

EGFR and HER3 expression in circulating tumor cells and tumor tissue from non-small cell lung cancer patients.

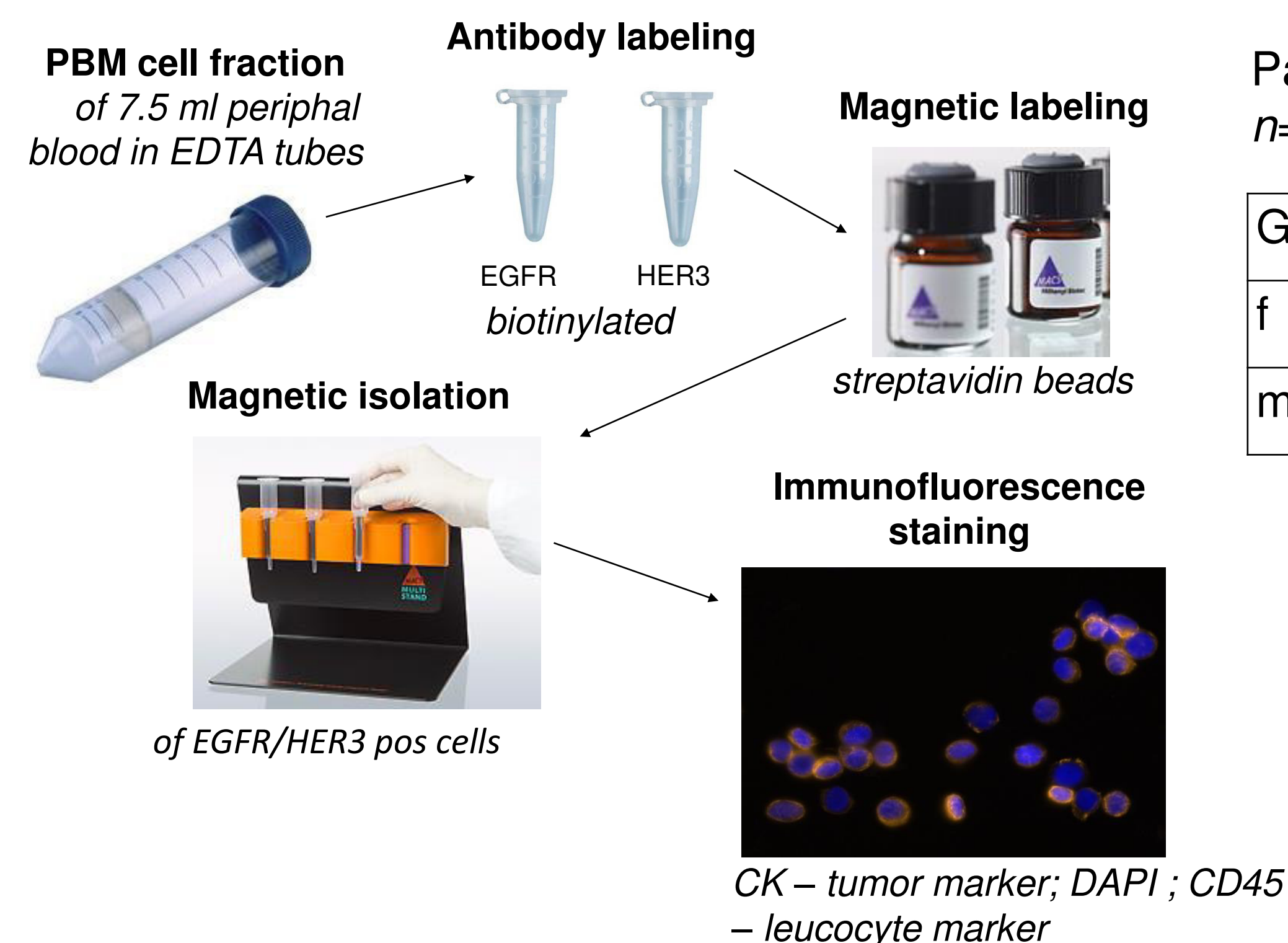
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INTRODUCTION

Liquid biopsy is the hot topic in cancer personalized medicine.

