Editorial: Obligate intracellular bacteria: Evasion and adaptative tactics shaping the host-pathogen interface

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Obligate intracellular bacteria are an important and fascinating group of microorganisms, as they are often pathogenic to humans and cause a significant clinical and public health burden worldwide. Adaptation to the obligate intracellular lifestyle implies an intimate and complex co-evolution with eukaryotic hosts over hundreds of millions of years. During this adaptation, these pathogens evolved sophisticated virulence mechanisms enabling them to grow intracellularly and resist host defences while minimizing damage to their hosts. This obligate intracellular nature is also a major research challenge, as these bacteria are typically not easy to handle and manipulate in the laboratory. However, over the last 15 years, several developments have significantly advanced understanding of the biology and virulence mechanisms of obligate intracellular bacterial pathogens. Some of these advances are covered in this Frontiers Research Topic.

Two reviews cover experimental models used to study Chlamydia trachomatis pathogenesis and evaluation of vaccines against Q fever (caused by Coxiella burnetii). Filardo et al. review the current knowledge on how C. trachomatis interacts with human prostate epithelial, Sertoli, and synovial cells and how studying Chlamydia survival and inflammatory host cell responses to infection in these cells aids elucidation of etiopathogenesis of Chlamydia-mediated male infertility, prostatitis, and reactive arthritis. On the importance of animal models as invaluable tools in preclinical evaluation of Q fever vaccine candidates and post-vaccination...
hypotheses regarding multiple potential functions of Tarp in promoting Chlamydia invasion.

**Ehrlichia chaffeensis** is the causative agent of human monocytic ehrlichiosis, an emerging tick-borne infectious disease. *E. chaffeensis* replication within monocytes and macrophages relies on multiple proteins. Rikihsia focuses on recent findings related to the role of EtpE-C on invasion, functions of *E. chaffeensis* effectors Etf-1, -2, and -3 to facilitate intracellular replication, and *Ehrlichia* hijacking of host membrane lipids.

Another key aspect of the virulence of obligate intracellular bacteria is their ability to control host cell death. Wang and Cull highlight the current knowledge, challenges, and future perspectives regarding involvement of tick programmed cell death machinery (apoptosis and autophagy pathways) in tick-pathogen interactions. A deeper understanding of how these mechanisms and their interplay impact pathogen acquisition, replication, and transmission will ultimately identify novel approaches to controlling tick-borne diseases.

Finally, two research papers explore the importance of cellular O2 levels and how this is perceived and explored by pathogens. To dissect the impact of O2 concentration on growth of *Chlamydia*, Thapa et al. investigate the role of host NADPH oxidases and functional mitochondria in chlamydial growth under normoxia and hypoxia. Interestingly, their data show that *C. trachomatis* require functional mitochondria and NADPH oxidase 4/p38 MAPK signaling for growth under normoxia, opening interesting hypotheses about how *Chlamydia* might switch their energy source depending on cellular O2 concentration.

HIF1α is an important regulator of cellular responses to hypoxia and regulates transcription of genes involved in immune responses, metabolic reprogramming, and anti-infective responses. Hayek et al., provide evidence that *C. burnetii* infection destabilizes HIF1α and alters expression of multiple HIF1α target genes. The *C. burnetii* effector(s) responsible for this destabilization and mechanistic consequences for disease outcome remain interesting open questions.

In conclusion, this Research Topic provides a diverse range of topics on host-pathogen interactions, ranging from experimental models, genomics and evolution, protein effectors and their functions, control of host programmed cell death, and the impact of O2 concentration on infection. We thank all authors who contributed their work and all reviewers for their time and insightful comments that led to this exciting collection of articles.

**Author contributions**

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