ARTICLES FOR DISCUSSION

1- New IASLC/ATS/ERS Classification and Invasive Tumor Size are Predictive of Disease Recurrence in Stage I Lung Adenocarcinoma. Yanagawa et al. JTO 2013; 8: 612

**Background**
- Approximately 20-30% of stage I lung cancer patients will die of recurrent disease
- The prognostic impact of the new proposed classification of lung adenocarcinoma has been studied but few have looked at the significance of size of invasion versus overall tumor size

**Methods**
- Prospectively maintained database of lung cancer 1998-2007, identified 191 adenocarcinomas stage I
- Mean 2.5 slides reviewed per case
- New classification used
  - each histologic components in 5% increments
  - overall classification based on predominant pattern
  - Secondary predominant pattern and lepidic pattern studied as well
    - Lepidic 0%, 5-35%, 35-70%, more than 70%
- 2 tumor sizes
  - The overall total tumor size 1cm or less, 1-2, 2-3, more than 3
  - Size of invasion, 0.5cm or less, more 0.5 to 1, 1-2, 2-3 and more than 3
- Visceral pleural invasion and LVI

**Results**
- 11 AIS (5.8%), 17 MIA (8.9%), 51 LP (26.7%), 52 PP (27.2%), 40 AP (20.9%), 20 SP (10.5%). No MP, no other histologic subtypes.
- Almost all (92%) treated by lobectomy and almost all (82%) had lymph node dissection
- Compared clinical path between different histologic subtypes. Stats significant for
  - Smoking history (more in solid)
  - Stage (AIS and MIA more stage IA)
  - LVI (none in AIS and MIA)
  - % lepidic component
  - Invasive tumor size
- 26 events either recurrence or DOD, med FU 61.4 mo
- DFS AIS-MIA 100%, LP 95%, PP 85%, AP 90%, SP 54%
  - Predominant growth pattern correlated with DFS
  - Total tumor size did not correlate with DFS
  - Size of invasion correlated
Lepidic component (35% and more better) and LVI also correlated, not 
pleural invasion

HR for solid vs non solid 4.08
HR for size of invasion 2.04
No mention of the secondary predominant….

Conclusion
- The main interest and significance is size of invasion would matter more than 
  overall size
- Histology matters but limited by lack of some of the other subtypes and basically 
  solid vs all others…..

2- Identification of Stage I Non-small Cell Lung Cancer Patients at High Risk for 
143:1365

Background
- The only published randomized clinical trial (the CALGB one is still ongoing) 
dates to 1995 and showed that recurrence rate was higher for sublobar resection 
(L-) compared to lobectomy (L+) with no differences in morbidity and mortality. 
No mention of differences in patterns of recurrence or associated factors

Aim
- Determine if incidence of L- increased since that time
- Look at differences in recurrence patterns
- Identify any risk factors that increases recurrence

Methods
- 2000-2006 all surgically resected patients with FU > 3 mos, no 2\textsuperscript{nd} 
  ary, no neo or adjuvant Radiation
  - 93 L- and 318 L=
- Looked at many (too many to list) clinical, surgical-related and histologic 
potential risk factors
- LR as ipsilat and N1-N3 vs DR
- Used SEER for aim 1
- Literature search for all publications on sublobar resection since 1995 (extensive 
in Table 8)

Results
- Patients with L- were older, worse lung function, fewer LN removed, smaller 
tumor size, lower T, shorter hospital stay, less chemo
- LR rate was not stat significant between both groups. At 2 years the same, but at 3 
  yrs increases in L- vs L+ group 23.9% vs 18.7% and 5 yrs 39.5 vs 24.6%
- For recurrence risk factors for 
  - L-, tumor size, tumor grade, and T1
  - L+, tumor size, LVI, Db, length hospital stay (LOS), RUL and in 
multivariate tumor size, DB, LOS
- LR more at the stump/staple line otherwise no differences in pattern and no 
difference in DR
• Survival rates 2, 3, 5yrs L- 84.5, 79.5 and 54.5%, L+ 90.5, 80.7, 64.5%, crude death rate 36.6 vs 25.2% (no comment if stat diff or not)
• For survival rate, risk factors for
  o L-, DB, tumor grade, age
  o L+, LVI, DB, tumor grade, LOS, histologic type
• Since 1995, increase in L- from 14-17% to 18-24% (despite the results from the 1995 studies)

