Summary

Over 50 % of the healthy population are carriers of fungi of the genus *Candida* most commonly the pathogenic *C. albicans*. Bacteria of the natural microbial flora and the immune system are able to keep *C. albicans* as a commensal. In the case of a weakening of the immune defence or imbalance of the normal micro – flora, the development of superficial, or in certain circumstances life – threatening systemic, *C. albicans* infections is possible.

C. albicans pathogenicity is influenced by different factors. On the fungal side are virulence attributes, like morphogenesis, adhesion factors and secreted hydrolytic enzymes of vital importance. Among these is the family of secreted aspartic proteases (Saps) of which ten members have so far been described. *In silico* studies presented in this thesis do not exclude the existence of an additional member. Similarities in sequences of the Sap proteins, and previous studies of the genes *SAP1* to *SAP6*, point at a functional specialisation of certain sub – groups of this family. Computer based analysis of putative transcription factor binding sites in the promoter regions of all *SAP* genes argue for differential regulation of the *SAP* gene expression. *In vitro* and *in vivo* analyses of *SAP* gene expression in different mutants, lacking certain transcription factors, support these results. Within these studies it was shown that the transcription factors Cph1 and Efg1, which play central roles in the regulation of morphogenesis, are involved in the regulation of the expression of the genes *SAP4* to *SAP6*. These data suggest that the reduced virulence of *Δcph1* and *Δefg1* mutants is at least partially due to the loss of expression of *SAP4* to *SAP6*.

The two proteases Sap9 and Sap10 take an exceptional position within the Sap family. In contrast to all other members of this family, these proteases are heavily glycosylated and localised via glycosylphosphatidylinositol (GPI) anchors at the cell surface. The construction of Protease – Gfp – fusion proteins verified the localisation at the cell surface of the two proteases, whereby Sap9 antigens were found mainly in the cell membrane and Sap10 antigens additionally in the cell wall.

The deletion of the genes *SAP9* and *SAP10* and the analyses of the resulting single and double mutants led to the conclusions that Sap9 and Sap10 play an important role in cell – surface integrity as well as for the cell separation process during budding. With this it has been shown for the first time that Sap proteases have a cellular function. Sap9 und Sap10 cleave at basic or dibasic processing sites and show a processing pattern similar to yapsins or the Kex2 protease from *Saccharomyces cerevisiae*. The over – expression in *C. albicans* of the *SAP9* gene in mutants lacking *KEX2* or *SAP10*, or of the *SAP10* gene in mutants lacking *KEX2* or *SAP9*, only partially restored the phenotypes of the wild – type. Therefore it must be assumed that Sap9 and Sap10 (as well as Kex2) despite functional overlap, process distinct target proteins of fungal origin. Sap9 may also have an autocatalytic processing activity. Additionally, deletion of these genes leads to altered adhesion properties to buccal epithelial cells and causes either an enhanced (*Δsap9*) or reduced (*Δsap10*) adhesion. However, both mutants show significantly reduced tissue damage in an *in vitro* model of oral epithelial infection.

Consequently, Sap9 and Sap10 possess a novel, dual role in both cellular processes and host – pathogen interactions. On the basis of the results presented in this thesis it is postulated that Sap9 and Sap10 proteases process proteins which are of fungal origin, are localised at the cell surface or passing through it and are involved in the structural assembly of the cell surface and adhesion.