25th IAP-Arab Division Conference
07-09 November 2013, Amman, Jordan

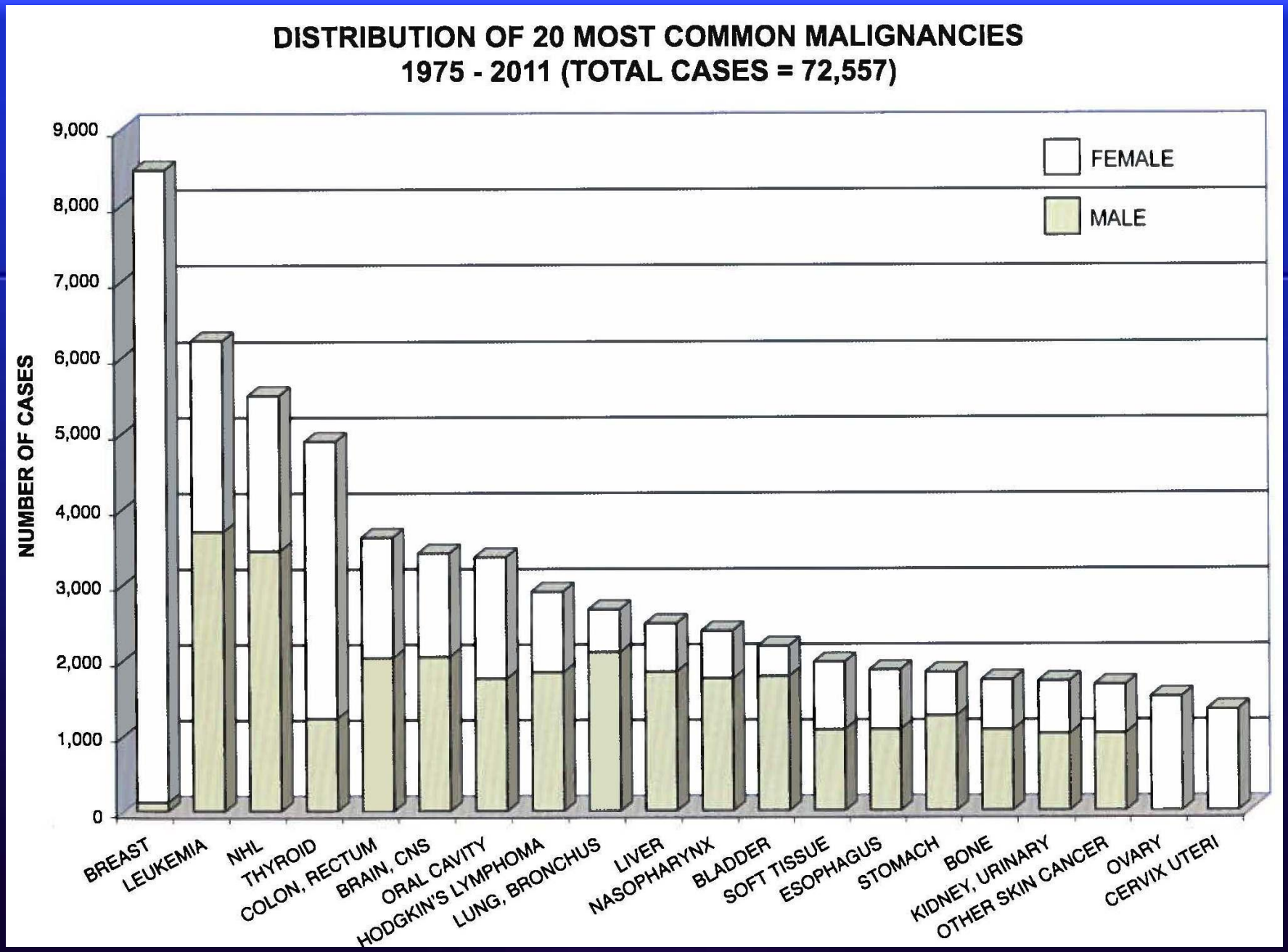
MOLECULAR PREDICTIVE MARKERS OF LUNG CARCINOMA: KFSH&RC EXPERIENCE

Fouad Al Dayel, MD, FRCPA, FRCPath
Professor and Chairman
Department of Pathology and Laboratory Medicine
King Faisal Specialist Hospital and Research Centre
Riyadh, Saudi Arabia

Lung Cancer

Leading cause of cancer mortality

- 1.4 million death/year worldwide (WHO, 2007)
- 160,000 death/year in USA (25% of all cancer death in USA)
- 5-year survival of lung cancer 6-15%



KFSH&RC Tumor Registry, 2011

TEN MOST COMMON MALIGNANCIES BY AGE GROUP AT DIAGNOSIS
1975 - 2011

SITE	AGE GROUP	No	%
BREAST	00 - 14	2	0.0
	15 - 39	2,618	30.9
	40 - 60	4,759	56.3
	>60	1,088	12.8

SITE	AGE GROUP	No	%
BRAIN, CNS	00 - 14	1,600	46.9
	15 - 39	904	26.5
	40 - 60	617	18.1
	>60	289	8.5

SITE	AGE GROUP	No	%
LEUKEMIA	00 - 14	2,773	44.6
	15 - 39	2,130	34.3
	40 - 60	980	15.7
	>60	333	5.4

SITE	AGE GROUP	No	%
ORAL CAVITY	00 - 14	42	1.3
	15 - 39	465	13.8
	40 - 60	1,406	41.9
	>60	1,445	43.0

SITE	AGE GROUP	No	%
NON-HODGKIN'S LYMPHOMA	00 - 14	839	15.3
	15 - 39	1,467	26.7
	40 - 60	1,766	32.1
	>60	1,421	25.9

SITE	AGE GROUP	No	%
HODGKIN'S LYMPHOMA	00 - 14	872	30.0
	15 - 39	1,517	52.3
	40 - 60	382	13.2
	>60	132	4.5

SITE	AGE GROUP	No	%
THYROID	00 - 14	100	2.0
	15 - 39	2,427	49.7
	40 - 60	1,668	34.1
	>60	693	14.2

SITE	AGE GROUP	No	%
LUNG	00 - 14	9	0.3
	15 - 39	166	6.2
	40 - 60	1,183	44.4
	>60	1,308	49.1

SITE	AGE GROUP	No	%
COLON, RECTUM	00 - 14	11	0.3
	15 - 39	648	17.9
	40 - 60	1,743	48.2
	>60	1,218	33.6

SITE	AGE GROUP	No	%
LIVER	00 - 14	77	3.1
	15 - 39	140	5.6
	40 - 60	1,067	43.0
	>60	1,195	48.2

KFSH&RC Tumor Registry, 2011

COMPARATIVE DATA - KFSH&RC vs SCR vs USA (% to TOTAL CANCER CASES)

SITE	KFSH&RC 2011 Analytics	SCR 2008 Saudis	USA 2011 Estimates
BREAST	16.7%	13.2%	14.6%
THYROID	9.5%	6.8%	3.0%
COLON, RECTUM	7.4%	10.2%	8.8%
LEUKEMIA	7.2%	6.6%	2.8%
NON-HODGKIN'S LYMPHOMA	5.1%	7.6%	4.2%
BRAIN, CNS	4.3%	2.8%	1.4%
HODGKIN'S LYMPHOMA	3.1%	3.5%	0.6%
LUNG, BRONCHUS	3.0%	4.1%	13.8%
BONE	2.4%	1.4%	0.2%
SKIN MELANOMA	0.2%	0.2%	4.4%
PROSTATE (% to MALES)	2.6%	6.3%	29.3%

KFSH&RC Tumor Registry, 2011

DISTRIBUTION OF 20 MOST COMMON MALIGNANCIES
2011 ANALYTIC CASES (TOTAL CASES = 2,292)

MALE

COLON, RECTUM 90 (9.3%)
LEUKEMIA 83 (8.6%)
NHL 71 (7.4%)
LIVER 62 (6.4%)
BRAIN, CNS 56 (5.8%)
THYROID 50 (5.2%)
KIDNEY, URINARY 49 (5.1%)
NASOPHARYNX 47 (4.9%)
LUNG, BRONCHUS 46 (4.8%)
BLADDER 40 (4.1%)
HODGKIN'S LYMPHOMA 40 (4.1%)
ORAL CAVITY 38 (3.9%)
STOMACH 29 (3.0%)
BONE 29 (3.0%)
SOFT TISSUE 28 (2.9%)
PROSTATE 25 (2.6%)
TESTIS 21 (2.2%)
ESOPHAGUS 19 (2.0%)
PANCREAS 19 (2.0%)
OTHER SKIN CA 17 (1.8%)

