Role of *Candida parapsilosis* secreted aspartyl proteinases in inflammation and regulation of innate immune evasion

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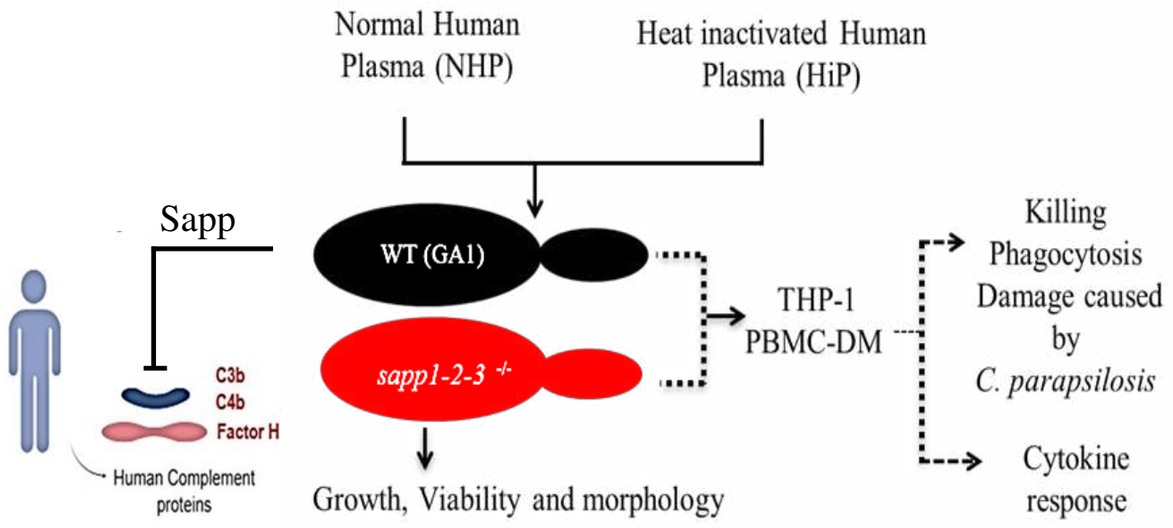
Abstract

Candida parapsilosis is an opportunistic fungal pathogen responsible for approximately 30% of candidaemia episodes in new-borns, and 10%–15% of *Candida* infections in adults worldwide. Fungal extracellular hydrolytic enzymes, especially secreted aspartyl proteinases (*Saps*) are important virulence factors of *Candida* species, that contribute to the development of disseminated candidiasis. Saps cause significant damage to epithelial cells, promote the escape of fungal cells during host innate immune attacks by cleaving host complement proteins and can also modulate the secretion of inflammatory cytokines. Although, several studies have investigated the role of *C. albicans* secreted aspartyl proteinases in its virulence, less is known about the precise role of *C. parapsilosis* secreted aspartyl proteinases (*SAPP*s) in host invasion, especially during complement evasion. Thus, we aimed to study the function of *C. parapsilosis* secreted aspartyl proteinases (candidaparapepsins) during host attack.

