

Title: Fungal-mediated Mg^{2+} competition shapes bacterial fitness and antibiotic resistance

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Abstract

Fungi and bacteria have been intimate partners for millennia. They cooperate or compete for resources in various environments, such as soil or infected host tissues with limited nutrients. Microbial cooperation and competition have profound implications for discovering novel antibiotics and developing strategies to treat infectious diseases. The fungus *Candida albicans* and the bacterium *Pseudomonas aeruginosa* are the primary causes of human polymicrobial infections. Such infections are often associated with increased antibiotic resistance and high mortality. To combat these infections, it is crucial to understand how these two species interact. We aim to uncover the causes and consequences of such fungal-bacterial competition, using these two species as an experimental model. We found that *C. albicans* can suppress bacterial viability in co-culture. Using bacterial transposon-sequencing (Tn-seq), we found 13 genes required for *P. aeruginosa* to protect itself from fungal competition, including a Mg^{2+} transporter, MgtA. Deletion in *mgtA* significantly reduces bacterial viability in co-culture, consistent with our Tn-seq result. We also found that adding Mg^{2+} in co-culture rescues viability of the *mgtA* deletion mutant, indicating *C. albicans* depletes Mg^{2+} to suppress bacterial viability. Furthermore, we discovered that Mg^{2+} competition is prevalent between multiple fungal and bacterial species. Lastly, we show that fungal-mediated Mg^{2+} depletion increases bacterial antibiotic resistance. We are currently investigating how such fungal-bacterial competition impacts the long-term evolution of bacterial antibiotic resistance. Overall, our finding reveals that Mg^{2+} competition is a novel mechanism of fungal-bacterial competition, highlighting the importance of understanding the role of this nutritional competition in polymicrobial infections and the potential of targeting this mechanism for therapeutic intervention.