[PS1.45]

Chlamydia trachomatis infection causes mitotic spindle pole defects independently from its effects on centrosome amplification.

A.E. Knowlton*, H.M Brown, T.S. Richards, L.A. Andreolas, R.K Patel, S.S. Grieshaber
University of Florida, United States

Chlamydiae are gram negative, obligate intracellular bacterial organisms, and *Chlamydia trachomatis* is the etiologic agent of the most commonly reported sexually transmitted disease in the United States. *Chlamydiae* undergo a biphasic life cycle that takes place inside a parasitophorous vacuole termed an inclusion. The inclusion associates intimately with host cell centrosomes, and this association is dependent upon the host motor protein dynein. We have previously reported that this interaction induces supernumerary centrosomes in infected cells, leading to multipolar mitotic spindles and inhibiting accurate chromosome segregation. Centrosome amplification and mitotic spindle defects are characteristic of many human cancers; however, pre-cancerous cells subjugate aberrant spindle pole formation by clustering multiple centrosomes to form bipolar spindles. Centrosome clustering is achieved through two distinct mechanisms, by dynein focusing to the mitotic spindle and initiation of the spindle assembly checkpoint (SAC). Our findings demonstrate that chlamydial infection causes mitotic spindle defects independently of its effects on centrosome amplification. Chlamydial infection dramatically increased the number of defective mitotic spindles in the mouse neuroblastoma cell line (N1E-115), a line well-characterized for its centrosome clustering abilities. We show that *Chlamydia* interferes with centrosome clustering outside of the canonical dynein/NuMA pathway, and a chlamydial infection has no affect on overall dynein activity or centrosome function. We demonstrate that chlamydial infection increases geometric spread of the centrosomes in interphase cells, and when we restrict the shape of infected cells we are able to decrease centrosome spread indicating *Chlamydia* directly affects the positioning of the centrosomes, the underlying microtubule network, and subsequent spindle architecture. We have determined that *Chlamydia* abrogates the important SAC delay resulting in disruption of centrosome clustering. These data suggest chlamydial infection exacerbates the consequences of centrosome amplification by inhibiting the cell's ability to suppress the effects of these defects on mitotic spindle organization.

Keywords: Chlamydia, Centrosomes, Spindles, Cell Cycle