

TITLE: ADP-Ribosylation Factor Like A (ArlA) IS INVOLVED IN THE ASEXUAL DEVELOPMENT AND VIRULENCE OF THE PATHOGENIC FILAMENTOUS FUNGI *Aspergillus fumigatus*.

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Filamentous fungi undergo polarized growth, from germination to hyphae elongation, to form a mycelia complex followed by asexual development with the appearance of conidiophores. The apical region of polarized growth of the fungus presents two different types of vesicles, among them, the micro and macrovesicles. The protein ADP-ribosylation factors (ARF) Like A (ArlA) belongs to the ARF group of proteins. They are monomeric GTP-binding proteins and belong to the Ras superfamily. This superfamily is additionally composed by four other families (RAB, RAN, RAS and RHO) that form a set of sub-systems responsible for the regulation of vesicle transport within the fungal cell, among other functions, such as signal transduction and regulation of vesicular traffic in the *Spitzenkörper*, which is at the region of apical growth of the hypha. In addition, the ARFs undergo the N-myristoylation process, an irreversible protein lipidation in which the myristoyl CoA myristate is covalently linked to a secondary glycine of the target protein (ARF), increasing its hydrophobicity. The ARF activity is also modulated by the action of ARF-GAP (GTPase Activating Protein - GcsA) and ARF-GEFs (Guanine nucleotide Exchange Factor – Sec7). *Aspergillus fumigatus* is an opportunistic saprophytic fungus that causes Allergic Bronchopulmonary Aspergillosis, Aspergilloma, and Invasive Pulmonary Aspergillosis (IPA). IPA is the most serious form of infection and it may be fatal to the patient with previously compromised immunity. Invasive fungal infection has increased significantly in recent years, making them important cause of morbidity and mortality in hospitalized or immunocompromised patients. In this study was proposed the construction of *arlA* null mutant as well the double-mutant $\Delta arlA \Delta gcsA$. *A. fumigatus* was able to develop in the absence of *arlA*, *gcsA* and with the deletion of both genes. Nevertheless, $\Delta arlA$ and $\Delta arlA \Delta gcsA$ have shown impaired colony growth and conidiophores development. The absence of lipids at the hypha tip, narrow cell wall, cell surface charge changes, altered biofilm formation and increased virulence have also been shown. Additionally, ArlA::GFP and GcsA::GFP are distributed throughout the *A. fumigatus* hypha cytoplasm and are present at the initial phase of asexual development. Therefore, ArlA and GcsA are involved in asexual development and virulence of *A. fumigatus*.

Key words: *Aspergillus fumigatus*, ADP-ribosylation Factor, GTPase activating protein, virulence, conidiogenesis.

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