Candida albicans promotes TSST-1 production in Staphylococcus aureus by depleting glucose and lifting CcpA-mediated repression of the tst gene

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Résumé

During menstruation, the gram-positive opportunistic pathogen *Staphylococcus aureus* can cause menstrual toxic shock syndrome (mTSS), a rare yet life-threatening disease, through the release of the superantigen TSST-1 (toxic shock syndrome toxin 1). Prolonged use of intravaginal menstrual products has been the main risk factor for mTSS, facilitating *S. aureus* growth in menstrual blood and TSST-1 production (Schlievert & Davis, 2020). However, various studies suggest the potential role of vaginal microbiota in mTSS development, including yeasts such as *Candida albicans* (Jacquemond et al., 2018; MacPhee et al., 2013; Maduta et al., 2024). Thus, this study investigated the potential role of vaginal *Candida* species, especially *C. albicans*, in the stimulation of TSST-1 production of *S. aureus*, through increased glucose depletion and relieving of CcpA-mediated gene repression.
Wild-type and slow glucose-depleting *C. albicans* strains were cultivated at 37∘C for up to 18h in Brain Heart Infusion, supplemented or not with glucose. Culture supernatants were mixed with *S. aureus* suspensions and incubated for 6h at 37∘C. TSST-1 levels were quantified by ELISA following exposure to fungal supernatant or control medium.

TSST-1 production was negatively correlated with glucose levels in both control medium and *C. albicans* supernatants. Limiting yeast glucose depletion delayed downstream TSST-1 production; glucose supplementation of supernatants inhibited toxin production of *S. aureus*. Deletion of the glucose-responsive regulator CcpA lead to increased TSST-1 production, independently of glucose levels in medium and supernatants. Furthermore, deletion of the

*Intervenant

exotoxin regulator SaeRS abolished TSST-1 production entirely.
In conclusion, CcpA inhibits TSST-1 production in high glucose conditions. Then, glucose depletion in medium by *C. albicans* during its growth, which lifts this repression, enabling SaeRS-mediated production of TSST-1 by S. aureus. These results highlight the importance of interkingdom microbial interactions and glucose availability in the regulation of *S. aureus* virulence and mTSS development.