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Immunoexpression of proteins involved in cytoskeleton remodeling in benign odontogenic lesions

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ABSTRACT

Objective: The present study was designed to analyze the immunolocalization of proteins involved in cytoskeleton remodeling, such as moesin and Rho-A, in benign odontogenic lesions that present with expansive growth and invasive clinical behavior.

Materials and methods: Expressions of moesin and Rho-A in odontogenic epithelium were evaluated by immunohistochemical analysis in 45 odontogenic lesions using monoclonal antibodies.

Results: Our results demonstrated strong membranous and cytoplasmic expressions of moesin in the epithelial cells in 66.7% and 44.4% of the odontogenic lesions, respectively. Furthermore, Rho-A expression in odontogenic epithelium was strong in the membrane and cytoplasm of 51.1% and 62.2% of the odontogenic lesions, respectively. A statistically significant correlation was found between the membranous and cytoplasmic expressions of moesin ($p = 0.000$) and those of Rho-A ($p = 0.048$) in odontogenic epithelial cells, while no statistically significant correlation was found between moesin and Rho-A expressions ($p > 0.05$).

Conclusions: The present study confirmed the strong expressions of moesin and Rho-A by odontogenic epithelial cells, suggesting their involvement in the development of benign odontogenic lesions. However, this study has failed to detect the connection between the moesin and Rho-A interaction in expansive growth and local invasiveness of these lesions.

1. Introduction

The proteins of the ezrin, radixin, moesin (ERM) family, which connect the plasma membrane and the cytoskeleton, have been the target in several studies for understanding their role in normal and neoplastic epithelia (Kobayashi, Sagara, & Masumoto, 2003; Martín-Villar, Megías, & Castel, 2006; Garcia et al., 2014; Assao et al., 2017).

Recent investigations have shown that members of the ERM family, especially moesin, may interact with the transmembrane proteins CD44 and podoplanin for maintaining and remodeling the cytoskeleton (Louvet-Vallée, 2000; Kobayashi et al., 2003; Maniti, Carvalho, & Picart, 2013). Thus, the frequent expression of moesin in the epithelial cells of skin and oral mucosa and in endothelial cells is associated with its role in the control of cytoskeletal processes (Kobayashi et al., 2003; Kobayashi, Sagara, & Kurita, 2004; Hirata, Nomachi, & Tohya, 2012). Furthermore, some in vitro studies showed that the activation of transmembrane proteins such as podoplanin and CD44 recruited the ERM proteins to activate intracellular signaling pathways that are triggered by GTPase Rho-A (Louvet-Vallée, 2000; Wicki & Christofori, 2007).

GTPase Rho-A, a protein belonging to the Ras superfamily, coordinates the regularization of the actin cytoskeleton through communication with the effector Rho-associated protein kinase (ROCK) (Spiering & Hodgson, 2011; O'Connor & Chen, 2013). Rho-A is present in the cytoplasm of cells and oscillates in inactive and active states; the activation occurs when the Rho-active GTP binds to the Rho-binding domain and releases its C-terminal domain, allowing interaction with moesin, thereby promoting changes in the cytoskeleton (Spiering & Hodgson, 2011; Hall 2012).

