Why the need for change?

- Lack of relevance beyond surgical pathology
- Emerging data
  - Genetics
  - Pathology
- Multidisciplinary diagnosis
  - Tumour boards / MDT
  - Correlation with radiology
- Therapy Diversity
  - Cytotoxic agents
  - Molecular targeted therapy
  - Adjuvant therapy
  - Surgical approaches
### 2015 WHO CLASSIFICATION

#### 1-1: Introduction
- 1-1A Lung cancer staging and grading
- 1-1B Rationale for classification in small biopsies and cytology
- 1-1C Terminology and criteria in non-resection specimens
- 1-1D Molecular testing for treatment selection in lung cancer

#### 1-2: Adenocarcinoma
- 1-2A Invasive adenocarcinoma
- 1-2B Variants of invasive adenocarcinoma
- 1-2C Minimally invasive adenocarcinoma

#### 1-3: Squamous cell carcinoma
- 1-3A Keratinizing and nonkeratinizing squamous cell carcinoma
- 1-3B Basaloid carcinoma
- 1-3C Preinvasive lesion: Squamous carcinoma in situ

#### 1-4: Neuroendocrine Tumours
- 1-4A Small cell carcinoma
- 1-4B Large cell neuroendocrine carcinoma
- 1-4C Carcinoid tumors
- 1-4D Preinvasive lesion: Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia

#### 1-5: Large cell carcinoma

#### 1-6: Adenosquamous carcinoma

#### 1-7: Sarcomatoid carcinoma

#### 1-8: Other carcinomas
- 1-8A: Lymphoepithelioma-like carcinoma
- 1-8B: NUT carcinoma

#### 1-9: Salivary gland-type tumours
- 1-9A Mucoepidermoid carcinoma
- 1-9B Adenoid cystic carcinoma
- 1-9C Epithelial-myoepithelial carcinoma
- 1-9D: Pleomorphic adenoma

#### 1-10: Papillomas
- 1-10A: Squamous papilloma
- 1-10B: Glandular papilloma
- 1-10C: Mixed squamous and glandular papilloma

#### 1-11: Adenomas
- 1-11A: Mixed type adenoma
- 1-11B: Adenomatoid adenoma
- 1-11C: Papillary adenoma
- 1-11D: Micronodular adenoma
- 1-11E: Muco gland adenoma

#### 1-12: Mesenchymal tumours
- 1-12A: Hamartoma
- 1-12B: Chondroma
- 1-12C: PEC/PEComatous tumours
- 1-12D: Congenital pulmonary hemangioendothelioma
- 1-12E: Diffuse lymphangiomatosis
- 1-12F: IMT
- 1-12G: Epithelioid haemangioendothelioma

#### 1-13: Lymphoproliferative disorders
- 1-13A: Marginal zone B-cell lymphoma of MALT origin
- 1-13B: Diffuse large B-cell lymphoma
- 1-13C: Lymphomatoid granulomatosis
- 1-13D: Nodular lymphoma
- 1-13E: Erdheim Chester disease

#### 1-14: Tumours of acute origin
- 1-14A: Germ cell tumours
- 1-14B: Intertumoral thymoma
- 1-14C: Malignant thymoma

#### 1-15: Metastases to the lung

### 2015 WHO CLASSIFICATION

#### 1-6: Adenosquamous carcinoma

#### 1-7: Sarcomatoid carcinoma

#### 1-8: Other carcinomas

#### 1-9: Salivary gland-type tumours

#### 1-10: Papillomas

#### 1-11: Adenomas

#### 1-12: Mesenchymal tumours, cont'd

#### 1-13: Lymphoproliferative disorders

#### 1-14: Tumours of acute origin

#### 1-15: Metastases to the lung

### Today's presentation

- Large cell carcinoma
  - Sarcomatoid tumours
- Adenocarcinoma
- Squamous cell carcinoma
- Adenosquamous carcinoma
- Neuroendocrine tumours
- Small sample diagnosis
- Integration of Molecular data in a clinically meaningful way
Large Cell Carcinoma: 2004 definition

**Definition**
Large cell carcinoma is an undifferentiated non-small cell carcinoma (NSCC) that lacks the cytological (and architectural) features of small cell carcinoma, adenocarcinoma, or squamous cell carcinoma.

