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Articles for Discussion

MUC4, a novel immunohistochemical marker identified by gene expression profiling, differentiates pleural sarcomatoid mesothelioma from lung sarcomatoid carcinoma.


Background: consensus on the IHC markers that differentiate sarcomatoid mesothelioma from lung sarcomatoid ca has not been reached. Histologic dx of sarcomatoid meso largely depends on the morphologic features, CK positivity and clinic-radiological and/or gross evidence of an extrapulmonary location. Calretinin and D2-40 are two commonly used positive markers for sarcomatoid meso, while no useful IHC markers for lung sarcomatoid ca are widely available.

Methods:

• Cases: 2005-14 SM (n=31) and lung SC (n=29) cases in one institution; dx based on clinical, gross, histologic findings; all SM located in extrapulmonary with pleurotrophic growth, all lung SC in lung parenchyma. Pathol dx confirmed by histologic findings and IHC panel.

• Gene expression analysis on 6 cases of SM and SC, each, FFPE tissue and validation of microarray expression data for relative quantitation.

• IHC: MUC4 (8G7, Santa Cruz Biothecnology), calretinin, D2-40, WT-1, AE1/AE3,p40, TTF1 (SP141), claudin-4

Results: Several novel genes are differently expressed between SM and SC.
• Real-time RT-PCR validated that MUC4 mRNA expression is negligible in all six SM and expression was observed in 5 of 6 lung SC.

• IHC profiles was expressed in 21 of 29 the lung SC (72%) but in none of SM (0/31, 0%).

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aCalculated by Fisher’s exact test of the positive rate between two groups.

Immunohistochemical score was semiquantified as follows: 0: 0%; 1+: 1–10%; 2+: 11–50%; 3+: >51% of spindled tumor cells.

Take home point:

MUC4 may be a additional helpful marker in the ddx of SM and lung SC.

Shared genetic predisposition in rheumatoid arthritis-interstitial lung disease and familial pulmonary fibrosis.


Background: RA-ILD is associated with higher mortality but its pathogenesis is not well studied. RA-ILD frequently present as UIP pattern compared to other connective tissue diseases. Familial pulmonary fibrosis (FPF) and RA-ILD share common risk factors such as smoking and the male sex. They hypothesized that RA-ILD and FPF share genetic risk factors and performed whole exome sequencing (WES) in RA-ILD patients to determine the contribution of mutations in genes previously linked to FPF.

Methods:

• Sturdy subjects: 101 consecutive independent RA-ILD patients recruited by a French network of ILD-expert pulmonologists and RA-expert rheumatologists from 10 university hospitals during 2013-15. 1010 in-house subjects without known autoimmune/inflammatory and/or pulmonary diseases served as healthy controls were.

• WES followed by restricted analysis of FPF-liked genes in RA-ILD patients. Then, TERT and RTEL1 molecular modelling and three-dimensional structural visualization, genotype-phenotype association analyses. Statistical analyses including power calculation, ancestry-inference analysis and burden test by excluding all outlier patients to avoid population stratification bias (i.e. adjustment for more stringent clustering of 100G subjects of European ancestry.)
Results:

Discussion: This genetic case-control association study provided evidence for an association between a panel of candidate genes (FPF-linked genes) and the “RA-ILD” phenotype (i.e. susceptibility to RA-ILD vs. controls). But the results do not provide information about the roles of these genes in 1) susceptibility to overall RA (RA vs. controls) or the 2) the risk of ILD in the RA population. Need for more study.

Take home point: Familial pulmonary fibrosis-linked genes including TERT, RTE1, PARN or SFTP may also contribute to RA-ILD susceptibility.


