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Analysis of Chlamydia pneumoniae-infected monocytes following incubation with a novel peptide, acALY18: A potential treatment for infection in Alzheimer's disease

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P1-327

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Article Outline

Background: Our laboratory has been studying the role of infection with the obligate intracellular bacterium, Chlamydia pneumoniae, in sporadic late-onset Alzheimer disease (LOAD). This infection may be a trigger for the pathology observed in LOAD as a function of initiating neuroinflammation following entry of the organism into the brain. We have hypothesized that one entry mechanism may be by blood-borne infected monocytes trafficking the infection into the brain. **Methods:** Our current studies focus on infection of monocytes in vitro followed by analysis of infection using immunofluorescence labeling and RTPCR-microarray techniques. In addition, we are studying a novel approach utilizing a unique peptide, acALY18, derived from the endogenously expressed endoplasmic reticulum protein TRPC1, to eradicate the organism at 24-48 hr post-infection, thereby limiting its capacity to develop into a chronic/persistent infection. The peptide appears to stimulate the innate immune system through activation of the inflammasome. **Results:** C. pneumoniae prominently and stably infected THP1 monocytes at 24-48hr. Numerous large inclusions were labeled using specific anti-chlamydial monoclonal antibodies. Monocyte gene expression, both for markers of innate and adaptive immunity as well as for Alzheime disease, was significantly altered. Three genes were up-regulated as compared to 45 genes down-regulated in the immunity array at 48hr post-infection, whereas in the Alzheimer array, 4 genes including those for cathepsins B and D were up-regulated as compared to 5 down-regulated. Intriguingly, following incubation of C. pneumoniae-infected cells with acALY18 peptide (25-50nM) at 24hr post-infection, there was a dramatic clearance of the organism from the monocytes (80% infected and untreated to 13-15% infected after treatment). Furthermore, gene regulation was altered following peptide treatment as there were 39 up-regulated including those for CASP1 and IL-1 at least 4 fold, and no genes down-regulated in the immunity array. **Conclusions:** Our data suggest that C. pneumoniae-infected monocytes are altered significantly to promote a chronic/persistent infection that may account for the presence of C. pneumoniae in LOAD. Furthermore, stimulating the innate immune response using the novel peptide, acALY18, promotes clearance of C. pneumoniae from infected monocytes; this peptide may be a viable candidate for treating C. pneumoniae infections in Alzheimer disease.