**ARTICLE INDEX**

**Articles for Discussion**


**Articles for Notation**

*Neoplastic*


Queisser MA et al. HOIL-1L Functions as the PKCζ Ubiquitin Ligase to Promote Lung Tumor Growth. Am J Respir Crit Care Med. 2014 Sep 15;190(6):688-98.


Non-neoplastic


Case Reports / Letters to the Editor


SUMMARIES - Discussion Articles


**Purpose:**
To evaluate whether there is prognostic value of KRAS mutational status in resected stage I lung adenocarcinomas.

**Methods:**
- Included patients had stage I NSCLC and underwent surgery with curative intent that underwent genotyping.
- Exclusion criteria: stage II, III, or IV disease; non-adenocarcinoma tumors; absent or failed genotyping, those that received adjuvant/neoadjuvant therapy; patients without adequate follow-up documentation or imaging.
- Allele-specific PCR-based SNaPshot.
- Demographic and clinical information collected.
- Patients assessed for recurrence, disease-free survival and overall survival.

**Results:**
- 312 patients were included in the final study cohort.
- 127 were KRAS-MUT, 185 were KRAS-WT (no significant difference in age, race, tumor size, functional status, medical comorbidies). More KRAS-MUT were smokers. 12 had additional (non-KRAS mutations).
- Other genetic alterations included 61 EGFR mutations and 32 other.
- Median follow-up was 36 months. 59 recurrences and 31 deaths. 17.3% of KRAS-MUT died (compared to 4.9% KRAS-WT) (p=0.0001).
- OS and DFS was significantly shorter in KRAS-MUT with a HR of 4.36. 3-year survival 84% vs. 95% in KRAS-MUT vs –WT.
- Of KRAS mutation status, tumor size, smoking status, se, and surgical procedure only KRAS is predictive for OS and DFS.
• Of KRAS mutations, codon 12 mutations found in 86%, and codon 13 in 9% and codon 61 in 5%.
• Codon 12 mutations had better DFS than other mutations (38.5 mos vs 25.7 mos), but no difference in OS.

Take home points:
• KRAS testing appears to independently indicate important prognostic information (in terms of DFS and OS) in surgically resected stage I lung adenocarcinoma.
• The prognostic information remains significant in univariate and multivariate analyses when stratifying by EGFR status.
• There appears to be codon-specific associations with prognosis (codons 13 and 61 being worse than codon 12).
• Potential implications for new therapies targeting P13K/AKT/mTRO pathways.

**Purpose:**
To evaluate the circulating-free tumor DNA status in EGFR mutated cases of NSCLC.

**Methods:**
- Tumor and duplicate plasma samples were collected from 1060 patients.
- EGFR tumor mutational analysis was performed via Scorpion ARMS-based EGFR detection kits (evaluating for 29 mutations across the EGFR gene).
- Data were analyzed using a data cutoff at 6 mos after the last patient had started treatment.
- Objective response rate was the primary end point.

**Results:**

<table>
<thead>
<tr>
<th>Plasma 1 EGFR Mutation Status, n</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor EGFR mutation status, n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>69</td>
<td>56</td>
<td>125</td>
</tr>
<tr>
<td>Negative</td>
<td>1</td>
<td>546</td>
<td>547</td>
</tr>
<tr>
<td>Total</td>
<td>70</td>
<td>582</td>
<td>652</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor EGFR mutation status, n</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>652</td>
<td>94.2</td>
<td>92.3-96.9</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>163.7</td>
<td>35.8-74.3</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>547</td>
<td>99.8</td>
<td>99.0-100.0</td>
</tr>
<tr>
<td>Positive-predictive value</td>
<td>70</td>
<td>98.6</td>
<td>92.3-100.0</td>
</tr>
<tr>
<td>Negative-predictive value</td>
<td>582</td>
<td>93.8</td>
<td>91.5-95.6</td>
</tr>
</tbody>
</table>

For the comparison of tumor and plasma data, the tumor DNA mutation status was adjusted for the mutations analyzed in circulating-free tumor DNA from plasma (i.e., for exon 19 deletions, L858R point mutations and T790M point mutations only).

