Conclusion: Supernatants of tumors primary culture of and serum of gastric cancer patients can stimulate the endothelium proliferation *in vitro*. PI correlated with TNF-α concentration. Serum stimulation showed the correlation between PI and pathomorphological features of tumors.

410 POSTER

Overexpression of angiogenic growth factors, VEGF, PDGF, and bFGF in head and neck squamous cell carcinoma in the betel quid chewing prevalent area

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Purpose: Head and neck squamous cell carcinoma (HNSCC), including cancers of the pharynx, larynx and oral cavity (ICD 140-149, except 147), is one of the ten most frequent cancers in the world. Angiogenic growth factors have been found associated with the aggressiveness of HNSCC. In this study, we evaluated the level of angiogenic growth factors, VEGF, PDGF and bFGF in paired normal and cancerous tissues from HNSCC patients to assess the association of these factors with clinical characteristics of the tumors.

Methods: A reverse transcription-quantitative PCR method was used to measure mRNA levels of VEGF, PDGF, bFGF in 112 paired (normal and cancerous) tissues from HNSCC patients. Clinical information was available for all patients. Analysis for correlation of these factors with clinical and histopathological parameters was done using the Pearson Chi-square test.

Results: Two-fold over-expression of VEGF, PDGF and bFGF were found 65%, 60% and 60% in the matched tumor tissue samples. Levels of VEGF and bFGF have clinical correlation with tumor differentiation ($P \approx 0.022$ and 0.05, respectively). Levels of these growth factors with other clinical and histopathological parameters were less associated.

Conclusion: Over-expression of angiogenic growth factors VEGF, bFGF, and PDGF were commonly found in head and neck cancer. This information may be further applied in clinical applications of diagnosis or therapeutics.

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Inhibitory effect of sulindac and sulindac sulfone (Exisulind)on tumour growth and angiogenesis

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Inhibition of tumour angiogenesis presents new method for cancer therapy in combination with conventional treatment.The aim of our study was to evaluate the effect of NSAID sulindac and its derivative EXISULIND, which lacks ant-COX activity, on: a) tumour-induced angiogenesis(TIA)test, which shows the earliest stage of angiogenic response, recruitment of endothelial cells from non-tumour vessels, similar to the process of metastases vascularisation, b) production of angiogenic growth factors in in vitro cultures of human cancer cells, c) growth of L-1 sarcoma tumour in syngeneic mice and its haemoglobin(Hb) content.

Results: Sulindac and EXISULIND suppressed mice skin cutaneous TIA induced by human lung, ovary, kidney and urinary bladder cells, suppressed bFGF production in lung and kidney cancer cell cultures, have delayed and diminished growth of L-1 sarcoma tumours.Hb content of tumours was lowered by EXISULIND only.

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Angiopoietins and the carcinogenesis of renal cell carcinoma (RCC)

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Introduction: Renal cell carcinoma (RCC) is the most common cancer developing in the kidney. Angiogenesis, the sprouting of preexisting capillaries is essential for tumor growth and progression. Angiogenesis is regulated by an orchestra of different angiogenic mediators. Angiopoietins are important regulators of angiogenesis. The angiopoietins 1 and 4 are active as maturation factors of the vascular wall, while angiopoietin 2 and 3 activity desintegrates the vascular wall and therefore leads to the initiation of vascular sprouting. In this study the role of the angiopoietins in the carcinogenesis and progression of RCC was investigated.

Methods: By RT-PCR we investigated the expression of the angiopoietins 1 to 4 in five different RCC cell lines, in human endothelial cells, in human fibroblasts and in tumor samples of 15 patients with RCC.

Results: None of the RCC cell lines produced any of the angiopoietins. Human endothelial cell produced the angiopoietins-2, -3 and -4. Human fibroblasts produced angiopoietin-1. Three of the tumor samples from patients with RCC produced angiopoietin-2. None of the tumor samples expressed any of the other angiopoietins.

Discussion: RCC cell lines did not produce any of the investigated angiopoietins. Based on these results we assume that angiopoietin-2 expressed in human RCC derives from tumor endothelium. However, the expression of angiopoietin-2 by tumor endothelium seemed to be downregulated in the majority of cases. Furthermore, expression of angiopoietin-1 by tumor infiltrating fibroblasts and expression of angiopoietin-3 and -4 by tumor endothelium was down regulated in all tumor samples investigated. Therefore we hypothesize that the down regulation of angiopoietins is an important step in the carcinogenesis of the majority of renal cell carcinomas. The co-expression of vegf and the tie-2 receptor is currently under investigation in our laboratory.

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Intratumoral vessels and proliferative index in lung adenocarcinoma

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Goal: To research and explore the intratumotal vessels, to examine the connection beteen tumor vascularization and proliferative index, as well as the expression of some biological markers.

Methods: Tissue sections from resected tumor specimens from 20 patients with lung adenocarcinomas are examined immunohistochemically for CD31,Ki-67(MIB-1), p53 and Synaptophysin. Diagnoses were confirmed by HE,PAS,Alcian blue.

Results: Out of 20 adenocarcinomas 12 were highly differentiated (7 with mixed subtypes,3 papillary and 2 acinar),2 were moderately differentiated and 6-low-differentiated solid adenocarcinomas. Availability of intratumoral microvasculature was confirmed immunohistologically by CD31 expression in all cases. For the highly differentiated adenocarcinomas networks of interconected angiogenic vessels were found, distributed in the tumor stroma around the acinar structures, in papillary axis and/or along the alveolar walls. In these cases all intratumoral vessels consist of and are covered by endothelial cells. In 3 low-differentiated adenocarcinomas with solid structures, thin-wall vessels were found, for which, in part of their wall, no endothelial cells were identified immunohistochemically. In these cases, tumor cell of adenocarcinoma exist as a vessel wall. Such vessels of microvasculature, for which there is no endothelial cell lining in part of their wall, and tumor cell perform the function of a vessel wall in this part of vessels wall, are found among tumor cells in solid adenocarcinoma. The proliferative index in 6 low-differentiated adenocarcinomas is higher than 50%, these tumors also express in a large extent the p53-from 45% to 95% of tumor cells population. Neuroendocrine divergent differentiation was established in 7 adenocarcinomas-4 highly differentiated and 3 low-differentiated adenocarcinomas.

Conclusion: Intratumoral vessels in highly differenriated adenocarcinomas are built of and covered by endothelial cells.In low-differentiated solid adenocarcinomas thin-wall intratumoral vessels of the microvasculature are found, in part of their wall there is a lack of endothelial cells, and tumor cells perform the function of vessel wall.The proliferative index in this low-differentiated adenocarcinomas is higher than 50%.