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# A ProteomicS study on *Chlamydia pneumoniae* -Induced Changes in Macrophages

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BACKGROUND: *Chlamydia* (*Chlamydophila*) *pneumoniae* is a small, morphologically and metabolically distinct gram-negative bacterium with obligately intracellular life cycle. It is the causative agent of human respiratory infections ranging from pneumoniae to dry cough, with 60-80% global seroprevalence. The tendency of *C. pneumoniae* to persist in macrophages even in the absence of exogenous triggers is well known, but the underlying host-chlamydial interactions driving the bacterial stress response remain elusive. OBJECTIVES: In this work, we describe changes in macrophage intracellular signaling pathways induced by *C. pneumoniae* infection. METHODS: Human THP-1-derived macrophages were infected with *C. pneumoniae* cardiovascular isolate CV6 and total cellular protein lysates were collected at 48 h and 72 h post-infection. Label-free quantitative proteome analysis combined with pathway analysis tools were used to identify patterns of differentially expressed proteins between infected and noninfected macrophages. RESULTS: A total of 2136 macrophage proteins were quantified in at least two out of three replicates for each sample. A one-way ANOVA (permutation-based false discovery rate 0.10) identified 214 proteins with significantly and consistently altered expression between the conditions. At 48 h post-infection, pathways associated with the positive regulation of NF-kappaB were stressed, while the negative regulation of cell cycle control was prominent at both 48 h and 72 h. The upregulation of S100A8 and S100A9 calcium-binding proteins, osteopontin and purine nucleoside phosphorylase LACC1 underlined the proinflammatory consequences of the infection, while the elevated NF-kappaB p100 levels in the infected macrophages implied interactions also with the noncanonical NF-kappaB pathway. Infection-induced changes in macrophage lipid metabolism were indicated by the upregulation of the scavenger receptor CD36 (cluster of differentiation 36) and ACAD10 (acyl coenzyme A dehydrogenase family member 10). The downregulated proteins were dominated by the mini chromosome maintenance (MCM) complex proteins 2 – 6, gamma glutamyl transferase 1 (GGT1) and fatty acid-binding protein 4 (FABP4). Collectively, this work represents a first proteomics study on *C. pneumoniae* – macrophage interactions and identifies several host cell proteins with yet unreported expression changes upon *C. pneumoniae* infection.

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