**TABLE 3.** EGFR Mutation Status Comparisons for Plasma 1 vs Plasma 2 Circulating-Free Tumor DNA Samples by EGFR Mutation Status Summary and Concordance (Screened Patients Evaluable for Both Samples, n = 224)

<table>
<thead>
<tr>
<th>Plasma 1 EGFR Mutation Status, n</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conformance</td>
<td>63</td>
<td>5</td>
<td>68</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>2</td>
<td>154</td>
<td>156</td>
</tr>
<tr>
<td>Specificity</td>
<td>65</td>
<td>159</td>
<td>224</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rate, %</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>96.9</td>
</tr>
</tbody>
</table>

**TABLE 4.** EGFR Mutation Status Comparisons for Plasma 1 vs Plasma 2 Circulating-Free Tumor DNA Samples by EGFR Mutation Subtype (Screened Patients Evaluable for Both Samples, n = 224)

<table>
<thead>
<tr>
<th>Plasma 1, n</th>
<th>Positive: Exon 19 Deletions</th>
<th>Positive: L858R</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive: exon 19 deletions</td>
<td>43</td>
<td>0</td>
<td>4</td>
<td>47</td>
</tr>
<tr>
<td>Negative</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>21</td>
<td>159</td>
<td>224</td>
</tr>
</tbody>
</table>

EGFR, epidermal growth factor receptor.
• 1060 patients were screened from 13 countries.
• 1033 tumor samples were available.
• \textit{EGFR} mutation status determined in 859 (81%), 118 (13.7%) of which were \textit{EGFR+}.
• Plasma 1 samples were available in 803/1060 including 82 (10.5%) mutation positive.
• Concordance between 652 matched tumor and plasma samples was 94.3% (sensitivity 65.7%; specificity 99.8%).
• 12 patients with unknown mutation status were identified as plasma mutation +
• Plasma 2 samples were available in 803/1060 including 65 mutation positive cases.
• Concordance between 224 matched plasma 1 and 2 samples was 97%.
• ORR for tumor mut+ 70%, tumor mut+ and plasma 1 mut+ 77, tumor mut+ and plasma mut- 59.5%.

\textit{Take home points}:
• There is high concordance, specificity, and sensitivity in tumor and circulating free DNA.
• \textit{EGFR} mutation status can be accurately assessed using circulating-free tumor DNA, although it cannot yet replace direct tumor testing.

**Purpose:**
To validate the prognostic value of the “new histologic classification” of lung primary adenocarcinoma subtypes in a large French cohort.

**Methods:**
- 407 consecutive lung adenocarcinomas (2001-2005) were reviewed and reclassified according to the IASLC/ATS/ERS classification.
- Graded into low, intermediate and high types.
- Clinical, pathological and molecular analysis were also performed.

**Results:**
- Patients underwent lobectomy (n=378) or pneumonectomy (n=29)
- 5- and 10-year survival was 53.2% and 32.6%, respectively.
- Low grade tumor in 1 patient, intermediate in 275 and high in 131 patients.
- KRAS in 34% and EGFR in 9.6%.
- Histologic grade was correlated with extent of resection, TTF-1 expression, vascular emboli and EGFR mutation.
- Mucinous histology was associated with KRAS mutation.
- Univariate analysis showed age, extent of resection, histologic grade, pleural invasion, vascular emboli, and T&N stage were all predictive of survival.
- Multivariate analysis, age, histologic grade and stage were independent prognostic factors.
Take home points:
- The IASLC/ATS/ERS appears to predict survival in French population.
- Histologic grade, again, correlates with clinical, pathologic and molecular parameters suggesting different oncogenic pathways.

**Purpose:**
To investigate and update the trends in lung cancer, in terms of histologic types and demographic characteristics, in the United States.

**Methods:**
- Surveillance, epidemiology and end results of histologically-confirmed lung cancer (including squamous, small cell, adenocarcinoma, large cell, and other types) were included.
- US whites and blacks diagnosed from 1977-2010 and white non-Hispanics, Asian/Pacific Islanders, and white Hispanics diagnosed from 1992-2010 were analyzed by sex and age.