FEMALE

BREAST 380 (28.6%)
THYROID 167 (12.6%)
LEUKEMIA 81 (6.1%)
COLON, RECTUM 79 (5.9%)
CORPUS UTERI 71 (5.3%)
ORAL CAVITY 59 (4.4%)
NHL 45 (3.4%)
OVARY 42 (3.2%)
BRAIN, CNS 42 (3.2%)
CERVIX UTERI 31 (2.3%)
LIVER 30 (2.3%)
SOFT TISSUE 30 (2.3%)
KIDNEY, URINARY 30 (2.3%)
HODGKIN'S LYMPHOMA 30 (2.3%)
BONE 26 (2.0%)
STOMACH 23 (1.7%)
LUNG, BRONCHUS 22 (1.7%)
NASOPHARYNX 16 (1.2%)
BLADDER 16 (1.2%)
EYE 16 (1.2%)

KFSH&RC Tumor Registry, 2011

WHO Classification of Lung Cancer

1967
1981
1999

Written by pathologists for pathologists

2004 Genetic and clinical information introduced (not current anymore)

2015 5th Edition

Lung Carcinoma

- Small cell carcinoma
- Non-small cell lung carcinoma (NSCLC)
  - Adenocarcinoma (including bronchioalveolar carcinoma BAC)
  - Adenosquamous carcinoma
  - Squamous cell carcinoma
  - Large cell carcinoma
  - Large cell neuroendocrine carcinoma

WHO Classification of Lung Cancer

Classification is based on resected specimen. On small biopsy, the differentiation of various subtypes of NSCLC is not reliable in many cases.

NSCLC - NOS

WHO Classification of Lung Cancer, 2004

Revised classification that emphasizes:

- **Integrated multidisciplinary approach for classification is needed**
- **Classification in small biopsies and and cytology specimen (was not addressed in 2004 WHO Classification)**
- **Tissue management by pathologists**

International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma

William D. Travis, MD, Elisabeth Brambilla, MD, Masayuki Noguchi, MD, Andrew G. Nicholson, MD,
Kim R. Geisinger, MD, Yasushi Yatabe, MD, David G. Beer, PhD, Charles A. Powell, MD, Gregory J. Riely, MD, Paul E. Van Schil, MD, Kavita Garg, MD, John H. M. Austin, MD, Hisao Asamura, MD, Valerie W. Rusch, MD, Fred R. Hirsch, MD, Giorgio Scagliotti, MD, Tetsuya Mitsudomi, MD, Rudolf M. Huber, MD, Yuichi Ishikawa, MD, James Jett, MD, Montserrat Sanchez-Cespedes, PhD, Jean-Paul Sculier, MD, Takashi Takahashi, MD, Masahiro Tsuboi, MD, Johan Vansteenkiste, MD, Ignacio Wistuba, MD, Pan-Chyr Yang, MD, Denise Aberle, MD, Christian Brambilla, MD, Douglas Flieder, MD, Wilbur Franklin, MD, Adi Gazdar, MD, Michael Gould, MD, MS, Philip Hasleton, MD, Douglas Henderson, MD, Bruce Johnson, MD, David Johnson, MD, Keith Kerr, MD, Keiko Kuriyama, MD, Jin Soo Lee, MD, Vincent A. Miller, MD, Iver Petersen, MD, PhD, Victor Roggli, MD, Rafael Rosell, MD, Nagahiro Saijo, MD, Erik Thunnissen, MD, Ming Tsao, MD, and David Yankelewitz, MD

Journal of Thoracic Oncology, Vol. 6, Number 2, February 2011

Major Changes of Proposed Classification

- Stop usage of “bronchioalveolar carcinoma”
- Addition of minimally invasive carcinoma
- Classification of invasive carcinoma according to predominant subtype

Journal of Thoracic Oncology, Vol. 6, Number2, February 2011

IASLC/ATS/ERS Classification of Lung Adenocarcinoma in Resection Specimens

- **Preinvasive lesions**
  - **Atypical adenomatous hyperplasia**
  - **Adenocarcinoma in situ (≤ 3 cm formerly BAC)**
- **Minimally invasive adenocarcinoma (≤ 3 cm lepidic predominant tumor with ≤ 5 mm invasion)**
- **Invasive adenocarcinoma**

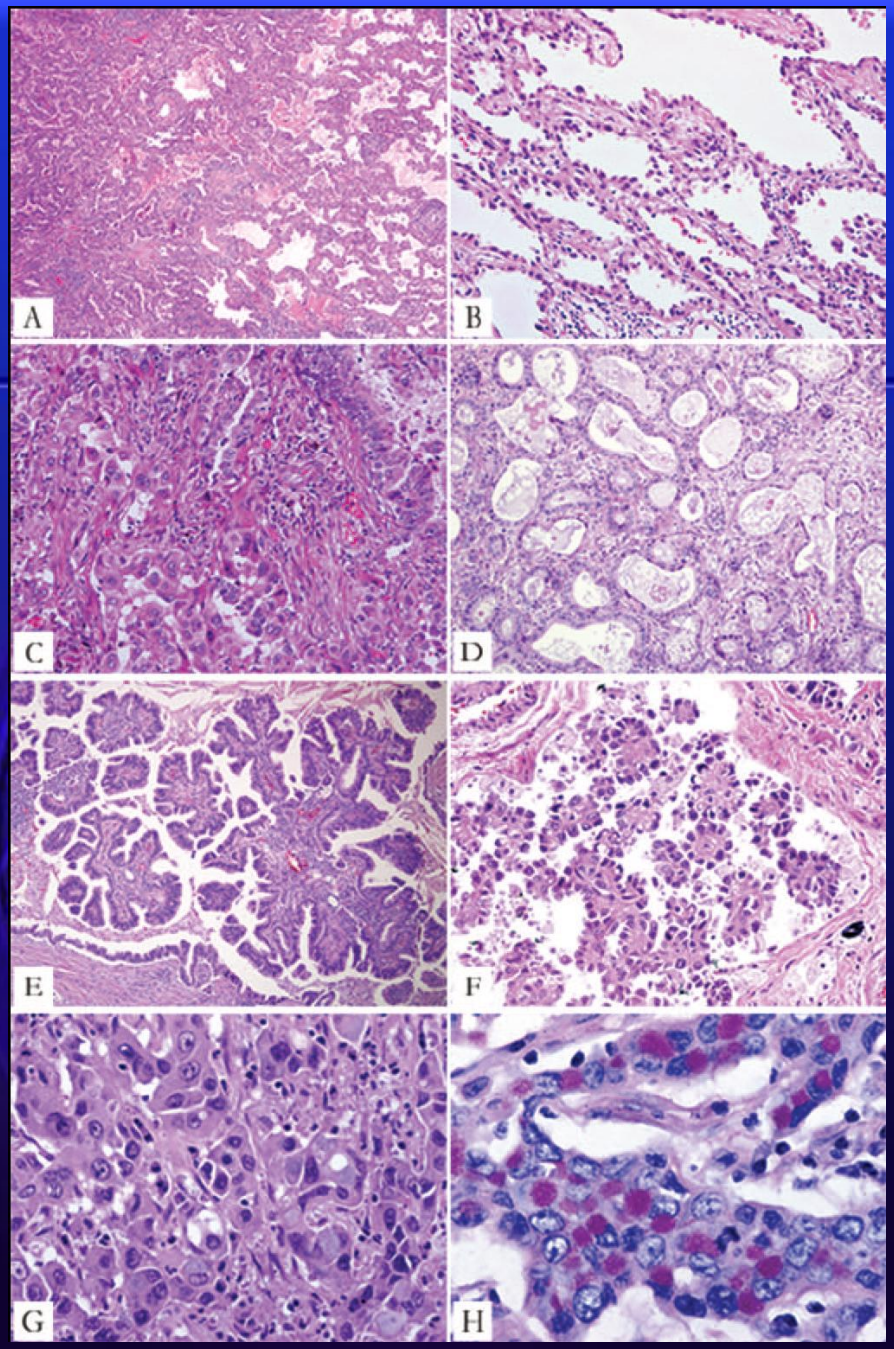
Journal of Thoracic Oncology, Vol. 6, Number2, February 2011

