

# H/KDEL receptors mediate host cell intoxication by a viral A/B toxin in yeast

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Microbial A/B toxins such as cholera toxin, *Pseudomonas* exotoxin A and the yeast killer toxin K28 all contain a KDEL-like amino acid motif at one of their polypeptide chains which ensures retrograde toxin transport through the secretory pathway of a target cell [1]. As key step in host cell invasion, each toxin binds to distinct plasma membrane receptors that are parasitized and utilized for toxin cell entry. Despite intensive efforts, some of these receptors are still unknown. Here we identify the yeast H/KDEL receptor Erd2p as membrane receptor of K28, a yeast viral A/B toxin carrying a C-terminal HDEL motif at its cell binding B/β-subunit. While initial toxin binding to the outer yeast cell wall is unaffected in cells lacking Erd2p, toxin binding to spheroplasts and in vivo toxicity strongly depend on the presence of H/KDEL receptors. Consistent with a role in toxin binding to spheroplasts, intracellular localization of Erd2p is not restricted to membranes of the early secretory pathway but rather extends to the plasma membrane where Erd2p can bind and internalize HDEL-bearing cargo such as K28 toxin, GFP<sup>HDEL</sup> and Kar2p [2]. Since human KDEL receptors are fully functional in yeast and capable to restore toxin sensitivity in the absence of endogenous Erd2p, toxin uptake by H/KDEL receptors at the eukaryotic cell surface might also contribute to the intoxication efficiency of A/B toxins carrying a KDEL-like motif at their non-cell binding A-subunit(s).

[1] M.J. Schmitt, F. Breinig, Nat. Rev. Microbiol. 4, 212-21 (2006).

[2] B. Becker, E. Gießelmann, A. Blum, J. Dausend, D. Rammo et al., Sci. Rep., under review.