Pulmonary Pathology Journal Club – April 2025

Presented by
Heather Chen-Yost, MD
Department of Pathology
University of Michigan, Ann Arbor, MI
Assisted by ChatGPT

Table of Contents:

Articles for Discussion

Page 3 Zhu Y, et al. Heterogeneity of molecular subtyping and therapy-related marker expression in primary tumors and paired lymph node metastases of small cell lung cancer. *Virchows Arch*. 2025;486(2):243-255.

Page 4 Ahn B, et al. Clinicopathologic and genomic analyses of SMARCA4-mutated non-small cell lung carcinoma implicate the needs for tailored treatment strategies. *Lung Cancer*. 2025;201:108445.

Page 5 Katsuragawa H, et al. Location of Fibroblastic Foci: Does the Lesion You Observe Really Suggest Usual Interstitial Pneumonia? *Modern Pathology*. 2025;38(3):100675.

Page 7 Moonen L, et al. OTP, CD44, and Ki-67: A Prognostic Marker Panel for Relapse-Free Survival in Patients with Surgically Resected Pulmonary Carcinoid. *Modern Pathology*. 2025;38(3):100677.

Summaries for Notation

Neoplastic Lung Disease

Page 8 Kawai H, et al. Expression patterns of HNF4α, TTF-1, and SMARCA4 in lung adenocarcinomas: impacts on clinicopathological and genetic features. *Virchows Arch*. 2025;486(2):343-354.

Page 8 Yao Z, et al. Primary pulmonary adenoid cystic carcinoma: A study of clinicopathological features and molecular alterations in twenty-one cases. *Lung Cancer*. 2025;201:108414.

Page 8 Huang L, Petersen RH. Tumour spread through air spaces is a determiner for treatment of clinical stage I non-small cell lung Cancer: Thoracoscopic segmentectomy vs lobectomy. *Lung Cancer*. 2025;201:108438.

Page 8 L'Imperio V, et al. Digital counting of tissue cells for molecular analysis: the QuANTUM pipeline. *Virchows Arch*. 2025;486(2):277-286.

Page 9 Fernandez-Bussy S, et al. Diagnostic performance of shape-sensing robotic-assisted bronchoscopy for pleural-based and fissure-based pulmonary lesions. *Thorax*. 2025;80(3):150-158.

Page 9 Kanathanavanich M, et al. Robotic-Assisted Bronchoscopy for the Diagnosis of Lung Lesions: Experience With the Use of Frozen Sections as an Aid to Confirm the

Localization of Lesions During the Procedure. *Archives of Pathology & Laboratory Medicine*. 2025;149(3):288-292.

Page 9 Zhang M, et al. Site-specific follow-up strategy for surgically resected patients with NSCLC based on ten-year follow-up data. Lung Cancer. 2025 Mar;201:108451.

Page 9 Goffinet S, et al V. EGFR status assessment using reflex testing targeted next-generation sequencing for resected non-squamous non-small cell lung cancer. Virchows Arch. 2025 Mar;486(3):531-539.

Page 10 Németh K, et al. TMPRSS2::ETS translocation in nonprostatic malignancies: an unexpected finding in thymic carcinoma and pulmonary adenocarcinoma. Virchows Arch. 2025 Mar;486(3):627-631.

Non-Neoplastic Lung Disease

Page 10 Kley AC, White AC. Parasitic Infections in Pulmonary and ICU Patients. *CHEST*. 2025;167(3):686-693.

Page 10 Ghanem M, et al. FGF21 Signaling Exerts Antifibrotic Properties during Pulmonary Fibrosis. *American Journal of Respiratory and Critical Care Medicine*. 2025 Mar;211(3):486-498

Reviews, Guidelines, and Consensus Statements

Page 10 Chou TY, et al. Differentiating Separate Primary Lung Adenocarcinomas From Intrapulmonary Metastases With Emphasis on Pathological and Molecular Considerations: Recommendations From the International Association for the Study of Lung Cancer Pathology Committee. *Journal of Thoracic Oncology*. 2025;20(3):311-330.

Page 11 Kattih Z, et al. Interstitial Lung Abnormality. *CHEST*. 2025;167(3):781-799.

Page 11 Hofman P, et al. Reflex biomarker testing in operable non-small-cell lung cancer: current challenges and recommendations. *Lung Cancer*. 2025;201:108107.

