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REVIEW

Taking control: reorganization of the host cytoskeleton by Chlamydia [version 1; referees: 5 approved]

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Abstract
Both actin and microtubules are major cytoskeletal elements in eukaryotic cells that participate in many cellular processes, including cell division and motility, vesicle and organelle movement, and the maintenance of cell shape. Inside its host cell, the human pathogen Chlamydia trachomatis manipulates the cytoskeleton to promote its survival and enhance its pathogenicity. In particular, Chlamydia induces the drastic rearrangement of both actin and microtubules, which is vital for its entry, inclusion structure and development, and host cell exit. As significant progress in Chlamydia genetics has greatly enhanced our understanding of how this pathogen co-opts the host cytoskeleton, we will discuss the machinery used by Chlamydia to coordinate the reorganization of actin and microtubules.
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Introduction

The Chlamydiaceae constitute a family of obligate intracellular bacteria that encompasses numerous species. With ~92 million new cases/year worldwide, Chlamydia trachomatis is the most frequent cause of bacterial sexually transmitted infections and is the leading cause of preventable infectious blindness called trachoma1-3. Trachoma is a significant problem in the developing world, where access to healthcare is limited and antibiotics are scarce. Chlamydia infections are also associated with chronic diseases and increased risk for cervical cancer4, making this infection a significant socioeconomic and medical burden in both developed and developing countries.

Chlamydiaceae exhibit a unique biphasic life cycle, cycling between a metabolically inactive but infectious small elementary body (EB ~200 nm) and a noninfectious metabolically active and dividing large reticulate body (RB ~800 nm). Chlamydia spends the majority of its life as an intracellular RB. Soon after invasion, EBs differentiate into RBs and replicate within a membrane-bound compartment called an “inclusion”. This obligate intracellular lifestyle required Chlamydia to develop an effective strategy to manipulate host cell pathways in order to ensure its survival and replication. Among the many pathways that Chlamydia co-opts, a common and intriguing target for all Chlamydia species has emerged: the host cytoskeleton. We will discuss the recent advances concerning the role played by the host cytoskeleton in the growth and structural maintenance of the chlamydial inclusion (see Figure 1).

Chlamydia trachomatis recruits actin to enter its host cell and uses microtubules to travel to the microtubule-organizing center

Because of their obligate intracellular nature, Chlamydiae have evolved very efficient ways to enter eukaryotic cells (Figure 1A). During infection, EBs attach to the host cell surface via a relatively weak electrostatic interaction with heparan sulfate moieties5. Then a stronger and more specific binding to a cellular receptor takes place, during which the majority of the EBs are internalized via an actin-dependent event6. While a number of receptors have been identified, including PDGFR β, β1-integrin, and Ephrin A2, depletion of a single receptor is not sufficient to block entry, suggesting that Chlamydia utilizes more than one receptor to invade its host cell7,8.

To promote entry into non-phagocytic epithelial cells, C. trachomatis delivers a translocated actin-recruiting phosphoprotein (Tarp, also known as CT456)9-11 into the host cytoplasm (Figure 1A). In a phosphorylation-dependent manner, Tarp recruits guanine nucleotide exchange factors that activate Rac1, a member of the Rho family of GTPases12-14, within the phosphorylation-activated Rac1 cassette cavae uses both Rac1 and Cdc42 to promote its entry, C. trachomatis recruits only Rac1, and not Cdc42 or RhoA15,16. Hijacking only one Rho GTPase family member is unique to C. trachomatis, as other intracellular bacteria including Salmonella and Shigella usually use multiple isoforms such as RhoA and Cdc4217-30. In addition to its Rac1 recruitment function, Tarp also directly binds to actin monomers and nucleates new unbranched actin filaments31,32. These linear filaments are then branched via the host Arp2/3 complex, which is activated by the Rac1 signaling pathway33,34. Thus, Tarp functions as both an actin nucleator and a signaling platform to locally remodel the actin cytoskeleton and promote Chlamydia invasion.

