Aim: The aim of this thesis was to measure a large spectrum of biomarkers in serum or plasma of patients with operable stage of NSCLC and to evaluate and compare the clinical utility of these biomarkers in the three most important clinical applications for NSCLC: diagnosis, prognosis and postsurgery follow up care.
Patients and methods: Total of 22 biomarkers with the most promising profiles were monitored: 8 standard tumor markers (cytokeratines Cyfra 21-1, TPA, TPS, and MonoTotal, CEA, SCC, TK, Chromogranin A) and 14 potential useful biomarkers including pro-inflammatory cytokines IL-6, IL-8, MCP-1, pro-angiogenic cytokine VEGF, matrix metaloproteinases MMP-1, MMP-2, MMP-7, MMP-9 and their inhibitors TIMP-1 and TIMP-2, adhesion molecules ICAM-1, VCAM-1, growth factor IGF-1, and PAI-1 stimulating tumor growth and angiogenesis. With a view of evaluating the clinical relevance of these markers for NSCLC we measured serum or plasma levels of these 22 markers in group of 93 patients with NSCLC undergoing radical surgery and in group of 20 patients with benign lung disease. For biomarker measurement were used conventional immunoanalytic routine methods (IRMA, REA, CLIA, MEIA, TRACE, ELISA) and multiplex immunoanalytic method.
Results: Cyfra 21-1, MonoTotal, TPA, TPS, CEA, SCC, Chromogranin A, TIMP-1, MMP-1, MMP-7, IL-6, MCP-1, VEGF, TK, and ICAM-1 were found to be significantly higher in patients with NSCLC in the moment of diagnosis or during follow up than in control individuals with benign lung disease. The mean serum levels of MMP-2, IL-8, TIMP-2, MMP-9, PAI-1, IGF-1 and VCAM-1 did not differ in the sera of NSCLC patients as compared with controls. The sensitivities for NSCLC diagnosis were in a wide range from 54,1% to 2,4% at 95% specificity. The highest sensitivity to distinguish between benign lung disease and NSCLC diagnosis was showed by cytokeratin markers (Cyfra 21-1, TPA, and MonoTotal), IL-6, and CEA. The best combination to distinguish between benign disease and NSCLC was achieved using CEA (>3,7 ng/m), Cyfra 21-1 (>2,0 ng/ml), IL-6 (>9,8 pg/m) and VEGF (>405 pg/ml), with a 75,6% sensitivity and 86,7% specificity, with a high predictive positive value of 97%. The sensitivities at 95% specificity for detection of disease progression during follow up were in a wide range from 52% to 4,8%. The highest sensitivity to distinguish between progression and remission status was showed by cytokeratin markers (Cyfra 21-1, TPA, and MonoTotal), TK, and CEA. We suggest that the combination of one cytokeratin (TPA or MonoTotal), Chromogranin A, MMP-7, and MCP-1 offers a good predictive value as survival predictors in NSCLC patients and for prediction of disease recurrence we found a valuable combination of one cytokeratin (TPA or MonoTotal) and one MMP (MMP-1 or MMP-7).
Conclusion: We can conclude that there has been no either appropriate parameter nor any combination of them currently usable for screening or early diagnosis of NSCLC. But some of the biomarkers could be very helpful in consideration of disease severity, treatment efficacy and prognosis estimation. As a result, this work should contribute to improve the therapeutic algorithm of patients with NSCLC and improve their long-term survival.