

The possible role of *Candida albicans* in the progression of dental caries

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An association between dental caries and *Candida albicans*, the most common fungus in human body, has been shown. However, the question that whether *C. albicans* acts as a caries pathogen or rather plays a role as a commensal microbe still exists. It is well known that dental caries is mainly caused by acids from bacterial fermentation. Acidogenic bacteria, such as *Mutans streptococcus* and *Lactobacilli*, have been considered as major pathogenic factors of dental caries for a long time, whereas various studies have shown that *Candida albicans* can adhere to dental hard tissues and dentinal collagen, and can produce organic acids and secrete collagenolytic enzyme, which may implicate the cariogenic capability of *Candida albicans* that cannot only demineralize the dental tissue, but also they can destroy organic structure of dentine. Paying attention to the role of *Candida albicans* in the progression of dental caries may advance knowledge of pathology and etiology of caries and offer additional approaches for the prevention and therapy of dental caries.

Keywords: *Candida albicans*; dental caries; acidogenic; mutans streptococcus

INTRODUCTION

Dental caries, one of the most prevalent chronic diseases of human beings worldwide (Pitts, 2004; Featherstone, 2007), is considered to be the consequence of demineralization of susceptible dental hard tissues caused by organic acids from bacterial fermentation of dietary carbohydrates (Fejerskov *et al.*, 2008). *Candida albicans* (*C. albicans*) is a commensal microbe that can be frequently isolated from various sites including oral cavity, laryngopharynx, intestines and vagina mucosa. It was reported that *C. albicans* can be found in the oral cavity of 40% normal subjects (Arendorf *et al.*, 1979) and 75% of individuals who wore dentures (Budtz-Jørgensen *et al.*, 1975). On the other hand, *C. albicans* can also act as an opportunistic pathogen with the ability to cause a variety of infections (Pappas *et al.*, 2004). For instance, thrushes in infant and chronic atrophic candidiasis (denture-induced stomatitis) in adult are the most

common clinical manifestation of oral candidiasis. Meanwhile, *C. albicans* has been frequently found from dental caries in recent decades (Lynch *et al.*, 1994; Beighton *et al.*, 1995; de Carvalho *et al.*, 2006). Some studies even have shown a significant association between *C. albicans* and dental caries in children and young adults (Moalic *et al.*, 2001; Beighton *et al.*, 2004; de Carvalho *et al.*, 2006). In addition, evidences from a variety of studies have demonstrated that *C. albicans* has the ability to produce organic acids by the means of fermenting carbohydrates (Samaranayake *et al.*, 1986) and shows adherence to saliva-coated hydroxyapatite (Cannon *et al.*, 1995), dental hard tissues (Sen *et al.*, 1997) and dentinal collagen (Makihiro *et al.*, 2002). These above might implicate that *C. albicans* has the ability to destroy dental hard tissues, and can be proposed to act as a caries pathogen in dental caries.

DISCUSSION

Oral bacteria in dental plaque with the acidogenic and

aciduric abilities (especially *Mutans streptococcus* and *Lactobacilli*) have been considered as major pathogenic factors of dental caries for a long time. However, oral cavity is a complexity of varieties of microorganisms including bacteria, fungus, and etc. According to the viewpoint of Marsh that any species with the ability of producing acids and tolerating the cariogenic environment can contribute to the disease process (Marsh *et al.*, 2006), there are undoubtedly other acidogenic microorganisms involved in dental caries. Therefore, with its capabilities, *C. albicans* may be proposed to play a significant role in dental caries progression.

