Fungal and fungal-like plant pathogens account for ~30% of crop losses worldwide, thus threatening the security of food supply needed to feed the growing human population. In nowadays agriculture, fungicides are used intensively to protect crops from fungal infections. Similarly, the incidence of severe clinical fungal infections is currently increasing, mainly due to increase in the number of individuals that are particularly susceptible because of age, medical interventions or having a compromised immune system. Despite the wide availability of different fungicide chemistries, resistance to each major class of fungicides has evolved. Most cases of antifungal resistance across plant pathogenic fungi and fungi of human clinical importance have resulted from independent parallel evolution. Interestingly, in the saprotroph an opportunistic human pathogen Aspergillus fumigatus, strains resistant to multiple azoles have been recovered from clinical and environmental samples, including agricultural soils. Although horizontal gene transfer might play a role in evolution and fungal adaptation, fungicide resistance arising through this route has not been reported yet.

Resistance to a specific fungicide can be conferred by different mechanisms including prevention of the fungicide from entering the fungal cell, actively removing the fungicide from the cell by activation of efflux pumps, or alteration of the target site rendering the fungus insensitive to the fungicide. Mutations resulting in conformational changes in target proteins are the most common form of resistance in both human- and plant-pathogenic fungi. For example, up to 30 different mutations have been reported to occur in CYP51, the target protein of azole fungicides, in the wheat pathogen, Zymoseptoria tritici. Selection of resistance depends upon individuals fit to survive and reproduce in the presence of the fungicide which may in turn be influenced by their genetic background. Limited genetic variation and fitness costs associated with specific resistance mutations may explain the low likelihood of resistance evolving in some pathogen populations compared to others. Therefore, the potential of a fungicide to select for resistant mutants in a given pathogen is key in risk assessment efforts taking into consideration the fungal populations and local aspects of fungicide use. Fungicide resistance is a continuous threat to agriculture and human health with important economic, environmental, and health impacts. This threat can be countered by diversifying the fungal management toolbox through the discovery of new antifungal chemicals and the deployment of integrated disease management tactics to optimize and limit fungicide input.
References