**Results:**
- Squamous and small cell carcinoma rates declined since the 1990s. This effect was seen less in women than in men.
- Adenocarcinoma rates decreased in men through 2005 and then rose from 2006-2010. The latter was, in fact, seen in each racial/ethnic and sex group.
- Male/female rate ratios declined among whites and blacks more than other groups.
- Recent rates among young women were higher than men for adenocarcinoma among all racial/ethnic groups and for other specified carcinomas among whites.
**Take home points:**

- US lung cancer trends vary by sex, histologic type, racial/ethnic group and age, reflecting historical cigarette smoking rates, duration, cessation, cigarette composition, and exposure to other carcinogens.
- Substantial excesses among men have diminished and higher rates of adenocarcinoma among young women have emerged as rates among men declined more rapidly.
- *EGFR* mutations and *ALK* rearrangements that occur primarily in adenocarcinomas are the primary basis for the molecular revolution that has transformed lung cancer diagnosis and treatment over the last decade.
SUMMARIES – Articles for Notation (Neoplastic)


_Purpose:_ To determine which ALK antibody clones provide the best agreement with ALK FISH.

_Methods:_ 303 lung adenocarcinomas were evaluated with ALK FISH and five ALK antibody clones (5A4; D5F3, ALK1, ALK01; SP8). All IHC examined by two pathologists.

_Results:_ 14 cases (4.6%) had ALK rearrangements by FISH. 5A4 & D5F3 stained 100% of the rearranged cases. 5A4 stained 12/14 cases, SP8 stained 9/14, ALK1 stained 7/14 and ALK01 stained 7/14.

_Take home points:_
- D5F3 exclusively stained rearranged cases with strong intensity without false-negative or false-positive cases.
- ALK IHC is an efficient and cost-effective approach to screening tumors for the rearrangement.


_Purpose:_ Establish the feasibility of implementing optimal clinical testing methods and algorithms for routine detection of ALK+ lung cancer.

_Methods:_ A reference study set of 28 lung adenocarcinomas was selected from ~2000 cases. 13 labs performed IHC (5A4, ALK1, D5F3 antibodies). 12 labs performed FISH. 3 labs performed a prospective parallel IHC/FISH on 411 consecutive clinical samples.

_Results:_ 22 cases were ALK+ and 6 were ALK- by FISH. Preoptimization IHC scores with 5AF and FISH showed correlation coefficients of 0.83 and 0.68, respectively. Optimization of IHC improved the intraclass correlation coefficients to 0.94. IHC/FISH testing in 373 informative cases showed 100% sensitivity and specificity for IHC vs FISH.

_Take home points:_
- Multicenter standardization may accelerate the adoption/implementation of ALK testing
- Appropriately validated IHC assays are a useful screen for ALK+ lung cancers.

*Purpose:* To evaluate the prognostic value of expression of apoptosis regulators in localized NSCLC.

*Methods:* Bcl-2, Bcl-xl, Mcl-1, pp32/PHAPI, and IncRNA MALAT-1 expression were evaluated in 383 NSCLC cases.

*Results:* Tumor histology was associated with expression of Bcl-2, Bcl-xl and Mcl-1. Only Bcl-2 demonstrated prognostic impact. Bcl-2 expression in non-adenocarcinoma was associated with increased overall survival. An interaction of Bcl-2 was observed with MALAT-1 LncRNA expression.

*Take home points:*
- Bcl-2 expression is specifically associated with improved survival in localized NSCLC.
- Bcl-2 and MALAT-1 LNC RNA appear to have an important interaction.


*Purpose:* To report the largest series, to-date, of indwelling pleural catheter tract-related metastases.

*Methods:* Single-center, retrospective review of IPCs inserted over a 44-month period.

*Results:* 110 IPCs placed in 107 patients. Catheter tract metastasis developed in 11 cases (10%): 9 with mesothelioma and 2 with metastatic adenocarcinoma. CTM often developed late (median, 280 days) following insertion. Long interval after IPC insertion was the sole significant risk factor for development of CTM.

*Take home points:*
- IPC-related CTM is uncommon but can complicate both mesothelioma and metastatic carcinoma.
- The duration of interval after insertion of IPC is the key risk factor.
- Symptoms are mild and respond well to radiotherapy.

**Purpose:** To determine whether DNA methyltransferase 3B is upregulated by transcriptional deregulation.

**Methods:** DNMT3B repression by FOXO3a was assessed in lung cancer cell, animal and clinical models.

**Results:** FOXO3a negatively regulates DNMT3B promoter activity by interacting with a binding element. Overexpression of FOXO3a or treatment with doxorubicin can result in further binding. Treatment with doxorubicin and Nutlin-3 (an MDM2 inhibitor) further enforces nuclear accumulation of FOXO3a resulting in decreased expression of DNMT3B. Decreased DNMT3B inhibits tumor growth and decreases methylation status of tumor suppressors. Clinically, lung CA patients with DNMT3B high, FOXO3a low and MDM2 high expression provies have poor prognosis.