Background: Although PD-L1 expression in a tumor has been shown to correlate with antitumoral effect by PD-1 inhibitor therapy, dependence on PD-L1 expression alone for patient selection for tx has been challenged. The interaction of immune cells and cancer cells shapes the immunosuppressive tumor microenvironment. For successful cancer immunotherapy, comprehensive knowledge of antitumor immunity as a dynamic spatio-temporal process is required for each individual patient. The
authors developed an immunogram for the cancer-immunity cycle by using NGS. Cancer-immunity cycle (CIC) consists of 1) Release of cancer Ag’s, 2) cancer Ag presentation, 3) priming and activation, 4) trafficking of T cells to tumors, 5) infiltration of T cells into tumors, 6) recognition of cancer cells by T cells, and 6) killing of cancer cells. Many ways to evaluate the antitumor immune responses, many strategies have been used. Recently, Blank et al (Science 2016;352:658-60) proposed the concept of the cancer immunogram to visualize general and local cancer immunity status in each patient. The concept was theoretically applied but not tested in practice. This study was done to develop an immunogram reflecting the CIC and applied to real patients with lung cancer for potential application for personalized cancer immunotherapy.

**Methods:** Whole exome sequencing and RNA sequencing were performed in 20 NSCLC patients (12 ADC; 7 with EGFR mutation, 7 SQC, 1 LCNEC) with resection but without any preop tx. All tumor and adjacent normal lung tissue samples obtained immediately after lung resection were stored in RNAlater RNA Stabilization Reagent (Qiagen, Hilden, Germany). DNA and RNA samples were prepared using either AllPrep DNA/RNA Mini Kits or AllPrep DNA/RNA/miRNA Universal Kits (Qiagen) according to the manufacturer’s protocol. Mutated neoantigens and cancer germline antigens expressed in the tumor were assessed for predicted binding to patients’ human leukocyte antigen molecules. The expression of genes related to cancer immunity was assessed and normalized to construct a radar chart composed of 8 axes reflecting seven steps in the cancer-immunity cycle (CIC). IHC was performed on FFPE for T cell and Tregs by CD3, CD8, FOXP3, and counterstained with hematoxylin. Images were captured and the positively stained area was quantified digitally with an image analysis software.

**Results:** Immunological status of an individual patient in terms of the cancer-immunity cycle can be depicted by the eight axes of immunogram scores (IGSs): IGS$_1$, existence of T-cell immunity in the tumor; IGS$_2$, tumor antigenicity; IGS$_3$, priming and activation; IGS$_4$, trafficking and infiltration; IGS$_5$, recognition of tumor antigens; and IGS$_6$ to IGS$_8$, suppressive factors inhibiting killing of cancer cells. IDO1, indoleamine 2,3-dioxygenase 1; ARG1, arginase 1; CG, cancer germline; PD-1, programmed cell death 1; PD-L1, programmed death ligand 1; aDC, activated dendritic cell; Treg, regulatory T cell; MDSC, myeloid-derived suppressor cell; HLA, human leukocyte antigen; CXCL9, C-X-C motif chemokine ligand 9; CCL5, C-C motif chemokine ligand 5.
Figure 5. Immunogram for the cancer-immunity cycle of 20 patients with NSCLC.

Axis 1 (IGS₁) represents putative existence of T-cell immunity in the tumor, axis 2 (IGS₂) represents tumor antigenicity, axis 3 (IGS₃) represents priming and activation of T cells, axis 4 (IGS₄) represents trafficking and infiltration, axis 5 (IGS₅) represents recognition of tumor antigens, axis 6 (IGS₆) represents absence of inhibitory immune cells, axis 7 (IGS₇) represents absence of immune checkpoint molecules, and axis 8 (IGS₈) represents absence of other inhibitory molecules. Immunograms of an individual patient with a T-cell–rich phenotype (A), an individual patient with a T-cell–intermediate phenotype (B), and a patient with a T-cell–poor phenotype (C). (D) Overlaid immunograms of nine patients with a T-cell–rich phenotype, five with a T-cell–intermediate phenotype, and six with a T-cell–poor phenotype. (E) Overlaid immunograms of adenocarcinomas with and without EGFR mutation (mut) and nonadenocarcinoma tumors.
Take home point: Now, personalized immunotherapy!

Aims: To evaluate PD-L1 expression by IHC together with genome-wide copy number alterations and immune infiltrate signature with clinicopathologic correlation in the largest already published cohort of 329 patients with malignant pleural mesothelioma (MPM).