Conclusions
• Make a point stating that comparison between studies on L- difficult because so many variables and defined/analyzed or not differently (in this study not much they didn’t analyzed)…. Their study does suggest increase in LR for L-, particularly in stump/staple line for tumors larger than 2 cm and higher grade….In fact grade was more predictive….Consider additional local therapy for better control in L- patients
• Still need to wait and see the outcome of CALGB study

3- Visceral Pleural Invasion Classification in Non–Small-Cell Lung Cancer in the 7th Edition of the Tumor, Node, Metastasis Classification for Lung Cancer: Validation Analysis Based on a Large-Scale Nationwide Database. Kawase et al. JTO 2013; 8:606

Background
• In 7th Ed of TNM, pleural invasion is classified as PL0, PL1 beyond the elastic layer, PL2 to the pleural surface, PL3 into parietal pleura. VPI = PL1 and :PL2 such as T1 size tumors with VPI are upgraded to T2 where T2 size tumors with VPI are not upgraded.
• This decision based on 5 retrospective studies and not on a large scale data base like used for the rest of TNM i.e. IASLC project.

Aim
• Retrospective analysis of over 5,000 patients from data submitted from 253 Japanese institution to Japanese Joint Committee of Lung Cancer Registry

Methods
• Retrospective registry study in 2010 on the outcome and clinicopathologic profiles of resected primary lung neoplasms in Japan.
  o Only primary lung cancers with FU at least 5 years
  o Extensive registry questionnaire for clinical, surgical, treatment, pathologic and outcome information. No info on how institutions evaluate VPI (and no pathologic review all questionnaire based).

Of the 11,663 patients, 4995 patients (42.8%) underwent curative resection for T1aN0, T1bN0, T2aN0, T2bN0, or T3N0 NSCLC.
• Patients with induction chemotherapy, radiotherapy, or both, residual tumor, metastasis were excluded.
• Statistics
  o OS for PL0, PL1, PL2 and T3 (PL3)
  o OS for pT1a, pT1b, pT2a and pT2b with or without VPI (PL1-PL2)

Results
OS for PL0 (n=3606), PL1 (n=727), PL2 (n=219), T3 (n=443) was 87%, 77%, 69%, 54%—multivariate does not mention effect of T.

OS for T1a VPI+ different than T1a VPI- but OS T1a VPI+ not different than T1b VPI- and T2a VPI-

OS for T1b VPI- different from T1b VPI+ but OS for T1b VPI+ not different than T2a VPI- and T2b VPI-

**Conclusions**

- Their study makes an argument for revisiting the TNM
  - The T1 with VPI+ do seen to do better than the T2 with or without VPI+ so lumping these T1 in with the T2 like the TNM does is less discriminatory.
  - *Question if you have a 2cm tumor with VPI+ how do you stage it? as T2a?*

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**Background**
• Eosinophilic bronchopulmonary diseases encompass a wide variety of diseases such as eosinophilic pneumonia, eosinophilic bronchitis, asthma.
• Recent case reports in Japan of patients with small airway disease, peripheral eosinophilia and alveolar eosinophilia, and lung biopsy showing eosinophilic bronchiolitis. However not clear if eosinophilic bronchiolitis a distinct clinical entity.

**Aim**
• Describe 6 patients with distinctive clinical, radiologic and functional features proposing a new disease called hypereosinophilic obliterative bronchiolitis

**Methods**
• Disease defined as:
  o Blood eosinophilia or BAL with eos>25% of differential
  o Persistent airflow obstruction on lung function tests, not improved by 4–6 weeks of inhaled corticosteroid therapy
  o 3) Lung biopsy demonstrating inflammatory bronchiolitis with prominent bronchiolar wall infiltration by eosinophils and/or characteristic direct HRCT features of bronchiolitis:
    • Direct features: poorly defined centrilobular nodules, branching opacities and tree-in-bud pattern.
    • Indirect features: mosaic attenuation on inspiratory CT and air-trapping pattern on end-expiration CT, and bronchial wall thickening.

**Results**
• 6 patients, 3M:3F, 40–47 yo, cough, SOB. None with systemic disease – all limited to except for 1 patient with nasal symptoms
• By definition met the above criteria
  o 1 patient had asthma, 2 had some response to inhaled steroids but had radiologic features not c/w asthma
• Pathology:
  o 1 bronchial bx showing ulceration with increased eos but changes not limited only to large airway like an eosinophilic bronchitis
  o 1 lung biopsy showed eosinophilic bronchiolitis but also an “eosinophilic granulomatous vasculitis” involving small arteries and capillaries
• All responded rapidly to steroids but recurred with tapering so long maintenance necessary

**Conclusions**
• Another ddx on our list of eosinophilic diseases, in particular eosinophilic bronchiolitis – different clinically than asthma, similar clinically to EP but radiologically different, and more extensive airway involvement than eosinophilic bronchitis


**Background**
- PNLH spectrum of reactive pulmonary lesions, characterized by florid germinal centers, interfollicular reactive lymphocytes, mild to moderate fibrosis and abundant plasma cells.
- Reactive lymphoid hyperplasia in other organs such as salivary glands, breast and skin associated with increased numbers of IgG4 plasma cells.

