308 Proffered Papers

invasion (P=0.013); greater cytoplasmatic expression was revealed with a univariate analysis in the female gender (P=0.0025); with the presence of extra-thyroid extension (P=0.037), perineural invasion (P=0.012) and multicentric tumors (P=0.005); 3) the greatest cytoplasmatic expression was associated to the greater Ki-67 expression and to the 3 compartments with the greater caspase-3 expression. In conclusion, it was shown the possible application of the galectin-3 as a tumor marker in well differentiated thyroid carcinoma and nucleolus expression, as an indicator of its metastasis potential.

1067 POSTER

Angiogenesis as an indicator of metastatic potential in papillary thyroid carcinoma

E. Stabenow¹, A. Ab'Saber², E. Parra-Cuentas², L. <u>de Matos³</u>, E. Eher², M. Tavares¹, V. Capelozzi², A. Ferraz¹. ¹Hospital das Clinicas –School of Medicine – University of Sao Paulo, Head and Neck Surgery, Sao Paulo, Brazil; ²Hospital das Clinicas – School of Medicine – University of Sao Paulo, Pathology, Sao Paulo, Brazil; ³School of Medicine – ABC's Foundation, Santo Andre, Brazil

Background: Angiogenesis is new blood vessel formation, a process that can lead to tumor development. Microvessel count has been correlated to metastasis in some neoplasias.

Purpose: To determine if measurement of microvessel density is useful in predicting metastasis to the cervical lymph node and prognosis in patients with papillary thyroid carcinoma.

Methods: A retrospective analysis was performed in 30 patients that had undergone total thyroidectomy. They were divided in 2 groups of 15 patients – with and without metastatic disease. Immunohistochemistry was used to detect expression of CD34 in archival paraffin-embedded papillary thyroid tumors, and microvessel density was calculated based on it. Association between microvessel density and the presence of metastasis, according to histological subtype, disease recurrence, and AMES prognostic index groups was determined through statistical analysis. Results: The median microvessel density for the patient group without metastasis (200.0 microvessels/mm²) was apparently, but not significantly, less than that observed among metastatic disease patients (254.4 microvessels/mm 2) (P = 0.20). When papillary carcinoma subtypes were analyzed, this difference became significant (P = 0.02): the follicular variant exhibited a greater microvessel density than the other subtypes, independent of metastasis presence. There was an apparent, but not significant, tendency for a larger median microvessel density in the group of patients that presented recurrence (294.4 microvessels/mm2 vs 249.6 microvessels/mm², P = 0.11). There was no relationship between risk level and microvessel density: in the low- and high-risk groups, the median MVD was 304.0 microvessels/mm² and 229.6 microvessels/mm², respectively (P = 0.27).

Conclusions: The results suggest that angiogenesis is more intense among metastatic tumors in the classic and the tall cell variants, indicating that microvessel count can be an indicator of the potential for metastasis in these subtypes of papillary thyroid carcinoma. Patients that developed recurrent disease had a tendency to exhibit higher angiogenesis; however, there was no association between microvessel density and the AMES prognostic index.

1068 POSTER

Human papillomavirus types in head and neck cancer: an analysis of patients with unresectable head and neck squamous cell carcinomas (HNSCC) treated with curative radiochemotherapy (RCT)

K. Lindel¹, E. de Villiers², A. Dietz³, F.X. Bosch⁴, B. Helmke⁵, K.J. Weber¹, J. Debus¹. ¹Universitiy of Heidelberg, Dept. of Radiation Oncology/Radiotherapy, Heidelberg, Germany; ²DKFZ, Division of Tumorvirus Characterisation, Heidelberg, Germany; ³Universitiy of Leipzig, Clinic of Rhino-otolaryngology and Head and Neck Surgery, Leipzig, Germany; ⁴University of Heidelberg, Clinic of Rhino-otolaryngology and Head and Neck Surgery, Heidelberg, Germany; ⁵Universitiy of Heidelberg, Institute of Pathology, Heidelberg, Germany

Intoduction: Over the past 15 years, human papillomavirus (HPV), the necessary cause of cancer of the cervix, has also been etiologically linked with a subset of HNSCC. The true prevalence of HPV and its influence on clinical outcome remain uncertain. Highly sensitive detection techniques, such as nested polymerase chain reaction (PCR) identified HPV DNA in a substantial proportion (30%-50%) of nonmelanoma skin cancer. Cutaneous HPV types might play a role in head and neck cancer but clinical data are missing.

Purpose: This study was performed to evaluate retrospectively HPV prevalence, genotypes and influence on clinical outcome in a subset of

patients with unresectable HNSCC treated with RCT in a multicenter randomized German trial at the University Hospital of Heidelberg, Germany. **Methods:** Thirty-six paraffin embedded biopsies of patients treated with curative RCT (total RT-dose 69.9, 600 mg/m²/dy 5-FU; 70 mg/m² carboplatin days 1–5 and 29–33) were analysed with single-phase primers FAP 69/64 and CP 65/70 and a nested PCR of FAP and CP to detect the majority of cutaneous and mucosal HPV types. The experimental findings were correlated with overall survival (OS), progression-free survival (PFS), distant metastases-free survival (DMFS).

