

## SUPPLEMENTARY INFORMATION

The MEK/ERK/miR-21 signaling is critical in Osimertinib resistance in EGFR-mutant non-small cell lung cancer cells

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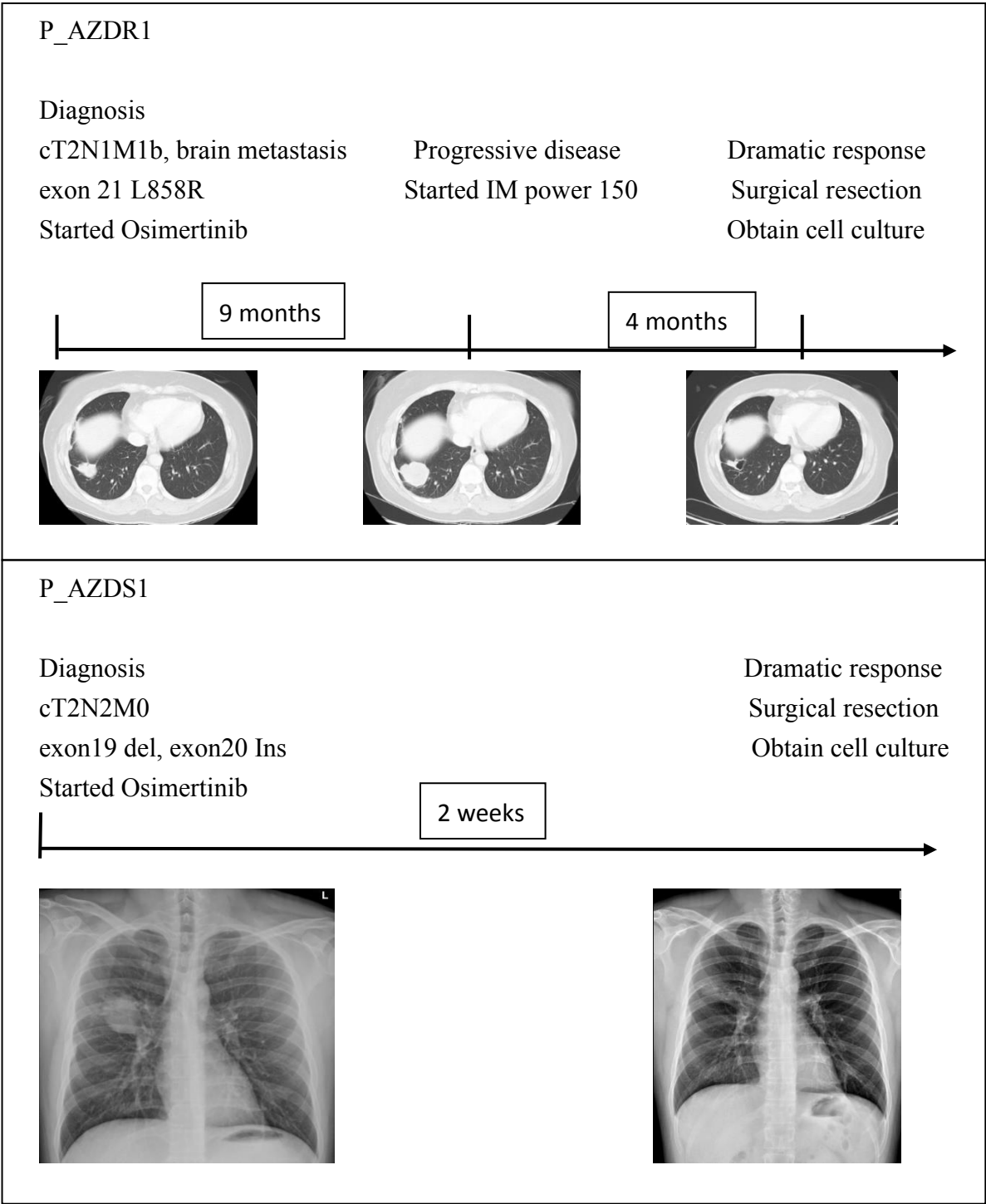
**Supplementary Table S1. Clinicopathological characteristics of NSCLC patients (N=20)**

Parameters	N	%
Age (years)	56.4 ± 2.8	
Gender (male)	20	100%
Smoke (n/%)	16	75%
Histology		
Adenocarcinoma (n/%)	16	60%
Squamous cell carcinoma (n/%)	4	40%
Pathological grade		
Poorly differentiated (n/%)	16	80%
Moderately differentiated (n/%)	3	15%
Well-differentiated (n/%)	1	5%
Tumor size		
> 5 cm (n/%)	10	50%
≤ 5 cm (n/%)	10	50%
Osimertinib responder		
Yes (n/%)	10	50%
No (n/%)	10	50%

