287. Biomarkers and other new methods for lung cancer

P2783 An evaluation of the potential for inhaled xenobiotics to develop cancer in the lung using an in vitro model of the human epithelial-airway wall

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Nano-objects (NOs) produced by combustion processes, such as the content contained in diesel exhaust particles (DEPs), can potentiate cell mutagenesis leading to lung cancer. Little is understood however, regarding the potential for engineered NOs to cause genotoxicity. The aim of this project was to use an in vitro human epithelial-airway epithelial cell layer (16HBE14o- cells) with human monocye derived macrophages (apical layer) and dendritic cells (basolateral layer), with different toxicological endpoints involved in NO-induced genotoxicity. Single- and multi-wall carbon nanotubes (SWCNTs/MWCNTs), as well as crocidolite asbestos fibres (CAFs) and DEPs caused no significant (p>0.05) cytotoxicity (lactate dehydrogenase release) up to 0.04mg/ml after 24hrs. Significant increases (p<0.05) in both LS and TNF-a levels at 0.005-0.04mg/ml over 24hrs were observed in both the apical and basolateral layers for all NOs. The NO-cell interaction (electron tomography) was only observed with macrophages and not with epithelial or dendritic cells. Initial analysis shows no changes in cell proliferation (BrDU assay) however, increased DNA damage (comet assay), possibly via an oxidant-related mechanism, in 16HBE14o- cells compared to control levels for NOs. We acknowledge the support of the European Respiratory Society, Fellowship LTRF-MC1572-2010 to Dr. MJD CLIFT.

P2784 Nitrosoglutathione reductase inhibition in the airway epithelium may contribute to lung cancer risk

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Background: S-Nitrosogluthathione (GSNO) is an endogenous bronchodilator. GSNO reductase (GSNOR) depletes airway GSNO; inhibitors are in development for asthma. However, GSNO can be tumorigenic by activating wild-type (wt) Ras though S-nitrosylation. We studied whether decreased GSNO reductase promotes wt Ras S-nitrosylation and activation in the lung.

Methods: Lung non-small cell cancer lines (H157; Calu-1; H266; Calu-3; H1650; AS41) were studied. Ras S-nitrosylation was studied by biotin substitution and immunoblot. Active GTP-Ras was assayed in a Raf-1RBD-binding ELISA. Certain cells were exposed to 1) 30 ppm NO in a sealed incubator; or 2) S-nitrosocysteine (CSNO, 10 μM), GSH (2mM) and NADH (300 μM) with or without the GSNO reductase inhibitor, C3 (100 μM, 10 min; from P. Sanghani). GSNO reductase activity (from J.S. Stamler) were compared with C57Black6 mice with and without intratracheal ethyl nitrite (EtONO, 10 μM).

Results: Wt Ras S-nitrosylation was increased relative to expression in cancer cell lines, though expression of was low. NO exposure for 5d, but not 2d, increased Ras S-nitrosylation relative to expression in vitro. S-Nitrosylation of Ras relative to total Ras expression was increased in the lungs of GSNO reductase -/- mice; and was increased in wt mice by EtONO. CSNO increased Ras activity. In the H1650 cells, this increase was partially augmented by the C3, though baseline expression and activity of GSNO reductase were low.

Conclusions: Though loss of GSNO reductase function may benefit asthma, it prevents wt Ras denitrosylation and inactivation. This effect is associated with tumorigenesis and may not be a good strategy for asthma treatment, particularly in smokers.

P2785 COPD as an independent risk factor for lung cancer in patients with bronchial squamous dysplasia

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Background: We evaluated airflow obstruction as a possible independent risk factor for lung cancer (LC) in patients with bronchial squamous dysplasia (SD).

