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Article / Book Information

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著者(和文)	ChenXinyue
Author(English)	Xinyue Chen
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論 文 要 旨
THESIS SUMMARY

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学生氏名： Student's Name	Chen Xinyue	指導教員（主）： Academic Advisor(main)	梶原　将
		指導教員（副）： Academic Advisor(sub)	

要旨（英文 800 語程度）
Thesis Summary (approx.800 English Words)

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 the biofilm formation by *C. albicans* and *C. glabrata*.

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. As the major organism for studying fungal pathogen, *C. albicans* has been well reported about genetic patterns relevant to the biofilm formation. This study on *C. albicans* focused on a cell wall β-1, 3-glucosyltransferase, Bgl2p about its role on the cell wall integrity and the

biofilm formation. *BGL2* was confirmed to be required for cell wall integrity in *C. albicans* by both the cell wall sensitivity assay and aggregation assay. Although it has been known that *BGL2* transcription increased during the biofilm formation, the metabolic activity of biofilm formed by *bgl2Δ/bgl2Δ* null mutant was detected to be similar with that of the wild type strain. Interestingly, through the observation by scanning electron microscope (SEM) imaging, there was a delay on the transition from yeast cell to filamentous cell during the biofilm formation by *bgl2Δ/bgl2Δ* null mutant. In this mutant, the expression of two transcriptional factor genes *CPH2* and *TEC1*, which are in the same regulatory pathway for filamentous transition, was detected to notably decrease 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 play a role in normal transition from yeast to filamentous cell morphology during the biofilm formation.

Since the biofilm formation by *C. glabrata* was not as well-studied as by *C. albicans*, a comprehensive genetic screening was accomplished by using gene mutant library in the study on the biofilm formation of *C. glabrata*. Five candidate genes were picked out and their systemic names in *C. glabrata* are CAGL0G08316g, CAGL0G06314g, CAGL0G08624g, CAGL0G06358g, CAGL0H06325g, respectively. The null mutant of each gene showed significant reduction in the biofilm formation by XTT assay, compared to the reference strain. The transcriptional expression of these five genes was also upregulated in the biofilm formation conditions, compared to those in planktonic cell growth conditions. Therefore, these results provided several new target genes involved in the biofilm formation by *C. glabrata*.

CAGL0H06325g (*CgSYN8*) and CAGL0G06358g (*CgSNC1*) were selected as the focused gene for the further research in these five above genes. Syn8p

and Snc1p in *S. cerevisiae* were identified as SNARE proteins, which are the key components of protein complex in membrane fusion of eukaryotic cells. Although Syn8p in *S. cerevisiae* has been known to act in the vesicle traffic between Golgi and PVC, this protein was firstly studied in *C. glabrata* in this study. 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* seemed to have no effect on the extracellular matrix production, but 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 in *S. cerevisiae* has been known to involve in the fusion between Golgi-derived secretory vesicles with the plasma membrane. Snc1p also showed slight effect on the vacuolar function and the biofilm formation by *C. glabrata*, but not as remarkable 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.

備考 ： 論文要旨は、和文 2000 字と英文 300 語を 1 部ずつ提出するか、もしくは英文 800 語を 1 部提出してください。

Note : Thesis Summary should be submitted in either a copy of 2000 Japanese Characters and 300 Words (English) or 1copy of 800 Words (English).