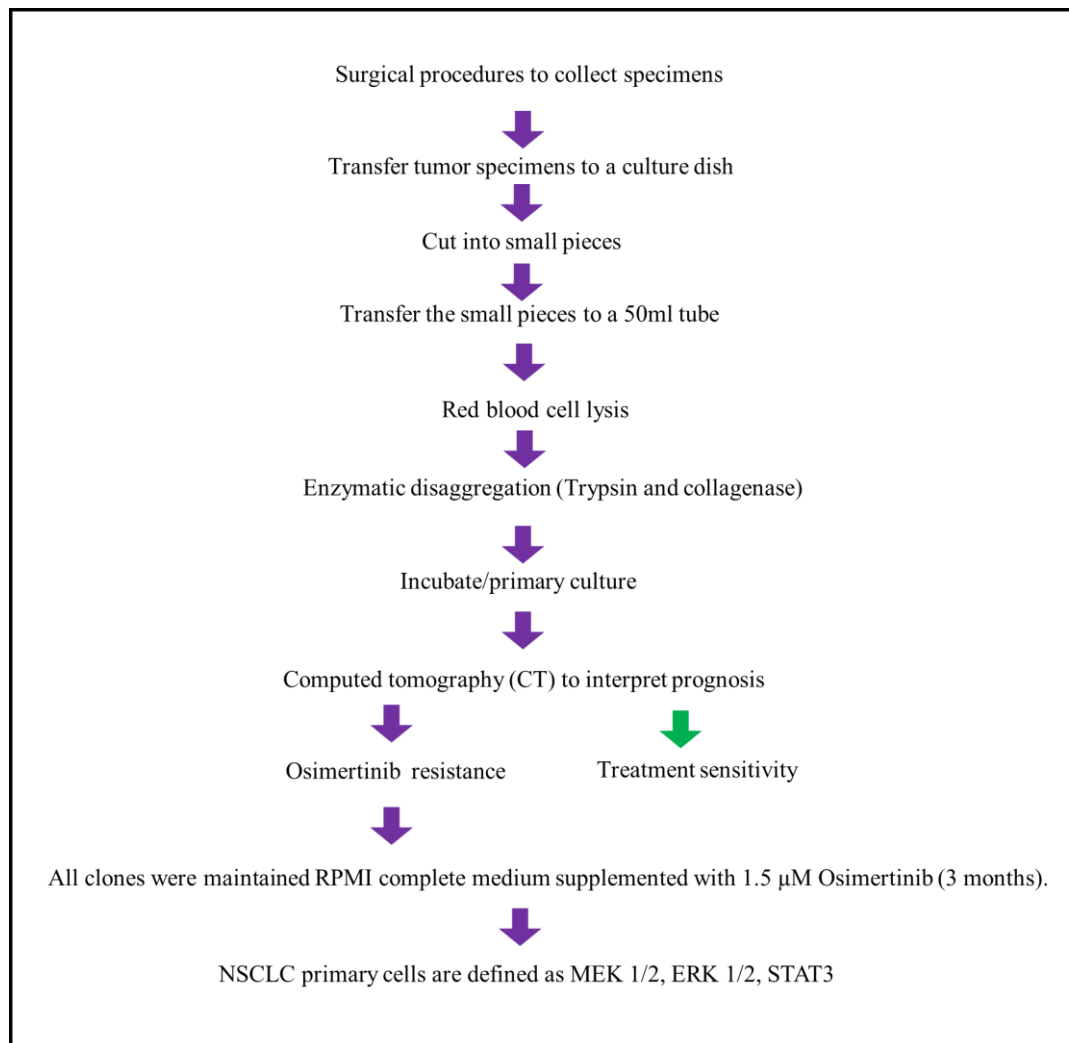
**Supplementary Table S2. qPCR primers**

<b>Gene name</b>	<b>Forward sequence</b>	<b>Reverse sequence</b>
FAP	ATGAGCTTCCTCGTCCAATTCA	AGACCACCAGAGAGCATATTTTG
ERK	ATGTCATCGGCATCCGAGAC	GGATCTGGTAGAGGAAGTAGCA
STAT3	CAGCAGCTTGACACACGGTA	AAACACCAAAGTGGCATGTGA
VIM	GACGCCATCAACACCGAGTT	CTTTGTCGTTGGTTAGCTGGT
A-SMA	AAAAGACAGCTACGTGGGTGA	GCCATGTTCTATCGGGTACTTC
E-cad	CGAGAGCTACACGTTCACGG	GGGTGTCGAGGGAAAAATAGG
$\beta$ -actin	CTGTCTGGCGGCACCACCAT	GCAACTAAGTCATAGTCCGC

