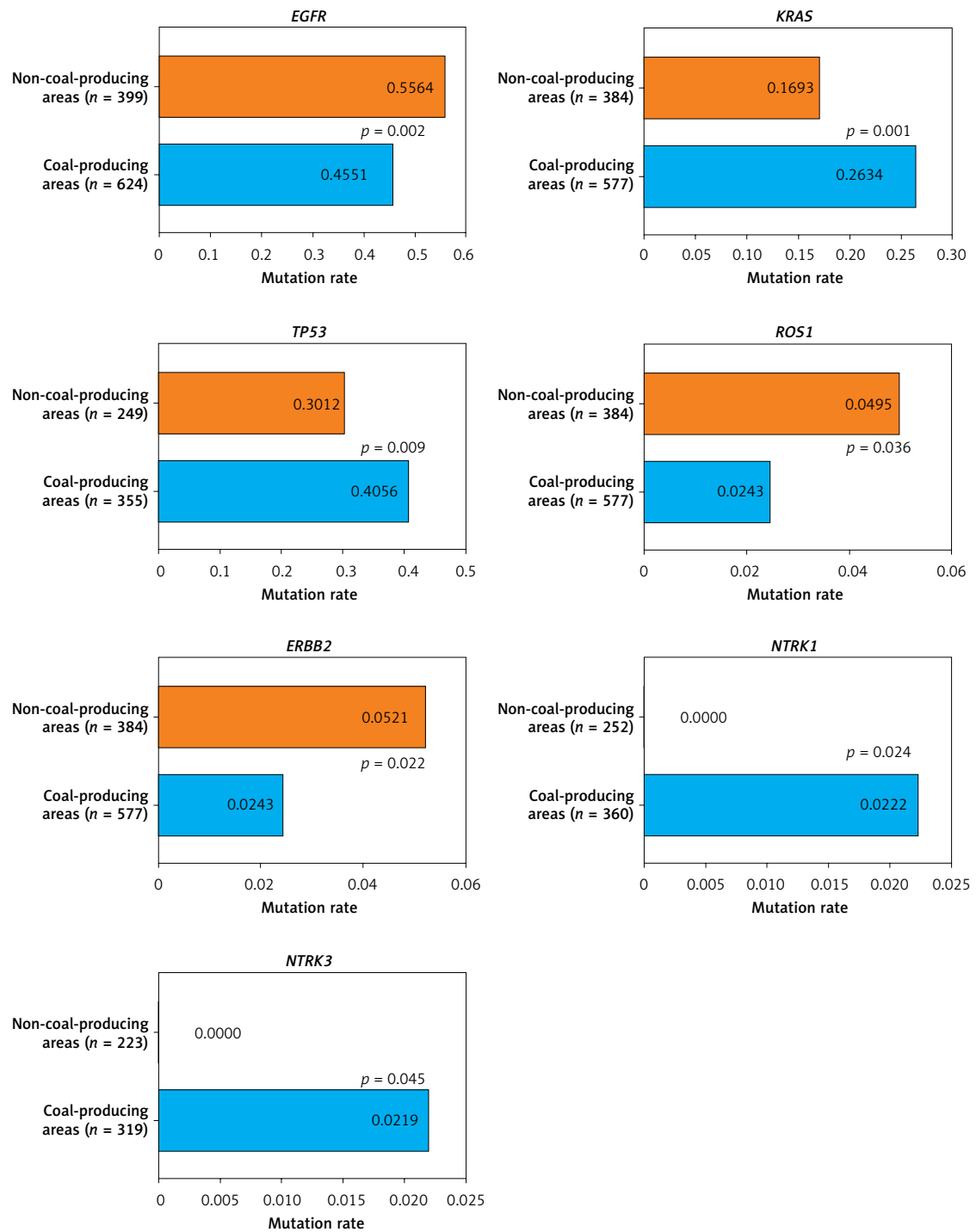
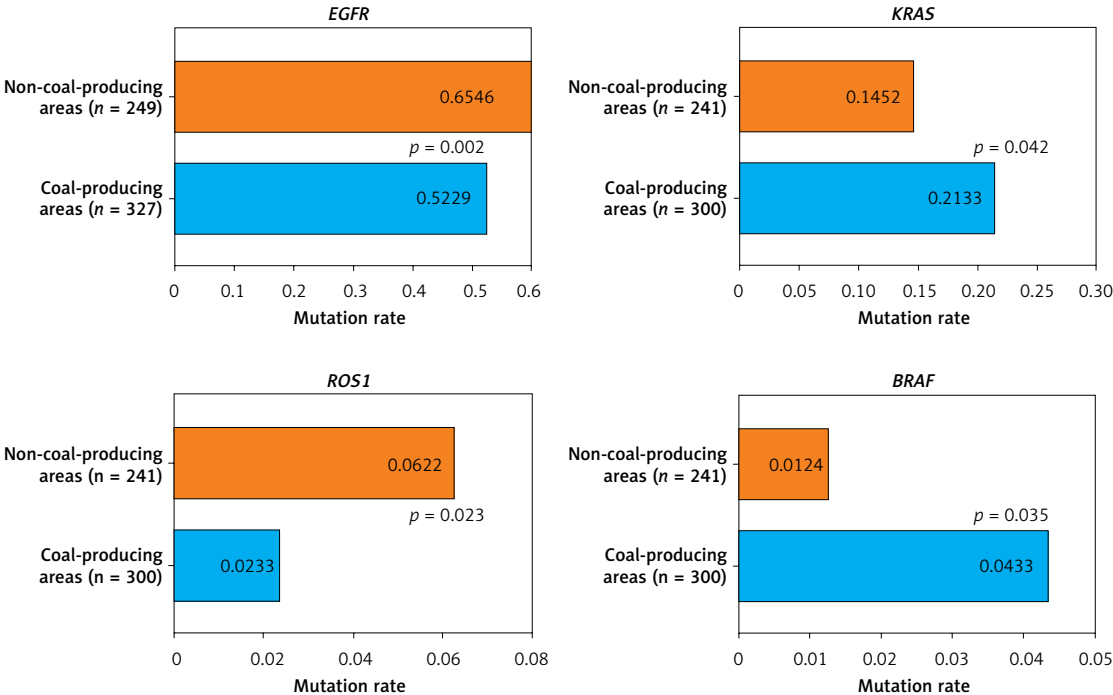
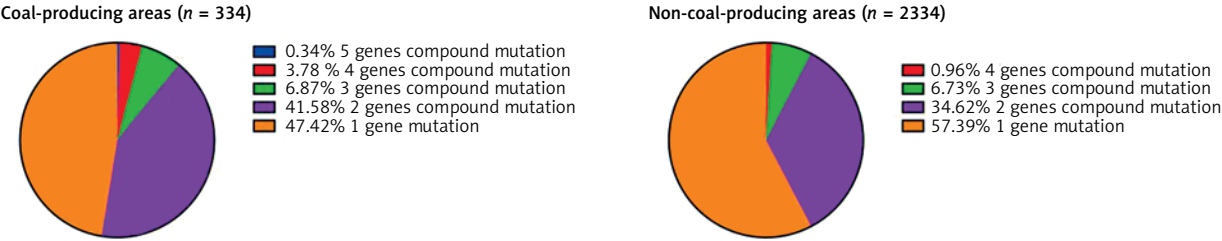