_The diagnosis requires a thoroughly sampled resected tumour, and cannot be made on non-resection or cytology specimens._

~10% of cases?

Large Cell Carcinomas: 2004

- Non-variant Large Cell Carcinoma, NOS
- Variant Large Cell Carcinomas
  - Basaloid Carcinomas
  - Large Cell Neuroendocrine Carcinomas
  - Lymphoepithelioma-like Carcinomas
  - Clear Cell Carcinoma
  - Large Cell carcinoma with Rhabdoid phenotype

2004
Large Cell Carcinoma variant:
Clear Cell Carcinoma
2015
A morphological description
Not a diagnosis

2004
Large Cell Carcinoma variant:
Large cell carcinoma
with rhabdoid phenotype
2015
A morphological description
Not a diagnosis

2004
Large Cell Carcinoma variant:
Lymphoepithelioma-like Carcinoma
2015
1.8 Other and unclassified carcinomas
Immunohistochemical studies show consistent strong staining with markers associated with Squamous cell carcinomas: p63, p40, CK5/6.

2004
Large Cell Carcinoma variant:
Large Cell Neuroendocrine Carcinoma

2015
1-4 Neuroendocrine Tumours
1-4B Large Cell Neuroendocrine Carcinoma

2004
Large Cell Carcinoma variant:
Basaloid Carcinoma

2015
1-3 Squamous Cell Carcinomas
1-3B Basaloid Carcinoma
Molecular studies in Basaloid carcinoma of lung


- DNA copy number aberrations
- mRNA expression pangenomic profiles
- Specific genetic profile
- ‘Squamous genes’ underexpressed
- SOX4 and IVL by IHC – 94% discrimination basaloid vs non-basaloid
- Very poor post-op survival

Large Cell Carcinoma – NOS: 2004

- Clinically and radiologically similar to other NSCLCs
  - Males, smoking related
  - Tend to be more peripheral, large masses, but not always
  - Pleural and Chest wall invasion common
  - Usual metastatic sites
Large Cell Carcinoma: IHC Lineage

Kerr KM et al, Lung Cancer 2012

SQC lineage
- p63
- p40
- CK5/6
- Strong/diffuse

AC lineage
- TTF1
- Napsin A
- Any staining

Well Differentiated
Squamous Cell Ca
Poorly Differentiated
Squamous Cell Ca
Well Differentiated
Adenocarcinoma
Poorly Differentiated
Adenocarcinoma

Pathologists will differ How they call marginal cases

A Genomics-Based Classification of Human Lung Tumors

The Clinical Lung Cancer Genome Project (CLCGP) and Network Genomic Medicine (NGM)

Histology original
- AD
  - n = 393
- LC incl LCNEC
  - n = 80
- SCLC
  - n = 48
- SQ
  - n = 245

Prediction
- AD
  - 91.4%
- LC
  - 48%
- LCNEC
  - 81%
- SCLC
  - 79%
- SQ
Large Cell Carcinomas - Mutations

<table>
<thead>
<tr>
<th>N</th>
<th>Country</th>
<th>EGFR</th>
<th>KRAS</th>
<th>ALK</th>
<th>BRAF</th>
<th>PIK3CA</th>
<th>MEX</th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>Italy</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>Italy</td>
<td>0</td>
<td>50%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>18</td>
<td>Japan</td>
<td>0</td>
<td>6%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>72</td>
<td>Scotland</td>
<td>0*</td>
<td>8.3%</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>102</td>
<td>USA</td>
<td>1</td>
<td>29%</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>20</td>
<td>Italy</td>
<td>1</td>
<td>40%</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>57</td>
<td>USA</td>
<td>1</td>
<td>43%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Overall prevalence</td>
<td>1%</td>
<td>25%</td>
<td>2%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mutations largely matched IHC lineage, where data are available.

