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22766 | Copine 1 counteracts pneumolysin-induced plasma membrane damage caused by *Streptococcus pneumoniae* infection

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Background & Aim: *Streptococcus pneumoniae* causes pneumonia, meningitis, and sepsis, leading to millions of hospitalizations and deaths annually despite vaccination efforts. Understanding bacterial interaction with host cells is key to developing innovative therapies. Pneumolysin (PLY), a *S. pneumoniae* virulence factor, forms pores in the host cell plasma membrane (PM) to disrupt cellular integrity and promote bacterial dissemination. Host cells rely on repair mechanisms to counteract PM damage induced by PLY(1). We recently identified Copine 1, a calcium-dependent phospholipid-binding protein, as a key player in this repair process(2) However, its precise role in PM repair remains unclear, which is the focus of this study. **Methods:** To ascertain if Copine 1 redistributed to PM damage sites, A549 (lung epithelial) or HeLa (cervix epithelial) cells were treated with purified PLY, infected with *S. pneumoniae,* or untreated. Protein localization was assessed by immunofluorescence confocal microscopy. To identify Copine 1 partners involved in PM repair, HEK 293T (kidney epithelial) cells expressing Copine 1 fused to a biotin ligase were non-intoxicated or intoxicated with PLY in the presence of exogenous biotin. Biotinylated proteins were purified and identified by mass-spectrometry. **Results:** Following both PLY intoxication and bacterial infection, Copine 1 was recruited to non-muscle myosin heavy chain IIA protein accumulations at the PM, which are PM sites associated with effective repair upon damage by other bacterial pore forming toxins (3,4). The results from the mass-spectrometry analysis are pending. **Conclusions:** These findings suggest, thus far, that Copine 1 counteracts PLY-mediated PM damage by participating in cortical actomyosin cytoskeleton remodeling.

Keywords: Bacterial infection, pneumolysin, plasma membrane repair, *Streptococcus pneumoniae*, therapeutic targets.

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