

Title: HEAT SHOCK AND CELL WALL STRESS INDUCE THE EXPRESSION OF HEAT SHOCK TRANSCRIPTION FACTOR HSFA AND HSP90 CHAPERONE IN *ASPERGILLUS FUMIGATUS*

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Abstract:

The filamentous saprophyte and human opportunistic fungal pathogen *Aspergillus fumigatus* is responsible for several human respiratory diseases, including the invasive pulmonary aspergillosis. Among the virulence determinants of this fungus, thermotolerance is one of the key features, being a prerequisite for the establishment of infection and maintenance of the pathogen inside the host. In *Saccharomyces cerevisiae*, the transcription factor Hsf1 is responsible for regulating the transcription of several heat shock proteins, such as Hsp90, Hsp70, Hsp60 and Hsp40 chaperones, which are part of the cellular program for heat adaptation. In addition, in yeast and in the fungal pathogen *Candida albicans* this transcription factor has been associated with the maintenance of the cell wall integrity (CWI). Here, we investigated the expression of the Hsf1 homolog in *A. fumigatus*, named as HsfA, and the molecular chaperone Hsp90 both in heat shock and cell wall stress. Temperature rise and cell wall stress induced by either congo red or caspofungin caused an increase in *hsfA* expression. The mRNA abundance of *hsfA* was also significantly increased in response to cell wall stress induced by caspofungin in the *pkcA*^{G579R}, $\Delta mpkA$ and $\Delta rlmA$ mutant strains, which encode components of the *A. fumigatus* CWI pathway. Furthermore, we observed by western blot experiments that HsfA protein abundance is also up-regulated under the same stress conditions. Interestingly, this increase in HsfA expression is accompanied by an increased in the Hsp90 molecular chaperone expression. These results highlight the importance of HsfA transcription factor for the adaptation of the fungus to heat shock and cell wall stress, and point out to the existence of a concise relationship between thermotolerance and CWI, possibly through the Hsp90 chaperone interaction with the CWI pathway components.

Keywords: *Aspergillus fumigatus*, heat shock, heat shock transcription factor, Hsf1.

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