Lepidic predominant pattern

Acinar adenocarcinoma

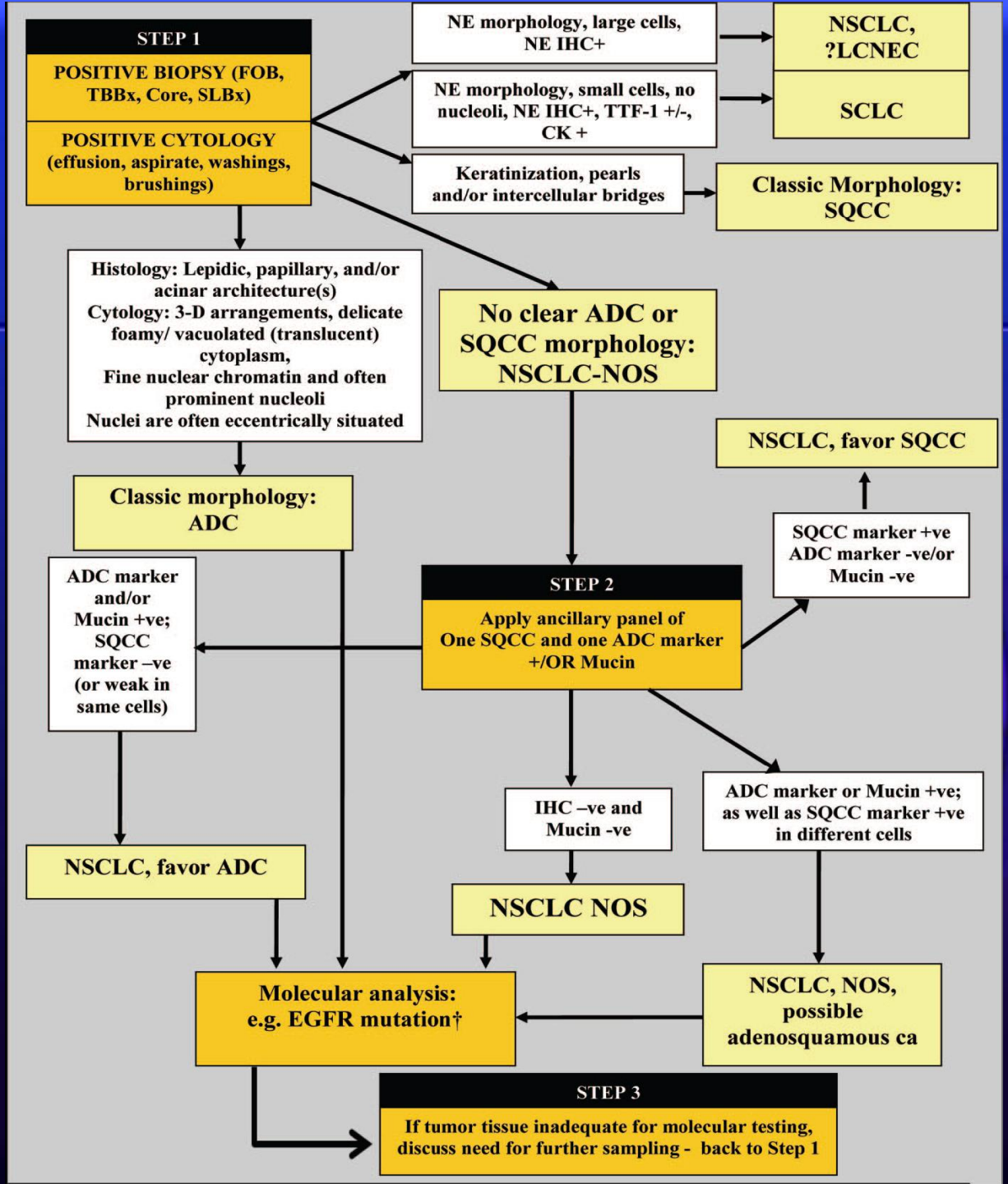
Papillary adenocarcinoma

Solid adenocarcinoma



Micropapillary adenocarcinoma

Journal of Thoracic Oncology, Vol. 6, Number2, February 2011



Journal of Thoracic Oncology, Vol. 6, Number2, February 2011

Lung Cancer

Immunohistochemical stains

- **Differentiate primary pulmonary adenocarcinoma from metastatic carcinoma**
- **Differentiate adenocarcinoma from squamous cell carcinoma**
- **Distinguish adenocarcinoma from mesothelioma**
- **Determine the neuroendocrine status of the tumor**

NCCN Guidelines Version 2.20, 2013

TABLE 1. Immunohistochemical Findings in Lung Biopsies of Poorly Differentiated Non-small Cell Carcinomas

Resection Diagnosis by WHO Criteria (No.Cases)	Biopsy IHC Number Positive/Total Stained (%)						Biopsy Diagnosis After IHC (No. Cases)
	CK7	TTF-1	Napsin A	p63	CK5/6	34βE12	
AC (20)	19/19 (100)*	16/20 (80)	11/19 (58)*	2/20 (10)	0/20 (0)	12/20 (60)	AC (16/20) NSCLC, NOS (4/20)
SCC (15)	9/15 (60)	0/15 (0)	0/15 (0)	15/15 (100)	11/15 (73)	15/15 (100)	SCC (14/15) NSCLC, NOS (1/15)
LCC (4)	3/4 (75)	2/4 (50)	0/4 (0)	0/4 (0)	0/4 (0)	0/4 (0)	AC (2/4) NSCLC, NOS (2/4)

*No tumor was present on the immunostained slide in 1 case.

AC indicates adenocarcinoma; IHC, immunohistochemistry; LCC, large cell carcinoma; NSCLC, Non-small cell lung carcinoma; NOS, not otherwise specified; SCC, squamous cell carcinoma; WHO, World Health Organization.

Am J Surg Pathol, Vol. 35 (1), Jan 2011

P40 is superior to P63 for SCC of lung.

Identification of driver mutations in tumor specimens from 1,000 patients with lung adenocarcinoma: The NCI's Lung Cancer Mutations Consortium (LCMC)

- *KRAS* 107 (25%)
- *EGFR* 98 (23%)
- *ALK* rearrangements 14 (6%)
- *BRAF* 12 (3%)
- *PIK3CA* 11 (3%)
- *MET* amplifications 4 (2%)
- *HER2* 3, (1%)
- *MEK1* 2(0.4%)
- *NRAS* 1 (0.2%)
- *AKT1* 0(0%)

In 60% tumor driver mutation detected

J Clin Oncol 29: 2011 (suppl; abstr CRA7506)

Lung Adenocarcinoma
Activating Oncogenes

Deletion and point Mutations

- **KRAS (30%)**
- **EGFR (15%)**

Gene Amplification
EGFR (6-9%)

Chromosomal rearrangement
EML4-ALK (5%)
ROS1 (2%)

EGFR, EML 4-ALK and KRAS are mutually exclusive

Molecular Testing Guideline for EGFR and ALK Tyrosine Kinase Inhibitors: Guideline from the College of American Pathologists, International Association for the Study of Lung Cancer, and Association for Molecular Pathology.

Archives of Pathology & Laboratory Medicine
June 2013, Vol. 137, No. 6, pp. 828-860

Testing for EGFR mutations and AlK gene rearrangements is recommended in the NCCN NSCLC guidelines for adenocarcinoma patients.

NCCN Guidelines Version 2.20, 2013

Lung Carcinoma

Distinction is critical between:

- **Adenocarcinoma**
- **Pure squamous cell carcinoma**
- **Pure small cell carcinoma**
- **Pure neuroendocrine carcinoma**

For EGFR and Alk testing

Lung Carcinoma

Lung carcinoma with mixed histology (adenosquamous, adeno/small cell) can have EGFR mutation or Alk rearrangement . Testing is required If possibility of adenocarcinoma component cannot be excluded.

Lung Cancer

It is important to retain sufficient tissue for molecular testing after establishing diagnosis of adenocarcnoma.

