malignant pleural effusion. This method can be used as more sensitive and accurate detection of KRAS mutations. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP) (No. 2014R1A2A1A11052422).

P1.01-077
Oncogenic Potential of a Novel HER2 755PL In-Frame (HER2PL) Mutation in Lung Adenocarcinoma

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Background: Never smoking Asian patients with lung adenocarcinoma are usually accompanied with recurrent occurring mutations of oncogenic drivers, such as EGFR, HER2, ALK fusions, ROS1 fusions etc. HER2 mutations were identified in approximately 2—4% of NSCLCs and these mutations were usually mutually exclusive with other driver mutations. Preclinical studies have suggested that overexpression of HER2 or mutations of the HER2 kinase domain are critical in oncogenic transformation and tumorigenesis. We found a novel HER2 755^{PL} in-frame (also called $HER2^{PL}$) mutation in a 52-year old never smoking lung adenocarcinoma patient. She did not have EGFR mutation. Patient was treated with a second generation of EGFR tyrosine kinase inhibitor (TKI), afatinib and had responded. However, the role of $HER2^{PL}$ mutation in lung tumorigenesis and its response to EGFR TKIs have never been addressed before. **Method:** We established a plasmid construct carrying a HER2 gene with $HER2^{PL}$ and transfected into normal murine fibroblasts, NIH/3T3 and human lung adenocarcinoma, NCI-H358 which express wide type EGFR. HER2 activation pathways were examined by western blots of phosphorylation of down-stream molecules with and without gefitinib and afatinib treatment. **Result:** Overexpression of $HER2^{PL}$ mutation can activate HER signaling pathways in both NIH/3T3 and NCI-H358. $HER2^{PL}$ mutation induces much higher phosphorylation of HER2 and downstream AKT signaling pathway compared to wide-type HER2. In addition, we found that HER2PL mutation can trigger HER2 signaling in ligand-independent manner and afatinib can significantly decrease $HER2^{PL}$ mutation-induced HER2 signaling pathway compared to a first generation of EGFR TKI, gefitinib. Furthermore, we found that the distribution of $HER2^{PL}$ mutation is in cytosol as well as on the membrane and the expression of p-HER2 (Tyr1221/1222) can be effectively attenuated with afatinib treatment in NCI-H358 stable lines using immunofluorescence assay. The cell growth and drug sensitivity to different generations of EGFR TKI in NCI-H358 lines transfected with $HER2^{PL}$ mutation are under investigation. **Conclusion:** This research may bring us new insights to understand the oncogenic significance of $HER2^{PL}$ mutation and be applied to relevant therapeutics. **Keywords:** afatinib, HER2 mutation

P1.01-078
Longitudinal Studies of Quality of Life in Advanced Non-Small Cell Lung Cancer Patients Undergoing First-Line Target Therapy

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Background: This paper studies the quality of Life (QoL) of taiwan advanced non-small-cell lung cancer (NSCLC) patients receiving first-line target therapy; QoL data into sexual scores using the European Organization for Research and Treatment of Cancer Quality of Life-Core 30 questionnaire EORTC QLQ-C30 and the QLQ-13 in patients with NSCLC. **Method:** From March 2016 to March 2017, patients with in a teaching hospital in southern Taiwan were recruited as the research participants, the patients with advanced or metastatic EGFR mutation-positive NSCLC who received gefitinib, erlotinib, or afatinib as first-line treatment, were invited to complete the EORTC QLQ-C30 and QLQ-C13 on a 5 time visit, the data was analyzed by using SPSS 20.0 software. **Result:** A total of 30 patients with NSCLC, The global health status showed differences between QOL before Target therapy and 4 and 12 weeks after commencing therapy, compared to baseline. Quality of life-30 scores were 35.6 ± 8.3 before therapy, 38.1 ± 7 after 4 weeks and 43.4 ± 6.8 after 12 weeks (P <0.000) (Table 1). For the other scales, at 12 weeks, improvement of insomnia, Pain, Dyspnea, Fatigue and Appetite loss, but worsening of diarrhea, Sore mouth and Dysphagia were observed (P <0.05). **Conclusion:** Longitudinal QoL assessments are important in advanced lung cancer patients because the data they provide could, for example, help to assess more patient areas and enable early recognition of arising symptom aggravation, there support for case management and health education.

