Scientists Unravel Mystery of Mycetoma Grain Formation

Groundbreaking Study Reveals Critical Role of Iron, Paving the Way for New Treatments

Osaka, Japan – A groundbreaking study led by a global research consortium offers new hope for patients with mycetoma, a neglected tropical disease. Researchers using an insect model and transcriptome analysis have unravelled the mechanism of iron regulation between host tissue and the mycetoma grain, a fungal mass characteristic of the disease. This discovery illuminates how the causative fungus invades and develops these protective grains within subcutaneous tissue, paving the way for new drug development and less invasive treatment strategies beyond surgical removal, potentially reducing the burden on patients significantly.

Mycetoma, a chronic infectious disease affecting impoverished communities, is characterized by the development of black grains within infected tissue. These grains shield the causative fungus from the immune system and antifungal agents, making treatment challenging and often requiring surgery or amputation. Until now, the process of grain formation has remained largely unknown.

A research group led by Specially Appointed Professor Imad Abugessaisa, in collaboration with Associate Professor Wendy van de Sande from Erasmus University Medical Center in the Netherlands, headed a consortium from RIKEN IMS (Japan), Erasmus MC (Netherlands), Maynooth University (Ireland), and the Mycetoma Research Center (WHO collaborating center on Mycetoma and Skin Neglected Tropical Diseases, Sudan). The team used state-of-the-art histology techniques, omics technologies, and computational biology to unravel the formation and development of mycetoma grains.

In their study, the consortium used an invertebrate model, *Galleria mellonella*, in which they could follow grain formation over time. By performing RNA analysis at different time points, they demonstrated that iron homeostasis in both host and pathogen plays an important role in mycetoma grain formation. These findings are an important milestone in the field of mycetoma research. Although the presence of grains was documented as early as 1840, how these grains form and which processes in both host and pathogen contribute have remained a mystery until now.

In this extensive study, the consortium showed that the primary mycetoma causative agent produces siderophores, fungal molecules that are excreted to scavenge iron and bring it back to the fungal cell. Furthermore, the amount of iron within the host appears to be important in either containing the fungus inside the grain or allowing it to grow actively outside the grain. Therefore, interfering with iron uptake might be a promising target for drug discovery.

Reflecting on the journey leading to this achievement, Professor Imad Abugessaisa stated, “In Wad Onsa, Sudan, a village with the world's highest prevalence of mycetoma, the disease leaves many disabled and impoverished, especially young people. Determined to make a difference, I partnered with Dr. Wendy van de Sande and secured funding from various organizations, including RIKEN, Erasmus MC, JSPS, and the GHIT Fund, to research this neglected disease. This publication highlights the importance of collaboration in achieving scientific breakthroughs and addressing societal needs.”

The article, “Iron regulatory pathways differentially expressed during *Madurella mycetomatis* grain development in *Galleria mellonella*,” is published in *Nature Communications* at DOI: https://doi.org/10.1038/s41467-025-60875-2.

Summary:

A groundbreaking study led by a global research consortium offers new hope for patients with mycetoma, a neglected tropical disease. Researchers using an insect model and transcriptome analysis have unravelled the mechanism of iron regulation between host tissue and the mycetoma grain, a fungal mass characteristic of the disease. This discovery illuminates how the causative fungus invades and develops these protective grains within subcutaneous tissue, paving the way for new drug development and less invasive treatment strategies beyond surgical removal, potentially reducing the burden on patients significantly.

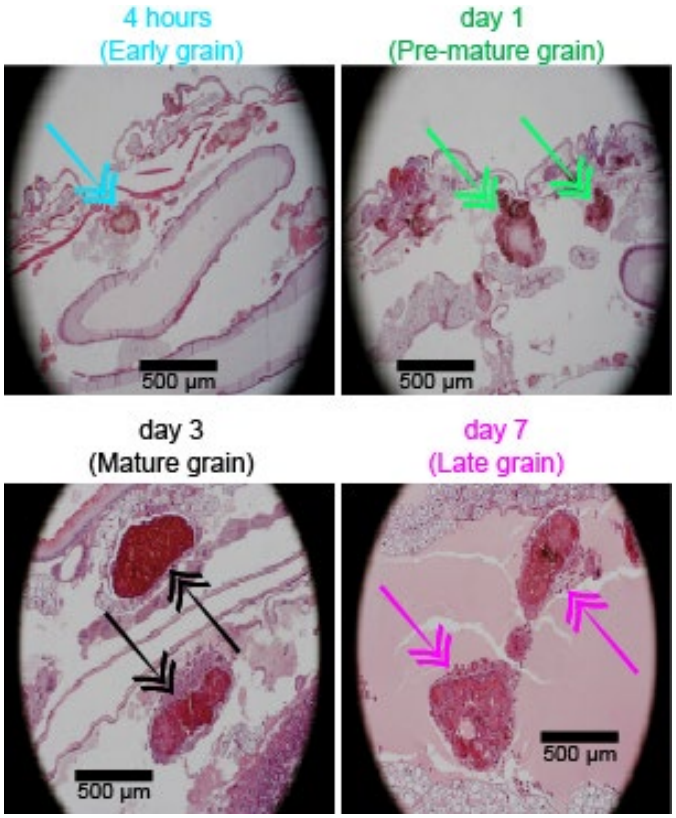

Fig. 1
Grain formation in the host was visualized 40 times magnified using H&E staining and light microscopy
Credit: 2025, Imad Abugessaisa et al., Iron regulatory pathways differentially expressed during *Madurella mycetomatis* grain development in *Galleria mellonella*, *Nature Communications*

