

P030 The response of intracellular *Salmonella enterica* serovar Typhimurium to TLR4 modulation of the host environment
**J.A.Wright, S.Töttemeyer, J.C. Hinton, I. Hautefort,
A. Thompson, D.J. Maskell and C.E. Bryant**
*Department of Veterinary Medicine, University of Cambridge.
Institute of Food Research, Norwich Research Park*

Toll-like receptor 4 (TLR4) is the principal receptor responsible for recognising, in association with the proteins MD2 and CD14, *Salmonella enterica* lipopolysaccharide. Stimulation of this receptor activates innate macrophage defences against *S.enterica*. TLR4 is required for controlling *S.enterica* serovar Typhimurium primary infection in the murine host. TLR4 plays a key role in regulating host gene expression in response to *Salmonella* infection, but it is unknown whether activation of these receptors results in changes in bacterial gene expression to respond to the changing host environment. We report the use of microarray analysis of *S.Typhimurium* gene expression during infection of bone-marrow derived macrophages from wild-type and TLR4^{-/-} mice. Comparative analysis of the bacterial transcriptome reveals 21 genes that are more highly expressed in wild-type macrophages than TLR4^{-/-} cells. These genes have putative functions in oxidative stress resistance, metal ion transport and acid resistance. Defined allelic replacement mutants have been generated in a number of these bacterial genes, and work is ongoing to further characterize their role in *Salmonella* biology, interaction with host macrophages and in primary infection of the murine host.