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Title: Autophagy and Mtb: a retrospective and a look ahead

Summary
Our studies conducted in late 1990s reported on the phosphatidylinositol 3-phosphate (PI3P) mechanism of the Mycobacterium tuberculosis (Mtb) phagosome maturation block. At that time we wondered whether there was any naturally occurring cellular process that could be used to advance Mtb phagosomal maturation. One of the prominent candidates considered was the process of autophagy, which is exquisitely dependent on PI3P generation, required for the massive intracellular membrane remodeling ensuing during autophagosome formation and their maturation into autolysosomes. When we used physiological, immunological, and pharmacological inducers of autophagy, such as starvation, IFN-γ, and rapamycin, we observed that these interventions enabled maturation of M. tuberculosis phagosomes into compartments with lysosomal properties. Numerous studies since these initial observations, both in vitro and in vivo, have addressed the role of autophagy in Mtb infection, inflammation, and pathogenesis. Here we will give an update on these studies and report on the most recent findings concerning overlaps between lysosomal and phagosomal membrane damage and the role of autophagy in Mtb pathogenesis.