Diagnostic Challenges in Molecular Work-Up: NGS vs Single-Gene Testing in Lung Cancer

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Importance of Molecular Diagnostics in NSCLC

- Non–small cell lung cancer (NSCLC) often harbors actionable driver mutations (e.g. *EGFR*, *ALK*, *ROS1*, *BRAF*, *MET exon 14*, *RET*, *NTRK*).
- Identifying these alterations is critical, as targeted therapies significantly improve patient outcomes.

Introduction

Purpose of pretreatment diagnosis

Mostly biopsy and cytology specimen

조직학적 진단

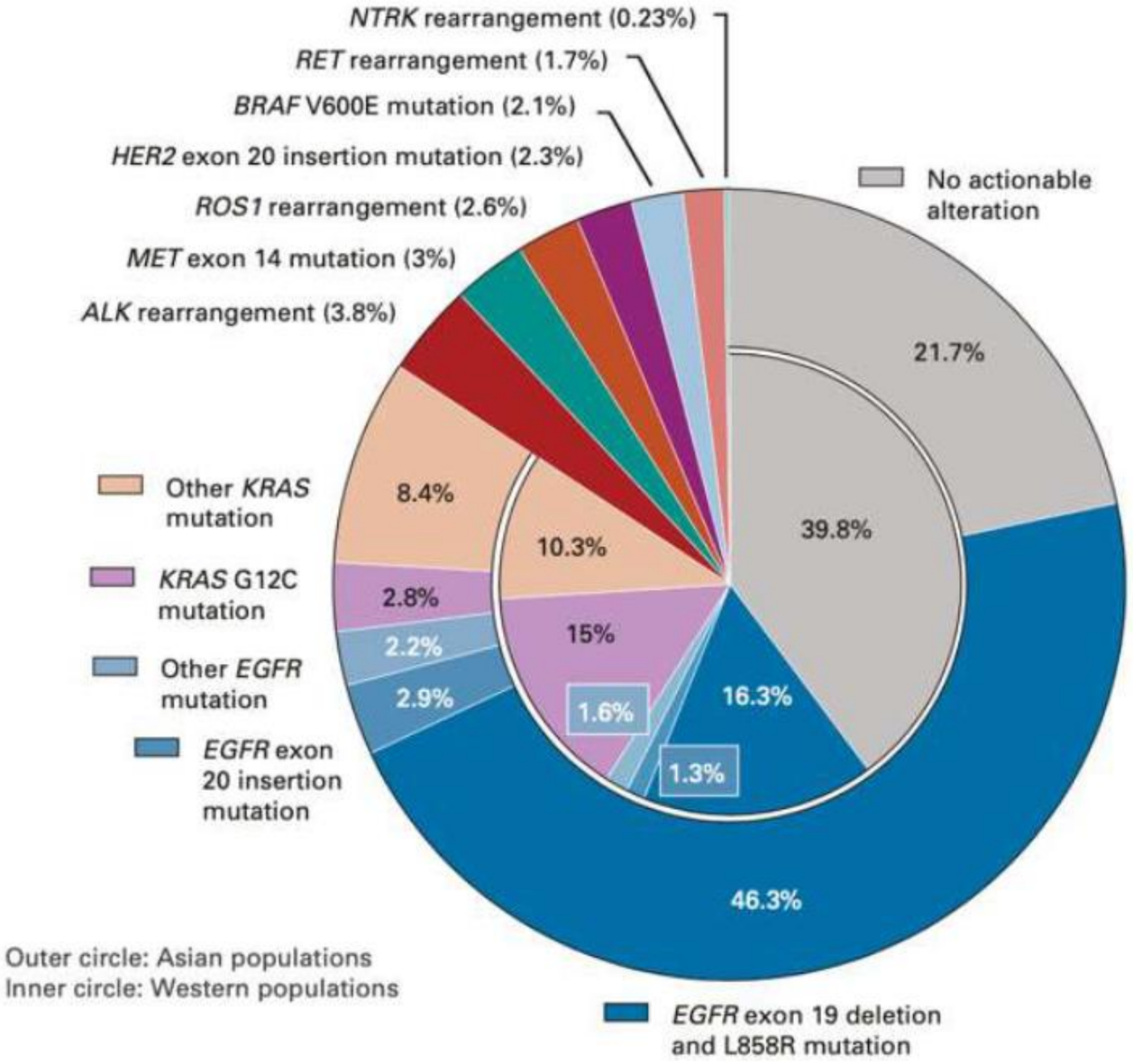
Struggle to preserve tissue

- 조직학적 진단을 위한
  면역조직화학검사 최소로 시행
- Reflex test 진행
- 여러 개의 블록으로 나누어 제작
- Microdissection

Biomarker test

대한폐암학회, *폐암 진료지침* 3판 p.82

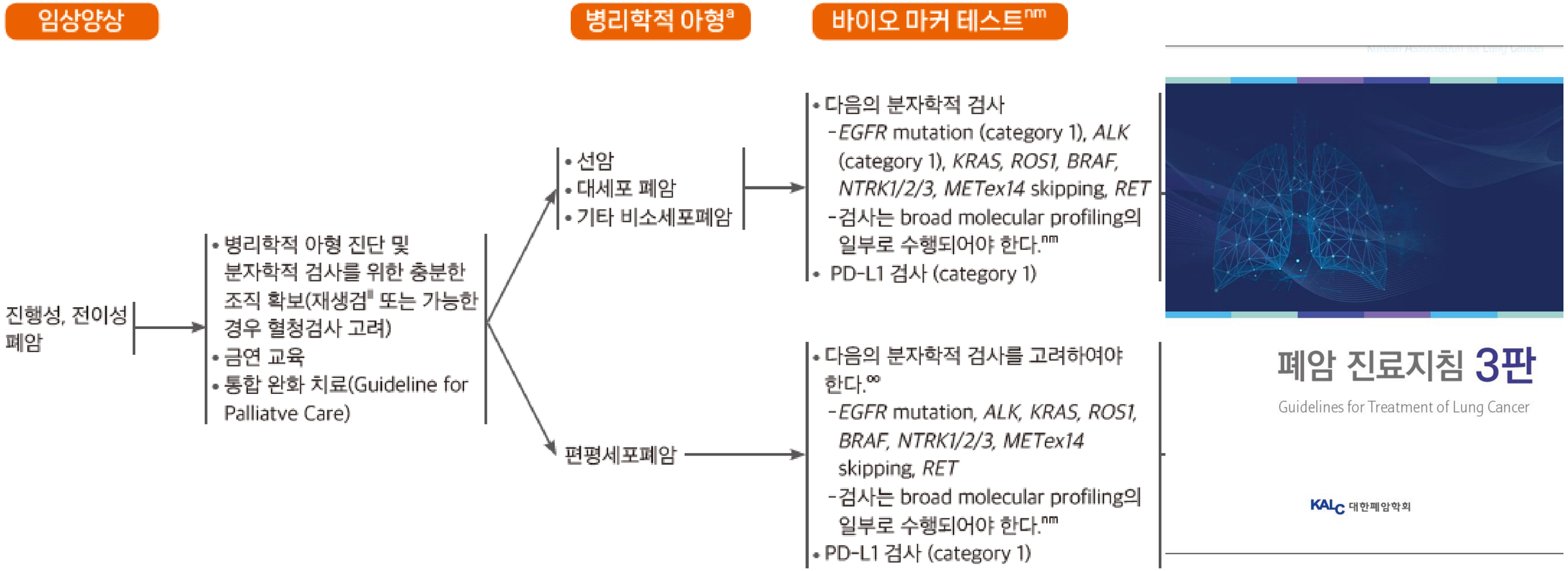
Introduction



Tan et al. J Clin Oncol 2022

General Guidelines for Biomarker Testing
- According to the Korean Association for Lung Cancer

Following CAP/ IASLC/ AMP, ASCO, and NCCN



2023 Guidelines for Treatment of Lung Cancer 3rd Ed. KALC

General Guidelines for Biomarker Testing
– According to the Korean Association for Lung Cancer

The key principles include:

1. Molecular testing for actionable genetic alterations and PD-L1 expression **should be performed for all patients with NSCLC**.

2. Actionable gene alterations
   - Essential genetic tests for NSCLC include EGFR, ALK, ROS1, and BRAF.
   - Tests for NTRK, MET, RET, HER2, and KRAS are recommended if EGFR, ALK, ROS1, and BRAF are negative, or as part of a comprehensive panel.

Biomarker tests in South Korea (2024)

Decision to perform tests?

