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Genetic analysis of multi-drug-resistance (MDR) in *Mycosphaerella graminicola (Zymoseptoria tritici)* field isolates.

Selim Omrane[1], Colette Audéon[1], Amandine Ignace[1], Clémentine Duplaix[1], Hind Sghyer[1], Lamia Aouini[2], Gert Kema[2], Anne-Sophie Walker[1]and Sabine Fillinger[1]

[1]INRA, AgroParisTech, UMR BIOGER, Avenue Lucien Brétignières, F78850 Thiverval-Grignon, France
[2]Plant Research International, Wageningen University, Wageningen, The Netherlands
sabine.fillinger@versailles.inra.fr

Multidrug resistance (MDR) is a common trait developed by many organisms to counteract chemicals and/or drugs used against them. The basic MDR mechanism is relying on an overexpressed efflux transport system that actively expulses the toxic agent outside the cell. In fungi, MDR (or PDR) has been extensively studied in *Saccharomyces cerevisiae* and *Candida albicans*, but also plant pathogenic fungi, e.g., *Botrytis cinerea*, *Oculimacula yallundae* and *Mycosphaerella graminicola* are concerned by this phenomenon. In agriculture, it is currently under investigation if MDR strains may threaten the efficacy of current fungicide treatments.
MDR strains were detected in septoria leaf blotch (*M. graminicola*) field populations since 2008. These strains are cross-resistant to fungicides with different modes of action due to active fungicide efflux. In a previous study, we identified the *MgMFS1* gene overexpressed in all tested MDR field strains (Omrane et al., 2015). This gene encodes a major facilitator membrane transporter whose inactivation abolished the MDR phenotype in at least one field strain.
We went out to identify the mutation(s) responsible for MDR phenotype in two isolated strains (MDR6 and MDR7). Crosses between both MDR strains showed that *mdr6* and *mdr7 loci* are closely linked. A bulk-segregant analysis coupled to next generation sequencing showed a clear co-segregation between phenotypes and the left arm of chromosome 7. This region harbors 14 genes including the gene. We identified a 519 bp insert (LTR-like) in both MDR strains as well as in other (but not all) MDR field strains. Genotyping of the progenies for the promoter insert showed a clear, but not exclusive correlation between the *MgMFS1* promoter insert and the MDR phenotype. These results indicate that the LTR-like insert is responsible for the MDR phenotype, potentially *via MgMFS1* overexpression, but also that an additional and independent mutation confers the MDR phenotype to strain MDR6.

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Omrane et al., Fungicide efflux and the MgMFS1 transporter contribute to the MDR phenotype in *Zymoseptoria tritici* field isolates (2015), *Env. Microbiol.*, in press