

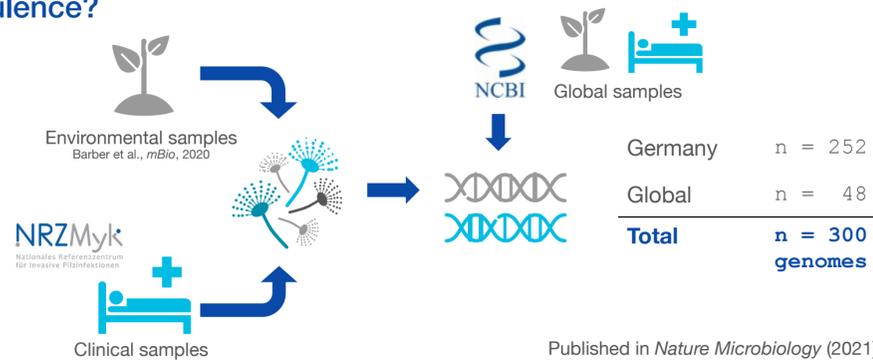
# Aspergillus fumigatus pan-genome analysis identifies genetic variants associated with human infection

Amelia E. Barber<sup>1,7,8</sup>, Tongta Sae-Ong<sup>2,8</sup>, Kang Kang<sup>2</sup>, Bastian Seelbinder<sup>2</sup>, Jun Li<sup>3</sup>, Grit Walther<sup>4</sup>, Gianni Panagiotou<sup>2,5</sup>, Oliver Kurzai<sup>1,4,6</sup>

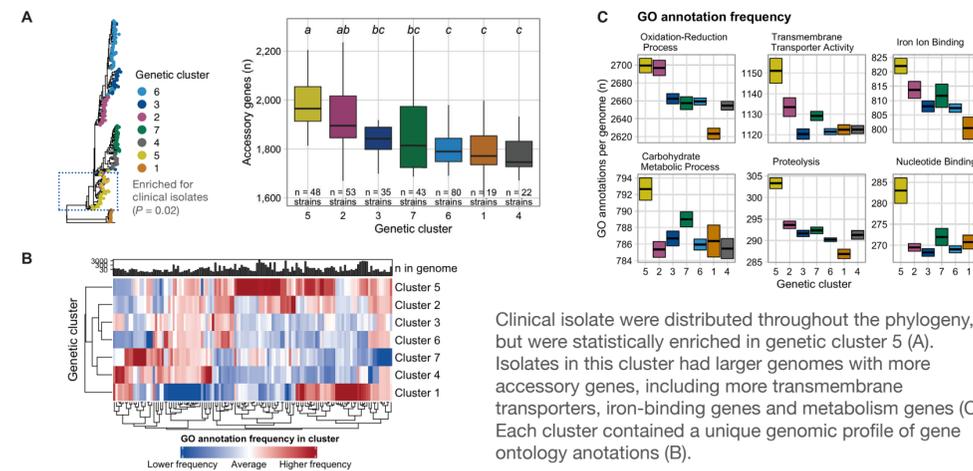
<sup>1</sup> Research Group Fungal Septomics, Leibniz-HKI, Jena, Germany. <sup>2</sup> Research Group Systems Biology and Bioinformatics, Leibniz-HKI, Jena, Germany. <sup>3</sup> City University of Hong Kong, Hong Kong, China. <sup>4</sup> National Reference Center for Invasive Fungal Disease (NRZMyk), Leibniz-HKI, Germany. <sup>5</sup> University of Hong Kong, Hong Kong, China. <sup>6</sup> Institute for Hygiene and Microbiology, University of Würzburg, Würzburg, Germany. <sup>7</sup> Present address: Junior Research Group Fungal Informatics, Leibniz-HKI, Jena, Germany. <sup>8</sup> Equal contribution.