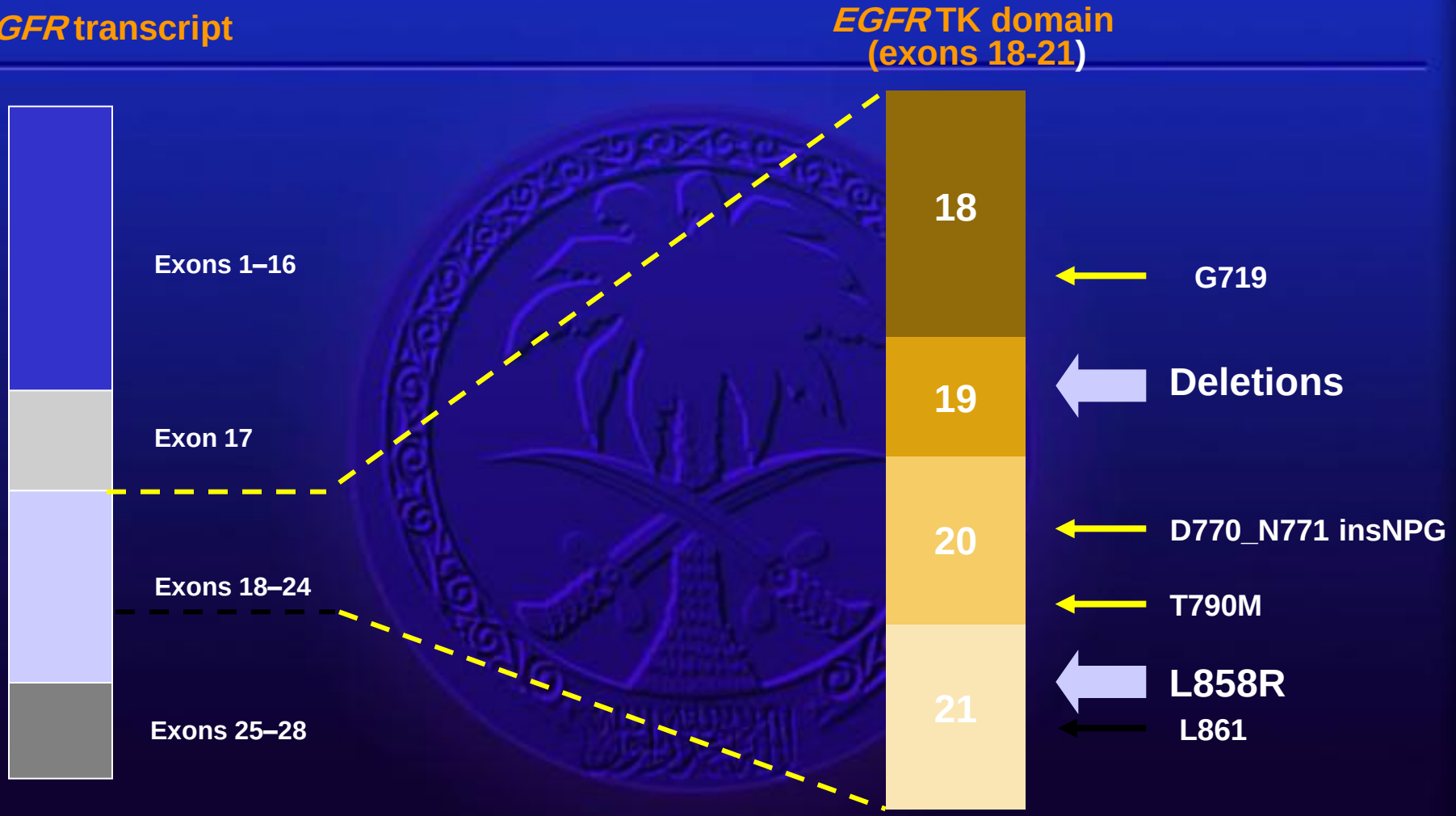
Lung Cancer

Molecular testing results should be available within 2 weeks of receiving samples to molecular labs.

- **EGFR mutations are seen more common (50%) in:**
  - **Women**
  - **Never smoker**
  - **Asian**

Selection of patients for EGFR mutation testing is dependent on subtype of lung cancer not on clinical information.

Common Mutations Identified in *EGFR* Gene



Riely GJ, et al. Clin Cancer Res 2006;12:839–44

EGFR TK Mutations

Common

- **Exon 19 in-frame deletion**
- **Exon 21 L858R mutation (Lysine to Arginine)**

Both mutations result in activation of TK domain and associated with sensitivity to TKI.

EGFR Mutations

- Exon 18 Gly719 (sensitive)
- Exon 19 deletion (sensitive)
- Exon 20 insertion (resistance)
- Exon 20 Thr790Met (acquired resistance)
- Exon 21 Leu858Arg (sensitive)

Frequency of EGFR Mutations in Lung Adenocarcinoma

- 32% in East Asia
- 7-15% in Caucasians
- 2% in African America
- About 30% in Saudi population (unpublished data)

- *Mitsudomi T, Yatabe Y. Mutations of the epidermal growth factor receptor gene and related genes as determinants of epidermal growth factor receptor tyrosine kinase inhibitors sensitivity in lung cancer. Cancer Sci. 2007;98(12):1817-1824*
- *Suda K, Tomizawa K, Mitsudomi T. Biological and clinical significance of KRAS mutations in lung cancer: an oncogenic driver that contrasts with EGFR mutation. Cancer Metastasis Rev. 2010;29(1):49-60.*
- *Reinersman JM, Johnson ML. Riely GJ, et al. Frequency of EGFR and KRAS mutations in lung adenocarcinomas in African Americans. J Thorac Oncol. 2011;6(1):28-31*

EGFR Mutation Testing in Saudi Arabian Lung Adenocarcinoma

Dr. Fouad Al Dayel,* Dr. Hamad Husaini,** Dr. Asma Tulbah,* Dr. Shamayel Mohammed,* Dr. Prashant Bavi, ***Dr. Halah Abalkhail*. *Pathology and Laboratory Medicine, ** Oncology Center, *** Research Center
King Faisal Specialist Hospital and Research Centre

مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

Introduction

Lung cancer is the fifth leading cause of cancer in males in Saudi Arabia. As per current World Health Organization (WHO), lung carcinoma is subdivided into small cell and non-small cell carcinoma (NSCLC). The latter compromise 70-80% of lung carcinoma and consists of heterogenous groups that is further divided into adenocarcinoma, squamous cell carcinoma and large cell carcinoma. Due to poor prognosis of lung cancer, there is an increasing need to find molecular biomarkers which can be used for diagnosis, risk stratification, early detection, treatment selection, prognosis and monitoring for recurrence. Increasing interest in adenocarcinoma of lung has been raised lately for various reasons. One reason is the increasing incidence of adenocarcinoma, which is now the most predominant histologic subtype. Other reason is the possible use of targeted therapy in cases showing EGFR mutations or ALK rearrangements.

Adenocarcinoma comprise approximately 70% of primary lung cancer in Saudi population.

Objectives

The aim of this study is to review the incidence of EGFR mutation in lung adenocarcinoma in Saudi patients.

Materials &Methods

Clinical data and genomic DNA was available from a cohort of 37 primary lung adenocarcinoma diagnosed at King Faisal Specialist Hospital and Research Centre(KFSH&RC) clinics. Ethical approval for the study was granted by the Research Advisory Council (RAC) at KFSH&RC.

The diagnosis was established histologically and confirmed by Immunohistochemistry. DNA from paraffin embedded tissue was manually extracted and was paired with histology-guided tissue macro-dissection to target tumor cells. The mutation status of EGFR exons 18-21 was evaluated using Polymerase chain reaction (PCR). Amplified products were purified and sequenced on an Applied Biosystems Genetic Analyzer 3730xl. Analysis and mutation nomenclature was based on GeneBank NM_005228.

Results

EGFR mutation was detected in 10 cases (27%). Of the 10 cases, 80% of mutations (deletions) were located in exon 19 and 10% in exons 20 and 21 respectively. All mutations detected conferred increased sensitivity to tyrosine kinase inhibitors (TKI).

