Effects of histatin 5 modifications on antifungal activity and kinetics of proteolysis.

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Details

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Abstract

Histatin 5 (Hst-5) is an antimicrobial peptide with strong antifungal activity against Candida albicans, an opportunistic pathogen that is a common cause of oral thrush. The peptide is natively secreted by human salivary glands and shows promise as an alternative therapeutic against infections caused by C. albicans. However, Hst-5 can be cleaved and inactivated by a family of secreted aspartic proteases (Saps) produced by C. albicans. Single-residue substitutions can significantly affect the proteolytic resistance of Hst-5 to Saps and its antifungal activity; the K17R substitution increases resistance to proteolysis, while the K11R substitution enhances antifungal activity. In this work, we showed that the positive effects of these two single-residue modifications can be combined in a single peptide, K11R-K17R, with improved proteolytic resistance and antifungal activity. We also investigated the effect of additional single-residue substitutions, with a focus on the effect of addition or removal of negatively charged residues, and found Sap-dependent effects on degradation. Both single- and double-substitutions affected the kinetics of proteolytic degradation of the intact peptide and of the fragments formed during degradation. Our

results demonstrate the importance of considering proteolytic stability and not just antimicrobial activity when designing peptides for potential therapeutic applications. This article is protected by copyright. All rights reserved.

Beteiligte Forschungseinheiten

Mikrobielle Pathogenitätsmechanismen Bernhard Hube Mehr erfahren

Leibniz-HKI-Autor*innen



Bernhard Hube

Details

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