Switching off protein 'thermostat' shuts down deadly fungal disease

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(PhysOrg.com) -- University of Toronto researchers have discovered that by switching off a protein "thermostat" that controls the growth and spread of lethal fungal infections, the disease may be halted.

Professor Leah Cowen and her team in the Department of Molecular Genetics discovered that a specific protein known as heat shock protein 90, or Hsp90, works as a temperature sensitive trigger for development of the potentially life-threatening fungus Candida albicans. By neutralizing Hsp90's function as a thermostat to jumpstart spread of the disease, C. albicans can be stopped in its tracks.

The research was published March 26 in the journal Current Biology.

Candida albicans can cause a wide range of disease from superficial infections such as yeast infections to life-threatening infections in the bloodstream. They can be especially lethal for people with compromised immune systems, such as those with AIDS or people undergoing treatment for cancer or organ transplantation, and they are the fourth leading cause of hospital acquired infectious diseases.

"We discovered that Hsp90 is the key temperature sensor governing the development of C. albicans. Using mouse models, we further found that by genetically inhibiting Hsp90, the result was complete clearance of the disease," said Cowen, Canada Research Chair in microbial genomics and infectious disease.

Cowen has spent many years focusing on Hsp90's role in enabling the evolution of fungal drug resistance and developing strategies to harness Hsp90 as a tool to block the emergence of drug resistance and render resistant pathogens more responsive to treatment. Working with Rebecca Shapiro, a graduate student in her new lab at U of T, Cowen became fascinated by the longstanding mystery in the field as to why elevated temperature was required for environmental conditions such as serum to induce filamentous growth in C. albicans.

Their discovery that Hsp90 provides a new mechanism to sense changes in temperature stimulated a fruitful collaboration with researchers at Duke University. Cowen's lab collaborated with Joseph Heitman's team at Duke to dissect the molecular mechanisms through which Hsp90 regulates this developmental transition. Together they screened hundreds of C. albicans mutants to uncover the identity of the proteins through which the Hsp90 thermostat works to regulate development. Cowen also teamed up with labs headed by Duke University's Aimee Zass and John Perfect to perform mouse model studies that established that inhibiting Hsp90 may provide a powerful therapeutic strategy for life-threatening fungal disease.

Provided by University of Toronto (news : web)