

PLOS Science Wednesday: Hi reddit, we're Johannes and Katja, and our research investigates the molecular processes that help chlamydiae pathogenic bacteria infect human hosts – Ask us Anything!

PLOSScienceWednesday¹ and r/Science AMAs¹

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Abstract

Hi Reddit, My name is Johannes Hegemann and I am Professor of Microbiology and Head of the Institute for Functional Microbial Genomics at the Heinrich-Heine-University in Düsseldorf, Germany. And my name is Katja Mölleken and I am a Senior Postdoctoral Fellow at the Institute for Functional Microbial Genomics at the Heinrich-Heine-University in Düsseldorf, Germany. Our research focuses on the molecular mechanisms that enable the pathogenic bacteria *Chlamydia trachomatis* and *Chlamydia pneumoniae* to infect their human hosts. This month, we published a study titled “Acquisition of Rab11 and Rab11-Fip2 – A novel strategy for *Chlamydia pneumoniae* early survival” in the journal PLOS Pathogens. Infection begins when the chlamydiae recognize specific receptors on their target cells, which triggers uptake of the bacteria. Once inside the cell, they establish a membrane-bound compartment termed an inclusion, in which they multiply before being released to infect new human cells. In our study we found that the nascent chlamydial inclusion actively recruits specific host proteins called Rab proteins into its membrane. These proteins define the inclusion as a so-called recycling endosome vesicle, within which the Chlamydiae hide out, so as to avoid degradation by the host cell's waste disposal system, the lysosome. Our findings help to understand how Chlamydiae establish the intracellular niche which is essential for their survival and release. We will be answering your questions at 1pm ET – Ask us Anything!

[REDDIT](#)

PLOS Science Wednesday: Hi reddit, we're Johannes and Katja, and our research investigates the molecular processes that help chlamydiae pathogenic bacteria infect human hosts – Ask us Anything!

PLOSSCIENCEWEDNESDAY [R/SCIENCE](#)

Hi Reddit,

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Wednesday: Hi reddit, we're
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research investigates the
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chlamydiae pathogenic

I'm curious, has this research helped you understand mycoplasma better, particularly in terms of how to prevent that type of infection or get rid of it?

I've also read that *C. pneumoniae* may also be a potential cause or contributor to Lyme disease, just curious as to what you think on that issue.

[Jenajen](#)

Johannes. During evolution each pathogen has developed its own specific way to establish a successful infection. So the fact that we understand better how chlamydia is hiding within the human cell does not automatically mean that we understand how mycoplasma, *E. coli* or other pathogens do it. However, now that we know more about the chlamydia tricks, we can check whether other pathogens may manipulate its host cell in a similar way. In fact, for mycoplasma a role of the membrane protein Rab7 has been discussed. The best way to prevent the infection is a vaccine. No vaccines against *Cpn* and *Mycoplasma* are available yet.

C. pneumoniae (*Cpn*) and Lyme disease. There is no literature that shows a causal association

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between Cpn and the disease.

Chlamydia and CFS=Chronic Fatigue Syndrome. It has been published that a significantly higher proportion of CFS patients have a Cpn infection compared to non-CFS control groups. However, the association of other pathogens with CFS seems to be much stronger .

Does this imply that it would be possible to develop a drug that targets these human proteins in order to treat chlamydia? Would this be a way of getting around drug resistance?

[-Metacelsus-](#)

Johannes. Targeting a human protein to treat an infection is always tricky as you will normally block the function of this human protein in all cells of your body...not only in those cells infected by chlamydia. Therefore, we will go after the chlamydial proteins which induce formation of this hiding-place within the human cell. Then we can search for small molecules which block the chlamydial protein. Our hope is that upon this treatment the human cell now will deliver the internalized chlamydia to the host cell's waste disposal system, the lysosome. I think that it will be hard to completely avoid drug resistance. However, the application of a combination of different drugs may reduce the likelihood to develop resistances.

Does this imply that it would be possible to develop a drug that targets these human proteins in order to treat chlamydia? Would this be a way of getting around drug resistance?

[-Metacelsus-](#)

Katja: We think one should not target the human protein but search for the chlamydial effector interacting with these human proteins. If you then find an inhibitor specific for the chlamydial protein you could specifically inhibit the infection. As I am not a pharmacologist I cannot say anything about drug resistance, but in the long term a resistance to any kind of treatment is always possible.

Thanks for the AMA! I have a few questions,

What is the upshot of knowing how the chlamydia bacteria go unnoticed/undegraded by the host?

As chlamydia is curable, is it solely the detection aspect that can be improved, or will this research allow for better cures/immunity vaccinations?

Can the methods/tools generated by this research be applied for use with other, more malicious bacterial infections?

Thanks again!

[HerbziKal](#)

Katja: To answer your questions: 1. When we followed the colocalization with different endosomal markers like Rab11 or Rab7, we found them continuously on the inclusion membrane like Rab11 or then off like Rab7. Which means they are not degraded (Rab7) and acquire recycling endosomal character. By this they disappear inside the cell. All this leads to finding the bacterial effector involved in these processes. This will be a potential therapeutic target. 2. Curing of an infection. If it's so easy to cure the infection why are there so many new infections/year? The numbers are increasing every year. The problem you have with antibiotic treatment is, that the bacteria linger in a persistent state during treatment and can be reactivated once treatment is finished. By this you have a flare up of infection

and you can spread the disease. In my opinion the only choice is a vaccine. 3. I think there is no hindrance to use the marker with other even more pathogenic bacteria. It is a nice way to describe the intracellular life of the bug.