Reflexively performed (60%)

Performed upon clinical request after diagnosis (33.3%)

Mixed (6.7%)

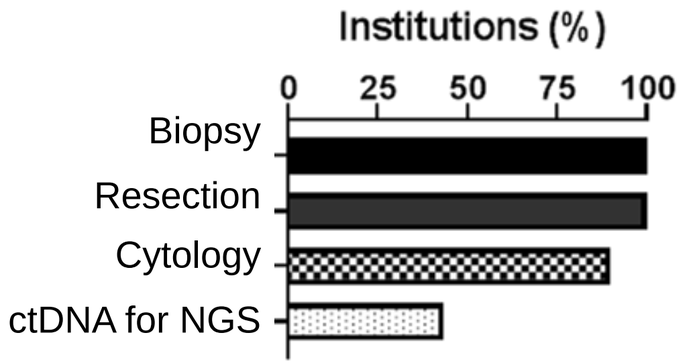
Upon biomarker test types, physician

If reflexively performed,

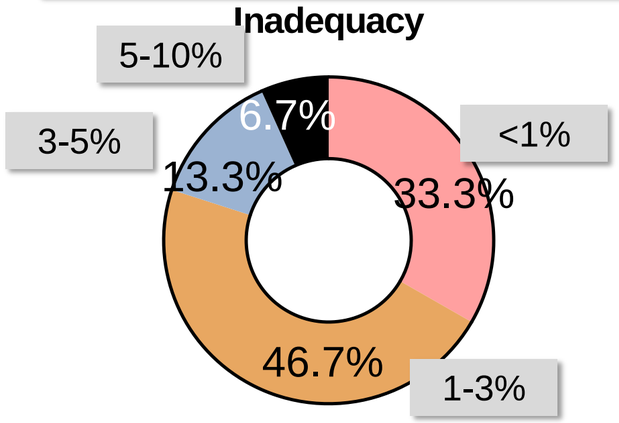
Performed in all tumors, regardless of the patient's stage (100%)

Performed only in metastatic or advanced tumors (0%)

Types of sample?



Inadequacy Frequency?



30 institutions

Types of molecular tests

Molecular tests vary by histologic subtype?

The same tests are performed for all NSCLC subtypes (60%)

Different tests are performed based on histologic subtype (40%)

- SqCC vs Non-SqCC (75%)
- Others (25%)

Generally, more types of tests are performed for non-SqCC than for SqCC.

For non-SqCC,

ALK = EGFR = PD-L1 (in all hospitals) > ROS1 > KRAS > BRAF

For SqCC,

PD-L1 (in all hospitals) > ALK = EGFR > ROS1 > KRAS > BRAF

For Small cell carcinoma,

Complete molecular subtyping X
POU2F3+ SCC reported (5/30, 16.7%)

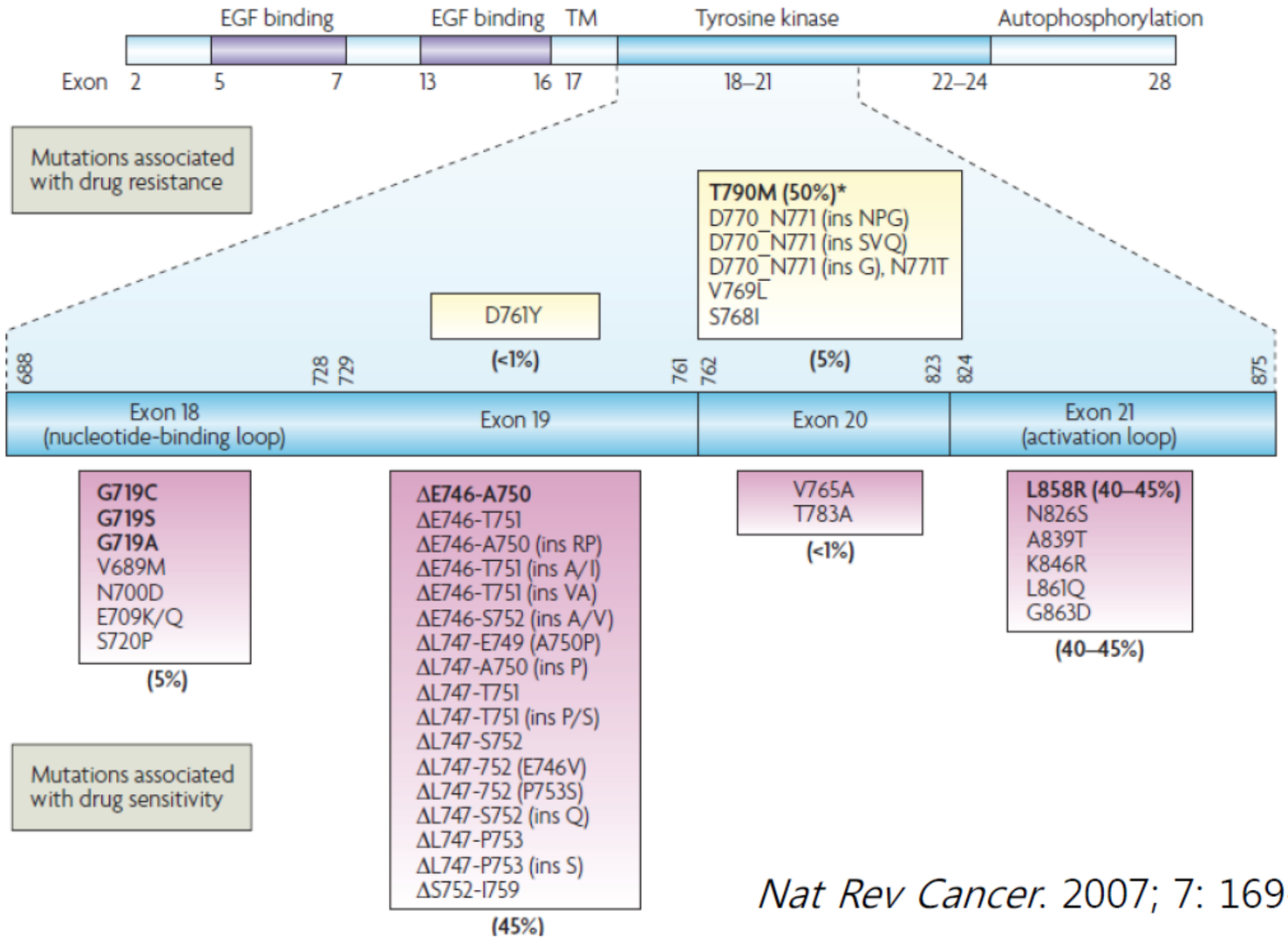
How to screen and detect the targetable oncogene?

	SNV	Fusion	CNV (Amp)	Etc
DNA	Pyrosequencing PCR-based method NGS	FISH Pyrosequencing NGS	FISH/CISH qPCR NGS	TMB (NGS~)
RNA		Fusion transcript (RT-PCR) NGS		
Protein	IHC (mutation-specific Ab)	IHC (expressed protein)	IHC (overexpression)	Expression-IHC (ex. PD-L1)
	EGFR, KRAS, BRAF	ALK, ROS1, NTRK1/2/3, RET	MET EGFR	
			MET	

Single gene tests

1. **Tissue availability**
   - Strategy for test selection when biopsy material is insufficient
2. **TAT**
   - Shortage of human and material resources
   - A less commonly performed test

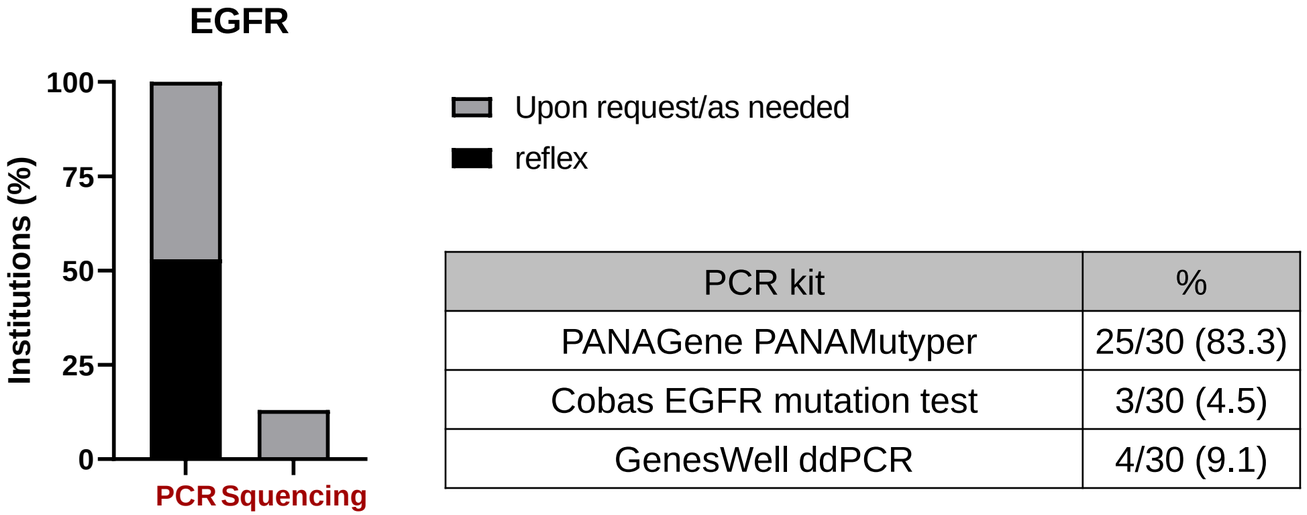
EGFR



Nat Rev Cancer. 2007; 7: 169-81.

