A *Staphylococcus* Quorum-Sensing Inhibitor Peptide That Is Fungicidal

Patrícia Damasceno Ribeiro¹, Valdirene Moreira Gomes² and Enrique Medina-Acosta¹

¹Laboratórios de Biotecnologia, ²Fisiologia e Bioquímica de Microrganismos, Centro de Biociências e Biotecnologia, Universidade Estadual do Norte Fluminense Darcy Ribeiro, Campos dos Goytacazes, RJ, Brazil. E-mail: pd_ribeiro@hotmail.com

Introduction: Sepsis and systemic mycosis are among the most feared opportunistic infections in the immunocompromised host, burned patients, open surgery patients, newborn and malnourished infants and pathologies associated with contaminated prosthetic devices. The increasing frequency of infections with multidrug-resistant opportunistic microbes demands specific enhancements of therapeutic development. Here we report that the *Staphylococcus* RNAIII-inhibiting synthetic peptide H₂N-YKPI7N-CONH₂ called RIP-6, known to interfere effectively with *Staphylococcus aureus* quorum-sensing dependent expression of virulence genes, exhibited fungicidal activity against *Candida albicans*, *Candida tropicalis* and *Saccharomyces cerevisiae*.

Material and Methods: Yeast cells (1x10⁴ CFU/mL) were cultured by triplicate in Sabouraud liquid medium in the presence of RIP-6 at final concentrations of 2.15 µM, 21.5 µM, 107.5 µM and 215 µM. Growth was monitored reading A₆₃₀ nm every 6 h. The ionic strength-dependent hemolytic activity was tested using Whole cells from EDTA-treated diluted in PBS or IGP. Aliquots were admixed with RIP-6 in the corresponding buffer at different final concentrations. For all *in vivo* experiments the intraperitoneal route of infection was used, while the follow-up treatments with 120 mg RIP-6/Kg or 150 mg RIP-6/Kg were performed intravenously at the radial vein of the tail.

Results and Discussion: RIP-6 killed growing yeasts at varying potencies and susceptibility was ionic environment-dependent (40-100 % susceptible at 2.15 µM in isotonic high ionic strength buffer). RIP-6 antifungal activity was unaffected by salt ions. In a study of the systemic antimycotic activity of RIP-6 in a mouse protection model of lethal infection, repeated administration of RIP-6 (8-25 mg/Kg/dose) to *Candida albicans*-infected mice delayed the onset of disease, suppressed disease progression, and increased survival, with no apparent systemic toxicity, resulting in 33 % long-term survival prophylactic efficacy.

Conclusions: These results suggested that the RIP-based therapy is an efficient strategy to eliminate polymicrobial infections.

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