**Aim**
- Investigate for the presence of increased IgG4 plasma cells in PNLH compared to MALT and other reactive lymphoid proliferations.

**Methods**
- Lymphoid lesions, all confirmed with appropriate IHC, molecular studies etc as needed, identified retrospectively from consultation files
  - 6 PNLH
  - 9 MALT
  - 8 FB
  - 8 intraparenchymal LN (IPLN)
  - 4 LIP
- IHC for IgG, IgG4 with identification of 3 areas of the highest numbers of positive cells
  - For 2 authors, count made from images taken from these areas
  - For 1 author, count made directly from slides
- Comparison between all entities for the mean number of IgG4 and IgG4/IgG ratio

**Results**
- Clinical hx
  - Available for 2 PNLH 1 normal serum IgG4, 1 serum IgG4 not done and no mention of steroid tx
  - For FB, 2 with RA, 1 chronic aspiration, 1 acute and chronic bronchiolitis, 1 UIP, 1 granulomatous interstitial pneumonia, 1 NSIP. No mention of serum IgG4 or treatment
  - For LIP, 1 with possible connective tissue disease, other 3 unknown. No mention of serum IgG4 or treatment
- Average IgG4 and ratio IgG4/IgG
  - PNLH 15-110 (78) / 0.19-0.60 – only mention mild varying degrees of fibrosis nothing about venulitis (except in discussion stating focal and quite subtle) or pattern of fibrosis
  - MALT 0-32 (4.4)/ 0-0.11
  - IPLN 0-40 (6.9)/ 0-0.24
  - FB 0/0
  - LIP 0-5 (2.3)/ 0-0.17
- All counts statistically different and independent from methods and assessors

**Conclusions**
- Interesting observation but still not good idea to the clinical significance (not enough available clinical and laboratory history).
  - Does not make this IgG4 sclerosing disease
  - Highlights caveat of making a dx of IgG4 disease on a small biopsy if all we have is increased IgG4 plasma cells without the other features
The consensus states Highly suggestive if 2 or more of the 3 morphologic features AND >50 IgG4 in surgical specimen and Probable is 2 or more of the 3 AND >20 IgG4 in small biopsy or if only 1 of the 3 histologic features

ARTICLES FOR NOTATION

Original article

Background
- Although IHC can usually assist in the distinction of MM versus carcinoma, in the case of sarcomatoid MM vs sarcomatoid Ca, it proves more variable.
- Although, IHC and some molecular test can assist us with the differential diagnosis between sarcomatoid MM/Ca versus malignant SFT or sarcomas such as SS, lack of staining, aberrant immunoprofile may pose a diagnostic challenge.
- p16/CDKN2A (located on 9p21) deletion has shown be useful in distinguishing benign from malignant mesothelial proliferation but role in the diagnosis of various sarcomatoid lesions of the pleural and lung not studied.

Aim
- To evaluate the frequency of 9p21 del by FISH in sarcomatoid lesions of the lung and pleura and assess its potential diagnostic role.

Methods
- Cases include
  - 32 sarcomatoid MM
  - 15 sarcomatoid Ca
  - 13 sarcomas (3SS, 1 intimal sarcoma of PA, 9 NOS)
  - 32 SFT (12 malignant and 20 benign)
- FISH for p16 and X;18

Results/Conclusions
- Results for del of p16 are
  - Sarcomatoid MM 81% (26)
  - Sarcomatoid Ca 53% (53)
  - Sarcoma 25% (3) -1 PA, 2 NOS, 0 SS with all 3 X;18+
  - SFT 12.5% (4) – 3 histologically malignant 3/12, 1/20 benign
- More prevalent in MM but still too much overlap to be diagnostically useful
- Interesting finding of more cases of p16 deletion in malignant SFT compared to benign ones but number low (3 vs 1)


Background
- BOOP usually responds to steroids but not always and relapses can occur

Aim
• To assess for the presence of prognostic morphologic and immunohistochemical features in BOOP