Methods: A total of 114 patients (111 men and 3 women) with at least 1 bronchial SD, at least 1 follow-up evaluation and normal baseline chest computed tomography (CT) were evaluated; 58 (51%) were COPD and 56 (49%) were non-COPD patients. Median age was 68 years (range:44-84 yr) and median follow-up duration was 21 months (range:4-98 months). Follow-up included periodic white light and autofluorescence bronchoscopy and chest CT. Expression of iNOS (inducible nitric oxide synthase) and EGFR (epidermal growth factor receptor) in bronchial epithelium biopsy specimens was evaluated by immunohistochemistry (IHC). Diagnosis of carcinoma in situ (CIS) and/or LC were follow-up endpoints. Results: Expression of iNOS and EGFR was closely related to patient COPD status (p=0.007 and p=0.018, respectively). COPD patients were more likely to have baseline high grade dysplasia (p=0.017), multiple dysplasias (p=0.045) and to develop a new dysplasia during follow-up (p=0.003). Progression to CIS or LC occurred more frequently in patients with COPD (p=0.012), positive EGFR (p=0.019), positive iNOS (p<0.001) and baseline high grade SD (p=0.035). Multivariate analysis showed that risk for progression was closely related to airflow obstruction (RR=0.959; 95% CI 0.923-0.987; p=0.044) and iNOS expression (RR=10.521; 95% CI 7.25-40.3; p=0.001).

Conclusion: In patients with bronchial SD, COPD is closely related to risk of progression to CIS or LC. This study supports the hypothesis that inflammation and oxidative stress promote lung carcinogenesis.

P2787 Role of systemic and bronchial oxidative stress and inflammation in lung cancer predisposition in patients with COPD

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Chronic airway inflammation such as that observed in COPD patients is a relevant contributor to lung cancer. Increased inflammation and oxidative stress levels have been shown in lung cancer lesions compared to non-tumor parenchyma.

Objectives: Levels of inflammation, redox balance, and angiogenesis were determined in the airways and blood of out-patients with lung cancer with and without COPD.

Methods: Oxidative stress, inflammation, angiogenesis, and growth factor levels were quantified (immunoblotting, ELISA, activity assays, and chemiluminescence) in the airways (bronchoscopy) and blood of: 1) patients with COPD and lung cancer (n=99), 2) patients with lung cancer without COPD (n=14), 3) patients with COPD without lung cancer (n=9), and 4) healthy subjects with no lung disease (n=12).

Results: In patients with COPD and lung cancer, blood superoxide anion, systemic oxidized DNA and proteins, and bronchial protein oxidation were increased compared to healthy controls. In patients with lung cancer, only protein oxidation was greater in their bronchi than in healthy controls. Antioxidant enzyme activity did not differ among groups in either blood or bronchi. TNF-alpha, interferon-gamma, and VEGF levels were higher in the blood and bronchi of patients with COPD and lung cancer and lung cancer only than in healthy controls.

Conclusions: While COPD induces an increase in systemic and bronchial oxidative stress in patients with associated lung cancer, the latter condition is related to greater content of proinflammatory cytokines and angiogenic factors in both blood and bronchi of the patients. Funded by: SEPAR, 2007, SOCAP 2007, MTV3-07-1010, 2009-SGR-393, & CIBERES.

P2787 Detection of patients with lung cancer out of a risk group by breath sample presentation to sniffer dogs

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Objective: Prognosis of patients with lung cancer (LC) largely depends on early diagnosis. Previous studies reported successful detection of LC in exhaled breath samples using sniffer dogs. However, questions remain concerning the discrimination potential of these approaches regarding LC and chronic inflammatory lung conditions, such as COPD.

Methods: In a prospective study we tested exhaled breath samples of patients with LC (group A), patients with COPD (group B) and healthy individuals (group C). Four sniffer dogs were trained to identify LC in human exhaled breath samples with each breath sample used only once. For analysing the diagnostic accuracy of LC detection, each dog performed the following tests in a standardized fashion: I) group A (n=10) vs group C (n=40), II) group A (n=5) vs group B+C (n=20), III) group A (n=10) vs group B (n=40).

Results: Sensitivity and specificity were in test I) LC vs healthy individuals 50% and 88% resp., in test II) LC vs mixed collective of COPD patients and healthy individuals 95% and 95% resp., and in test III) LC vs COPD 80% and 95% resp. Overall test sensitivity was 90% (CI 0.78-0.97), specificity 72% (CI 0.51-0.88), PPV 86% (CI 0.74-0.94) and NPV 78% (CI 0.56-0.93), inter-rater variability k=0.46 given the experimental conditions. Tests were analysed for confounders (study population, smoking habits, nutrition, medication).

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P2788
A new possibility of process monitoring in lung cancer: Volatile organic compounds detected with ion mobility spectrometry to follow the success of the therapeutic process
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Introduction: Lung cancer is mostly detected when it is already too late for surgery. But even when tumours can still be operated, there has not been a simple, convenient way of observing any follow-up parameters such as PSA in prostate cancer. With the non-invasive analysis of Volatile Organic Compounds (VOCs) in exhaled breath using ion mobility spectrometry (IMS) we get the chance to step up in this development.

