Mode of action of *L. pneumophila* effector proteins

L. pneumophila employs a conserved mechanism to establish in mammalian and protozoan host cells a unique replication compartment, the ER-associated *Legionella*-containing vacuole (LCV) (**Fig. 1**). LCVs avoid fusion with lysosomes but interact with distinct organelles and communicate with different vesicle trafficking routes, such as the endosomal, secretory, and retrograde pathways. LCVs can be purified and subjected to proteomics and reconstitution assays (1).

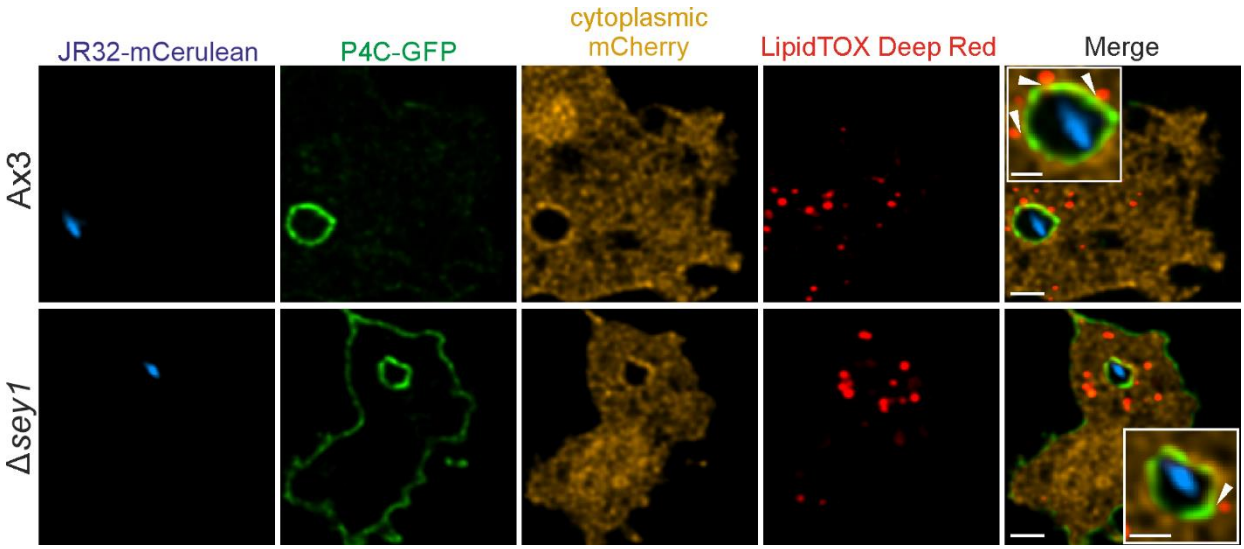

Fig. 1. Atlastin/Sey1 promotes lipid droplet recruitment to intact LCVs. Fluorescence micrographs of *Dictyostelium discoideum* Ax3 or Δ*sey1* producing the LCV/PtdIns(4)*P* marker P4C-GFP and cytosolic mCherry, fed overnight with 200 µM sodium palmitate and infected (MOI 10, 1 h) with mCerulean-producing *L. pneumophila* JR32, fixed with PFA and stained with LipidTOX Deep Red. Examples are shown for contact between lipid droplets and the LCV membrane (white arrowheads). Scale bars: overview (2 µm), inset (1 µm) (2).

To govern LCV formation and other pathogen-host interactions, *L. pneumophila* employs a type IV secretion system, which translocates the astonishing number of more than 300 different “effector proteins” into host cells, where they undermine pivotal processes and organelles. We investigate effectors modulating phosphoinositide lipids (3), or the retromer coat complex (4, 5), as well as the small Ran GTPase (6, 7) and the large GTPase atlastin/Sey1 (2, 8). Using macrophages, epithelial cells, *Dictyostelium* and *Acanthamoeba* amoebae, we currently study how *L. pneumophila* subverts the ER, mitochondria, lipid droplets (2), and host cell metabolism to promote intracellular bacterial replication. To mechanistically study these pathogen-host cell interactions, we employ genetic, biochemical, structural biological and cell biological approaches.

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