Nascent C. trachomatis-containing inclusions then use the minus-end-directed microtubule motor dynein to move from the cell periphery to the microtubule-organizing center (MTOC), where the inclusion resides for the duration of the life cycle35 (Figure 1B). This is a pathogen-driven event in which the inclusion protein CT850 is involved through its interaction with the dynein light chain DYNLT136. At the MTOC, Src family kinases control the tight association between inclusions and centrosomes37. Additional inclusion proteins including IncB, CT101, and CT222 are concentrated at these contact points between inclusions and centrosomes, suggesting their potential contribution to the transport of the inclusion38. In fact, during Chlamydia psittaci infection, IncB has been shown to interact with Snapin, which also binds dynein, thus connecting the inclusion to the microtubule network39. The association of inclusions with the MTOC is a common characteristic for a number of Chlamydia species, suggesting that this event is essential for Chlamydia’s life cycle. One possibility is that the MTOC brings host organelles and chlamydial inclusions in close proximity, thus facilitating the transfer of nutrients and lipids from the host to the inclusion. Additionally, the clustering of the inclusions at the MTOC is necessary for the homotypic fusion of inclusions to take place during C. trachomatis infection, as the dissociation of the inclusions from the MTOC inhibits this fusion event40. Homotypic fusion is critical for C. trachomatis pathogenicity, as non-fusing mutants grow significantly slower than their wild-type counterparts33,41. In particular, C. trachomatis strains that do not undergo homotypic fusion are also replication-defective and cause significantly milder disease in humans42-45. Given the importance of microtubule-based transport of the inclusion in Chlamydia development, additional unidentified Chlamydia effectors are likely involved in this process.

Chlamydia creates microtubule cages to support the development of its inclusion

Around 12 hours post-infection (PI), microtubules likely assemble around the inclusion under the control of the chlamydial effector CT223/IPAM, which has been shown to alter microtubule organization through the host centrosomal protein of 170 kDa (CEP170) in transfected cells46 (Figure 1C). There, microtubules encasing the inclusion are stabilized, which allows them to undergo post-translational modifications (PTMs), including detyrosination and acetylation47,48 (Figure 1D). These PTMs influence microtubule structure and depolymerization rates49 and have been implicated in the relocation of the Golgi apparatus around the chlamydial inclusion50,51. In most cells, dynamic microtubules have a half-life of about 5–10 minutes, while modified microtubules can persist for hours52, suggesting that Chlamydia utilizes these PTM microtubules to establish a stable long-term relationship with its host. Detyrosination is the best-characterized modification and involves the removal of the carboxy-terminal tyrosine from α-tubulin by tubulin carboxypeptidase, thus exposing a glutamic acid as the new C-terminus53.
Figure 1. Reorganization of the host cytoskeleton during Chlamydia trachomatis infection. (A) Entry during which a translocated actin-recruiting phosphoprotein (Tarp) induces actin polymerization; (B) transport of the nascent inclusion to the microtubule-organizing center (MTOC) using CT850; (C) formation of microtubule cages around the inclusion, in which CT223 is likely involved, and microtubule-dependent movement of lipid droplets (LDs) and multi-vesicular bodies (MVBs) towards the inclusion; (D) post-translational modifications of microtubule cages and positioning of Golgi mini-stacks around the inclusion controlled by CT813/InaC; (E) structural scaffolds of actin, septins, and intermediate filaments reinforce the growing inclusion membrane in a CT813-dependent manner; (F) Chlamydia exits the host cell using CT228-dependent extrusion (left) or through cell lysis (right).

Interestingly, stable microtubules are involved in the repositioning of organelles. During infection, the Golgi is a major source of host lipids, including sphingomyelin and cholesterol. To enhance access to these lipids, Chlamydia induces the fragmentation of the Golgi into mini-stacks, which are then recruited around the inclusion in a microtubule-dependent manner. In addition to controlling Golgi positioning, detyrosinated microtubules are involved in other trafficking events, including the recycling of endocytosed transferrin and the dispersal of lipid droplets, which are also co-opted by Chlamydia. Lipid droplets and multi-vesicular bodies are redirected towards the chlamydial inclusion along microtubules to provide fatty acids, which are important for Chlamydia replication. The endoplasmic reticulum (ER) has also been associated with stable microtubules, in particular acetylated microtubules, along which ER tubules slide. Chlamydia hijacks the ER and promotes the formation of ER-inclusion contact sites, which are important for the transfer of lipids.
of lipids to the inclusion. During *Chlamydia* infection, the acetylated microtubules that surround the inclusion could enable the ER to slide towards the inclusion, thus allowing IncD/CERT to interact with the ER-resident proteins VAPA/VAPB and form ER-inclusion contact sites. Although treatment with nocodazole, which disrupts microtubules, failed to prevent ER accumulation around the inclusion, acetylated microtubules are notoriously resistant to nocodazole treatment and may still be present following treatment.

