**Evasion of autophagy mediated by *Rickettsia* surface protein OmpB is critical for virulence**

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***Nature Microbiology*** volume 4, pages2538–2551(2019)

**Presenter:** Bing-Chang Yang **Date/Time:** 2020/03/05 17:10-18:00 **Commentator:** Jenn-Wei Chen **Location:** Room 601, Med College Building **Background:**

The intracellular life cycle of *Rickettsia* begins when bacteria adhere to and invade host cells. They subsequently escape theprimary vacuole into the cytosol, where they replicate and mustevade antimicrobial autophagy, a process that removes intracellular pathogens similarly to damaged organelles such as mitochondria**.** Several facultative intracellular bacterial pathogens that grow inthe host cell cytosol have evolved mechanisms to evade autophagicrecognition**.** *Rickettsia* are highly adapted to the intracellular environment and thus have probably also evolved mechanisms to evade autophagic recognition**.** However, the bacterial factors that protect *Rickettsia* fromthe formation of a polyubiquitin coat are unknown.**Objective/Hypothesis:**

The authors aimed to understand the role of bacterial proteins of *Rickettsia* in shielding against autophagic recognition.

# Results:

The authorassessed strains with transposon (tn) mutations in ompA, ompB, sca2 and hrtA (encoding the 17-kDa antigen). They found that *R. parkeri* requires OmpB, but not Sca2-mediated actin mobilization, to avoid polyubiquitylation. Once in the cytosol, ompBSTOP::tn bacteria exhibited increased association with membranes resembling phagophores, which localized near one bacterial pole or partly surrounding bacteria. However, ompBSTOP::tn and WT bacteria were comparable in their relatively rare localization within double-membrane vacuoles or electron-dense lysosomal compartments at 1 hour post infection and OmpB is required for the formation of this halo. They developed an approach that combined polyubiquitin enrichment from the surface fraction of bacteria with mass spectrometry to detect Lys-diGly (diGly) remnants, a signature for ubiquitin. However, they identified a bacterial peptide of OmpA with diGly remnants that was consistently enriched in fractions from ompBSTOP::tn bacteria and OmpA was detected in His-ubiquitin-enriched fractions from ompBSTOP::tn but not WT bacteria. And then they infected both HMECs and BMDMs, and then stained for the autophagic receptors p62 and NDP52 and found that more than 30% of ompBSTOP::tn bacteria colocalized with p62 and NDP52 at 1h.p.i. in both cell types and in HMECs at 72h.p.i. In vivo, they infected C57BL/6 mice with WT or ompBSTOP::tn bacteria, but they were unable to recover any ompBSTOP::tn bacteria from any organ within the window of 2 to 72h.p.i.

# Conclusion:

The results of this study have revealed OmpB acts as a protective shieldto inhibit antimicrobial autophagy and as a critical virulence factorin *Rickettsia* pathogenesis.

# References:

1. Galluzzi, L. et al. Molecular defnitions of autophagy and related processes. EMBO J. 36, 1811–1836 (2017).