In Non-Small Lung Cancer (NSCLC) Circulating Tumour Cells (CTCs) are detected in rather few patients and numbers with the FDA-approved EpCam (epithelial marker) based CellSearch® system and other current methods. Therefore, the aim of this study is to establish an EpCAM-independent CTC isolation technique by using the two clinically relevant epithelial markers *EGFR* & *HER3* for CTC enrichment.

MATERIAL & METHODS Magnetic Cell Separation (MACS)



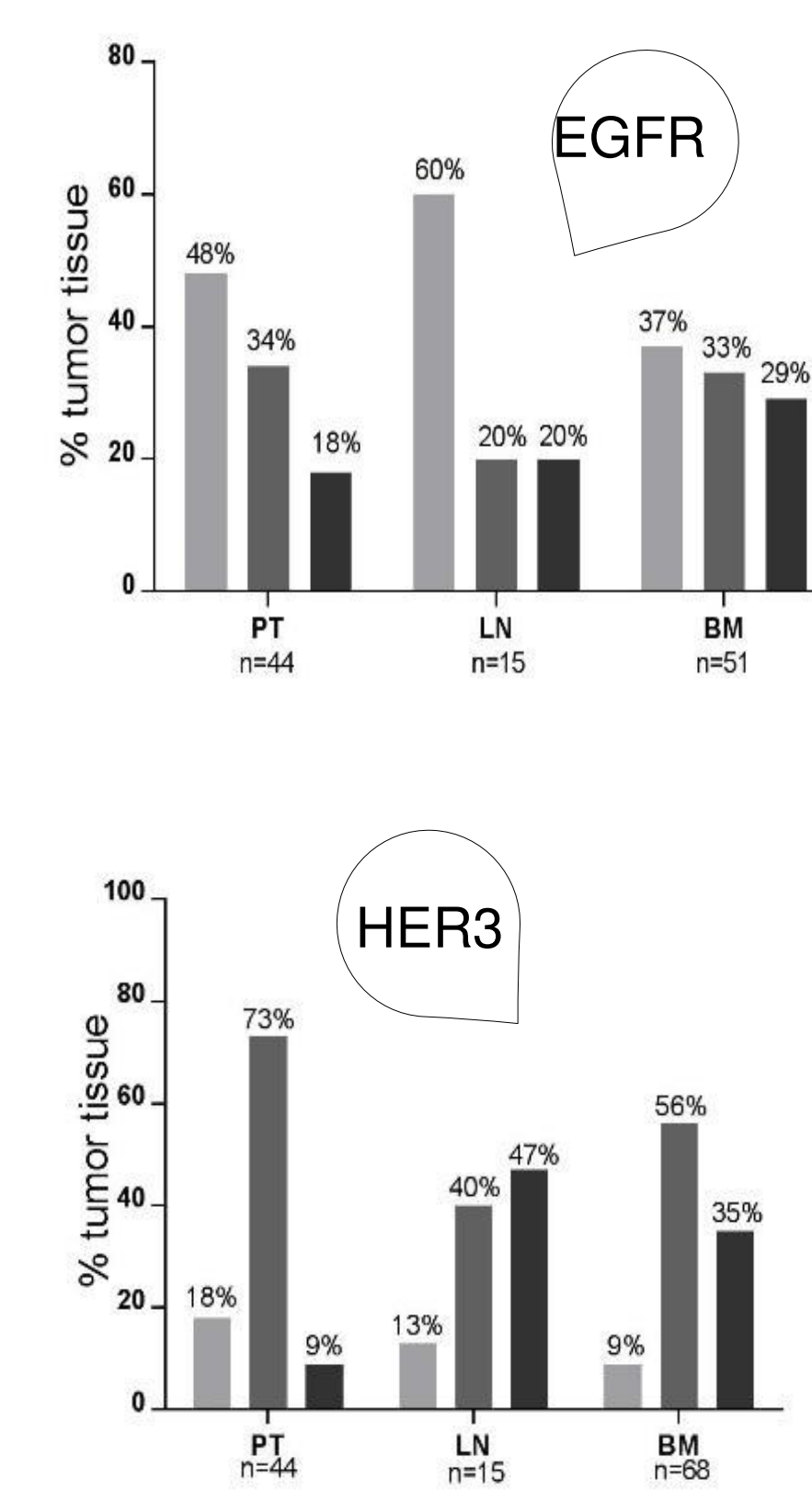
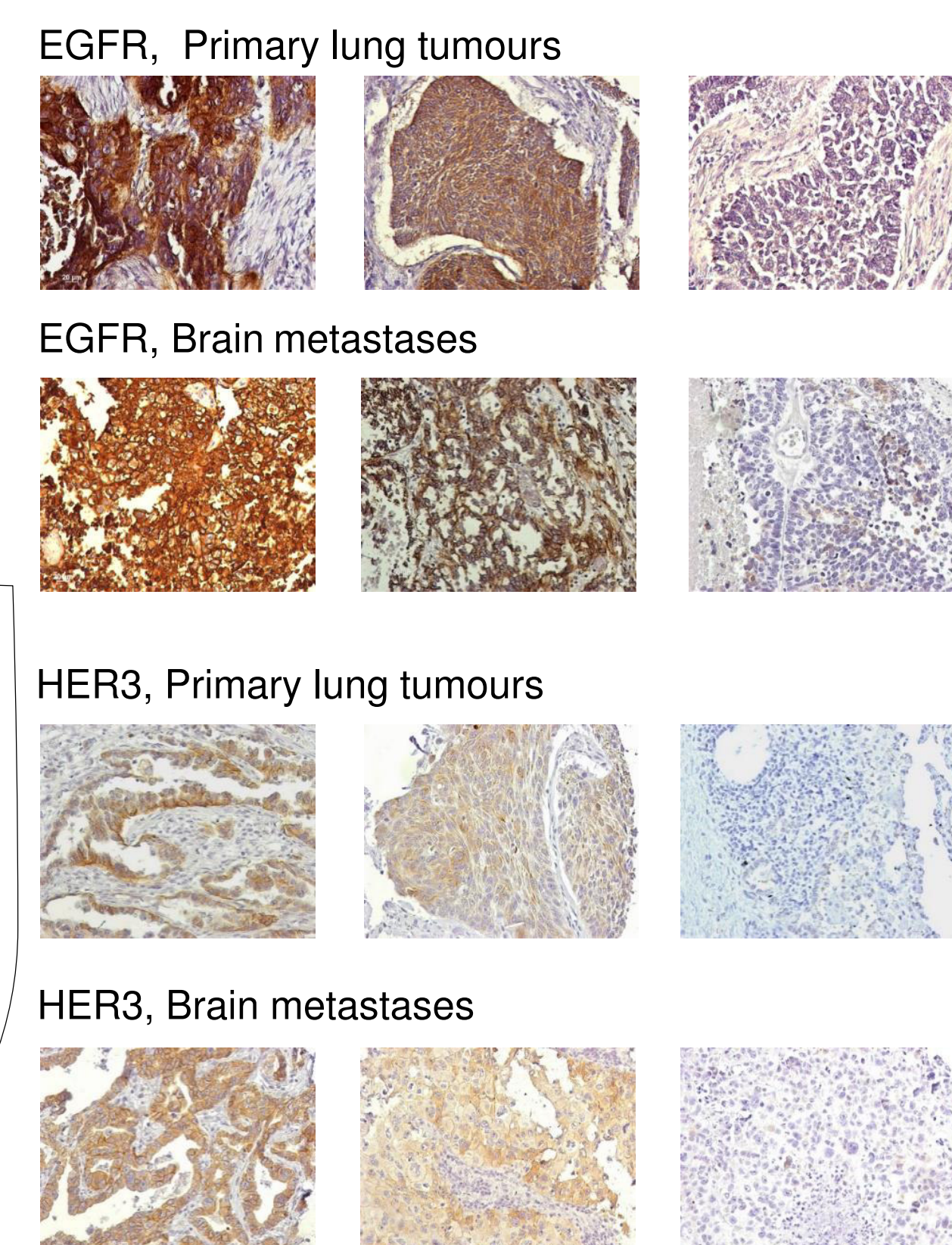
Patient cohort
n=45; median age (range): 63 y (41 – 85)