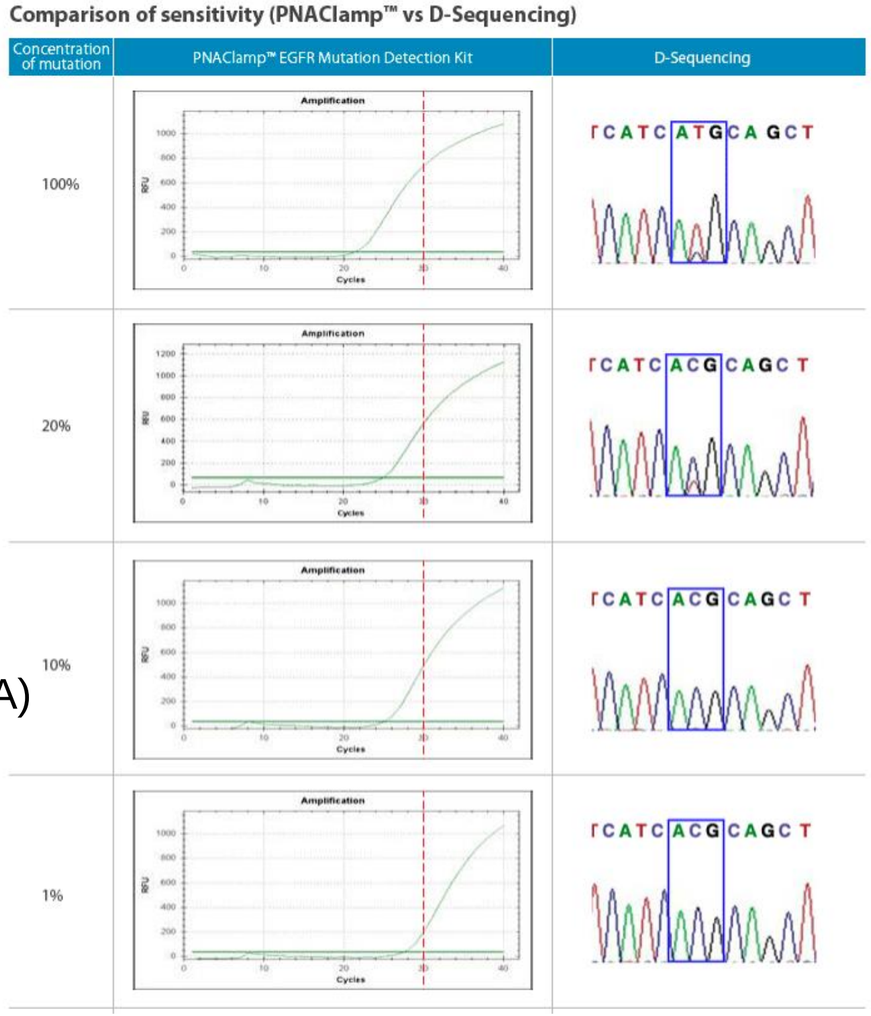
EGFR

PCR-based assays are more sensitive and require lower DNA input than direct sequencing.



PCR kit	%
PANAGene PANAMutyper	25/30 (83.3)
Cobas EGFR mutation test	3/30 (4.5)
GenesWell ddPCR	4/30 (9.1)

- Cobas® EGFR Mutation Test v2, Roche Molecular Systems (Roche, IN, USA)
- PNAClamp™ Mutation Detection Kit EGFR (ver.2) (panagene, Korea)
- GenesWell ddEGFR Mutation Test (Gencurix, Seoul, Korea)



50% of Ex20ins were not detected

		Sample	DNA	Detection limit	Time	Detection				
						Exon18	Exon19	Exon20	Exon21	Total
	Cobas EGFR mutation test	FFPE; plasma	150 ng* (50 minimum)	1.3~13.4% (1~5%)	4:00* (6-8h)	G719X (3)	Ex19Del (29)	S768I T790M Ex20Ins (5)	L858R (2) L861Q	42
semi-quantitative	PANAGene PANAMutyper	FFPE; plasma	300ng	<1%	2:40* (4-6h)	G719X (3)	Ex19Del (29)	S768I T790M Ex20Ins (10)	L858R (2) L861Q	47
Quantitative;	GenesWell ddPCR	FFPE; plasma	270 ng*	<1% most sensitive	0:40* 2:40* 1:30* (6-8h)	G719X (3)	Ex19Del (59)	S768I T790M Ex20Ins (33) C797X (4)	L858R (2) L861Q	107

More Labor intensive
Need an additional equipment

* According to datasheet

NGS: all novel EGFR mutation can be detected

ALK

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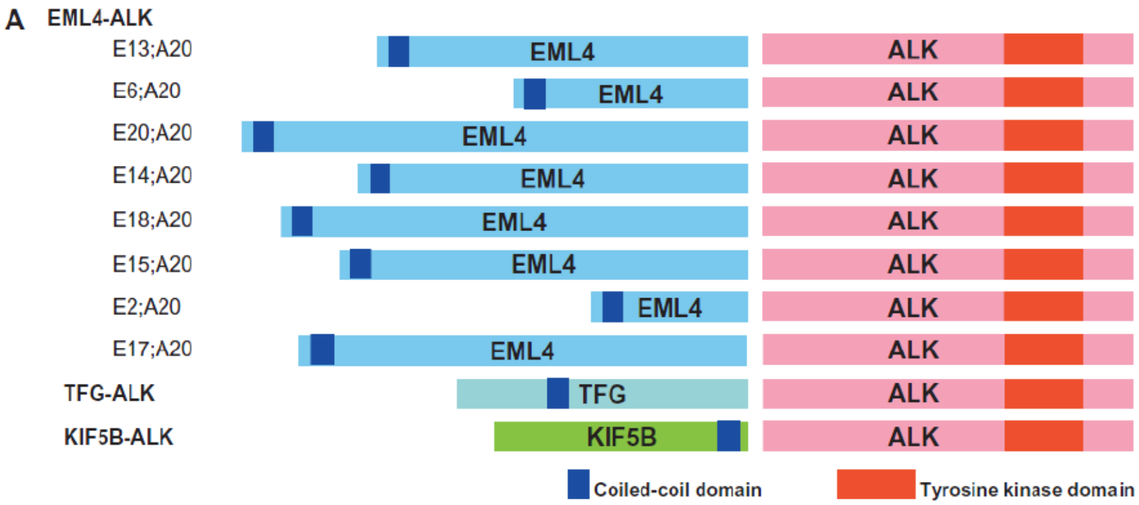
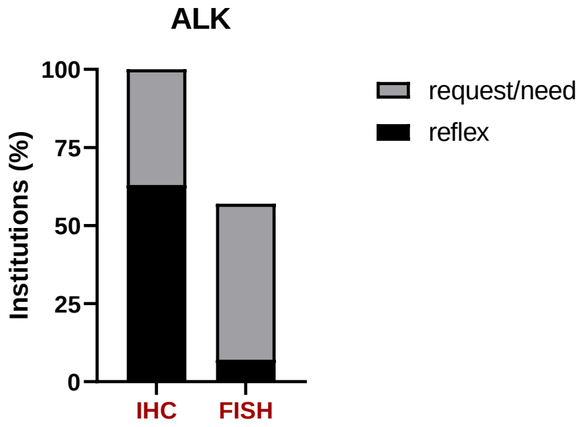
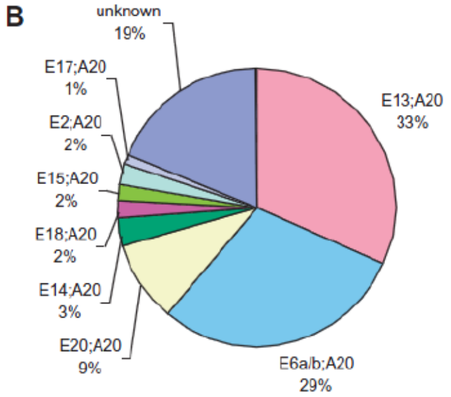
Variants of ALK fusions







