Niacinamide Helps Combat Candida Albicans

Byron's Comments:

A novel new way to help correct Candida imbalance.

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.

From press release:

A team of scientists from the Institute for Research in Immunology and Cancer (IRIC) of the University of Montreal have identified vitamin B3 as a potential antifungal treatment.

Led by IRIC Principal Investigators Martine Raymond, Alain Verreault and Pierre Thibault, in collaboration with Alaka Mullick, from the Biotechnology Research Institute of the National Research Council Canada, the study is the subject of a recent article in Nature Medicine.

Infections by the yeast Candida albicans represent a significant public health problem and a common complication in immunodeficient individuals such as AIDS patients, cancer patients undergoing chemotherapy and recipients of organ transplants. While some treatments are available, their efficacy can be compromised by the emergence of drug-resistant strains.

The current study shows that a C. albicans enzyme, known as Hst3, is essential to the growth and survival of the yeast. Researchers found that genetic or pharmacological inhibition of Hst3 with nicotinamide, a form of vitamin B3, strongly reduced C. albicans virulence in a mouse model. Both normal and drug-resistant strains of C. albicans were susceptible to nicotinamide. In addition, nicotinamide prevented the growth of other pathogenic Candida species and Aspergillus fumigatus (another human pathogen), thus demonstrating the broad antifungal properties of nicotinamide.

“There is an urgent need to develop new therapies to kill C. albicans because it is one of the leading causes of hospital-acquired infections and is associated with high mortality rates,” explains Martine Raymond, who is also a professor at the University of Montreal Department of Biochemistry. “Although many issues remain to be investigated, the results of our study are very exciting and they constitute an important first step in the development of new therapeutic agents to treat fungal infections without major side effects for patients.”

Martine Raymond is Principal Investigator in the Yeast Molecular Biology Laboratory. Alain Verreault is Principal Investigator in the Chromosome Biogenesis Laboratory. Pierre Thibault is Principal Investigator in the Proteomics and Bioanalytical Mass Spectrometry Laboratory. The research received funding from the Canadian Institutes for Health Research and the National Science and Engineering Research Council of Canada.

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
Institute for Research in Immunology and Cancer (IRIC) of the University of Montreal

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