Ataxia-Telangiectasia Mutated Kinase (ATM) Regulates Mitochondrial Homeostasis In *Aspergillus nidulans*

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**INTRODUCTION:** ATM is a phosphatidylin-3-kinase-related protein kinase that functions as a central regulator of DNA damage response in eukaryotes. In humans, mutations in ATM cause the devastating neurodegenerative disease Ataxia-Telangiectasia. Previously, our group characterized the homologue of ATM (AtmA) in the filamentous fungus *Aspergillus nidulans*. In addition to its role in DNA damage response AtmA also plays a role in polarized hyphal growth. Recently, we also observed that AtmA is impaired in glucose uptake. Here, we report that loss of *A. nidulans* AtmA controls mitochondrial homeostasis.

**MATERIAL AND METHODS:** Oxygen consumption was monitored polarographically by an oxygraph equipped with a Clark-type oxygen electrode. Germlings and conidia were incubated with MitoTracker Green FM and Nonyl-Acridine Orange and visualized on an Observer Z1 fluorescence microscope (Carl Zeiss) and analysed by flow cytometry, respectively. Oxidative stress was detected after incubation with H₂DCFDA.

**RESULTS AND DISCUSSION:** Mitochondrial respiration was measured in the wild-type and \(\Delta \text{atmA}\) strains in a respiration medium. After addition of Antimycin A, we observed an increase in 30% of alternative oxidase activity in \(\Delta \text{atmA}\), which was fully inhibited by addition of SHAM. Accordingly, the alternative oxidase gene (\(\text{aoxA}\)) expression was higher in the mutant than in the wild-type strain. When TMPD/Ascorbate was added as a substrate, a decrease in the complex IV activity was shown in the \(\Delta \text{atmA}\) strain. The ROS levels in the \(\Delta \text{atmA}\) strain were about 60% higher than in the wild-type strain. Interestingly, the \(\Delta \text{atmA}\) strain exhibits an increase of 60% in mitochondrial mass as assessed by staining with MitoTracker Green FM and Nonyl-Acridine Orange, suggesting a defect in intracellular destruction of abnormal mitochondria (mitophagy).

**CONCLUSION:** These results suggest that loss of AtmA causes a defect mitochondrial homeostasis.

Key words: *Aspergillus nidulans*, ATM, mitochondria,

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