Tiny molecules protect from the dangers of sex

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Pathogenic fungi have been found to protect themselves against unwanted genetic mutations during sexual reproduction, according to researchers at Duke University Medical Center. A gene-silencing pathway protects the fungal genome from mutations imposed by a partner during mating.

This pathway was discovered in Cryptococcus neoformans, a fungus that commonly infects humans, causing over one million cases of lung and brain infection each year, and more than 600,000 deaths. A related species, Cryptococcus gattii, is causing an expanding outbreak in the Pacific Northwest that is of considerable public health impact and concern.

"This discovery of how the genome is protected during sex might be leveraged as an Achilles' heel in the battle against C. neoformans, which frequently causes life-threatening illness in people," said senior author Joseph Heitman, M.D., Ph.D., chair of the Duke Department of Molecular Genetics and Microbiology. "This protective silencing effect also operates in some animals, and our studies demonstrate that the pathway operates to defend the genome during sexual reproduction."

Sexual reproduction in fungi produces airborne spores that are readily inhaled into the lungs and thought to be the source of human infections. Thus, agents that block fungal sex might stop the risk of infection at the source.

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C. neoformans uses a novel sex-induced RNAi (RNA interference) genome defense system that protects by effectively "silencing" the DNA, so that it is not vulnerable to repeated genes and transposable elements that could cause mutations.

The silencing system protects the genome from changes that might be imposed by transposable elements of DNA, called "jumping genes," that are also more active during the sexual cycle, said Xuying Wang, Ph.D., a postdoctoral associate who works in the Heitman lab.

Through deep sequencing of the small RNAi pieces which mediate the silencing in C. neoformans, the team also identified abundant small RNAs which map to repetitive transposable elements that could cause mutations if not silenced.

These small RNAs were absent in mutant strains (rdp1) that were studied. One group of transposable elements was greatly expressed during mating of rdp1 mutant strains and these fungi showed an increased transposition and mutation rate in the next generation, leading the researchers to conclude that the RNAi pathway squelches transposon activity during the sexual cycle.

Provided by Duke University Medical Center