

# Predicting the risk of a common fungal infection after stem cell transplantation

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In silico genetic analysis in mice has led to the discovery of a gene affecting susceptibility to a severe fungal infection in transplant recipients. In a study published June 20th in the open-access journal *PLoS Genetics*, investigators from Duke University Medical Center, the National Institute of Environmental Health Sciences, Roche Palo Alto, the Fred Hutchinson Cancer Research Center, and the National Jewish Medical and Research Center found that genetic variation within the plasminogen gene in mice and men affects susceptibility to a severe and life-threatening fungal infection.

Invasive infection with *Aspergillus fumigatus* is a common and life-threatening infection among severely immunocompromised individuals. Despite aggressive surveillance and prophylaxis, its incidence in hematopoietic stem cell transplant recipients hovers around 10%, and the three-month mortality rate is approaching 30%.

Lead investigators Aimee Zaas and David Schwartz examined the susceptibility of different inbred mouse strains for developing invasive aspergillosis after receiving immunosuppressive therapy. The inbred strains exhibited significant and reproducible differences in survival after inhalational exposure to the fungus.

Co-author Gary Peltz and colleagues recently developed an in silico method for genetic analysis in mice that was used to analyze this survival data, which led to the rapid identification of genetic variation within the plasminogen gene as a potential susceptibility factor. Therefore, it is

possible that polymorphisms in human plasminogen may also affect susceptibility. Analysis of a cohort of bone marrow transplant recipients indicated that a human plasminogen allele also affects the risk of contracting this disease.

Peltz, who is now at Stanford University, stated: "This is the first study that used a multi-species genetic mapping approach to identify genetic susceptibility factors for a severe infection."

Identification of a genetic polymorphism that influences infection after transplantation has important implications for pre and post transplant care, and possibly for the management of other immune-compromised patients. Genetic testing could identify high-risk individuals who may benefit from the use of broad-spectrum antifungal agents or enhanced monitoring for infection. It is important to emphasize, however, that further research and evaluation is required before clinical applications can be developed.

Source: Public Library of Science

[www.plosgenetics.org/doi/pgen.1000101](http://www.plosgenetics.org/doi/pgen.1000101)

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