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Katerina Wolf and Kenneth A. Fields

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Type I IFNs are induced during microbial infections and have well-characterized antiviral activities. TRAF3 is a signaling molecule crucial for type I IFN production and, therefore, represents a potential target for disarming immune responses. Chlamydia pneumoniae is a human pathogen that primarily infects respiratory epithelial cells; the onset of symptoms takes several weeks, and the course of infection is protracted. C. pneumoniae has also been associated with a variety of chronic inflammatory conditions. Thus, typical C. pneumoniae infections of humans are consistent with an impairment in inflammatory responses to the microorganism. We demonstrate that infection of epithelial cells with C. pneumoniae does not lead to IFN-β production. Instead, infected cells are prevented from activating IFN regulatory factor 3. This effect is mediated by C. pneumoniae–dependent degradation of TRAF3, which is independent of a functional proteasome. Hence, it is likely that C. pneumoniae expresses a unique protease targeting TRAF3-dependent immune effector mechanisms.

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The respiratory epithelium represents a major site for entry of pathogenic microorganisms. Therefore, the epithelial cell lining of the respiratory tract plays a pivotal role in innate immune defense against bacterial and viral pathogens. Innate immune recognition of microbial products is an essential component of this defense and is mediated by germline-encoded pattern recognition receptors (PRRs). PRRs detect pathogen-associated molecular patterns that signal the presence of a foreign microorganism to the host TLRs. These receptors, which are members of the TNFR family, represent the best-characterized class of PRRs. TLRs are localized in the cytoplasmic or endosomal membranes; of the 10 functional TLRs identified in humans, human bronchial epithelial cells express functional TLR1–6 (1). Ligation of a TLR initiates a cascade of signaling pathways that proceed in either a MyD88-dependent (TLR1, TLR2, TLR4, TLR5, and TLR6) or TRIF-dependent (TLR3 and TLR4) manner. MyD88-dependent pathways drive the induction of various inflammatory cytokines, whereas TRIF-dependent pathways are responsible for the induction of type I IFNs in addition to inflammatory cytokines (2). Another group of PRRs include RNA helicases, retinoic acid-inducible gene-I (RIG-I), and melanoma differentiation–associated gene 5 (MDA5), which recognize viral dsRNA in the cytoplasm and lead to the production of IFN-α/β (3–5).

Transduction of various signals, including those initiated from all PRRs, requires participation of TNFR-associated factors (TRAFs). TRAFs are intracellular signaling molecules that serve as both adaptor proteins and E3 ubiquitin ligases. TRAF1 and TRAF2 are constitutively associated and ubiquitously expressed together with TRAF3 and TRAF6 in most cell types, whereas expression of functional TRAF5 is mainly restricted to immune cells (6). K63-linked autoubiquitination of TRAF proteins is essential for the assembly of downstream signaling effectors. The engagement of TLR3 or TLR4 leads to TRIF-dependent K63-linked ubiquitination of TRAF3. This ubiquitinated TRAF3 is crucial for downstream activation of kinases TBK1 and IKKe that catalyze the phosphorylation of IFN regulatory factor 3 (IRF3) and subsequent induction of IFN-β (7–9). K63-linked ubiquitination of TRAF3 also plays a role in transduction pathways initiated from RIG-I and MDA5 by binding directly to activated mitochondrial antiviral signaling protein (MAVS) (10, 11). Thus, TRAF3 represents a key signaling molecule in multiple transduction pathways, and deficiency in this adapter molecule impairs IFN-α/IFN-β induction by TLR3, TLR4, TLR7/8, TLR9 (8, 9), RIG-I, and MDA5 (10). In addition to IRF3, type I IFNs are regulated by the transcription factor IRF7, which is activated upon stimulation of endosomal TLR7/8 and TLR9 in immune cells, leading to the generation of primarily IFN-α (10). Although the importance of type I IFNs in the innate immune response to viral infections is well characterized, their role during the course of bacterial infections is less clear.

