Hot or Not - The Heat Shock Factor1 (HSF1) is essential for Candida albicans cellular functioning

The opportunistic human pathogen, *Candida albicans* hinges on the heat shock factor-1 (*HSF1*), a client protein of the well-established heat shock chaperone (protein folding helper), *HSP90* for proficiently modulating thermal stress response. In addition to its implications in reciprocation to heat shock, *HSF1* is essential for sustaining the viability and virulence of *C. albicans*. The underpinnings that, the conditional mutant of the heat shock factor-1 (*HSF1*) in *C. albicans* displays enhanced susceptibility not only towards a plant alkaloid, berberine, but also to diverse antifungal drugs has been previously established by us.

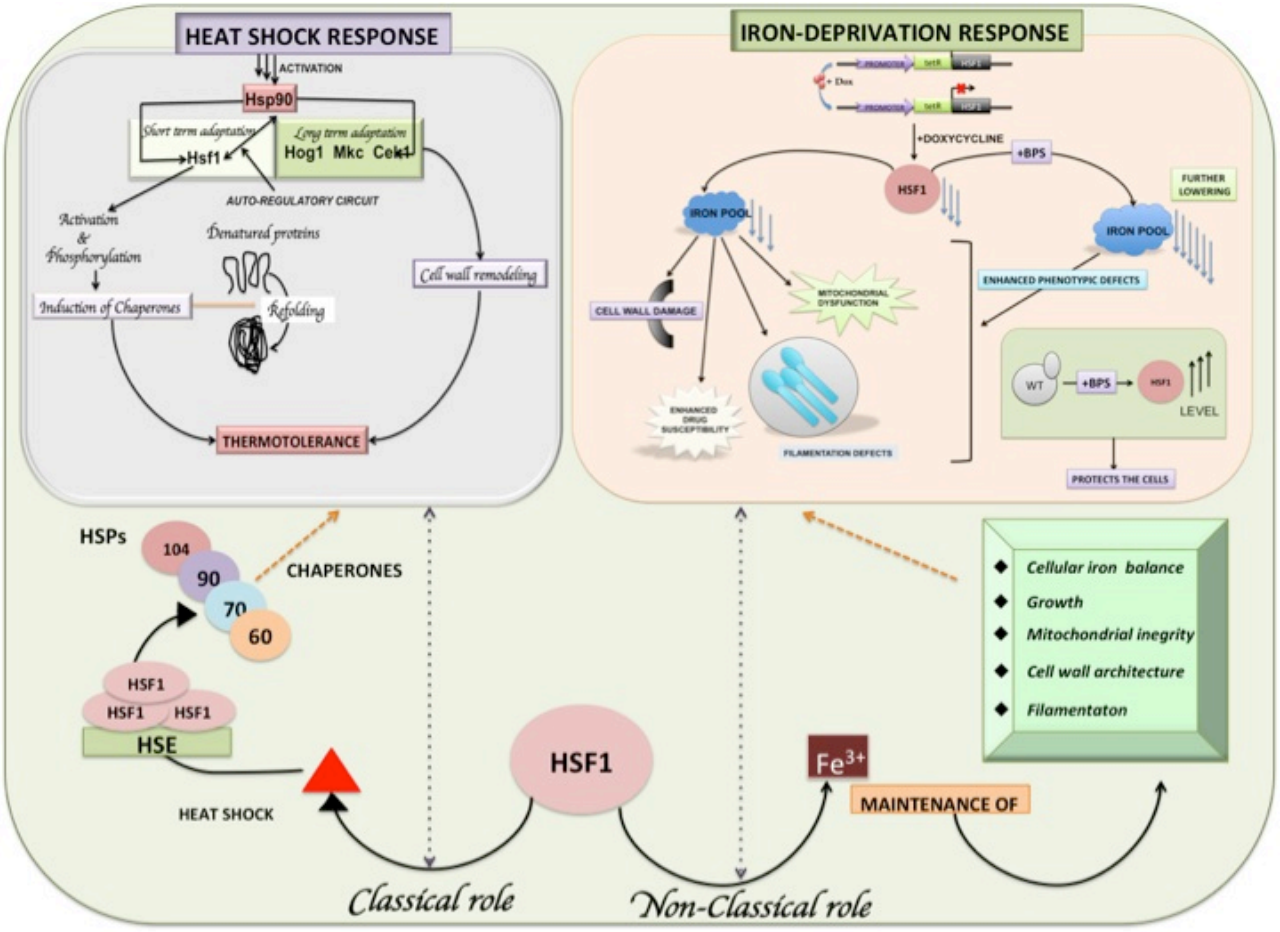

Fig. 1. Model highlighting the heat shock and non-heat shock responsive roles of HSF1.

The present study reveals an additional phenotype, related to non-heat shock responsive levels of *HSF1* where, an intricate relationship between cellular iron and *HSF1* mediated drug susceptibility

of *C. albicans* is disclosed. For instance, at 30°C, the conditional deletion of *HSF1* leads to lowering of intracellular iron pools resulting in enhanced drug susceptibility, dysfunctional mitochondria, and compromised cell wall integrity. Notably, all of these non-heat shock phenotypes observed could be rescued upon exogenously supplemented iron. The novel phenotypes presented by the mutant at basal conditions i.e. at 30°C, however, do not appear to be directly linked to the global regulation of iron-dependent gene expression. External chelation of iron of *HSF1* mutant cells led to severe growth defects and apparently triggers an iron starvation signal in the cell thus, demonstrating that *HSF1* is essential for *C. albicans* cells to tolerate the iron deprivation stress. Additionally, *HSF1* also influences a predominant attribute governing the virulence of *C. albicans*, i.e. is its morphogenetic plasticity wherein, the conditional mutant of *HSF1* portrayed inability to form hyphae even under solid hypha inducing conditions.

Taken together, besides the well-documented roles of *HSF1* in reciprocation of thermal stress, the present study illuminates its novel roles under basal conditions and provides molecular insights into its role in iron deprivation and drug tolerance of *C. albicans*.

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