differences between the different exosomal RNA extraction methods.

Conclusion: Among these methods, ExoRNEasy™ kit seems to provide the highest yield of RNA. No significant differences were found between sample groups of hsa-miR-1228-3p expression among all the used methods and we suggest that hsa-miR-1228-3p should be considered as a stable endogenous control for exosomal microRNA analysis.

Keywords: exosomes, miRNA, exosomal isolation, NSCLC biomarker

P2.08
Gene Fusions Detected in Non-Small Cell Lung Carcinoma (NSCLC) and Small Cell Lung Carcinoma (SCLC)

Track: Biology and Pathogenesis

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Background: Gene fusions, first thought to be limited to hematologic malignancies and soft tissue sarcomas, are taking on more importance in many solid tumors. For instance, functional ESR1 fusions in breast cancer are now associated with resistance to hormonal therapy. In NSCLC, *ALK*-, *RET*-, and *ROS1*-rearrangements are frequently targeted with available kinase inhibitors. However, much remains unknown regarding other chromosomal gene rearrangements. The purpose of this study is to report fusion assay results performed at a multi-omic tumor profiling facility to identify potentially novel or uncommon fusions in a variety of thoracic carcinoma.

Method: In total, 356 NSCLC and 20 SCLC were profiled using the ArcherDx FusionPlex Assay at a CAP/ISO/CLIA-certified laboratory (Caris Life Sciences) using FFPE specimens. Fifty-two genes were analyzed for potential gene fusions. Fusion-positive specimens were confirmed using in-situ hybridization and/or Sanger sequencing. Depending on available specimen, tumor samples were evaluated by immunohistochemistry (IHC), and next generation sequencing (NGS) for co-occurring biomarkers.

Results: Overall, 32 fusion transcripts in 31 of 356 NSCLC specimens contained a previously reported or novel fusion (8.7%). Fusion transcripts were found in adenocarcinoma (78.1%, 25/32) followed by SCC (15.6%, 5/32) and carcinoma, NOS (6.3%, 2/32). One NSCLC specimen contained two co-occurring fusions (EML4-ALK, PRKCG-PRKCB) and 40.6% (13/32) were either ALK (n=8), *RET* (n=2), or *ROS1* (n=3) rearrangements. More than once detected fusions included *MSMB* (n=3), *ERG* (n=2), *MAST2* (n=2), and *PRKCA* (n=2). Notable fusions included *BRD4*, *FGFR3*, *MET*, and *NTRK3* detected in single cases. Sequencing analysis by NGS revealed no co-occurring deleterious mutations in *BRAF, EGFR, ERBB2, MET, NRAS*. However, *KRAS* G12 mutations were detected in 22.6% (7/31) fusion-positive specimens, all of which were adenocarcinomas. PD-L1 expression was detected in 30.4% (7/23) of fusion-positive specimens. Only one fusion (*SYN2-PPARG*) was identified in SCLC.

Conclusion: ArcherDx FusionPlex Assay is a laboratory validated assay for detection of fusions involving ALK, RET, and ROS1, and some additional directly targetable fusions. The presence of mutant KRAS and/or PD-L1 in fusion-positive NSCLC could be used for novel drug combinations. These results could be useful to direct patients to clinical trials for relevant drugs. Further studies are warranted to explore the role of fusions in driving various cancers.

Keywords: NSCLC, SCLC, fusion gene, FFPE

P2.09
cMET in NSCLC: Expression, Amplification and Mutations

Track: Biology and Pathogenesis

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Background: Targeted therapies have gained a lot of attention in non-small cell lung cancer, including several cMET inhibitors against non-small cell lung cancer (NSCLC). Nowadays, cMET amplification is used as a standard biomarker for patient selection; however there is still discussion about the cut-off value. More recently, splicing variants of cMET, which show exon 14 skipping, are gaining importance since it has been shown that patients harboring this mutation can

respond to cMET directed targeted therapy. In this study, we explored the occurrence of cMET aberrations and their correlation with cMET expression in a population of 155 primary EGFR-TKI naive NSCLC tumors. We also evaluated cMET expression and amplification in corresponding metastases. Finally, given the link between the EGFR and cMET pathways, the EGFR status was also studied.