Chlamydia pneumoniae is a Gram-negative, obligate intracellular bacterium that infects mucosal surfaces of the human respiratory tract, causing pneumonia, bronchitis, pharyngitis, and sinusitis. Epidemiological data suggest that most people are infected and reinfected throughout life (12). Therefore, C. pneumoniae represents an invader commonly encountered by respiratory defenses. The pathogen has also been associated with a variety of chronic diseases, such as reactive arthritis, sarcoidosis, asthma, chronic obstructive pulmonary disease, multiple sclerosis, Alzheimer’s disease, and atherosclerosis (13). However, the role of the pathogen in the course of chronic diseases is unknown. C. pneumoniae undergoes a developmental cycle in which two functionally and morphologically distinct cell types are recognized. The infectious cell type, which is specialized for extracellular survival and...
transmission, is termed the “elementary body”; the intracellular, vegetative cell type is called the “reticulate body.” Upon internalization of *C. pneumoniae* by a host cell, the bacterium proceeds with a developmental cycle that occurs entirely within a membrane-bound vesicle termed an “inclusion.” The chlamydial inclusion does not fuse or interact with endosomes or lysosomes during productive growth of the microorganism within an epithelial cell (14–16). Conversely, *C. pneumoniae* cannot escape the endosomal/lysosomal fusion upon invasion of an immune cell, such as a macrophage, where the pathogen is destined for degradation (17).

In this study, we demonstrate that *C. pneumoniae* has evolved a unique mechanism to disarm essential aspects of innate immunity. Unlike other chlamydial species, infection of epithelial cells with *C. pneumoniae* does not lead to IFN-β production. Moreover, the microorganism actively suppresses type I IFN induction, because infection interferes with stimulation of cells with polyinosinic-polycytidylic acid (poly[I:C]), the synthetic analog of dsRNA. Finally, we provide systematic evidence that *C. pneumoniae* targets TRAF3 for degradation. Therefore, *C. pneumoniae* infection blocks type I IFN induction by preventing phosphorylation and nuclear translocation of IRF3.

**Materials and Methods**

**Cell culture and organisms**

*C. pneumoniae*, AR-39 purchased from American Type Culture Collection (Manassas, VA), was propagated in HeLa cells and purified using MD-76R, as previously described (18). HeLa 229 and A549 cells were also obtained from American Type Culture Collection. Subconfluent monolayers of cells were infected with *C. pneumoniae*. AR-39 at the indicated multiplicity of infection (MOI) by incubation with chlamydial inoculum in a 37°C incubator for 2 h with occasional agitation. Chlamydial-infected and uninfected cells were cultured in RPMI 1640 (Invitrogen, Carlsbad, CA) for HeLa cells and F12K for A549 cells supplemented with 10% FBS (Sigma, St. Louis, MO) and in the presence of 1 mM sodium deoxycholate, and protease inhibitors (Roche, Indianapolis, IN). Precleared cell lysates were incubated with anti-HA Abs, followed by incubation with a 50% slurry of protein A-Sepharose (Sigma). The protein A-bound immunocomplexes were subjected to Western blot analysis and probed with anti-MAVS Abs, as described above.

**Coelectroporation of host and chlamydial cell lysates**

Uninfected HeLa cells transfected with HA-TRAF3 and pUNO-hIPS1 were lysed in RIPA buffer containing 50 mM Tris (pH 7.4), 150 mM NaCl, 1% Nonidet P-40, 0.1% SDS, 0.5% sodium deoxycholate, and protease inhibitors (Roche, Indianapolis, IN). Precleared cell lysates were incubated with anti-HA Abs, followed by incubation with a 50% slurry of protein A-Sepharose (Sigma). The protein A-bound immunocomplexes were subjected to Western blot analysis and probed with anti-MAVS Abs, as described above.

**ELISA**

Culture media of uninfected or *C. pneumoniae*–infected HeLa cells were collected at different time points p.i. and centrifuged at 20,000 × *g* for 10 min, and IFN-β was measured in supernatants using an ELISA kit (PBL, Piscataway, NJ), according to the manufacturer’s instructions. Uninfected or *C. pneumoniae*–infected A549 cells were either mock treated or transfected with 0.5 μg/ml poly(I:C) at 48 h, as described above. Culture media were collected 20 h posttransfection, and levels of IFN-β were quantified by ELISA. The Student *t* test was used to analyze data.