Supplementary Figure S1. Comparison of mutation occurrences of EGFR, KRAS, TP53, ROS1, ERBB2, NTRK1 and NTRK3 genes in the studied lung adenocarcinoma patients



Supplementary Figure S2. Comparison of mutation rates of EGFR, KRAS, ROS1 and BRAF genes in the studied females, non-smokers and individuals with lung adenocarcinoma



Supplementary Figure S3. Frequency of compound gene mutations in NSCLC individuals

Supplementary Table SI. Clinical demographics, pathology, region distribution and the studied 17 genes' mutation details of all participants

Supplementary Table SII. Experimental methods for the detection of the studied 17 genes in detail

Method	Kit	Company/ Institution	Gene	Number
ARMS-PCR	EGFR Mutations Detection Kit	Amoy Diagnostics	EGFR	73
NGS	8-Gene NGS Panel	Life Healthcare	EGFR/ALK/ROS1/KRAS/BRAF/RET/MET/ERBB2	400
NGS	17-Gene NGS Panel	Life Healthcare	EGFR/ALK/ROS1/KRAS/BRAF/RET/MET/ERBB2/ NRAS/PIK3CA/NTRK1/TP53/FGFR1/KIT/ PDGFRA/NTRK2/NTRK3	547
NGS	55-Gene NGS Panel	Life Healthcare	≥EGFR/ALK/ROS1/KRAS/BRAF/RET/MET/ ERBB2/NRAS/PIK3CA/NTRK1/TP53/FGFR1/ KIT/PDGFRA/NTRK2/NTRK3	3
NGS	58-Gene NGS Panel	Life Healthcare	≥EGFR/ALK/ROS1/KRAS/BRAF/RET/MET/ ERBB2/NRAS/PIK3CA/NTRK1/TP53/FGFR1/ KIT/PDGFRA/NTRK2/NTRK3	7
NGS	499-Gene NGS Panel	Life Healthcare	≥EGFR/ALK/ROS1/KRAS/BRAF/RET/MET/ ERBB2/NRAS/PIK3CA/NTRK1/TP53/FGFR1/ KIT/PDGFRA/NTRK2/NTRK3	1
NGS	618-Gene NGS Panel	Life Healthcare	≥EGFR/ALK/ROS1/KRAS/BRAF/RET/MET/ ERBB2/NRAS/PIK3CA/NTRK1/TP53/FGFR1/ KIT/PDGFRA/NTRK2/NTRK3	4
NGS	876-Gene NGS Panel	Life Healthcare	≥EGFR/ALK/ROS1/KRAS/BRAF/RET/MET/ ERBB2/NRAS/PIK3CA/NTRK1/TP53/FGFR1/ KIT/PDGFRA/NTRK2/NTRK3	3
NGS	16-Gene NGS Panel	KingMed Diagnostics	Containing EGFR/ALK/ROS1/KRAS/BRAF/RET/ MET/ERBB2/NRAS/PIK3CA/NTRK1/NTRK2/ NTRK3	8
NGS	26-Gene NGS Panel	KingMed Diagnostics	Containing EGFR/ALK/ROS1/KRAS/BRAF/ RET/MET/ERBB2/NRAS/PIK3CA/NTRK1/TP53/ FGFR1	64
NGS	60-Gene NGS Panel	KingMed Diagnostics	Containing EGFR/ALK/ROS1/KRAS/BRAF/ RET/MET/ERBB2/NRAS/PIK3CA/NTRK1/TP53/ FGFR1/KIT/PDGFRA	8
NGS	599-Gene NGS Panel	KingMed Diagnostics	≥EGFR/ALK/ROS1/KRAS/BRAF/RET/MET/ ERBB2/NRAS/PIK3CA/NTRK1/TP53/FGFR1/ KIT/PDGFRA/NTRK2/NTRK3	2
Total				1120

