

# *Chlamydia* Biology

From Genome to Disease

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Cover design: A chlamydial inclusion imaged by expansion microscopy. HeLa 229 cells were infected at an MOI of 1 with the dual fluorescent reporter strain *C. trachomatis* mCh(Gro<sub>L2</sub>) and GFP(OmcA<sub>L2</sub>) (Cortina *et al.*, 2019, <https://doi.org/10.1371/journal.pone.0217753>) and imaged by expansion microscopy at 30 hours post infection, as described by Kunz *et al.* (2019, <https://doi.org/10.3389/fcimb.2019.00276>). The image shows a single inclusion containing a population of chlamydiae that is undergoing asynchronous RB-to-EB conversion, as detected by differential expression of mCherry from the early *GroESL* promoter (shown in magenta) and/or GFP from the late *omcAB* promoter (shown in cyan). This image was kindly provided by Tobias Kunz, Ralph Götz and Thomas Rudel (University of Würzburg, Germany), who used the dual fluorescent reporter strain generated by Maria-Eugenia Cortina and Isabelle Derré (University of Virginia).

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# Foreword

When Ming Tan, one of the editors and a contributor to this new volume on *Chlamydia*, called me earlier this summer to ask if I would be willing to write a few words about the book, I was delighted and honoured to have the opportunity to get a sneak preview of the contents. We chatted for a few minutes about new work that is under way on all aspects of chlamydiae biology, genetics and genomics, and host immune responses to chlamydiae. These are exciting times for *Chlamydia* researchers, and this excitement is reflected in each of the chapters that you, the reader, have before you. It is hard to believe that it has been nearly a decade since the last compendium of progress on *Chlamydia* research was published, and this volume provides a timely update. The editors, Drs Tan, Hegemann and Sütterlin, have done a superb job in organizing the book to provide cohesiveness between the broad areas covered. They have assembled a first-rate group of experts that nicely blends contributions from well-established, veteran researchers and highly talented newer investigators. This symbolic passing the mantel is, I think, extremely important for continued progress. The editors also have blended expertise in areas that run the gamut from clinician researchers to cell biologists and molecular geneticists. In short, there is something for everyone here.

The volume begins, quite appropriately, with chapters that describe both *Chlamydia trachomatis* and *C. pneumoniae* and human diseases they cause or are implicated in. It is most interesting to me that despite excellent physician awareness, quick and reliable diagnostic tests and effective treatment methods for *C. trachomatis* infection, the worldwide infection rates are increasing. This likely attests to the remarkable traits this microbe exhibits

as a pathogen. We clearly need more research on the basic biology of chlamydiae to gain a better appreciation of early interactions with the host cell, intracellular survival strategies, host responses, and paths of transmission. It is very clear that during the past decade we have learned a great deal about chlamydiae and their interaction with the host. Several contributions are dedicated to informing us about how these pathogens invade, establish their intracellular niche, and co-opt host cell processes for their own benefit. There are chapters that combine expertise in chlamydiae biology (e.g. Hans Hegemann, Rey Carabeo, Kevin Hybiske, Isabelle Derré) and host cell biology (e.g. Christine Sütterlin). The propagation of chlamydiae is now known to be anything but straightforward and George Liechti, Patrick Viollier, Gilbert Greub and Tony Maurelli provide us with a very nice update on chlamydiae division and differentiation. Perhaps the most new knowledge developed during the past 10 years is in chlamydiae genetics and genomics. These topics are beautifully covered in three chapters. Christopher Rosario, Katelyn Soules, Scott Hefty and Ming Tan cover gene regulation; Colette O'Neill, Ian Clarke and Derek Fisher cover genetics; and Vitor Borges, Patrick Hyden, João Paulo Gomes and Thomas Rattei cover genomics. These chapters serve as an integrating theme for the book and help us to understand how new genetic and genomic information may have valuable practical applications. These chapters also showcase some of the newer investigators charged with moving this field forward. The response of the host to chlamydiae is not neglected in this volume. Cell-autonomous defence, an important feature of all intracellular infections, is discussed by George Häcker and Thomas Rudel. A discussion

of innate immunity is led by Uma Nagarajan and adaptive immunity is discussed by Taylor Poston, Toni Darville and Ray Johnson. An update on the ever-elusive chlamydial vaccine is tackled in a chapter by Luis de la Maza and his colleagues. Simon Graspeuntner, Peter Timms, Jan Rupp and Bonnie Quigley provide an interesting chapter on the interface between chlamydiae and the microbiome. This is an area of particular interest to me, and one that could provide useful pathogenesis-related insights. We all know that there is much more to the study of chlamydiae than work on human disease. Konrad Sachse and Nicole Borel provide an overview of chlamydiae that are important as veterinary pathogens, and Alice Taylor-Brown, Tamara Halter, Adam Polkinghome and Matthias Horn give us valued insights on the ubiquity of chlamydiae in the biosphere. It would appear that wherever eukaryotic cells are found, chlamydiae are likely to – I almost wrote invade – but perhaps integrate in symbiotic relationships – may be a better way to put it. Finally, all chlamydiae must be studied in the context of the host cell and often

work requiring animal models are needed. This is especially true for understanding pathogenesis of disease and protection from disease. Guangming Zhong, Alison Quayle, Ashok Aiyar and Tianyuan Zhang conclude the volume with a discussion of the pros and cons of animal models in the study of chlamydial infections and how these systems may be put to best use to study host responses and disease.

When Ming and I were on the phone talking about some of the newest work being done, his enthusiasm was infectious. I found I could almost bring back that feeling of excitement I had many years ago when I sat in Jim Moulder's lab. I recalled how Jim always said that he wanted to know the evolutionary adaptations chlamydiae have made to succeed in the intracellular environmental niche. I am sure that Jim would be pleased to know that we are getting closer to the goal thanks to the efforts of many, including those who contributed to this book. Please allow me to add my thanks to all of you. I know that this volume will be a wonderful addition to the literature. Keep up the good work!

Gerry Byrne  
August 2019  
Jamestown, RI

# A note on usage

In the book, we have used the following terms with their respective formatting (Capitals and *italics*):

- chlamydia: single bacterium
- chlamydiae: multiple bacteria
- chlamydial: adjective (equivalent to ‘bacterial’)
- *Chlamydia*: Genus name
- *Chlamydiaceae*, *Parachlamydiaceae*: Family name
- *Chlamydiales*: Order name (includes *Chlamydia* and *Chlamydia*-related bacteria)
- *Chlamydiae*: Phylum name

For practical purposes *Chlamydiales* and *Chlamydiae* are equivalent because there is only one order,

*Chlamydiales*, in the phylum *Chlamydiae*. We prefer *Chlamydiales* because *Chlamydiae* is easily confused with the generic term, chlamydiae.

The above italicization rules conform with the ASM style, which italicizes names of all bacterial taxa. However, some taxonomy nomenclature systems do not italicize names above family, i.e. they would use *Chlamydiales* and *Chlamydiae* for the order and phylum, respectively. We have deferred to authors of some chapters in the book on this usage.

More details on the usage of *Chlamydia* terms and taxonomy can be found in Bavoil, P., Kaltenboeck, B., and Greub, G. 2013. In *Chlamydia* veritas. Pathog. Dis. 67, 89–90.

MT: To my mother, Helen

JHH: To the most influential women in my life, Ursula and Angelika

CS: To my sons, Toby and Lucas