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OPINION ARTICLE

The Tussle Between Mycobacteria and Host: To Eat or Not To Eat

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Abstract Autophagy is a catabolic process of cellular homeostasis evolutionarily conserved in eukaryotes. To block infection of intracellular bacterial pathogens, metazoans deploy autophagy for pathogen clearance through phago-lysosome formation and specific bactericidal peptides. Although an array of research have publicized the host regulatory factors, the function of bacterial effectors are yet to be understood in detail. In this article, we focus on the autophagic response to one of the most successful intracellular bacteria *Mycobacterium tuberculosis*.

Keywords Tuberculosis · Autophagy · Host–pathogen interaction · Virulence factors · Mycobacteria · *Mycobacterium tuberculosis*

Mycobacterium tuberculosis, the causative agent of tuberculosis, has probably killed more people than any other microbial pathogen in the history of human civilization. The emerging drug-resistant forms of *M. tuberculosis* coupled with HIV co-infection pose a threat never felt before. Although various reasons have been suggested for development of drug resistance among different microbes [1], the ways with which *M. tuberculosis* adapt and improvise in order to survive remains a mystery. Apart from possessing a plethora of regulatory proteins for its survival and pathogenicity [2, 3], it is also known to secrete a gamut of virulence factors to thwart of host immune-defence [4]. This scenario warrants investigation both towards search of new drug targets as well as discovery of new drugs [5–7]. Fortunately in the recent years several drugs have been developed to address the issue of multi-drug resistance tuberculosis, two prominent examples being TMC-207 (bedaquiline) which is already granted approval and 24-desmethylrifampicin (a rifamycin derivative), a drug found to be effective against multidrug-resistance tuberculosis [8, 9]. Although studies are underway to see the effect of newer candidates against mycobacterial infections, we are ignorant about the effect of anti-mycobacterial antibiotics on host–pathogen tussle especially in autophagy networks. One study indicates that azithromycin blocks autophagy pathway and its long term use predispose cystic fibrosis patients to non-tuberculous mycobacterial infections [10]. However, the mycobacterial infection process comprises of a complicated patho-physiology which needs to be thoroughly understood before therapeutic intervention.

Autophagy is a protective cellular process ubiquitously present in eukaryotic organisms. Although the facets of autophagy have been known for quite some time, recent advances in the past decade have thrown new light on autophagy as an immune-defence mechanism against tuberculosis infection. It is now perceived that host deploy autophagy to tackle *M. tuberculosis* in two different ways: one to eradicate mycobacteria by promoting the autophagosome–lysosome fusion and the other to deliver mycobactericidal peptides/enzymes in the mature lysosomal vesicles [11]. However, the ability of *M. tuberculosis* to utilize its virulence factors to avoid the phago-lysosomal fusion and establish the infection is well documented [4]. Despite decades of ongoing research on various aspects of tuberculosis, we are still data deficient on the exact

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