Objectives: To develop a non-invasive technique of analysing new tumour markers in order to find a follow up biomarker for an improved monitoring of the treatment of lung cancer patients.

Methods: Exhaled breath from 33 lung cancer patients was collected and analysed with an IMS device before and after lung surgery. The patients were split into groups according to the tumour histology. Additional conditions such as COPD, medication and former radiation or chemotherapy were also taken into consideration. Furthermore, the results were statistically analysed.

Results: There were several peaks which showed differences between the pre- and post-surgery groups (such as ‘EV’ norm: 0.062 in squamous cell carcinoma). Further results will be presented in box plots.

Conclusion: As the results show differences between the peaks before and after surgery, the analysis of VOCs in exhaled air might be a new non-invasive possibility of monitoring the process of lung cancer therapy. In future research it would be interesting to carry out further investigations on long-term patient observations after defined time intervals.
describes a proof of principle study for discriminating NSCLC from COPD using an electronic nose.

Methods: 66 newly diagnosed (nd) NSCLC patients in the lung cancer group were compared to 73 COPD patients using a Cyto秤ne 320 (Smith Detection) electronic nose. Gas samples were taken immediately after exhalation and raw files were transferred to a self-developed pattern recognition software (DiagNose) to learn a common pattern for each ndNSCLC and COPD and then group each file DiagNose software employs neuronal network principles for pattern recognition.

Results: Pattern analysis of all files correctly identified 62 of the 73 samples as COPD and 39 of the 66 samples as Carcinoma patients (sensitivity 84%; specificity 89%).

Discussion Patterns derived from breath analysis of NSCLC and COPD patients analyzed with a special software based on neuronal network techniques were able to correctly discriminate between cancer and COPD patients in the major-ity of cases. Sensitivity and Specificity were both high. Further improvements with even more sophisticated algorithms may further improve these results. Our study demonstrates the potential of pattern recognition for early detection of lung carcinoma in a population risk.

**P2793**

**Neutrophil elastase levels is higher in patients with lung cancer than chronic obstructive pulmonary disease**

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Neutrophil elastase (NE) is a specific serine proteinase and it is a modulator of inflammation. Systemic and pulmonary inflammation has been associated with both non-small cell lung cancer (NSCLC) and chronic obstructive pulmonary disease (COPD). Still, an exact role of NE in pathogenesis of NSCLC, COPD and in coexistence of both diseases is unknown. The aim of the study was to evaluate NE levels in NSCLC with and without COPD.

Methods: Serum and BAL fluid (BALF) levels of NE were measured by enzyme-linked immunosorbent assay (ELISA) in 28 patients with NSCLC, 20 patients with moderate COPD, 25 patients with NSCLC and moderate COPD (NSCLC/COPD) and 10 healthy non-smoking individuals (HI). Peripheral blood and BALF were collected from each patient before any treatment.

Results: Serum NE levels were significantly higher in groups with NSCLC, NSCLC/NL/COPD, compared to COPD or HI (620±67.7 ng/mL and 609±8.8±52.7 ng/mL vs 409±261.6 ng/mL and 243±23.9 ng/mL, p<0.05). BALF NE levels were lower in NSCLC/COPD than in COPD or HI but significantly higher NE levels was found in groups with NSCLC: NSCLC/COPD (1.47-fold), NSCLC/COPD (1.53-fold) compared to COPD (1.21-fold, p<0.05) or HI (basal level). Serum NE levels were correlated with the clinicopathological status of patients with NSCLC.

Conclusions: Our data suggest a higher levels of NE both in NSCLC and NSCLC/COPD than in COPD or HI.

**P2794**

**The eosinophil infiltration of lung cancer tissue and its relationship with the expression of IL-5**

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Objective: Some studies showed that high eosinophil infiltration in lung cancer tissues was associated an improved prognosis. And the other studies showed the high expressed of IL-5 in lung cancer cells. IL-5 has emerged as a main controlling cytokine for eosinophil production, activation, and recruitment. However, there was little data associating IL-5 production with eosinophilia in lung cancer. We studied the eosinophil infiltration and the expression of IL-5 in tissue specimens from lung cancer patients and analyzed the correlation between the eosinophil infiltration and IL-5 expression of lung cancer tissue.

