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論 文 要 旨

THESIS SUMMARY

系・コース： Department of, Graduate major in	ライフエンジニアリング　系コース	申請学位（専攻分野）： Academic Degree Requested	博士 Doctor of (Philosophy)
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要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words ）

The pathogenic fungi *Candida albicans* and *C. glabrata* rank as the first and the second leading cause of candidiasis. It is reported that they cause hepatic cell apoptosis by producing reactive oxygen species (ROS). The NADPH oxidase genes (*CgNOX1* and *CaFRE8*), which generate the ROS in these fungi, play a critical role during this process. Moreover, the role of *NOX* genes from *C. glabrata* under oxidative stress remains unknown. Therefore, it is of interest to understand and role of *CgNOX1* under these specific conditions and the regulation of expression from the *CgNOX1* and *CaFRE8* promoters.

In Chapter 2, I compared the transcript expression of *CgNOX1* under both specific conditions by RT-qPCR. It is observed that there is a significant increase in *CgNOX1* after co-incubation or H_2O_2 treatment. Moreover, the ROS level was strongly induced under H_2O_2 stress, while the *nox1Δ* mutant failed to induce this phenomenon. This suggests that *CgNOX1* plays a critical role in the oxidative stress response in *C. glabrata*.

In Chapter 3, I investigated the effect of *CgNOX1* gene on the inflammation response of hepatocytes. It is found that IL-6 concentration and transcript expression were induced in HC cells after *C. glabrata* infection. The lack of *CgNOX1* reduced the IL-6 induction. However, NLRP3 inflammasomes and related genes were inactivated in hepatic cells in this study.

In Chapter 4 and Chapter 5, I constructed GFP-tagged *C. glabrata* and *C. albicans* containing the promoters of *CgNOX1* and *CaFRE8*. The GFP signals of *C. glabrata CgNOX1-EGFP* were detectable in some cells but not all cells. But after co-incubation and H_2O_2 treatment, no GFP fluorescence was visible in the strain. In *C. albicans FRE8Δ/ACT1pt-yEGFP-CYC1t* strain, the GFP signals were significantly increased after co-incubation and treatment with hydrogen peroxide. The result was confirmed with transcript level. Therefore, this strain could be a promising model for conducting quantitative analysis of the *CaFRE8* promoter

activity.

In Chapter 6, I established five GFP-tagged *C. albicans* strains, each with a different deletion of the *CaFRE8* promoter region spanning 500 bp upstream of the gene. The GFP fluorescence of all the GFP-tagged strains was dateable and showed no meaningful difference. Then, I checked the GFP mean fluorescence intensity and transcript expression among six GFP-tagged strains during the co-incubation with hepatic cells. During the process, it was determined that the region from -500 bp to -401 bp in the upstream sequence of the gene is considered a core region. In addition, it was observed that the -99 ~ 0 region of the *CaFRE8* promoter might play a critical role under conditions of oxidative stress.

In conclusion, *CgNOX1* plays an important role in *C. glabrata* during infection of human hepatocytes and oxidative stress response. Furthermore, in *C. albicans*, the core regions in the upstream sequences of the *CaFRE8* gene were identified during contact with HC cells and under oxidative stress. The identification of the core sequence upstream of *CaFRE8* may contribute to a better understanding of its recognition by hepatocytes and its response to oxidative stress in *C. albicans*.