Host and *Brucella* gene expression biosignatures in an *in vitro* model of infection

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Brucella natural infections occur primarily through mucosal membranes. HeLa cells, as non-professional phagocytic cells, have been used to investigate adhesion, internalization, intracellular trafficking and survival and replication of brucellae. Post-infection global gene expression profiles of *both* agent and host have yet to be analyzed. The goals of this study were to characterize the transcriptome of *Brucella* and *Brucella*-infected host cells during the initial infectious process for understanding the initial strategies employed for the pathogen to survive and replicate intracellularly and to identify perturbations of major gene(s) modulating critical cellular pathways during initial infection. Our initial results revealed that the intracellular replication of *B. melitensis* in HeLa cells begins after an initial adaptation period of 4h post-infection. Analysis of microarray results using classical statistical methods revealed 161 (35 up- and 126 down-regulated) and 115 (86 up- and 29 down-regulated) genes differentially expressed in intracellular *B. melitensis*, and 152 (45 up- and 107 down-regulated) and 957 (733 up- and 224 down-) altered genes in infected cells compared to non-infected ones at 4 and 12 h post-infection, respectively. *Brucella* genes related with transcription/translation (transcriptional regulators, ribosomal proteins) and metabolic processes (carbohydrate, lipid and amino acid transporters, kinases, dehydrogenases) were down-regulated at 4 but were up-regulated at 12 h post-infection. Among others, host genes related to apoptosis (caspase 1 & 3), cell cycle (cyclin, histone deacetylase) and MAPK signaling (MAPK1, 6 & 8) pathways were differentially expressed at both time points. Dynamic Bayesian modeling analysis identifies host and *B. melitensis* candidate mechanistic genes. To verify this *in silico* predictions, knocked down HeLa cells and *B. melitensis* mutants on candidate mechanistic genes were interacted with *B. melitensis* WT and non-transfected HeLa cells respectively, and their interaction followed up to 12 h post-infection. Our preliminary results characterized candidate genes important in *B. melitensis* infection to non-professional phagocytic cells as a preliminary approach to characterize and understand the *B.abortus*: host initial interactions as diagnostic biosignatures.