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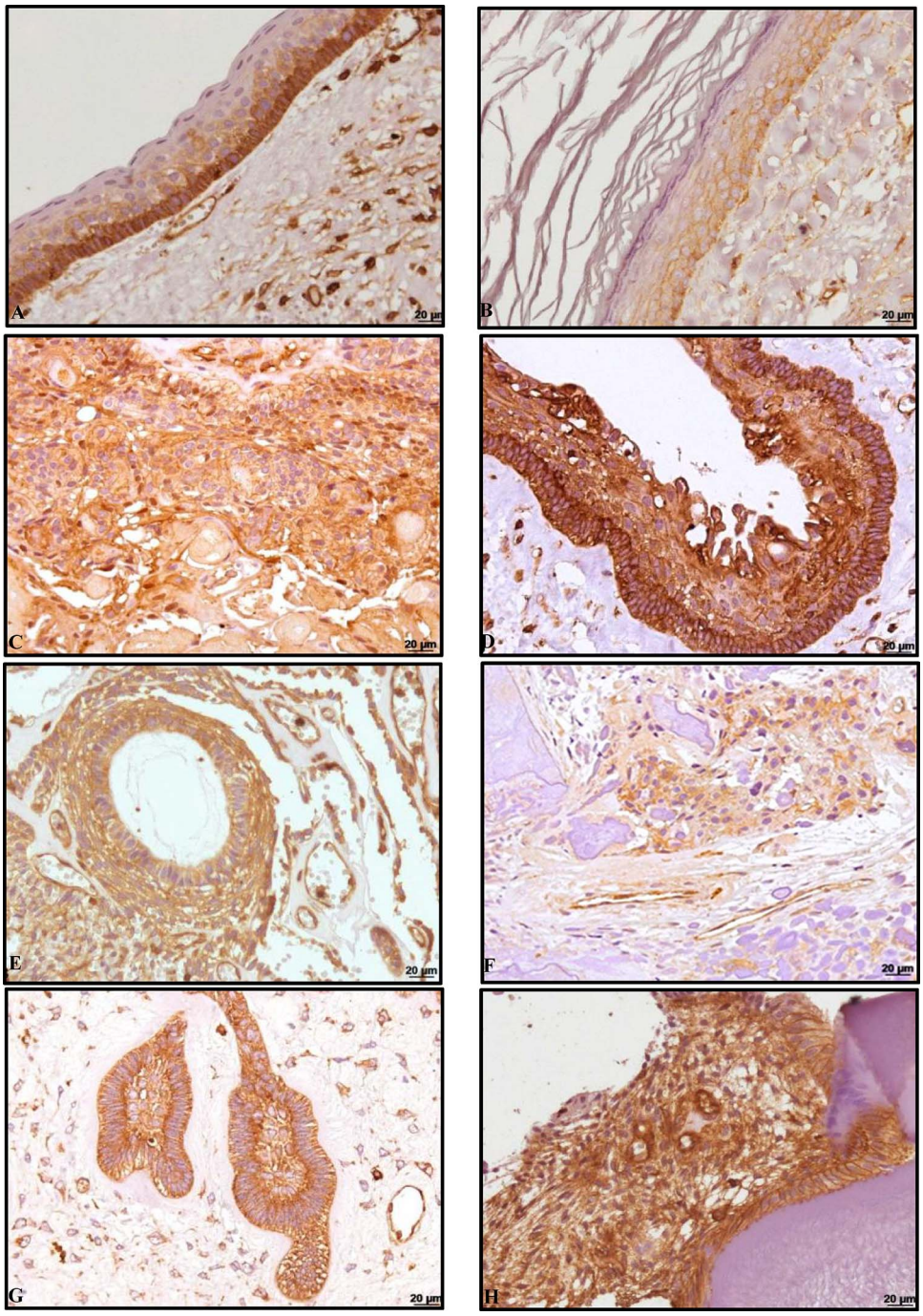

Fig. 1. Expression of moesin in benign odontogenic lesions. A – Keratocystic odontogenic cyst; B - Orthokeratinized odontogenic cyst; C - Calcifying odontogenic cyst; D - Ameloblastoma; E -Adenomatoid odontogenic tumors; F - Calcifying epithelial odontogenic tumor; G - Ameloblastic fibromas; and H - Odontomas.

In addition, moesin and Rho-A are involved in epithelial–mesenchymal transition (EMT), a morphological process characterized by dissolution of epithelial cell–cell adhesion, reorganization of the actin cytoskeleton, and increased cell matrix contacts that induce enhanced migratory and invasive capabilities (Martín-Villar et al., 2006; Haynes, Srivastava, Madson, Wittmann, & Barber, 2011). In malignant tumors, moesin is an EMT marker, and its overexpression was independently associated with poor outcome (Madan et al., 2006; Schlecht et al., 2012; Wang et al., 2012).

Considering that moesin participates with Rho-A in important signaling pathways to perform various functions of normal and neoplastic epithelial cells, the present study was designed to analyze the immunolocalization of moesin and its relationship with the Rho-A expression in benign odontogenic lesions that show expansive growth and invasive clinical behavior. To our knowledge, this is the first report that has analyzed moesin and Rho-A immunoexpressions in benign odontogenic lesions.

2. Materials and methods

This study used surgical specimens of odontogenic lesions that were obtained from the Laboratory of Pathology, Bauru School of Dentistry, University of São Paulo, between 1963 and 2009 for analysis. The lesions were selected on the basis of the following inclusion criteria: (i) patients who have been diagnosed with odontogenic cyst or tumor according to the classification of the World Health Organization (El-Naggar, Chan, Gandis, Takata, & Slootweg, 2017) and (ii) availability of the paraffin block with sufficient and representative amount of material for microscopic analysis.

The samples consisted of 45 benign odontogenic lesions: 23