Methods: Eosinophil infiltration was detected by Chromotrope-2R staining and IL-5 was detected by immunohistochemistry in 45 lung cancer tissues and 328 controls, who were high expressed of IL-5 in lung cancer cells. IL-5 has emerged as a main controlling cytokine for eosinophil production, activation, and recruitment. However, there was little data associating IL-5 production with eosinophilia in lung cancer. We studied the eosinophil infiltration and the expression of IL-5 in tissue specimens from lung cancer patients and analyzed the correlation between the eosinophil infiltration and IL-5 expression of lung cancer tissue.

Results: IL-5 was detected by immunohistochemi stry in 45 lung cancer tissues and 36 squamous cell carcinoma cases. In the high eosinophilic infiltration cases, the counting of eosinophil infiltration and IL-5 expression of lung cancer tissue.

Conclusions: Association of genetic polymorphisms of matrix metalloproteinase (MMP)14 to the susceptibility of non-small cell lung cancer

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Background: Matrix metalloproteinase (MMP)14 is a cell surface proteinase that displays a broad spectrum of activity against extracellular matrix components and promotes the invasion/metastasis of cells. MMP14 is overexpressed in NSCLC, and the level is correlated with poor survival. We investigate the MMP14-165 TT genotype associated with GG/GT genotypes (an OR of 1.84, 95% CI 1.22-2.77, p=0.005), MMP14 +7096 CC genotype associated with TT/TC genotypes (an OR of 1.79, 95% CI 1.19-2.70, p=0.005), and MMP14 +8153 GA genotype associated with GG genotypes (an OR of 2.07, 95% CI 1.36-3.14, p=0.001).

Methods: Through a case-control study design, genomic DNA samples isolated from peripheral lymphocytes of 267 NSCLC patients and 328 controls, who were high expressed of IL-5 in lung cancer cells. IL-5 has emerged as a main controlling cytokine for eosinophil production, activation, and recruitment. However, there was little data associating IL-5 production with eosinophilia in lung cancer. We studied the eosinophil infiltration and the expression of IL-5 in tissue specimens from lung cancer patients and analyzed the correlation between the eosinophil infiltration and IL-5 expression of lung cancer tissue.

Results: Pattern analysis of all files correctly identified 62 of the 73 samples as COPD and 39 of the 66 samples as Carcinoma patients (sensitivity 84%; specificity 89%).

Discussion Patterns derived from breath analysis of NSCLC and COPD patients analyzed with a special software based on neuronal network techniques were able to correctly discriminate between cancer and COPD patients in the major-ity of cases. Sensitivity and Specificity were both high. Further improvements with even more sophisticated algorithms may further improve these results. Our study demonstrates the potential of pattern recognition for early detection of lung carcinoma in a population risk.

Conclusions: A significant association between the polymorphisms of MMP14 gene and the susceptibility to NSCLC was demonstrated.

**P2796**

**The expression and clinical significance of PD-L1*CD68* macrophages in peripheral blood mononuclear cells of non-small cell lung cancer**

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Purpose: To explore the roles of PD-L1* (programmed death-1 ligand 1) CD68* macrophages in peripheral blood mononuclear cells (PBMCs) of non-small cell lung cancer (NSCLC) by flow cytometry (FCM).

Materials and methods: 60 squamous cell carcinoma patients, 60 adenocarcinoma patients and 60 healthy controls were recruited in the study. PD-L1*CD68* macrophages were isolated from PBMCs of the 180 persons with FCM.

Results: Squamous cell carcinoma and adenocarcinoma patients had higher PD-L1*CD68* macrophages expression compared to healthy controls (P<0.000) and P=0.013 respectively), and PD-L1*CD68* macrophages from squamous cell carcinoma were higher than that from adenocarcinoma group [19.03±12.28%] vs [14.21±11.86%], P<0.001].

Conclusions: PD-L1*CD68* macrophages in PBMCs have marked relationship with squamous cell carcinoma and adenocarcinoma, especially can produce profound effect on squamous cell carcinoma.

**P2797**

**Circulating CD133+ stem cells in lung cancer patients**

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The presence of circulating tumor cells in lung cancer patients are potentially...
responsible for the spread of cancer. Lung cancer stem cells (LCSCs) found in the tumor samples express both: CD133 and Epithelial Cell Adhesion Molecule (EpCAM). Previously we observed that CD133(+) stem cells are present in the lung cancer tissue. The aim of this study was to identify LCSCs in circulation and to correlate their proportion with the histological type of lung cancer and the stage of the disease.