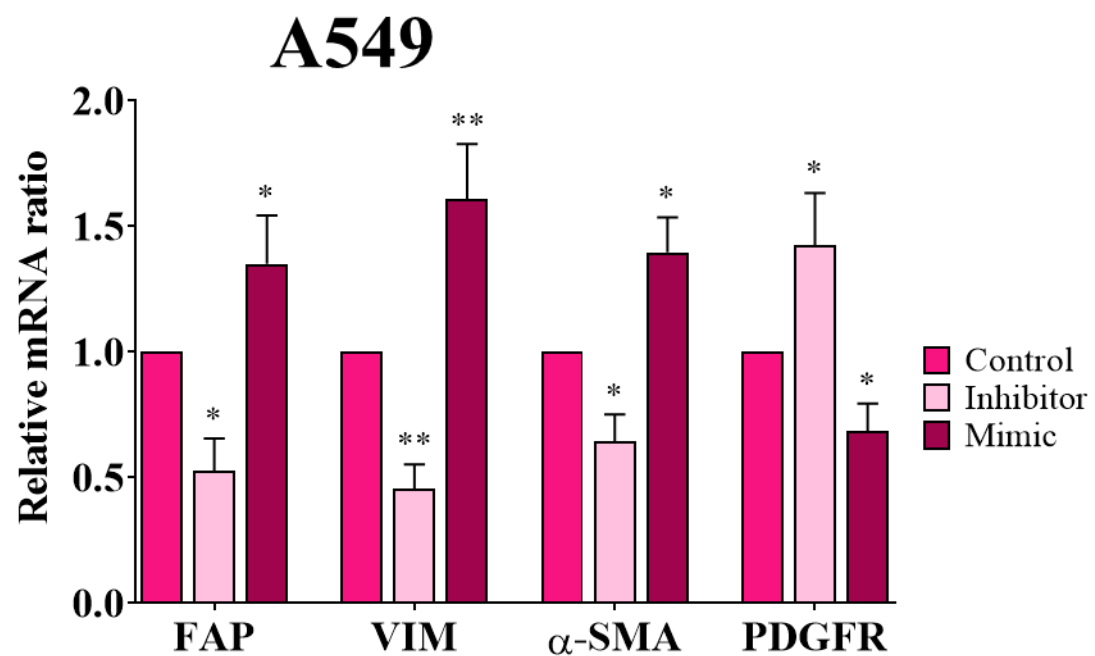
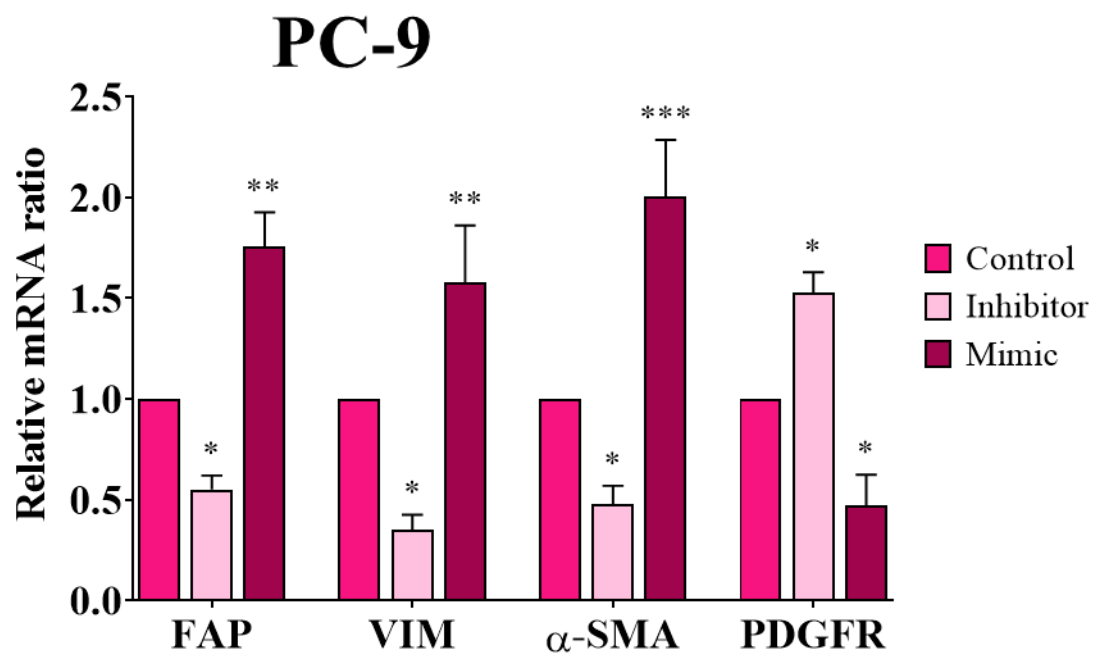
**Supplementary Figure S1** The representative examples of Osimertinib-resistant and Osimertinib-sensitive cell lines deriving from patients (computed tomography).