**Results**

**Infection of epithelial cells with *C. pneumoniae* does not induce IFN-β**

An IFN-β response elicited during productive infection of epithelial cells with *C. pneumoniae* has not been demonstrated. Buss et al. (20) reported that, in human endothelial cells, *C. pneumoniae* induce production of IFN-β via MAVS-dependent IRF3 and IRF7 activation during the first 16 h p.i. However, in that study, endothelial cells were infected with *C. pneumoniae* inoculum that had not undergone purification through diatrizoate meglumine plus diatrizoate sodium, formally known as renografin, described by Caldwell et al. (21). Instead, a crude *C. pneumoniae* preparation was used (20). Renografin purification of chlamydial organisms is routinely employed for all chlamydial species, because it removes significant amounts of cellular debris from lysed eukaryotic cells, as well as reticulate bodies, which are released with elementary bodies during sonication of infected cells at the end of the chlamydial cycle. Therefore, we compared IFN-β production during infection of HeLa cells with MD-76R (diatrizoate meglumine plus diatrizoate sodium) purified and crude *C. pneumoniae* inoculum using ELISA assays. Although IFN-β secretion was not detected in culture media obtained from cells infected with purified *C. pneumoniae*
at 16, 22, or 40 h p.i., the cytokine was clearly detected in media of cultures infected with crude inoculum (Fig. 1A). MD-76R–purified C. trachomatis, L2 at 40 h p.i. was included as a positive control. It is highly likely that the crude chlamydial inoculum contains ample amounts of cellular debris, including nucleic acid, which might be responsible for activation of host cells. Indeed, unlike purified C. pneumoniae, the crude inoculum contain high levels of the eukaryotic cytoplasmic protein Hsp90 and nuclear TATA box binding protein, TBBP (Fig. 1B). The lack of IFN-β production in cells infected with purified C. pneumoniae was further confirmed in A549 lung epithelial cells at 65 h p.i. (Fig. 1C). Moreover, in C. pneumoniae–infected cells transfected with poly(I:C), the production of IFN-β detected in the culture medium was inhibited by >50% compared with uninfected poly(I:C)-stimulated cells (Fig. 1C). The percentage reduction in the levels of IFN-β corresponded to the number of infected cells, because ~50–60% of cultures contained chlamydial inclusions (data not shown). These data demonstrate that infection of epithelial cells with purified, intact C. pneumoniae does not stimulate IFN-β production at any time p.i. and suggests that the microorganism actively impairs generation of IFN-β in infected cultures.

C. pneumoniae prevents IRF3 activation in infected cells

We further confirmed that C. pneumoniae inhibits IFN-β production in infected HeLa cells in which the infection of cells at an MOI of 1 is easily and consistently achievable. Stimulation of uninfected cells with poly(I:C) for 4 h caused significant cytotoxicity, which was detected by the presence of a large number of rounding cells compared with the mock-treated cells. This cytotoxic effect of poly(I:C) appeared to be greatly reduced in cultures infected with C. pneumoniae for 64 h (Fig. 2A). In epithelial cells, the induction of IFN-β is initiated upon phosphorylation and nuclear translocation of the transcription factor IRF3. Therefore, we examined the activation status of IRF3 in Chlamydia-infected cultures. As expected, the Ser396-specific phosphorylation of IRF3 was detected in uninfected cells transfected with poly(I:C) but not in quiescent cells. Interestingly, IRF3 phosphorylation was not detected in C. pneumoniae–infected cultures, even in cells stimulated with poly(I:C) (Fig. 2B). These data were further confirmed by probing of nuclear extracts for IRF3. Nuclear translocation of IRF3 was detected in uninfected cells and cells infected with C. trachomatis, L2 at 24 h p.i. but not in C. pneumoniae–infected cells at 64 h p.i. upon induction with poly(I:C) (Fig. 2C). C. trachomatis was included as a positive control, because infection of cultures with this chlamydial species induces expression of IFN-β (25). C. trachomatis–infected cells were harvested at 24 h p.i. because of the differences in chlamydial growth rate.