Results: Ten out of 36 tumors were positive for high risk cutaneous HPV-types(1 ct HPV 5, 3 HPV 8, 4 ct HPV 9, 1 HPV 20, 2 ct HPV 48, 2 ct HPV 50, 2 HPV 76, HPV 79) Seven biopsies showed multiple HPV-DNA. HPV-infection was independent of tumor site (oropharynx versus hypopharynx) Kaplan-Meier survival estimates showed no difference in OS, PFS and DMFS between patients with HPV positive compared to negative tumors. Conclusion: The role of cutaneous HPV in oncogenetic processes is not yet clarified, but they might also play a role in HNSCC. In contrary to our previous data which demonstrated HPV 16 positive HNSCC have a better prognosis than HPV negative tumors, there seems to be no evidence of a positive influence on clinical outcome or preferred tumor localization for tumors positive for cutaneous HPV.

1069 POSTER

Loss of heterozygosity on chromosomes 2q21 and 19p13.2 in oxyphilic thyroid cancers

K. Stankov^{1,2}, A. Pastore², L. Toschi², J. McKay³, F. Lesueur⁴, J.L. Kraimps⁵, D. Bonneau⁶, M. Volante⁷, M. Papotti⁸, G. Romeo².

¹ Clinical center Novi Sad, Biochemistry, Novi Sad, Serbia; ² University of Bologna Medical School, Medical Genetics, Bologna, Italy; ³IARC, Genome Analysis Group, Lyon, France; ⁴ Centre National de Genotypage, Evry, France; ⁵ Jean Bernard Hospital, Endocrine Surgery, Poitiers, France; ⁶ Centre Hospitalier Universitaire d'Angers, Génétique Médicale, Angers, France; ⁷ University of Turin, Biomedical Sciences and Oncology, Torino, Italy; ⁸ San Luigi Hospital Orbassano, Torino, Italy

Hürthle thyroid tumors are characterized by frequent numerical chromosomal aberrations, including aneuploidy or polyploidy, losses and gains of some chromosomal regions and DNA fragmentation. In recent years great attention has been paid to the combined analysis of morphological and genetic features of oxyphilic tumors and to the elucidation of their pathogenesis. We analyzed for loss of heterozygosity (LOH) of the candidate regions for TCO (Thyroid Tumor with Cell Oxyphilia) and NMTC1 (Non-Medullary Thyroid Carcinoma 1), two loci already mapped on chromosomes 19p13.2 and 2q21 respectively. Matched normal and tumor DNA samples from 70 patients with sporadic oxyphilic thyroid tumors and 20 with sporadic follicular tumors were subjected to microsatellite analysis using 10 markers on 19p13.2 and 6 markers on 2g21. This approach led us to the observation of a more significant LOH in oxyphilic than in follicular tumors. Allelic loss in tumor samples was evenly distributed in both 19p13.2 and 2q21 regions, in accordance with the established linkage of TCO and NMTC1 for inherited tumors. In order to investigate the possible contribution of both susceptibility loci in oxyphilic tumors, the family which led to the original mapping of TCO locus was reanalyzed for the markers in the 2q21 region. This led to the exclusion of linkage with the NMTC1 locus and to the refutation of the digenic inheritance hypothesis at least in this family.

1070 POSTER
Cimetidine: a lethal weapon against malignant salivary gland tumor?

M. Fukuda¹, M. Ishikawa¹, N. Suka¹, Y. Horiuchi¹, K. Kusama², H. Sakashita¹. ¹Meikai University, Second Department of Oral and Maxillofacial Surger, Sakado, Saitama, Japan; ²Meikai University, Department of Oral Pathology, Sakado, Saitama, Japan

Background: It has been reported that cimetidine inhibits the growth of glandular tumor such as colorectal cancer, however, the effect of cimetidine against salivary gland tumor is still unknown. We demonstrated previously that human salivary gland tumor (HSG) cells spontaneously express neural cell adhesion molecule (NCAM) and that the proliferative activity of HSG cells could be controlled via homophilic binding mechanism. In the present study, we investigated whether cimetidine could prevent the growth of HSG cells

Materials and methods: The HSG cell line, derived from a human submandibular salivary gland, was established by Shirasuna et al. and three human oral squamous cell carcinoma cell lines, HSC-2, 3 and Ca9-22 were respectively maintained in 25 cm² culture flasks at 37°C in a humidified 5% CO2 incubator until required. Northern-blot, Western-blot analysis and MTT assay were performed. Morphological observation of