Gene that governs toxin production in deadly mold found

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For the growing number of people with diminished immune systems - cancer patients, transplant recipients, those with HIV/AIDS - infection by a ubiquitous mold known as Aspergillus fumigatus can be a death sentence.

The fungus, which is found in the soil, on plant debris and indoor air, is easily managed by the healthy immune system. But as medical advances contribute to a growing population of people whose immune systems are weakened by disease or treatment, the opportunistic fungus poses a serious risk.

Now, however, scientists may have found a master switch, an über gene, that seems to control the mold's ability to make poison. The new finding was reported today (April 12) in the journal *Public Library of Science Pathogens* by a team led by Nancy P. Keller, a biologist from the University of Wisconsin-Madison.

"There is a growing problem with medical fungi in the United States," says Keller, a UW-Madison professor of plant pathology and medical microbiology. "Aspergillus fumigatus is among the most important."

Like many fungi, Aspergillus fumigatus makes a variety of poisons, presumably to give the microbe a competitive advantage in the environments it inhabits. In humans with suppressed immune systems, the mold can cause a number of diseases with mortality rates of 60 percent or more.

"The infection can be treated, but not easily," Keller explains. "Once an immunocompromised individual gets any fungal disease, it's pretty hard to treat, and the treatments themselves are often toxic. There is a 60-90 percent mortality rate with invasive aspergillosis."

Thus, knowing how the fungus makes its chemical arsenal is important and opens an avenue to devising novel treatments that can disarm the pathogen before it does its dirty work.

In fungi, there are typically many genes at work making toxins and other chemical metabolites. The genes tend to be clustered in groups on the organism's genome. In Aspergillus fumigatus, there are as many as 22 such gene groupings.

How those posses of genes are triggered and governed, however, has been a mystery. But now Keller's group has found that a key gene known as LaeA controls at least half of those toxin-producing gene clusters, suggesting there may be a way to modulate the virulence of the deadly microbe.

"We now have a very good idea that (the gene) is central to the toxic nature of the fungus," Keller says.

The LaeA gene, she believes, is like a maestro, directing the mold's toxin-producing genes in an orchestrated chorus that, in the right host, can be fatal.

Knowing this, Keller explains, "suggests that if you can find a way to regulate the activity of LeaA you might have a novel target" for new therapies to treat Aspergillus fumigatus infection.

"The gene is not expressed all the time, which means there must be a signal that says 'turn me on.'"

Removing the gene from the equation, she says, may cripple the microbe's ability to infect and sicken people.

"The loss of LaeA results in a great decrease in the repertoire of secondary metabolites, which appears to impact the infection process," making the gene an ideal prospect for new ways to fight infection.

Source: University of Wisconsin-Madison