lesions and squamous cell carcinomas of the oral cavity. However, no mutations were detected during oral cancer progression.

doi:10.1016/j.oos.2009.06.579

### P3.54. Modulated aberrant expression of Aurora A by osteopontin is associated with poor prognosis in oral cavity squamous cell carcinoma

C.-Y. Chien [a,*], C.-H. Chen [a], F.-M. Fang [b]

[a] *Department of Otolaryngology, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Taiwan*
[b] *Department of Radiation Oncology, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Taiwan*

**Introduction:** The explosion of microarray studies has promised to shed light on the identification of disease markers. To find novel, undefined prognostic factors, we used the expression profile of poor prognostic factor of OCSCC, *osteopontin*, a secreted protein, as a template to search for and compare transcriptome expression profiles in a OCSCC microarray database.

**Methods:** The semiquantitative RT-PCR, western blot, and IHC approaches were used to evaluate the RNA and protein expression of Aurora A in paired OCSCC patients' specimens. Immunohistochemistry analysis of Aurora A expression was assessed in 256 OCSCC patients who underwent tumor resection between 1996 and August 2005 without previous radiotherapy. Results were correlated with clinicopathologic characteristics using univariate and multivariate analyses. The correlation between OPN and Aurora A was also assessed in OCSCC specimens. The Aurora A expression level was explored in human oral cancer cell lines by OPN stimulating.

**Results:** Among these syn-expression candidate targets, *Aurora A* (*STK6/STK15*) is identified as one of the correlated genes (Pearson's correlation coefficient = 0.62, $p = 0.001$). Here, we showed that the mRNA and protein levels of Aurora A were significantly overexpressed in OCSCC compared to adjacent non-cancerous tissues and normal oral mucosa by semiquantitative RT-PCR, western blot and IHC. The cumulative 5-year survival rate was significantly correlated with a relatively advanced tumor stage, positive nodal status, TNM stage, and strong expression of Aurora A. Thus, elevated Aurora A expression is an indicator of poor survival. From semiquantitative RT-PCR, western blot and IHC staining data, OPN and Aurora A exhibit highly positive correlations in OCSCC specimens. Moreover, stimulation of oral cancer cells with OPN results in an increase in Aurora A protein expression.

**Discussion:** These finding suggest that Aurora A are not only an important prognostic factor but also a new therapeutic target in the OPN/Aurora A pathway for OCSCC treatment.

doi:10.1016/j.oos.2009.06.580

### P3.55. Genetic polymorphisms and risk of oral cancer

L.P. Karen-Ng [a], Z.A.A. Rahman [b,*], S. Hamid [c], M.T. Abraham [d], I.A. Razak [a], R.J. Raja-Latifah [a]

[a] *Oral Cancer Research and Coordinating Centre (OCRCC), University of Malaya, Malaysia*
[b] *Department of Oral Maxillofacial Surgery, Faculty of Dentistry, University of Malaya, Malaysia*
[c] *Cancer Research Initiatives Foundation (CARIF), Subang Jaya, Selangor, Malaysia*
[d] *Oral Maxillofacial Surgery Unit, Hospital Tengku Ampuan Rahimah, Klang, Ministry of Health, Malaysia*

Oral cancer is considered a multifactorial disease where multiple exposures interact with the individual genetic background resulting in risk modulation. Genetic polymorphisms of carcinogen-metabolizing enzyme genes have been associated with the risk of oral cancer.

This study was done to investigate the role of single nucleotide polymorphisms (SNPs) within genes of phase I (CYP1A1) and phase II of the xenobiotic metabolism (GSTM1, GSTT1, GSTP1) and its association with oral cancer risk.

An unmatched case–control study was conducted using 207 newly diagnosed oral cancer patients and 116 non-cancer subjects selected from the OCRCC database. Peripheral blood was obtained from consented individuals and the CYP1A1, GSTM1, GSTT1 and GSTP1 genotypes were determined using polymerase chain reaction (PCR) and restriction enzyme digestion (RFLP). Simple and multiple logistic regression yielding odds ratio (OR and aOR) were employed to measure the association between genetic polymorphisms and risk of oral cancer.

In comparing cases and controls for CYP1A1 polymorphism, the OR was 0.843 (95% CI 0.534–1.330) while the OR for GSTM1 null genotype relative to GSTM1 non-null was 0.987 (95% CI 0.627–1.554). The OR for GSTT1 null genotype was 0.866 (95% CI 0.541–1.388) relative to GSTT1 non-null genotype. The OR for GSTP1 polymorphism genotype, as compared to the wild-type genotype, was 0.680 (95% CI 0.397–1.164). Although all OR values of CYP1A1 and GSTs polymorphisms indicated reduced risk against oral cancer risk, neither CYP1A1, GSTM1 or GSTT1 null nor GSTP1 polymorphisms genotype was revealed as significantly associated with oral cancer risk.

