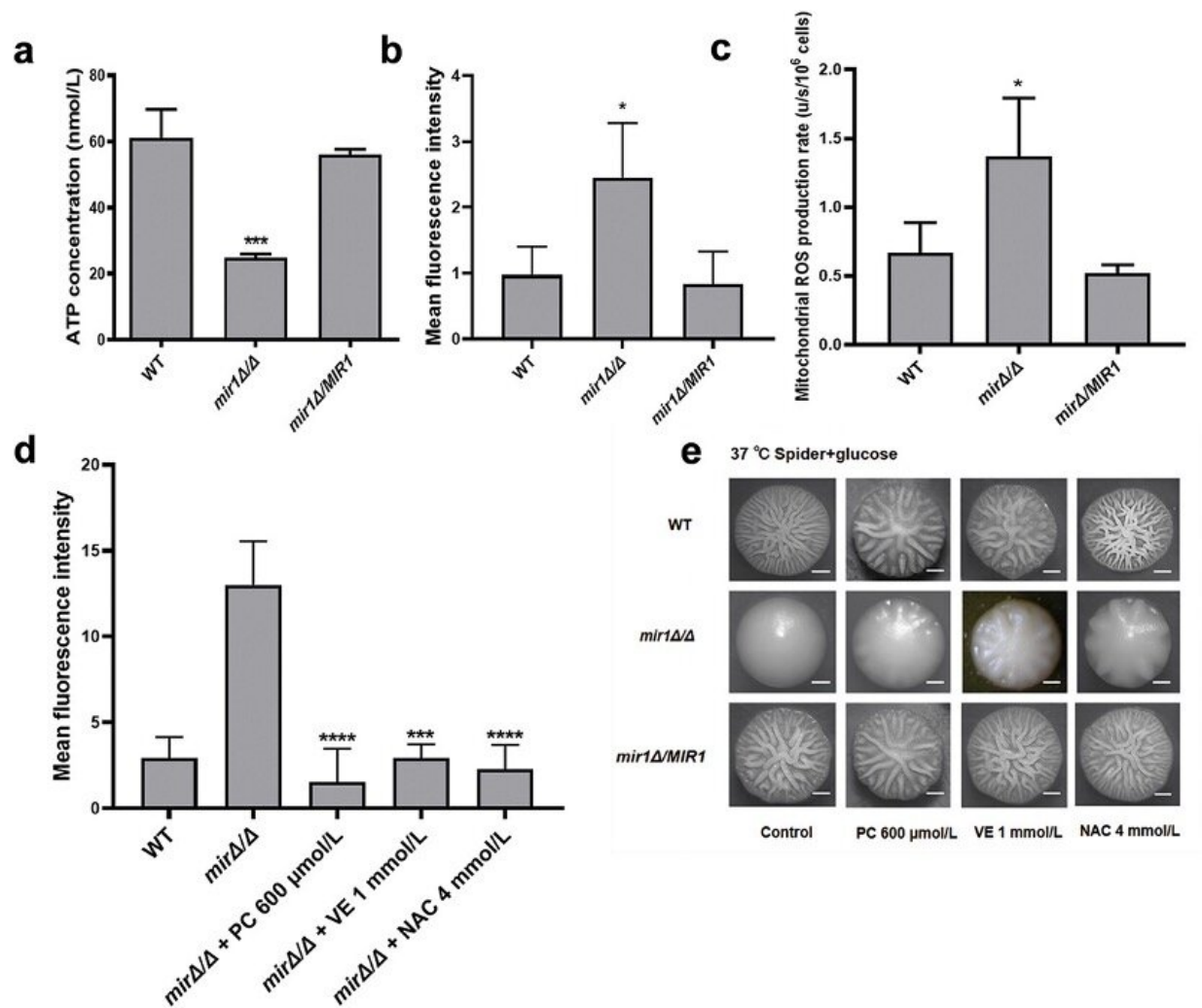


Study finds mitochondrial phosphate carrier plays an important role in virulence of *Candida albicans*