Table 1 Evaluation of the quality of life of patients using the QLQ-C30 and QLQ-LC13 questionnaire

	Before therapy Mean (SD) (N = 30)	After 1 weeks Mean (SD) (N = 30)	After 4 weeks Mean (SD) (N = 30)	After 8 weeks Mean (SD) (N = 30)	After 12 weeks Mean (SD) (N = 29)
QLQ-C30 areas					
Global	35.6±8.3	38.6±5.9**	38.1±7	38.2±5.6	43.4±6.8***
Physical	72.2±25.1	72.4±24	72.7±23.9	73.8±23.2*	74.7±22.9**
Role	71.1±25.1	75±23.1	75.6±20.5	74.4±20.1	76.4±19.8
Emotional	86.7±10.5	89.7±9.5*	91.7±9.9**	91.4±8.7*	92±8.3*
Cognitive	66.1±15.8	67.2±15.2	68.3±15.7	68.9±14.7	70.1±14.1*
Social	63.3±26.3	66.7±19.2	71.1±16.6	71.1±18.7	71.3±19
Symptom scales/items					
Fatigue	20.4±20.1	15.9±14.8	10±12.6**	10±13.3**	11.5±13.8***
Pain	16.7±16.7	7.8±18.6*	6.1±15.2**	3.3±10***	3.4±10.2***
Nausea	0±0	0.6±3	0.6±3	0±0	0±0
Dyspnoea	21.1±23.5	10±15.3**	4.4±14.2***	2.2±8.3***	1.1±6.1***
Sleep disturbance	22.2±19.9	12.2±16.1*	6.7±13.3***	6.7±13.3***	8±14.3***
Appetite loss	21.1±20.2	14.4±16.5	12.2±18.2*	8.9±14.7**	9.2±17.3***
Constipation	1.1±6	1.1±6	0±0	0±0	0±0
Diarrhoea	1.1±6	22.2±23.3***	30±18***	32.2±18.2***	18.4±16.6***
Financial impact	16.7±18.8	14.4±16.5	7.8±14.1	7.8±14.1	9.2±14.9
QLQ-LC13 areas					
Coughing	32.2±20.2	16.7±16.7***	8.9±14.7***	10±15.3***	10.3±17.7***
Dyspnoea	17±19.2	10.7±12.3*	4.4±8.4***	3.3±7.1***	4.2±8.5***
Haemoptysis	0±0	0±0	0±0	0±0	0±0
Sore mouth	0±0	12.2±21.9**	10±15.3**	6.7±13.3	6.9±13.5**
Dysphagia	0±0	5.6±12.4	8.9±14.7*	5.6±12.4*	4.6±11.5*
Peripheral neuropathy	0±0	0±0	0±0	0±0	0±0
Hair loss	0±0	0±0	0±0	0±0	0±0
Chest pain	10±15.3	1.1±6***	0±0	0±0	0±0
Pain in arm or shoulder	2.2±8.3	0±0	0±0	1.1±6	0±0
Other pain sites	6.7±18.1	7.8±18.6	4.4±14.2	2.2±8.3	1.1±6.1*

*P<0.05,**p<0.01, ***P<0.001, compared with before therapy.