Method: Therapy naïve resection samples were collected at the Antwerp University Hospital and the Onze-Lieve-Vrouw Hospital Aalst. The expression of EGFR and cMET was determined by immunohistochemistry (Ventana, clones 3C6 and SP66 respectively), while cMET amplification was examined by in situ hybridization (Ventana, MET DNP and CEN7 DIG probes). EGFR mutations and cMET splice site mutations were detected by Sanger sequencing. Deep sequencing of cMET was performed with the custom designed TPME kit (Multiplicom) and sequenced on Illumina MiSeq. Significant correlations were tested using the Chi^2 and kappa test (SPSS 23).

Results: In 146/155 tumors cMET expression could be determined; 73/146 samples showed high (2+ or 3+ score) cMET expression and 4/118 samples showed amplification (ratio $\geq$ 2). No significant correlations could be determined between cMET expression and histological subtype of NSCLC (p=0.065), differentiation degree (p=0.468) and cMET amplification (p=0.214). However, a significant correlation was found between cMET expression, EGFR expression (p=0.015) and EGFR mutations (p=0.029). Splice site mutation regions were sequenced in 87/155 samples, all of which were wild-type. However, deep sequencing revealed 2 patients with splice site mutations. When comparing cMET amplification between the primary tumor and the corresponding metastases (n=40), only one sample showed amplification in the metastases and not in the primary tumor. Hence, cMET expression showed a significant correlation between primary tumors and their metastases (kappa=0.003).

Conclusion: The overall results of our study are in agreement with earlier data. Moreover, we showed that overall expression levels of cMET in primary tumors and metastases are very similar despite large intratumor heterogeneity. The two patients with cMET splice site mutations, both showed a high cMET expression and one patient had a ratio of cMET/CEN7 of 2. In conclusion, this study shows that high cMET expression in most NSCLC samples does not originate from presently known genetic cMET aberrations. High cMET expression is likely to be caused by temporary changes in transcription and translation, influenced by EGFR-signaling, miRNAs or other regulatory mechanisms.

Keywords: cMET, NSCLC, cMET amplification, cMET expression

P2.10
Clinical and Pathological Characteristics of ALK Positive Lung Cancer Patients. Instituto Oncológico Nacional — Panama

Track: Biology and Pathogenesis

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Background: ALK rearrangement is present in 4% - 6% of all patients with NSCLC. The mean age of presentation is 52 years with predominance in males and in light or never smokers. ALK is a novel therapeutic target with an excellent response to treatment with specific tyrosine kinase inhibitors (i. e. crizotinib).

Method: We retrospectively reviewed the medical records of patients with ALK positive lung cancer from february 2014 to june 2016. The objective was to describe the clinical and pathological characteristics of our patients to see if we correlate with the epidemiology usually described.

Results: ALK rearrangement was evaluated in 223 patients diagnosed with lung cancer and 16 of the cases were positive, representing 7%. The mean age of diagnosis was 63,3 years (37 — 89) and 68,8% of patients were females. 93,5% had a PS from 0 — 2. Only 26,7% never smoked. The adenocarcinoma type represented the 93,7% and 25% were described with a mucinous pattern. Most of the cases were detected with FISH with 81,3%. Stage IV disease was present at diagnosis in 68.8% and the rest were locally advanced (Stage IIIA and IIIB). Common sites of metastases were the contralateral lung (31,3%), bone (18,8%), (12,5%) and only 1 patient had brain metastases. 11 of 14 (78,5%) patients with metastatic disease were exposed to crizotinib in first line treatment, but the data is still immature to report efficacy.

Conclusion: The incidence of ALK rearrangement in Panama (7%) is similar to the incidence reported in other studies. In contrast, although for now this is a small series of cases, our patients presented with a slightly older mean age, female predominance and smoking history was positive in most of them. Stage IV