

Aspergillus fumigatus: Development of New Drugs and Potential Molecular Targets

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Abstract

Aspergillus fumigatus is an opportunistic and saprophytic fungus that may cause a range of pathological conditions with invasive pulmonary aspergillosis being considered the most severe. The cells of all living organisms are programmed to self-destruct under certain conditions. Apoptosis is the best known way of programmed cell death. In some fungi, its occurrence has been confirmed and related to important biological processes such as development, aging, stress responses and pathogenesis. The apoptosis pathway in *A. fumigatus* is still poorly understood. New study prospects have emerged in order to combat the fungus *Aspergillus fumigatus*. In this sense, natural products and medicinal plants have great importance in the development of new drugs used in human medicine. The apoptosis has emerged as a key regulator of fungal growth, demonstrating that intermediates of this pathway may be potential targets for new drugs. In addition to this fact, natural products are promising sources of new therapeutic agents discovery.

Keywords: *Aspergillus fumigatus*; Signaling pathways; Saprophytic fungus; Programmed cell death

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Aspergillus fumigatus is currently the main fungal pathogen spread in the air. It's able to cause various disease states in humans, including the most severe and invasive aspergillosis. The high mortality rate of this disease requires intense efforts to reveal the basic principles involved in the pathogenicity of this fungus [1].

The high capacity of the fungus to become drug resistant as well as the limited drug production has been problematic. This raises the need for the development of new effective drugs to be used as strategies to minimize fungus resistance [2]. Therefore, the study of genes participants in important signaling cascades which may enable the use of these as targets for the design of new specific drugs to combat the fungus is crucial.

There are several signaling pathways that may be important in the *A. fumigatus* infectious process. The process of apoptosis or programmed cell death is responsible for maintaining the balance in the body and can be triggered by several factors. However, the apoptotic process is directly related to a complex signaling network and several proteins that remain to be elucidated in *A. fumigatus* [3]. The study and understanding of apoptosis

pathway in *A. fumigatus* may efficiently interfere and point out to exclusive targets to the fungus.

The development of drugs for the control of pathogenic fungi has been relatively neglected. Consequently, there is an urgent need to reveal new therapeutic ways to treat this disease [4-7].

Natural products and especially medicinal plants have great importance for the development of new drugs used in human medicine. The plant kingdom has significantly contributed to the development of new drugs to be used in the treatment of various diseases [4].

In addition, the pharmacological research of active ingredients of medicinal plants has provided important advances in the therapeutic management of many diseases, wherein several substances found in plants have been used as useful targets for pharmacological, physiological and biochemical studies [4,8].

Brazil is the country with the largest plant genetic biodiversity in the world [9]. Moreover, considering the enormous wealth

of Brazilian flora, there is still a huge and untapped natural source of plant secondary metabolites with numerous chemical and medicinal properties not yet revealed [8].

Our research group is part of a rich plant biodiversity region, the Brazilian Cerrado, the second largest biome in South America, being very attractive in the study of active substances from medicinal plants that can be used as prototypes for the development of new drugs.

Given the difficulty of diagnosis and the ineffectiveness of current antifungal, which decisively contribute to the high mortality caused by invasive aspergillosis, it highlights the need to search for new therapeutic targets that are efficient and particular of this fungus. Thus, the natural processes that occur in this microorganism can be focus of potential investigations. This is reinforced by the fact that targeting studies engaged to find new bioactive molecules from plants are crucial since natural products are promising sources of discovery of new therapeutic agents.

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