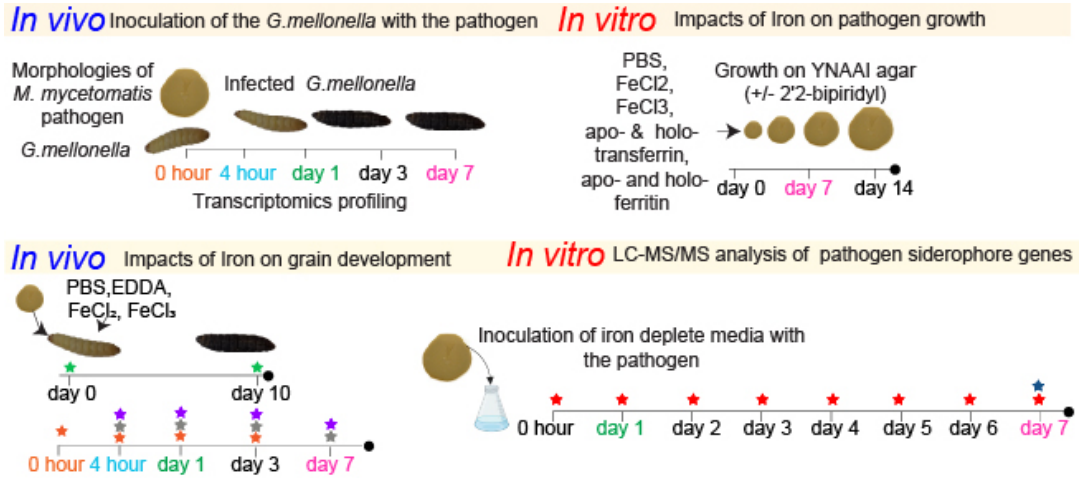

Fig. 2
Overall view of the study. In vivo and in vitro, study of the grain development and impact of iron.
Credit: 2025, Imad Abugessaisa et al., Iron regulatory pathways differentially expressed during *Madurella mycetomatis* grain development in *Galleria mellonella*, *Nature Communications*

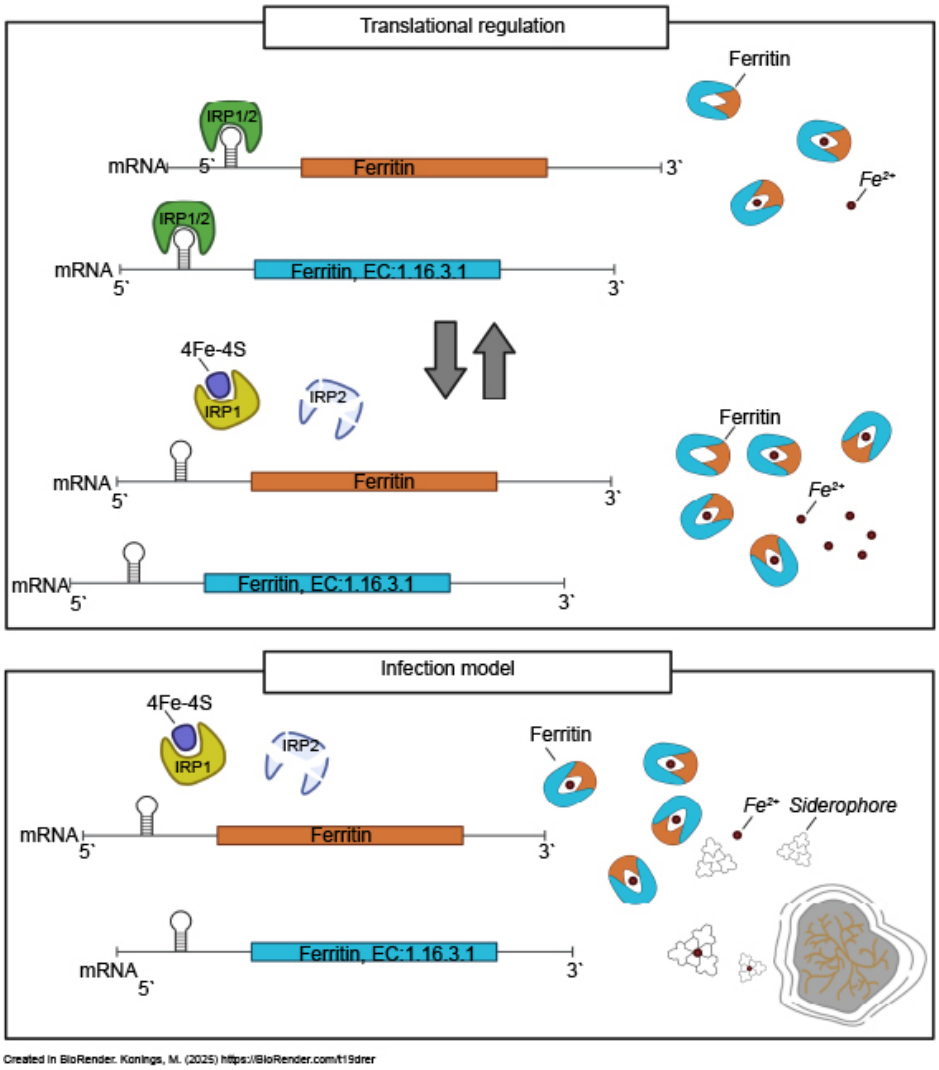

Fig. 3
Snapshot of different analysis showing gene expression changes, expression of iron genes and impacts of iron on pathogen growth
Credit: 2025, Imad Abugessaisa et al., Iron regulatory pathways differentially expressed during *Madurella mycetomatis* grain development in *Galleria mellonella*, *Nature Communications*

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