* EGFR c.2508C>T; p. R836R (SNP) in a Basaloid Ca

Diagnosis of Large Cell Carcinoma: 2015

Definition
Large cell carcinoma is an undifferentiated non-small cell carcinoma (NSCC) that lacks the cytological, architectural, and immunohistochemical features of small cell carcinoma, adenocarcinoma, or squamous cell carcinoma. The diagnosis requires a thoroughly sampled resected tumour, and cannot be made on non-resection or cytology specimens.

The diagnosis of large cell carcinoma is only made when additional staining (Immunohistochemistry and/or mucin stains) is negative, unclear, or not available.

2015: Adenocarcinoma: Solid subtype
Tumour progression and de-differentiation

Pathologists will still differ how they call marginal cases !!!!

ICD-O code Large cell carcinoma 8012/3

Based on their immunohistochemical profiles, three subtypes of large cell carcinoma can be distinguished:
- Large cell carcinoma with null immunohistochemical features
- Large cell carcinoma with unclear immunohistochemical features
- Large cell carcinoma with no additional stains

30% of former cohort remains?
Undifferentiated carcinoma which is not Small Cell (or LCNEC) IN A RESECTION SPECIMEN

Mucin Stain
> 5 vacuoles in at least each of 2 hpf

no

yes

Immunohistochemistry
P63/p40/CK5-6……

TTF1/Napsin A……

‘Squamous’ positive

‘Adeno’ positive

Both’ positive: Discrete and >50% each

Solid adenocarcinoma

Adenosquamous carcinoma

Non-keratinising Squamous cell carcinoma

Which markers and how much staining?

For Adenocarcinoma

• TTF1 ★

• Napsin A

• Surfactant apoproteins

• CK7

• Definite staining but it can ★ be weak and patchy. Which clone?

For Squamous Cell Carcinoma

• P63 ★

• P40 ★

• CK5/6 ★

• Desmocollin

• 34betaE12

• Strong and diffuse staining ONLY ★

Morphologically poorly differentiated lesions do (relatively) badly.

1-7: Sarcomatoid Carcinomas

1-7A Pleomorphic, Spindle cell and Giant cell carcinomas

1-7B Carcinosarcoma

1-7C Pulmonary Blastoma
Pleomorphic, Spindle cell and Giant cell carcinomas

**Definition**
Pleomorphic carcinoma is a poorly differentiated non-small cell lung carcinoma that contains at least 10% spindle and/or giant cells, with the remainder of the tumour showing squamous cell carcinoma, adenocarcinoma, or undifferentiated non-small cell carcinoma.

Spindle cell carcinoma consists of an almost pure population of epithelial spindle cells, with no differentiated carcinomatous elements.

Giant cell carcinoma consists almost entirely of tumour giant cells (including multinucleated cells), with no differentiated carcinomatous elements.

Sarcomatoid Carcinomas

- Many are combined with ‘standard’ NSCLC elements
  - Adenocarcinoma
  - Squamous cell carcinoma
  - Large Cell carcinoma
- Pure forms are very rare
  - Giant cell carcinoma
  - Spindle cell carcinoma
‘Relatively’ Pure Spindle Cell and Giant Cell Carcinoma are extremely rare

Pleomorphic / Sarcomatoid Carcinoma Lineage

<table>
<thead>
<tr>
<th>No of Cases</th>
<th>Country</th>
<th>EGFR mutations</th>
<th>KRAS mutations</th>
<th>BRAF/ALK/PIK3CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>61</td>
<td>Korea</td>
<td>15% exon19del 11% L858R exon21</td>
<td>10%</td>
<td>-</td>
</tr>
<tr>
<td>17</td>
<td>Japan</td>
<td>18% 67% exon19del 33% L858R exon21</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>13</td>
<td>Italy</td>
<td>0</td>
<td>37%</td>
<td>-</td>
</tr>
<tr>
<td>27</td>
<td>Italy</td>
<td>-</td>
<td>22%</td>
<td>-</td>
</tr>
<tr>
<td>35</td>
<td>Scotland</td>
<td>0</td>
<td>28.6%</td>
<td>0</td>
</tr>
</tbody>
</table>

Kaira K et al. J Thorac Oncol 2010
Pelosi G et al. Mod Pathol 2004
A malignant epithelial tumour with glandular differentiation or mucous production by tumour cells

New IASLC/ATS/ERS Adenocarcinoma classification

- What was wrong with ‘WHO 2004’?
  - Mixed adenocarcinoma
  - Bronchioloalveolar carcinoma
  - Small diagnostic samples
- New ‘solutions’ for 2015
  - Predominant pattern subtyping
  - Adenocarcinoma in situ
  - Minimally invasive adenocarcinoma
  - Multifocal tumours
  - Predictive sub-typing by IHC
Post operative survival vs **predominant pattern** in pulmonary adenocarcinoma – five patterns

Adjuvant therapy?