Gender %		Histological type		Metastases	
f	35.4	SCC	3	Single	14
m	64.6	ADC	41	Multiple	27
		LCC	1	M0	4

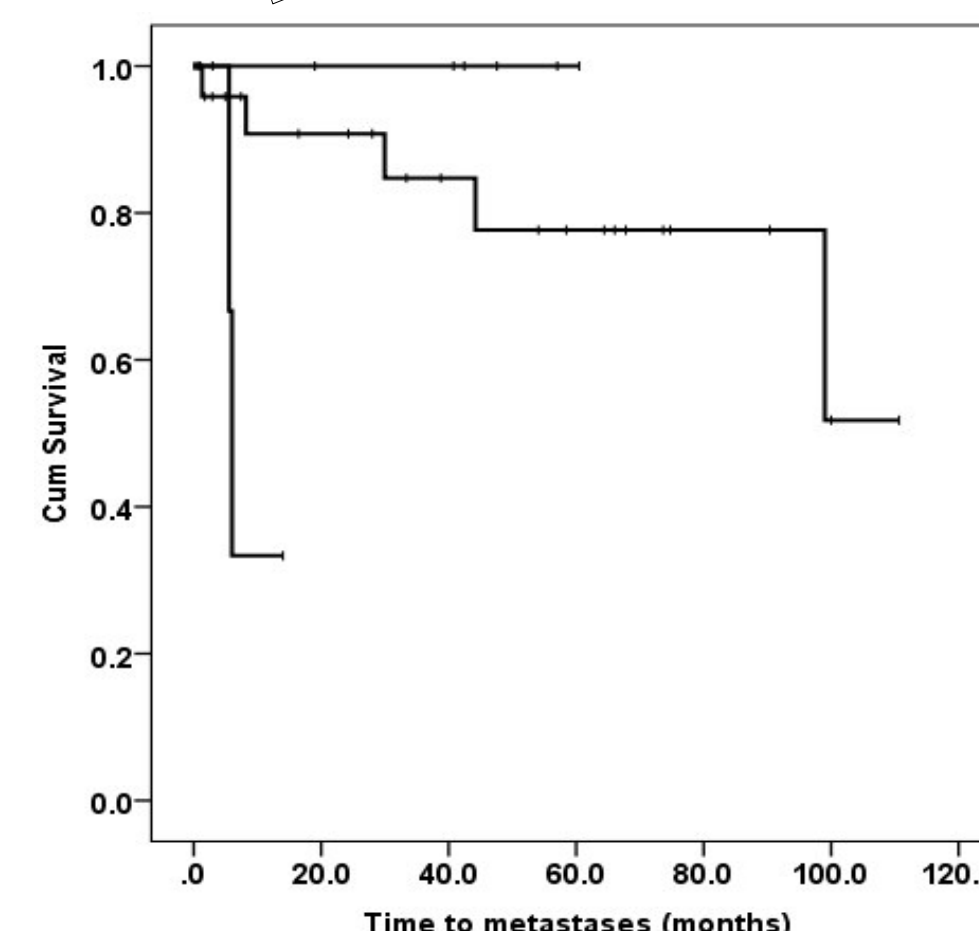
EGFR mut		UICC Stage	
Exon 19 del	7	III	5
wt	30	IV	40
Not screened	8		

