein-Protein Interactions, Cell-Cell Spreading