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RESEARCH NEWS STORY

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Chiba University

How an Immune Cell Receptor Dampens the Fight Against Fungal Infection

Researchers clarify a previously underexplored immunoregulatory mechanism in aspergillosis, paving the way for improved clinical management

People are constantly exposed to fungal spores, including those of *Aspergillus fumigatus*, but individuals with weakened immune systems may develop life-threatening infections. In a recent study, researchers from Japan clarified the mechanisms by which the dendritic cell immunoreceptor (Dcir) suppresses neutrophil activity during infection with *A. fumigatus*. Their findings highlight Dcir as a potential therapeutic target for aspergillosis and suggest promising research avenues in the field of immunology.

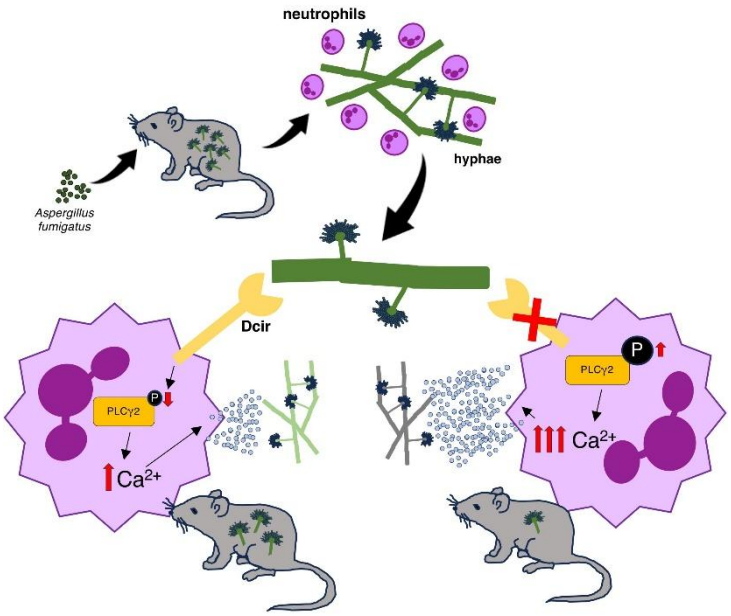

Image title: The role of Dcir during infection with *Aspergillus fumigatus*
Image caption: Dcir recognizes *Aspergillus fumigatus* hyphae and dampens the degranulatory activity of neutrophils. Without Dcir, neutrophils show enhanced fungicidal activity, and the host's ability to eliminate the pathogen is improved.
Image credit: Associate Professor Shinobu Saijo from Chiba University, Japan
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People are exposed to millions of fungal spores every day, even potentially harmful ones like those from *Aspergillus fumigatus*. For most individuals, this constant exposure is harmless, as the immune system efficiently clears the spores without causing illness. However, for a growing number of people with weakened immune systems due to cancer, organ transplants, or chronic diseases, *Aspergillus* spores can lead to life-threatening infections known as aspergillosis. Thus, understanding the specific immune mechanisms that fight fungal infections is essential for developing therapies and improving outcomes for those affected.

Scientists have long studied a family of sensor proteins called C-type lectin receptors (CLRs), which are crucial for detecting and eliminating pathogens. Most CLRs act like a car's gas pedal, initiating powerful immune responses to attack invading microbes. However, one specific CLR, the dendritic cell immunoreceptor (Dcir), is a known immunoregulator that instead acts like a brake, dampening immune responses. While its role in limiting inflammation and autoimmunity is well-documented, its precise function during fungal infections remains unclear.

In a recent study, a research team led by Associate Professor Shinobu Saijo and Assistant Professor Fabio Seiti Yamada Yoshikawa of the Medical Mycology Research Center at Chiba University, Japan, tackled this knowledge gap. Using mouse models, the team investigated how Dcir influences the host response to *Aspergillus fumigatus*, focusing on how it affects a key immune cell type. The study was published in Volume 16 of the journal *Frontiers in Immunology* on August 4, 2025.

