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Toxosomes: How Cells Dispose of an Undigestable Membrane Pore Complex

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Pore forming toxins (PFT) are thought to be important virulence factors of many pathogenic bacteria, and there is a growing interest in innate defense mechanisms against PFT. Based on the early observation that target cells of *S. aureus* α-toxin, archetype of the small β-barrel-pore forming toxin family, may recover from a substantial drop of cellular ATP, the concept was advanced that repair of manifest membrane lesions is an important aspect of cellular defense against PFT. Recently, we found that endocytosis of plasma membrane lesions is a decisive event for the rescue of *S. aureus* α-toxin target cells. Although this provided an explanation for the *ad hoc* reconstitution of plasma membrane integrity, the question remained how target cells ultimately dispose of pore complexes, which were previously shown to be rather resistant to proteolytic degradation *in vitro*.

Using internal radiolabeling, mass spectrometry, ultracentrifugation, electron microscopy and fluorescence microscopy we studied the fate of α-toxin after encounter with epithelial target cells.

The study revealed that epithelial cells are in fact unable to destroy internalized α-toxin pore complexes, but that they return the undegradable material to the extracellular milieu in the context of exosome-like particles, here referred to as *toxosomes*.

The data constitute the first paradigm for exocytosis of a bacterial toxin by target cells. The mechanisms involved in this process and implications for pathology are discussed.

Keywords: exosomes, S. aureus, alpha-toxin, pore forming toxins