Recently, we have shown that the chlamydial protein CT813 (also called InaC) is critical for promoting microtubule modifications during infection through its interaction with and activation of the small host GTPases ARF1 and ARF4, supporting prior data showing interactions between CT813 and ARF proteins (Figure 1D). It is unclear how the CT813:ARF complex is able to influence microtubule PTMs. However, inhibitors of RhoA and ROCK (Rho-associated protein kinase) decrease the number of inclusions associated with stable microtubules, suggesting that both of these proteins are involved in this process.

There is evidence demonstrating that RhoA triggers microtubule stabilization via its interaction with the mammalian homolog of Diaphanous (mDia). The activation of mDia generates capped microtubules, thus preventing catastrophic microtubule disassembly. Interestingly, DIAPH2 was identified in an RNAi screen in Drosophila S1 cells as important for chlamydial inclusion development. It would be interesting to determine whether *C. trachomatis* co-opts mDia to stabilize microtubules and generate the post-translationally modified microtubule cages around the inclusion, particularly since mDia is also involved in actin polymerization.

**Chlamydia trachomatis builds actin scaffolds around its inclusion to promote inclusion stability**

As the inclusion continues to grow, actin and intermediate filaments associate with the inclusion (Figure 1E). This association increases progressively from ~20 hours PI until the end of *Chlamydia*s intracellular life cycle. Disruption of the actin cytoskeleton results in the rupture of the inclusion membrane and the leakage of *C. trachomatis* into the host cytoplasm, demonstrating that the maintenance of the inclusion’s integrity requires intact actin cages. Interestingly, RhoA—but not ROCK—also plays a major role in this event, as it is recruited to the inclusion and its depletion results in a substantial loss of actin scaffolds around the inclusion.

The chlamydial protein CT813 is the only effector identified to date to regulate actin recruitment around the inclusion (Figure 1E). Interestingly, this function of CT813 appears to be independent of its role in regulating post-translationally modified microtubule cages, as the overexpression of CT813 in wild-type *Chlamydia* results in the loss of post-translationally modified microtubules but not actin cages. Together, these data suggest that both CT813 and RhoA participate in actin cage formation and microtubule stabilization. While microtubule stabilization also depends on ARF1/ARF4 and ROCK, actin polymerization does not require ROCK. The role of ARF in the formation of actin cages remains unclear, as depletion of ARF does not affect actin polymerization.

Recently, the actin cytoskeleton has been implicated in Golgi reorganization during infection. Using chemical mutagenesis, it has been suggested that CT813 organizes Golgi mini-stacks around the inclusion through the formation of actin cages. However, a CT813-overexpressing *Chlamydia* strain that has actin but no post-translationally modified microtubule cages displays a defect in Golgi organization around the inclusion. This suggests that it is the CT813-dependent induction of post-translationally modified microtubule cages that controls Golgi organization. Therefore, the exact role of the actin cytoskeleton in organelle repositioning during *Chlamydia* infection is still unclear.

**Chlamydia uses the actin cytoskeleton to exit host cells by extrusion**

*Chlamydia* exits the host cell through two mutually exclusive mechanisms: extrusion and cell lysis (Figure 1F, left and right, respectively). Note that to exit their host cells using the lytic process, *Chlamydia* must extricate themselves from the cytoskeleton structures that encase the inclusion, in particular the actin scaffold. Pgp4, a transcription factor encoded by the chlamydial plasmid, is essential for actin depolymerization prior to cell exit, as the deletion of this regulatory gene prevents actin disassembly and completely blocks *Chlamydia* exit. The chlamydial protease activity factor, which cleaves intermediate filaments, is also involved in cell exit, but it does not play a role in actin disassembly.