Flow cytometry was applied to identify LCSCs in the peripheral blood of 20 patients with lung cancer in IIB, IV stage of the disease. Blood samples were stained with anti-CD133 and anti-EpCAM antibodies. LCSCs were also studied in the resected lung cancer tissue samples from 7 patients.

Putative LCSCs of CD133(+)/EpCAM(+) phenotype were found in the tumor samples from 6/7 patients and constituted 0.01-1.32% of the tumor cells. Analysis of the peripheral blood samples revealed the presence of CD133(+) cells in 16/20 cases (mean 0.95%), EpCAM(+) cells in 16/20 cases (mean 1.25%) and the CD133(+) and EpCAM(+) cells in 5/20 cases (mean 0.07%). We did not find EpCAM(+) cells in patients with small cell lung cancer (4 patients). We observed higher proportion of CD133(+) cells in patients with NSCLC stage of disease (with presence of distant metastases) when compared with those with intrapulmonary spread (p<0.08).

We concluded the presence of the putative lung cancer stem cells in the tumor samples and the presence of the CD133(+)/EpCAM(+) cells in the circulation of lung cancer patients. Our study may have important implications in understanding of the mechanisms of the metastases spreading.

P2798 Evaluation of IL-6 level in serum and bronchoalveolar lavage fluid of patients with non-small cell lung cancer (NSCLC)

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Aim: To study the relationship between the interleukin-6 (IL-6) level in serum and bronchoalveolar lavage fluid (BALF) and non-small cell lung cancer (NSCLC).

Methods: The concentration of IL-6 in serum or BALF of 48 NSCLC patients, 56 patients of pulmonary inflammatory diseases (PID) and 26 normal controls were measured by ELISA.

Results: The concentration of IL-6 in BALF of NSCLC patients was significantly higher than that of PID patients and normal controls (P<0.01). The concentration of IL-6 in sera of NSCLC patients was higher than that of normal controls (P<0.01) but not statistically different from that of PID patients. In patients with NSCLC, the serum IL-6 level was modestly higher than that of PID patients, but this difference was not statistically significant (P=0.05). Serum IL-6 level was higher in NSCLC of advanced stages (stage IIIa, IIb and IV), as compared with that in NSCLC patients of early stages (stage Ia-IIb). BALF IL-6 level of NSCLC patients at different stages was not different. IL-6 level (in serum but not in BALF) of PID patients correlated with the serum concentration of C reactive protein (r=0.69).

Conclusion: IL-6 in BALF might be used as a marker for NSCLC. Serum IL-6 level might be an indicator for the stage of NSCLC. The serum IL-6 can also indicate the severity of acute lung inflammatory response.

P2799 Magnolol can induce apoptosis in non-small cell lung cancer via caspase-independent pathway

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Magnolol is a traditional Chinese herbs drug purified from Magnolia officinalis which has multiple pharmacological properties such as antioxidant and anti-inflammatory effects. Magnolol exhibited remarkable inhibitory effects on tumor growth. However, the effect of Magnolol on non-small cell lung cancer (NSCLC) has not been clarified. In this study, the NSCLC cell lines (A549, H520, H441 and HPAEC) were treated with different concentrations (0-100μM) of Magnolol for 24 hrs and the cytotoxic effect of Magnolol positively correlated with its concentration. Moreover, the chemotherapy drug Cisplatin at the dose of 25μM had the same cytotoxic effect as Magnolol at 80μM on NSCLC cell lines. Flow cytometry assay revealed that pretreatment with Magnolol at the dose of 80μM for 24 hours could induce apoptosis in A549 cells. We also illustrated that Magnolol-induced apoptosis in A549 cells involved mitochondria and nuclear proteins of NSCLC cells were lined by western blotting after treatment with Magnolol at various concentrations for 6hr, and the results revealed that apoptosis-inducing factor (AIF) and endonuclease G (Endo G) induced by Magnolol translocated from mitochondria to nucleus, suggesting that the Magnolol-induced apoptosis is mediated through caspase-independent pathway. In conclusion, Magnolol can induce apoptosis of NSCLC cells. In addition, the apoptosis in NSCLC cells involves, most likely, caspase-independent pathway in NSCLC cells.

