CHAPTER 1

INTRODUCTION

The importance of fungi as infective agents, especially in opportunistic systemic infections has grown considerably in recent years. The increase of fungal disease is due to numerous factors, such as the increased use of antibiotics therapy and advances in medical technique which have resulted in an increase in the use of invasive procedures. Expansion of the fields of oncology and transplantation has led to an increase in the number of immunocompromised and vulnerable patients, and there is a growing problem with AIDS. Yeasts belonging to the genus *Candida* are major fungal pathogens for the immunocompromised host. *Candida* is pervasive pathogens capable of causing both local and systemic infections in hospitalized patients (1). During the 1980s, the *Candida* was the fourth most common nosocomial pathogens in intensive care units and accounted for 10% of all bloodstream infections and 25% of all urinary tracts infection in the intensive care unit setting (2, 3).

The frequency of nosocomial candidemia increased dramatically over the decade from 1980 through 1989. The reviewed secular trends in nosocomial bloodstream infections among hospitals surveyed as part of the National Nosocomial Infection Surveillance (NNIS) system and found that the rate of nosocomial candidemia increased by almost 500% in large teaching hospitals and by 219% to 370% in small teaching hospitals and large nonteaching hospitals, respectively (4). *Candida* causes 40 to 50% of deep fungus infections in lymphoma patients and 44 to 80% of infections in leukemic patients in various series. At Stanford University in California, U.S.A., in one series it was noted that over a third of such infections in this host were fatal (1).

Table 1. Most commonly isolated nosocomial pathogens hospital – wide and in ICUs : National Nosocomial Infections Surveillance system, October 1986 – December 1990 (5).

Area surveyed, pathogens	No. of isolates (% of total)
Entire hospital	
Escherichia coli	19,100 (13.7)
Staphylococcus aureus	15,553 (11.2)
Enterococci	14,820 (10.1)
Pseudomonas aeruginosa	14,087 (10.1)
Coagulase – negative staphylococci	13,517 (9.7)
Candida species	9,804 (7.1)
Enterobacter species	8,728 (6.3)
Klebsiella pneumoniae	6,841 (4.9)
Proteus mirabilis	4,915 (3.5)
Serratia marcescens	2,042 (1.5)

Area surveyed, pathogens	No. of isolates (% of total)
ICUs	
P.aeruginosa	2,390 (12.4)
S.aureus	2,377 (12.3)
Coagulase – negative staphylococci	1,964 (10.2)
Candida species	1,963 (10.1)
Enterobacter species	1,666 (8.6)
Enterococci	1,661 (8.6)

Table 2. Distribution of fungi causing nosocomial infections : National Nosocomial Infections Surveillance system, January 1980 – April 1990 (5).

Pathogen	No. of isolates (% of total)
Candida species	19,621 (72.1)
Fungi unspecified	2,907 (10.7)
Torulopsis species	1,884 (6.9)
Aspergillus species	311 (1.1)
Other	2,477 (9.1)
Total	27,200 (100)

Over 100 species of *Candida* have been identified, *Candida albicans* is the species most commonly isolated from clinical material and generally accounts for 50 % to 70% or more of cases of invasive candidiasis (2, 6). In common with many fungal species, *Candida albicans* is most frequently isolated as a yeast pathogen in human (7). But in the recent reports suggest that shifts have occurred in the distribution of infections caused by species of *Candida* other than *Candida albicans*. A number of reports have documented infections caused by *Candida tropicalis, Candida glabrata, Candida parapsilosis, Candida krusei, Candida lusitaniae*, and *Candida dubliniensis* (8, 9, 10, 11, 12, 13).

Table 3. Proportions of systemic candidal infections due to particular species, according to data from various institutions (11).

Candida species	Percentage of infections reported Per reference		
	Wingard, J.R.	Rex, J.H., et al	Iowa*
Candida albicans	54	56	59
Candida tropicalis	25	17	12
Candida glabrata	8	13	11
Candida parapsilosis	7	10	10
Candida krusei	4	2	3
Others	2	2	5

* : Unpublished data from the University of Iowa (1984 – 1993)

For the pathogenesis such as a commensal organism of the mucous membranes, *Candida albicans* becomes invasive when some aspect of host immunity becomes impaired. This statement is not meant to imply that the organism plays a very benign role in pathogenesis. Instead, several virulence factors, each of which promotes the successful colonization or invasion of various tissues (12). The cell wall of the organism is essential to its success as a pathogen, since it is required for growth, rigidity and protection against osmotic insult, and is the site of contact between the organism and its environment. Cell surface ligands and receptors promote colonization of host cells and tissues. A proteolytic enzyme (acid carboxyl protienase) associated with the cell surface and external environment is probably responsible for tissue invasion, which occurs as the organism undergoes to its filamentous form. This conversion is thought to be important to the infectious process. The cell wall is the structure responsible for the characteristic shape of each cellular form, and it is the site of interaction between the organism and the

host. Information about the wall components and their organization is important in understanding for the role in cell integrity and host – parasite interactions (13).

Most of the biological functions related to pathogenicity and virulence reside in the fungal cell wall, since as the outer most part of the cell, the cell wall is the structure that mediates the host – fungus interplay (4). This includes the triggering and modulation of host immune responses, which in case of cell wall of *Candida albicans* is a significant source of antigens appears to rely on a complex interplay between natural and adaptive immunity, posing interesting challenges to the host (14, 15). Especially prevalence in subjects infected by the human immunodeficiency virus with severe functions and numerical deficits in $CD4^+$ T - lymphocytes, which are critical components of cell – mediated immunity (CMI) (16). Candidal antigens may stimulate specific cell – mediated and humoral immune responses (HIMR), and there is a renewed interest in the study of the host antibody response to *Candida albicans* (14, 17 – 24). The identification and characterization of immunodominant antigens eliciting potent immune responses during candidiasis could have important repercussions for developing novel diagnostic, prophylactic, and therapeutic techniques for candidiasis (25). Detection of antibodies against *Candida* are important to study the immunological response to the infection and may also aid in the serodiagnosis of *Candida* disease (26).

The ideal " antigenic marker" for local and deep infections needs to meet certain in order to be useful in the diagnosis of candidiasis. First, it has to be expressed in all strains of *Candida albicans* and under different growing conditions. Second, it has to be expressed and trigger the immune response during infection, preferably at the early stage. Finally, it should not elicit a major immune response during the interactions of *Candida albicans* with host as a component of the normal flora. Immunoblot analysis of the serological response is a useful tool for the identification of immunogenic fungal components that elicit a specific antibody response in invasive disease. The detection of these particular cellular components will significantly to adapt