Saccharomyces cerevisiae var. *'boulardii'* infections: from diagnosis to in-host microevolution

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Saccharomyces 'boulardii'

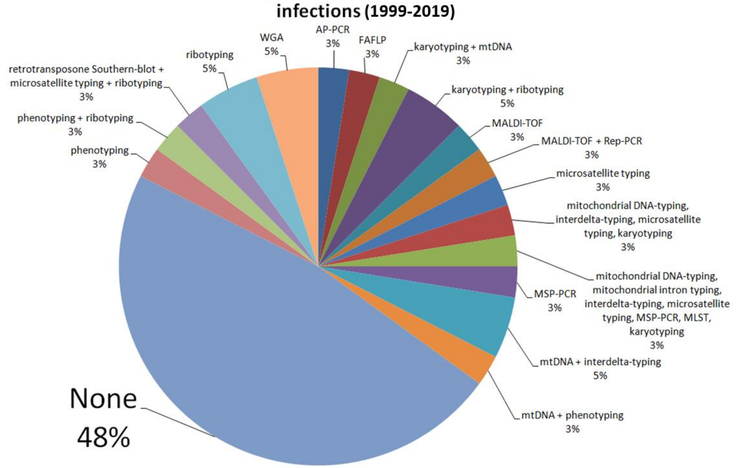
- Recently, the subtype *S. 'boulardii'* has become an ingredient in many **probiotic supplements**.
- **Positive health effects:**
  - effect against *Clostridium difficile* and cholera toxins
  - antimicrobial activity
  - modulation of gut flora
  - reduction of inflammatory cytokine levels
- **Treatment:** diarrheal disorders (acute colitis, *C. difficile*-related diarrhea)

Problems

Yeast probiotics infections (first in 1991)
- local or systemic mycosis
- published fungemia cases

Predisposing factors
- critical illness; ICU admission
- antibiotics and probiotics use
- immunosuppression

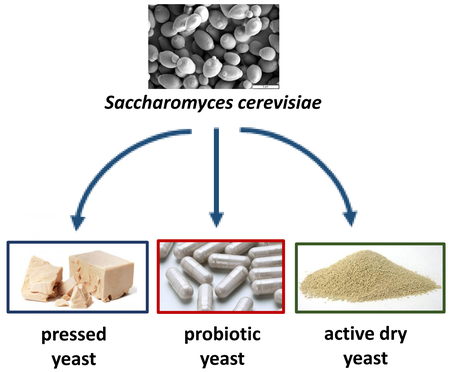
Methods used for strain-level typing of presumably probiotic-derived yeast infections (1999-2019)



Diagnosis of yeast probiotic infection

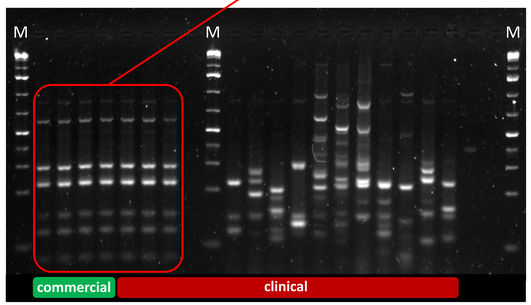
Subtyping

S. cerevisiae is a potentially emerging fungal pathogen and as a species it is not homogeneous. Instead it can be divided into clades and several clinical isolates have been identified in these phylogenetic groups. Although PCR-fingerprinting methods are applicable for subtyping, routine clinical mycological diagnostics rarely uses such methods.
However subtyping would be a prequisite to understand how and why infections arise from products containing live yeasts, such as probiotics.



Multiplex PCR

Based on our genotyping results we combined interdelta, *YLR177w*, *YOR267c*, and the ITS region primers into a single multiplex reaction. For probiotics and probiotic-derived clinical isolates, our multiplex PCR resulted in an easily recognizeable band pattern which consists of six bands in three groups plus a single band. The other, non-probiotic related clinical isolates displayed different band patterns clearly distinguishing them from the probiotic group.



Imre A. et al., A new, rapid multiplex PCR method identifies frequent probiotic origin among clinical *Saccharomyces* isolates, *Microbiological Research* **227**, 126298 (2019)

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Live Q&A session:
Tuesday, April 28
2:02 - 2:04 PM

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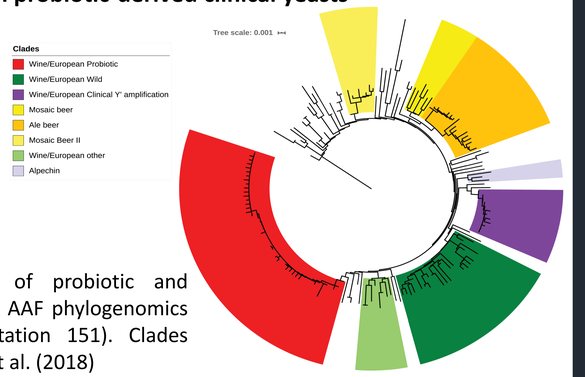
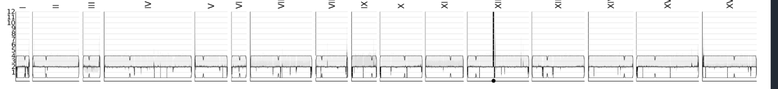
mtDNA and genome structure variation analysis in probiotic-derived clinical yeasts

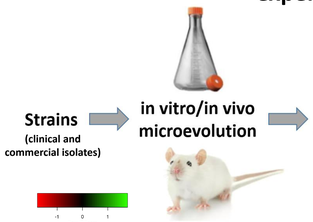


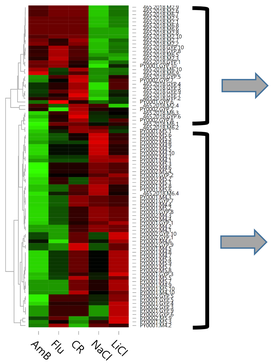
mtDNA phylogeny of probiotic and related yeasts using AAF phylogenomics (see PEQG presentation 151). Clades according to Peter et al. (2018)

Combined coverage plot for 43 probiotic and derived clinical isolates shows that genome structure variations are rare (1 tetraploid, 4 aneuploid (> diploid), 1 aneuploid (<diploid), 37 diploid)



Identification of traits under selection during experimental infection





clinical isolate and subclones

Amphotericin B	Fluconazole	Congo Red	NaCl	LiCl

commercial isolates and subclones

Amphotericin B	Fluconazole	Congo Red	NaCl	LiCl

tolerant less tolerant