Analysis showed a lack of evidence to support the association between the genetic polymorphisms of CYP1A1, GSTM1, GSTT1 and GSTP1 and risk of oral cancer.

doi:10.1016/j.oos.2009.06.581

### P3.56. CYP1A1, GSTM1 and GSTT1 polymorphisms and oral cancer – Correlation with patients' status at 2-year, age of onset, nodal status, tumor size and stage

M.T. Abraham [a,*], L.P. Karen-Ng [b], W.M.N. Ghani [b], R.B. Zain [b], R.J. Raja-Latifah [b], S.C. Cheong [c]

[a] *Oral Maxillofacial Surgery Unit, Hospital Tengku Ampuan Rahimah, Klang, Ministry of Health, Malaysia*
[b] *Oral Cancer Research and Coordinating Centre (OCRCC), University of Malaya, Malaysia*
[c] *Cancer Research Initiatives Foundation (CARIF), Subang Jaya, Selangor, Malaysia*

Altered expression of xenobiotic enzymes such as CYP1A1, GSTM1 and GSTT1 has been reported in some malignant tumors including oral cancer. However, the correlation between these enzymes and clinicopathologic parameters has not been well documented. The aim of this study was to investigate the associations between CYP1A1, GSTM1 and GSTT1 polymorphisms with patients' status at 2-year, age of onset, nodal status, tumor size and disease stage. A total of 195 oral cancer patients were included in this study. Peripheral blood was obtained from consented individuals and CYP1A1, GSTM1 and GSTT1 genotypes were determined using PCR and restriction enzyme digestion. Chi-square test and simple logistic regression yielding odds ratio (OR) was employed for comparison of all parameters except for age of onset where *t*-test was used. Patients with GSTM1/GSTT1 polymorphism were associated with almost triple increased risk of mortality at 2-year after the first being diagnosed (OR 2.79, 95% CI 1.22–6.36). Mean age of onset

was higher in those with GSTT1 null (60.82 ± 10.61 years) and GSTM1/GSTT1 polymorphism genotype (59.48 ± 11.30 years) compared to lower mean age of onset for those with GSTT1 non-null (58.15 ± 11.97 years) and GSTM1/GSTT1 wild-type genotype and these observations were not significant. There was also no significant difference between CYP1A1 and GSTM1 polymorphisms and age of onset. Positive nodes are associated with high CYP1A1 polymorphism, GSTM1 null and GSTM1/GSTT1 polymorphism (59.7%, 56.5% and 72.6%, respectively) and low GSTT1 null (29.0%). For tumor size of more than 2 cm, there was higher percentage of GSTT1 null genotype (92.7%) as compared to those with tumor size of less than 2 cm ($p = 0.035$). Polymorphisms of all three genes were higher in late stage compared to early stage disease. However, statistically, these observations were not significant. In conclusion, no association was observed between CYP1A1 and GSTM1 polymorphisms and all clinicopathologic parameters studied. This study also showed that for GSTM1/GSTT1 and GSTT1 polymorphisms, association was seen with patients' status at 2-year and tumor size respectively, indicating that the GST genotypes may be important indicators for the patients' status and tumor size in oral cancer.

doi:10.1016/j.oos.2009.06.582

### P3.57. Vascular endothelial growth factor-C and lymphatic marker expressions in oral cancer

A.S. Almeida [a,*], S.E.S. Faustino [a], S. Nonogaki [b], G. Landman [c], L.P. Kowalski [c], D.T. Olveira [a]

[a] *University of São Paulo – Bauru Dentistry School, Brazil*
[b] *Adolfo Lutz Institute, Brazil*
[c] *AC Camargo Cancer Hospital, Brazil*