EML4-ALK Variants

E13;A20	E13;A20 (variant 1), E13;ins69 A20
E6;A20	E6a/b;A20 (variant 3a/b)
E20;A20	E20;A20 (variant 2), E20;ins18A20
E14;A20	E14;ins11del49A20(variant 4'), E14;del12A20 (variant 7)
E18;A20	E18;A20 (variant 5')
E15;A20	E15 del19;del20A20 (variant 4)
E2;A20	E2;A20 &E2;ins117A20 (variant 5a/b)
E17;A20	E17;ins68A20

NSCLC Cell lines

H3122 and DFCI032 contain E13;A20. H2228 contain E6;A20

IHC Ab	%
D5F3	80.0
Both D5F3 / 5A4	16.7
5A4	3.3

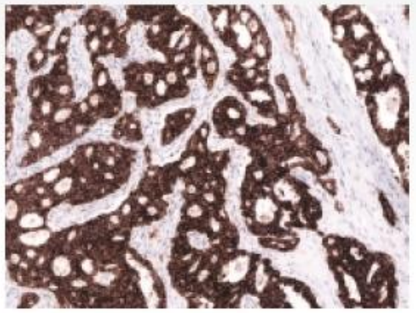
ALK (D5F3) CDx
Sensitivity 81-100%,
specificity 91-100%

FISH Ab	%
Vysis ALK Break Apart	95.5
ALK Break Apart (ZytoVision)	4.5

Eur J Cancer 2010;46:1773–1780

ALK IHC kit

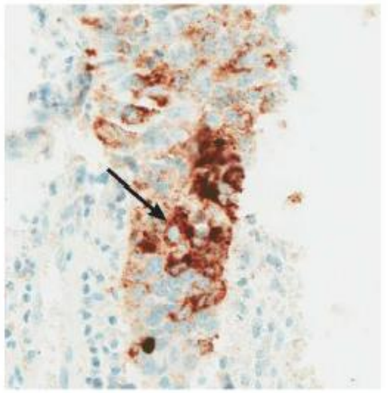
VENTANA ALK (D5F3) CDx Assay



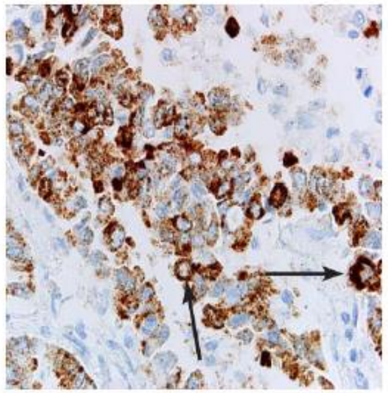
Catalog Number:	790-4796
Ordering Code:	06687199001
Quantity:	50 tests
Controls:	Appendix
Isotypes:	IgG
Clone Name:	D5F3
Species:	Rabbit Monoclonal
Localization:	Cytoplasmic
Regulatory Status:	IVD, FDA Approved (PMA)

VENTANA ALK (D5F3) CDx Assay is intended for the qualitative detection of the anaplastic lymphoma kinase (ALK) protein in formalin-fixed, paraffin-embedded (FFPE) non-small cell lung carcinoma (NSCLC) tissue stained with a BenchMark XT automated staining instrument. It is indicated as an aid in identifying patients eligible for treatment with XALKORI® (crizotinib).

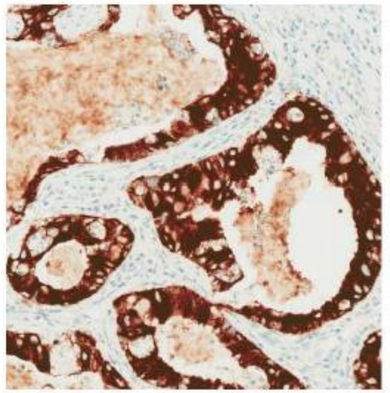
Clinical Diagnosis Positive



Few strong cytoplasmic staining tumor cells

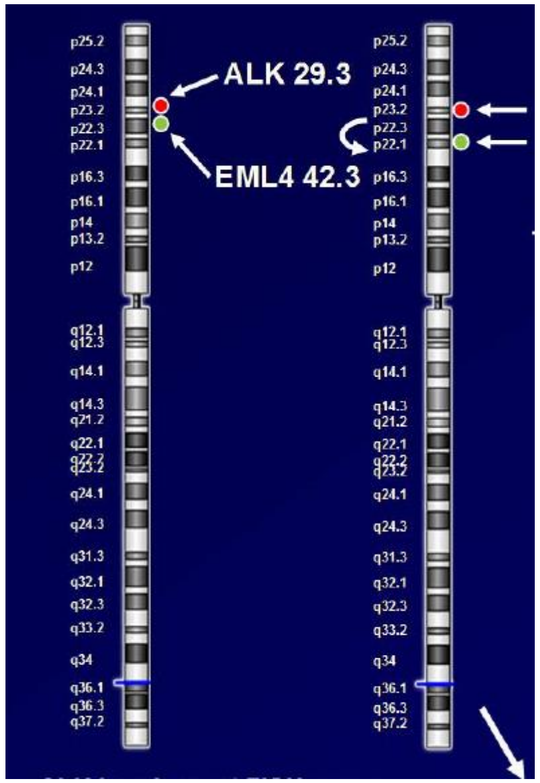


Strong cytoplasmic staining tumor cells



Homogeneously strong cytoplasmic staining within tumor cells

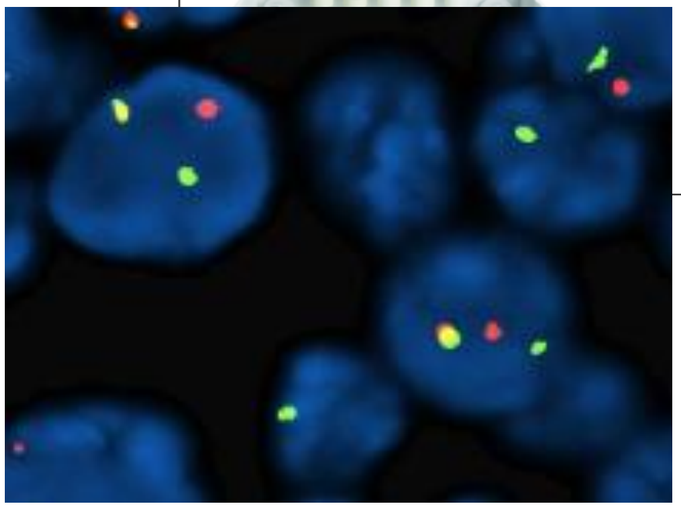
Labor-intensive
Requires a high level of expertise.
→ **Shift to IHC (or NGS)**



Product Description

Intended Use
The Vysis ALK Break Apart FISH Probe Kit is intended to detect rearrangements involving the ALK gene via fluorescence in situ hybridization (FISH) in formalin-fixed paraffin-embedded (FFPE) non-small cell lung cancer (NSCLC) tissue specimens.

Reduce variability with ready-to-use components
- Premixed, optimized probes
- ALK positive control slides
- ALK negative control slides
- Ready-to-use slide preparation reagents



Fusion partner?
In-frame?

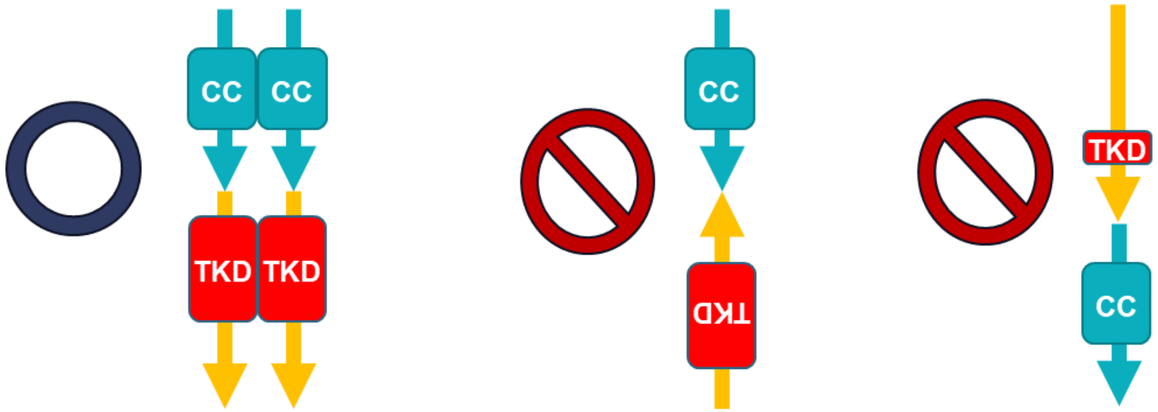
J Clin Oncol 2009;27:4247–4253

The Requirements for Fusion to be Functional

1. The fusion should retain the **protein coding frame**
   - The orientation of two gene should be the same (sense to sense)
   - The fusion should not induce frameshift

