学位論文要約
Extended Summary in Lieu of the Full Text of a Doctoral Thesis

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学位論文題目：
Thesis Title　　pathobiological role of cleft palate transmembrane protein 1 family proteins in oral squamous cell carcinoma

学位論文要約：
Summary of Thesis

Purpose
Cleft palate transmembrane protein 1 (Clptm1) and its paralog protein, Cisplatin resistance-related protein 9 (CRR9) constitute a highly conserved protein family, from *Caenorhabditis elegans* to *Homo sapiens*. In the present study, we examined the clinicopathological and biological significance of Clptm1 and CRR9 expression in oral squamous cell carcinoma (OSCC).

Methods
Ninety-eight OSCC tissue specimens were immunohistochemically stained with specific antibodies to Clptm1 and CRR9. The immunoreactivity of Clptm1 and CRR9 was then correlated with clinicopathological factors, including the prognosis of patients. siRNA-mediated gene silencing of *CRR9* followed by cell proliferation, Matrigel invasion, anoikis assay, and gelatin zymography were performed using cultured OSCC cells. Subsequently, immunohistochemical examination including double staining was performed to determine the correlation between CRR9 and Bcl-xL expression in OSCC cells.

Results
Non-tumorous oral squamous cells exhibited vague, weak, or little cytoplasmic staining with anti-Clptm1 and CRR9 antibodies. By contrast, robust Clptm1 and CRR9 immunoreactivity was found at the cancer invasion front in 55 and 54 of the 98 OSCC tissue specimens, respectively. Notably, CRR9 immunoreactivity was associated with more than 5 mm of depth of invasion, poor prognosis of the patients, and smoking habits ($P < 0.05$). siRNA-mediated gene silencing of *CRR9* did not alter the cell proliferation but decreased Matrigel invasion and impaired anoikis resistance in cultured Ca9-22 and SAS cells. CRR9 and anti-apoptotic Bcl-xL expression levels were correlated in pT1 OSCC tissue specimens.

Conclusion
Clptm1 and CRR9 were overexpressed in many OSCC tissues. In particular, CRR9 expression may promote tumor development and have a significant poor prognostic value in OSCC, possibly through conferring invasion ability and resistance to apoptotic stimuli possibly related to Bcl-xL expression. CRR9 could be a novel molecular target for patients with OSCC.