P1.02-001
SLFN11 Expression in Early Stage Non-Small Cell Lung Cancer Predicts Benefit from Adjuvant Chemotherapy with Taxane and Platinum

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Background: No predictive biomarker for cytotoxic chemotherapy is approved for clinical use. Schlafen family member 11 (SLFN11) protein is widely reported as sensitizing to DNA-damaging agents. Epigenetically mediated suppression of SLFN11 is associated with poor response to platinum in patients with ovarian and lung cancer. Pre-clinical lung cancer models suggest that SLFN11 expression may be a useful biomarker of response to cisplatin, PARP inhibitors and topoisomerase inhibitors. Tumor expression of SLFN11 is assessed by immunohistochemistry, RNA expression or DNA methylation; no standard method exists. We used mass spectrometry to quantify SLFN11 protein in archived samples of patients with early stage NSCLC treated with taxane plus platinum (TP) and correlated proteomic expression of SLFN11 with survival. **Method:** We obtained archived tissue sections representing 594 patients with lung cancers of multiple subtypes. A

board-certified pathologist marked the tumor areas, which were microdissected and solubilized. In each liquefied tumor sample, 60 protein biomarkers including SLFN11 were quantified with selected reaction monitoring mass spectrometry. Patients were stratified by a SLFN11 cutoff of 100 amol/ug, based on the proteomic assay's limit of quantification. Survival outcomes were assessed with Kaplan-Meier and Mantel-Cox log-rank analyses. **Result:** Among 86 TP-treated early stage NSCLC patients, those with SLFN11 protein levels above the cutoff (n=51) had better progression-free survival (PFS) than patients with SLFN11 levels below the cutoff (HR: 2.26; 95%CI: 1.08-4.72; p=0.052). Similar differences in PFS were found in the subset of patients with NSCLC (n=77) (HR: 2.79; 95%CI: 1.29-6.05; p=0.030). Differences in overall survival by SLFN11 expression were not statistically significant. In a group of untreated patients (n=440), there were no differences in PFS between patients with high and low expression of SLFN11. **Conclusion:** Mass spectrometric evaluation of SLFN11 retrospectively identified responders to platinum-containing chemotherapy and could be used to predict response for platinum-containing therapy and warrants further validation. Multiplexed proteomics can quantitate SLFN11 simultaneously with other therapeutically relevant proteins (eg, HER2, ALK, ROS1) to inform therapy selection at initial diagnosis and upon relapse. **Keywords:** chemotherapy, SLFN11, Predictive biomarker

P1.02-002
Diagnostic Utility of MUC4 Expression to Differentiate Epithelioid Mesothelioma from Lung Adenocarcinoma and Squamous Cell Carcinoma

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Background: Malignant mesothelioma is a highly aggressive asbestos related cancer with poor prognosis and its diagnosis and differentiation from various cancers is challenging. In addition to histological features, many positive and negative immunohistochemical markers are needed to differentiate epithelioid mesothelioma from lung adenocarcinoma and/or squamous cell carcinoma. The positive mesothelial markers calretinin, WT-1, D2-40, CK5/6; positive lung adenocarcinoma markers, TTF-1, Napsin-A, Claudin-4, CEA; and positive squamous cell markers, P40, P63, CK5/6, MOC31 are routinely used. However, these markers are not sufficient and novel markers have to be identified. **Method:** Patients and Histologic Samples Pathological specimens (formalin-fixed paraffin-embedded tissue blocks) of 65 epithelioid mesothelioma and 60 lung adenocarcinoma and 57 squamous cell carcinoma were obtained from the archives of the Department of Pathology, Hiroshima University. All histological sections were reviewed and reclassified according to recent 2015 WHO classification and was confirmed by histologic findings and an immunohistochemical marker panel recommended by 2012 IMIG update to practical guidelines Immunohistochemical Procedures and Evaluation of Expression of MUC4 Immunohistochemical staining was performed using the Ventana Benchmark GX automated immunohistochemical station (Roche Diagnostics, Tokyo, Japan). Cells showing nuclear staining for calretinin, WT1, p40, p63, and TTF-1, cytoplasmic staining for MUC4 and napsin A, membranous staining for D2-40, MOC-31, and claudin-4 or membranous and/or cytoplasmic staining for CK5/6 and CEA were regarded as 'positive'. Positive Immunoreactivity was semi quantified scored from 0 to 3+. **Result:** MUC4 positivity was present in 50/60(83.3%) cases, case of adenocarcinoma and 50/56(89.3%) cases of squamous cell carcinoma but none of 65 epithelioid mesotheliomas (0%). Among lung adenocarcinoma cases, 21 cases showed score 3+, 9 cases 2+ and 20 cases score +1. In lung squamous cell carcinoma, 21 cases score 3+, 10 cases score 2+ and 19 cases score 1+. The sensitivity and specificity of MUC4 to differentiate epithelioid mesothelioma from lung adenocarcinoma were 100% and 83.3% respectively with accuracy rate of 92%. Similarly, sensitivity and specificity of MUC4 to differentiate epithelioid mesothelioma from lung squamous cell carcinoma 100% and 89.3% respectively with accuracy rate of 95%. MUC4 expression showed sensitivity of 100%, but lower specificity of 86.2% and accuracy rate of 91.2% than CEA or Claudin-4 expression. However, it showed better sensitivity, specificity and accuracy rate than that of MOC-31. **Conclusion:** MUC4 is an additional negative immunohistochemical marker to differentiate epithelioid mesothelioma from lung adenocarcinoma and/or squamous cell carcinoma. **Keywords:** MUC4, Epithelioid mesothelioma, lung adenocarcinoma & squamous cell carcinoma