2. **Tyrosine kinase domain** should be preserved

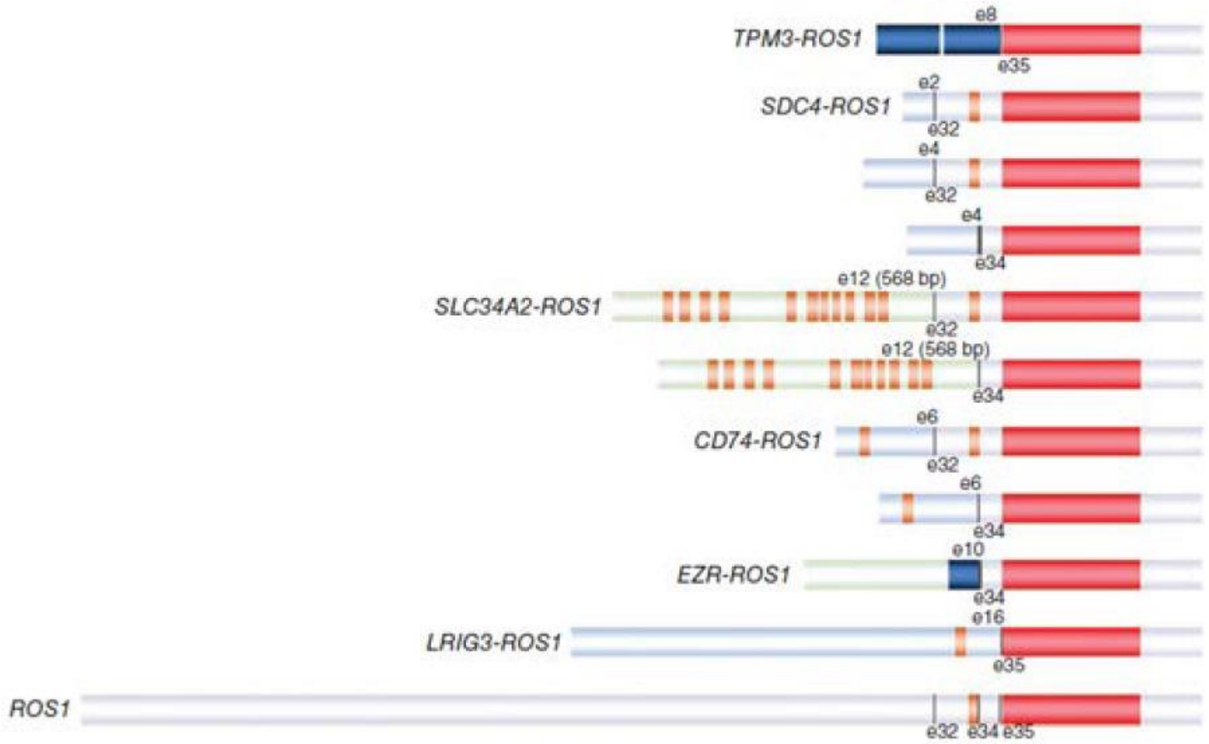
3. Partner gene should have ability to form **dimers/oligomers**
   - Example of dimerization domain: coiled-coil, leucine zipper, …



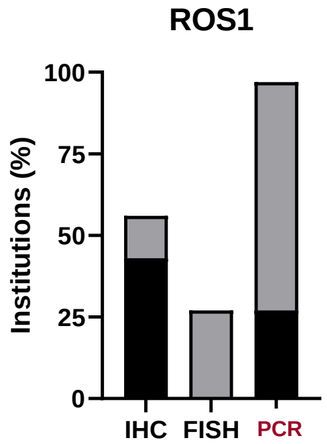
Slide from prof. Lee boram (SMC)

ROS1

Variants of ROS1 **fusions**



Nat Med 2012;18:378-81.



IHC Ab	%
SP384	94.1
D4D6	5.9

PCR kit	%
AmoyDx	100

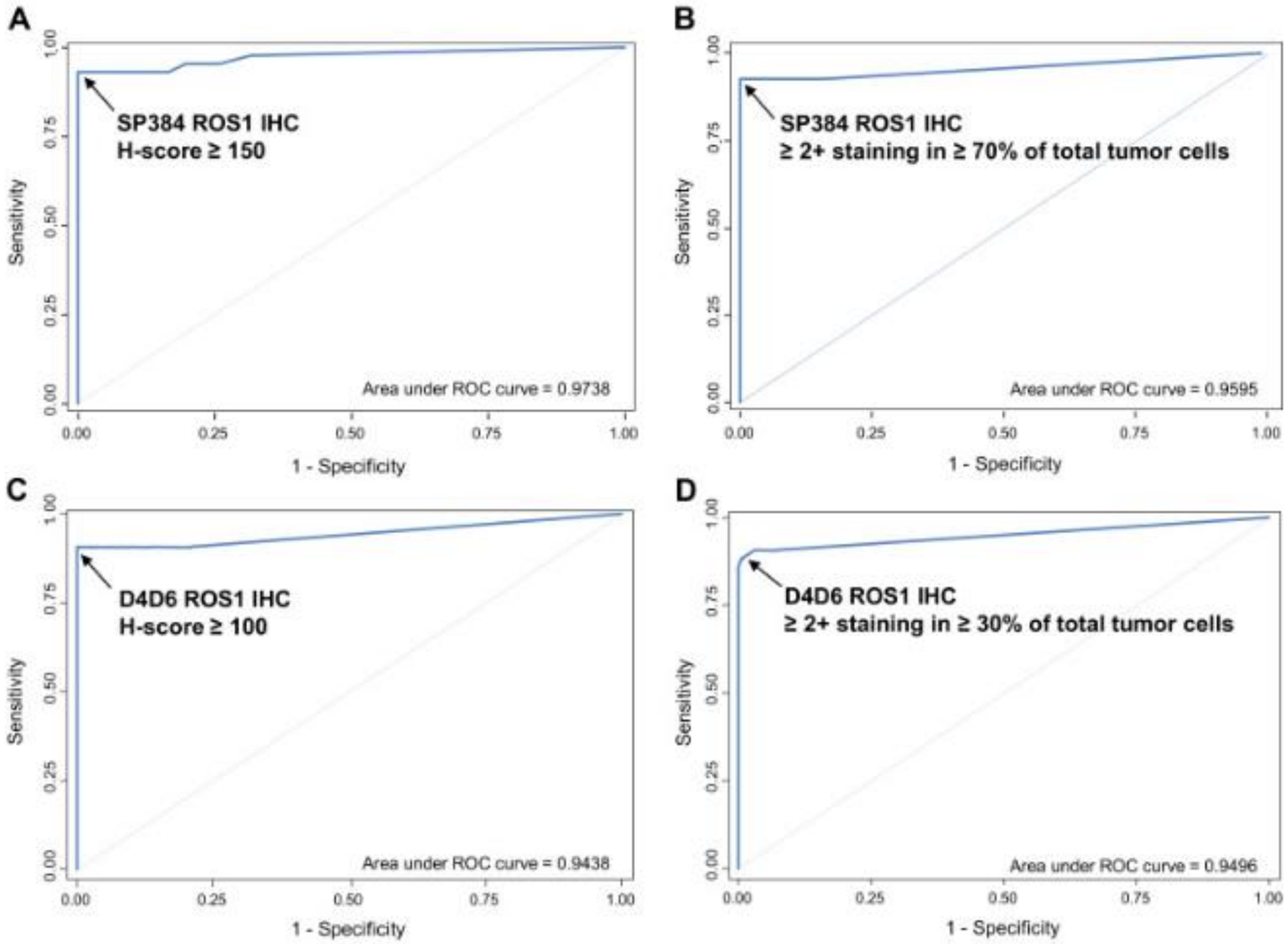
about 43% screen with IHC first, then confirm with PCR

The ROSING Study

SP384
- H-score ≥ 150
- 2+ ≥70% of tumor cells
➔ 93% sensitivity + 100% specificity

D4D6
H-score ≥ 100
➔ 91% sensitivity + 100% specificity

EGFR, ALK, KRAS 등 key alteration negative시, PCR 고려



Assessment of a New ROS1 Immunohistochemistry Clone (SP384) for the Identification of ROS1 Rearrangements in Patients with Non-Small Cell Lung Carcinoma: the ROSING Study. J Thorac Oncol. 2019 Dec;14(12):2120-2132.

