TITLE: Azole agricultural fungicides and selective pressure of resistant phenotypes in *Aspergillus fumigatus*

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Triazoles are also widely used for the control of phytopathogenic fungi, and the increase in fungal resistance to agricultural fungicides represents an emerging problem. The relationship between resistance in environmental and clinical strains is based on similarity in the mechanism of action of agricultural fungicides and triazoles drugs. Exposure to a triazole fungicide can select a resistant strain resistant, phenomenon knows as "cross-resistance". *Aspergillus fumigatus* is a soil species and is the main etiological agent of Aspergillosis. Some strains, both environmental and clinical present mutations in the *Cyp51A* gene leading to resistance to azoles compounds. Mutations in the *Cyp51A* gene result in the production of enzyme with alterations in its three-dimensional conformation leading to lower azole-target affinity and antifungal resistance. These mutations were attributed to the extensive exposure of *A. fumigatus* environmental strains to triazole fungicides. The objective of this study is to evaluate the hypothesis of environmental origin of mechanisms of resistance to triazoles, in clinical and environmental isolates of *A. fumigatus*, modulated by exposure to agricultural fungicides. An experimental garden plot, part organic and part regularly exposed to fungicide difenoconazole, was constructed and the soil was inoculated with 4 non-mutant and wild type phenotypes of *A. fumigatus*. We assessed the pressure of fungicide over the inoculated strains with monthly sprays, followed by soil periodic recovery of *A. fumigatus* colonies. Up to now we recovered 745 colonies. Azole MICs, both fungicides and drugs, were determined (Dry Plates, Eiken, Japan). The MIC ranges for itraconazole, voriconazole, ravuconazole, posaconazole, metconazole, tebuconazole and difenoconazole intervals were: 0.5-1 mg/L, 0.5-1 mg/L, 0.12-0.25 mg/L, 0.06-0.5 mg/L, 0.25-0.5 mg/L, 1-2 mg/L and 0.5-1 mg/L, respectively. After 7 months of regular fungicide exposition the soil recovered colonies fail to present resistance to azole compounds. We performed DNA sequencing targeting β tubulin gene to confirm the species of all recovered colonies. We concluded that the emergence of non wild-type *A. fumigatus* strains in environmental under fungicides effects is a not a straightforward event and possibly demands larger amount of fungicide or extensive period of exposition time.

Key- Words: *Aspergillus***,** azole drugs, fungicide, gene mutation

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