

AmoyDx Essential NGS panel (LC 10), One Solution Covering Tumor Tissue and Plasma for detection of EGFR and cMET alterations (alts) in NSCLC

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Key Takeaway

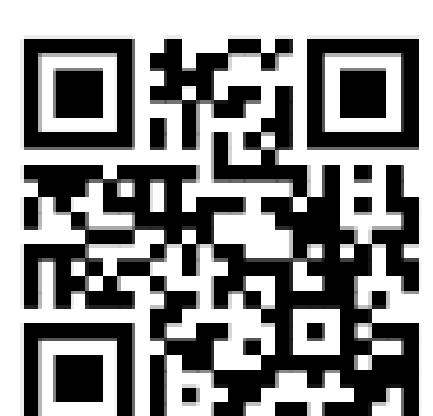
AmoyDx LC10 NGS Panel provides a comprehensive solution for detecting key driver mutations in lung cancer, enabling simultaneous analysis of both tissue and plasma with a unified platform. Utilizing dual-end capture ddCapture[®] technology, LC10 ensures high sensitivity and specificity, even in low-input or challenging samples, making it a powerful tool for precise and reliable mutation detection in clinical diagnostics. Given the tissue sample unavailability and quality issue, an integrated approach combining tissue and plasma sequencing enhances the identification of actionable mutations, ultimately guiding more effective treatment strategies.

Conclusions

ctDNA is a reliable tool for treatment guidance in stage IIIB-IV NSCLC, effectively detecting both primary driver mutations and acquired resistance.

The variant allele frequency in ctDNA from patients with stage I-IIIa was lower than stage IIIB-IV, indicating a lower amount of ctDNA shedding occurring in NSCLC early stage (I-IIIa).

The LC10 NGS panel offers a comprehensive solution for detecting alterations in both tissue and ctDNA, expanding sample accessibility and streamlining NSCLC diagnosis and treatment.



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Disclosures

Min Qing, Xiaofang Zhuo, Chengjuan Xiong, Longen Zhou, Flora Berisha are full employee of Johnson & Johnson.

Xing Li, Cheng Li, Yin Shi, Xuejun Chen, Zhenjun Tan and Changbin Zhu are full employee of AmoyDX.

Introduction

- Approximately 50% of Asian non-small cell lung cancer (NSCLC) patients carry EGFR and MET alterations with available targeted therapies.
- Current commercial testing systems often use different NGS platforms for tissue and plasma analysis, limiting direct comparability and sample accessibility.
- Liquid biopsy strongly complements clinical diagnosis needs in situations where tissue is inaccessible or with low-quality in NGS testing¹ (~10%-15% failure rate).
- By providing a unified NGS platform, LC10 enhances mutation detection accuracy and supports more informed treatment decisions for NSCLC patients.

Methods

LC10 Detection Methodology

- The LC10 applies to both FFPE tissue and plasma. Using ddCapture[®] dual - end capture, it boosts recovery and specificity for accurate detection (Fig. 1). It needs 50 ng tissue DNA or 10 ng cfDNA, and supports 10,000X sequencing for mutation identification. The LC10 panel can detect alterations in 10 NSCLC key driver genes (Table 1).

