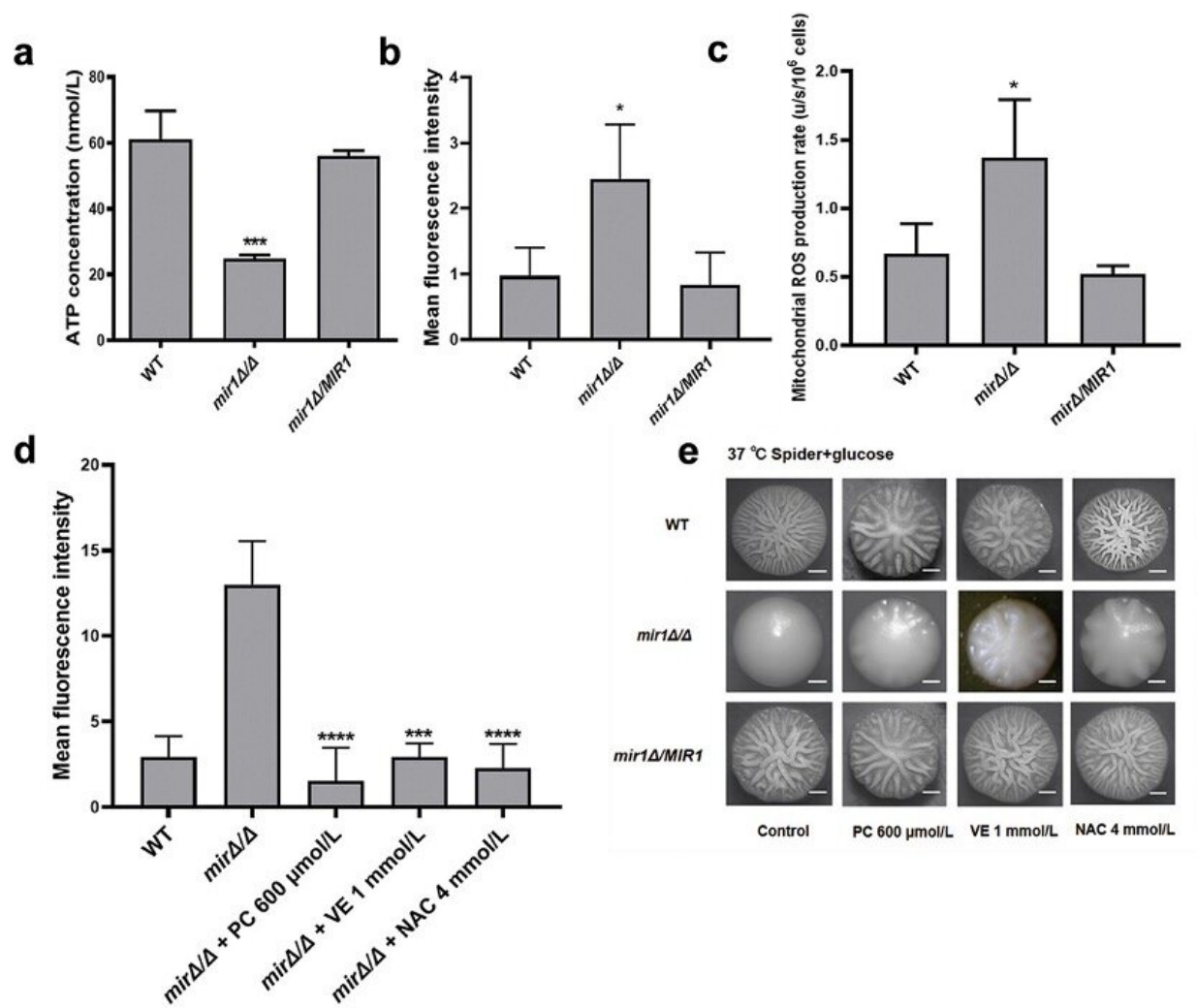


Study finds mitochondrial phosphate carrier plays an important role in virulence of *Candida albicans*

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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)

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