Initial experiments revealed that mice lacking Dcir (or 'Dcir-knockout') were significantly better at clearing the fungal infection from their lungs and spleen compared to wild-type mice. To understand why the absence of this receptor improved the immune response, the team focused on neutrophils, which are the primary immune cells responsible for combating this type of infection. They discovered that the protective effect of Dcir deficiency was entirely dependent on neutrophils, as depleting these cells in Dcir-knockout mice eliminated the enhanced fungal clearance they had previously observed.

The researchers then moved on to *in vitro* experiments, for which they isolated neutrophils from the Dcir-knockout mice. "*Neutrophils eliminate pathogens via phagocytosis, programmed cell death, oxidative stress, and degranulation*," explains Dr. Fabio Seiti Yamada Yoshikawa. "*We sought to pinpoint the exact effector mechanism through which Dcir regulates fungicidal activity against A. fumigatus*." The team confirmed that these neutrophils were more effective at killing fungal hyphae—the filamentous structures that make up the main body of the fungus—through degranulation. This is a powerful process in which neutrophils release their internal store of enzymes, destroying pathogens too large to be engulfed. Neutrophils from Dcir-deficient mice exhibited significantly higher degranulation activity, which the researchers linked to increased intracellular calcium mobilization and the activation of a specific signaling protein called PLCγ2. Conversely, when they blocked the degranulation process with a drug, the protective effect of Dcir deficiency disappeared, both *in vitro* and in the mouse model.

By acting as a negative regulator of neutrophil degranulation, Dcir essentially puts a brake on the immune system, limiting its effectiveness against *A. fumigatus*. Overall, these findings

broaden our understanding of CLR functions in host defense, highlighting an additional level of complexity in host–fungi interactions that could be leveraged in clinical practice. "*The identification of Dcir as a receptor involved in the host defense to Aspergillus fumigatus suggests that it can be a potential target for pharmacological interventions, helping in the treatment of patients affected by this infection,*" notes Dr. Saijo. "*Our work thus opens new avenues of investigation that can help improve the current understanding of aspergillosis and its management*."

Further research will focus on whether genetic variations in the *Dcir* gene are associated with the severity of aspergillosis in humans and on identifying the specific molecules on *Aspergillus* that Dcir recognizes. With any luck, these efforts will ultimately lead to better options for those at higher risk of fungal infection.

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About Associate Professor Shinobu Saijo from Chiba University, Japan
Dr. Shinobu Saijo is an Associate Professor at the Division of Molecular Immunology, Medical Mycology Research Center at Chiba University, Japan. Her research focuses on molecular immunology, especially cytokines at the interface of health and disease. She has over 70 scientific publications on these topics.

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Reference:
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Authors: Fabio Seiti Yamada Yoshikawa[1], Rikio Yabe[1,2], Shota Torigoe[3,4,5], Sho Yamasaki[1,3,6,7], and Shinobu Saijo[1]
Affiliations: (1) Division of Molecular Immunology, Medical Mycology Research Center, Chiba University, Japan
(2) Cancer Immunology Project, Department of Diseases & Infection, Tokyo Metropolitan Institute of Medical Science, Japan
(3) Laboratory of Molecular Immunology, Immunology Frontier Research Center, Osaka University, Japan
(4) Department of Mycobacteriology, Leprosy Research Center, National Institute of Infectious Diseases, Japan
(5) Research Center for Biosafety, Laboratory Animal and Pathogen Bank, National Institute of Infectious Diseases, Japan
(6) Department of Molecular Immunology, Research Institute for Microbial Diseases, Osaka University, Japan
(7) Center for Infectious Disease Education and Research (CiDER), Osaka University, Japan
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Contact: Shinobu Saijo
Medical Mycology Research Center, Chiba University
Email: saijo@faculty.chiba-u.jp

Academic Research & Innovation Management Organization (IMO), Chiba University
Address: 1-33 Yayoi, Inage, Chiba 263-8522 JAPAN
Email: cn-info@chiba-u.jp