@frau\_dr\_barber  
www.barber-lab.com

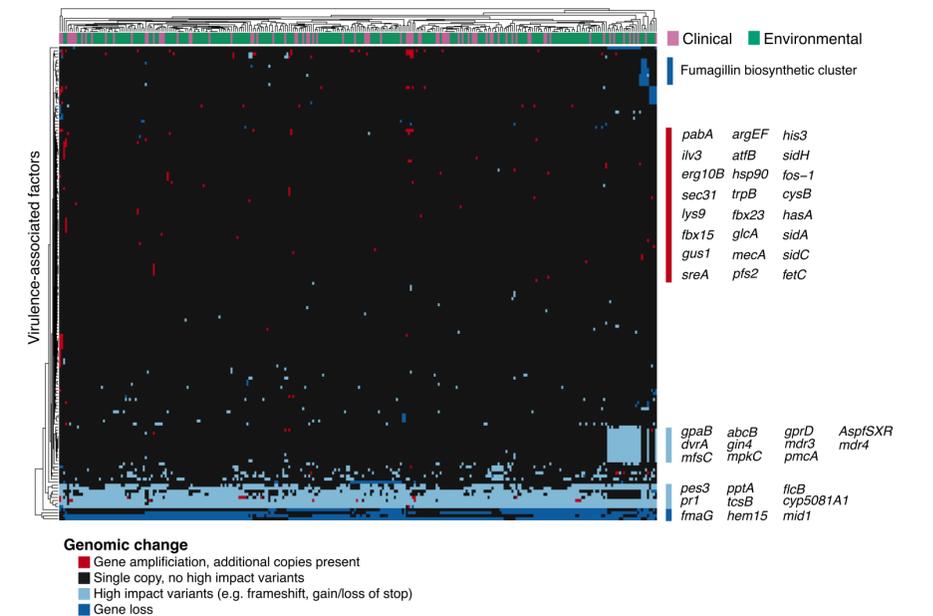
What is the genomic diversity of *A. fumigatus* and how does it impact virulence?



Genetic clusters have distinct genomic profiles - and one cluster is enriched for clinical isolates

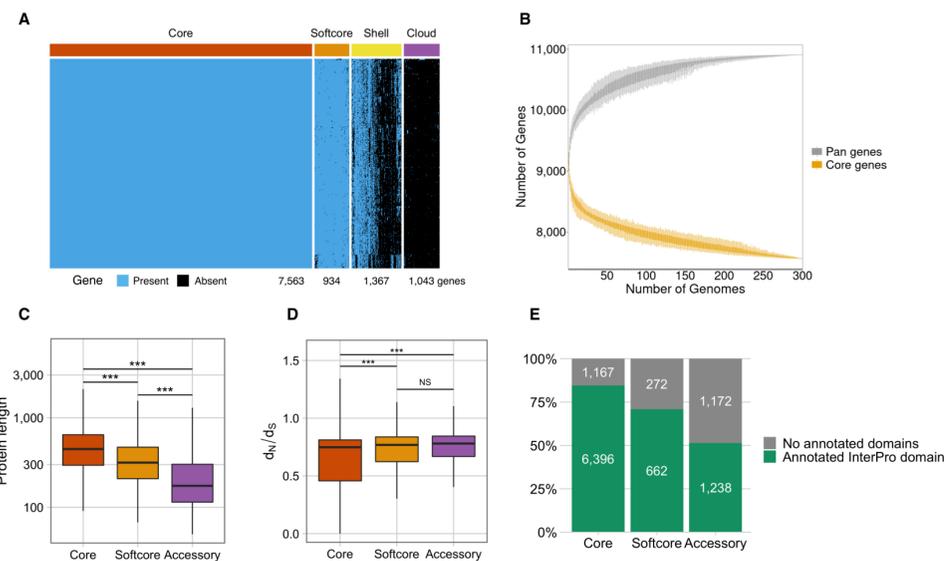


*A. fumigatus* exhibits genetic variation in virulence-associated genes



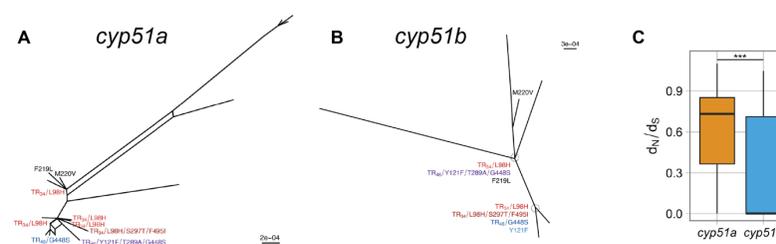
43% of virulence-associated genes examined (155/36) exhibited high-impact genetic variation among isolates, such as gene loss or duplication.

The pan-genome of *A. fumigatus*



(A) Of the 10,907 non-redundant orthogroups identified, only 7,563 (69%) were found in all genomes. (B) The number of total genes identified did not increase after ~250 genomes. (C-E) Accessory genes are shorter in length (C), under a lesser degree of purifying selection (D) and less frequently possess an annotated function.

Triazole targets genes display distinct phylogenetic networks and imbalanced levels of stabilizing selection



*A. fumigatus* contains two paralogous copies of the triazole target gene, *cyp51*. A phylogenetic network of *cyp51a* and flanking sequence (A) contained conflicting genetic information (illustrated by parallel bands), suggestive of genetic recombination at the locus. No splits were observed in *cyp51b* (B). *cyp51b* is also under a stronger degree of stabilizing selection than *cyp51a* (C).

Conclusions

16-22% of each isolate's genome was not conserved among the 300 samples, including ~500 non-Af293 genes per isolate.

Notable genetic variation is present between genetic clusters - including variation in virulence-associated genes.

One reference strain and genome are not enough to capture the heterogeneity of *A. fumigatus*!