Case Reports

Page 11 Hsu YR, et al. YAP1::TFE3 fusion in a case of malignant TFE3-rearranged PEComa of the lung: expanding the spectrum of pulmonary PEComa-like mesenchymal neoplasms. Virchows Arch. 2025 Mar;486(3):621-626

Page 11 Badar F, et al. A 52-Year-Old Woman With Shortness of Breath and Left Lower Back Pain. *CHEST*. 2025;167(3):e83-e87

Page 11-12 Petrarulo S, et al. ABCA3-related interstitial lung disease in a young woman. *Thorax*. 2025;80(3):186-187.

Page 12 Kalsi HS, et al. Endobronchial obstruction of the left middle lobe. *Thorax*. 2025;80(3):184-185.

Page 12 Lérias, S., et al. Molecular characterization of a thymic neuroblastoma in an adult associated with inappropriate antidiuretic hormone secretion syndrome. *Virchows Arch* (2025). https://doi.org/10.1007/s00428-025-04085-7

Articles for Discussion

1) **Zhu Y, et al. Heterogeneity of molecular subtyping and therapy-related marker expression in primary tumors and paired lymph node metastases of small cell lung cancer. *Virchows Arch*. 2025;486(2):243-255.**

Background

- Recent advances in molecular subtyping (NE high - ASCL1, NEUROD1, and NE low- POU2F3, YAP1) and therapy-related markers (DLL3, MYC, PD-L1, MHC I) have provided insights into small cell lung cancer (SCLC).
- However, intertumoral and intratumoral heterogeneity has been reported, particularly between primary tumors and mediastinal lymph node (LN) metastases.
- Purpose: Investigate whether LN metastases accurately reflect the molecular profile of primary tumors.

Methods

Retrospective study analyzing formalin-fixed paraffin-embedded (FFPE) whole tissue blocks from 46 surgically resected SCLC patients with primary tumors and paired LN metastases

- 2 senior pathologists evaluated- Hematoxylin & Eosin (H&E), neuroendocrine (NE) markers (CD56, chromogranin A, synaptophysin).
- Immunohistochemistry (IHC): Additional staining for molecular subtype markers (ASCL1, NEUROD1, POU2F3, YAP1) and therapy-related markers (DLL3, MYC, PD-L1, MHC I).
- Scoring:
    - PD-L1 expression was assessed using a combined positive score (CPS) and percentage positivity.
    - Other markers were evaluated using an H-score (0-300).
- Statistical analysis
    - Correlation between molecular markers and clinical outcome: Spearman's rank correlation, Wilcoxon matched-pairs signed-rank test, and Kaplan-Meier survival analysis.

Results

- Molecular subtyping:
    - Primary tumors and LN metastases showed heterogeneous expression of SCLC subtypes.
    - No single dominant molecular subtype correlated with PD-L1 expression.
- Therapy-related markers:
    - PD-L1 and MHC I expression was less present in LN metastasis versus primary tumor
    - Metastatic tumors
        - NEUROD1 and DLL3 expression was stronger
        - POU2F3, MYC, PD-L1, and MHC I expression was weaker
- 15 patients had a change in molecular subtyping pattern when looking at LN
    - Higher number of NE-phenotypes identified using LN metastasis
- The major subtypes in LN metastasis were SCLC-A (ASCL-1 dominant) and SCLC- AN (ASCL1/NEUROD1), which can be inconsistent with the molecular profile of the primary tumor.
- Prognostic implications:
    - ASCL1 expression correlated with improved progression-free survival (PFS) in primary tumors but not in LN metastases.
    - PD-L1 expression in LN metastases correlated with poor overall survival (OS)
    - No significant difference in OS and PFS between NE-high and NE-low groups in both primary tumor and LN mets
    - TNM and post-operative chemotherapy were independent prognostic markers regardless of molecular subtypes

Take Home Message:

- Molecular subtyping on LN metastasis for SCLC may not accurately reflect the molecular profile of the tumor
- PD-L1 expression might be lower in LN metastasis
- While they did not find a significant survival difference between NE-low and NE-high SCLCs, there was a better outcome in NE-low SCLC, matching literature
- TNM is still independent of molecular subtypes

---

2) Ahn B, et al. Clinicopathologic and genomic analyses of SMARCA4-mutated non-small cell lung carcinoma implicate the needs for tailored treatment strategies. *Lung Cancer*. 2025;201:108445.

