[PS2.32]

Different Regulation of Iron Uptake and Storage of Typ A and Type B Strains of *F. tularensis* Influences Their Susceptibility to H_2O_2 Induced Killing

HL Lindgren*, MH Honn, AS Sjöstedt

Department of Clinical Microbiology, Clinical Bacteriology, and Laboratory for Molecular Infection Medicine Sweden (MIMS), Umeå University, SE-90185 Umeå, Sweden

Francisella tularensis, the causative agent of tularemia, is one of the most infectious bacterial pathogens known and is classified as a category A select agent and a facultative intracellular bacterium. Why type A strains (subspecies *tularensis*) of *F. tularensis* cause a more severe form of tularemia than type B (subspecies *holarctica*) strains of the bacterium is not known. In this study we have identified marked phenotypic changes between the subspecies since we show that type A strains store less intracellular iron than type B strains. The type A strain SCHU S4 was less susceptible than the type B strains FSC200 and the attenuated live vaccine strain (LVS) to H_2O_2-induced killing. H_2O_2 is a major factor mediating macrophage-mediated bactericidal activity. The activity of the H_2O_2-degrading enzyme catalase was similar between the strains so this did not explain their different susceptibility. Instead iron appeared to be a factor promoting the susceptibility of FSC200 and LVS to H_2O_2 since their resistance to H_2O_2-induced killing was enhanced if their iron pool was reduced. By real-time PCR it was demonstrated that FSC200 and LVS expressed higher levels of genes related to iron uptake and storage relative to SCHU S4 and this likely explains their high intracellular iron content. Together, the results suggest that type A strains have a restricted iron uptake and storage, which is beneficial for their resistance to H_2O_2-induced killing. This may be an important factor for the higher virulence of this subspecies of *F. tularensis* as reactive oxygen species including H_2O_2 are important bactericidal components during tularemia.

Keywords: Iron, Hydrogen peroxide, Francisella tularensis