**Methods**

- 91 cases of BOOP 1995-2010, 72 idiopathic and 19 secondary, by wedge bx (56), TBBX (11), core bx (9), pneumonectomy (15).
- IHC for CD34, CD31, D2-40, COLIV, COLIII, CD68, PDGFR, VEGF

**Results/Conclusions**

- 77.85% treated with steroids, 62 (81%) with good response, 15 (19%) with no response
  - 6 DOD
  - 14 D other causes
  - 49 stable or slowly progressive
- Good prognostic markers overall
  - Younger than 38 yrs
  - Non-smokers
  - Large plugs
  - Patchy lesions
- Good prognostic markers for lary BOOP
  - All 12 cases with cells positive for CD68, VEGF, presence of collagen IV and absence of collagen III had excellent response to steroids and no relapse
- In summary, BOOP with more collagen III do more poorly


**Background**

- Identification of EGFR mutations essential for the treatment of NSCLC. Different methods available and no recommendations for the best test (sensitivity, accuracy, amount of DNA, TAT…)

**Aim**

- 2-center comparison of 3 methods cobas (AS-PCR), Sanger and Therascreen (ARMS)

**Methods**

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300 vendor - purchased FFPET NSCLC specimens

114 randomly selected specimens + 13 previously characterized specimens + 6 chosen for rare mutations

8 specimens with <1% tumor content

1 specimen with invalid results for all methods

124 evaluable specimens

Site 1: cobas EGFR test and Sanger
Site 2: cobas EGFR test and Therascreen EGFR test
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**Results/Conclusions**
- Cobas and Therascreen had less invalid rates and was more sensitive than Sanger in detecting mutations
- Cobas and Therascreen were comparable and reproducible, both with low TAT (1 day)
- Cobas uses less DNA and has automated reporting
- In summary, sounds like Cobas would be a better assay….

4- Sex-determining region Y-box 2 amplification in preneoplastic squamous lesions of the lung. Schneider et al. Human Pathol 2013; 44:706

**Background**
- Inv SQCC occurs through of progression of preinvasive lesions of increased severity into full invasion. This progress has been associated with acquired, cumulative molecular abnormalities, mostly in the form of chromosomal losses, but also mutations (p53) and methylation (p16).
- SOX2 is involved in the carcinogenesis of SQCC of many different organs and increase amplification of SOX2 in progression from low-grade dysplasia to invasive has been hypothesized.

**Aim**
- Evaluate SOX2 amplification in a spectrum of pre-invasive to invasive SQCC and determine if SOX2 amplification identifies patient a risk of progressing into invasive SQCC

**Methods**
- 46 total pre-neoplastic lesions from 3 groups of patients
  - Group C with 18 patients with NSCLC (17 SQCC and 1 ADC)
    - 9 metaplasia
    - 1 low grade dysplasia
    - 4 high grade dysplasia
    - 6 CIS
  - Group T with 11 cases of pneumonectomies, explant for non-neoplastic lung diseases
    - 11 metaplasia
    - 7 low grade dysplasia
    - 2 high grade dysplasia
    - 0 CIS
  - Group S with 17 patients surveillance biopsies from patients with prior SQCC
    - 16 metaplasia
    - 1 low grade dysplasia
    - 1 high grade dysplasia
    - 5 CIS
- SOX by IHC and FISH

**Results/Conclusions**
- IHC expression was identical in all 3 groups and was present in all squamous lesions throughout the thickness of the lesions vs in normal/hyperplastic present only in basal layer
• Amplification not seen in metaplasia or low grade dysplasia, only in some cases of high grade/CIS and SQCC. Only one case had enough tissue for FISH in all lesion and showed AMP in both the high grade/CIS and SQCC not low grade
• In summary, IHC not useful to discriminate between grades of squamous precursors. AMP could be used to separate low grade from high/CIS
• Comments: the true classification is technically mild, mod, severe dysplasia, CIS. They don’t make a specific comment but suspect mod and severe lumped as high grade.

