A peptide derived from the highly conserved protein GAPDH is involved in tissue protection by different antifungal strategies and epithelial immunomodulation.

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Abstract

Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) has an important role not only in glycolysis but also in nonmetabolic processes, including transcription activation and apoptosis. We report the isolation of a human GAPDH (hGAPDH) (2-32) fragment peptide from human placental tissue exhibiting antimicrobial activity. The peptide was internalized by cells of the pathogenic yeast Candida albicans and initiated a rapid apoptotic mechanism, leading to killing of the fungus. Killing was dose-dependent, with 10 μg ml (3.1 μM) and 100 μg ml hGAPDH (2-32) depolarizing 45% and 90% of the fungal cells in a population, respectively. Experimental C. albicans infection induced epithelial hGAPDH (2-32) expression. Addition of the peptide significantly reduced the tissue damage as compared with untreated experimental infection. Secreted aspartic proteinase (Sap) activity of C. albicans was inhibited by the fragment at higher concentrations, with a median

effective dose of 160 mg l(-1) (50 µM) for Sap1p and 200 mg l(-1) (63 µM) for Sap2p, whereas Sap3 was not inhibited at all. Interestingly, hGAPDH (2-32) induced significant epithelial IL-8 and GM-CSF secretion and stimulated Toll-like receptor 4 expression at low concentrations independently of the presence of C. albicans, without any toxic mucosal effects. In the future, the combination of different antifungal strategies, e.g., a conventional fungicidal with immunomodulatory effects and the inhibition of fungal virulence factors, might be a promising treatment option.

Involved units

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