

Publication

3D correlative electron microscopy reveals continuity of Brucella -containing vacuoles with the endoplasmic reticulum

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Entry of the facultative intracellular pathogen; Brucella; into host cells results in the formation of endosomal; Brucella; -containing vacuoles (eBCVs) that initially traffic along the endocytic pathway. eBCV acidification triggers the expression of a type IV secretion system that translocates bacterial effector proteins into host cells. This interferes with lysosomal fusion of eBCVs and supports their maturation to replicative; Brucella; -containing vacuoles (rBCVs). Bacteria replicate in rBCVs to large numbers, eventually occupying most of the cytoplasmic volume. As rBCV membranes tightly wrap each individual bacterium, they are constantly being expanded and remodeled during exponential bacterial growth. rBCVs are known to carry endoplasmic reticulum (ER) markers; however, the relationship of the vacuole to the genuine ER has remained elusive. Here, we have reconstructed the 3-dimensional ultrastructure of rBCVs and associated ER by correlative structured illumination microscopy (SIM) and focused ion beam/scanning electron microscopic tomography (FIB/SEM). Studying; B. abortus; -infected HeLa cells and trophoblasts derived from; B. melitensis; -infected mice, we demonstrate that rBCVs are complex and interconnected compartments that are continuous with neighboring ER cisternae, thus supporting a model that rBCVs are extensions of genuine ER.

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