Researchers examine potential drug pathway to combat Pneumocystis

December 14 2016, by Cedric Ricks

A study led by University of Cincinnati (UC) researchers is offering new insight in how the fungus Pneumocystis, thrives in the lungs of immune-comprised individuals, where it can cause a fatal pneumonia.

The study, "Functional characterization of the Pneumocystis carinii Inositol Transporter 1," is currently available in the online edition of the journal, *MBio* and details the use of mouse models to identify a new drug therapy for the potential treatment of Pneumocystis pneumonia, inositol transport.

These obligate fungal pathogens, Pneumocystis, must transport inositol—a sugar-like nutrient essential for life in most organisms—obtained from the mammalian lung using a specific transporter, explains Melanie T. Cushion, PhD, senior associate dean for research and professor of internal medicine at the UC College of Medicine.

"Identifying a drug to inhibit the transporter will kill these fungi because they can't synthesize inositol as they lack two enzymes to do so," says Cushion. "The transporters in humans and Pneumocystis are sufficiently different that inhibitors of the fungal transporter are not likely to impact the mammalian transporters. If that's the case, no toxicity is expected with this new line of drugs."

These fungi are immune to common current anti-fungal therapies, and the gold standard therapy, trimethoprim sulfamethoxazole, often results

in life-threatening allergic reactions in many patients. In the journal article, researchers characterized the transport of inositol in the fungus and found that it was highly selective for inositol and did not transport any other molecules, explains Cushion.

For individuals living with HIV/AIDS, Pneumocystis jirovecii, causes a lethal pneumonia (PCP) despite the use of combined antiretroviral therapy in patients, says Cushion. The mortality rate from PCP is about 15 percent in HIV positive populations in the United States and other developed countries, while in the developing world or underserved populations in the U.S. the mortality rate approaches 80 percent, she explained.

An advance in combating Pneumocystis could also help transplant patients who are on immunosuppressive drugs for life and other patients receiving these therapies for ailments such as rheumatoid arthritis, says Cushion.

More information: Melanie T. Cushion et al. Functional Characterization ofInositol Transporter 1, *mBio* (2016). DOI: 10.1128/mBio.01851-16

Provided by University of Cincinnati