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The molecular genetic study on biofilm formation by *Candida* species

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Introduction

Candida species is the major cause of fungal infection in the world. To date, *C. albicans* and *C. glabrata* are considered as the first and second major causes of systemic candidiasis. Not only existing as planktonic cells, *Candida* species is also capable of developing into surface-attached microbial communities called as biofilm. The biofilm formation by *Candida* species is one of pathogenic factors on human infections and is generally observed on the implant devices in human body. Because of the distinct characteristic architecture and phenotypic properties, the biofilm has increased resistance to antimicrobial treatment and host immune defense compared to the planktonic cells. However, the mechanism of biofilm formation by *Candida* species has not been studied well. Therefore, this research is a molecular genetic study on biofilm formation by *C. albicans* and *C. glabrata*.

Results and discussion

In this study, the biofilm formation model on multi-well plates was used to form *Candida* biofilm *in vitro*. Based on this simple and productive method, a system of biofilm formation model on silicone material was developed in this study, which was supposed to simulate the fungal infection on the silicone medical devices. In the study on the biofilm formation by *C. albicans*, the role of a cell wall protein, Bgl2p was focused. Although the metabolic activity of biofilm formed by *bgl2Δ/bgl2Δ* mutant was detected to be similar with that of the wild type strain, the delay on the transition from yeast cell to filamentous cell was observed by SEM during the biofilm formation. In this mutant, the expression of two transcriptional factor genes

CPH2 and *TEC1*, which are in the same regulatory pathway, was repressed especially during the biofilm formation. Taken together, lack of Bgl2p in *C. albicans* was suggested to influence the transcriptional expression of *CPH2* and *TEC1* genes and then lead to the delay on the transition from yeast to filamentous cell morphology during the biofilm formation.

In the study on the biofilm formation by *C. glabrata,* a comprehensive genetic screening was accomplished by using gene mutant library and five candidate genes were found out to be involved in the biofilm formation by *C. glabrata*. The transcriptional expression of these five genes was also upregulated in the biofilm formation conditions, compared to those in planktonic cell growth conditions.

CgSYN8 and *CgSNC1* were selected as the focused gene for the further research in these five. Syn8p and Snc1p in *S. cerevisiae* were identified as SNARE proteins, acting in membrane fusion. This study indicated *syn8Δ* mutant was defective not only in the metabolic activity of biofilm, but also in the morphological structure and the biomass of biofilm. Deletion of *SYN8* also led to notable decrease in the adhesion ability during the biofilm formation, which may link to the repression of two adhesin genes, *EPA10* and *EPA22*. Furthermore, in addition to the abnormal vacuolar morphology, the hypersensitivity to Hygromycin B and various ions in *syn8Δ* mutant suggested that Syn8p is required for normal vacuolar function in *C. glabrata*. Snc1p also showed slight effect on the vacuolar function and biofilm formation by *C. glabrata*, but not as significant as Syn8p. Therefore, the SNARE proteins Syn8p and Snc1p were predicted to be relevant to vacuolar function and then it was supposed that the active vacuolar function is required for the biofilm formation by *C. glabrata*. These findings provided more understanding on the virulence factors of *Candida* species and more information for future clinical treatment.