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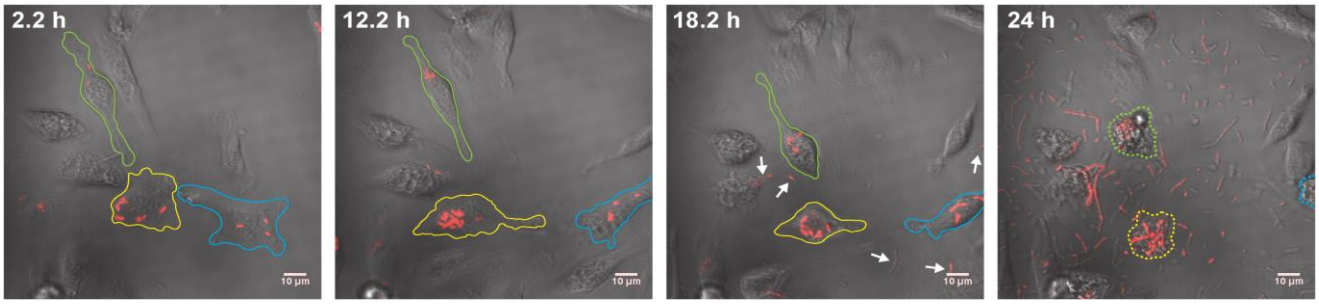
Yersinia pestis is a facultative intracellular pathogen that causes the human disease known as plague. Growing evidence indicates that intracellular growth in macrophages is important for *Y. pestis* virulence. Upon phagocytosis, *Y. pestis* alters the maturation of the phagosome to generate a protective compartment within the cell known as the *Yersinia* containing vacuole (YCV). Key steps in the generation of the YCV include inhibition of YCV acidification, expansion into a spacious vacuole, and acquisition of the autophagic markers. However, the mechanisms used by the bacterium to subvert the normal phagosome maturation process and generate the YCV have not been defined. Our long term goals are to elucidate the mechanisms by which *Y. pestis* evades macrophage killing and define the contribution of intracellular survival to *Y. pestis* virulence.

Recently we discovered that *Y. pestis* manipulates the host endocytic recycling pathway to survive in macrophages. Moreover, we have demonstrated that *Y. pestis* recruits Rab1, Rab4 and Rab11 to the YCV. Importantly, we also discovered that *Y. pestis* manipulation of Rab11b disrupts global endocytic recycling in the macrophage. Together these data suggest the hypothesis that *Y. pestis* specifically targets and recruits Rab11 to the YCV to avoid phagolysosome maturation and generate a replicative niche within macrophages.

Currently we are expanding on these initial findings to further define how *Y. pestis* manipulates Rab11 and the host recycling machinery to generate the YCV. Specifically, we seek to answer two key questions. First, how does *Y. pestis* recruit Rab11 to the YCV (**Aim 1**)? Second, how does Rab11 recruitment impact the remodeling of the YCV (**Aim 2**)? Specifically, what other components of the recycling pathway does Rab11 recruit to the YCV and do these components directly contribute to YCV biogenesis and intracellular survival?

Answering these questions will fill a critical gap in our understanding of how *Y. pestis* is able to subvert normal phagosome maturation and survive within this intracellular niche. Furthermore, through understanding how *Y. pestis* manipulates the host recycling and inflammatory pathways we can gain novel insight into the interactions between these pathways in the context of normal cell biology.



Intracellular survival of *Y. pestis* in macrophages: Primary peritoneal macrophages were infected with fluorescent *Y. pestis* (red) and monitored by live confocal microscopy for 24 h. To track Individual infected macrophages over the course of the infection, they are highlighted by colored outlines. Dotted outlines represent dead macrophages

Working model of YCV biogenesis