Heptahelical receptors GprC and GprD of *Aspergillus fumigatus* are essential regulators of colony growth, hyphal morphogenesis, and virulence.

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Abstract

The filamentous fungus Aspergillus fumigatus normally grows on compost or hay but is also able to colonize environments such as the human lung. In order to survive, this organism needs to react to a multitude of external stimuli. Although extensive work has been carried out to investigate intracellular signal transduction in A. fumigatus, little is known about the specific stimuli and the corresponding receptors activating these signaling cascades. Here, two putative G-protein-coupled receptors, GprC and GprD, were characterized with respect to their cellular functions. Deletion of the corresponding genes resulted in drastic growth defects as hyphal extension was reduced, germination was retarded, and hyphae showed elevated levels of branching. The growth defect was found to be temperature dependent. The higher the temperature the more pronounced was the growth defect. Furthermore, compared with the wild type, the sensitivity of the mutant strains toward environmental stress caused by reactive oxygen intermediates was increased and the mutants displayed an attenuation of virulence in a murine infection model. Both mutants,

especially the DeltagprC strain, exhibited increased tolerance toward cyclosporine, an inhibitor of the calcineurin signal transduction pathway. Transcriptome analyses indicated that in both the gprC and gprD deletion mutants, transcripts of primary metabolism genes were less abundant, whereas transcription of several secondary metabolism gene clusters was upregulated. Taken together, our data suggest the receptors are involved in integrating and processing stress signals via modulation of the calcineurin pathway.

Involved units

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