Thanks for this! A few questions:

1. Does your research revealing how Chlamydiae "hide out" in intracellular inclusions have any implications for new approaches or tactics for fighting the infection?
2. Is it known if other pathogenic bacteria employ similar tactics within host cells? If not, would you predict this a general strategy or specific to Chlamydia species?
3. How do Chlamydia species fare in terms of antibiotic resistance? What is the current state of 'standard' main line treatments, to your knowledge?

Thank you!

[nickfree](#)

Katja: I have to admit that I'm a basic researcher no pharmacologist but one has to be careful since the bacteria hide in a system which is essential for the cell. So if you choose this as a target you have to be aware of the consequences on "healthy" cells. To your second question: We know that most intracellular bacteria have evolved strategies to establish their specific niche. Some hide from lysosomes like Chlamydia, Salmonella & Mycobacterium while others only grow when engaged to the lysosome like Coxiella. The most common mechanism is to secrete specific effector proteins in order to manipulate the host cell to achieve their specific goals. These effectors manipulate all types of endocytic components like Rabs, GEFs or GAPs. Unfortunately I cannot answer what is the current main line of treatment, but we know that the bacteria can become resistant and most importantly undergo persistence. If they reappear after antibiotic treatment you don't know by which mechanism. Therefore vaccination is the only option.

Hi! Thanks so much for doing this AMA.

I'm currently a freshman at university, and I'm interested in doing what you do as a career. Were there any standout classes or concepts that helped you as you went on to graduate school and then to postdoctoral research? Anything you specifically look for in candidates?

[dragonxwings](#)

Johannes. Everything in biology is connected. Thus, I advise my students to take unrelated courses to get a feeling of how complex biological processes are. Don't specify too early, go and try to get a broad picture. During your studies certain aspects / questions will quicken your interest. Whatever you do, do so with passion.

Why are you trying to help chlamydia infect humans, shouldn't you be doing the opposite? ;-)

[fakename5](#)

Katja: As a basic researcher you want to know the WHY and HOW ;-). And maybe by understanding why and how we will be able to treat the disease better. Therefore we have to find the puzzle piece on the bacterial side to do so.

Hi! What is it about chlamydia that makes it so easily treatable? Do other STI's have more complex defense mechanisms?

[MoPuWe](#)

Johannes. It might not be so easy to treat a chlamydial infection. Yes, antibiotic treatment is effective. However, if chlamydia face a stress situation they have the ability to differentiate into a persistence state. For example, in in vitro experiments treatment with the antibiotics penicillin causes persistence. Once you remove the antibiotics the chlamydia differentiate back to normal and continue their infection cycle. Moreover, the fact that many chlamydial infections come with no symptoms, impede an efficient treatment. Therefore, a vaccine is the only way to prevent a chlamydial infection. I do not know whether other STI pathogens have more complex defense mechanisms.

Hi! What is it about chlamydia that makes it so easily treatable? Do other STI's have more complex defense mechanisms?

[MoPuWe](#)

Katja: As said before I think chlamydia are not easily treatable. Although antibiotics are available and working, chlamydial persistence is a huge problem. Because after the antibiotic treatment the infection reoccurs and tissue damage is enhanced. In case of bacterial STIs antibiotics are nowadays the common choice, but in my opinion you will need a specific drug for a specific target in order to be effective. And this holds true for viruses and bacteria. I am not a medical doctor or pharmacologist but isn't in all cases the long term goal to establish a vaccine in order to get rid of any of these bugs?

Hi, so now that you've established how *C. pneumoniae* establishes a niche within the cell, how does this change how we approach targeting treatment/prevention of infection? As a side note, I have very limited knowledge on current treatments and prevention in this area. Keep up the good work.

[MobBank](#)

Katja: I think with our results we have a chance to find the chlamydial effector involved in the establishment of the niche. And this is a new potential target for maybe a small molecule inhibitor which would specifically inhibit the chlamydial infection.

Why chlamydia? How did you get into it?

[zZEmmEZz](#)

Johannes. Quite some years ago I was playing squash with a MD who told me that there was he had no tool at hand to diagnose an infection with *Chlamydia pneumoniae*. Could I help? At that time I was running the DNA synthesizer to produce oligonucleotides. And thus we developed a PCR method to diagnose *C. pneumoniae*. From then on I was smitten with *C. pneumoniae*.

Isn't chlamydia easily treated with antibiotics? Why bother studying it further?

[ozmio](#)

Katja: Is it really easily treated with antibiotics? As I said before the numbers of chlamydial infections are increasing in the last years and with this the consequences of for example female infertility. If it's all so easy why are the infections not eliminated? The hypothesis in the research field is that the

treatment elucidates stress and the pathogen reacts with the mechanism of persistence. In this state they cannot be targeted by antibiotics and the symptoms disappear. After the treatment the bacteria reactivate their life cycle. The patients have reoccurring infections and can spread the pathogen. So we need to study Chlamydia to find some more effective treatment or even better a vaccination.

Isn't chlamydia easily treated with antibiotics? Why bother studying it further?

[ozmio](#)

Johannes. Yes, a chlamydia infection can be treated with antibiotics. but only if you know about the infection. Therefore, the development of a vaccine is the only safe way to avoid a chlamydial infection. Our lab has actually identified chlamydia proteins which are prime candidates for a subunit vaccine. In collaboration with immunologists we are currently testing them.

Hi and thanks for joining us today.

With chlamydia rates in countries like Fiji where some antenatal populations see upwards of 50%, do you think mass drug administration for STIs (similar to trachoma initiative) would be an effective elimination strategy?

[PHealthy](#)

Johannes. The best way to eliminate the chlamydia pathogens will be the development of a vaccine. Because whole organism vaccines did not work (this was tested about 50 years ago in Africa) a subunit vaccine consisting of several chlamydial proteins is required. We have identified several candidate proteins and immunological studies are under way to test their efficiency.