**Take home points:**
- FOXO3a transcriptionally represses DNMT3B expression.
- MDM2 overexpression may attenuate the above repression.
- Co-treatment with Nutlin-3 and doxorubicin is a novel therapeutic strategy.


**Purpose:** To assess whether EGFR mutation status is associated with objective response rate progression-free and overall survival in patients with advanced NSCLC treated with chemotherapy.

**Methods:** Meta-analysis of published reports investigating the effects of chemotherapy I patients with NSCLC stratified by EGFR mutation status.

**Results:** ORR was significantly higher in patients with EGFR mutations in prospective studies but not in retrospective studies. No obvious association between EGFR mutation and PFS in prospective or retrospective series. EGFR mutation and OS associations also not seen in prospective studies, but was noted in retrospective studies.

**Take home point:**
- EGFR mutation in advanced NSCLC may be associated with higher ORRs to chemotherapy but are not associated with differential PFS and/or OS.

**Purpose:** To retrospectively compare the volume doubling time (VDT) on serial CT of NSCLC with EGFR mutation with that of NSCLC without EGFR mutation.

**Methods:** 102 histopath-proven NSCL were reviewed with helical CT.

**Results:** The median VDT of all patients was 188 days. EGFR mutation was noted in 35/102 pts. The VDT in EGFR+ was longer than the 67 EGFR- (676 vs 139 days). The VDT of adenocarcinoma (305 days) was longer than that of squamous cell carcinoma (81 days).

**Take home point:**
- EGFR+ is associated with longer VDT (corroborating less-aggressive character).


**Purpose:** To evaluate serum free fatty acid biomarkers in lung cancer.

**Methods:** Serum from 55 patients with lung cancer were matched with 165 similar pulmonary patients without lung cancer.

**Results:** Arachidonic acid, linoleic acid and their metabolites were 1.8 to 3.3-fold higher in 37 patients with adenocarcinoma vs 111 patients without. Concentrations of FFA and metabolites were similar in 18 patients with SqCC and 54 control subjects.

**Take home point:**
- Serum FFA and their metabolites demonstrate good sensitivity and specificity for identification of lung adenocarcinoma.


**Purpose:** To evaluate GRIM-1 expression in NSCLC and its interactions with GRP78.

**Methods:** 40 surgical specimens evaluated for GRIM-1 and GRP78 expression.
Results: Lower expression of GRIM-1 in NSCLC was shown at both the protein and mRNA level (compared to normal tissues). Tumors showed higher basal expression of GRP78 protein and mRNA. In NSCLC tissues, weaker staining for GRIM-1 and stronger GRP78 staining was observed. No correlation between GRIM-1 expression and clinical characteristics was observed. GRP78 expression was significantly correlated with TNM stage.

Take home points:
- Expression of GRIM-1 and GRP78 was negatively correlated in NSCLC tissues.
- Down-regulation of GRP78 by GRIM-1 provides a potential mechanism for their interaction.


Purpose: To evaluate testing methods for HER2 in lung adenocarcinoma and the concordance of methods.

Methods: HER2 protein expression analyzed by IHC, FISH, and DISH on tissue microarray composed of lung adenocarcinoma from 243 consecutive patients. EGFR, KRAS and HER2 mutations also evaluated for.

Results: IHC+ in 6 (2.5%) cases. HER2 amplification observed in 5 (2.1%) by FISH and in 9 (3.7%) by DISH. HER2 by IHC and FISH were significantly associated. Overall concordance between FISH and DISH was 96.7%. 109 (49.9%) tumors were EGFR+, 25 (11.2%) were KRAS+, and 6 (2.7%) had HER2 mutations. 2/6 cases with HER2 mutation showed amplification by FISH and DISH.

Take home points:
- HER2 overexpression, amplification, and mutation are uncommon in lung adenocarcinoma.
- HER2 mutated cases tended to show amplification.
- HER2 testing may be useful in lung adenocarcinoma patients to determine whether patients are eligible for anti-HER2 agents.
- DISH is superior to FISH for detection of amplification.

11. Queisser MA et al. HOIL-1L Functions as the PKCζ Ubiquitin Ligase to Promote Lung Tumor Growth. Am J Respir Crit Care Med. 2014 Sep 15;190(6):688-98.