Sample Distribution

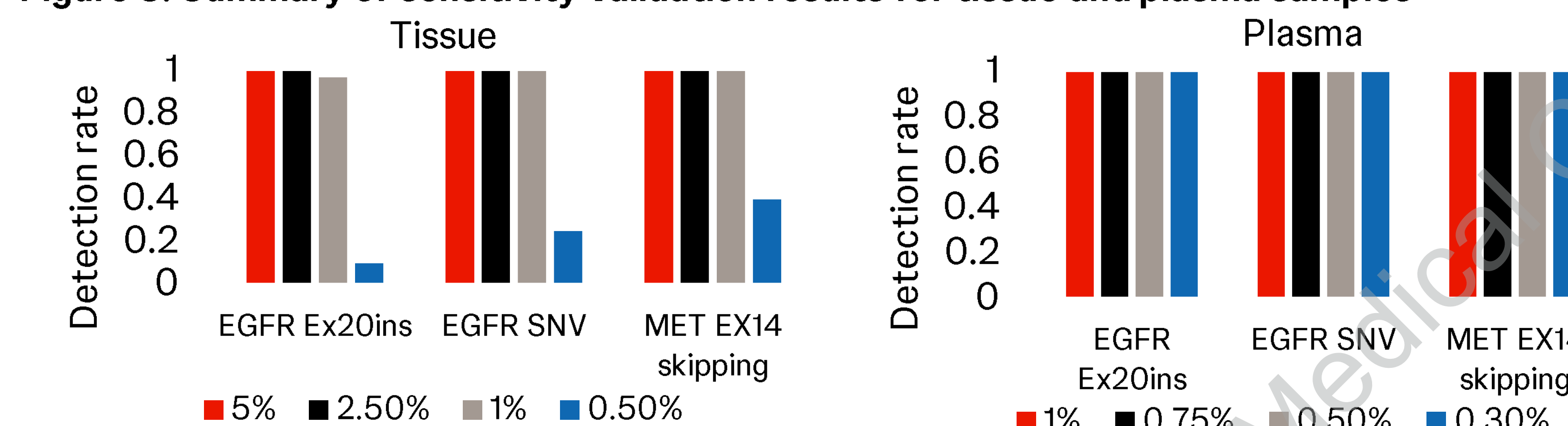
- For analytical validation, we used clinical samples with variously diluted mutations (EGFR Ex20ins, Ex19del, L858R, MET Ex14 skipping), 11 plasmids in HEK-293T cells with 3rd TKI EGFR resistance mutations, plus 131 plasma and 156 tissue samples.
- In clinical validation, paired blood and tumor tissue from 323 NSCLC patients were analyzed by LC10 panel. Total 7 tissue samples were failed, while all plasma samples were successfully tested. Finally, 316 paired samples were included in the analysis.

Results

Confirmation of the Limit of Detection (LoD) Performance of LC10 with Cell Lines and Clinical Samples

- LOD was confirmed as 1% for tissue and 0.3% for plasma for EGFR SNV, Ex20ins and MET ex14 skipping (Fig. 3).
- Using 131 tissue and 156 plasma samples, the concordance between LC10 and amplicon-based NGS assay was 100% in both tissue and plasma.

Figure 3. Summary of sensitivity validation results for tissue and plasma samples



LC 10	Amplicon-based NGS				LC 10	Amplicon-based NGS			
		Pos	Neg	Total			Pos	Neg	Total
	Pos	35	0	35		79	0	79	
	Neg	0	96	96		0	77	77	
	Total	35	96	131		79	77	156	
	PPA	100% (95%CI: 90.1%-100%)				100% (95%CI: 95.4%-100%)			
	NPA	100% (95%CI: 96.2%-100%)				100% (95%CI: 95.3%-100%)			

