Genetic and biochemistry analyses of the natural resistance to the fungicide fenhexamid in the phytopathogenic fungus Botrytis pseudocinerea

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INRA, AgroParisTech UMR1290 BIOGER, BP01, F78850 Thiverval-Grignon, France

E-mail: Walker@versailles.inra.fr

The *Botrytis* species complex responsible for grey mould disease on grapevine is composed of two species: *Botrytis cinerea* the major one (about 90%) and *Botrytis pseudocinerea.* Despite their genetic polymorphism, these species cannot be morphologically distinguished. However, they do differ in their response to several fungicides, especially to the sterol biosynthesis inhibitor fenhexamid. While *B. cinerea* is sensitive to this hydroxyanilide, *B. pseudocinerea* is naturally resistant. Enzyme assays showed that in *B. pseudocinerea* the fenhexamid target enzyme, the sterol 3-ketoreductase was less sensitive to fenhexamid. In addition, a strong synergism between fenhexamid and sterol 14α-demethylation inhibitors (DMIs) known to inhibit Cyp51, a cytochrome P450 monooxygenase was observed in *B. pseudocinerea*. These results could suggest detoxification of fenhexamid by cytochromes P450. The *cyp684* gene showing the strongest similarity to *cyp51* among all *B. cinerea* cytochrome P450 genes was found strongly overexpressed in the presence of fenhexamid in *B. pseudocinerea*. In this work, we studied separately the effect of *B. pseudocinerea erg27* polymorphism, *erg27* encoding 3-ketoreductase, and of the recently identified cytochrome P450 gene, *cyp684*, on resistance to fenhexamid, respectively by *erg27* gene, and *cyp684* inactivation. In parallel, metabolization studies are conducted to identify metabolites and test their activity on *Botrytis* spp.