Purpose: To determine the mechanism for PKC zeta down-regulation in lung cancer.
Methods: HOIL-1L, HOIP, SHARPIN and PKCz were evaluated by Western blot and/or q-RT-PCR in different cell lines. Gain/Loss of function experiments were performed as well as tumor growth studies in animal models.

Results: During hypoxia, PKCz is ubiquitinated and degraded by HOIL-1L. In vitro assays showed HOIL-1L to ubiquitinate PKCz at Lys-48. In xenograft models, HOIL1L is silenced. HOIL-1L expression is regulated by HIFs. The actions of HOIL-1L were independent of LUBAC.

Take home points:
- The data in this study provide primary evidence of a mechanism of cancer cell adaptation to hypoxia.
- Silencing of HOIL-1L impairs lung tumor growth.
- HOIL-1L expression predicts survival of lung cancer patients.


Purpose: To evaluate the expression profile of napsin A, TTF-1, CK5/6, p40 and p63 in pulmonary neuroendocrine tumors.

Methods: 52 typical carcinoids, 8 atypical carcinoids, 7 small cell carcinomas, and 1 large cell NE carcinoma were stained for the above markers.

Results: Napsin A, p63, p40, and CK5/6 were consistently negative in NE tumors. TTF-1 was positive in 52/52 TCs, 4/8 ACs, 5/7 SCLCs, and 0/1 LCNEC.

Take home points:
- Pulmonary NE tumors have a distinct but non-specific immunoprofile.
- They are napsinA-/p40-/p63=/CK5/6-/TTF-1+/-. 


Purpose: To evaluate the prognostic impact of the Japanese nodal classification and its ability to define favorable N2 disease in resected NSCLC.

Methods: 496 patients with NSCLC that underwent lobectomy with nodal dissection were retrospectively analyzed.

Results: 67 cases with N2 disease identified. The outcome of resected N2a-2 NSCLC was more poor than N2a-1 group (28% vs 62% 5-year OS). Multivariate
analysis revealed that N2a-2 was an independent prognostic factor. Patients with N2a-2 showed more involved nodes and stations, less skip metastasis and more locoregional recurrence. No significant difference in OS and FS between N1 and N2a-1.

*Take home point:*
- The Japanese nodal classification is able to identify a favorable N2 subgroup in resected NSCLC.


*Purpose:* To evaluate GP88 tissue expression in localized/locally advanced lung cancer and serum GP88 levels in advanced disease.

*Methods:* GP88 expression was determined by IHC in NSCLC patients, 85 with stage I-II disease and 40 with stage IIIa. Correlation with clinical outcome was performed. Serum GP88 level, via enzyme immunoassay, was obtained from patients with stage IIIb/IV disease.

*Results:* GP88 was expressed in in > 80% of adenocarcinoma and SqCC in contrast to normal lung and SCCs. Inverse relationship of GP88 expression and survival in resected NSCLC. Decrease in PFS for GP88 expression.

*Take home point:*
- GP88 may be an important prognostic biomarker in localized and advanced disease.


*Purpose:* To assess the reproducibility of a set of histopathologic features of SqCC in relation to other poorly differentiated NSCLCs and to assess the value of IHC in improving the diagnosis.

*Methods:* 37 resection specimens with SqCC, LCC, basaloid carcinoma, sarcomatoid carcinoma, LEL carcinoma and solid AdC were evaluated by histology and assessed for added value of stains in the diagnosis by pathologists on the panel.

*Results:* Kappa scores, by histology alone, were .46 SqCC, .25 LCC, .27 Basaloid, .52 sarcomatoid, LEL .56, and .21 solid AdC. With the use of stains, the kappas improved for SqCC (.57) and for solid AdC (.63).
**Take home point:**
- Stains improved reproducibility of histological diagnosis of SqCC and AdC.


*Purpose:* To investigate lung cancer risk associated with chronic bronchitis, emphysema, tuberculosis, pneumonia and asthma.

*Methods:* Information from 12,739 case subjects and 14,945 control subjects from 7 case-control studies in Europe and Canada were pooled. Multivariate logistic regression models were used to investigate the relationship between individual diseases and co-occurring condition.

*Results:* Chronic bronchitis and emphysema were associated with lung CA after accounting for other disease and smoking. A positive relationship with pneumonia (diagnosed 2 years or less before lung CA) and lung CA was observed. Asthma had an inverse association with lung CA.

