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Researchers surprised by results of lung, mold study

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Researchers led by Montana State University have found a surprising condition that occurs in the lungs after an invasion of a common mold that can cause deadly infections in humans.

In the most oxygen-rich environment in the body - the lungs - the scientists discovered a shortage of oxygen. The shortage resulted from inflammation and invasive growth of the mold, which greatly reduced the oxygen available to the pathogenic mold *Aspergillus fumigatus*.

The mold is generally found in hay, soils and compost piles and can cause a variety of lung infections when inhaled by humans. The most lethal is invasive aspergillosis, which can kill 30 to 90 percent of its victims depending on the patient population. Most susceptible are people who have had organ transplants, HIV, chemotherapy or other medical treatments that weaken their ability to fight off infection.

"We think this (the lack of oxygen) is a really big stress on the pathogen," said Nora Grahl, a doctoral candidate at MSU.

Grahl led the study that's adding knowledge to the field of infectious disease and was published in the July 21 issue of *PLoS Pathogens*. Based in Dr. Robert Cramer's laboratory in MSU's Department of Immunology and Infectious Diseases, the study was the first to show a strong link between hypoxia, or low oxygen levels in the lungs, and fungal infections , Grahl said. She added that the research was unique because little research has been done on the microenvironments encountered by

Aspergillus fumigatus in such detail during infection.

The study was conducted in mice and showed a variety of ways that the lungs and mold respond to each other. The scientists noted, for example, that low levels of oxygen are just one of many challenges that mold has to overcome before it can cause a lung infection. When the shortage occurs, though, microbes may adapt through fermentation or other changes in metabolism. An important finding of the study was that the mold's fermentation could also influence the host immune response to the pathogen.

Cramer said most microbes can use fermentation to generate energy during hypoxia, but Grahl has also found mutant strains of the mold that use respiration instead. As a result, the researchers are interested in continuing to study respiration as it relates to Aspergillus fumigatus pathogenesis.

Grahl said she learned that the PLoS Pathogens paper - her first published paper as lead author -- had been accepted for publication while attending the fourth Federation of the Societies of Biochemistry and Molecular Biology (FEBS) Conference on Human Fungal Pathogens in France. After presenting her research there in May, she won an Outstanding Young Investigator Award for her work.

Provided by Montana State University