Protein kinase a and high-osmolarity glycerol response pathways cooperatively control cell wall carbohydrate mobilization in *Aspergillus fumigatus.*

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Abstract

Aspergillus fumigatus mitogen-activated protein kinases (MAPKs) are involved in maintaining the normal morphology of the cell wall and providing resistance against cell wall-damaging agents. Upon cell wall stress, cell wall-related sugars need to be synthesized from carbohydrate storage compounds. Here we show that this process is dependent on cAMP-dependent protein kinase A (PKA) activity and regulated by the high-osmolarity glycerol response (HOG) MAPKs SakA and MpkC. These protein kinases are necessary for normal accumulation/degradation of trehalose and glycogen, and the lack of these genes reduces glucose uptake and glycogen synthesis. Alterations in glycogen synthesis were observed for the sakA and mpkC deletion mutants, which also displayed alterations in carbohydrate exposure on the cell wall. Carbohydrate mobilization is

controlled by SakA interaction with PkaC1 and PkaR, suggesting a putative mechanism where the PkaR regulatory subunit leaves the complex and releases the SakA-PkaC1 complex for activation of enzymes involved in carbohydrate mobilization. This work reveals the communication between the HOG and PKA pathways for carbohydrate mobilization for cell wall construction.IMPORTANCEAspergillus fumigatus is an opportunistic human pathogen causing allergic reactions or systemic infections such as invasive pulmonary aspergillosis, especially in immunocompromised patients. The fungal cell wall is the main component responsible for recognition by the immune system, due to the specific composition of polysaccharide carbohydrates exposed on the surface of the fungal cell wall called pathogen-associated molecular patterns (PAMPs). Key enzymes in the fungal cell wall biosynthesis are a good target for fungal drug development. This report elucidates the cooperation between the HOG and PKA pathways in the mobilization of carbohydrates for fungal cell wall biosynthesis. We suggest that the reduced mobilization of simple sugars causes defects in the structure of the fungal cell wall. In summary, we propose that SakA is important for PKA activity, therefore regulating the availability and mobilization of monosaccharides for fungal cell wall biosynthesis during cell wall damage and the osmotic stress response.

Involved units

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