Supplementary Table SIII. Mutation rates of driver mutations in NSCLC individuals tested by NGS

Gene	Total	Coal-producing areas				Non-coal-producing areas				P-value
		Total	WT	MUT	Rate	Total	WT	MUT	Rate	
<i>EGFR</i>	1120	681	379	302	44.35%	439	208	231	52.62%	0.007
<i>ALK</i>	1047	630	608	22	3.49%	417	397	20	4.80%	0.292
<i>ROS1</i>	1047	630	614	16	2.54%	417	397	20	4.80%	0.050
<i>KRAS</i>	1047	630	468	162	25.71%	417	351	66	15.83%	< 0.001
<i>BRAF</i>	1047	630	605	25	3.97%	417	406	11	2.64%	0.247
<i>RET</i>	1047	630	611	19	3.02%	417	403	14	3.36%	0.757
<i>MET</i>	1047	630	623	7	1.11%	417	412	5	1.20%	0.896
<i>ERBB2</i>	1047	630	615	15	2.38%	417	396	21	5.04%	0.021
<i>NRAS</i>	647	381	379	2	0.52%	266	265	1	0.38%	1.000
<i>PIK3CA</i>	647	381	365	16	4.20%	266	251	15	5.64%	0.399
<i>NTRK1</i>	647	381	372	9	2.36%	266	264	2	0.75%	0.211
<i>TP53</i>	639	376	221	155	41.22%	263	180	83	31.56%	0.013
<i>FGFR1</i>	639	376	371	5	1.33%	263	260	3	1.14%	1.000
<i>KIT</i>	575	340	329	11	3.24%	235	233	2	0.85%	0.059
<i>PDGFRA</i>	575	340	335	5	1.47%	235	234	1	0.43%	0.409
<i>NTRK2</i>	575	339	339	0	0.00%	236	236	0	0.00%	N/A
<i>NTRK3</i>	575	339	332	7	2.06%	236	236	0	0.00%	0.024

Supplementary Table SIV. Mutation rates in *KRAS* in NSCLC individuals with or without a smoking history

KRAS					
Coal-producing areas	Total	Mutation	WT	Mutation rate	P-value
Smoking	181	63	118	34.81%	0.001
Non-smoking	449	99	350	22.05%	
KRAS					
Smoking	Total	Mutation	WT	Mutation rate	P-value
Coal-producing	181	63	118	34.81%	0.007
Non-coal-producing	90	17	73	18.89%	
KRAS					
Non-smoking	Total	Mutation	WT	Mutation rate	P-value
Coal-producing	449	99	350	22.05%	0.013
Non-coal-producing	327	49	278	14.98%	
KRAS					
Non-coal-producing areas	Total	Mutation	WT	Mutation rate	P-value
Smoking	90	17	73	18.89%	0.369
Non-Smoking	327	49	278	14.98%	
KRAS mut and WT					
	Total	Smoking	Non-smoking	Smoking rate	P-value
Coal-producing areas	630	181	449	28.73%	0.010
Non-coal-producing areas	417	90	327	21.58%	

Supplementary Table SV. Comparison of detection rates of NSCLC driver gene mutations in plasma and tissue

Gene	Plasma				Tissue				P-value
	Positive	%	Negative	%	Positive	%	Negative	%	
<i>EGFR</i>	83	39.71%	126	60.29%	481	53.27%	422	46.73%	< 0.001
<i>KRAS</i>	18	8.61%	191	91.39%	209	23.15%	694	76.85%	< 0.001
<i>TP53</i>	22	10.53%	187	89.47%	212	23.48%	691	76.52%	< 0.001
<i>ERBB2</i>	6	2.87%	203	97.13%	29	3.21%	874	96.79%	0.799
<i>NRTK3</i>	1	0.48%	208	99.52%	6	0.66%	897	99.34%	1.000