**Selection by Stage**

**Selection by Adenocarcinoma Predominant pattern Histology?**

What is (was) bronchioloalveolar carcinoma (BAC)?

- Localised non-invasive adenocarcinoma
  - Non-mucinous
  - Mucinous
- Invasive adenocarcinoma with BAC components or features
- Multifocal advanced adenocarcinomas
  - Mucinous BAC
  - Non-mucinous forms
  - ‘alveolar cell carcinoma’
**Bronchioloalveolar carcinoma (BAC)**

An adenocarcinoma with a pure bronchioloalveolar pattern and NO EVIDENCE of stromal, vascular or pleural invasion.

WHO Classification of Lung Tumours, 1999 & 2004
Minimally Invasive Adenocarcinoma?

Features which may appear to indicate a more aggressive tumour.....

....in a lesion <3cm diameter....... 

.....but which DO NOT, in practice, increase metastatic risk.

- Recognition of this lesion?
- How to treat this lesion?
- Have we created a ‘monster’?

Boland JM et al. Mod Pathol 2012; 25 supp2,474A
'Moderate to Good agreement'

In situ adenocarcinoma or invasive adenocarcinoma?

The nature of the ‘lepidic’ tumour.

Is all lepidic (BAC) pattern really adenocarcinoma-in-situ?
Invasive mucinous adenocarcinoma (formerly mucinous BAC)

- consolidation
- air bronchograms
- multifocal subsolid nodules/masses

Adenocarcinoma - Cribriform pattern: Solid or Acinar?
Spread Through Alveolar Spaces: STAS

The bronchial epithelium derives from a different stem cell compartment than the peripheral Terminal Respiratory Unit.
Adenocarcinoma 2015

- **Definition**
  Invasive adenocarcinoma is a malignant epithelial tumour with glandular differentiation, mucin production, or pneumocyte marker expression. The tumours show an acinar, papillary, micropapillary, lepidic, or solid growth pattern, with either mucin or pneumocyte marker expression. After comprehensive histological subtyping in 5-10% increments, the tumours are classified according to their predominant pattern.

- **ICD-O codes**
  - Adenocarcinoma 8140/3
  - Lepidic adenocarcinoma 8250/3
  - Acinar adenocarcinoma 8551/3
  - Papillary adenocarcinoma 8260/3
  - Micropapillary adenocarcinoma 8265/3
  - Solid adenocarcinoma 8230/3

- **1-2: Adenocarcinoma**
  - 1-2A Invasive adenocarcinoma
  - 1-2B Variants of invasive adenocarcinoma
  - 1-2C Minimally invasive adenocarcinoma
  - 1-2D Preinvasive lesions
    - 1-2D-i: Atypical adenomatous hyperplasia
    - 1-2D-ii: Adenocarcinoma in situ

- **Squamous cell carcinoma**
  - Only TWO defining features
    - Keratinisation
    - Inter-cellular bridges
Squamous Cell Carcinoma: Variants

- Basaloid
  - Keep. Genuine evidence of poorer prognosis
- Papillary
  - Not sure. Just a growth pattern? HPV associated?
- Small Cell
  - What is it? No publications since 2004
- Clear Cell
  - No. Cytological change common in lung cancer
- Microcystic
- 'Creeping carcinoma'
  - Early disease. Less aggressive
- Peripheral squamous cell carcinoma

Squamous Cell Carcinoma

1-3A Keratinizing and Non-keratinizing SCC
Squamous cell carcinoma is a malignant epithelial tumour that either shows keratinization and/or intercellular bridges, or is a morphologically undifferentiated non-small cell carcinoma that expresses immunohistochemical markers of squamous differentiation.