While the lytic pathway requires actin depolymerization to proceed, extrusion is regulated by an acto-myosin-mediated mechanism. Extrusion involves the protrusion of the intact membrane-bound inclusion out of the cell and the pinching off of the inclusion into a separate compartment. The resulting extruded inclusion is surrounded by the actin cytoskeleton, the host plasma membrane, and a thin layer of cytoplasm between plasma and inclusion membranes. Extrusion requires N-WASP-mediated actin polymerization and myosin II-dependent contraction of stable actin filaments. The septin family of cytoskeletal proteins regulates actin fiber formation on the inclusion membrane through an unknown mechanism. Interestingly, RhoA is also involved in this process, where it specifically regulates the final stage of extrusion—pinching off and separation of the extrusion from the host cell.

The signals that dictate whether *Chlamydia* exits the host cell by lysis or extrusion are not well understood. However, the Chlamydial inclusion protein CT228 has been shown to play a central role in this process. CT228 recruits the MYPT1 subunit of myosin phosphatase to microdomains on the inclusion membrane early during infection. MYPT1-mediated phosphorylation of myosin light chain II (MLC2) favors extrusion-mediated exit, while the depletion or dephosphorylation of MLC2 shifts the balance.
towards the lytic pathway. Thus, *Chlamydia* establishes local cytoskeletal signaling networks on the inclusion membrane to direct its escape from the host cell.

Concluding remarks

*Chlamydia* has evolved efficient mechanisms to hijack essential components of the host cytoskeleton. The successful establishment of *Chlamydia*’s intracellular niche and dissemination of infectious progeny relies on the proper spatial and temporal control of both actin and microtubules. To orchestrate this balance, *Chlamydia* employs effector proteins to recruit host proteins to the inclusion membrane and modulate the activity of host cytoskeletal signaling networks. Recent work has only begun to shed light on the identity of these chlamydial effector proteins. Recent advances in *Chlamydia* genetics and the expansion of the *Chlamydia* genetic toolbox now provide the tools necessary to dissect the molecular pathways and the chlamydial effectors that control the interactions between the chlamydial inclusion and the host cytoskeleton. Identifying these mechanisms is important not only for understanding *Chlamydia* pathogenesis and developing novel therapeutics but also because it has the potential to identify new host cellular pathways that regulate the cytoskeleton.

Competing interests

The authors declare that they have no competing interests.