Pathology Images

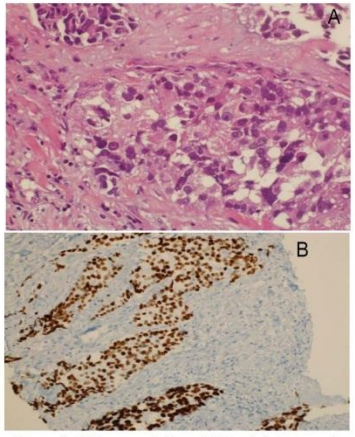
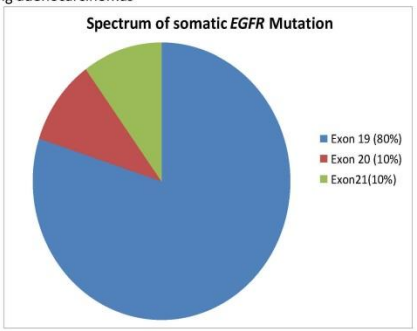


Figure 1 A)Representative H&E of Adenocarcinoma of lung B) IHC stains for TTF-1 that shows nuclear staining in primary lung adenocarcinomas



Mutation Analysis

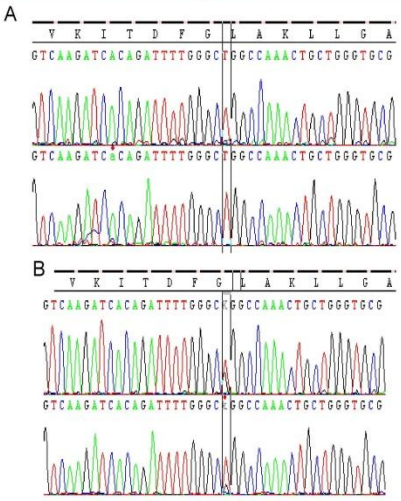


Figure 2. Mutation analysis of EGFR. A representative chromatogram from Normal control (A) and case submitted for mutation analysis (B) exhibiting L858R in exon 21.

Conclusion

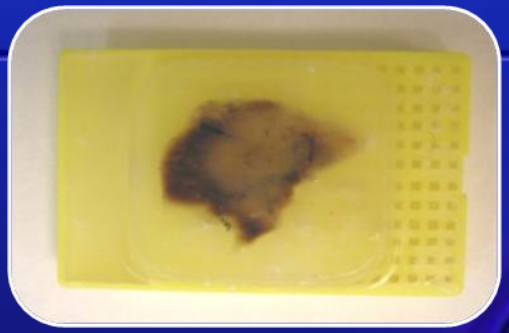
The incidence of EGFR mutation in lung adenocarcinoma in our patients (27%) is slightly higher than western population (15-23%). To our knowledge, this is the first molecular analysis of EGFR gene mutational analysis in lung adenocarcinoma in Saudi Arabia.

Resistance to EGFR-TKIs

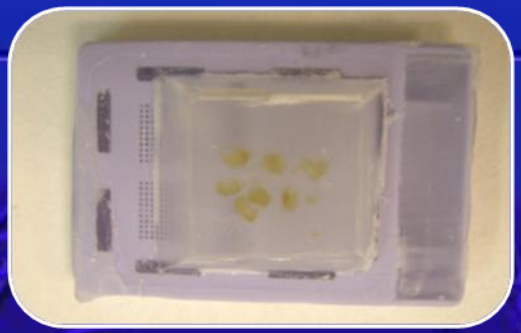
- **Primary resistance**
  - KRAS mutations and Alk gene rearrangement
  - EGFR mutations not sensitive to EGFR TKIs (rare, ~2%) – ex 20 insertion
  - BRAF mutations (rare, ~3%)
- **Acquired resistance**
  - Second EGFR mutation: T790M (50% of cases)
  - MET amplification (some)
  - Pi3k mutations
  - Transformation to small cell lung ca

Tissue Sampling Methods in NSCLC

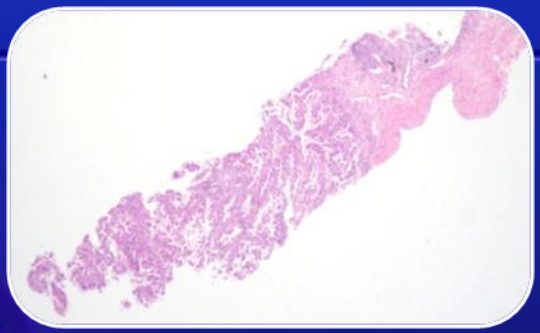
- Three main methods of obtaining tumour samples



Excised during surgery



Bronchoscopic biopsy (for central lesions)



Guided needle biopsy (for peripheral lesions)

- Preservation of DNA is essential (e.g. formalin-fixed, paraffin-embedded tumour sample)
- Preferably use primary tumour tissue
  - when this is not available, may consider metastatic tissue, pleural effusion or blood

Testing for Mutation

Tumor Sample Collection

Sectioning (at least 50% tumors)

DNA Extraction

Amplification

Sequencing

EGFR Testing Method

- Direct (Sanger) sequencing
- Pyrosequencing
- High resolution melting analysis
- Polymerase chain reaction (PCR), allele specific hybridization
- Real time PCR
- Whole exome sequencing
- Whole genome sequencing

Limitations of Mutation Detection by Direct Sequencing

- Sequencing will not detect proportions of tumor cells below the sensitivity level (25%)
- Microdissection routinely used to increase tumor content (eliminate non-neoplastic areas)
- Blocks or unstained sections for DNA extraction should be from the most cellular areas with >50% tumor cells
- Select sections without excessive inflammatory response

Adequacy of EGFR Testing

- Adequacy is determined by malignant cells content and DNA quality and not sample type
- Specimen should be fixed in 10% NBF for 6-48 hours
- Cell blocks are preferred over smears for cytology samples

ALK-rearranged Adenocarcinoma

- 2-7% of adenocarcinomas
- Younger patients
- Never smoking
- Higher stage
- Solid tumor growth, frequent signal cells with abundant intracellular mucin

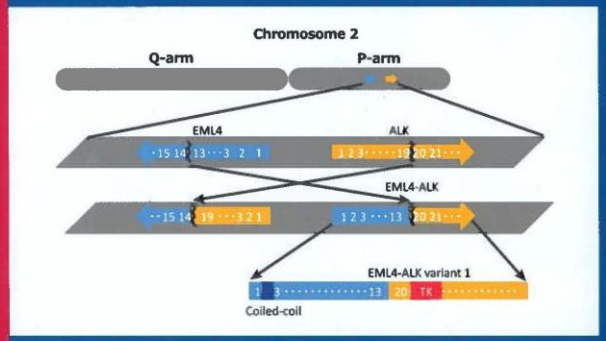
Similar to EGFR mutation positive patient except they are younger and male

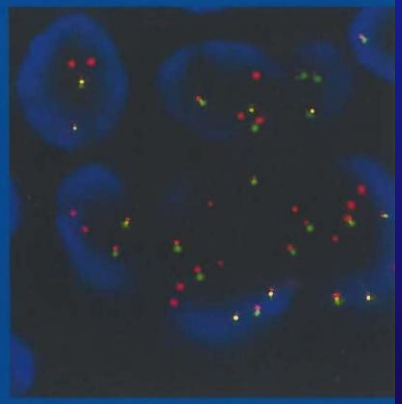
IASLC

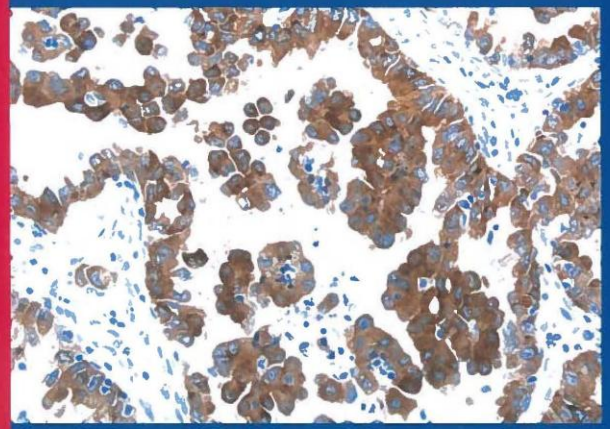
Conquering Thoracic Cancers Worldwide

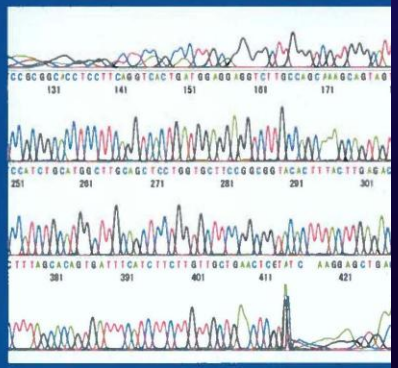
EDITED BY
MING SOUND TSAO, MD, FRCPC
FRED R. HIRSCH, MD, PHD
YASUSHI YATABE, MD, PHD