Background

- SMARCA4 (BRG1) mutations are increasingly recognized as a distinct subset of non-small cell lung cancer (NSCLC).
- Prior studies have suggested that SMARCA4-mutated NSCLC often presents with aggressive behavior and poor response to standard therapies.
- This study aims to identify the clinical and histologic characteristics of SMARCA4-mutated NSCLC and treatment response and prognosis.

Methods

- Cohort: NSCLC samples from the AMC-NGS NSCLC cohort and The Cancer Genome Atlas (TCGA-LUAD).
- Genomic Analysis: Whole-exome sequencing and targeted panel sequencing were performed to characterize SMARCA4 mutations and co-occurring genomic alterations.
- Histologic Features: Pathologic slides were reviewed by two pathologists for tumor morphology and differentiation patterns. TTF- and PD-L1 immunophenotypes were documented when available. Additional IHC makers for anti-BRG1, TTF-1, MAGEA4, CT45A, and PRAME were performed
- Treatment Response: Clinical outcomes for patients treated with pemetrexed-platinum chemotherapy and immune checkpoint inhibitors (ICI) were analyzed.
- Statistical analysis
    - Chi-squared test or Fisher's exact tests for categorical variables.
    - Kaplan-Meier survival analysis.
    - Cox proportional hazard model for multivariable survival analysis.

Results

- 50 SMARCA4-truncated and 63 non-truncated cases with a control of 462 SMARCA4-wild-type cases
- Clinicopathologic Characteristics:
    - SMARCA4-truncated NSCLC
        - More common in male smokers
        - 75% presented as poorly differentiated adenocarcinoma.
        - Tumors frequently lacked glandular differentiation and had solid or rhabdoid morphology.
    - Non-truncated NSCLC
        - Weaker male predilection, more never-smokers

        - Adenocarcinoma most frequent histologic type
        - Most had solid pattern, but less than in the mutated group
- Genomic Alterations:
    - SMARCA4-truncated group
        - CT45, MAGE, GAGE, CTAG1B, PRAME, and LIN28B were upregulated
        - Frequent co-occurring mutations in TP53 and STK11 were identified
    - SMARCA4-non-truncated showed more frequent driver gene mutations (*EGFR, KRAS, ALK/ROS/RET*)
- IHCs
    - Loss of BRG1 only seen in the SMARCA4-truncated group
    - Focal and diffuse TTF-1 staining was seen in 14% and 34% of SMARCA4-truncated NSCLC
    - SMARCA4-non-truncated cases had lower frequency of immunoreactivity for MAGEA4, CT45A, and PRAME
- Clinical Outcomes:
    - SMARCA4-truncated group had worse OS than the wild-type group
    - Pemetrexed-platinum chemotherapy showed poor clinical benefits in SMARCA4-truncated and non-truncated groups compared to wild-type group
    - Immune checkpoint inhibitors (ICIs) had variable efficacy,

Take Home Message

- SMARCA4-truncated NSCLCs are predominately in male smokers and are more likely to be poorly differentiated adenocarcinomas.
    - Non-truncated were more likely to be conventional adenocarcinomas with no predilection to sex
- Standard chemotherapy and ICIs have suboptimal response rates for both SMARCA4-truncated and non-truncated groups
- Targeting CTA expression could offer a novel therapeutic approach.

---

3) Katsuragawa H, et al. Location of Fibroblastic Foci: Does the Lesion You Observe Really Suggest Usual Interstitial Pneumonia? *Modern Pathology*. 2025;38(3):100675.

Background

- Fibroblastic foci (FF) are considered a hallmark of UIP but can be seen in other fibrotic ILDs
- Study Aim: Does the specific location of FF within lung tissue correlate with a UIP diagnosis versus other fibrotic ILDs (NSIP, fibrotic HP, collagen vascular disease-related ILD)

Methods

- Study Design: Retrospective histopathologic analysis of 83 lung explant specimens.
    - 24 diagnosed with IPF, 11 with idiopathic NSIP, 36 with CV-ILD, 12 with FHP
    - Excluded unclassifiable cases and PPFE
- Histologic Analysis:
    - Reviewed by 2 pathologists
    - Fibroblastic foci were identified and mapped within lung specimens using an annotation tool (HALO-AI imaging software)

- 4 categories of distribution: Peripheral (subpleural, paraseptal), intralobular along alveolar wall, centrilobular, and distorted or dense fibrotic lesion (ie: in fibrotic areas where intact alveoli are not present)
- Counted number of total FFs in each location