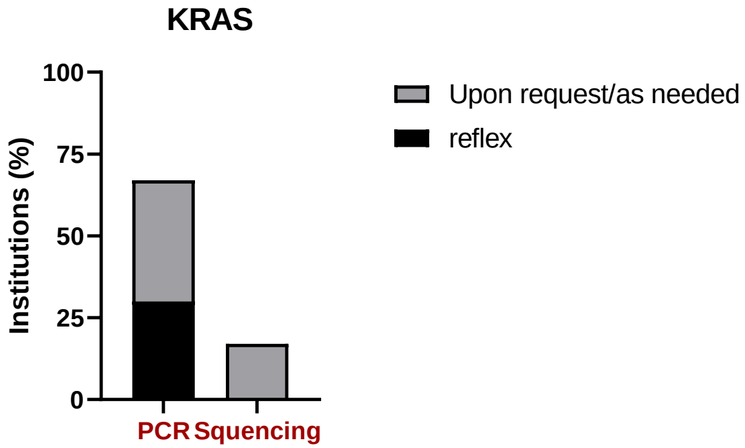
AmoyDx ® ROS1 Gene Fusions Detection Kit

***ROS1* Gene Fusions Detected by the Kit**

Reagent	Spliced Gene & Exon			ROS1 Spliced Exon
ROS1 Reaction Mix ①	*SLC34A2* exon4 *SDC4* exon2	*SLC34A2* exon13del *SDC4* exon4	*CD74* exon6	32
ROS1 Reaction Mix ②	*SLC34A2* exon4 *SDC4* exon4	*SLC34A2* exon13del *EZR* exon10	*CD74* exon6	34
ROS1 Reaction Mix ③	*TPM3* exon8	*LRIG3* exon16	*GOPC* exon8	35
ROS1 Reaction Mix ④	*GOPC* exon4			36

RNA: ~300ng (50~800 ng/uL *6uL)
Time: 2:40
- cDNA 1:00
- PCR 1:40

KRAS



PCR kit	%
PANAGENE (Oncotector Mutation Detection Kit)	100

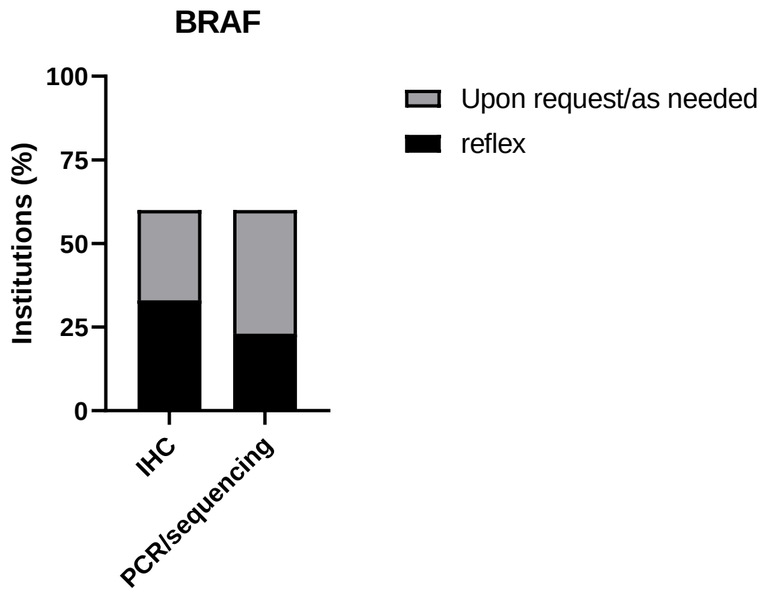
Time: 2:20
DNA: 40ng (10ng*4)
Detection limit: ~2%

G12A
G12D
G12R
G12C
G12S
G12V
G13D

BRAF

BRAF (VE1) IHC
- Sensitivity: 95-100%
- Specificity: 95-100%

PNAClamp BRAF mutation kit
Detection limit: 1%
DNA: 10ng/uL
Time: 1:40
Detect: V600 mutation



IHC Ab	%
VE1	100

PCR kit	%
PNAClamp BRAF Mutation Detection Kit	78.6
Direct Sequencing	14.3
Biosewoom Real-Q BRAF V600E Detection Kit	7.1

33% start with IHC as a reflex test (screening) and confirm with PCR or sequencing

Real-world assessment of the BRAF status in non-squamous cell lung carcinoma using VE1 immunohistochemistry: A single laboratory experience (LPCE, Nice, France). Lung Cancer. 2020 Jul;145:58-62

EP06.03-21 Usefulness of Immunohistochemistry for the Detection of BRAFV600E in Lung Cancer: A Multicenter Retrospective Study in China, Yuan, P. et al. JTO 2023, 18;11, S491 - S492

MET, RET, HER2 and NTRK1/2/3

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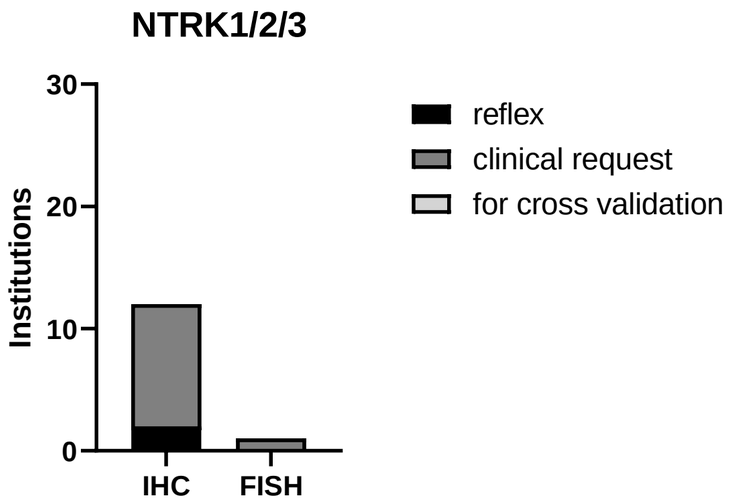
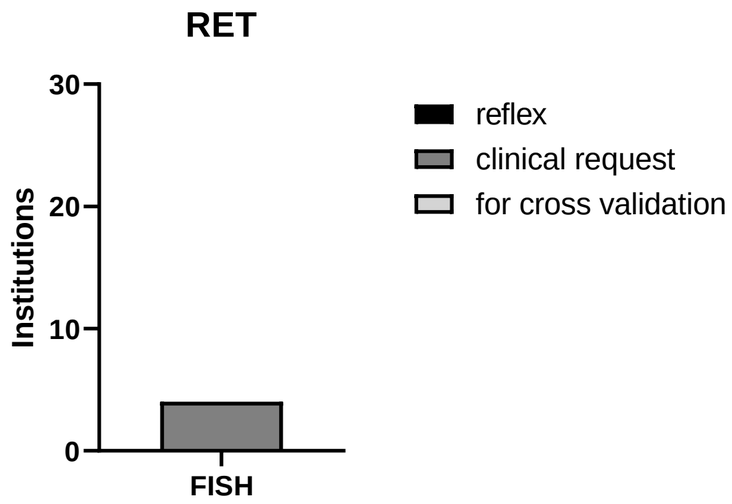
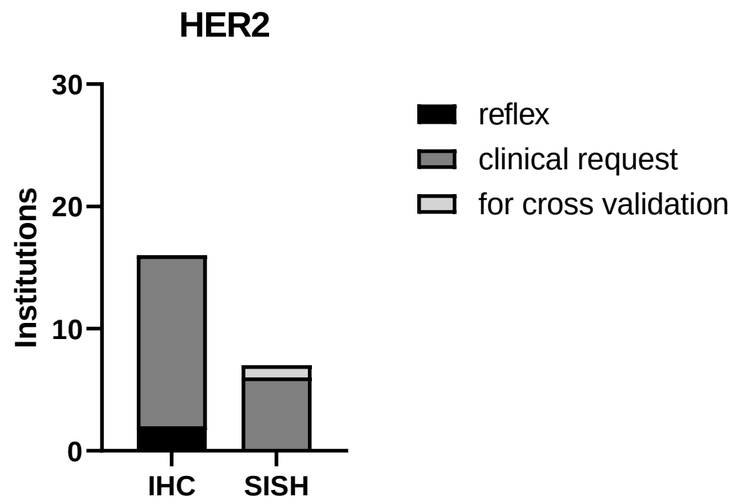
NGS testing for NTRK, MET, RET, and HER2 is recommended by the Korean Society of Pathologists.







IHC Ab	%
VENTANA® pan-TRK (EPR17341)	100

FISH	%
SPEC RET Break Apart FISH Probe RUO kit(Abbott)	100

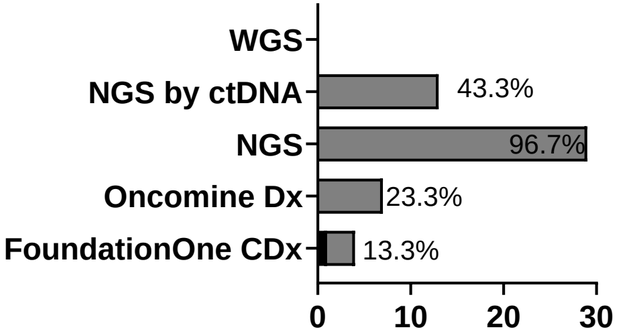
IHC Ab	%
4B5	100

Comprehensive genomic test (NGS by tissue)

1. Tissue availability
2. TAT
3. Difficulty in interpreting complex results and generating reports

Types of molecular tests

For Broad molecular testing,



Two institutions stated that WGS is set up but not yet in use.