May 22 2024



Cells grown on spider + glucose (100 mmol/L) agar medium for 3 days were harvested and used for mRNA extraction. To investigate the effect of antioxidants, spider + glucose (100 mmol/L) agar medium was added with 4 mmol/L NAC. Expression levels of the selected genes were assessed by RT-qPCR. (a) Relative mRNA levels of some hypha-related genes in *Candida albicans* wild-type, *mir1*Δ/Δ, and *mir1*Δ/*MIR1* strains. (b) Effect of the antioxidant NAC on the mRNA levels of some hypha-related genes in the *mir1*Δ/Δ mutant. Credit: Mycology

In a paper [published](#) in *Mycology*, Professor Yan Wang's team found that in both nematode and murine infection models, the lack of MIR1 gene, which encodes mitochondrial phosphate carrier, can lead to severe virulence defects in *Candida albicans*.

Further studies showed that [virulence](#) defects were associated with defects in hyphal formation and [reactive oxygen species](#) (ROS) production. This study shows that MIR1 plays an important role in *C. albicans* mitochondrial function, filamentation and virulence, and may be a promising antifungal target.

In the *Caenorhabditis elegans* candidiasis model, the survival rate of the wild-type strain infected group dropped to about 20% at 120 h, while the survival rate of the *mir1*Δ/Δ-infected group remained about 90% at 120 h. Similar results were obtained in the murine model. None of the mice infected with *mir1*Δ/Δ mutant died during 21 days of observation, while all of the mice infected with the wild type or the *mir1*Δ/*MIR1* mutant died within 8 days.

The team decided to further investigate why MIR1 plays an important

role in virulence of *C. albicans*. Hyphal formation is an important virulence factor for *C. albicans* to invade the host and exert virulence. The team studied the hyphal formation ability of *mir1* Δ/Δ mutants under different culture conditions.

Interestingly, the *mir1* Δ/Δ mutant exhibited severe filamentation defects on the hypha-inducing agar media, including YPD + serum, Lee, Spider + glucose, SLAD, SLD, and YPS. They further found that the loss of *MIR1* resulted in non-fermentable carbon utilization defects, ATP reduction, and reactive oxygen species (ROS) accumulation in *C. albicans*.

The antioxidant proanthocyanidins, vitamin E, and N-acetyl cysteine could reduce intracellular ROS level and partially rescue the filamentation defects of the *mir1* Δ/Δ mutant. Thus, the loss of *MIR1* led to a loss of virulence in *C. albicans*, and this effect was related to the defects in hyphal formation caused by ROS accumulation.

Then a new question arises: How does ROS accumulation affect the formation of hyphae in *C. albicans*? Was it due to the blockage of the hyphal-promoting signaling pathways?

The team tested the expressions of 11 hypha-related genes and they found that many of the genes, including *ECE1*, *HWP1*, *HGC1*, *HYR1*, *CST20*, *CEK1*, *CPH1*, *CYR1*, *TPK1*, *EFG1* and *RIM101*, were down-regulated in the *mir1* Δ/Δ mutant. Moreover, these down-regulations could be partially rescued by the addition of the antioxidant NAC. Collectively, ROS inhibited hyphal formation of *mir1* Δ/Δ mutant, partially by down-regulating the expressions of hypha-related genes.

"This study shows *MIR1* plays a vital role in respiration, filamentation and virulence of *C. albicans*, and disrupting respiration through blocking the mitochondrial phosphate carrier may be an effective antifungal

strategy," said Professor Wang.

More information: Qiao-Ling Hu et al, Mitochondrial phosphate carrier plays an important role in virulence of *Candida albicans*, *Mycology* (2024). [DOI: 10.1080/21501203.2024.2354876](https://doi.org/10.1080/21501203.2024.2354876)

Provided by Tsinghua University Press

Citation: Study finds mitochondrial phosphate carrier plays an important role in virulence of *Candida albicans* (2024, May 22) retrieved 22 June 2024 from <https://phys.org/news/2024-05-mitochondrial-phosphate-carrier-plays-important.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--