Comparative genomics of environmental *Aspergillus fumigatus* and the role of agricultural azoles on the emergence of resistance

Amelia E. Barber^{1,2}, Jennifer Born⁴, Ivo Schliebner⁴, Antonia Lange^{1,2}, Holger B. Deising⁴, and Oliver Kurzai^{1,2,3}

¹Leibniz Institute for Natural Product Research and Infection Biology - Hans Knöll Institute. Jena, Germany. ²National Reference Center for Invasive Fungal Infections. Jena, Germany. ³Institute for Hygiene and Microbiology, University of Würzburg. Würzburg, Germany. ⁴Institute of Agricultural and Nutritional Sciences. Martin Luther University Halle-Wittenberg. Halle (Saale), Germany

Investigating the link between agriculture and drug resistance in *Aspergillus fumigatus*

≈60% of azole-resistant *A. fumigatus* isolates do not possess known *cyp51a* mutations

Over the last decade there has been a rapid and global emergence of azole resistance in the ubiquitous fungal pathogen *Aspergillus fumigatus*. The dominant resistance mechanism is of environmental origin, suggesting that resistance is emerging through a selective pressure applied by the widespread usage of azole antifungals in agriculture. However, the influence of these fungicides on the ecology of *A. fumigatus*, as well as the downstream consequences for agriculture and medicine remain largely unknown.

5% of agriculturally-isolated *A. fumigatus* isolates show resistance to medical azoles

A. fumigatus was isolated from soil samples obtained from farms in Germany practicing organic agriculture and those practicing conventional agricultural using azole fungicides.

	Agricultural Azoles			Medical Azoles		
	Tebu	Difeno	Prothio	Itra	Vori	Posa
Overall	27.3%	88.9%	1.9%	6.0%	5.1%	1.9%
	59/216	192/216	4/216	13/216	11/216	4/216
Conventional	30.3%	86.6%	2.5%	7.6%	7.6%	2.5%
	36/119	103/119	3/119	9/119	9/119	3/119
Organic	23.7%	91.8%	1.0%	4.1%	2.1%	1.0%
	23/97	89/97	1/97	4/97	2/97	1/97
	Resazurin			VIP Check		

Isolates from conventional agriculture have a higher resistance rate than those originating from organic agriculture. Isolates resistant to medical azoles frequently possess elevated MICs against agricultural azoles, indicating cross resistance.

Itraconazole	Voriconazole	Posaconazole
6.0% (13/216)	5.1% (11/216)	1.9% (4/216)
Genotype: 8 WT <i>cyp51a</i> 4 TR/L98 1 Pending	Genotype: 8 WT <i>cyp51a</i> 4 TR/L98	Genotype: 4 TR/L98

Bio type®
Diagnostic GmbH

Large scale whole genome sequencing to probe the influence of azoles on the ecology of agriculturally-isolated *A. fumigatus*

Randomly-selected isolates from the same conventional field are widely distributed among a panel of clinical isolates. Phylogeny inferred from TRESP typing. (Garcia-Rubio *et al.* 2016).

330 isolates submitted for WGS to answer questions including:

- Is there a change in the strain population before *vs.* after the growing season and azole application?
- Are there differences in the populations present on conventional *vs.* organic fields?
- Through comparison with clinical strains, can we identify fungal determinant critical for human infection?

GEFÖRDEBT VOM

FRIEDRICH-SCHILLER-UNIVERSITÄT JENA

Contact

Amelia Barber, PhD
amelia.barber@hki-jena.de