

Candidalysin is a fungal peptide toxin critical for mucosal infection.

Moyes DL*, Wilson D*, Richardson JP*, Mogavero S*, Tang SX, Wernecke J, Höfs S, Gratacap RL, Robbins J, Runglall M, Murciano C, Blagojevic M, Thavaraj S, Förster TM, Hebecker B, Kasper L, Vizcay G, Iancu SI, Kichik N, Häder A, Kurzai O, Luo T, Krüger T, Kniemeyer O, Cota E, Bader O, Wheeler RT, Gutschmann T, Hube B, Naglik JR (2016) Candidalysin is a fungal peptide toxin critical for mucosal infection. *Nature* 532(7597), 64-68.

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Abstract

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Cytolytic proteins and peptide toxins are classical virulence factors of several bacterial pathogens which disrupt epithelial barrier function, damage cells and activate or modulate host immune responses. Such toxins have not been identified previously in human pathogenic fungi. Here we identify the first, to our knowledge, fungal cytolytic peptide toxin in the opportunistic pathogen *Candida albicans*. This secreted toxin directly damages epithelial membranes, triggers a danger

response signalling pathway and activates epithelial immunity. Membrane permeabilization is enhanced by a positive charge at the carboxy terminus of the peptide, which triggers an inward current concomitant with calcium influx. *C. albicans* strains lacking this toxin do not activate or damage epithelial cells and are avirulent in animal models of mucosal infection. We propose the name 'Candidalysin' for this cytolytic peptide toxin; a newly identified, critical molecular determinant of epithelial damage and host recognition of the clinically important fungus, *C. albicans*.

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