IASLC ATLAS OF ALK TESTING IN LUNG CANCER

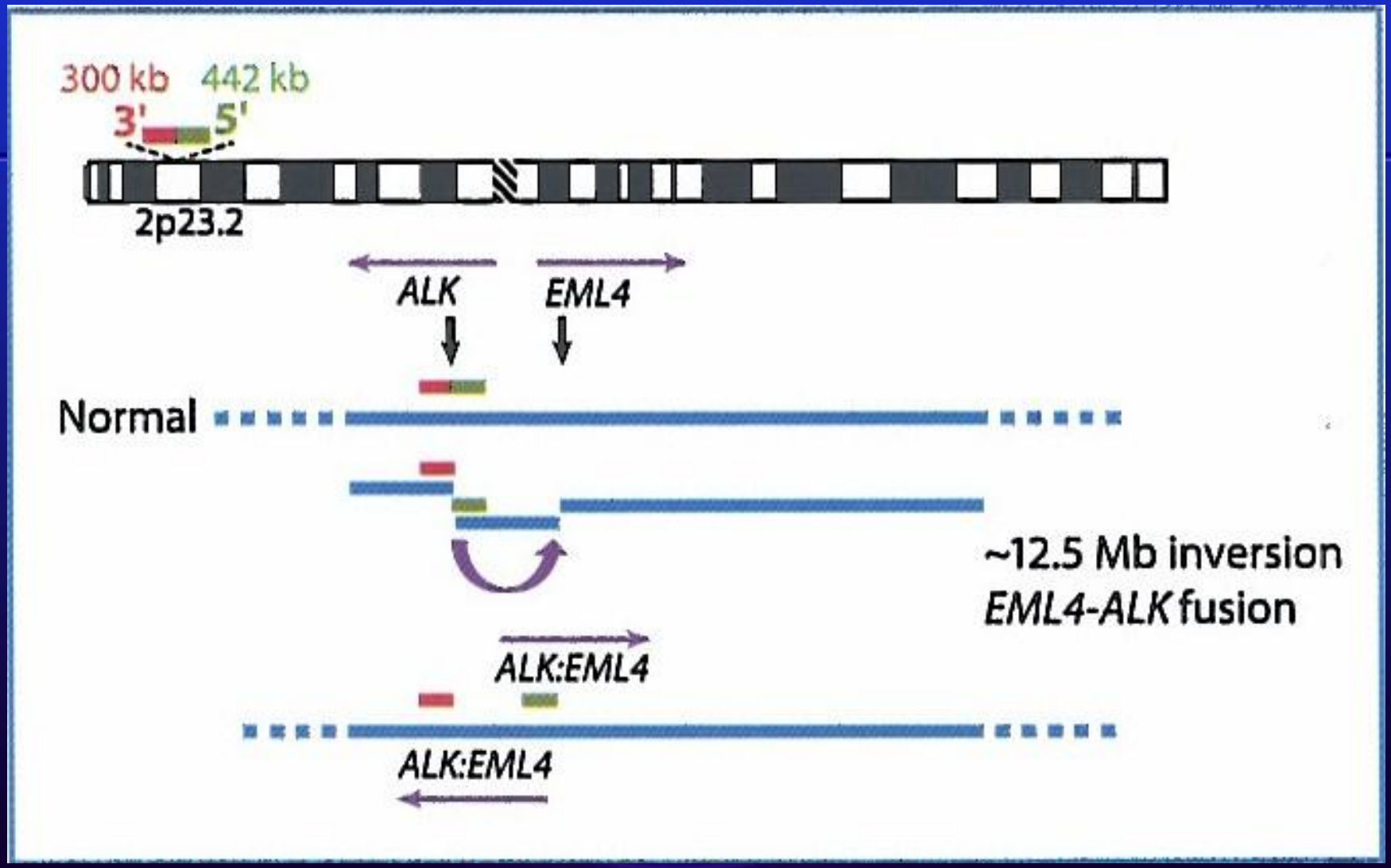






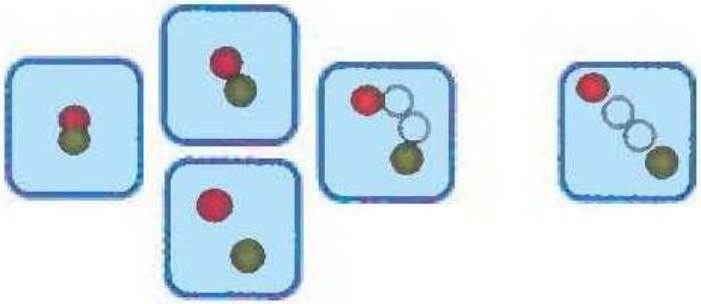


INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER


300 kb
442 kb
3'
5'
2p23.2
ALK
EML4
Normal
~12.5 Mb inversion
EML4-ALK fusion
ALK:EML4
ALK:EML4

SIGNAL CLASSIFICATION

Patterns observed in native *ALK*



Red and green separated by <2 signal diameters

Classified as negative

Red and green separated by ≥2 signal diameters

Classified as positive

Patterns observed in split 3'-5' *ALK*

Red and green separated by ≥2 signal diameters

Classified as positive

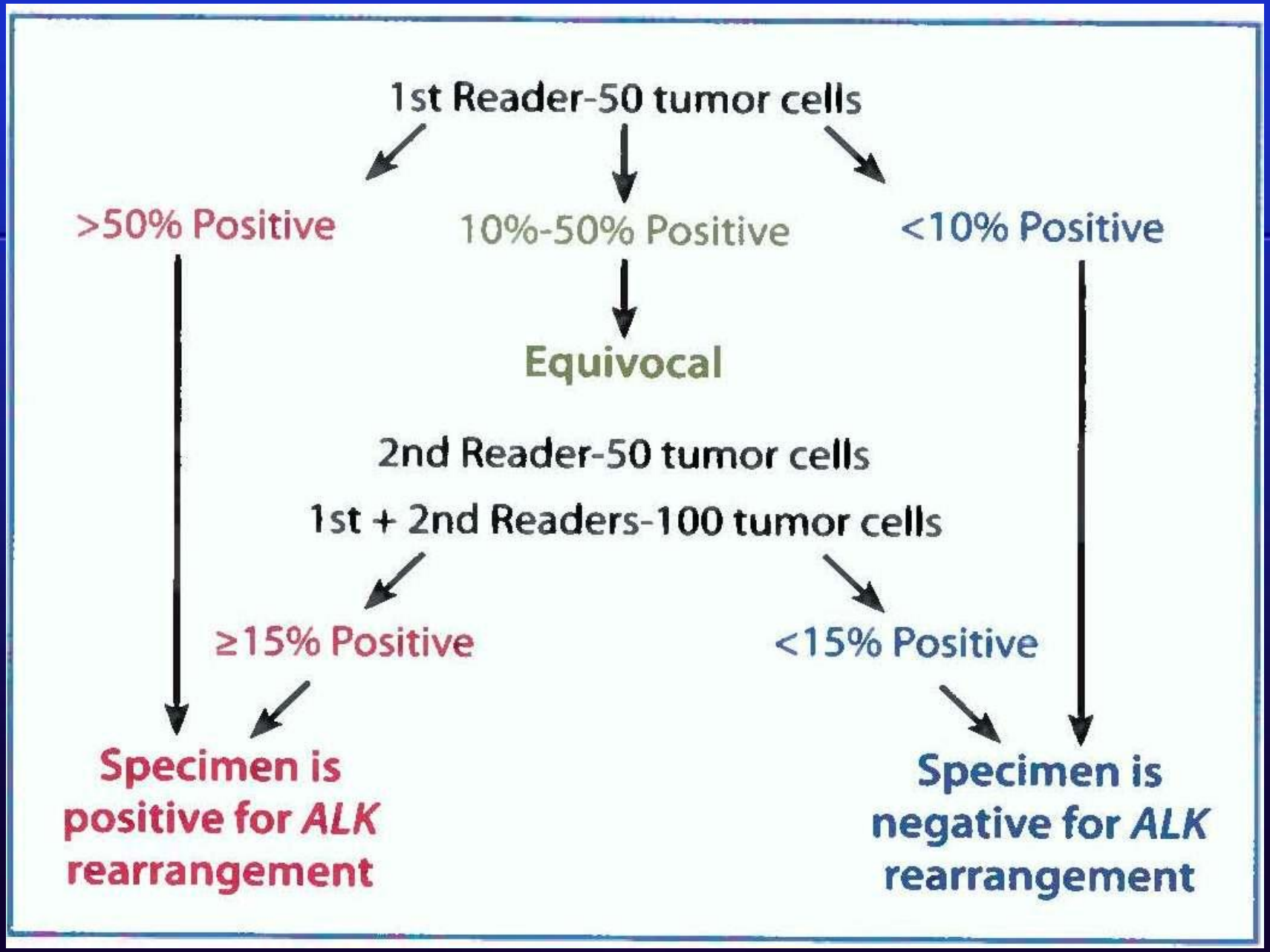
Red and green separated by <2 signal diameters