1-3B Basaloid Carcinoma
Basaloid carcinoma is a poorly differentiated malignant epithelial tumour that presents in its pure form as a proliferation of small cells with lobular architecture and peripheral palisading. These cells lack squamous morphology, but show immunohistochemical expression of squamous markers. Tumours with a keratinizing or non-keratinizing squamous cell component, but a basaloid component of > 50%, are also classified as basaloid carcinoma.

1-3C Pre-invasive disease – Squamous dysplasia and Carcinoma in situ
Adenosquamous Carcinoma

**Definition**
A carcinoma showing components of both squamous cell carcinoma and adenocarcinoma, each component comprising at least 10% of the tumour.

_IHC-defined solid adenocarcinoma and non-keratinising squamous cell carcinoma are accepted for this diagnosis, provided the IHC is unequivocal and the respective zones are discrete and >10% each_

---

**LCC-NOS: adenosquamous carcinoma by IHC**

- 22% showed possible adenocarcinoma lineage
- 48% showed possible squamous cell carcinoma lineage
- 1.6% showed a possible adenosquamous lineage
Which are the Neuroendocrine tumours?

Tumours of the Lung: WHO 2004

- Squamous cell carcinoma
- Small cell carcinoma
- Adenocarcinoma
- Large cell carcinoma
- Adenosquamous carcinoma
- Sarcomatoid carcinoma
- Carcinoid tumour
- Salivary-type carcinomas

1-4: Neuroendocrine tumours

High Grade Neuroendocrine tumours

- 1-4A: Small cell carcinoma
- 1-4B: Large cell neuroendocrine carcinoma (LCNEC)

Low Grade Neuroendocrine tumours

- 1-4C: Carcinoid tumours
  - Typical Carcinoid
  - Atypical Carcinoid

Precursor lesion

- 1-4D: Diffuse idiopathic pulmonary neuroendocrine hyperplasia (DIPNECH)
Large Cell Neuroendocrine Carcinoma
Pulmonary Carcinoid tumours

- Clearly different from High Grade NE tumours
  - Aetiology
  - Morphology
  - Biology
  - Genetics
- Proliferative activity important in definition
  - Can ‘cell cycle’ IHC assist in this distinction?
- ‘Peripheral’ spindle cell carcinoids are different?

Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia

Carcinoid, Large Cell Carcinoma and Adenocarcinoma all distinct
SCLC and LCNEC could not be distinguished at a molecular level
NSCLC subtyping in small samples

- Prevalence depends on sample type & origin
- Morphological diagnostic accuracy relatively low
  - Lack of reliable cellular features in adenocarcinoma
  - Overinterpretation of ‘squamoid’ appearances
  - Undifferentiated areas
  - Tumour heterogeneity

- NSCLC-NOS
  - Majority (66%) are adenocarcinoma

**Predictive IHC in NSCLC-NOS**

- Utilise sparingly, interpret with care
- Does not ‘confirm’ diagnosis
- Reduces ‘NOS rate’ to under 10%, but cannot abolish it

- Essentially ‘qualifies’ NSCLC-NOS
  - NSCLC-NOS
  - NSCLC, ‘favour squamous’ (p63, p40, CK5/6)
  - NSCLC, ‘favour adenocarcinoma’ (TTF1)

---

**Subtyping NSCLC: How good?**

- Predictive IHC has ‘levelled the playing field’
- Better diagnosis possible on poorer specimens

---

**Predictive IHC in NSCLC-NOS**

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- Essentially ‘qualifies’ NSCLC-NOS
  - NSCLC-NOS
  - NSCLC, ‘favour squamous’ (p63, p40, CK5/6)
  - NSCLC, ‘favour adenocarcinoma’ (TTF1)
Patterns of adenocarcinoma and ‘mutation’

**KRAS**
- Codons 12, 13, 61
- Solid or poorly differentiated
- Invasive Mucinous
- CD74-NRG1 fusion

**EGFR**
- Tyrosine kinase domain
- Exon 18-21

**TRU**
- Adenocarcinomas
- AIS, lepidic, papillary and micropapillary
- TTF1 positive
- Non-smoking, female, Asian

**ALK rearrangements**
- Several partners recognised
- Solid or poorly differentiated
- Mucinous signet ring cells
- TTF1 positive
- Non-smoking