Taken from paper- Figure 3

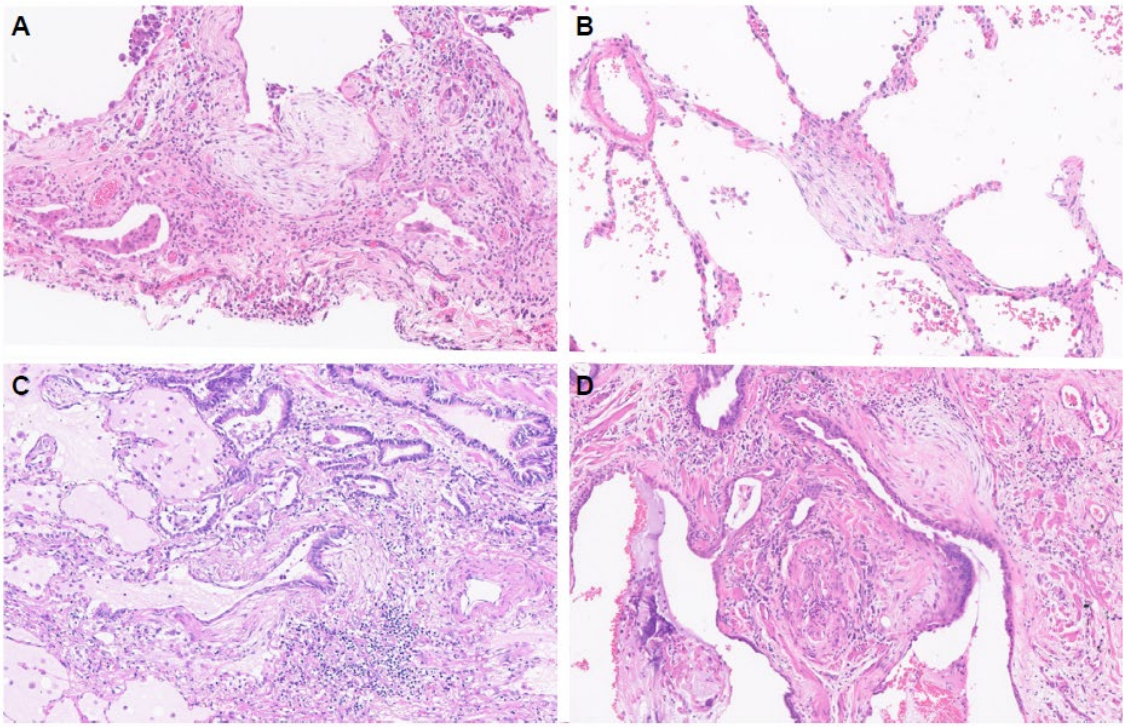

Figure 3.
Examples of the location of fibroblastic foci (FF). (A) Peripheral FF. (B) Alveolar FF. (C) Centrilobular FF. (D) Distorted/dense fibrosis FF.

- Statistical Analysis:
  - Fisher exact tests for categorical variables
  - Kruskal-Wallis and Wilcoxon tests for continuous variables

<u>Results</u>

- Fibroblastic Foci Location:
  - IPF had higher total FFs and higher numbers of pFF and dFF than NSIP and CVD-ILD
  - cFF were observed more in FHP than IPF
  - aFF were higher in CVD-ILD than in FHP

<u>Take Home Message:</u>

- Location of FFs can correlate with ILDs
  - Peripheral and distorted -> IPF
  - Centrilobular -> FHP
  - Alveolar wall -> CVD
- Limitations
  - CVD was heterogeneous group

---

4) **Moonen L, et al. OTP, CD44, and Ki-67: A Prognostic Marker Panel for Relapse-Free Survival in Patients with Surgically Resected Pulmonary Carcinoid. *Modern Pathology*. 2025;38(3):100677.**

Background

- Current prognostic markers are limited for pulmonary carcinoids, and better stratification of recurrence risk is needed.
- CD44, a glycoprotein involved in cell adhesion and metastasis, has been associated with poor prognosis in various cancers.
    - With OTP, both have been identified as molecular markers to ID patients at risk for disease relapse in pulmonary carcinoids
- Ki67's prognostic value in pulmonary carcinoids remains debated.
- Study aim: IHC panel of OTP, CD44, and Ki-67 can better indicated relapse-free survival (RFS)

