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Genetic links to fungal infection risk identified

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(PhysOrg.com) -- Two genetic mutations that may put individuals at increased risk of fungal infections have been identified by scientists from UCL and Radboud University, increasing understanding about the genetic basis of these infections and potentially aiding the development of new treatments.

The two separate studies, published today in the New England Journal of Medicine, mark a significant step in the understanding of genetic susceptibility to fungal diseases. The findings have implications for people suffering from chronic mucocutaneous candidiasis (CMC), as well as more common infections like vaginal candidosis (thrush).

The UCL-led research focused on patients from multiple generations of a large family who had suffered from serious recurrent fungal infections that proved lethal in some of those affected. DNA sequencing and genetic mapping techniques enabled the researchers to identify that this family had a recurrent mutation in a gene called CARD9. The team from Radboud University in the Netherlands discovered that a mutation in the gene Dectin-1 is associated with increased susceptibility to vaginal infections by fungi (primarily of the genus Candida).

When these two genes are working correctly, Dectin-1 senses the presence of fungi and prompts the immune cells to send signals that result in CARD9 setting off a molecular response in the immune system to protect against these microorganisms. If Dectin-1 or CARD9 are mutated or missing, the immune system struggles to control Candida and

may allow local or even systemic (affecting the entire body) infections to develop.

Both studies involved researchers from across the world. Critical experiments to prove the causality of the CARD9 mutation were done at the Technical University of Munich, Germany, where mice lacking the corresponding gene had been shown to be susceptible to fungal infections. Similarly, demonstration of the molecular mechanisms leading to the loss of fungi recognition by mutated Dectin-1 in mice had been performed by the University of Aberdeen.

Professor Mihai Netea, who led the team from Radboud University, said: "Although the process of host response to fungal infection has previously been studied in mice, it is very interesting to see that it is the same in humans. The new results show that the mechanisms to protect against fungal infections have been largely conserved by evolution between mice and humans, which is not necessarily the case for other microbes."

Corresponding author Professor Bodo Grimbacher, UCL Infection & Immunity and Consultant Immunologist at The Royal Free Hospital, said: "This discovery enables further insights in the interaction between fungi and the human immune system and may pave the way for future therapeutic options in patients suffering from Candida infections."

More information: The paper 'Susceptibility to fungal infections due to homozygous mutation in CARD9' is published in the latest edition of the *NEJM*. http://content.nejm.org/cgi/content/short/361/18/1727

Source: University College London (news : web)