

# Bacterial Evasion of the Host Immune System

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Cover design adapted from images provided by Pedro Escoll, showing *Legionella pneumophila* (red) replicating within a human primary macrophage.

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# Preface

Humans have an intimate relationship with bacteria as we harbour in our bodies a considerable amount of bacteria, known as our microbiota (Thaiss *et al.*, 2016). Indeed it has been demonstrated that a close interaction between our cells and the commensal microbes in our gut is essential for human health. However, humans also have contact with pathogenic bacteria and the infectious diseases that these cause continue to be a major threat to human health: predictions suggest that over the next few decades, these will account for one of five deaths globally (Mathers and Loncar, 2006). For example in 2015 the World Health Organization stated that tuberculosis (caused by *Mycobacterium tuberculosis*) was one of the top 10 causes of death worldwide (WHO, 2015). Another example is antibiotic-resistant *Salmonella*: it accounts for more than 100,000 infections in the USA per year (Medalla *et al.*, 2017). In a time when emergence of antibiotic resistance in bacteria is occurring worldwide, understanding how bacteria cause disease is the key to finding new therapeutic approaches to tackle infection. The study of host–pathogen interactions, in particular the interaction with the host immune system, is an essential area of research.

The immune system is thus composed of a combination of mechanisms and specialized cells (i.e. immune cells) that evolved in eukaryotes to constantly monitor the homeostasis of the host. Disruption of such homeostasis, for example during tissue damage, infection or tumour development activates the immune system (Goldszmid *et al.*, 2014). For bacterial pathogens, escaping the host immune system is thus essential for successful multiplication and the establishment of an infection. Indeed, failure of the immune system to deal with pathogenic bacteria and recover homeostasis has life-threatening consequences, as seen in immunocompromised individuals. In this volume we present a collection of timely reviews on the most current research in bacterial evasion of the host immune system.

Life is communication and all living systems communicate with their neighbours. The immune system is key in the establishment of this cross-talk between eukaryotes and bacteria. However, pathogenic bacteria are able to *hack* into this communication, causing *confusion* in the immune system and allowing them to evade defence mechanisms, subvert and exploit host functions in their benefit, and replicate within the host during infection, causing disease which can be fatal.

Pathogenic bacteria have evolved sophisticated mechanisms to exploit host functions and evade their recognition by immune cells during infection. One of these strategies is the injection of bacterial proteins (*effectors*) into the host cells during infection, a topic reviewed in Chapter 1. In Chapter 2, Pucciarelli and García-del Portillo review another interesting strategy; the *camouflage* of bacterial surface components during infection in order to alter the recognition of pathogenic signatures.

In the recent years, research on immunity against pathogenic bacteria has been focused on innate immunity, the first line of defence against infection. Among innate immune

cells, macrophages have received special attention as these immune cells are professional phagocytes that engulf and analyse bacteria, recognizing pathogenic signatures and further orchestrating immune responses with the adaptive immune system (composed by B and T lymphocytes) to fight infection. Macrophages are therefore the first line guardians against infection, but many pathogenic bacteria *manipulate* these cells to prevent an effective immune response. In Chapter 3, Wan *et al.* review the mechanisms by which pathogenic bacteria subvert macrophage functions.

In addition to the innate and adaptive immune systems mentioned above, another essential part of any immune system, ‘cell-autonomous immunity’ (also called cellular self-defence), has been discovered. Cell-autonomous immunity operates in every cell of an organism and guards both individual immune and non-immune cells against the immediate threat of infection. It cooperates with conventional immunity (i.e. the innate and adaptive systems) and permits any cell to trigger the activation of an immune response. Not surprisingly, pathogenic bacteria also harbour mechanisms to disrupt these systems too. For instance, bacteria can subvert autophagy in an infected cell, thereby evading this catabolic process which removes undesirable material (including intracellular pathogens) within the cell. Chapter 4 analyses the consequences of bacterial modulation of autophagy on the immune response to infection. Furthermore, the recognition of bacterial components by cellular inflammasomes is another key self-defence mechanism against intracellular pathogens, a topic examined in Chapter 5.

Later in the volume, once the players, strategies and mechanisms have been presented, and in order to have a broad view of the mechanisms used by specific bacteria to evade the immune system, we provide an overview of *the whole dance* in two reviews examining the specific evasion strategies used by two important human pathogens during infection. The evasion strategies developed by *Salmonella* are discussed in Chapter 6, while the strategies utilized by *Mycobacterium* are reviewed in Chapter 7. Finally, we close this *volume* with a look into plant pathogens and plant immunity in Chapter 8.

In summary, this volume provides the reader with an overview of important current research on bacterial evasion of the immune system, a topic that is not only exciting but also essential for the elucidation of the mechanisms bacteria use to cause infection.

## References

- Goldszmid, R.S., Dzutsev, A., and Trinchieri, G. (2014). Host immune response to infection and cancer: unexpected commonalities. *Cell Host Microbe* 15, 295–305. <https://doi.org/10.1016/j.chom.2014.02.003>.
- Mathers, C.D., and Loncar, D. (2006). Projections of global mortality and burden of disease from 2002 to 2030. *PLOS Med.* 3, e442.
- Medalla, F., Gu, W., Mahon, B.E., Judd, M., Folster, J., Griffin, P.M., and Hoekstra, R.M. (2017). Estimated incidence of antimicrobial drug-resistant nontyphoidal *Salmonella* infections, United States, 2004–2012. *Emerging Infect. Dis.* 23, 29–37.
- Thaiss, C.A., Zmora, N., Levy, M., and Elinav, E. (2016). The microbiome and innate immunity. *Nature* 535, 65–74. <https://doi.org/10.1038/nature18847>.
- World Health Organization (2015). Global tuberculosis report 2015. 20th Edition. WHO/HTM/TB/2015.22

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