Niacinamide Helps Combat Candida Albicans

Study Title:

Modulation of histone H3 lysine 56 acetylation as an antifungal therapeutic strategy

Study Abstract:

Candida albicans is a major fungal pathogen that causes serious systemic and mucosal infections in immunocompromised individuals. In yeast, histone H3 Lys56 acetylation (H3K56ac) is an abundant modification regulated by enzymes that have fungal-specific properties, making them appealing targets for antifungal therapy. Here we demonstrate that H3K56ac in C. albicans is regulated by the RTT109 and HST3 genes, which respectively encode the H3K56 acetyltransferase (Rtt109p) and deacetylase (Hst3p). We show that reduced levels of H3K56ac sensitize C. albicans to genotoxic and antifungal agents. Inhibition of Hst3p activity by conditional gene repression or nicotinamide treatment results in a loss of cell viability associated with abnormal filamentous growth, histone degradation and gross aberrations in DNA staining. We show that genetic or pharmacological alterations in H3K56ac levels reduce virulence in a mouse model of C. albicans infection. Our results demonstrate that modulation of H3K56ac is a unique strategy for treatment of C. albicans and, possibly, other fungal infections.

Study Information:

1.Hugo Wurtele, Sarah Tsao, Guylaine Lépine, Alaka Mullick, Jessy Tremblay, Paul Drogaris, Eun-Hye Lee, Pierre Thibault, Alain Verreault, Martine Raymond. Modulation of histone H3 lysine 56 acetylation as an antifungal therapeutic strategy Nature Medicine 2010 July
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