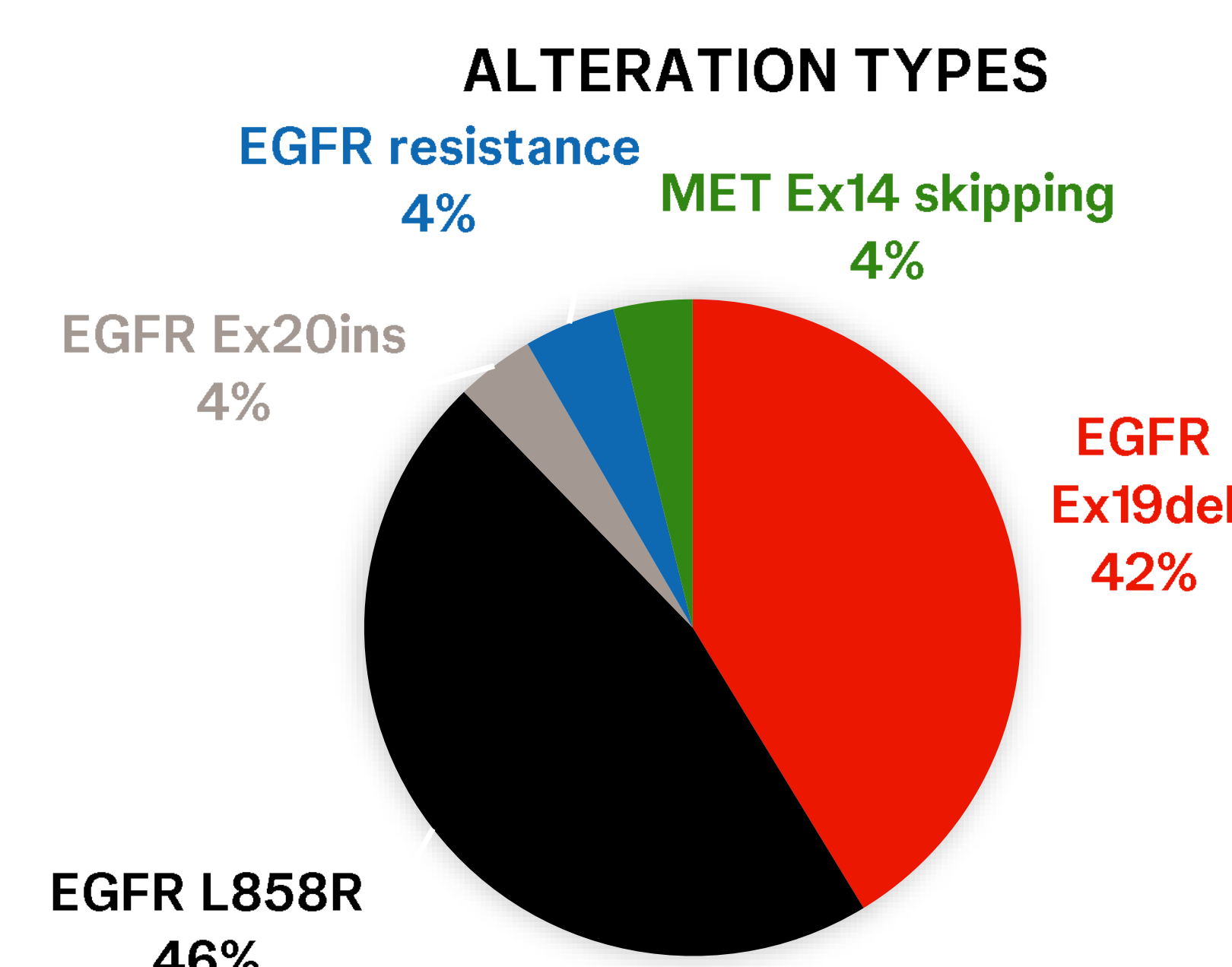
* Pos: Positive; Negative: Neg; PPA: Positive Percent Agreement; NPA: Negative Percent Agreement.

Patient Characteristics and Tissue Alterations

- A total of 316 patients with paired tissue and plasma were enrolled mainly from lung adenocarcinoma patients, including 198 patients from stage I - IIIa and 118 from stage IIIB - IV. Among these, 154 (48.7%) tissue samples were confirmed harboring actionable alterations. Regarding treatment history, 79.7% of patients were treatment-naïve, while 20.3% had experienced disease progression following prior treatments, such as Gefitinib, Osimertinib, and chemotherapy (Fig. 4). The EGFR and MET alteration distribution were shown in Fig. 4 and Table 2.

