6 Summary

Chlamydophila pneumoniae is an important widespread respiratory pathogen causing sinusitis, bronchitis and (community acquired) pneumoniae. However, a brought geographic diversity and periodicity with varying incidence rates of *C. pneumoniae*-mediated CAP-cases has been demonstrated. In addition, a repetitive or (chronic) persistent infection has been associated with an increase in chronic diseases like COPD, bronchial asthma or arteriosclerosis and subsequent (cardio-) vascular lesions.

In our studies, we could demonstrate, that

1) *Chlamydophila pneumoniae* is able to infect different bronchial and alveolar epithelial cells. Subsequently a multitude of proinflammatory (patho-)mechanisms, characteristic for acute and chronic pulmonary diseases like release of cytokines, expression of epithelial adhesion molecules, enhanced interaction of leukocytes and infected epithelial cells as well as an alteration in the surfactant regulation was initiated. It turned out that epithelial cells played a dual role during this process, mediating an overwhelming inflammatory reaction by releasing anti-inflammatory mediators like prostaglandins or nitric oxide.

2) Endothelial cells of different origin (HUVEC, HAEC) are key target cells for *Chlamydophila pneumoniae*. Infection was followed by a sustained inflammatory reaction of the endothelium with expression of adhesion molecules and cytokines, as well as subsequent recruitment of blood monocytes and PMN into the subendothelial matrix, essential pathogenic mechanisms for the development of atherosclerotic lesions. During the process of bacterial adhesion, invasion and intracellular survival central signal transduction pathways (increase in $[Ca^{2+}]_i$, MAPK-activation, transnuclear shift of NF-κB) were activated. Effects demonstrated were specific for *C. pneumoniae*, *C. trachomatis* did also infect, but did not activate human endothelial cells.

3) Endothelial Nod-proteins acted as key intracellular pattern recognition receptors to mediate a profound and prolonged target cell activation and might be the interface between chronic/persistence infection and onset of (chronic) vascular diseases.

Further studies are now required to determine the relationship between distinct steps of initial attachment, the chlamydial development cycle, importance of different chlamydial virulence factors and initiation of host cell signalling pathways that could lead to target cell damage and inflammation which in turn may result in or may promote chronic diseases like COPD, bronchial asthma or atherosclerosis.