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Rhodococcus equi phagosomes: arrest for a rest

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Rhodococcus equi is a Gram positive pathogen which is closely related to mycobacteria and, like them, has a thick, hydrophobic cell wall core composed of mycolic acid compounds. *R. equi* can cause severe –often fatal- bronchopneumonia in its natural host, the foal, and in immunosuppressed humans. In infected foals, *R. equi* multiplies in macrophages supported by a virulence-associated plasmid, and eventually lyses the host cell by necrosis (1, 4).

We have described that *R. equi* halts phagosome maturation at a step following an early endocytic one and before reaching a late endocytic stage (2). The proton-pumping vATPase is excluded, phagosome pH is neutral at 3 h of infection (3).

We have recently screened a transposon library of *R. equi* for mutants that are compromised in inhibition of phagolysosome formation and we identified two mutants which are compromised in the Fatty Acid Synthase (FAS) II pathway which is required (in rhodococci and mycobacteria) for the elongation of mycolic acids. In pathogenic mycobacteria, knocking out these genes is lethal, whereas *R. equi* multiplies normally in broth culture without a functional FAS II pathway. The mutants have increased phagolysosome formation but eventually reach a privileged compartment. Transfer of the extractable lipids from wild type versus mutant bacteria onto *E. coli* carrier cells leads to reduced and normal phagolysosome formation, respectively, demonstrating the central role of these long-chain (glyco-)lipids in inhibition of phagolysosome formation.

Additionally, we have observed that a secreted protein encoded by the virulence-associated plasmid is central in inhibiting phagosome acidification (but not phagolysosome formation or cytotoxicity). We can now dissect the requirements for inhibition of phagosome acidification and fusion with lysosomes (5). The current status of this research will be presented.

This lab's major contributions to this are:

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2. Fernandez-Mora, E., M. Polidori, A. Lührmann, U.E. Schaible and A. Haas (2005) *Traffic* 6: 635.
3. von Bargaen, K., M. Polidori, U. Becken, G. Huth, J.P. Prescott & A. Haas (2009) *Infect. Immun.* 77: 5676.
4. von Bargaen, K. & A. Haas (2009) *FEMS Microbiol. Rev.* 33: 870.
5. Schaible, U. E. & A. Haas (eds): *Intracellular Niches of Microorganisms. A pathogen's guide through the host cell.* WILEY-BLACKWELL Press, 2009

Keywords: phagosome, phagolysosome, cytotoxicity, membrane trafficking