I. STEP: IMMUNOHISTOCHEMISTRY

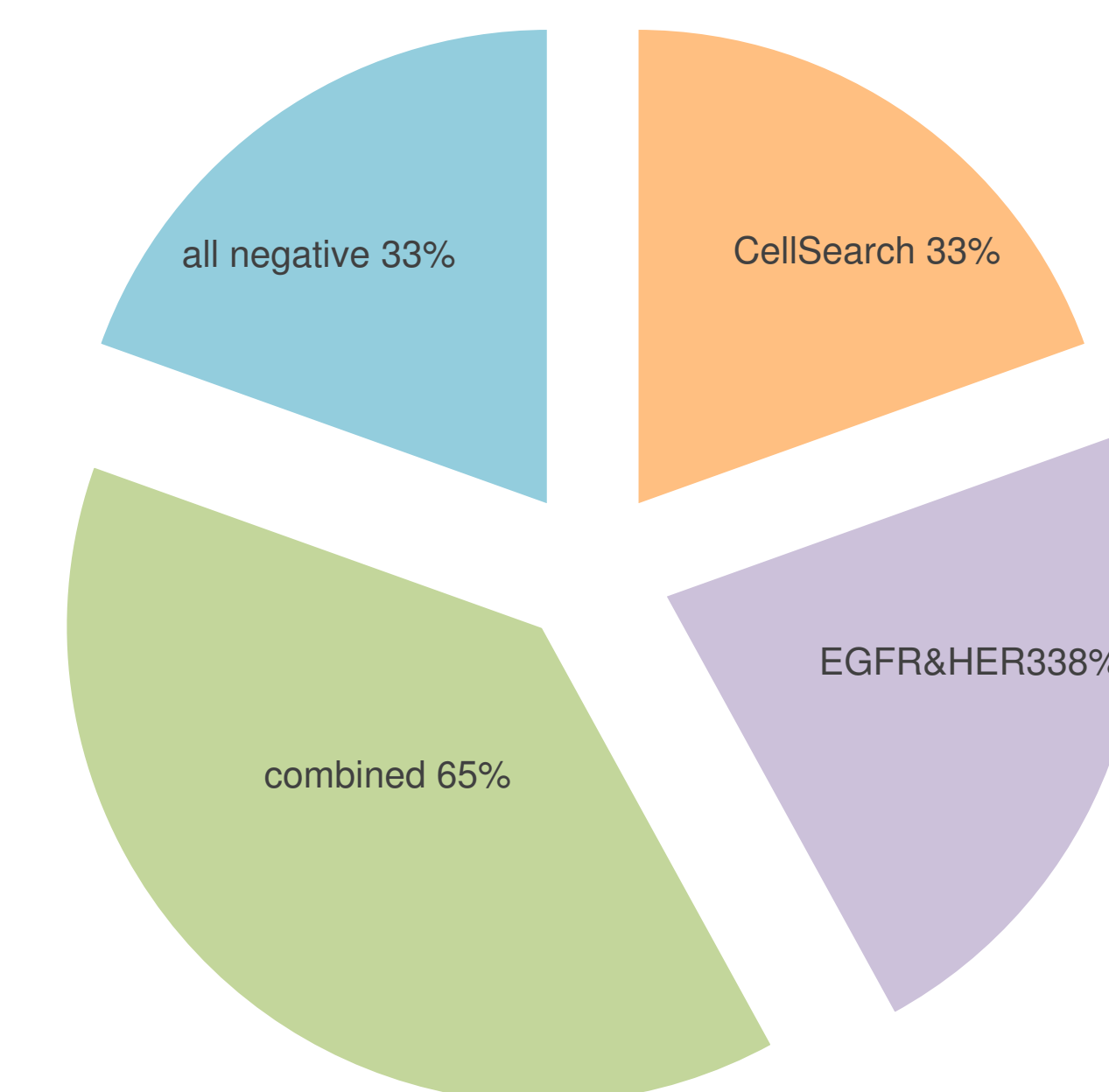
- Background: EGFR and HER3 (member ErbB protein family) are overexpressed in brain metastases of NSCLC patients^{1,2}



HER3 expression in primary NSCLC tumors is significantly associated with a decreased time to metastatic progression (p=0.006; log-rank test).