Methods:

- Tissue microarrays were constructed and stained with PD-L1 (E1L3N, Cell Signaling Technology, Danvers, MA), CD4, CD8, and FOXP3.

- PD-L1 positivity is defined as ≥5% membranous positivity while high PD-L1 positivity as ≥50%. IHC scoring was by 4 investigators.

- Quantitation for CD4+, CD8+, FOXP3+ lymphocytes was performed by Leica Aperio ositive pixel count algorithm, and expressed as the # of cells /1000 tumor cells. A subset was validated by manual count. an average of the counts i all

- Genomic DNA from a representative subset of 113 patients was used for genome-wide copy number anlysis. 1mm cores were taken from tumor blocks corresponding to sections marked by a
pathologist author. Copy number profiles were studied by OncoScan Express SNP arrays (Affymetrix, Santa Clara, CA) and data were processed with Nexus Express. % genome alteration was computed as a proxy for genomic instability, and statistical analyses were used to relate copy number aberrations to other variables.

Results:

• IHC: 130 of 311 (41.8%) evaluable MPM were PD-L1+ and 30 (9.64%) were high PD-L1+; Strong correlation between PD-L1 expression and non-epithelioid histologic subtype. PD-L1+ tumors showed significantly increased CD4+ and CD8+ cell infiltration but not FOXP3+ cell infiltration; high PD-L1+ tumors have had higher level of infiltration in all types of T-cells.

• Patients with PD-L1+ tumors had a trend toward poorer OS (p=0.15). Those with high PD-L1+ tumors were associated with a significant worse survival (p<0.001) in univariate analysis but not in multivariate analysis.

• Higher % genome alteration was associated with epithelioid histological subtype and poorer survival (p=0.04) but not with PD-L1 expression.

Take home point: PD-L1 expression was associated with non-epithelioid MPM, poor clinical outcome, and increased immune infiltrates. Increased genomic instability did not correlate with PD-L1 expression but was associated with poorer survival.

Histological analysis of vasculopathy associated with pulmonary hypertension in combined pulmonary fibrosis and emphysema: comparison with idiopathic pulmonary fibrosis or emphysema alone.


Background: CPFE patients often have PH as do IPF and COPD patients. Little has been reported on the pathological features of pulmonary vasculatures, esp. in whole lung tissue. This study was to evaluate the pulmonary vasculopathy in an autopsy series of patients with CPFE and compare with the findings in IPF alone and emphysema alone.

Methods: From 1613 subjects who attended the Japanese Red Cross Medical Centre from 12/1992-7/2015, they selected 16 CPFE, 11 IPF alone, and 23 with emphysema cases with available clinical data as well as compatible HRCT and dx of PH based on 5th World Symposium on PH in Nice. Patients with connective tissue disease, drug-induced lung disease, HP or other forms of secondary IP were excluded. Pts with PH related to left heart ds, CTEPH, portal hypertension, congenital heart ds or HIV infection were also excluded. Pulmonary vasculopathy was evaluated with the following procedure: 1. Fibrotic, emphysematous and preserved areas of each tissue were chosen, 2. Three pulmonary arteries (200-300 µm in diameter) accompanying the respirator or terminal bronchioles were randomly selected from each area, 3. Vasculopathy was evaluate according to the Heath-Edwards scoring system,
4. Three scores were averaged to give a final score of the area, 5. Cellular and/or fibrotic intimal thickening and muscularization in the interlobular veins and venules were assessed in the same areas selected above, and 6. Changes such as medial hypertrophy and/or intimal thickening in the arterioles along the alveolar ducts (<100 µm) were evaluated in the same areas.