Figure 4. Patient characteristics and mutation distribution

The patient characteristics	
Characteristics	No. of Patient(%)
Age, years, median (range)	59 (24-87)
Sex, n	
Male	163 (51.6%)
Female	153 (48.4%)
Histologic type, n	
LUAD	271 (85.7%)
LUSC	34 (10.8%)
Others	11 (3.5%)
Stage, n	
I-IIIa	198 (62.7%)
IIIB-IV	118 (37.3%)
Treatment status, n	
Treatment naïve	252 (79.7%)
Progression	64 (20.3%)



References

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- JAMA Oncol. 2022 Sep 1;8(9):1328-1332.
- Cancer Med. 2023 Apr;12(7):7982-7991.
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Figure 1: Workflow of ddCapture[®]

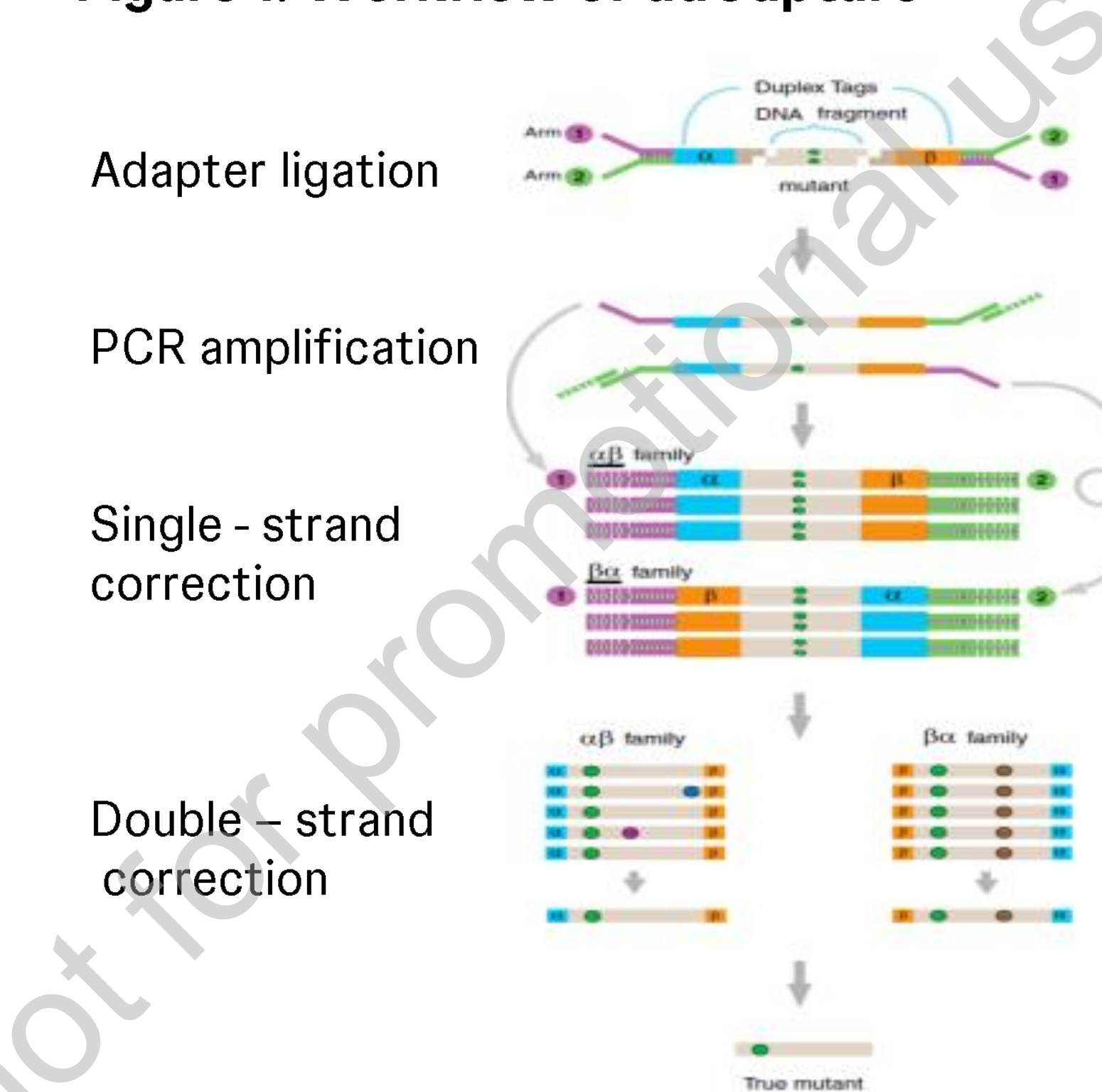


Table 1: Gene list of AmoyDx LC10

EGFR	ALK	ROS1	KRAS	BRAF
MET	RET	HER2	NRAS	PIK3CA

Figure 2: Sample Distribution

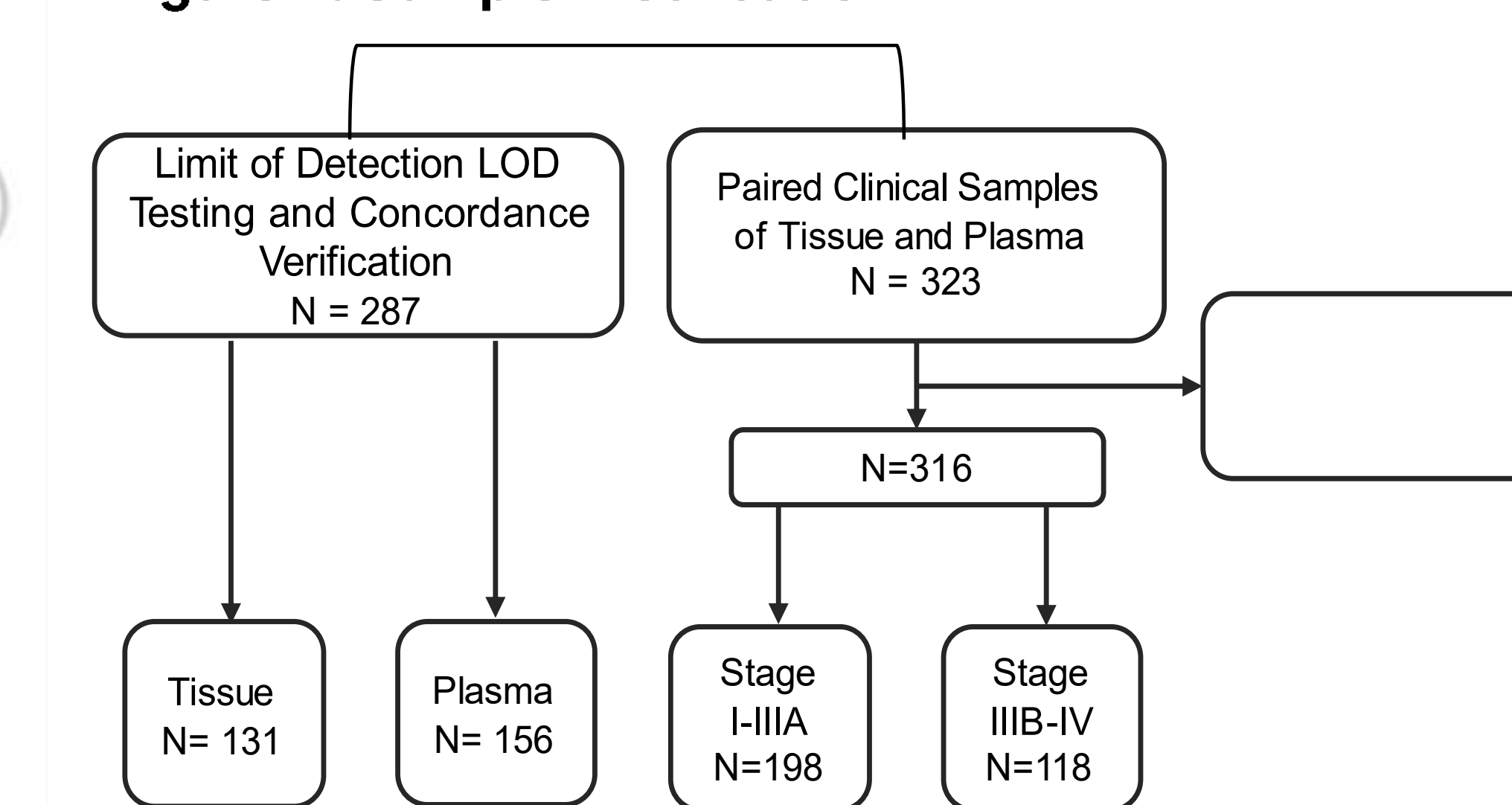


Table 2: EGFR and MET alteration distribution

Alteration type	Alteration site	N
EGFR L858R	p.L858R	75
	p.E746_A750del	31
	p.L747_P753delinsS	7
	p.E746_S752delinsV	5
	p.L747_A750delinsP	4
	p.L747_T751del	4
	p.L747_T751delinsP	3
	p.E746_T751delinsI	2
	p.S752_I759del	2
	p.E746_A750delinsAP	1
	p.E746_P753delinsVS	1
EGFR EX19del	p.E746_T751delinsA	1
	p.E746_T751delinsV	1
	p.E746_T751delinsVA	1
	p.E746_K754delinsISE	1
	p.L747_K754delinsQQ	1
	p.L747_S752del	1
	p.L747_S752delinsQ	1
	p.A763_Y764insFQEA	3
	p.P772_H773insNP	1
	p.P772_H773insQ	1
	p.N771_P772insT	1
EGFR resistance	p.C797S	3
	p.E709K	2
	p.G796S	2
MET EX14 skipping	c.2888-20_2888-9del12	1
	c.2888-1G>A	1
	c.2888-48_2888delins10	1
	c.3004_3028+3del28	1
	c.3028+1G>T	1
	c.3028G>C	1

Concordance between Plasma and Tissue

- In the 118 samples from patients with stage IIIB - IV, the PPA is 75.4% and the NPV is 100% (Table 3), which was consistent with previous studies²⁻³.