The purpose of this study was to evaluate the clinical significance of VEGF-C and podoplanin expression in 42 well-differentiated oral squamous cell carcinomas (OSCC), with and without lymph node involvement, including eight verrucous carcinoma, treated at the Department of the Head and Neck Surgery and Otorhinolaryngology, AC. Camargo Cancer Hospital, São Paulo, from 1980 to 2000. Patients were evaluated according the demographic, clinical and microscopic parameters. In addition, we investigated the histopathological malignancy index and the immunohistochemistry expression of VEGF-C and podoplanin by malignant cells in the invasive front tumor. Chi-square test or Fisher's exact test was used to analyze the association of VEGF-C and podoplanin with the variables above in OSCC patients. The 5 and 10-year survival rates were calculated by Kaplan–Meier method. Most of OSCC, including verrucous carcinoma, showed a high expression of VEGF-C by malignant cells. The OSCC patients with high expression of VEGF-C showed a tendency, without statistical significance, of local and/or regional recurrence. The overexpression of podoplanin was significantly associated with the male gender ($p = 0{,}037$), with T1 and T2 stage ($p = 0{,}037$), with I and II clinical stage ($p = 0{,}027$) and with the presence of glandular infiltration ($p = 0{,}003$). The local and regional recurrences were detected more frequently in OSCC with high expression of podoplanin, without statistical significant difference. The overall survival rates and cancer specific survival rates for OSCC patients with high VEGF-C expression and the overall survival rate for OSCC patients with podoplanin overexpression were lower than those of OSCC patients with low expression of these proteins. The cervical lymph node involvement was significant prognostic factor ($p = 0{,}001$) for patients with oral cancer. These results suggest that the overexpression of VEGF-C and podoplanin by malignant cells and regional lymph node involvement are indicative factors of an unfavorable clinical outcome and poor prognosis for patients OSCC.

doi:10.1016/j.oos.2009.06.583

### P3.58. The expression of e-cadherin, cd44, and p53 in lip carcinoma with positive neck metastasis

A. Ntomouchtsis *, C. Tsompanidou, K. Papzisis, D. Mangoudi, K. Vahtsevanos, K. Antoniades

*Theagenio Cancer Hospital Thessaloniki, Greece*
*Aristoteles University of Thessaloniki, Greece*

**Introduction:** Lip carcinoma is one of the most common malignant tumor in oral and maxillofacial region. In advanced stages with regional metastasis it has a poor prognosis. E-cadherin and CD 44 molecules play a role in cell-to-cell adhesion; p53 is associated with cellular proliferation and cell death.

**Methods:** To determine the expression of the E-cadherin, CD44, and p53, and to establish their prognostic value and their clinical significance in the lip carcinoma. Immunohistochemical study of the E-cadherin, CD44, and p53 proteins in 33 lip squamous cell carcinoma, that were presented from the beginning with regional neck metastasis or they presented positive lymph notes after the surgical intervention of the primary lesion, over a period of 10 years. The data obtained were subjected to uni- and multi-variate statistical analyses. There were included only patients with a follow up over 5 years.

**Results:** Only 26 of the 33 cases with lip carcinoma provided enough data to be evaluated. Immunostaining for CD44 was positive in 11 cases (42.31%), with more intense positivity in low histological grade tumors. Positivity of E-cadherin was noticed in only one case of the lip carcinomas (3.85%). In the 26 cases only 9 expressed the p53 protein (34.62%). The expression of p53 was stronger in high histological grade carcinomas and in tumors with high maximal thickness.

**Conclusions:** Since all our patients had a poor prognosis, it seems that decreased E-cadherin and CD 44 expression and over expression of p53 in cancerous tissue correlates with this outcome in lip carcinoma patients. Detection of the expression of these proteins is useful to confirm the risk for cervical lymph node metastasis; further studies are encouraged to reveal the detail mechanisms in formation of lymph node metastatic focus.

doi:10.1016/j.oos.2009.06.584

### P3.59. Significant differences in p63,and Ki67 expression in oral dysplasia from patients with or without oral squamous cell carcinoma: A retrospective longitudinal study

R. Czerninski [a,*], M. Granit [a], I. Kaplan [b]

[a] *Hebrew University, Hadassah School of Dental Medivcine, Israel*
[b] *Institute of Pathology, Rabin Medical Center and Sackler School of Medicine, Tel-Aviv University, Israel*

**Background:** Prediction of transformation of oral dysplastic lesions to carcinoma is currently impossible. Recent studies have shown that clinical and microscopic findings in oral dysplasia and oral squamous cell carcinoma (OSCC) are associated with a wide array of changes in molecular markers including p63, p53, p16 (tumor suppressor genes) and Ki67 (proliferation marker).

**Aim:** To compare p16, p63, p53 and Ki67 expression levels in oral dysplastic lesions between patients with and without a history of transformation to OSCC.

**Methods:** Sixty-five archival formalin fixed, paraffin embedded samples of dysplasia and OSCC from 30 patients with multiple oral lesions were submitted for immunohistochemistry for ki67, p53,