5- MET and EGFR Mutations Identified in ALK-Rearranged Pulmonary Adenocarcinoma. Molecular Analysis of 25 ALK-Positive Cases. Boland et al. JTO 2013; 8:574

Background
• ALK rearrangement identified in 5% of ADC, usually mutually exclusive from other gene mutations such as EGFR and K-ras, however rare reports of ADC with EGFR and ALK
• Patients with ALK may become resistant to crizotinib
• Role of additional targets in resistant cases or as other potential therapeutic target still unknown

Aim
• To assess for known potential driver mutations or therapeutic targets in ALK+ ADC

Methods
• 25 cases ALK+ by IHC and FISH
• DNA extracted and testing done on MassArray (Sequenom) based lung cancer screening panel of 187 mutations in 10 genes (EGFR, KRAS, BRAF, ERBB2, JAK2, AKT1, AKT2, KIT, MET and PIK3CA).
• MET amplification by FISH

Results
• 5 cases (20%) had an additional genomic abnormality
  o 1 EGFR del L747-S752 in Exon 19
  o 4 mutations in MET thought to be germline (none with amplification by FISH)

Conclusions
• Results argue for broad testing and not by algorithm
Implications for treatment when a patient has both ALK and EGFR + not known
• In cases where MET may not be germline, protein encoded by MET is also inhibited by crizotinib

6- Histology-Related Associations of ERCC1, RRM1, and TS Biomarkers in Patients with Non–Small-Cell Lung Cancer: Implications for Therapy. Maus et al. JTO 2013; 8:582

Background
• For most NSCLC, standard treatment remains chemotherapy platin based combined with another drug class including pemetrexed
• Reported differences in response between AD and SQCC
Aim
- Hypothesized that there is an association between histology and gene expression of ERCC1, RRM1 and TS to explain this difference in response.

Methods
- Used tumors from a commercial genetic testing and seems like the testing results were from that company
- Did statistical analysis but without outcome data (including tumor response).

Results/Conclusions
- AD 1136, SQCC 457, NOS 947, med age 67, 48% women
- Statistical differences between gene expression of all3, with lower expression in AD than SQCC but **large range with much overlap of the ranges**
  - ERCC1 AD 1.82 (0.04-24.79) vs SQCC 2.48 (0.27-14.34)
  - RRM1 AD 1.06 (0.23-13.95) vs SQCC 2.41 (0.41-33.19)
  - TS AD 2.5 (0.39-68.0) vs SQCC 4.1 (0.14-59.3)
- The assumption is that low level expression associated with better response thus AD often do better with this regimen but with the absence of any correlation with outcome, can’t really conclude anything….What would have been interesting is even within a subgroup like AD if the cases with higher expression would have done worse…

7- Clinical application of immunocytochemical detection of ALK rearrangement on cytology slides for detection or screening of lung adenocarcinoma. Tanaka et al. Lung Cancer 2013; 80: 289

Background
- TBNA often the only method of diagnosis for NSCLC
- More cells in the smears than in the tissue

Aim
- Compare IHC to ICC (immunocytochemistry) for the detection of ALK in these specimens

Methods
- TBNA on 18 patients, 7 of which also had positive ALK by IHC (on?)
- Both methods quantified by 3 pathologists 0, 1, 2+, with 1 and 2+ considered +.
- Correlation with FIH and RT-PCR

Results/Conclusions
- 6 of the 7 IHC+ ALK were also ICC + and the 11neg remained neg so great correlation between both
- And correlation between IHC and FISH/PCR was 2 FISH +, 1 neg, 3 ind and 1 of the ind +PCR….Interestingly the neg ICC/pos IHC was neg by FISH so maybe ICC better?
- In summary can screen for ALK on cytologic smears from TBNA


Background:
Some studies have suggested that lung cancer at risk of developing brain metastasis may harbor specific molecular alterations. The role of ALK is predisposing to brain metastasis is controversial thus the aim of this study.

**Methods:**
- All patient that undergone brain surgery for lung metastasis 1990-2011 were eligible
- TMA with 2 1.5mm punches
- FISH assessing for translocation and amplification and IHC for ALK

**Results:**
- 175 BM with 16 matched primary tumors
  - 151 AD, 5 SQCC, 9 ADSQCC, 7 LCC, 7 LCNEC
- FISH + in 7 AD (4 with ELM4 and 3 with another partner), in 2 ADSQCC (1 ELM4 1 other partner), in 1 LCC (with other partner). FISH amp in 16 AD< 2 SQCC, 1 LCC. IHC + in 4 AD, 1 ADSQCC (identical to FISH with ELM4)
- **100% concordance between BM and lung primary**

**Conclusion:**
- Similar rate of ALK translocation in cases of BM to generally reported
- Not sure why looked at AMP and significance of ALK AMP, at least does not predict for tx response


**Background**
- Can be difficult to separate benign pleural effusions from metastatic adenocarcinoma and malignant mesothelioma on morphology only