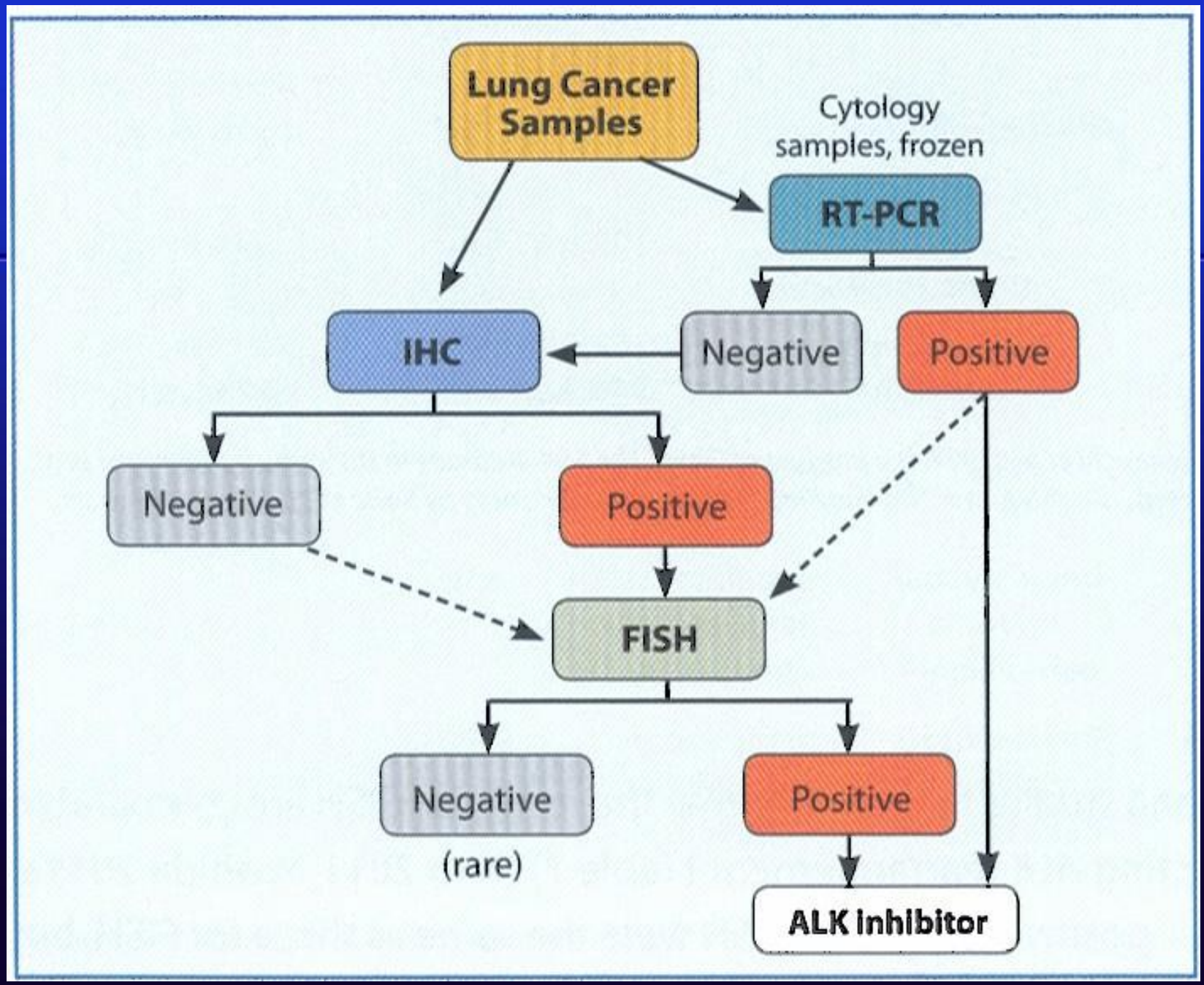
Classified as negative

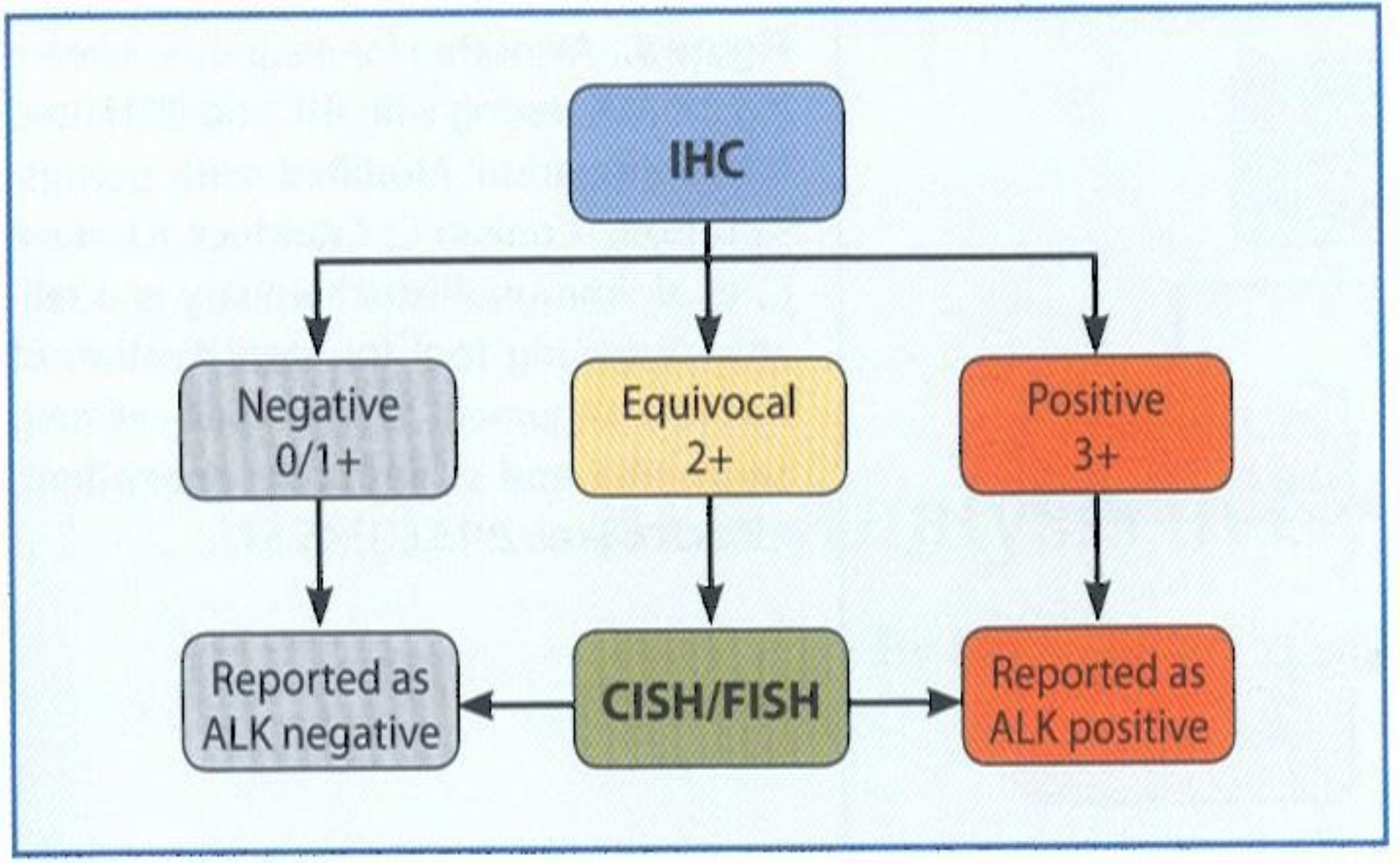
SPECIMEN CLASSIFICATION

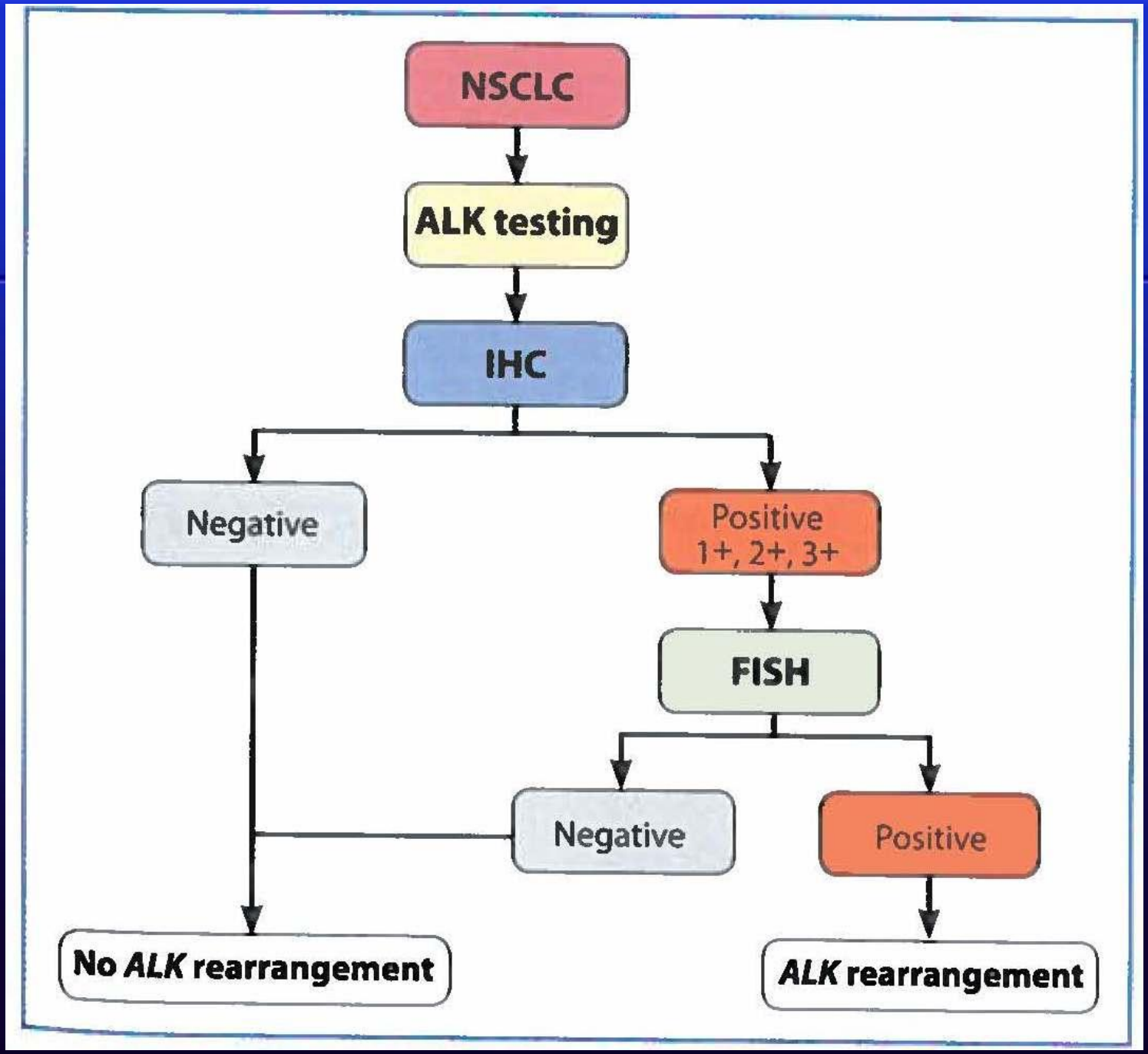
Nonrearranged tumors:
Rearrangement-positive cell rate
<15% of cells

Rearranged tumors:
Rearrangement-positive cell rate
≥15% of cells


1st Reader-50 tumor cells
>50% Positive
10%-50% Positive
<10% Positive
Equivocal
2nd Reader-50 tumor cells
1st + 2nd Readers-100 tumor cells
≥15% Positive
<15% Positive
Specimen is positive for ALK rearrangement
Specimen is negative for ALK rearrangement


Lung Cancer Samples
Cytology samples, frozen
RT-PCR
Negative
Positive
IHC
Negative
Positive
FISH
Negative
(rare)
Positive
ALK inhibitor


IHC
Negative
0/1+
Equivocal
2+
Positive
3+
Reported as
ALK negative
CISH/FISH
Reported as
ALK positive


NSCLC
ALK testing
IHC
Negative
Positive
1+, 2+, 3+
FISH
Negative
Positive
No ALK rearrangement
ALK rearrangement

Frequency of ALK Gene Rearrangement in Saudi Lung Cancer

Dr. Fouad Al Dayel,* Dr. Hamad Husaini,** Dr. Asma Tulbah,* Dr. Shamayel Mohammed,* Dr. Halah Abalkhail*,
Dr. Prashant Bavi, *** Dr. Khawla Al Kuraya***
*Pathology and Laboratory Medicine, ** Oncology Center, *** Research Center
King Faisal Specialist Hospital and Research Centre

مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

Introduction

Lung carcinoma is the fifth common cancer affecting Saudi men. Recently, translocation of the anaplastic lymphoma kinase (ALK) gene is found to play a predictive role in adenocarcinoma tumor genesis.

The ALK gene codes for tans membrane glycoprotein with tyrosine kinase activity. In frame rearrangement with the known fusion partners places the ALK kinase domain under the control of different gene promoter, which results in chimeric protein with constitutive tyrosine kinase activity.

