Title: Cell Invasion, Macrophage Survival and Inflammatory Cytokine Levels Produced among the Closely Related Serovars Salmonella Enteritidis and Salmonella Dublin

Authors: Campioni, F.¹, Gomes, C.N.¹, Rodrigues, D.P.², Costa, R.G.², Bergamini, A.M.M.³, Tiba-Casas, M.R.⁴, Falcão J.P.¹


Abstract: Salmonella Enteritidis and Salmonella Dublin are closely related serovars that share antigenic and genetic properties. However, they differ significantly in their pathogenic potential, with S. Enteritidis colonizing chickens, and causing gastroenteritis in humans and S. Dublin causing systemic infection in cattle and occasionally infecting humans resulting in severe invasive disease. In light of the great importance of the infections caused by these two closely related serovars, the aims of this study were to compare the cell invasion to human epithelial cells (Caco-2) and bovine epithelial cells (MDBK), the capacity to survive and multiply inside human (U937) and chicken (HD11) macrophages of 25 S. Enteritidis and 25 S. Dublin strains isolated in Brazil between 1983 and 2016. Moreover, the levels of the inflammatory cytokines IL-8, IL-1β, IL-6, IL-10, IL-12p70 and TNF produced by Caco-2 cells in response to 10 selected strains of each serovar, were analyzed by flow cytometer. S. Enteritidis and S. Dublin strains studied showed similar percentages of cell invasion either in human epithelial cells (75%) or in bovine epithelial cells (73%). S. Dublin strains survived better (80%) in human macrophages than S. Enteritidis strains (65%) (P<0.05). Moreover, both serovars had a similar rate of multiplication (3x) inside U937 macrophages after 8 hours of incubation. Regarding the capacity to survive in chicken macrophages, S. Dublin had a similar invasion rate (70%) in comparison to S. Enteritidis strains (67%) (P>0.05). However, S. Dublin strains multiplied better (2x) than serovar Enteritidis strains (1x) inside HD11 macrophages after 8 hours of incubation (P<0.05). In addition, 70% of the S. Dublin strains analyzed in the cytokine assay did not stimulate the production of any of the cytokines except for IL-8, while 70% of the S. Enteritidis strains stimulate the production of all the six cytokines investigated. In conclusion, the better capacity of the S. Dublin studied to survive and multiply inside macrophages, as well as the low induction of cytokine production might explain the better ability of strains of this serovar to evade the host immunity response and cause invasive disease in comparison to serovar Enteritidis strains.

Keywords Salmonella Enteritidis, Salmonella Dublin, Cell invasion, Macrophages, Cytokines