P1.02-003
Prevention of Adriamycin-induced Cardiac Damage by NAD-Modulation Prevention of Adriamycin-induced Cardiac Damage by NAD-Modulation

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Background: Adriamycin (ADR), a potent anticancer chemotherapeutic agent, is used to treat a variety of human neoplasms. However, its clinical use is hampered by severe side effects including cardiotoxicity. It has been reported that ADR-induced cardiotoxicity is related to myocardial oxidative stress, disruption of cellular and mitochondrial Ca^{2+} homeostasis and DNA damage. Nevertheless, the remedy for ADR cardiotoxicity is still not developed. Here we describe the effect of NAD^+/NADH modulation by NQO1 enzymatic action on ADR-induced cardiotoxicity in mice. **Method:** C57BL/6 male mice were intraperitoneally injected with ADR. Before and after exposure to ADR, the mice were orally administrated with WK0202, a substrate of NQO1, (20 mg/kg body weight of mice). Cardiac biomarkers (CPK, Trop I, LDH and SGOT) in plasma levels, oxidative biomarkers and mRNA levels of pro-inflammatory cytokines were determined to compare cardiac toxicity of each experimental group.C57BL/6 male mice were intraperitoneally injected with ADR. Before and after exposure to ADR, the mice were orally administrated with WK0202, a substrate of NQO1, (20 mg/kg body weight of mice). Cardiac biomarkers (CPK, Trop I, LDH and SGOT) in plasma levels, oxidative biomarkers and mRNA levels of pro-inflammatory cytokines were determined to compare cardiac toxicity of each experimental group. **Result:** Cardiac biomarkers in sera, oxidative biomarkers, and mRNA levels of pro-inflammatory cytokines were significantly increased in ADR-treated mice. However, these increases were significantly alleviated by WK0202. We also demonstrated that the downfall in SIRT1 and SIRT3 activities is critically involved in ADR-induced cardiotoxicity through acetylation of NF-κB p65 and p53. However, increase of NAD^+/NADH by WK0202 through NQO1 enzymatic action attenuated ADR-induced cardiotoxicity through recovery of SIRT1 and SIRT3 activities and subsequent deacetylation of NF-κB p65 and p53. **Conclusion:** WK0202 has a protective effect against ADR-induced acute cardiotoxicity through NQO1 enzymatic action. Therefore, WK0202 might be a new therapeutic option for preventing chemotherapy-associated side effects. **Keywords:** Cardiotoxicity, NQO1, Adriamycin