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# Is maspin immunolocalization a tool to differentiate central low-grade mucoepidermoid carcinoma from glandular odontogenic cyst?

**Marilena Vered***, **Irit Allon, Amos Buchner, Dan Dayan**

*Department of Oral Pathology and Oral Medicine, School of Dental Medicine, Tel Aviv University, Tel Aviv 69978, Israel*

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## Summary

Mucoepidermoid carcinoma (MEC) of the salivary glands has a low-grade variant (LGMEC), which may be found within the jawbones. LGMEC shares a number of histopathological similarities with glandular odontogenic cysts (GOC) of the jawbones. Maspin has been identified in several benign and malignant salivary gland neoplasms. We investigated the immunolocalization of maspin in LGMEC and GOC and evaluated its potential to distinguish between these two entities. Cases of LGMEC ($n = 6$), GOC ($n = 8$) and various odontogenic cysts with marked mucous metaplasia (OCMM, $n = 7$), which served as controls, were immunohistochemically labeled for the binding of an antibody directed against maspin. Immunomorphometry was performed separately for maspin-immunopositive epithelial cells and epithelial-mucous cells in either their nuclear or cytoplasmic compartments. Results were presented as the volume fraction (Vv) of each element. The Vv of the maspin-immunopositive epithelial-mucous cytoplasm and nuclei was significantly higher in LGMEC than in GOC and OCMM ($p < 0.001$ and $p = 0.026$, respectively). In the epithelial cells, no significant differences were observed among the lesions ($p > 0.05$). It is suggested that the high levels of maspin in the epithelial-mucous cells (in both cytoplasm and nuclei) in LGMEC may serve as a tool to distinguish it from GOC. This may be useful especially in equivocal cases and in small incisional biopsy samples.


*Corresponding author. Tel.: +972 3640 9305; fax: +972 3640 9250.
*E-mail addresses:* mvered@post.tau.ac.il (M. Vered), allonirit@yahoo.com (I. Allon), buchner@post.tau.ac.il (A. Buchner), ddayan@post.tau.ac.il (D. Dayan).

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## Introduction

The odontogenic epithelium and the salivary gland epithelia share a common origin, namely, the epithelium of the stomatodeum (Ten Cate, 1994). Both begin their embryonic development as a thickening within the epithelial lining of the stomatodeum during weeks 5–6 of gestation. Although each of these epithelial types develops into completely different and highly specific functioning organs, the neoplastic cells within the various pathologic lesions derived from both the odontogenic and salivary gland epithelia may show common cytomorphological features, such as basaloid, columnar-to-cuboidal cells with a palisading appearance, clear cells and epithelial-mucous secreting cells.

A rare type of developmental odontogenic cyst, glandular odontogenic cyst (GOC), may demonstrate an aggressive biological behavior (Waldron, 2002). It is generally accepted that such a cyst has an odontogenic origin; however, it shows gland-like features reminiscent of salivary gland tumors, thus reflecting the common origin of the odontogenic and salivary gland epithelia (Ellis and Auclair, 1996; Waldron, 2002).

On rare occasions, salivary gland tumors arise centrally within the jawbones. Their origin is attributed to neoplastic transformation of odontogenic epithelium, mainly dentigerous cysts (Ellis and Auclair, 1996), or to salivary gland tissue entrapped within the jawbones dating from the embryonic development (Bouquot et al., 2000). The most common central salivary gland tumor is mucoepidermoid carcinoma (MEC) of the low-grade type (LGMEC), a malignant neoplasm, with low metastatic potential (Ellis and Auclair, 1996). Central LGMEC of the jawbones is indistinguishable in both architecture and immunohistochemical phenotype of the cells from its salivary gland counterpart (Pires et al., 2004), and has histological features that overlap with those of GOC (Ellis and Auclair, 1996; Waldron, 2002). Differentiation of LGMEC from GOC bears both treatment and prognostic implications.

Mammary serine protease inhibitor (maspin) was originally described in breast myoepithelium by Zou et al. (1994), and has since been detected in various normal glandular tissues, such as the prostate, pancreas, ovary and salivary glands, as well as in several benign and malignant types of epithelial neoplasms (Futscher et al., 2002). The tumor suppressor qualities of maspin have been reported in breast (Zou et al., 1994), prostate (Pierson et al., 2002) and oral cavity carcinoma (Xia et al., 2000; Vered et al., 2008). The inhibitory role of maspin has been described in different stages of tumor formation and progression, including degradation of basal laminae following serine protease activities, connective tissue invasion, tumor-induced angiogenesis and development of metastases (Solomon et al., 2006). Maspin is a useful prognosticator of tumor progression and patient survival, e.g., in oral and breast cancer (Sabbatini et al., 2000; Xia et al., 2000). Its presence is related to sensitization of tumor cells to apoptosis (Lockett et al., 2006).

The purpose of this study was to examine the immunohistochemical localisation of maspin in LGMEC, in comparison with GOC, and to assess its use as a marker to distinguish between these entities.

## Materials and methods

### Study cases

Cases of GOC ($n = 8$), LGMEC ($n = 6$) and various odontogenic cysts (radicular and dentigerous) with mucous metaplasia (OCMM, $n = 7$), which served as a control group, were retrieved from the archival files of the Department of Oral Pathology and Oral Medicine, School of Dental Medicine, Tel-Aviv University.

All samples were formalin-fixed and paraffin wax-embedded. Five micrometer-thick sections were cut and stained with hematoxylin and eosin, and mucicarmine (Mayer's Mucicarmine, Bio-Optica, Milano, Italy) using conventional protocols.

### Immunohistochemistry

Three micrometer-thick sections were cut and mounted on positively charged microscope slides (Optiplus™, Biogenex, San Ramon, CA, USA). These were then labelled immunohistochemically for binding of an anti-maspin antibody. After dewaxing and rehydrating by conventional methods, antigen retrieval was performed by incubating with NucleArDecloaker™, pH = 9.5 (Biocare Medical, Walnut Creek, CA, USA), in a pressure cooker for 12 min. Sections were then incubated with a mouse monoclonal primary antibody directed against maspin (EAW24, diluted 1:75, incubated overnight at 4 °C; Novocastra, Newcastle upon Tyne, UK) and binding was revealed using a Broad Spectrum Poly HRP conjugate ready-to-use kit (Zymed, San Francisco, CA, USA), employed according to manufacturer's instructions. Sections were reacted with AEC substrate-chromagen kit (Zymed, San Francisco,