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108P
Genetic polymorphisms in glycolytic pathway are associated with the prognosis of patients with early stage non-small cell lung cancer

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Background: This study was conducted to investigate whether polymorphisms of genes involved in glycolysis are associated with the prognosis of patients with non-small cell lung cancer (NSCLC) after surgical resection
Methods: Forty-four single nucleotide polymorphisms (SNPs) of 17 genes in glycolytic pathway were investigated in a total of 782 patients with NSCLC who underwent curative surgical resection. The association of the SNPs with overall survival (OS) and disease free survival (DFS) were analyzed.
Results: Among the 44 SNPs investigated, four SNPs (ENO1 rs227****A>G, PFKM rs1116****C>T, PFKP rs11*****C>T, PDK2 rs37*****G>A) were significantly associated with survival outcomes in multivariate analyses. When stratified by tumor histology, three SNPs (ENO1 rs227****A>G, PFKM rs11*****C>T, and PDK2 rs37*****G>A) were significantly associated with OS and/or DFS only in squamous cell carcinoma, whereas PFKP rs11*****C>T exhibited a significant association with survival outcomes only in adenocarcinoma. When the four SNPs were combined, OS and DFS decreased as the number of bad genotypes increased (Ptrend = 9×10^{-4} and 2×10^{-5}, respectively). Promoter assays showed that ENO1 rs227****G allele had significantly higher promoter activity compared to the rs227****A allele ($P = 3\times10^{-4}$).
Conclusions: The four SNPs, especially ENO1 rs227****A>G, may be useful for the prediction of prognosis in patients with surgically resected NSCLC. The effect of SNPs of glycolytic genes on survival of NSCLC may differ depending on tumor histology. Further studies are needed to confirm our findings and to understand the role of glycolysis in determining prognosis in lung cancer.
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109P
ALK activates ERK5, in both neuroblastoma and lung cancer – a putative therapeutic target in cancer treatment

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Background: ALK, a receptor tyrosine kinase, has been identified as one partner in a wide variety of translocation events which mediate an oncogenic response in different cancer types. A number of small tyrosine kinase inhibitors (TKIs) have been developed that act to inhibit ALK activity, the most studied of these being crizotinib, a small competitive ATP-binding inhibitor currently in clinical use in the treatment of ALK positive NSCLC patients. Initial treatment of ALK^+ neuroblastoma patients treated with crizotinib has not provided as clear cut responses as those observed in other cancer types, whereas with ALK^+ NSCLC patients it acquires resistance to crizotinib. The data accumulated thus far suggests that monotherapy may not be the solution for all ALK^+ neuroblastoma and NSCLC patients, and that individualized combinations of specific drugs might be a future solution to address the disease.
Methods: Xenograft tumor models, western blotting, proliferation assay using resazurin, cell lines used ALK and EGFR positive NSCLC cells.
Results: ERK5, a.k.a. BMK1, is suggested to play a vital role in proliferation, differentiation, and survival. Previously, we have shown that ERK5 activated by ALK through the pathway PI3K/Akt/PKB/MEKK3, which contributes to cell growth of neuroblastoma cell lines. Pharmacological inhibition or siRNA of ERK5 results in decrease in growth of NSCLC cell lines, whereas in combination with ALK inhibitor seems to be more effective both in vitro and in vivo.
Conclusions: Taken together, our results indicate that ERK5 plays an important role in ALK and EGFR positive NSCLC cases, suggesting that targeting ERK5 might be a potential therapeutic target worthy of future exploration for NSCLC patients.
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110P
Predictive and prognostic role of T-regulatory cells in resected non-small cell lung cancer

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Background: Lung cancer is the leading cause of cancer-related mortality and responsible of 1.6 million deaths per year through worldwide. Surgical resection with negative margin combined with the adjuvant therapy [except for stage IA and IB (<4 cm)] is the standard treatment for early stage Non-small cell lung cancer (NSCLC). Early stage NSCLC, however, has relapse rate over 40% mostly at distant sites. Therefore, high relapse rate necessitates urgent novel biomarker for these patients. In this study, we aim to evaluate the predictive and prognostic role of FOXP3+ Treg cells along with well-defined clinicohistopathological factors in early stage non-small cell lung cancer (NSCLC).
Methods: FOXP3 expression in tumor infiltrating lymphocytes (TIL) was examined by immunohistochemical staining from resected early stage 48 NSCLC patients. Data of patients were analyzed retrospectively. FOXP3 expression status along with common clinicohistopathological prognostic factors were evaluated retrospectively.
Results: Median age of patients was 62 years-old (range 43–78). Mean follow-up, median overall survival (OS), and disease free survival (DFS) were 49, 49, and 30 months, respectively. FOXP3 expression was positive in 23 (47.9%) patients. Adjuvant chemotherapy (4 cycle of cisplatin-vinorelbine) were given to 16 patients (33.3%) at physician discretion. Increased rate of FOXP3 expression are associated with worse OS and DFS with p value of 0.016 and 0.032, respectively. In the patients with high FOXP3 expression, platin based adjuvant chemotherapy had

showed detrimental effect on DFS and OS with p value of 0.029 and 0.154 (40 vs 21 months), respectively.
Conclusions: These results suggest that FOXP3 expression in TIL has a better prognostic potential in resected NSCLC. Our findings also highlight the very high-risk group in resected NSCLC patients with high FOXP3 staining intensity who did not get any benefit even disfavor from adjuvant platin chemotherapy.
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111P
Deltex-1 single nucleotide polymorphism rs1732786A>G is associated with the prognosis of surgically resected non-small cell lung cancer

