ABSTRACT

Principal Investigator: Takuji Oka

Grant Title: Fundamental studies on galactomannan biosynthesis in filamentous fungi

Objective: Fungal-type galactomannan (FTGM) is a major cell wall polysaccharide in pathogenic *Aspergillus* species. Its biosynthesis and intracellular transport pathways are potential targets for the development of antifungal drugs. However, the precise mechanisms by which FTGM is transported to the cell surface, as well as the regulatory networks of related nucleotide sugar metabolism, remain largely unknown. To elucidate these processes, this study primarily investigated the role of glycosylphosphatidylinositol (GPI) anchors in FTGM transport and thoroughly examined the intracellular nucleotide sugar supply network driven by UDP-glucose 4-epimerases in *Aspergillus*.

Results and Discussion: Deletion of GPI anchor biosynthetic genes resulted in the loss of FTGM from the cell wall, revealing that the GPI anchor itself functions as a direct carrier for transporting FTGM to the cell surface. Furthermore, regarding the fundamental supply of sugar donors in *Aspergillus* sp., we elucidated the distinct yet coordinated roles of two UDP-glucose 4-epimerases, UgeA and UgeB. UgeA strictly acts as the primary supplier of UDP-galactose for FTGM biosynthesis. In contrast, UgeB possesses broader substrate specificity, catalyzing the interconversion of UDP-GlcNAc and UDP-GalNAc to maintain diverse nucleotide sugar pools. This UgeB-mediated supply is essential for the synthesis of other indispensable cell wall components and for adaptation to cell wall stress. The functional divergence between UgeA and UgeB is of great interest for understanding fungal cell wall integrity. Taken together, these results demonstrate that nucleotide sugar biosynthetic pathway and GPI-mediated transport are potential targets for future antifungal drug design.

References:

1. Kadooka, C., Yakabe, S., Hira, D., Futagami, T., Goto, M., and Oka, T. (2025) Functional redundancy and divergence of UDP-glucose 4-epimerases in galactose metabolism and cell wall biosynthesis in *Aspergillus nidulans*. ***Fungal Genet Biol*** 177, 103972
2. Oka, T., Kadooka, C., Tanaka, Y., and Hira, D. (2026) Structure and biosynthetic mechanisms of galactomannans in filamentous fungi. ***Biochim Biophys Acta Gen Subj*** 1870, 130960
3. Yakabe, S., Kadooka, C., Matsuzawa, T., Kawai, Y., Noguchi, M., Hira, D., Goto, M., and Oka, T. (2026) Intracellular β-glucosidase regulates cellulase expression and development in *Aspergillus nidulans*. ***Appl Microbiol Biotechnol.*** 10.1007/s00253-026-13851-9