Methods



Results

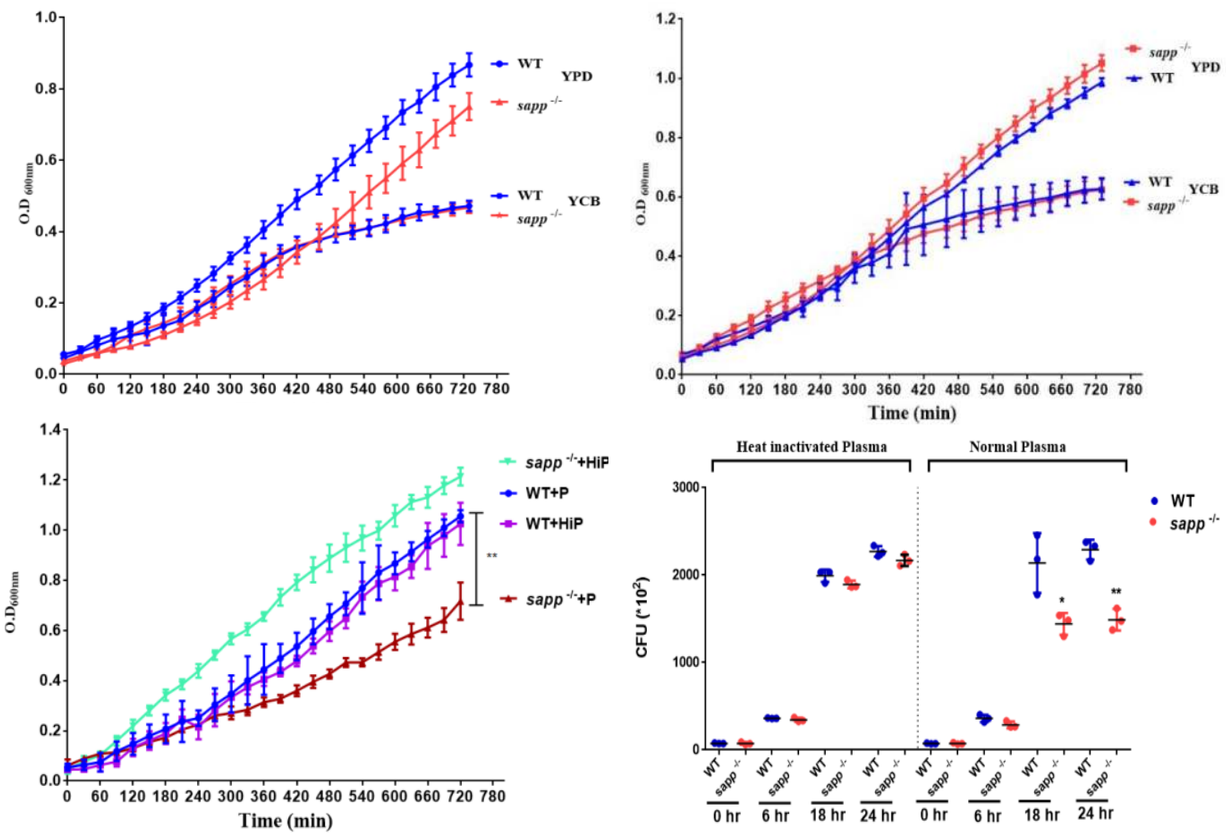


Figure 1. Growth kinetics of wt (GA1) and *sapp1-2-3* $^{-/-}$ strains in YPD, YCB medium and in the presence of human serum.

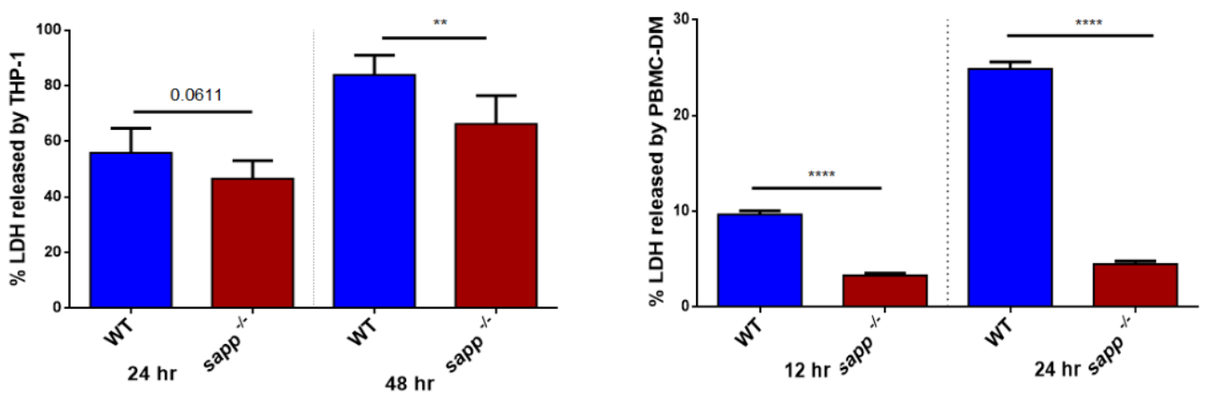


Figure 2. Host cell damage after infection with *C. parapsilosis* wt and *sapp1-2-3*$^{-/-}$ cells.

