Selective macroautophagy (hereafter referred to as autophagy) describes a process in which cytosolic material is engulfed in a double membrane organelle called an autophagosome. Autophagosomes are carriers responsible for delivering their content to a lytic compartment for destruction. The cargo can be of diverse origins, ranging from macromolecular complexes to protein aggregates, organelles, and even invading pathogens. Each cargo is unique in composition and size, presenting different challenges to autophagosome biogenesis. Among the largest cargoes targeted by the autophagy machinery are intracellular bacteria, which can, in the case of *Salmonella*, range from 2 to 5 μm in length and 0.5 to 1.5 μm in width. How phagophores form and expand on such a large cargo remains mechanistically unclear. We used HeLa cells infected with an auxotrophic *Salmonella* to study the process of phagophore biogenesis using in situ correlative cryo-ET. We show that host cells generate multiple phagophores at the site of damaged Salmonella-containing vacuoles (SCVs). The observed double membrane structures range from disk-shaped to expanded cup-shaped phagophores, which have a thin intermembrane lumen with a dilating rim region and expand using the SCV, the outer membrane of Salmonella, or existing phagophores as templates. Phagophore rims establish different forms of contact with the endoplasmic reticulum (ER) via structurally distinct molecular entities for membrane formation and expansion. Early omegasomes correlated with the marker Double-FYVE domain-Containing Protein 1 (DFCP1) are observed in close association with the ER without apparent membrane continuity. Our study provides insights into the formation of phagophores around one of the largest selective cargoes.

You can find part of the story here: [https://www.pnas.org/doi/10.1073/pnas.2221712120](https://www.pnas.org/doi/10.1073/pnas.2221712120)