Table 3. Concordance between plasma and tissue

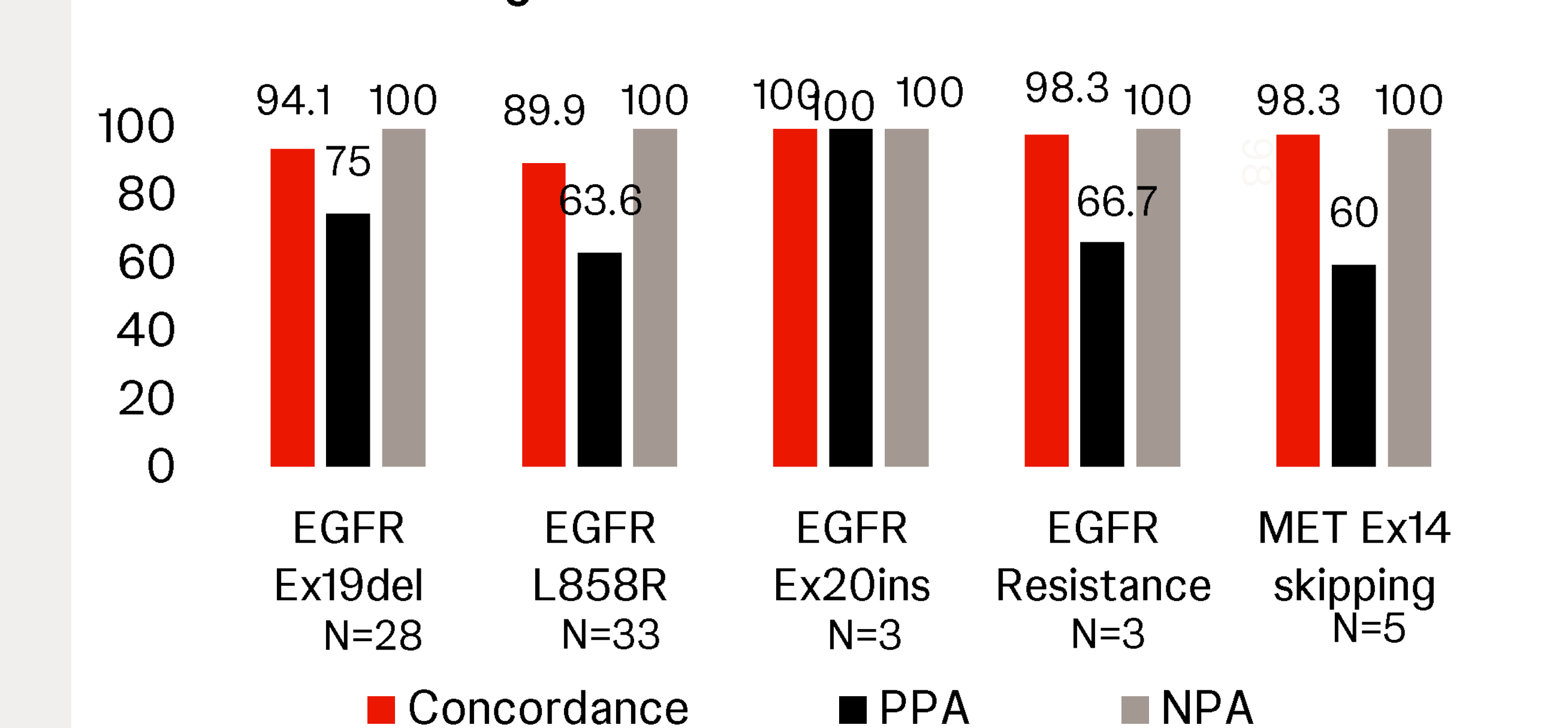
LC10 Plasma	LC10 Tissue		
	Pos	Neg	Total
Pos	49	0	49
Neg	16	53	69
Total	65	53	118
PPA	75.4% (95%CI: 63.7%-84.2%)		
NPA	100% (95%CI: 93.2%-100%)		

* Pos: Positive; Negative: Neg; PPA: Positive Percent Agreement; NPA: Negative Percent Agreement.

Detection Performance of LC10 at Various Alteration Site in Plasma

- In samples from stage IIIB - IV, the concordance rates for EGFR Ex19del, L858R, Ex20ins, EGFR resistance mutations and MET Ex14 skipping were 94.1%, 89.9%, 100%, 98.3% and 98.3%, respectively. The PPA for EGFR 19del, L858R, Ex20ins, EGFR resistance mutations and MET Ex14 skipping were 75%, 63.6%, 100%, 66.7% and 60% respectively (Fig. 5).

