Oral epithelium reacts to microbial challenges by eliciting a defensive response that includes the production of antimicrobial peptides. **Objectives:** The present study aimed to investigate the expression of human b-defensins (hBDs)-1, 2 and 3 in experimental oral candidiasis. **Methods:** Reconstituted human oral epithelia were infected with six different Candida species, and a wild type C. albicans isolate and five of its mutants. hBD peptide and mRNA expression in the epithelia were examined by immunohistochemistry and in situ hybridization, respectively. **Results:** The expression of hBDs was induced after 12 h of infection with the wild type C. albicans, but this response was not observed for the noninvasive hyphal mutants or the secreted aspartyl proteinase (Sap) mutants. Furthermore, hBD expression was not detected after 48 h in the epithelia infected with either C. albicans wild type isolate or its invasive hyphal and SAP mutants. Most of the non-albicans-Candida were capable of inducing the expression of hBDs in epithelia after 24 or 48 h of infection. **Conclusions:** These Candida-host interaction patterns suggest that the oral epithelia possess mechanisms for sensing the early invasion of C. albicans through recognition of the presence of hyphae and Saps of Candida and respond to the insult by producing antimicrobial peptides. This hyphal-invasion-dependent-inhibition of hBD expression in oral epithelium that undermines the host surveillance system represents a hitherto undescribed novel pathogenic mechanism of C. albicans. Supported by Hong Kong Research Grants Council (RGC HKU 7310/00M, 7518/05M & 7339/02M).