

Genome-wide signals of positive evolution in fungal pathogen *Aspergillus fumigatus* reveals environmental adaptation strategies

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Genome-wide scans for positively selected genes (PSGs) provide insights into the dynamics of genome evolution, the genetic basis of differences between species, and the functions of individual genes. We present the most comprehensive examination of fungal PSGs to date, using the available 18 high-coverage *Aspergilli* genome assemblies. The increased phylogenetic depth of this dataset results in improved statistical power, and permits species-specific tests to be applied. Because of the pathogenic nature of *Aspergillus fumigatus* towards immunocompromised host, we applied branch-site test1 of positive selection considering the *A. fumigatus* as the foreground branch and obtained 122 genes showing positive selection ($q < 0.05$). Our results show that several genes involved in conidia growth evolved under positive selection. Hence to adapt to the host or any environment fungal growth and advantageous mutation for conidia are fixed under positive selection. Functions enriched with PSGs include signal transduction, metabolism, mitochondrial activity, regulation of transcription and several connected terms. These aid the strategies of *A. fumigatus* to adapt to diverse environments. Moreover, functional enrichment of PSGs interacting host proteins shows overrepresentation of adaptive (symbiosis related Gene Ontology (GO) category) and immunomodulatory pathways. Additionally, the components of host immune pathways were also enriched which suggests host imposed pressure on PSGs in accordance with a host-pathogen arms race or adaptive selection to survive hostile environments. Identifying PSGs and the critical amino acid sites provides a basis for functional studies that may also increase our understanding of their underlying molecular mechanisms of action. Additionally, it may lead to the identification of variation at functionally important sites, as well as eventually using this information can be used in the rational drug designing, if the PSG is essential for *A. fumigatus* growth or survival. Taken together, based on our results we concluded that positive selection indeed plays a crucial role in the evolution of *A. fumigatus*. We also provide valuable targets for further research on the mechanisms of immune evasion and host-pathogen interactions for this serious human pathogen.

Reference

1. Yang Z, dos Reis M. 2011. Statistical properties of the branch-site test of positive selection. *Mol Biol Evol.* 28:1217-1228.

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