

The *smiA* gene is required for proliferation, growth and proper function of Cell Wall Integrity Pathway in *Aspergillus fumigatus*

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Aspergillus fumigatus is known as an opportunistic pathogenic fungus responsible for the majority of infections, such as invasive pulmonary aspergillosis in immunosuppressed patients. Inside the host, fungi species respond to the environmental stimuli through signal transduction cascades, linking the external signals to proper intracellular responses. Among the several strategies involved in the regulatory system that controls fungal cellular responses is the Cell Wall Integrity (CWI) pathway, which is mainly responsible for the *de novo* synthesis and remodeling of fungal cell wall. It is known that *Sacharomyces cerevisiae* gene *SMI1 (KNR4)* acts modulating the activity of CWI pathway, regulating cell wall synthesis. To assess the function of *smiA* gene in cell wall maintenance in *A. fumigatus*, a null mutant ($\Delta smiA$) mutant strain was isolated. $\Delta smiA$ shows defects in asexual structures such as abnormal conidiophore. In addition, the deletion strain presented severe growth defects and very decreased conidiation on minimal and complete medium, displaying white colonies, which indicates complete absence of conidia pigmentation. The null mutant is more sensitive to all compounds tested such as congo red, calcofluor white, caspofungin, caffeine and SDS when compared to the wild-type and complemented strain, suggesting a role for *smiA* in cell wall integrity. Interestingly, these $\Delta smiA$ defects were not recovered by the addition of sorbitol as osmotic stabilizer. The caspofungin paradoxical effect was also absent in the mutant strain. In addition, $\Delta smiA$ strain is completely avirulent in the *Galleria mellonella* model. Altogether, our data suggest that *smiA* plays an important role in cell wall maintenance, being closely involved in *A. fumigatus* sporulation, proliferation and growth, in addition to be determinant for the CWI pathway proper signaling.

Key words: null mutant, white colonies, cell wall maintenance, growth.

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