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References

1. WHO: World Health Organization: Global prevalence and incidence of selected curable sexually transmitted infections overview and estimates. Geneva, WHO. 2005.
2. Gerbase AC, Rowley JT, Mertens TE: Global epidemiology of sexually transmitted diseases. *Lancet* 1998; 351 Suppl 3: 2–4. PubMed Abstract | Publisher Full Text
3. CDC: Sexually Transmitted Disease Surveillance 2011. Atlanta: US Department of Health and Human Services. 2012: 1–184. Reference Source
4. Romano Carratelli C, Nuzzo I, Cozzolino D, et al.: Relationship between *Chlamydia pneumoniae* infection, inflammatory markers, and coronary heart diseases. *Int Immunopharmacol.* 2006; 6(5): 848–53. PubMed Abstract | Publisher Full Text
5. Ezzahren R, Stassen FR, Kuvvers HR, et al.: *Chlamydia pneumoniae* infections augment atherosclerotic lesion formation: a role for serum amyloid P. *APMIS.* 2006; 114(2): 117–26. PubMed Abstract | Publisher Full Text
6. Abdelrahman YM, Belland RJ: The chlamydial developmental cycle. *FEMS Microbiol Rev.* 2005; 29(5): 949–59. PubMed Abstract | Publisher Full Text
7. Scicluna MA: Recent advances in *Chlamydia* subversion of host cytoskeletal and membrane trafficking pathways. *Microbes Infect.* 2011; 13(6): 527–35. PubMed Abstract | Publisher Full Text | Free Full Text
8. Su H, Raymond L, Rockey DD, et al.: A recombinant Chlamydia trachomatis major outer membrane protein binds to heparan sulfate receptors on epithelial cells. *Proc Natl Acad Sci U S A.* 1996; 93(20): 11143–8. PubMed Abstract | Publisher Full Text | Free Full Text
9. Carabeo RA, Grieshaber SS, Fischer E, et al.: *Chlamydia trachomatis* induces remodeling of the actin cytoskeleton during attachment and entry into HeLa cells. *Infect Immun.* 2002; 70(7): 3793–803. PubMed Abstract | Publisher Full Text | Free Full Text
10. Ewelt CA, Cesaay A, Kim JH, et al.: RNA interference screen identifies Abi kinase and PDGFR signaling in *Chlamydia trachomatis* entry. *PLoS Pathog.* 2008; 4(3): e1000211. PubMed Abstract | Publisher Full Text | Free Full Text
11. Subbarayal P, Kanukakaran K, Winkler A, et al.: Ephrin A2 receptor (EphA2) is an invasion and intracellular signaling receptor for *Chlamydia trachomatis*. *PLoS Pathog.* 2015; 11(4): e1004846. PubMed Abstract | Publisher Full Text | Free Full Text | *F1000 Recommendation*
12. Clifton DR, Fields KA, Grieshaber SS, et al.: A chlamydial type III translocated protein is tyrosine-phosphorylated at the site of entry and associated with recruitment of actin. *Proc Natl Acad Sci U S A.* 2004; 101(27): 10166–71. PubMed Abstract | Publisher Full Text | Free Full Text | *F1000 Recommendation*
13. Jewett TJ, Miller NJ, Dooley CA, et al.: The conserved Tarp actin binding domain is important for chlamydial invasion. *PLoS Pathog.* 2010; 6(7): e1000997. PubMed Abstract | Publisher Full Text | Free Full Text
14. Parrett CJ, Lenoci RV, Nguyen B, et al.: Targeted Disruption of *Chlamydia trachomatis* Invasion by In Trans Expression of Dominant Negative Tarp Effectors. *Front Cell Infect Microbiol.* 2016; 6: 84. PubMed Abstract | Publisher Full Text | Free Full Text | *F1000 Recommendation*
15. Jewett TJ, Alvarado S, Ohr RJ, et al.: Analysis of *Chlamydia trachomatis* Tarp harbors distinct G and F actin binding domains that bundle actin filaments. *J Bacteriol.* 2013; 195(4): 708–16. PubMed Abstract | Publisher Full Text | Free Full Text
16. Carabeo RA, Grieshaber SS, Hasenkamp A, et al.: Requirement for the Rac GTPase in *Chlamydia trachomatis* invasion of non-phagocytic cells. *Traffic.* 2004; 5(6): 418–25. PubMed Abstract | Publisher Full Text
17. Subtil A, Wyplosz B, Baláša ME, et al.: Analysis of *Chlamydia* caviar entry sites and involvement of Cdc42 and Rac activity. *J Cell Sci.* 2004; 117(Pt 17): 3923–33. PubMed Abstract | Publisher Full Text
18. Hänisch J, Köhn R, Wozniczka M, et al.: Activation of a RhoA/myosin II-dependent but Arp2/3 complex-independent pathway facilitates Salmonella invasion. *Cell Host Microbe.* 2011; 9(4): 273–85. PubMed Abstract | Publisher Full Text | *F1000 Recommendation*
19. Suzuki T, Mimuho H, Miki H, et al.: Rho family GTPase Cdc42 is essential for the actin-based motility of *Shigella* in mammalian cells. *J Exp Med.* 2000; 191(11): 1905–20. PubMed Abstract | Publisher Full Text | Free Full Text
34. Al-Zeer MA, Al-Younes HM, Kerr M, Suchland RJ, Rockey DD, Bannantine JP, Pannekoek Y, van der Ende A, Eijk PP, Pannekoek Y, Spaargaren J, Langerak AA.

29. Mital J, Hackstadt T: Salmonella Peris L, Wagenbach M, Lafanechère L, Jewett TJ, Fischer ER, Mead DJ, et al.

28. Pannekoek Y, Spaargaren J, Langerak AA, Mital J, Hackstadt T: Salmonella Peris L, Wagenbach M, Lafanechère L, Jewett TJ, Fischer ER, Mead DJ, et al.

26. Patel JC, Galán JE: 2013; 104: 716–27.

25. Mital J, Hackstadt T: 2013; 104: 716–27.

24. Mital J, Lutter EI, Barger AC, et al.: Chlamydia trachomatis inclusion membrane protein CT850 interacts with the dynexin light chain DYNLT1 (Tectex). Biochem Biophys Res Comum. 2015; 462(2): 165–70.

23. Richards TS, Knowton AE, Grisheber SS: Chlamydia trachomatis homotypic inclusion fusion is promoted by host microtubule trafficking. BMC Microbiol. 2013; 13: 185.