Results: Age, sex, smoking hx in three groups were similar. DLco was significantly lower (p=0.001) in CPFE and trend of higher eSPAP by Echo (46 mmHg, range 40-51; p=0.052). In the fibrotic, emphysematous and preserved areas in the CPFE group, arteriopathy and venous-venular changes were worse in the fibrotic area than in the emphysematous and preserved areas. No significant differences in arteriolar changes were identified among these areas, however. Among the CPFE, IPF and emphysema groups, there are no significant differences in the arterial or venous-venular abnormalities in the fibrotic and emphysematous areas. However, in the preserved area, CPFE group showed more prevalent arteriolar and venous-venular changes than IPF and emphysema groups.

Discussion: Limitation of this study includes no right heart cath data available except 1 pt, small number of patients with selection bias. CT criteria of PH (pulmonary trunk diameter of >28.6mm, main PA/asc aorta diameter ratio of >1) were met in only a few CPFE patients, suggesting that few of them may have developed clinical PH as well.

Take home point: Pulmonary arterial-arteriolar and venous-venular changes in the preserved area in CPFE patients may play a role in the pathogenesis of PH.

Articles for Notification

Neoplastic


Background: Sarcomatoid ca (SC) of the lung based on the current WHO2015 criteria may include heterogeneous group of cases that likely include unrelated clinicopathologic entities. Recent advances in the IHC and molecular characteristics of SC allowed a different diagnostic approach and the need for identifying parameters that could facilitate reclassification of such tumors. They proposed a novel
approach to the classification of SC in an attempt to streamline clinical management and identify patients who would benefit from targeted therapies.

**Methods:** 86 cases of SC (17 pleomorphic and 12 spindle cell ca) found in the surg path file of MD Anderson Cancer Center was reclassified according to the following algorithm. Of note, they excluded carcinosarcomas and biphasic pulmonary blastomas as they consider them as different clinicopathologic entities.

Based on the new system, they were able to reanalyze the spectrum of these lesions as ACA, sarcomatoid type (n=36, 42%), SQCC sarcomatoid type (n=13, 15%), dediff ACA (n=13, 15%), LCC sarcomatoid type (n=24, 28%). T stage was the only factor associated with prognosis on multivariate analysis.

**Take home point:** They purported that their new classification system of SC would more accurately guide patient management and facilitate targeted therapies.

**Prognostic impact of GATA binding protein-3 expression in primary lung adenocarcinoma.** Hashiguchi T et al. *Hum Pathol* 2017;63:157-64

**Background:** GATA3 expression may be seen in mammary luminal gland, Th2 lymphocytes, CNS, kidney, and hair follicles of the skin, etc. Several tumors have been reported to be positive for GATA3 including breast and bladder ca; decreased GATA3 expression in these two tumors is associated with poor px. On the other hand high GATA3 expression in neuroblastoma or soft tissue sarcomas may portend a poor survival. Reports are not available in on GATA3 expression in relation to clinicopathologic features and patient survival in primary lung cancer. This study was designed to
investigate the association between GATA3 expression and lung ADC, for a potential use of GATA3 immunohistochemical expression as a prognostic marker.

**Methods:** 95 completely resected lung ADC cases collected in a single institution during 2007-9, excluding those who had chemo and/or radiation therapy before surgery, path stage IIB and IV, or cases with metachronous lung cancer. GATA3 IHC was performed and scored. Association between GATA expression and clinicopathologic factors including survival (OS, DFS) were analyzed.

**Results:** 49 cases with high GATA3 expression were associated with lymphatic and vascular invasion, and identified as independent risk factors for worse OS and DFS.

**Take home point:** GATA3 IHC could be a potential prognostic marker.


**Background:** 1-2% of NSCLCs show ROS1 rearrangement, usually associated with never smoking history, younger age and ADC histologic type. 72% of Patients with NSCLC harboring ROS1 fusion can respond to ROS1-targeted therapy. 71-80% of ROS1 fusion respond to crizotinib. Although genetic alterations of KRAS, EGFR, and ALK, main oncogenic drivers in NSCLC, are generally regarded mutually exclusive, there have been some conflicting findings in the literature.

**Methods:** From MGH, they identified patients who underwent ROS1 testing (FISH, targeted RNA sequencing, FoundationOne NGS or a commercial real-time PCR assay) along with testing of additional oncogenes including KRAS, EGFR and ALK testing. Clinicopathologic features and genetic testing results were reviewed.