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Background: Notch signaling pathway has been implicated in the prognosis of non-small cell lung cancer (NSCLC). This study was conducted to determine the association between single nucleotide polymorphisms (SNPs) in the Notch pathway genes and survival outcomes of surgically resected NSCLC.
Methods: 252 SNPs in 28 candidate genes involved in Notch pathway genes were extracted from the SABioscience, a Quiagen company (http://www.sabiosciences.com). After quality control, 64 SNPs were analyzed in the discovery set (n = 354). A replication study was performed (n = 772). All polymorphisms were genotyped using SEQUENOM's MassARRAY® iPLEX assay according to instructions of the manufacturer. The genotype association with overall survival (OS) and disease-free survival (DFS) were analyzed.
Results: Among the 64 SNPs analyzed in the discovery set, 8 SNPs were significantly associated with OS or DFS. Among the 9 SNPs, the association was consistently observed only for DTX1 rs1732786A>G in the validation set. In combined analysis, the rs1732786A>G was significantly associated with better OS and DFS (adjusted HR [aHR] for OS, 0.81; 95% CI, 0.68–0.95; P = 0.01; aHR for DFS, 0.82; 95% CI, 0.72–0.94; P = 0.003; under codominant model). When categorized by pathological stage, the rs1732786A>G was found to be significantly associated with late stage (adjusted HR [aHR] for OS, 0.73; 95% CI, 0.60–0.89; P = 0.002; under codominant model).
Conclusions: Our results suggest that the DTX1 rs1732786 A>G could be a useful marker for predicting the prognosis of patients with early stage NSCLC.
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112P
Macrophage inhibitory cytokine-1 as a biomarker for diagnosis and prognosis of stage I–II non-small cell lung cancer

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Background: Non-small cell lung cancer (NSCLC) is the leading cause of cancer death and has a poor prognosis. Biomarkers should be established to improve patient care especially in early-stage NSCLC. The macrophage inhibitory cytokine-1 (MIC-1) can promote tumor invasiveness and metastasis. Therefore, our aim was to delineate the diagnostic and prognostic value of serum MIC-1 in patients with early-stage NSCLC.
Methods: A total of 152 consecutive patients with stage I–II NSCLC were retrospectively reviewed and underwent follow up after total resection of tumor. Serum MIC-1 level was evaluated in patients and 229 healthy controls, and was correlated with clinical features and prognosis of patients.
Results: The level of MIC-1 of NSCLC patients was significantly higher than that of controls (P < 0.001). A threshold of 1000 pg/ml could be used to diagnose early-stage NSCLC with 96.5% specificity and 71.3% sensitivity (area under curve, 0.912; 95% CI, 0.886–0.939). Higher level of MIC-1 was associated with elder age (>60 years old) at diagnosis (P = 0.001) and female gender (P = 0.03). There was a significant difference between the overall survival for patients with high level of MIC-1 (⩾1000 pg/ml) and low level of MIC-1(log rank, P = 0.045). The overall 3-year survival rate in patients with high level of MIC-1 was significantly lower than that of patients with low MIC-1 level (84.0% vs. 97.8%, P < 0.05). Cox regression revealed that a high level of MIC-1 was a potential risk factor (HR = 7.848, 95%CI, 1.044–58.979) for compromised overall survival.
Conclusions: The high level of serum MIC-1 might be served as a potential biomarker for diagnosis and poorer outcome in patients with early-stage NSCLC. The clinical significance could be evaluated in future studies with larger sample size.
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113P
Enumeration and molecular characterization of circulating tumor cells in lung cancer patients using the GILUPI CellCollector

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Background: Analysis of tumor biopsy material represents only assessable tumor and represents the state at the time of diagnosis. This approach neglects tumoral heterogeneity changes occurring during disease progression. However, during systemic therapies tumors undergo molecular changes and usually develop resistance mechanisms. Reevaluation of tumors after therapy, at disease progression and before new treatment initiation would be informative for the selection of appropriate next steps. However, re-biopsies are not often feasible and can cause morbidity. Liquid biopsy, i.e. isolating and analyzing circulating tumor cells (CTCs), can be an additional source of diagnosis, prognosis, evaluation of treatment efficacy, and molecular tumor evolution and metastatic sites. The GILUPI CellCollector®, an intravascularly in-dwelling device, screens blood for CTCs directly in the vein of the cancer patient. The device has specific