P2800 Emerging prognostic biomarkers in non small cell lung cancer patients: Impact of treatment with nimesulide (COX-2 inhibitor) combined with chemotherapy

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To date, the treatment outcome of non small cell lung cancer (NSCLC) is still unclear and satisfactory and new treatment options are urgently needed. The present study was designed to: 1) evaluate the effects of the antiangiogenic drug: nimesulide (NSAID, a COX-2 inhibitor) combined with chemotherapy on NSCLC treatment progress, 2) Evaluate the role of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF), as prognostic indicators in NSCLC. 3) Correlate the above parameters levels with the clinicopathological status of the patients during the therapy. The study included 30 NSCLC patients:

Methods: The patients were divided to: group I, included 17 patients received chemotherapy alone and group II included 13 patients received the same chemotherapy with Nimesulide and 10 as controls. Serum and biopsies were taken for all patients on admission and 3 weeks after the completion of treatment.

Results: Serum and tissue levels of VEGF and bFGF, were significantly higher in NSCLC patients and decreased significantly after treatment specially in group II compared to group I. The serum and tissue levels of the studied parameters decreased significantly in the responders as compared to resistant cases. The response rate after combined therapy was 69% versus 53% after chemotherapy alone.

Conclusion: In conclusion, Nimesulide appears to boost the efficacy of the traditional chemotherapy as its co-administration showed encouraging effects on improving and normalization of the proangiogenic parameters and in turn the vascular supply of tumors. This may have good impact on the patient outcome, prolongation of their survival rate and prognosis.

P2801 Investigation of biomarkers for pulmonary carcinosarcomatous lymphangitis in patients with lung cancer

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Introduction: It is a crucial issue to perform differential diagnosis on the newly emerging interstitial opacities with dyspnea in the advanced lung cancer patients during chemotherapy. Many possible causes of these image findings should be considered, such as interstitial slightly raised, recurrent diseases, inflammatory effects. Magnolol exhibited remarkable inhibitory effects on tumor growth. However, the effect of Magnolol on non-small cell lung cancer (NSCLC) has not been clarified. In this study, the NSCLC cell lines (A549, H520, H441 and HPAEC) were treated with different concentrations (0-100μM) of Magnolol for 24 hrs and the cytotoxic effect of Magnolol positively correlated with its concentration. Moreover, the chemotherapy drug Cisplatin at the dose of 25μM had the same cytotoxic effect as Magnolol at 80μM on NSCLC cell lines. Flow cytometry assay revealed that pretreatment with Magnolol at the dose of 80μM for 24 hours could induce apoptosis in A549 cells. We also illustrated that Magnolol-induced apoptosis in A549 cells involved mitochondria and nuclear proteins of NSCLC cell lines were lined by western blotting after treatment with Magnolol at various concentrations for 6hr, and the results revealed that apoptosis-inducing factor (AIF) and endonuclease G (Endo G) induced by Magnolol translocated from mitochondria to nucleus, suggesting that the Magnolol-induced apoptosis is mediated through caspase-independent pathway. In conclusion, Magnolol can induce apoptosis of NSCLC cells. In addition, the apoptosis in NSCLC cells involves, most likely, caspase-independent pathway in NSCLC cells.

Aim: To establish biomarkers for PCL of lung cancer.

Method: Serum samples are collected from the subjects, which includes patients with lung cancer with lymphangitis (Lym, n=7), with enlarged lymph nodes (LCN, n=4), without lymphangitis or enlarged lymph nodes (LC, n=7), interstitial pneumonia including drug-induced, infections, and pulmonary carcinosarcomatous lymphangitis (PCL). The treatments for these diseases are different from each other, but urgent matters.

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Aim: To establish biomarkers for PCL of lung cancer.
Methods: Plasma MP-TF activity was measured in 33 patients with LC of different stages. Blood was collected at the time of inclusion; MP were collected by ultracentrifugation; TF activity was measured with a one stage clotting assay. Informed consent was obtained from all patients.

Results: The blood of patients with stage IV LC had a higher MP-associated TF activity compared to stage III (45.56 [14.88-143.70] vs. 9.45 [3.47-16.23] arbitrary U/mL) (median [interquartile range]); p < 0.05 by Mann-Whitney test (fig. 1).

Conclusions: MP-associated TF activity increases in late stage LC. This observation is consistent with the hypothesis that MP-associated TF is involved in LC progression.