**Results:** Among 62 patients with ROS-rearranged NSCLC in their cohort, none harbored concurrent ALK fusions or EGFR activating mutations, while 2 cases (3.2%) had KRAS mutations. No concurrent mutations in BRAF, ERBB2, PIK3CA, AKT1, MAP2K1.

**Take home point:** ROS1 rearrangements rarely overlap with alterations in other targetable oncogenes.

*Overexpression of Rsf-1 correlates with poor survival and promotes invasion in non-small cell lung cancer.* Zhang X et al. Virchows Arch 2017;470:554-60

**Background:** Among the genes within the 11q13.5 amplicon, Rsf-1 (also known as HBXAP) has been proposed as a candidate cancer-associated gene with the highest correlation between DNA copy number and RNA copy number in ovarian cancer tissues. The role of Rsf-1 in the lung has not been known.
Methods: 61 patients with primary lung cancer treated with resection (2005-2007) in a hospital in China underwent IHC. Using cell lines, they performed siRNA tx, western blot analysis, Matrigel invasion assay and luciferase reporter assay as well.

Results/Take home point: They demonstrated that Rsf-1 was overexpressed in lung cancer and associated with poor survival. Rsf-1 regulated cell invasion through MMP2 and NF-κB pathway. Another potential prognostic marker...


Background: A study, participated by Ventana, Caris, and Pfizer, presented data on the Ventana ALK (D5F3) CDx Assay.

Methods: NSCLC specimens prospectively tested for ALK status by FISH in the PROFILE 1014 clinical trial of crizotinib vs. chemotherapy (n=1,018, including 178 ALK+ and 754 ALK- specimens) were evaluated using the ALK (D5F3) CDx Assay. Hazard ratios for PFS comparing crizotinib and chemo for ALK-IHC+ pts and ALK-FISH+ pts, as well as for concordance with the enrollment ALK FISH assay were determined.

Results/Take home point: overall agreement rates were 94.3% with 53 discrepant cases, of which 25 were ALK-FISH+/IHC- and 28 were ALK FISH-/IHC+. Between-reader agreement rates for ALK IHC involving three independent laboratories were >98%. The hazard ratios using observed outcomes were 0.401 for ALK FISH+/IHC+ and 0.407 for all ALK-FISH+ cases tested with ALK-IHC vs. 0.454 for all ALK-0FISH+ cases enrolled in the trial. ALK IHC provides an effective option to accurately and rapidly identify patients with ALK+ NSCLC. The outcome data for ALK FISH-/IHC+, the most pressing question, were not available for analysis, however.


Background: Somatic mutations in ERBB2 have been reported in 1-2% of lung ADC and previous case series have suggested clinical tumor responses using anti ERBB2 small molecules and antibody therapies.

Methods: They reported the outcomes of 9 patientst with metastatic lung ADC with ERBB2 mutations being treated with ERBB2-targeted therapies.

Results/Take home point: 4 of their 9 patients responded with duration of response ranging from 3-10 months, with subsequent PIK3CA mutation and ERBB2 copy number gain as potential resistance
mechanisms. Yet another potential targeted therapy and providing with more rationale for the NGS panel testing of advanced NSCLCs.

**Comaprisson of segmentectomy and lobectomy in stage IA adenocarcinomas.** Zhao ZR et al. J Thorac Oncol 2017;12:890-96

**Background:** They compared the survival after lobectomy and segmentectomy among pts with pathological stage IA ADC having pT1b tumor (size 2cm or less) by 8th AJCC TNM system

**Methods:** 7,989 patients were identified in the registry and propensity scores generated from logistic regression on pre op characteristics were used to balance the selection bias of undergoing segmentectomy. OS and lung cancer-specific survival were compared in propensity score-matched groups.