NGS

- 96.7% (29/30) of institutions
- In-house (72.4%) + Outsourced (27.6%)

NGS by ctDNA

- 43.3% (13/30) of institutions
- In-house (38.5%) + Outsourced (61.5%)

Custom panel (7.4% of institute)

Types	No of Genes	n
Lung cancer	75	1
Solid tumor	50-546	4

Commercial panel (92.6% of institute)

Types	No of Genes	n
Lung cancer	23	2
Solid tumor	323-550	29

Commercial panel provider,

Illumina (53.3%) | Thermo Fisher (46.7%)

Oncomine Dx Target Test

- 23.3% (7/30) of institutions
- Upon clinical request (100%)
- Through pathology department (100%)
- In-house (28.6%) + Outsourced (71.4%)

NGS

- 96.7% (29/30) of institutions
- Upon clinical request (100%)
- Through Pathology (86.2%), Clinical Laboratory department (3.4%) and Joint management with Clinical Laboratory department (10.3%)
- In-house (72.4%) + Outsourced (27.6%)

NGS by ctDNA

- 43.3% (13/30) of institutions
- Upon clinical request
- Through Pathology (53.8%) and Clinical Laboratory Department (46.2%)
- In-house (38.5%) + Outsourced (61.5%)
- TSO500 ctDNA (1) + 랩지노믹스OTD (1) + 자체 (3) + Unknown/not answered (8)

Category	Oncomine Dx Target Test	FoundationOne CDx	Oncomine Comprehensive Assay Plus (OCA plus)	TruSight Oncology 500 (TSO500)
Manufacturer	Thermo Fisher	Foundation Medicine (Roche)	Thermo Fisher	Illumina
Number of Genes	**46**	**324**	**517**	**523**
Targets	SNV, indel, fusion, CNV	SNV, indel, fusion, CNV, MSI, TMB	SNV, indel, fusion, CNV, TMB, MSI	SNV, indel, fusion, CNV, TMB, MSI
DNA Input	≥ 10 ng	≥50–200 ng	≥ 20 ng (recommended 80–100 ng)	≥ 40 ng
RNA Input	≥ 10 ng	_	≥ 20 ng	≥ 40 ng
TMB/MSI Reporting	X	O	O	O
Companion Dx Approval	O (EGFR, ALK, ROS1, BRAF)	O (FDA-approved for 20+ drugs)	X	X
Turnaround Time (TAT)	3–5days	10–14days (USA)	3-5days	5–7days
Key Features	Fast, clinically approved test for key lung cancer markers	Widely used comprehensive panel with FDA approvals; outsourced analysis	Broad in-house tumor profiling	Broad research-grade panel, strong RNA fusion coverage

Tumor purity >20%

Oncomine Dx Target Test (ODxTT)

비소세포성 폐암 동반진단 NGS 검사의 유용성

- 단 한번의 검사로 23종 유전자 변이를 검출하여 추가적인 생검 필요성 감소
- 적은 양의 환자 검체로 신속하게 진단하여 치료 방향 설정 시간 단축
- 동반진단으로 4종 유전자 변이에 대한 표적치료제 대상 환자 빠르게 선별

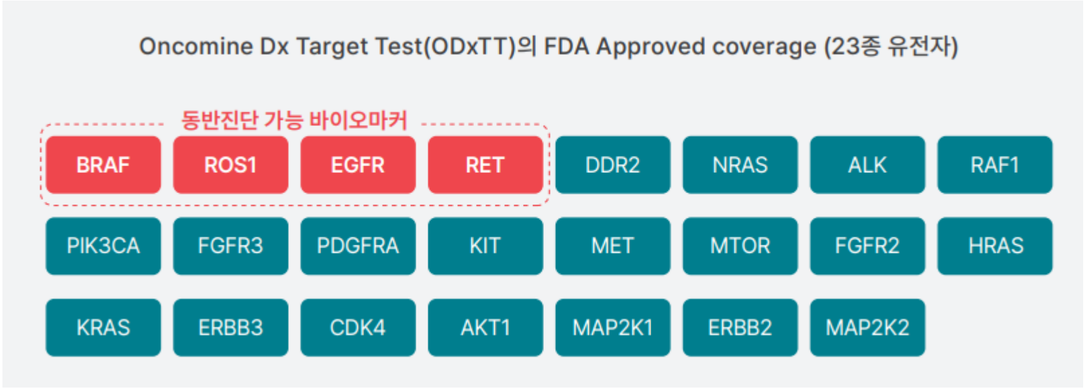
유전자	변이	동반진단 가능 치료제
BRAF	*BRAF* V600E	RAFINLAR® + MEQSEL® (dabrafenib in combination with trametinib)
ROS1	*ROS1* fusion	XALKORI® (crizotinib)
EGFR	*L858R*, exon 19 deletions	IRESSA® (gefitinib)
	exon 20 insertions	RYBREVANT™ (amivantamab)
RET	*RET* fusion	RETEVMO® (selpercatinib)

All genes included in the Oncomine Dx Target Test

DNA panel, hotspot genes	*AKT1*	*FGFR2*	*MAP2K1*
	ALK	*FGFR3*	*MAP2K2*
	AR	*GNA11*	*MET*
	BRAF	*GNAQ*	*MTOR*
	CDK4	*HRAS*	*NRAS*
	CTNNB1	*IDH1*	*PDGFRA*
	DDR2	*IDH2*	*PIK3CA*
	EGFR	*JAK1*	*RAF1*
	ERBB2	*JAK2*	*RET*
	ERBB3	*JAK3*	*ROS1*
	ERBB4	*KIT*	*SMO*
	ESR1	*KRAS*	
RNA panel, fusion drivers	*ABL1*	*ETV4*	*NTRK2*
	ALK	*ETV5*	*NTRK3*
	AXL	*FGFR1*	*PDGFRA*
	BRAF	*FGFR2*	*PPARG*
	ERBB2	*FGFR3*	*RAF1*
	ERG	*MET*	*RET*
	ETV1	*NTRK1*	*ROS1*

List of companion diagnostics
EGFR (E19del, L858R, 20ins), BRAF, ROS1, RET

List of analytic validation
KRAS MET PIK3CA



Category	Thermo Fisher OCA Plus	Illumina TruSight Oncology 500
Sequencing Method	Amplicon-based target sequencing (DNA + RNA)	Hybrid capture-based target sequencing (DNA + RNA)
Number of Genes	517 genes (DNA + RNA) –fusion 49	523 genes (DNA), 55 genes (RNA fusion)
Detectable Variant Types	SNV, Indel, CNV, Fusion, Splice variants	SNV, Indel, CNV, Fusion, Splice variants
Fusion D… Method		…nowl…
TMB Ana…		…TMB)
MSI Anal…		…vity)
HRD Ana…		…omic…
Input Ma… (FFPE)		
Turnarou…		
Analytica… Sensitivit…		
Analytica… Specificit…		
Bioinform… Platform	…al reporting	
Panel Cost (per sample)	상대적 저렴; 장기 초기 비용 상대적으로 저렴	시퀀싱 장비 고가

- 신속성+자동화 **(Hands-on time 짧음)**
- 낮은 시료 요구량
- 상대적으로 낮은 비용
- 숙련도 요구 낮음 **(실험 + 자동보고서 생성-NGS** 해석 경험이 적은 기관도 결과 활용 용이)
- **HRD** 지표 제공 **(score** 제공)

- **긴 TAT**
- **높은 시료요구량**
- **높은 비용**
- **숙련도 요구 (실험 + BI)**
- **HRD** 지표 부재 **(개발 중)**

- Homopolymer error 등으로 false call 가능 + primer 부위에 변이가 있는 경우 해당 allele 증폭 실패 가능
- 상대적으로 낮은 **throughput (**대형과제 부적합)
- 데이터 형식 제한: **illumina**에 비해 **raw data customizing** 분석 어려움.

