Host factors involved in intracellular growth and proliferation of *Salmonella*

Salmonella serovars are facultative, intracellular pathogens which cause a range of diseases of humans and animals including acute and chronic forms of gastroenteritis, diarrhea, as well as systemic infections which can lead to septicemia and long-lasting secondary health effects such as urinary tract disorders and chronic arthritis. Furthermore, both humans and animals may become asymptomatic carriers of the pathogen. The pathogenesis of *Salmonella* is generally characterized by invasion of non-phagocytic cells of the intestinal epithelia, followed by uptake by phagocytic cells of the immune system such as macrophage, dendritic cells and neutrophils. Unlike many other bacterial pathogens, *Salmonella* serovars are capable of survival and even growth in host immune cells, a characteristic which contributes to spread within the host within lymphoid tissues and inner organs.

Our work has been concerned with factors, both bacterial and host-associated, which contribute to the intracellular growth and proliferation of *Salmonella* within host cells. We have identified a novel gene involved in *Salmonella* resistance against host antibacterial peptides, and identified a negative regulator of both flagellar biosynthesis and invasion gene expression which may be involved in the switch between the extra- and intracellular lifestyles of this pathogen. More recently, we have discovered that *Salmonella* is able to utilize a host cell process in order to acquire nutrients to support intracellular growth independent of bacterial *de novo* biosynthesis or uptake systems.

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Selected Publications:

Le Bourhis, L., J. G. Magalhaes, T. Selvanantham, L. H. Travassos, K. Geddes, J. H. Fritz, J. Viala, K. Tedin, S. E. Girardin, D. J. Philpott (2009) Role of Nod1 in mucosal dendritic cells during *Salmonella* pathogenicity island 1-independent *Salmonella enterica* serovar Typhimurium infection. *Infect. Immun*. 77:4480-4486.

Pfeiffer, V., A. Sittka, R. Tomer, K. Tedin, V. Brinkman and J. Vogel (2007) A small non-coding RNA of the invasion gene island (SPI-1) represses outer membrane protein synthesis from the *Salmonella* core genome. *Mol. Microbiol*. 66:1174-1191.

Sittka, A., V. Pfeiffer, K. Tedin and J. Vogel (2007) The RNA chaperone Hfq is essential for the virulence of *Salmonella typhimurium*. *Mol. Microbiol*. 63:193-217.

Thompson, A., M. Rolfe, S. Lucchini, P. Schwerk, J.C.D. Hinton and K. Tedin. (2006) The bacterial signal molecule, ppGpp, mediates the environmental regulation of the invasion and intracellular virulence gene programs of *Salmonella*. *J. Biol. Chem*. 281:30112-30121.