**Results/Take home point:** 564 (7.1%) underwent segmentectomy. Pts with lobectomy was better in OS and lung cancer-specific survival for the entire cohort. However, after 1:2 propensity score matching, segmentectomy (n=552) was no longer associated with worse survival. This study suggests that patients in stage IA with pT1a tumor may be potentially treated with segmentectomy provided that it is confirmed by prospective randomized trials.

**Correlation between classic driver oncogene mutations in EGFR, ALK, or ROS1 and 22C3-PD-L1 >50% expression in lung adenocarcinoma.** Rangachari D et al. J Thorac Oncol 2017;12:878-83

**Background:** A retrospective study from Beth Israel Deaconess to examine the frequency of overlap between EGFR, ALK and ROS1 abnormalities and PD-1 expression that are often tested for selection of first-line therapies in advanced lung cancer.

**Methods:** 71 pairs of patients with lung ADC were analuzed for PD-L1 by IHC using 22C3 pharmDx kit and evaluad for co-occurrence of genomic aberrations and clinicopathologic characteristics.

**Results/Take home point:** specimens included surgical resection, small bx’s (core needle or Tbbx), and cytology cell blocks. A PD-L1 tumor proportion score of ≥50% was seen in 29.6% of tumors. Of 19 tumors with EGFR mutations, ALK FISH+, or ROS1 FISH+ tumrs, 18 had a PD-L1 score less than 50% and only 1 showed PD-L1 score of at least 50%. Tumors with a PD-L1 score of at least 50% were significantly associated with smokingstatus compared with tumors with a PD-L1 score of less than 50%. PD-L1 core of ≥50% seldome overlaps with presence of driver oncogenes with approved targeted therapy. Possible grouping of the tumors for tx decision: oncogene+/PD-L1 enriched/all biomarker-.

Take home point: LAG3 is expressed on TILs in some NSCLC patients and its expression was higher in nonADC and correlated with PD-1/PD-L1 expression and poor px. Another emerging prognostic marker that may or may not stand the test of time.

Precision immunotherapy; dynamics in the cellular profile of pleural effusions in malignant mesothelioma patients. Lievense LA et al. Lung Cancer 2017;107:36-40

Take home point: A proof of concept study with limited sample size that showed the composition of pleural effusion is dynamic and influenced by tx and also the immune cell composition of pleural effusion may not reflect the status in the tumor tissue.


Take home point: As in other non-Caucasian populations, the number needed to test to identify one ALK+ patient was much lower in never smokers at 9, as opposed to 22 and 293 in light and heavy smokers, respectively.


Background: Expression of p16 and cytogenetic abnormalities of CDKN2A were correlated with clinical features and outcome in a large cohort of thymic carcinomas at Mayo Clinic Rochester

Methods: 27 thymic carcinomas identified over a 50 year period (1963-2013) were stained with p16 and underwent FISH for CDKN2A.

Results/Take home point: Loss of p16 expression was seen 12 of 26 pts (46.2%) and correlated homozygous CDKN2A deletion that was seen in and 4 of 22 (18.2%). Loss of p16 expression was associated with worse recurrence and metastasis free survival as well as OS. Thymic sq cell ca patients with loss of p16 expression were younger. Both could be potential prognostic biomarkers in thymic carcinomas and also suggest a potential role for CDK4/6 inhibitors.
Recurrent NAB2-STAT6 gene fusions in oestrogen receptor-a expression in pulmonary adenofibromas. Fusco N et al. Histopathology 2017;70:906-17

**Take home point:** They studied 7 cases of adenofibromas for IHC and EM and also performed molecular study on microdissected sampled to evaluated the presence of NAB2-STAT6 fusion genes and MED12 exon 2 mutations in their discrete components. As controls, SFT, pulmonary hamartomas and breast fibroadenomas was also analyzed. They found that the stromal elements pertain to the fibroblastic lineage and show ER overexpression in 71% while the epithelium consists of TTF1/e-cadherin+ bronchiolar elements. A highly recurrent NAB2-STAT6 fusion variant (exon 4-exon 2) was detected only in the stroma, but not in the epithelium. No MED12 mutations were identified. Pulmonary adenofibromas harbor the molecular hallmark of SFT and thus might be related to SFT.