- High sensitivity + **specificity**
- 유전자 **coverage** 넓음, 균일한 **coverage**
- **Novel alteration (unknown variant, fusion..)**
- 대규모 병원 적합:**high throughput**
- 광범위한 활용: 동일 플랫폼으로 다양한 연구 가능, **Illumina** 생태계와 연계 가능**(WES, WGS, ctDNA..)**

Single gene test vs NGS

	Single-Gene Testing	NGS
Comprehensiveness	Single-gene test; predefined targets	multi-gene coverage + multiple mutation types in parallel; uncover rare or unexpected variants (for resistance work-ups, NGS provides a broader view of tumor evolution)
Analytical Sensitivity	Sanger (15-20%); PCR based (1-5% → <1%)	Comparable or even more sensitive
TAT	Shorter TAT	Longer (2-3wks)
Cost/ Reimbursement	ALK (IHC), EGFR, ROS1, BRAF, KRAS (PCR) +NTRK1/2/3, MET, RET, HER2 Cumulative test cost: less expensive Patient's final burden: much lower	–
Tissue requirement	Cumulative, more	Less
Interpretation	A binary result for known targets.	Challenge of interpreting complex results Labor intensive

Selection of mutation test as routine platform

Reimbursement

In-house setting | Analytic platform

Turnaround time

Tissue requirement

Institutional preference

Current Best-Practice Paradigm: Finding the Balance

- NGS panel testing has emerged as the preferred strategy for comprehensive mutation analysis.

- The **optimal strategy** often combines both approaches.
  - Rapid single-gene tests may be used for certain critical markers (to expedite treatment decisions), while broad NGS panels provide a comprehensive profile.
  - Histologic Dx + PD-L1 + EGFR/ALK/(KRAS/ROS1/BRAF)
  - NGS

Comprehensive genomic test (NGS by liquid bx)

Liquid Biopsy in NSCLC

Liquid biopsy

- Analyze circulating tumor DNA (ctDNA) in the patient's blood (plasma) to detect cancer-related genetic alterations.

Techniques for Liquid Biopsy Molecular Testing:

- *Targeted single-mutation tests:* EGFR plasma test
- *Plasma NGS*

"plasma-first" approach: NILE study (Noninvasive vs. Invasive Lung Evaluation).
In NILE, treatment-naive advanced NSCLC patients had tissue testing and parallel plasma NGS (Guardant360); comparable sensitivity for finding drivers

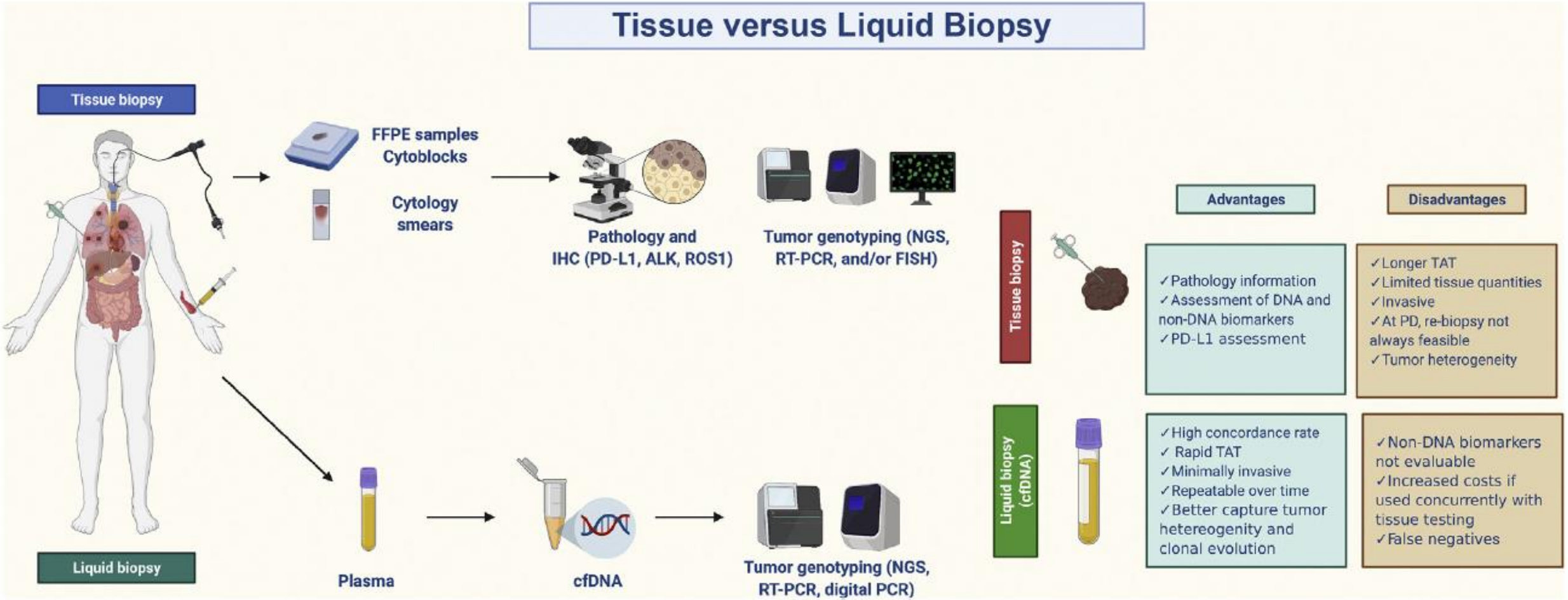
Detection of Resistance Mutations (Upon Progression):
liquid biopsy allows us to survey the tumor's new genetic landscape at progression in a less invasive way,

Monitoring and Emerging Applications: treatment monitoring and minimal residual disease (MRD) assessment.

However, the main current guideline-endorsed uses of liquid biopsy are:
(1) as a complement at baseline if tissue is an issue, and
(2) at acquired resistance to detect new mutations.

플랫폼 (개발사)]	cfDNA	포함 유전자 수	검출 변이 종류	특징 및 승인 여부
Guardant360 CDx (Guardant Health)	5-30ng	~74	SNV, Indel, Fusion (주요 6 genes), CNV + MSI qualitative result	FDA 승인 동반진단 검사 Lung: EGFR E19del, L858R, T790M, Ex20ins; ERBB2 mutation; KRAS G12C 전세계 임상 활용 넓음, 보고서에 치료 가이드 포함
FoundationOne Liquid CDx (Foundation/Roche)	20ng	300+	SNV, Indel, Fusion, CNV + TMB, MSI	FDA 승인 동반진단 검사 Lung: ALK, EGFR E19del, L858R 광범위 패널로 포괄적 분석 가능
Illumina TSO 500 ctDNA (Illumina)	20ng	523	SNV, Indel, Fusion, CNV + TMB, MSI	RUO 대형 패널 (임상시험/연구용) 자체 NGS 장비로 시행, 대용량 정보 산출
Roche AVENIO (Roche)	10-50ng	17 (targeted) 77 (expanded)	SNV, Indel, Fusion, CNV (패널에 따라 다름)	RUO 3종 패널 (Targeted/Expanded/Surveillance) 맞춤 선택 가능, MRD 특화 패널 포함
Oncomine LB (Thermo Fisher)	20ng	50여 개 (Pan-Cancer) Lung cancer panel (11 genes; >150 hotspots)	SNV, Indel, Fusion (hotspot 위주), CNV 일부	RUO Ion Torrent 기반 패널 빠른 시퀀싱 사이클, 저비용 LDT 활용

Liquid Biopsy in NSCLC (cfDNA Testing and Applications)



Liquid Biopsy for Advanced NSCLC: A Consensus Statement From the International Association for the Study of Lung Cancer, JTO 2021

NGS by liquid biopsy

고려대학교구로병원 KOREA UNIVERSITY GURO HOSPITAL

"negative plasma test does not guarantee the absence of mutation"

Category	Tissue Biopsy (NGS)	Liquid Biopsy (ctDNA-based NGS)
comprehensive	Tumor heterogeneity	Global snapshot of tumor heterogeneity Non-DNA biomarker or protein expression detectionX
Sensitivity	High – Direct analysis of tumor cells; high DNA input and allele frequency	Moderate – Depends on ctDNA levels; Limited in early or low-volume disease or brain metastasis
Specificity	Very high – Detected variants are tumor-derived	High – True positives likely; CHIP-related mutations
Types of Detectable Variants	Broad – SNVs, fusions, CNVs, TMB, MSI	Broad, but with lower limit of detection – SNVs, *selected fusions/CNVs; TMB, MSI*
Cost	Similar	Similar
Patient Convenience	Low – Requires invasive sampling	Very high – Noninvasive blood draw; minimal discomfort; easily repeatable
Sample Limitations	Limited by tumor location/quantity; insufficient/poor-quality tissue common	Easy to collect, but ctDNA may be absent or low; possible contamination by leukocyte gDNA
Clinical Use	Essential for initial diagnosis and therapy selection; pathology and molecular profiling	Useful for therapy monitoring, resistance mutation detection, MRD tracking, recurrence surveillance
TAT	~2–3 weeks for result	Faster turnaround (~7–10 days); ideal for dynamic monitoring

CHIP = Clonal Hematopoiesis of Indeterminate Potential
TP53, DNMT3A, TET2, ASXL1, PPM1D, SF3B1, JAK2…

Korea: 20 days vs 15days (median)

감 사 합 니 다