Since most surfaces in the oral cavity are bathed in saliva, adhesion of *C. albicans* to saliva-coated surfaces is an important early step involved in the colonization of oral cavity (Marsh *et al.*, (Cannon *et al.*, 1995). It has been confirmed that with the assistance of salivary proteins (Cannon *et al.*, 1995; ÓSullivan *et al.*, 1997), *C. albicans* can readily adhere to mucosa epithelial cells (Douglas *et al.*, 1985), acrylic (Edgerton *et al.*, 1993; Mariana *et al.*, 2004), dental hard tissues (Sen *et al.*, 1997; Kinirons *et al.*, 1983; Damm *et al.*, 1988) and collagen (Makihira *et al.*, 2002). While the adherence of *C. albicans* to mucosal surfaces and acrylic is the important prerequisite for the development of oral candidiasis, the attachment to dental tissues and collagen may provide *C. albicans* an opportunity to involve in the dental caries progression. Furthermore, salivary component that contains the proline-rich proteins is not only active in providing receptors for adhesion of *C. albicans* to enamel pellicles, but also can be absorbed to streptococcal surfaces and promote the adhesion of *C. albicans* (ÓSullivan *et al.*, 2000). Thus, salivary proteins may act as a ligand for the interactions between *C. albicans* and oral bacteria that may aid *C. albicans* to participate into the dental caries development. Besides, it might be necessary to note an interesting phenomenon described in the study by Sen *et al.* that *C. albicans* can detect the cracks and grooves, follow the ridges of cavity and finally penetrate into dentinal canal (Sen *et al.*, 1997). And this character of *C. albicans* may be considered as an obvious difference from that of classical cariogenic bacteria.

Since acidification that leads the demineralization of dental tissues plays the most important role in the progression of dental caries (Featherstone, 2004), the acidogenicity of microbes can be considered as one of the typical characters of caries pathogen. The mode of acid production by *C. albicans* (Klinke *et al.*, 2009) is quite different from lactobacilli in which acidogenicity is mainly based on the secretion of lactic. It is supposed that there are at least two processes that can be predicted in vivo involve in the acidification of a surrounding environment by yeast cells: 1) *C. albicans* produces several organic acids including pyruvic acid and acetate (Samaranayake *et al.*, 1986; Collins *et al.*, 1991), 2) abundant H^+

-ATPase on the plasma membrane of yeasts pumping out protons from the cell is induced by glucose and makes a contribution to the acidification (Bowman *et al.*, 1986; Manavathu *et al.*, 1999). Some studies have shown that in an environment with a pH below 5.5, which is relevant for caries formation, acidification by *Mutans streptococcus* decreases considerably and ceases around pH 4.2 (de Soet *et al.*, 1991), whereas *C. albicans* can still secrete acid at pH 4.0 (Klinke *et al.*, 2009). Furthermore, the study by Nikawa *et al.* showed that *C. albicans* was capable of dissolving the hydroxyapatite at an approximately 20-fold rate higher than *Mutans streptococcus*, despite a lower number of yeast cells in the culture (Nikawa *et al.*, 2003). These studies above may indicate *C. albicans* is capable of producing acids and demineralizing dental tissue in vivo.

In addition to the adherence to dentinal collagen, *C. albicans* can also produce an enzyme that can degrade the collagen. Kaminishi *et al.*, in 1986 (Kaminishi *et al.*, 1986) isolated one collagenolytic enzyme from *C. albicans* which was reported later by Hagihara *et al.* (Hagihara *et al.*, 1988). This enzyme can nonspecifically degrade both the cross-linked β and non-cross-linked α chains, which are components of the dentinal collagen, then the organic structure of dentine is destroyed as a result.

In summary, the mechanisms involved in the role of *C. albicans* in the process of dental caries can be concluded as follows: 1) adhesion to a variety of surfaces and interaction with other microorganisms, especially the typical cariogenic bacteria such as *Mutans streptococcus*, 2) the ability of producing organic acid that dissolve the hydroxyapatite of dental hard tissue, 3) production of an enzyme that can degrade the dentinal collagen.

Although Majjala *et al.* claimed that *C. albicans* did not invade carious dentine and the results of their study did not support the proposal that *C. albicans* plays a significant role in dentine caries pathology (Majjala *et al.*, 2007), we should not turn a blind eye to the potential cariogenic abilities of *C. Albicans* and the possible role of *C. albicans* in the dental caries progression. Meanwhile, much further studies are needed to verify the role of *C. albicans* in the progression of the dental caries.

CONCLUSION

Taking account of capabilities such as adherence to dental tissues with a high affinity, acid extrusion and collagenolytic enzyme secretion, it can be assumed that *C. albicans* may make a significant contribution in the caries process. It is noteworthy that the mechanism of its acid production is different and the ability of *C. albicans* to degrade the dentinal collagen is unique. Therefore, it is speculated that paying attention to the role of *C. albicans*

in the progression of dental caries may advance the understanding of pathology and etiology of dental caries and offer additional approaches for the prevention and therapy of dental caries.

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