Chlamydia pneumoniae and airways inflammation:

An investigation of the host cell-pathogen relationship

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ABSTRACT

C. pneumoniae is an obligate intracellular bacterium that has been implicated in the pathogenesis of chronic airways diseases such as asthma and COPD. *C. pneumoniae* undergoes a biphasic developmental cycle, alternating between infectious and non-infectious forms. However, it may also enter into a persistent state whereby it undergoes limited growth and division. It is this persistent state which may be of particular importance in the development of chronic airway inflammation and disease. A variety of cells are susceptible to *C. pneumoniae* but the relationship between *C. pneumoniae* and host cells with relevance to airways inflammation is not well described. The current studies were undertaken to investigate the host-cell pathogen relationship, with the aim of measuring basic immune responses and how these responses may allow persistent infection to develop. Utilising a combination of flow cytometry and ELISA's I have examined cytokine and surface molecule expression of cells in response to *C. pneumoniae* exposure. Airway epithelial cells were shown to respond to *C. pneumoniae* stimulation by increasing IL-8 and IL-6, cytokines involved in the recruitment and activation of inflammatory cells to the primary site of infection. My studies also show that monocytes respond to *C. pneumoniae* by increasing cytokine production. Increased concentrations of *C. pneumoniae* significantly increased IL-10 but decreased IL-12 monocyte expression, possibly causing an imbalance between Th2 and Th1 responses. Expression of surface molecules indicative of cellular activation, were increased by *C. pneumoniae* on monocytes, neutrophils and to a lesser extent on lymphocytes. In addition, monocytes reduced costimulatory molecule expression which may lead to diminished T cell activation, failure to clear infection and promote the development of persistent *C. pneumoniae* infection. Theses studies show that *C. pneumoniae* modulates a range of basic immune responses of the host cell. Costimulatory molecule expression by monocytes may play a role in determining whether primary *C. pneumoniae* infection is cleared and this coupled with inadequate T cell activation may lead to persistent infection which is associated with chronic respiratory diseases such as COPD and asthma.