**Supplementary Figure S2** Primary cancer cell isolation process.



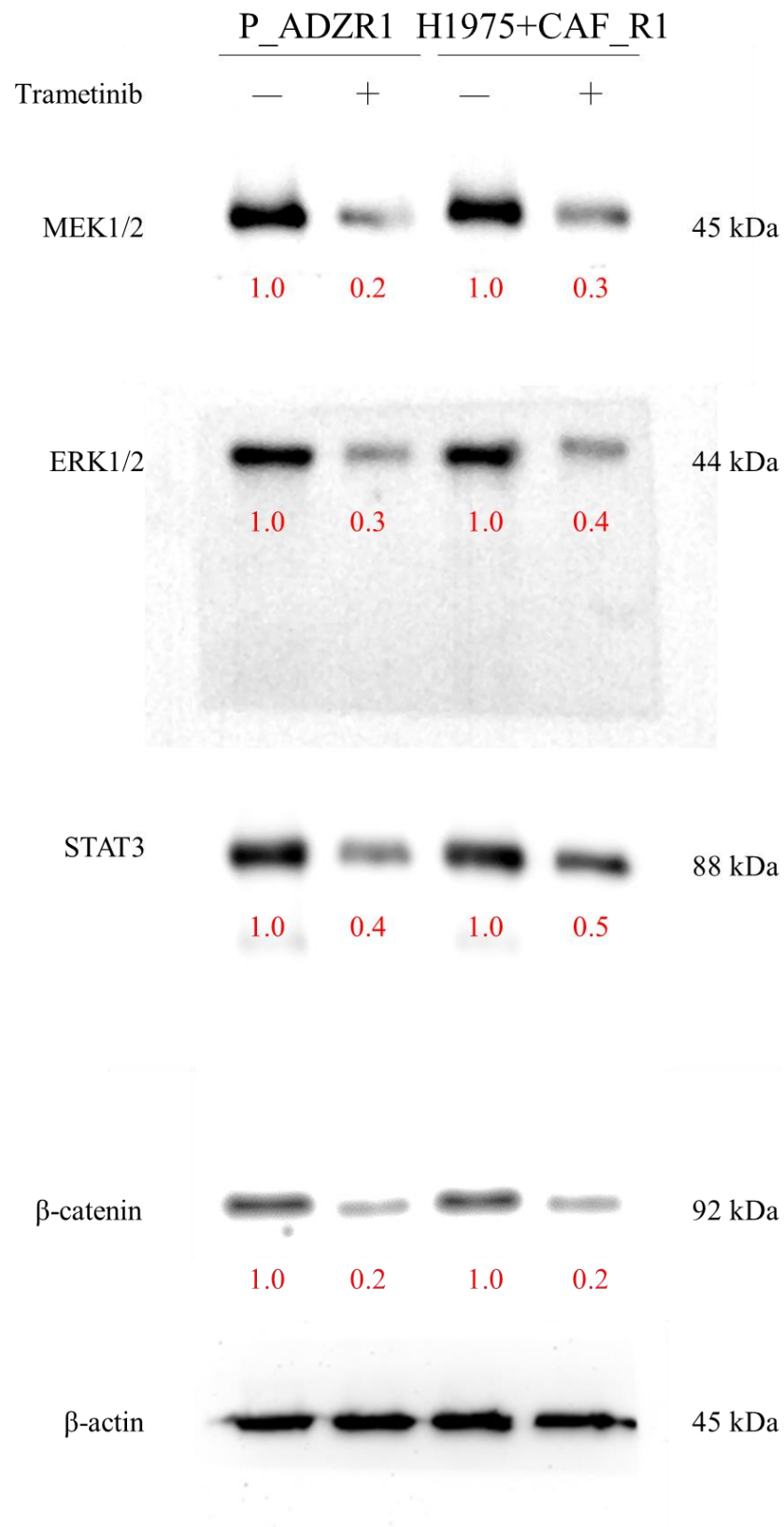
**Supplementary Figure S3** Inhibiting mir-21-5p does the job in commercial cell lines (PC9 and A549).



**Supplementary Figure S4.** Full-size blots of Figure 2F



**Supplementary Figure S5.** Full-size blots of Figure 3F





**Supplementary Figure S6.** Full-size blots of Figure 4C.