**Aim**
- To look at the role of FISH for aneuploidy of chromosomes 11 and 17

**Methods**
- 200 cytology cases classified as pos, neg, suspicious. Gold standard for + was histology. Gold standard for negative was clinical, radiologic FU. Cytology reclassified as True Pos, True Neg, False Pos, False Neg.
- FISH as usual and determination of cut-off for aneuploidy

**Results/conclusions**
- 82 + cytologies, all TP, all FISH +
- 51 – cytologies, 3 FN all 3 FISH+, 48 TN but FISH not done? (not clear reading the data)
- 67 suspicious, 43 TP and 23 TN with 1 FISH+
- So FISH could be excellent to separate + vs – fluids BUT results of FISH on negative cases not clear and seems like there are NO cases of mesothelioma where this would really matter. All malignant effusions described are metastatic adenocarcinoma….

**Case reports**
- 69 yo male smoker with central lung mass
- By H&E (picture shown) and IHC (p63 and CK5+, TTF-1 – and no mucin on PAS-D) looks like true squamous cell carcinoma
- ALK rearrangement by FISH, BRAF V600E mutated and EGFR and k-ras wild type
- Take Home message: Although recommendations for molecular studies are for non-SQCC, considering how dire the prognosis of lung cancer is, even if rare event, should we restrict testing?

2- A 52-Year-Old Smoker with an Incidental Pulmonary Nodule. Das et al. Chest 2012; 141: 1346
- 52yo male presenting with productive cough found to have a 9mm nodule. 35 pack-yr smoker no other history
- Dx and review on clear cell/sugar tumor of the lung

3- Difference in Clonality as a Tool for Differential Diagnosis of Primary Versus Secondary Lung Neoplasms. Leuzzi et al. JTO 2012; 7:934
- 68 yo woman presenting with 2 synchronous nodules in LUL and RUL, one a grade 3 adenocarcinoma and second grade 2 adenocarcinoma.
- Performed EGFR mutational analysis in both and found an exon 19 microdeletion (ΔE746–A750) in the LUL adenocarcinoma and an exon 21 mutation (L858R) in the RUL one, supporting synchronous primaries rather than metastasis.
- Raises interesting issues as how to test EGFR in cases of synchronous as well as metachronous adenocarcinomas. We don’t always get all nodules biopsies, assumption of EGFR status based on one nodule.
- Raises interesting issues as to clonality. In this case being 2 different mutations, can make this assumption but EGFR being + in about 20% if one case neg other mutated is it enough? Could this mean EGFR heterogeneity? So probably not the best test for clonality but can be useful.

Review articles
- Very similar to original publication with more justifications of why the proposed changes, suggestions on how to gross, do gross-radiologic correlation, description of correlation with molecular findings, discussion on grading and implications for TNM staging

Very similar to original publication but much more directive in terms of what stains to do, when to do them, how to sign out the cases, how to strategically use tissue to allow molecular studies

- Review based on literature AND opinions from experts
- Review on the criteria to distinguish benign vs malignant mesothelial proliferation for both epithelial and spindled.
- Review the cytologic features of MM, discuss the challenges of making such a dx on cytology but makes no recommendation
- Review the morphologic spectrum of MM epithelial and sarcomatous, with section on peritoneal ones
- Reviews IHC (Comment that labs should choose their own panel ideally markers with 80% specificity and sensitivity) and discussion on DDX with different types of carcinomas and emphasis on issues with peritoneal cancers, with sarcomas.
- Review of molecular markers in MM (including use of p16!), on EM
- Helpful clues and pitfalls of diagnosing MM

- Extensive review on ILD including clinical updates based on clinical trials of diseases such as IPF, LAM, Sarcoidosis and HSP
- Review on basic/translational research as it relates to ILD including TGF, extracellular matrix and surfactant.

- Very nice and detailed review on pulmonary fibrosis with focus on IPF and brief mention of NSIP, COP
- In summary, IPF is thought to be a multifactorial disease where a genetically susceptible host develops the disease due to various potential injuries (GERD, virus etc). This leads to various cell injury, cytokine release, cellular stress, cell proliferation and interaction.

- Excellent review on the last 3 extensive studies including the TCGA whole genome study on SQCC and description of all potential driver mutations and druggable targets.
- Also review on all the currently opened clinical trials with novel cytotoxic agents and targeted therapy
- Finally review of all the promising targets

- Detailed review about the rarer mutations in EGFR and their known/unknown potential for sensitivity or resistance to EGFR inhibitors. Several tables that details these studies.