ALK gene rearrangement can identify patients with adenocarcinoma who are sensitive to ALK inhibitors. However, no data are available on the prevalence of ALK rearrangements changes in Middle Eastern population. Therefore, we carried out this study to evaluate the prevalence of ALK rearrangements in lung adenocarcinoma of Saudi patients.

Objectives

The aim of this study is to determine the prevalence of ALK rearrangement in lung adenocarcinoma of Saudi patients..

Materials &Methods

ALK gene rearrangements were studied using fluorescence in situ hybridization (FISH) on 97 adenocarcinoma samples utilizing tissue microarray format. ALK gene translocations identified by BAC clone RP11-328L16 were studied by the break part probe from Vysis (Abott Molecular, II, USA) to detect chromosome 2p23 rearrangements.

Results

Ninety seven (97) lung adenocarcinoma cases were evaluated. There were 3 cases exhibited ALK gene rearrangement (3%). All of these 3 cases was moderately differentiated adenocarcinoma. None of our cases showed signet cells or abundant intracellular mucin.

Pathology Images

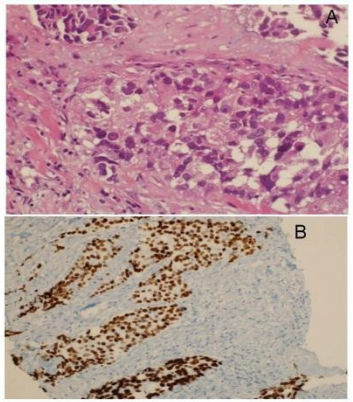


Figure 1 A)Representative H&E of Adenocarcinoma of lung B) IHC stains for TTF-1 that shows nuclear staining in primary lung adenocarcinomas

Conclusion

This is the first study that reveals frequency of ALK translocation in a ethically unique cohort of Saudi lung cancer patients. The findings of this study show that incidence of ALK adenocarcinoma is similar to the published western data and these patients can benefit from targeted therapy like Crizotinib- a dual ALK and MET inhibitor that has shown promising results in clinical trials.

FISH

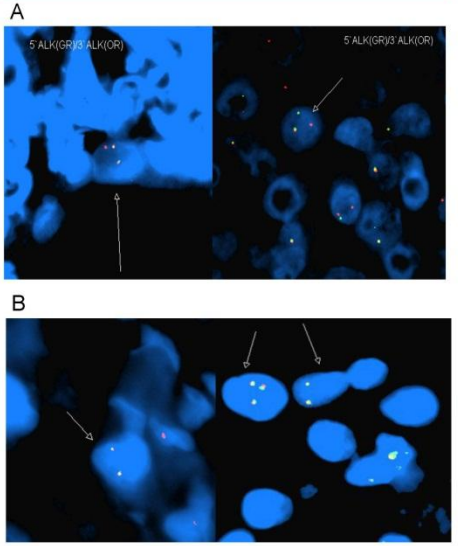


Figure 2. *In situ* hybridization method for the detection of ALK alterations in lung adenocarcinoma sample showing cells with ALK rearrangement (A) and normal cases (B)

Cancer is a disease of genome. Today we have the technology to understand the alterations of these genes using exome sequencing, transcriptome sequencing and whole genome sequencing.