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ACTIVITY OF CATHEPSIN D IN NON SMALL CELL LUNG CANCER

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The aim of the present study was to evaluate the cathepsin D activity in NSCLC depending to the morphologic pattern and stage of the disease. The material for examinations was obtained intraoperative from patients with lung carcinoma (35 men and 4 women, aged between 40-70 years). The activity of cathepsin D was assayed in supernatants and sediments of tissues homogenates obtained by the centrifuge, using the denaturated hemoglobin. The enzyme activity was evaluated on the ground of the amount of liberated tyrosine assayed by the method of Folin and Ciocalteau. The protein level was determind by the method of Lowry. The activity of cathepsin D in supernantants and sediments of neoplastic tumors as well as of lung tissue surrounding a tumor was significantly higher than the enzyme activity in nonmalignant lung diseases (tuberculoma, emphysema) /p<0.05/. The supernatant of lung cancer reveals the activity of cathepsin D: 102.35 ± 23.2Tyr nM/g protein for macrocellular carcinoma, 74.3 ± 14.3Tyr nM/g protein for planoepithelial carcinoma, 65.43 ± 38.8Tyr nM/g protein for adenocarcinoma. The sediment of lung cancer reveals the activity of cathepsin D : 38.86 ± 15.8 Tyr nM/g protein for macrocellular carcinoma, 33.3 ± 10.6 Tyr nM/g protein for adenocarcinoma and 20.76 ± 9.8 Tyr nM/g protein for planoepithelial carcinoma. Increasing activity of the enzyme was not depend on the stage of the disease. The study suggests that activity of cathepsin D in lung cancer tissue depend on the degree of tumor differentiation.

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PACLITAXEL/CISPLATIN IN STAGE IIIB/IV NON-SMALL-CELL LUNG CANCER

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Paclitaxel (Taxol®) as single agent has shown promising activity in advanced non-small-cell lung cancer (NSCLC). In our phase II trial, we have determined the efficacy of paclitaxel combined with cisplatin. Inclusion criteria were good performance status, adequate renal as well as bone marrow function and no prior chemotherapy. Patients with signs of severe cardiac or hepatic dysfunction, pregnancy, clinical manifest neuropathy or manifest cerebral metastasis were excluded. Twenty patients with histologically proven NSCLC stage IIIB or IV were treated with paclitaxel (175 mg/m^2) as 3-hour infusion after standard premedication on day 1 and cisplatin (50 mg/m^2 daily) on days 1 and 2 with antiemetic therapy and sufficient pre- and posthydration. Treatment cycles were repeated every 3 weeks. Progressive disease resulted in discontinuation of treatment. All 20 patients were evaluable for response and toxic effects. Partial responses were seen in 7 patients (35%), no change in 9 patients (45%) and progressive disease in 4 patients (20%). Major side effects included leukopenia (WHO Grade 4 in 1 patient), anemia, alopecia and dose-limiting neurotoxicity (WHO Grade 3 in 1 patient). No severe hypersensitivity reaction has been observed. Thus paclitaxel/cisplatin has shown good antitumor activity in patients with advanced NSCLC and should be further evaluated in this disease.

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PREVENTIVE ONCOLOGY AND NICOTINE ADDICTION: A HYPOTHESIS

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Nicotine dependence is important for preventive oncology, which is to be demonstrated by using the lung cancer model. High tar exposure is very much related to lung cancer risk. A mathematical model was developed in order to demonstrate the dose response relationship between tar exposure and lung cancer risk (Kunze, Vutuc; 1980). There is another relationship between lung cancer risk and nicotine dependence. Representative data on the epidemiology of nicotine dependence for Austria show a medium to very high nicotine dependence for 36% of the population, 64% had a modest dependence (using the Fagerström Test for Nicotine Dependence). First results from a field study with lung cancer patients indicate a high proportion of heavy dependent smokers in that group. This study will be the first of its kind to show a relationship between nicotine dependence and lung cancer risk.

