

## Orthokeratinization-related factors in the oral dysplasia-squamous cell carcinoma sequences

Tatsuya Abé<sup>1</sup>, Satoshi Maruyama<sup>2</sup>, Manabu Yamazaki<sup>1</sup>, Hamzah Babkair<sup>1</sup>, Jun Cheng<sup>1</sup>, Takashi Saku<sup>1</sup>

<sup>1</sup>Divisions of Oral Pathology, Department of Tissue Regeneration and Reconstruction, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

<sup>2</sup>Oral Pathology Section, Department of Surgical Pathology, Niigata University Hospital, Niigata, Japan

**OBJECTIVE:** Keratin (K) 10-positive (+) orthokeratotic epithelial dysplasia (OKD) of the oral mucosa is one of the background conditions of oral squamous cell carcinoma (SCC). We wanted to profile keratinization-related factors in those lesions to examine how the K10+ phenotype is processed during the oral carcinogenetic pathway.

**STUDY DESIGN:** We performed immunohistochemistry in surgical materials from oral dysplasia-carcinoma sequence lesions. Oral SCC cell lines were also investigated by immunofluorescence, western blotting, and PCR.

**RESULTS:** Immunohistochemically, in addition to K10, caspase-14 and filaggrin were strongly positive in OKD, while they were not in normal to dysplastic epithelia. In differentiated carcinoma in-situ and well-differentiated SCC, caspase-14 and filaggrin were positive in keratinized areas. Caspase-14 expressions in both mRNA and protein levels were confirmed in oral SCC cell lines such as ZK-2, HSC-2, and HSC-4.

**CONCLUSIONS:** Some molecular mechanism related to orthokeratinization could be involved in the sequential oral cancerization.