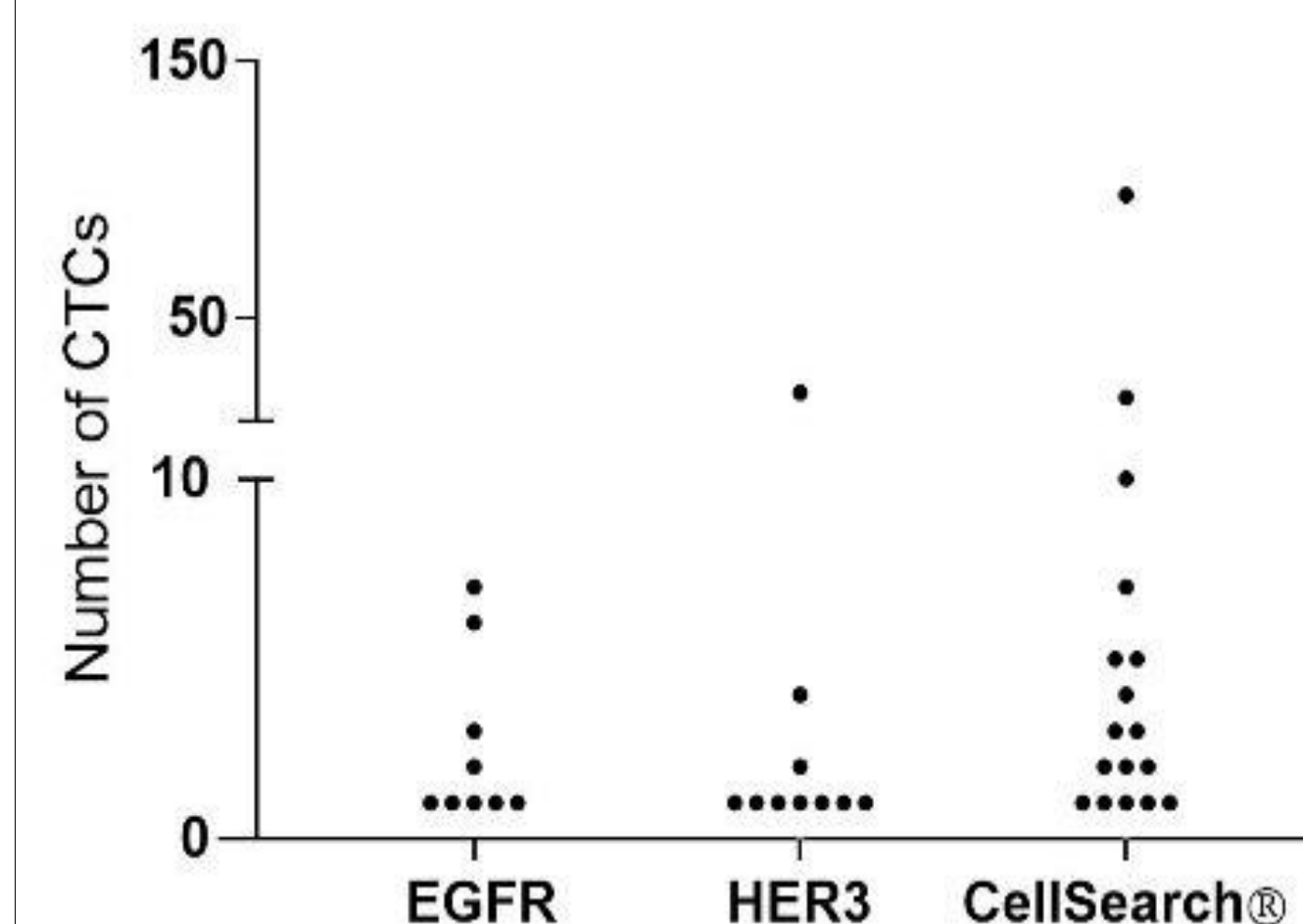


II. STEP: MACS



Significantly higher detection rates when combining the methods in comparison to either single use CellSearch (p = 0.0023) or magnetic cell separation with EGFR/HER3 (p = 0.0109).

