Journal of Hard Tissue Biology 20[2] (2011) p125-132

CODEN-JHTBFF, ISSN 1341-7649

## Original

# Co-expression of BMP-2 and -7 in the Tumoral Epithelium of CEOT with Selective BMP-7 Expression in Amyloid Materials

**Chong H. Siar[1], Keisuke Nakano[2], Phuu P. Han[3], Mihoko Tomida[4], Hidetsugu Tsujigiwa[5], Hitoshi Nagatsuka[5], Kok H. Ng[6] and Toshiyuki Kawakami[2]**

*[1]Department of Oral Pathology, Oral Medicine and Periodontology, Faculty of Dentistry, University of Malaya, 50603 Kuala Lumpur, Malaysia*
*[2]Hard Tissue Pathology Unit, Matsumoto Dental University Graduate School of Oral Medicine, 1780 Hirooka-Gobara, Shiojiri 399-0781, Japan*
*[3]School of Dentistry, University of Southern California, 925 West 34th Street, Los Angeles, CA 90089-0641 USA*
*[4]Department of Oral Physiology, Matsumoto Dental University School of Dentistry, 1780 Hirooka-Gobara, Shiojiri 399-0781, Japan*
*[5]Department of Oral Pathology and Medicine, Graduate School of Medicine, Dentistry & Pharmaceutical Science, Okayama University, 2-5-1 Shikata-cho, Okayama 700-8525, Japan*
*[6]formerly Unit of Stomatology, Cancer Research Centre, Institute for Medical Research, Jalan Pahang, 50588 Kuala Lumpur, Malaysia*
(Accepted for publication, May 2, 2011)

Abstract: The calcifying epithelial odontogenic tumor (CEOT) is a benign but locally-invasive odontogenic neoplasm believed to take origin from the stratum intermedium of the developing tooth germ. Bone morphogenetic proteins (BMPs) are multifunctional signaling molecules that regulate diverse cellular processes including epithelial-mesenchymal interactions during odontogenesis. Aberrant BMP activity has been enumerated in the ameloblastoma but information about its distribution in the CEOT remains limited. The aim here was to investigate BMP expression in CEOT and to speculate on its significance. Immunolabelling for BMP-2 and BMP-7 was performed on archival tissues of six CEOT cases and the level of expression was quantified as negative (0), mild (+), moderate (2+) and strong (3+). Results disclosed that CEOT epithelium demonstrated co-expression of BMP-2 and -7 suggesting upregulation of these proteins at sites of tumor differentiation. Distribution patterns were distinct with some overlap. Their localizations were largely membranous and/or cytoplasmic. Amyloid-like materials strongly expressed BMP-7 but were nonreactive for BMP-2, implicating that these signaling proteins play differential roles in the formation of these extracellular products. Mineralized substances including Liesegang rings were mostly negative for both BMPs suggesting that calcification process is associated with repression of these molecules. Stromal endothelium and fibroblasts were stained variably positive. BMP was heterogeneously detected in the CEOT epithelium at the tumor advancing front suggesting their upregulation at active sites and downregulation in quiescent areas. Present findings suggest that BMP-2 and BMP-7 most likely play differential roles in the cellular differentiation and progression of CEOT. BMP-7 accumulation within amyloid-like protein is a novel finding.

Key words: Bone morphogenetic proteins (BMPs), BMP-2; BMP-7, Calcifying epithelial odontogenic tumor (CEOT), Amyloid, Liesegang rings

## Introduction

The calcifying epithelial odontogenic tumor (CEOT) is a benign but locally-invasive odontogenic neoplasm that accounts for approximately 0.4-3% of all odontogenic neoplasms[1-4]. It is unique for its tumoral growth pattern and the presence of amyloid materials that may become calcified[2]. The CEOT is believed to originate from remnants of the dental lamina or stratum intermedium of the developing tooth germ[3]. Clinically, CEOT has been reported in all age groups, peaking at age 40 years and shows an even sex distribution[2-6]. The mandible is more frequently involved than the maxilla, and the molar region is the site of predilection. Most CEOTs occur centrally in the jaws and appear as unilocular or multilocular radiolucencies with occasional radiopaque deposits or association with an unerupted tooth. Peripheral variants are rare[1]. Microscopically, the tumor is characterized by presence of sheets, strands, or discrete islands of polyhedral epithelial cells supported by a fibrous connective tissue stroma [2-4]. These tumor cells have hyperchromatic and pleomorphic nuclei. Their cytoplasm is deeply eosinophilic with well-delineated borders and prominent intercellular bridges. A clear cell variant has also been reported[4]. A distinguishing feature

Corresponding to: Dr. Toshiyuki Kawakami, PhD, Professor, Hard Tissue Pathology Unit, Matsumoto Dental University Graduate School of Oral Medicine, 1780 Hirooka-Gobara, Shiojiri 399-0781, Japan. Phone: +81-263-51-2035; Fax: +81-263-51-2035; E-mail: kawakami@po.mdu.ac.jp