22. Parnekov Y, Spaargaren J, Langerak AA, et al.: Interrelationships between polymorphisms of incA, fusogenic properties of Chlamydia trachomatis strains, and clinical manifestations in patients in The Netherlands. J Clin Microbiol. 2005; 43(5): 2441–5.

21. Suchland RJ, Rockey DD, Bannantine JP, et al.: Isolates of Chlamydia trachomatis that occupy nonfusogenic inclusions lack IncA, a protein localized to the inclusion membrane. Infect Immun. 2001; 69(7): 4564–6.

20. Patel JC, Galán JE: 2013; 104: 716–27.

19. Gundersen GG, Maxfield FR: Cell dynein to traffic to the microtubule-organizing center in a p50 dynamitin-nucleator of actin. J Cell Sci. 2001; 114(24): 9040–4.

18. Mital J, Hackstadt T: Salmonella Peris L, Wagenbach M, Lafanechère L, Jewett TJ, Fischer ER, Mead DJ, et al.

17. Patel JC, Galán JE: 2013; 104: 716–27.

16. Mead DJ, Patel JC, Galán JE: 2013; 104: 716–27.

15. Harms A, Bosch M, Reddy BJ, et al.: AMPK activation promotes lipid droplet dispersion on detyrosinated microtubules to increase mitochondrial fatty acid oxidation. Nat Commun. 2015; 6: 7176.

14. Coccioha JL, Kumar Y, Fischer ER, et al.: Cytoplasmic lipid droplets are translocated into the lumen of the Chlamydia trachomatis parasitophorous vacuole. Proc Natl Acad Sci U S A. 2008; 105(27): 9379–84.

13. Giambarbera T, Capmany A, Romao M, et al.: The late endocytic Rab39a GTPase regulates the interaction between multivesicular bodies and chlamydial inclusions. J Cell Sci. 2015; 128(16): 3068–81.

12. Friedman JR, Webster BM, Mastronarde DN, et al.: ER sliding dynamics and ER-membrane contacts occur on acetylated microtubules. J Cell Biol. 2010; 190(3): 363–70.

11. Faiers M, Dunn JD, Graneke JA, et al.: Integrating chemical mutagenesis and whole-genome sequencing as a platform for forward and reverse genetic analysis of Chlamydia. Cell Host Microbe. 2015; 17(5): 716–25.

10. Agaisse H, Derré I: STIM1 is a Novel Component of ER-Chlamydia trachomatis Inclusion Membrane Contact Sites. PLoS One. 2015; 10(4): e0125671.

9. Copeland JW, Treisman R: 2014; 5: 145–58.

8. Herms A, Bosch M, Reddy BJ, et al.: Actin intermediate filaments stabilize the Chlamydia trachomatis vacuole by forming dynamic structural scaffolds. Cell Host Microbe. 2008; 4(2): 169–69.

7. Kokes M, Dunn JD, Graneke JA, et al.: Mapping and characterizing the host protein network in Chlamydia trachomatis infection. Nat Rev Mol Cell Biol. 2001; 3(8): 723–9.

6. Palazzo AF, Cook TA, Alberts AS, et al.: mDia mediates Rho-regulated formation and orientation of stable microtubules. Nat Cell Biol. 2001; 3(8): 723–9.

5. Mita J, Lutter EI, Barger AC, et al.: A Chlamydia effector recruits CEP170 to reprogram host microtubule organization. J Cell Sci. 2015; 128(18): 3420–34.

4. Pannekoek Y, Spaaranger J, Langerak AA, et al.: Normal IncA expression and fusogenicity of inclusions in Chlamydia trachomatis. Infect Immun. 2001; 69(7): 4564–6.

3. Parnekov Y, van der Ende A, Eijk PP, et al.: Normal IncA expression and fusogenicity of inclusions in Chlamydia trachomatis isolates of the incA477T mutation. Infect Immun. 2001; 69(7): 4564–6.

2. Suchland RJ, Rockey DD, Bannantine JP, et al.: Isolates of Chlamydia trachomatis that occupy nonfusogenic inclusions lack incA, a protein localized to the inclusion membrane. Infect Immun. 2001; 69(7): 4564–6.

1. Lutter EI, Barger AC, Nair V, el al.: F1000Research 2017, 6(F1000 Faculty Rev):2058 Last updated: 01 DEC 2017

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