C. pneumoniae targets host TRAF3

In epithelial cells transfected with poly(I:C), the signaling cascade leading to IRF3 activation is primarily initiated from MDA5, which recognizes this dsRNA analog (26). Ligation of MDA5 to dsRNA leads to the recruitment of MAVS, followed by activation of TRAF3 through direct association with MAVS (10, 27). Formation of TRAF3-dependent K63-linked polyubiquitin chains in induced cells is essential for activation of TBK1-IKKε kinases that phosphorylate IRF3. Conversely, in cells treated with poly(I:C) in the absence of a transfecting reagent, the dsRNA enters the cell via endocytosis and initiates the TLR3-signaling pathway, leading to the activation of IRF3 and NF-κB (reviewed in Ref. 28). Interestingly, unlike with C. trachomatis, infection of cultures with C. pneumoniae in HeLa cells treated with poly(I:C) for 1 h in the absence of a transfecting reagent prevented phosphorylation of the cytoplasmic NF-κB inhibitor, IκBα, indicating that the pathogen is also capable of inhibiting signaling initiated from TLR3 (Fig. 3A). The transduction pathways initiated from both MDA5 and TLR3 converge at one critical signaling molecule, TRAF3. Indeed, in C. pneumoniae–infected and uninfected cells cotransfected with HA-TRAF3 and pUNO-hIPS1, TRAF3 was immunoprecipitated together with MAVS from uninfected cells but not from C. pneumoniae–infected cultures. The coprecipitation of TRAF3 and MAVS was detected in Chlamydia-infected cells treated with chloramphenicol, indicating that bacterial protein synthesis is required to prevent MAVS binding to TRAF3 (Supp-
Therefore, we analyzed TRAF3 levels during *C. pneumoniae* infection. In A549 cells, which contain detectable amounts of endogenous TRAF3, the infection with *C. pneumoniae* resulted in lower levels of the signaling molecule as early as 24 h p.i. compared with uninfected cells. This decrease in TRAF3 was detected throughout the course of infection (Fig. 3B). These results indicate that *C. pneumoniae* targets host TRAF3 during infection.

The possibility that *C. pneumoniae* may degrade TRAF3 was investigated in uninfected and chlamydiae-infected HeLa cells ectopically expressing HA-TRAF3. It was demonstrated that overexpression of TRAF3 does not activate any known transduction pathway (29). Whole-cell lysates were harvested at 64 h p.i. for *C. pneumoniae*-infected cells and at 24 h p.i. for *C. trachomatis*, L2–infected cells and probed with TRAF3-specific Ab. In contrast with uninfected and *C. trachomatis*–infected cells, this signaling molecule was not readily detectable in *C. pneumoniae*–infected cultures (Fig. 4A), raising the possibility that TRAF3 is degraded. We performed transcriptional analysis of TRAF2, TRAF3, and TRAF5 in uninfected and *C. pneumoniae*–infected HeLa cells to rule out the possibility of alterations at the transcriptional level. Indeed, the mRNA message of all of the analyzed genes, including TRAF3, was not lower than in uninfected cultures (Supplemental Fig. 2). Furthermore, we examined the overexpression of TRAF3 in *C. trachomatis*, serovar D–infected cells; the levels of the signaling molecule remained unaltered (Supplemental Fig. 3). Therefore, the apparent TRAF3 degradation was a *C. pneumoniae*–specific phenomenon requiring bacterial translation (Fig. 4A). The levels of TRAF3 degradation correlated with the number of cells infected with *C. pneumoniae*, because more TRAF3 was detected at a lower MOI (Fig. 4B). Conversely, the ectopic expression of TRAF2 in HeLa cells was unaffected by *C. pneumoniae* or *C. trachomatis* (Fig. 4C).

### Treatment of infected cells with protease inhibitors does not prevent *C. pneumoniae*–induced TRAF3 degradation

TRAF3 is an adaptor protein that also acts as an E3 ubiquitin ligase, a function essential for K63-linked autoubiquitination (30), whereas K48-linked ubiquitylation of TRAF3 marks this signaling molecule for proteasome-dependent degradation (31, 32). Interestingly, only K63-linked polyubiquitin chains are stimulated directly by TRAF3, whereas other cytoplasmic E3 ligases execute K48-linked ubiquitination (30, 33). It was recently demonstrated...
that TRAF3 degradation in A549 cells is mediated by the E3 ligase Triad3A and is prevented by the proteasome inhibitors lactacystin and MG132 (33). Therefore, we investigated whether the degradation of TRAF3 during infection of epithelial cells with *C. pneumoniae* depends on the host proteasome. Uninfected and *C. pneumoniae*–infected HeLa cells ectopically expressing TRAF3 were treated with lactacystin for 15 h. None of the lactacystin concentrations tested prevented TRAF3 degradation in *C. pneumoniae*–infected cells (Fig. 5A). We were unable to exploit the alternative proteasome inhibitor MG132 in this assay, because treatment of cultures with MG132 for 15 h resulted in toxicity and cell death (data not shown). Instead, we used a cell-free lysates approach (24) to further investigate the mechanism of TRAF3 degradation. A total of 5 × 10^6 uninfected HeLa cells expressing TRAF3 was lysed using a Parr Cell Disruption Bomb, and the cell lysates were coincubated for 1 h with different amounts of *C. pneumoniae* lysates in the presence or absence of 20 µM MG132. The level of TRAF3 degradation was detected by probing immunoblots with anti-TRAF3 mAb. Probing with anti-actin was used as a loading control.