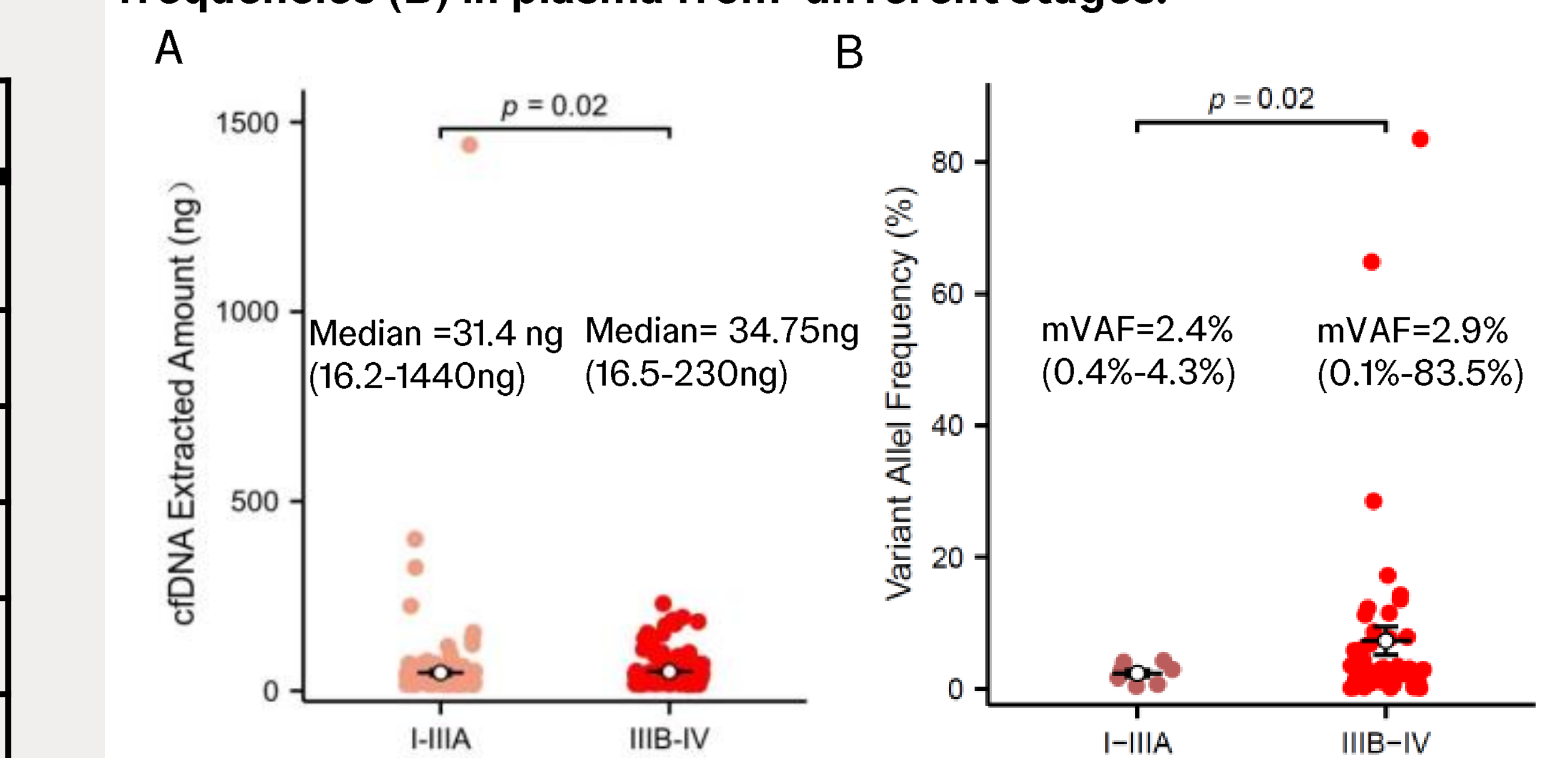
Figure 5. Concordance between LC10 plasma and tissue at specific alterations for stage IIIB-IV cohort



Comparison on ctDNA Release in Stage I - IIIa and Stage IIIB-IV

- The extracted cfDNA amount from 10 ml peripheral blood collected from patients with stage I - IIIa was slightly lower than stage IIIB-IV (median: 31.4 vs 36.5 ng, Fig.6A).
- The variant allele frequency (VAF) in ctDNA from patients with stage I-IIIa (median VAF 2.4% with a narrow range 0.4%-4.3%) was relatively lower than stage IIIB-IV (median VAF 2.9% with a wide range 0.1%-83.5%, Fig.6B). The result is consistent with previous findings that the release of ctDNA is associated with the tumor stage⁵⁻⁶.

Figure 6. Comparison of Variant cfDNA amount(A) and allele frequencies (B) in plasma from different stages.



Lung Cancer