**Take home point:** Circulating (cell-free) nucleic acids (cfDNA/cfmiRNAs) epigenetically modulated during cell transformation. Hypermethylation of tumor suppressor genes is frequently observed in cancers, and such epigenetic changes are potential markers for detecting and monitoring tumors. Moreover, the same predictive biomarkers can be used as therapy targets, maybe one day!


**Take home point:** This study reports that younger patients (<40 of age at dx) showed a distinctly unique prevalence of oncogenic genetic alterations including ALK (p<.001), HER2 (p<.001), ROS1(p=.033), and RET (trend only p=.108), which is not a huge surprise.

Non-neoplastic


**Background:** This study sought to determine the test characteristics of non-definitive HRCT patterns for histopathological UIP.

**Methods:** Patients with bx-proven ILD and non-definitive HRCT scans were identified from UCSF and Mayo Clinic Rochester. Test characteristics for HRCT patterns as predictors of UIP on surgical lung bx were derived and validated in independent cohorts.
Results: In the test cohort, 64 of 385 (17%) had possible UIP pattern on HRCT; 31 of 385 (83%) had inconsistent with UIP pattern. 113 of 385 (29%) patients had histopathological UIP pattern in this cohort. Possible UIP pattern had a specificity of 91.2% and a positive predictive value (PPV) of 62.5% for UIP on surgical lung bx. The addition of age, sex and total traction bronchiectasis score improved the PPV. Inconsistent with UIP pattern demonstrated poor PPV (22.7%). HRCT pattern specificity was nearly identical in the validation cohort (92.7%). The substantially higher prevalence of UIP pattern in the validation cohort improved the PPV of HRCT patterns.

Take home point: A possible UIP pattern on HRCT has high specificity for histopathological UIP but the PPV is highly dependent on the underlying prevalence of histopathologic UIP in the population. Thus, they showed that in some settings, the inclusion of additional clinical and radiographic information to non-definite imaging findings is required to identify groups of pts with a high probability of histopathological UIP.

Fluorescent quantitative PCR detection of Mycobacterium tuberculosis in tissue sections from granulomatous lesions retrieved using EDTA. Wang X et al. J Clin Patho 2017;70:390-4

Take home point: Compared to AFB or Auramine O stains and amplicafication of fluorescent quantitative PCR without EDTA retrieval, fluorescent quantitative PCR with EDTA retrieval improves detection rate of TB/non-TB mycobacteria and increases the sensitivity.

Reviews, Letters, Editorials


Background: They sought to address MGMT as a biomarker in the oncogenesis and opportunity of turning this gene into a drugable target in NETs of the lung. Studies on brain tumors have shown that MGMT promoter methylation is considered a strong predictive factor for a favorable outcome of tx with temozolomide, an alkylating agent.

Methods: A systematic literature review of MGMT in NSCLC and SCKC and other lung NETS to evaluate whether MGMT is a prognostic and.or predictive factor to select pts with lung cancer who can benefit from tx with temozolomide.

Results/Take home point: In NSCLC MGMT promoter methylation is not a prognostic and predictive factor, hence termozolamide has no place, while SCLC and NET patients with a MGMT promoter methylation has yet to be confirmed, suggesting it as a potentially personalized treatment.
Advances in the diagnosis and management of well-differentiated and intermediate-differentiated neuroendocrine tumors of the lung. Wolin EM. Chest 2017;151:1141-6

Mostly discusses the treatment options for the typical and atypical carcinoid tumors of the lung.


A nice review on CTC, which would be a good preparation for this technique coming to our door eventually, though not yet for the prime time.


A generic but updated review on diagnostic approaches for ILDs.


Very nice update on PH with all recent literature that should be a handy reference.


The immune score as a further prognostic indicator in carcinoid tumors. Roncati L et al. Chest 2017:151:1186

A very short letter to the editor asserting that “brisk” TIL in carcinoid tumor correlates with good px and vice versa.


I think macrophage is always a potential culprit for many diseases in the lung....


A historical review.
