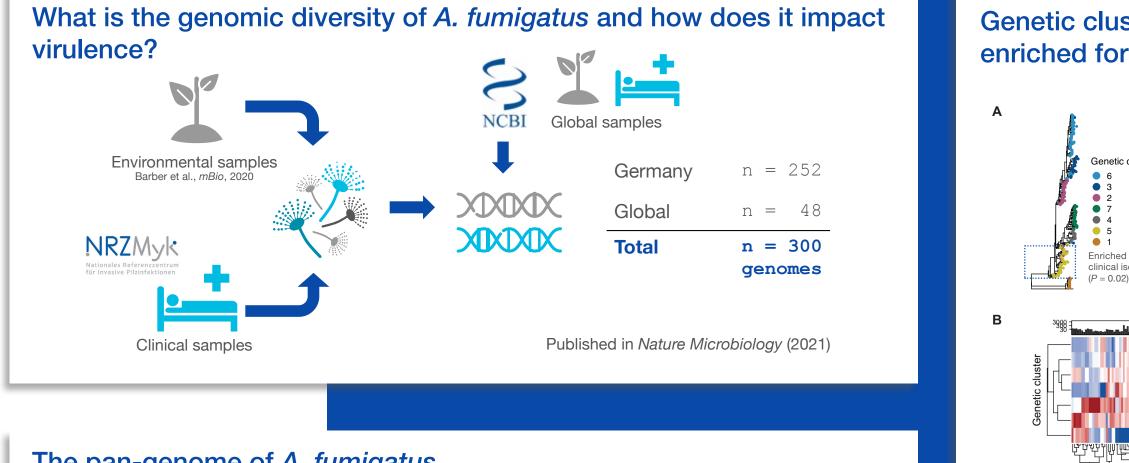


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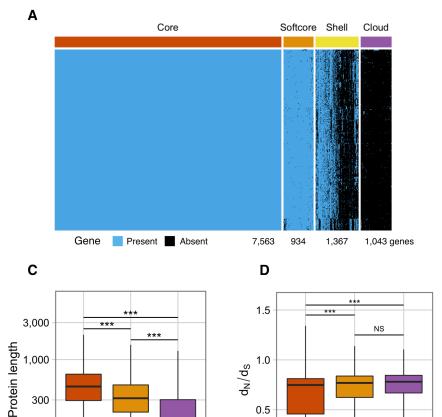
Aspergillus fumigatus pan-genome analysis identifies genetic variants associated with human infection

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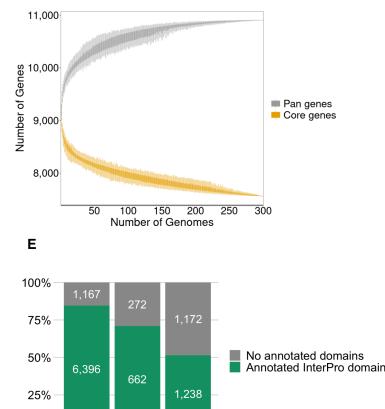
Research Group Fungal Septomics, Leibniz-HKI, Jena, Germany.² Research Group Systems Biology and Bioinformatics, Leibniz-HKI, Jena, Germany.³ City University of Hong Kong, China.⁴ National Reference Center for Invasive Fungal Disease (NRZMyk), Leibniz-HKI, Germany. ⁵ University of Hong Kong, Hong Kong,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



The pan-genome of *A. fumigatus*



Core Softcore Accessory



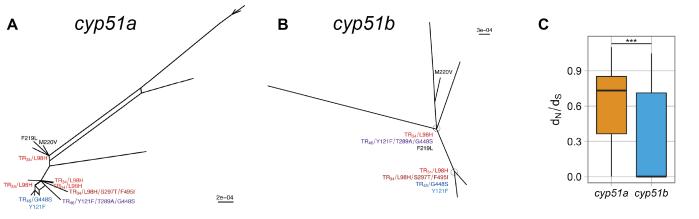
Core Softcore Accessory

(A) Of the 10,907 non-redudant 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 posess an annotated function.

Core Softcore Accessory

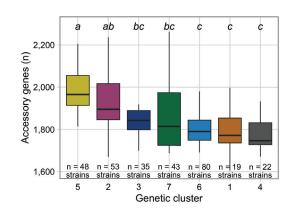
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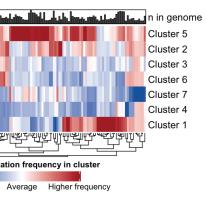
Triazole targets genes display distinct phylogenetic networks and imbalanced levels of stabilitizing selection

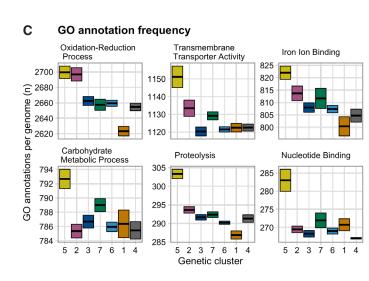


A. fumigatus contains two paralogous copies of the triazole target gene, cyp51. A phylogenetic network of cyp51a and flanking sequence (A) contained conflicting genetic information (illustrated by parallel bands), suggestive of genetic recombination at the locus. No splits were observed in *cyp51b* (B).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

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

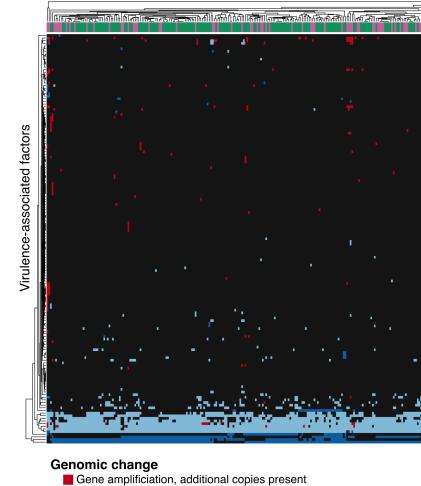






Clinical isolate were distributed throughout the phylogeny, but were statistically enriched in genetic cluster 5 (A). Isolates in this cluster had larger genomes with more accessory genes, including more transmembrane transporters, iron-binding genes and metabolism genes (C). Each cluster contained a unique genomic profile of gene ontology anotations (B).

A. fumigatus exhibits genetic variation in virulence-associated genes



Single copy, no high impact variants

Gene loss

High impact variants (e.g. frameshift, gain/loss of stop)

DFG

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

Conclusions

für Bildung und Forschung

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

---- BALANCE

//// MICROVERSE

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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*!

Clinical Environmental	
pabAargEFhis3ilv3atfBsidHerg10Bhsp90fos-1sec31trpBcysBlys9fbx23hasAfbx15glcAsidAgus1mecAsidCsreApfs2fetC	
gpaB abcB gprD AspfSX dvrA gin4 mdr3 mdr4 mfsC mpkC pmcA pes3 pptA flcB pr1 tcsB cyp5081A1	R

