

The Expression of Estrogen Receptor and Bcl2 in *Candida albicans* May Represent Removal of Functional Barriers among Eukaryotic and Prokaryotic Cells

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Abstract

Introduction: Although there are several structural characteristics separating prokaryotic cells from eukaryotic cells, we still believe that functional similarities can make differences. The relationship between estrogen exposure and pathogenicity of *Candida albicans* has been investigated for a long time.

Study Objectives: To investigate the expression of estrogen receptor and BCL2 in *Candida albicans*.

Methodology: *Candida albicans* (ATCC) was cultured in Sabouraud Dextrose Broth (SAB) for 24 hrs at 37°C. A tube containing broth medium (SAB) with *C. albicans* was centrifuged to concentrate the amount of *C. albicans* for 5 minutes (3000 RPM). A sample of the sediment was transferred into slides to make smears of *C. albicans*. Immunohistochemical localization of estrogen receptor (ER), and BCL2 proteins was carried out using indirect immunoperoxide techniques.

Results: Both ER and BCL2 proteins were localized in *C. albicans*. The localization was observed mainly in the nucleus, and to lesser extent in the cytoplasm of *C. albicans*. Hyphae form of *C. albicans*.

Conclusion: Our preliminary findings showed that the effects of estrogen and its receptor on *C. albicans* is deeper than it was thought, and the growth of *C. albicans* may follow similar mechanisms as involved in host cells and this is expected to widen our understanding of interactions between prokaryotic and eukaryotic cells.

Keywords: *Candida albicans*; Estrogen Receptor; BCL2; Localization; Immunohistochemistry

Introduction

Candida albicans

Fungi have been recognized as one of the main etiologic agents causing diseases to human, particularly among immunocompromised patients [1]. *Candida albicans* is the most prevalent fungal species involved in human diseases [1,2]. *C. albicans* exists in different areas in human body including skin, gastrointestinal tract and the vulvovaginal tract [3].

C. albicans has the ability to change its form according to environmental conditions as factors of virulence. *C. albicans* has a biochemical system composed of proteins that can bind to steroids such as estrogen binding protein (Ebp1). In humans, estrogens can control

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the process of proliferation and differentiation through ERs. It has been demonstrated that there is an effect of 17 β -estradiol on morphological changes of *C. albicans* from the yeast-to-hypha via EBP1 in *C. albicans* through using an ebp1 [4].

It has been reported that estrogen elevating levels are considered as risk factors for developing disease [5,6]. Other studies reported the association between increased estrogen levels in pregnancy period and increased vaginal colonization with *C. albicans* [7-9]. Furthermore, exogenous estrogens including oral contraceptives have been reported to be associated with increased colonization of *C. albicans* [5,6,9].

Estrogen has important roles in cell proliferation in the intestine, skin, and liver [10-12]. Tae., *et al.* [13] showed that estrogen increased the expression of Bcl-2 following spinal cord injury (SCI) in rats.

Study Objective

The main objective of this study was to investigate the expression of estrogen receptor and BCL2 in *Candida albicans*.

Methodology

Candida albicans (ATCC) was cultured in Sabouraud Dextrose Broth (SAB) for 24 hrs at 37°C. A tube containing broth medium (SAB) with *C. albicans* was centrifuged to concentrate the amount of *C. albicans* for 5 minutes (3000 RPM). A sample of the sediment was transferred into slides to make smears of *C. albicans*.

Immunohistochemical localization of estrogen receptor (ER), and BCL2 proteins was carried out using indirect immunoperoxide techniques. Smears containing yeast cells were fixed in 100% ethanol for 5 minutes, and then incubated with 1% hydrogen peroxide for 30 minutes to neutralize endogenous activity of peroxidase activity. Following washing with phosphate buffer saline (pH 7.2) for 5 minutes, slides were incubated with 1% bovine serum albumin for 10 minutes to eliminate non-specific reactions. Using pap pen, a circle was drawn round the smear area in each slide to retain the fluids over the smear. Slides labeled for estrogen receptor were incubated with estrogen receptor (Dako, code M7047, clone 1d5) diluted 1/100 for 1 hour, and those labeled for BCL-2 were incubated with BCL-2 (code M0887, clone 124) for 1 hour. Slides were washed with phosphate buffer saline (pH 7.2) for 5 minutes, then slides were incubated with biotinylated secondary antibodies for 15 minutes, washed with phosphate buffer saline (pH 7.2) for 5 minutes, incubated with streptavidin conjugated with peroxidase enzyme for 15 minutes. A chromogen (DAB) was used to view the reaction, and then slides were washed with tap water to end the reaction. Finally, slides were stained with hematoxylin as a counter stain for 10 seconds, washed with tap water, dehydrated and mounted.

Results

Expression of ER

Candida cells showed that ER was expressed in both forms round and hyphae forms, but hyphae forms exhibited stronger expression in nucleus and moderate expression in cytoplasm.

Expression of BCL-2

Candida cells showed that BCL-2 was expressed in both forms round and hyphae forms, but hyphae forms exhibited stronger expression in cytoplasm and moderate expression in nucleus.

Discussion

Although the data in this study is little, but I think that it has strong impact for the following reasons: previous studies conducted in candida and estrogen have put the focus on estrogen binding protein, rather than on ER directly as in this study [4].

The potential that estrogen available within the conditions involving the existence of *Candida albicans* will not only effect on their virulence, but their proliferation because estrogen accelerates the proliferation of cells [10-12].

From the previous context, we think that the relationship between estrogen and *Candida albicans* is deeper than we thought before. Furthermore, as far as similar mechanisms are involved in proliferation between prokaryotic cells such as *Candida albicans* and host cells, it is highly possible to include that the interaction and interactivity between cells will shift to a next level in which prokaryotic cells may send messages as what is called cross-talk and impact their equilibrium. More work is needed to better understanding and the door will be open for more discussions and questions [14].

Conclusions

Our preliminary findings showed that the effects of estrogen and its receptor on *C. albicans* is deeper than it was thought, and the growth of *C. albicans* may follow similar mechanisms as involved in host cells and this is expected to widen our understanding of interactions between prokaryotic and eukaryotic cells.

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