**Discussion**

Type I IFNs are pleiotropic cytokines secreted by a variety of cells and are known to act in an autocrine, as well as paracrine, manner. Type I IFNs are primarily composed of multiple IFN-α subtypes and a single IFN-β and represent an essential component of the innate immune response to viral infections in humans. Secreted IFNs mediate antimicrobial activities by binding the IFN-α/β receptor (IFNAR), leading to heterodimerization of STAT1 and STAT2. The heterodimer forms a complex with IRF9 and is translocated into the nucleus where it interacts with the IFN-stimulated response element. This ultimately drives the induction of transcription of type I IFN–responsive genes. The importance of type I IFNs in the innate response to numerous viruses is well

**FIGURE 4.** *C. pneumoniae* degrade host TRAF3. (A) Whole-cell lysates of uninfected and *C. pneumoniae*–infected at 64 h p.i., or *C. trachomatis*–infected at 24 h p.i. HeLa cells transfected with HA-TRAF3. Immunoblots were probed with anti-TRAF3 Abs. (B) *C. pneumoniae* cultures infected at an MOI of 1 or 0.5 and uninfected cells were transfected with HA-TRAF3. Resolved material was probed with anti-TRAF3 mAb. (C) Uninfected and chlamydial-infected HeLa cells transfected with Flag-TRAF2 were probed with anti-Flag mAb. Immunoblots probed with anti-actin were used as a loading control.

**FIGURE 5.** Degradation of TRAF3 is not inhibited by lactacystin or MG132. (A) Uninfected HeLa cells and cells infected with *C. pneumoniae* were transfected with HA-TRAF3 and treated with different concentrations of lactacystin for 15 h. Immunoblots were probed with anti-TRAF3 and anti-TRAF2 Abs. (B) Uninfected cells transfected with HA-TRAF3 were disrupted using a Parr Cell Disruption Bomb (1500 psi/5 min). HeLa cell lysates were coincubated with various amounts of *C. pneumoniae* lysates in the presence of absence of 20 µM MG132. The level of TRAF3 degradation was detected by probing immunoblots with anti-TRAF3 mAb. Probing with anti-actin was used as a loading control.

**FIGURE 6.** *C. pneumoniae* inhibits multiple signaling pathways by degradation of TRAF3. Upon stimulation of either MAVS- or TRIF-dependent signaling pathways, *C. pneumoniae* interferes with the signaling cascade by targeting host TRAF3. This prevents transduction of the inducing signal to IRF3, thereby suppressing the IFN-β response.
established. Although type I IFNs are induced, the role of this cytokine during the course of bacterial infections is less-well defined.

TRAF3 is a key signaling molecule involved in multiple pathways that lead to generation of type I IFNs and is essential for the innate immune response to a broad range of infections. K63-linked autoubiquitination of TRAF3 is crucial for activation of IRF3 upon induction of cells with numerous stimuli. However, the signaling molecule also plays an important role as a negative regulator of various transduction pathways (31). For instance, in quiescent cells, TRAF3 binds to NF-kB inducing kinase. Upon induction of the noncanonical NF-kB pathway, TRAF3 undergoes nself-mediated K48-linked ubiquitination and proteosomal degradation, releasing NF-kB inducing kinase, which results in phosphorylation of IKKα and p100 (NF-kB2) processing (34). Furthermore, degradative ubiquitination of TRAF3 is also required for MyD88-independent MAPK activation (30). Although C. pneumoniae inhibits induction of IFN-β upon MDA5 and TLR3 engagement (Fig. 6), it is highly likely that by targeting TRAF3, the pathogen modulates a great number of transduction pathways within its eukaryotic host.