Methods

- Study Design: Retrospective cohort study on pulmonary carcinoid cases.
    - Match patients with relapse (local and/or distant, n=57) to those without relapse (n=113) for a 1:2 ratio
- 4 pathologists were involved and evaluated
    - Necrosis: Absence/presence, percentage, type
    - Mitotic count: Number of mitoses per 2 mm^2, averaged for 3 fields
- Immunohistochemistry (IHC): CD44 and Ki67 expression assessed via IHC.
- Scoring System:
    - OTP and CD44: Membranous staining intensity and percentage of positive tumor cells.
    - Ki67: Percentage of positively stained tumor nuclei.
- Statistical Analysis:
    - Kaplan-Meier survival curves for RFS. Cutoff values determined using time-dependent areas under ROC curve
    - Cox proportional hazards regression for independent prognostic factors.

Results

- Atypical carcinoid tumors were more common in the relapse cohort
- No significant difference between resection status between recurrence and non-recurrence groups
- Decreased OTP and CD44 expression, increased Ki-67 proliferation index associated with a negative impact on RFS
- Risk stratification shows significant difference in RFS
    - Low risk of relapse (Ki-67 <5% AND OTP H-score >50 AND CD44 H-score >30)
    - High risk of relapse (Ki-67 >5% OR OTP H-score <50 OR CD44 H-score <30)
- Showed high reliability among the pathologists for stratifying risk

Take Home Message

- A combination of OTP, CD44, and Ki-67 can help with the prediction of RFS in pulmonary carcinoids
    - Low risk of relapse (Ki-67 <5% AND OTP H-score >50 AND CD44 H-score >30)
    - High risk of relapse (Ki-67 >5% OR OTP H-score <50 OR CD44 H-score <30)

Articles for Notation

Neoplastic

Kawai H, et al. Expression patterns of HNF4α, TTF-1, and SMARCA4 in lung adenocarcinomas: impacts on clinicopathological and genetic features. *Virchows Arch*. 2025;486(2):343-354.

Purpose: Describe the morphology, IHC, and prognosis of HNFα-mutated lung adenocarcinomas. To note, the paper stratified HNFα-mutated lung adenocarcinomas according to whether they arise from the terminal respiratory unit (TRU) or not.

Take-home message: HNF4α-positive non-mucinous adenocarcinomas represent a distinct subgroup with high-grade morphology, poor prognosis, high frequency of *KRAS* mutations, and frequent SMARCA4 loss.

- HNF4α-positive TRU-type adenocarcinoma showed frequent TTF-1 positivity.

Yao Z, et al. Primary pulmonary adenoid cystic carcinoma: A study of clinicopathological features and molecular alterations in twenty-one cases. *Lung Cancer*. 2025;201:108414.

Purpose: To identify unique molecular alterations and clinical feature associations of adenoid cystic carcinomas (ACCs) originating from the lung.

Take-home message:

- Positive MYB staining with proven MYB rearrangements (n=15, 71.4%). Notch1 gene expression was prominent in solid-basaloid ACCs (n=3) and metastatic ACCs.
- Rate of lymph node metastasis was higher in patients with ACCs without MYB rearrangement.

Huang L, et al. Tumour spread through air spaces is a determiner for treatment of clinical stage I non-small cell lung Cancer: Thoracoscopic segmentectomy vs lobectomy. *Lung Cancer*. 2025;201:108438.

Purpose: Analyze the prognostic significance of STAS for clinical stage I NSCLC- Segments vs. lobectomy

Take-home message:

- Clinical stage I NSCLC patients with STAS, lobectomy is superior to segmentectomy, providing better overall survival and recurrence-free survival.
- Lobectomy is the preferred approach for STAS-positive patients, highlighting need for preoperative STAS assessment.

L'Imperio V, et al. Digital counting of tissue cells for molecular analysis: the QuANTUM pipeline. *Virchows Arch*. 2025;486(2):277-286.

Purpose: The study aims to develop a new computation tool to estimate tumor cellular fraction in non-small cell lung cancers (QuANTUM).

Take-home message:

- AI-based image analysis can be as good as traditional histopathologic assessment with manual counting with comparable tumor cell fraction estimates, though they generally tend to undercount.
- AI is more effective at detecting CNVs previously undetected by pathologists.