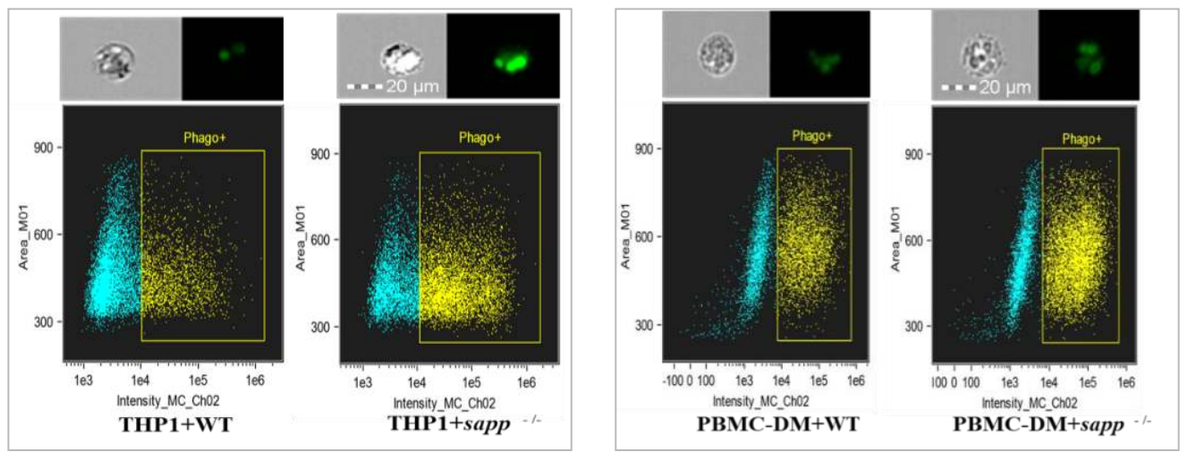


Figure 3. Phagocytosis of fungal cells by THP1 and PBMC-derived macrophages.

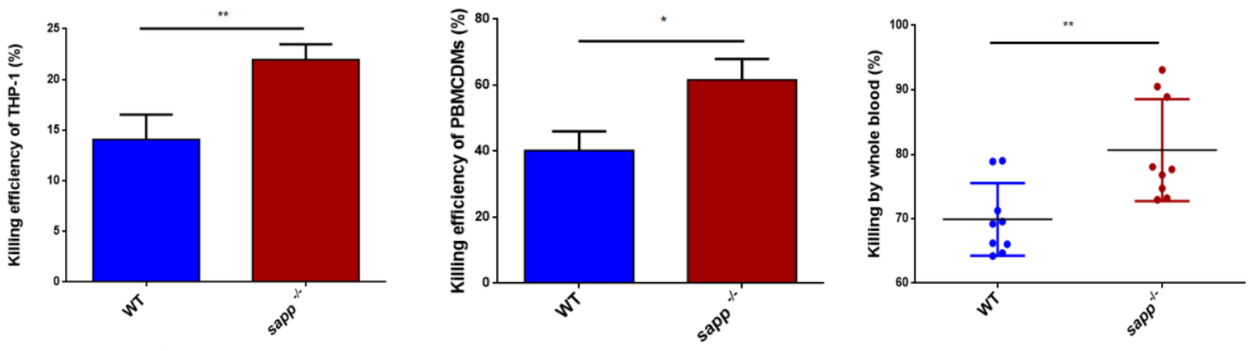


Figure 4. Yeast cell survival following incubation with host cells.