The majority of data describing chlamydial infections and IFN production comes from in vitro and in vivo studies with Chlamydia muridarum. C. muridarum is a murine pathogen that has been established as a mouse model of genital infection because it shares many aspects of acute genital infection with C. trachomatis in women (35). The production of type I IFNs in mice infected with C. muridarum appeared to be more beneficial to the microorganism than to the host. IFNAR−/− mice were able to resolve genital infection faster and displayed reduced pathology in the oviduct compared with wild-type (WT) mice (36). In C. muridarum–infected mouse macrophages, the expression of IFN-β was induced in a MyD88-dependent manner, yet the survival of chlamydial infection is more transmissible to chlamydial survival in macrophages obtained from WT mice (37). Conversely, IFN-β production in mouse oviduct epithelial cells was primarily TLR3 dependent (i.e., MyD88 independent) (38). The production of IFN-β was also described in McCoy cells infected with C. trachomatis, serovar L2 (39), and Kad et al. (25) detected significant upregulation of IFN-β gene expression in C. trachomatis–infected HeLa cells. Unlike with C. muridarum, no difference in chlamydial burden was detected in lungs of WT, IFNAR−/−, and IRF3−/− mice infected with C. pneumoniae (40). A great number of studies described diverse effects of C. pneumoniae on various cell types in vitro, including the production of IFN-β in endothelial cells (20). However, it is absolutely essential to clearly distinguish whether the observed effects are caused directly by the pathogen or by cellular debris that may enter the host cell together with the bacterium. Furthermore, it is important to differentiate between immune responses to productive chlamydial growth and chlamydial degradation when C. pneumoniae cannot avoid fusion with the lysosomal pathway within an infected cell (17). In this study, we demonstrated that during productive infection of human epithelial cells with purified, intact C. pneumoniae, the pathogen does not induce production of IFN-β. Furthermore, C. pneumoniae induces species-specific degradation of the host signaling molecule TRAF3, thereby preventing activation of IRF3. The impaired transduction pathway initiated from MDA5 was detected in epithelial cell lines, such as HeLa, A549, but also in HEK 293 cells (data not shown), all of which support C. pneumoniae growth, and the levels of inhibition corresponded closely to the number of infected cells. Chlamydial protein synthesis was required for all of the events caused by the bacterium. In addition, the treatment of C. pneumoniae–infected cells with the proteasomal inhibitors lactacystin and MG132 did not prevent TRAF3 degradation; coincubation of chlamydial and host cell lysates resulted in degradation of the signaling molecule, suggesting that C. pneumoniae utilizes a species-specific protease that targets TRAF3. Although chlamydiae reside within membrane-bound inclusions during their intracellular growth, insertion of chlamydial proteins into the inclusion membrane, as well as secretion of chlamydial effectors into the host cytoplasm, is essential for successful exploitation of the eukaryotic cell. Chlamydiae use sophisticated strategies to evade host immune responses. C. trachomatis and C. pneumoniae secrete a serine protease designated chlamydial protease/proteasome–like activity factor (CPAF) into the host cytosol. CPAF is responsible for degradation of several eukaryotic components, but it primarily targets the regulatory factor X5 and upstream stimulation factor 1, both of which are required for MHC Ag expression (41). Moreover, chlamydiae employ a Tail-specific protease that cleaves the p65/RelA subunit of NF-kB1 into 40- and ~22-kDa fragments, preventing NF-kB activation during chlamydial infection (24). Due to inability of CPAF and Tail-specific protease to cleave their respective targets in 8 M urea, the target specificity of these two chlamydial proteases was recently questioned (23). We detected the degradation of TRAF3 even in the presence of 8 M urea (Figs. 3, 4), which suggests that targeting of the signaling molecule is not an artifact of postlysosome degradation. Our data represent a critical shift in understanding C. pneumoniae pathogenesis. Although it is postulated that the pathogen elicits numerous proinflammatory responses by host cells, we propose that, during productive infection with purified C. pneumoniae, the bacteria actively modify and impair the host immune system, which prevents or significantly delays chlamydial recognition and efficient elimination. Indeed, C. pneumoniae seems to utilize species-specific strategies that are comparatively more efficient than those used by C. trachomatis to avoid or delay recognition by the host innate immunity. It was established that C. pneumoniae intercepts the signaling pathway from IL-17R in IL-17–stimulated epithelial cells by sequestering the adaptor molecule Act1 to the chlamydial inclusion membrane (42). The degradation of TRAF3 represents another unique tactic of C. pneumoniae that may significantly contribute to protracted or asymptomatic respiratory infections and/or chronic infections associated with this pathogen.

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Disclosures

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