Fernandez-Bussy S, et al. Diagnostic performance of shape-sensing robotic-assisted bronchoscopy for pleural-based and fissure-based pulmonary lesions. *Thorax*. 2025;80(3):150-158.

Purpose: This study evaluates the diagnostic performance and safety of radial endobronchial ultrasound (R-EBUS) for detecting pleural and fissure-based lesions

Take-home message:

- R-EBUS provides a high diagnostic yield, particularly for malignancies, while maintaining a favorable safety profile.
- Cryobiopsy had the highest diagnostic yield as compared to forceps and FNA.

Kanathanavanich M, et al. Robotic-Assisted Bronchoscopy for the Diagnosis of Lung Lesions: Experience with the Use of Frozen Sections as an Aid to Confirm the Localization of Lesions During the Procedure. Archives of Pathology & Laboratory Medicine. 2025;149(3):288-292.

Purpose: The study aims to evaluate the diagnostic yield of RAB with FS analysis and compare it with standard bronchoscopic approaches

Take-Home Messages:

- RAB has a high diagnostic yield compared to conventional bronchoscopy, and frozen section analysis demonstrated high concordance with final histopathologic diagnoses.

Zhang M, et al. Site-specific follow-up strategy for surgically resected patients with NSCLC based on ten-year follow-up data. Lung Cancer. 2025 Mar;201:108451.

Purpose: 10 year follow-up results for resected NSCLC patients including recurrence rates based on histology, patterns of adenocarcinoma, TNM stage, and presence of ground-glass opacities (GGO) on imaging

Take-Home Messages: Study involved 2359 patients.

- No recurrence was observed in patients with pure GGO lung adenocarcinomas or lepidic adenocarcinomas.
- For pure solid nodules, squamous cell carcinoma had lower recurrence risk in thorax, brain, and bone.
- TNM stage and vascular invasion correlated with recurrence.

Goffinet S, et al. EGFR status assessment using reflex testing targeted next-generation sequencing for resected non-squamous non-small cell lung cancer. Virchows Arch. 2025 Mar;486(3):531-539.

Purpose: Describe the clinicopathological, molecular features, and prognostic factors of resected *EGFR*-mutant non-squamous NSCLCs evaluated with reflex NGS and RT-PCR

Take Home Message

- 153 patients were evaluated, and almost all had adenocarcinomas (151/153). Most had single common *EGFR* mutations (77% cases)
- RT-PCR had good agreement with NGS to detect an *EGFR* mutation
- 41% of patients had a mutation co-occurring with *EGFR*, *EGFR/TP53*- mutated tumors were associated with positive PD-L1 expression
- Shorter event-free survival was recorded in patients with *EGFR* exon 18 and *TP53* exon 7 mutations

Németh K, et al. TMPRSS2::ETS translocation in nonprostatic malignancies: an unexpected finding in thymic carcinoma and pulmonary adenocarcinoma. Virchows Arch. 2025 Mar;486(3):627-631.

Purpose: TMPRSS2::ETS gene fusion is a common genetic event in prostate carcinoma. This study aims to see if this fusion is present in other nonprostatic malignancies.

Take Home Message:

- NGS analysis of 1758 tumors (68 from prostate, rest from non-prostate malignancies).
- Two non-prostate cancers were found to have a TMPRSS::ETS fusion- lung adenocarcinoma and thymic carcinoma.
- Suggests that this fusion is non-specific and reliance on clinical and immunohistochemical findings takes precedence.

Non-Neoplastic

Kley AC, et al. Parasitic Infections in Pulmonary and ICU Patients. *CHEST*. 2025;167(3):686-693.

Purpose/Take-home message: Case series discussing parasitic infections seen in pulmonary and critical care medicine. No pathology pictures, but a short review.

Ghanem M, et al. FGF21 Signaling Exerts Antifibrotic Properties during Pulmonary Fibrosis. Am J Respir Crit Care Med. 2025 Mar;211(3):486-498.

Purpose: Analyze to see if modified FGF21 could exert antifibrotic properties in the lung. Currently, PEGylated human FGF21 analogs can decrease liver fibrosis in patients with NASH

Take-home message:

- Patients with IPF had higher FGF21 concentrations and decreased KLB concentrations.
- In mice studies, treatment with PEGylated FGF21 mitigated lung fibrinogenesis, and FGF21 and KLB inhibited alveolar type 2 cell apoptosis.

