Comparative genomic analysis reveals a critical role of de novo nucleotide biosynthesis for *Saccharomyces cerevisiae* virulence.

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Abstract

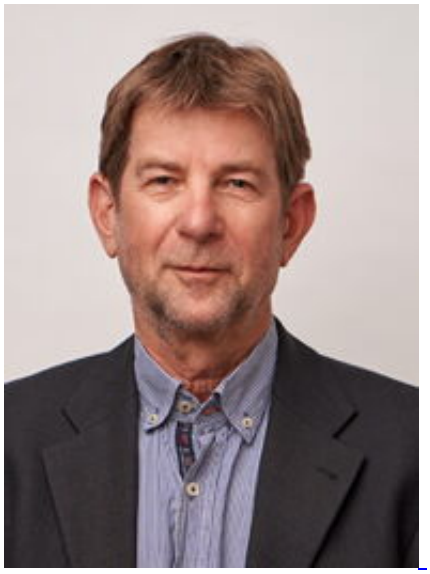
In recent years, the number of human infection cases produced by the food related species Saccharomyces cerevisiae has increased. Whereas many strains of this species are considered safe, other 'opportunistic' strains show a high degree of potential virulence attributes and can cause infections in immunocompromised patients. Here we studied the genetic characteristics of selected opportunistic strains isolated from dietary supplements and also from patients by array comparative genomic hybridization. Our results show increased copy numbers of IMD genes in opportunistic strains, which are implicated in the de novo biosynthesis of the purine nucleotides pathway. The importance of this pathway for virulence of S. cerevisiae was confirmed by infections in immunodeficient murine models using a GUA1 mutant, a key gene of this pathway. We show

that exogenous guanine, an end product of this pathway in its triphosphorylated form, increases the survival of yeast strains in ex vivo blood infections. Finally, we show the importance of the DNA damage response that activates dNTP biosynthesis in yeast cells during ex vivo blood infections. We conclude that opportunistic yeasts may use an enhanced de novo biosynthesis of the purine nucleotides pathway to increase survival and favor infections in the host.

Beteiligte Forschungseinheiten

Mikrobielle Pathogenitätsmechanismen Bernhard Hube Mehr erfahren

Leibniz-HKI-Autor*innen



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