Histology, IHC and mutation

**Histology vs Mutation**

<table>
<thead>
<tr>
<th>Histology</th>
<th>IHC</th>
<th>Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adeno-Carcinoma</td>
<td>15%</td>
<td>35.8%</td>
</tr>
<tr>
<td>Probable Adeno (by IHC)</td>
<td>5.8%</td>
<td>45.8%</td>
</tr>
<tr>
<td>Squamous Carcinoma</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Probable Squamous (by IHC)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>MUC5AC/5GS</td>
<td>10%</td>
<td>7.3%</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**TTF 1 vs Mutation**

<table>
<thead>
<tr>
<th>TTF 1 positive</th>
<th>TTF 1 negative</th>
<th>Mutation detected only TTF 1+ were tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGR mutation</td>
<td>15%</td>
<td>2.5%</td>
</tr>
<tr>
<td>KRAS mutation</td>
<td>33%</td>
<td>36%</td>
</tr>
<tr>
<td>BRAF mutation</td>
<td>2.5%</td>
<td>2.1%</td>
</tr>
<tr>
<td>ALK fusion</td>
<td>4.2%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

Kret A et al. Lung Cancer Jan, 2015; suppl 1

IHC and Predictive testing

<table>
<thead>
<tr>
<th>ALK translocation</th>
<th>ALK tyrosine kinase inhibitors (TKIs)</th>
<th>Screening tool but potentially a primary response predictor</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR mutation</td>
<td>EGFR TKIs</td>
<td>L858R well detected. Anti-ex19del lack sensitivity</td>
</tr>
<tr>
<td>EGFR wild type</td>
<td>Anti-EGFR MoAb (Cetuximab)</td>
<td>EGFR IHC</td>
</tr>
<tr>
<td>ROS1 translocation</td>
<td>Crizotinib</td>
<td>Lower specificity</td>
</tr>
<tr>
<td>MET upregulation</td>
<td>Anti-MET agents</td>
<td>Poor success so far</td>
</tr>
<tr>
<td>BRAF mutation</td>
<td>BRAF TKIs</td>
<td>Limited experience</td>
</tr>
<tr>
<td>RET translocation</td>
<td>Cabozantinib</td>
<td>Not so effective</td>
</tr>
<tr>
<td>PD-L1 expression</td>
<td>Anti-PD1 and PD-L1 MoAbs</td>
<td>Appear predictive in some circumstances</td>
</tr>
</tbody>
</table>

FGFR1 amplification
- Biomarker issues
- Definition of amplification
- 20% may be overestimate?
- Ponatinib – FGFR1 inhibitor

**Discoid Domain Receptor 2 mutation**
- Prevalence 3.8%
- Good in vitro target – miRNA & Dasatinib
- Limited clinical evidence

PI3Kinase
- ~30% amplification
- ~ENI mutations – addictive?? inhibitors exist

**MET**
- Inhibitors exist
- So far no success

**EGFR**
- TKI vs MoAb
- Mutations – rarity (vIII – 8%)
- Targeting the receptor

**IGFR1**
- Figlutumab
- Some effect in squamous toxicity

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- Mutations – rarity (vIII – 8%)
- Targeting the receptor

**IGFR1**
- Figlutumab
- Some effect in squamous toxicity
A word of caution

‘There is nothing more dangerous (or expensive) than making diagnoses on the basis of immunohistochemical profiles in disregard of the cytoarchitectural features of the lesion.’

Rosai J 2010; in Dabbs, DJ. Diagnostic Immunohistochemistry. Theranostic and genomic applications

A word of caution

‘Alas, this is true for any other special technique applied for diagnostic purposes to human tissue, molecular biology being the latest and most blatant example’

Rosai J 2010; in Dabbs, DJ. Diagnostic Immunohistochemistry. Theranostic and genomic applications

WHO Classification of Lung Cancer: New look?

• Some changes in definition
• New category – NE tumours
• Re-distribution based on molecular data leading to a MUCH greater importance of immunohistochemistry