Reviews, Guidelines, and Consensus Statements

Chou TY, et al. Differentiating Separate Primary Lung Adenocarcinomas From Intrapulmonary Metastases With Emphasis on Pathological and Molecular Considerations: Recommendations From the International Association for the Study of Lung Cancer Pathology Committee. Journal of Thoracic Oncology. 2025;20(3):311-330.

Purpose: Updated recommendations from the IASLC Pathology Committee, focusing on pathologic and molecular approaches to distinguish separate primary lung cancers (SPLCs) from intrapulmonary metastases (IPMs).

Take-Home Messages:

- Histologic assessment alone can accurately differentiate SPLCs from IPMs in some cases, particularly when tumors exhibit markedly different histologic subtypes. However, when the histology overlaps, molecular profiling significantly improves classification accuracy.

- Single-gene assessments (e.g., EGFR alone) are inadequate, and a broader mutational and copy number analysis is preferred.

Kattih Z, et al. Interstitial Lung Abnormality. *CHEST*. 2025;167(3):781-799.

Purpose: Radiology review of findings for ILD classification

Take-home message:

- Review describes what features radiologists consider to be interstitial lung abnormalities (ILAs) and the risk of progression based on these findings.
- Algorithm proposed based on ILAs and the percentage of involvement to help with clinical management (pg 795) and a classification system for ILA, high risk for ILD progression, probable ILD, and ILD (pg 796).

Hofman P, et al. Proposal of real-world solutions for the implementation of predictive biomarker testing in patients with operable non-small cell lung cancer. Lung Cancer. 2025 Mar;201:108107.

Purpose: Review detailing 3 challenges and proposed solutions to optimize biomarker testing for NSCLC

Take-home message:

- Biomarker testing in operable NSCLC should be routinely requested
- Practice tissue conserving techniques or use alternative sample types (liquid biopsy, cytology) to allow for sufficient biomarker testing
- Use a multigene NGS panel

Case Reports

Hsu YR, et al. YAP1::TFE3 fusion in a case of malignant TFE3-rearranged PEComa of the lung: expanding the spectrum of pulmonary PEComa-like mesenchymal neoplasms. Virchows Arch. 2025 Mar;486(3):621-626

Summary: 64-year-old with a left lingular lung mass. Histology showed nested and sheet-like growth of large epithelioid cells with eccentric nuclei, prominent nucleoli, and abundant granular eosinophilic cytoplasm. TFE-3 was diffusely positive.

Diagnosis: TFE3-rearranged malignant perivascular epithelioid cell tumor (PEComa) harboring a YAP1::TFE3 gene fusion.

Badar F, et al. A 52-Year-Old Woman with Shortness of Breath and Left Lower Back Pain. *CHEST*. 2025;167(3):e83-e87

Summary: 52-year-old with worsening shortness of breath and left lower back pain. PET scan showed avid consolidation in LUL measuring 4.8 x 3.9 (SUV 10.6) and LLL measuring 8.7 x 5.2 (SUV 13.4).

Diagnosis: Primary pulmonary Hodgkin lymphoma (PPHL).

Petrarulo S, et al. ABCA3-related interstitial lung disease in a young woman. *Thorax*. 2025;80(3):186-187.

Summary: 25-year-old who presents with a 6-month history of progressive exertional dyspnea, chest pain, and mild hemoptysis.

Diagnosis: Cryobiopsy showed mixed NSIP-like pattern with diffuse pneumocyte hyperplasia and alveolar hemorrhage. NGS found a germline ABCA3 gene mutation- Notable as ABCA3 plays a role in normal surfactant production and alveolar capillary development.

Kalsi HS, et al. Endobronchial obstruction of the left middle lobe. *Thorax*. 2025;80(3):184-185.

Summary: 48-year-old former smoker with 1-year history of breathlessness, persistent cough, and recurrent chest infections. CT scan found an obstructing lesion in left bronchus

Diagnosis: Polypoid endobronchial lipoma.

Lérias, S., et al. Molecular characterization of a thymic neuroblastoma in an adult associated with inappropriate antidiuretic hormone secretion syndrome. *Virchows Archive* (2025). https://doi.org/10.1007/s00428-025-04085-7

Summary: 72-year-old male presenting with SIADH syndrome and an anterior mediastinal mass

Diagnosis: Neuroblastoma with copy number alterations of chromosome 3 and gain of *PIK3CA* gene