

Evolution of multifungicide resistance in fungal pathogens populations

Pathogenic fungi are well-known for causing life-threatening diseases in humans as well as for causing economically important diseases in agricultural crops. Antifungal medication in humans, and fungicide application in crop plants is required for managing diseases caused by this group of microorganisms. However, most of these fungicides are site-specific (i.e. they act against only one specific target site in the fungal cell). This specific activity increase the risk of selection out strains of resistant fungus to the fungicide because just one mutation is required in the organism to overcome the action of the fungicide, compared to fungicides with multiple sites of action. Mechanisms of fungicide resistance in fungi include: prevent a fungicide from entering the cell or remove the fungicide from the cell, as well as to inactivate the fungicide from inhibiting its target. As an evolutionary process, none of these mechanisms acts alone because the emergence of drug resistance is based on selection for organisms that have an enhanced ability to survive and reproduce in the presence of a drug, which is achieved by activation of fungal stress responses that support the short-term cellular adaptation to the fungicide, but also to promote genetic instability, facilitating the emergence of stable drug resistant mutants, and increasing of genetic diversity. Because the genome instability presented by the resistant mutant, after a treatment with other class of site-specific fungicide, these individuals will present a rapid breakthrough to resistance for the new fungicide, and then the individuals of the population will become multidrug or multifungicide resistant (MFR), that is, individuals that show resistance to two or more fungicides.

Recent reports indicate that multifungicide resistant populations of *Botrytis cinerea*, the causal agent of gray mold on strawberry, are increasing over the time in the United States. According to a proposed theory of evolution of MFR populations of *B. cinerea*, the process is based on the stepwise accumulation of resistance to single fungicide classes due to continuous selection and diversification (i.e. genetic flux through migration). Furthermore, a new report documented experimental probe for support of selection by association in the evolution of MFR populations of *B. cinerea*. The concept of selection by association is based on the assumption that an isolate with resistance to different classes of site-specific fungicide would be selected in the field by each of the chemical that carry resistance, which is also referred as Indirect selection of resistance or “Genetic Hitchhiking”. Nevertheless, the dissemination of MFR organisms in the field seems to be moderated because a reduced fitness, but more studies are needed to support this information.

References

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