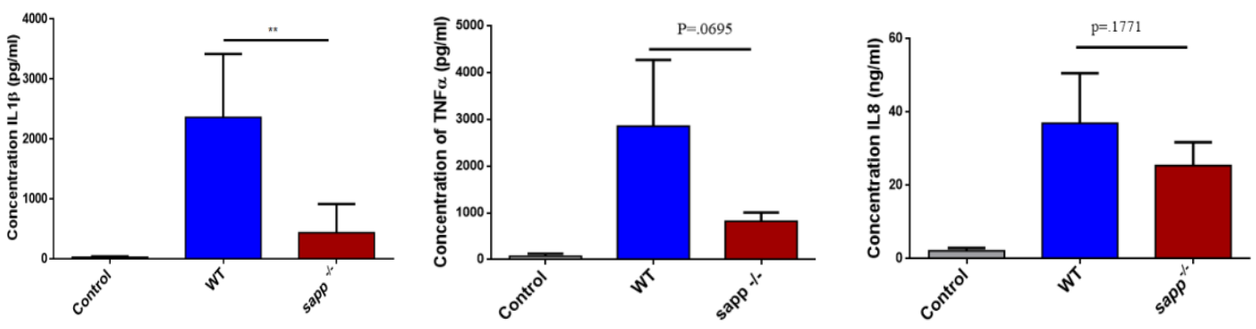


Figure 5. Cytokine production by PBMC-DMs upon stimuli with fungal cells.

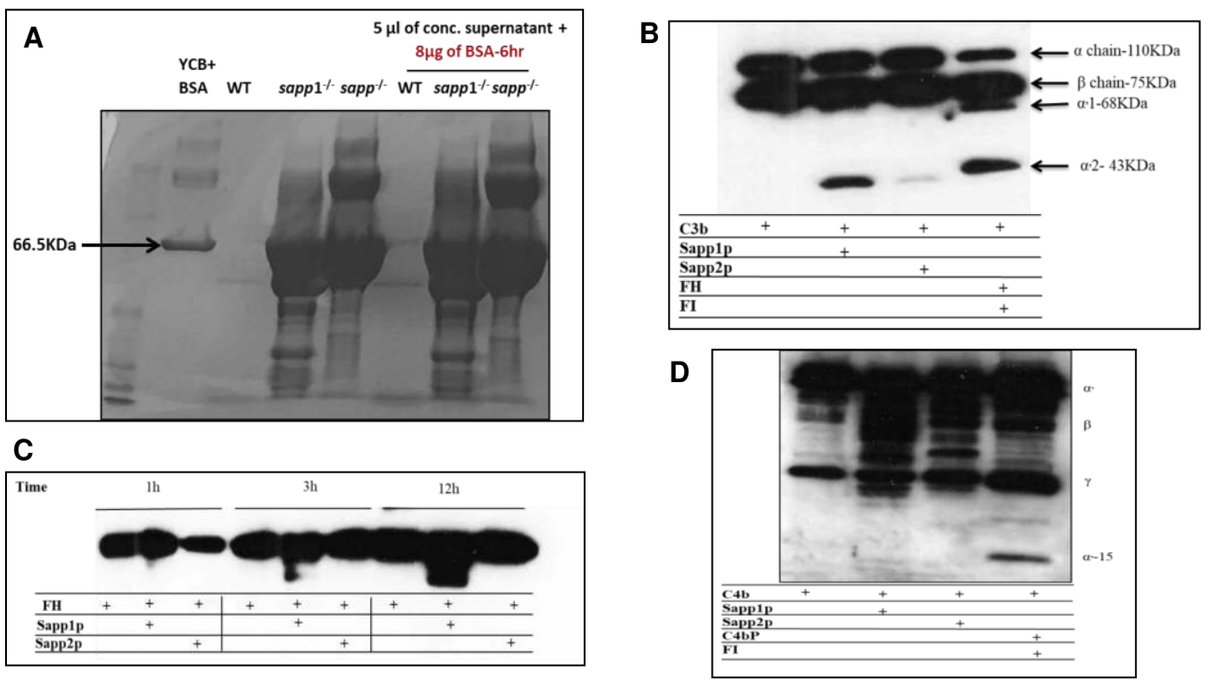


Figure 6. Sapp1p and Sapp2p can cleave the BSA in media (A), can cleave human complement protein the C3b (B), cleave RCA member FH (B) and can also cleave C4b (D).

Conclusion

Our results indicate that the *sapp1-2-3* $^{-/-}$ mutant strain is more susceptible to the presence of human plasma, phagocytosed and killed more efficiently by macrophages and causes less damage to PBMC-DMs compared to wt. Furthermore, Sapps can cleave major human complement protein.

Acknowledgements

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References

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