*Take home points:*
- After accounting for co-occurring respiratory disease, chronic bronchitis and emphysema continue to have a positive association with lung CA.


*Purpose:* To determine the availability of biopsy specimens that could be used for genomic studies and to identify tumors for initial oncogene analysis.

*Methods:* DNA was extracted from 6 tumors (3 primary, 3 metastatic) and analyzed by SEQUENOM.

*Results:* An activating M918T RET somatic mutation was identified in a metastatic SCLC tumor.

*Take home point:*
- A sub-population of SCLC patients may benefit from TKI targeted therapy.

**Purpose:** To evaluate thymic epithelial tumors for keratin expression.

**Methods:** 83 thymic tumors were evaluated for keratin expression.

**Results:** 14 thymic epithelial tumors (11 type B2 and B3, 3 thymic carcinomas) showed highly reduced expression of at least one keratin marker. 3 cases showed complete keratin loss. 13/14 cases showed strong nuclear p63 expression.

**Take home points:**
- Loss of keratin expression is an important diagnostic pitfall in thymic neoplasms and may lead to confusion with TLL.
- Loss of keratin in type B2 and B3 thymomas can be seen in 5% of cases.
- A panel of epithelial markers including p63 should be used to ensure the correct diagnosis of keratin-negative mediastinal tumors.


**Purpose:** To identify potential targets of therapy for SCLC not currently searched for in routine practice.

**Methods:** DNA from 98 SCLCs was subjected to NGS and analyzed for genomic alterations.

**Results:** 386 alterations were identified (~3.9 alterations / tumor). 52 (53%) of cases harboured at least 1 actionable alteration with potential to personalize therapy. The most common alterations were P53 (86%), RB1 (54%) and MLL2 (17%).

**Take home point:**
- >50% of SCLC cases have at least 1 actionable alteration.


**Purpose:** To analyze the association between class III/IV POU genes and proneural/neuroendocrine phenotype lung cancers.

**Methods:** 7 SCLC cell lines, 12 NSCLC cell lines and a human kidney cell line were evaluated by RT-PCR and Western blot analysis for POU transcription factors.
Results: Class III/IV POU gene expression was generally restricted to SCLC cells. However, the forced expression of class III/IV POU genes in the NSCLC cell lines induced the expression of neuroendocrine-specific markers (neural cell adhesion molecule 1, synaptophysin, and chromogranin A) and proneural transcription factors (achaete-scute homolog-like 1, NeuroD1, and thyroid transcription factor 1) in various degrees.

Take home points:
- The expression of class III/IV POU genes is important for the proneural/neuroendocrine differentiation of lung cancer cells.
SUMMARIES – Articles for Notation (Non-neoplastic)


**Purpose:** To evaluate the efficacy of different PCR methods for detecting Mycobacterium species in FFPE tissues.

**Methods:** 110 FFPE specimens (56 nonmycobacterial, 32 MTB, and 22 non TB mycobacteria (determined by AFB culture)) were evaluated with N-PCR, RT-PCR, and 3 different commercial RT-PCR methods.

**Results:** N-PCR, in-house RT-PCR and AdvanSure RT-PCR correlated well with AFB cultures. N-PCR sensitivity (87.5%) was higher than RT-PCR methods. All PCR methods had high specificities (98.2-100%).

**Take home points:**
- Well-designed RT-PCR and N-PCR can help to identify MTB in FFPE specimens.


**Purpose:** To determine if new smoking-related ILD phenotypes could be identified.

**Methods:** International group of clinicians, radiologist and pathologists evaluated 141 cases of idiopathic interstitial pneumonia. 41 cases of IIP has a smoking history. Radiologists and pathologists used a score sheet to note presence/absence of selected features and impression of smoking relatedness.

**Results:** Phase 1 suggested that preserved forced vital capacity with disproportionately reduced diffusing capacity of the lung for carbon monoxide, and various radiographic and histopathological findings were smoking-related features. In phase 2, the kappa coefficient among clinicians was 0.16 (95% CI 0.11–0.21), among the pathologists 0.36 (95% CI 0.32–0.40) and among the radiologists 0.43 (95% CI 0.35–0.52) for smoking-related features. Eight of the 100 cases were felt to represent a potential smoking-related interstitial lung disease.
Take home points:
• Smoking-related features of interstitial lung disease were identified in a minority of smokers and were not specific for smoking.