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PARAMETERS OF IMMUNOLOGICAL RESPONSE IN LUNG CANCER PATIENTS.

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24 patients with lung cancer were enrolled into this study. They were divided into groups according to hystological diagnosis, stage of disease and performance status.
Parameters of acute phase response (CRP, AGP, ACT, profile of glicosilation of AGP & ACT) and cellular response (lymphocytes T, subpopulations CD4 & CD8, Il-2R+, HLA-DR antigen, T4/T8 rate) were examined in the blood of the patients.
The number of patients in each studied group was too small to conduct the precise statistical analysis. The preliminary results suggest as follows:
1. Parameters of inflamatory response in patients in extensive stage of SCLC are higher than in patients with limited stage of SCLC.
2. Antychymotripsin concentration is higher in patients with advanced disease and worst performance status.
3. There are more lymphocytes with Il-2 receptor in the blood of patients in extensive stage of SCLC and more lymphocytes with HLA-DR in those with limited stage.
4. In patients with NSCLC: the higher stage of disease is, the higher the parameters of acute phase response are.
The study is continued.

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THE ROLE OF VATS (VIDEOTHORACOSCOPY) IN THE STAGING OF LUNG CANCER.

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Having been almost accepted universally the use of the neoadjuvant therapy in the treatment of the lung cancer at stadium 3 N2 positive, we think the use of VATS is necessary for an exacter pre-operative staging that aims at recognizing a larger and larger number of patients to start at a neoadjuvant therapy and to avoid exploratory thoracotomy. In fact VATS permits the evaluation of lymph nodes not accessible at mediastinoscopy and allows the biopsy of both the visceral and parietal pleural surfaces and pulmonary parenchymal lesions. It sometimes delineates lesions that aren't visible at CT scanning.
Since 1993 in the 1 st. Department of General Surgery, we have considered necessary the use of VATS for some patients that seem to be risky after CT. No morbidity or mortality has been noted. Opposite the other examinations VATS is more aggresive (one lung ventilation and position of patient) and permits sometimes after a completed staging the excution of a definitive surgical treatment. Considering that a better treatment follows a increase in survival, we hope that VATS will became an standard technique for the evaluation and treatment of lung cancer.

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THE ROLE OF BASIC FIBROBLAST GROWTH FACTOR (bFGF) IN HUMAN NON SMALL CELL LUNG CANCER (NSCLC).

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The expression of bFGF was investigated in human NSCLC lines of primary and metastatic origin. In 8 of 10 cell lines bFGF was detected in cytoplasm by immunocytochemistry. In cytosol preparations levels ranging from 377 to 1299 pg/mg protein were found by ELISA. Western blot analysis confirmed the presence of 18, 21 and 28 kDa bFGF isoforms in cell extracts. Specific mRNA for bFGF was demonstrated in 8/10 NSCLC cell lines by Northern blotting and RT-PCR. To investigate the potential role of bFGF as autocrine growth factor in NSCLC, cell lines were incubated with agents - Suramin 1-1000µg/ml, Pentosanpolysulfate (PPS) 1-1000µg/ml, oligonucleotides bFGF-AS, -S, NS 1-5µM - that are interfering with bFGF activity and expression. Cell proliferation was significantly inhibited by Suramin but not by PPS or oligonucleotides-AS. Furthermore, Heparin-Sepharose fractions of NSCLC cytosol preparations stimulated the proliferation of freshly isolated human umbilical endothelial cells. In paraffin embedded surgery specimens bFGF was detected by immunocytochemistry in cytoplasm of NSCLC cells irrespective of the histologic type (5 squamous cell, 1 large cell, 5 adeno ca.). Our results show that bFGF is expressed in NSCLC both in vitro and in vivo and suggest that bFGF may contribute to neoangiogenesis in human NSCLC. Therapies aimed at interruption of this paracrine loop my be clinically relevant in this disease.