Number of saprophytic yeast species are now known to be causing various elements in human and animals. Many types of yeast are common microflora of humans and become invasive when host is compromised due to long term treatment with anti-neoplastic or immune suppressing drugs. Considering these two facts, the aim of the present study was to identify the uptake of saprophytic yeasts by animal cell lines. This *in vitro* model was further used to characterize the invasion of by pathogenic yeast namely *Candida albicans*. The invasion of epithelial cells is a virulence determinant of infiltrating *Candida albicans* infections. The tight junction assembly which is an important cellular structure of host imparts mechanical integrity and barrier function to the epithelial cells and was probed during invasion process. Molecular modifications brought about to surmount the barrier function of epithelial cells during the invasion process are hitherto unascertained.

The main findings in the thesis can be summarized as follows:

1. The epithelial barrier is made up of several proteins of which Zonula Occludens-1 is a principal player. This study attempts to elucidate the role of ZO-1 during *C. albicans* invasion. Chimeric GFP-ZO-1 expressing HEK-293T cells upon infection with *C. albicans* showed co-localization of actin and ZO-1 at the site of hyphal invasion.

2. The actin binding region of ZO-1 was essential for its localization at the invasion site.

3. C-terminal proline-rich domain of ZO-1 protein which contains actin binding region (ABR) was involved in its recruitment at the site of *C. albicans* invasion.
4. Conversely, the PDZ domains present at the N-terminal are not required for ZO-1 localization at the site of invasion.

5. Inhibition of actin polymerization by Cytochalasin D decreased the sites of *C. albicans* invasion.

6. Other TJ proteins like claudin-1, claudin-4, and JAM-A were also recruited at the invasion site in rabbit corneal epithelial cell line.

7. The loss of barrier function was demonstrated by reduction in the electrical resistance across MDCK monolayers that were exposed to spent medium harvested after growth of hyphal stage of *C. albicans*.

8. In addition, MDCK monolayers that were exposed to spent medium harvested after growth of hyphal stage of *C. albicans* also showed increased paracellular permeability.

9. These changes in TEER and permeability were attributed to the loss of ZO-1 during invasion without altering cell morphology.

10. Depletion of ZO-1 protein in MDCK cells accomplished by expression of ZO-1 shRNA resulted in higher invasion frequency while over-expression of ZO-1 led to decreased *C. albicans* invasion.

11. Treatment of MDCK monolayers with hyphal spent media led to a significant increase in transcription of TJP-1 gene whereas yeast spent media did not change mRNA levels in comparison to untreated monolayers. Early infection with *C. albicans* hyphae also does not change host mRNA level.

12. FRAP analysis demonstrated that ZO-1 localization at *C. albicans* invasion site is active.

13. Loss of ZO-1 with actin in buccal mucosa of immune-suppressed rats infected by *C. albicans* hyphae was observed.

14. Various yeast isolates from different clinical scenario were identified by DNA sequence information of PCR amplified ITS region. The identification of different yeast isolates from various patients revealed that 70% of the isolates
belonged to the genus *Candida*, while remaining 30% of the isolates were yeasts not belonging to genus *Candida*.

15. The purported saprophytic yeasts were characterized for internalization by mammalian cells *in vitro*, by staining the F-actin. These non-Candida clinical isolates, either in yeast or hyphal forms, were efficiently internalized by human epithelial cells. The internalization was marked by a process of actin polymerization surrounding the invading yeast.

Overall, this study demonstrates the disruption of barrier function during *C. albicans* invasion due to the loss or re-localization of ZO-1 protein. Such active uptake by epithelial cells signifies traversal of cell barrier by yeast cells during infection *in vivo*. 