CTC enumeration



→ first diagnoses

EGFR enrichment

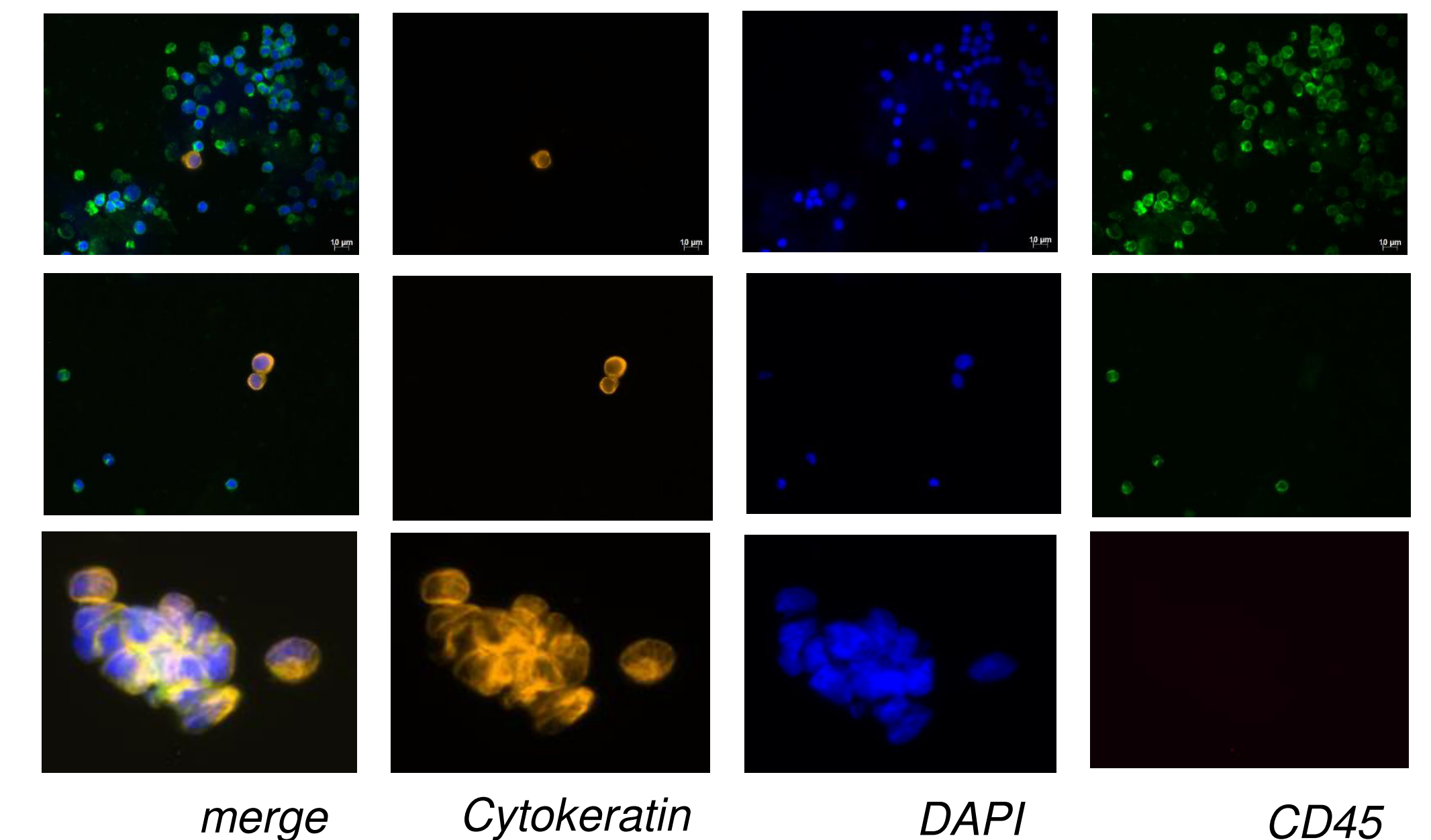
→ progress

HER3 enrichment

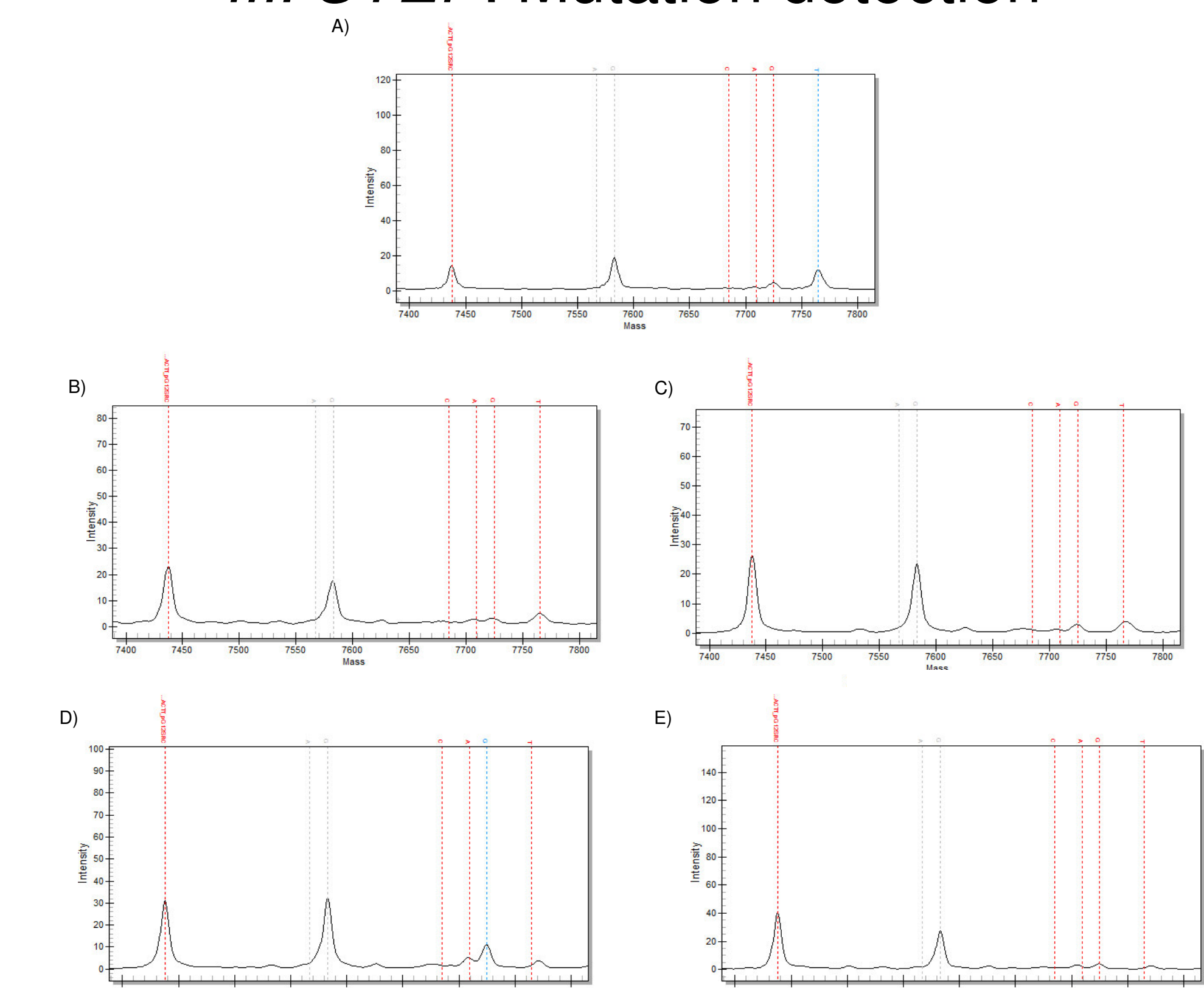
→ progress

21 single cells + 10 clusters

HER3 enrichment



III. STEP: Mutation detection



Molecular analysis of primary lung tumor tissue (PT), corresponding circulating tumor cell cluster and three single CTCs to proof tumourigenic origin. MassARRAY system (iPLEX Lung) shows heterozygous mutation for KRAS G12S in PT. (A) Same mutation is seen in the CTC cluster (B) and in one single CTC (C), whereas two single CTCs (D,E) show no mutation for KRAS.

CONCLUSION

- EGFR and HER3 are suitable markers for the detection of CTC in NSCLC patients
- CTC isolation with the combination of EGFR/HER3 enrichment and the CellSearch® system allows CTC identification in a significantly higher fraction than either method alone (significant negative correlation by Cohen's kappa = -0.280)
- Isolated CTCs are suitable for downstream molecular characterization
- Challenge in NSCLC: heterogeneity → further research for the identification of subpopulations
- Implementation of multi-centred studies needed

LITERATURE

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- Sun M, et al. HER family receptor abnormalities in lung cancer brain metastases and corresponding primary tumors. *Clinical cancer research: an official journal of the American Association for Cancer Research*. 2009;15:4829-4837. doi: 10.1158/1078-0432.ccr-08-2921.

Offenlegung potentieller Interessenkonflikte:
Keine.

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