



**KALC 2022**

Korean Association for Lung Cancer International Conference  
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# Molecular Genetic and Epigenetic Features in Smokers and Non-Smokers with Non- Small Cell Lung Cancer

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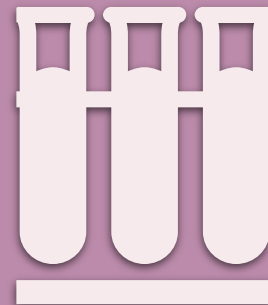
# The aim of the study

to investigate the mutational burden of the tumor and methylation features of the promoter regions of the *HOXA9*, *MARCH11*, *PTGDR*, and *UNCX* genes in patients with non-small cell lung cancer, depending on the smoking status.



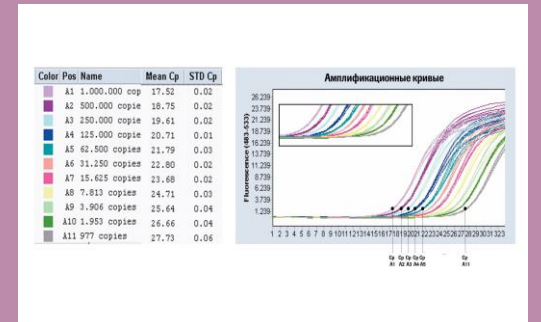
mutational burden of the tumor

- 48 genes



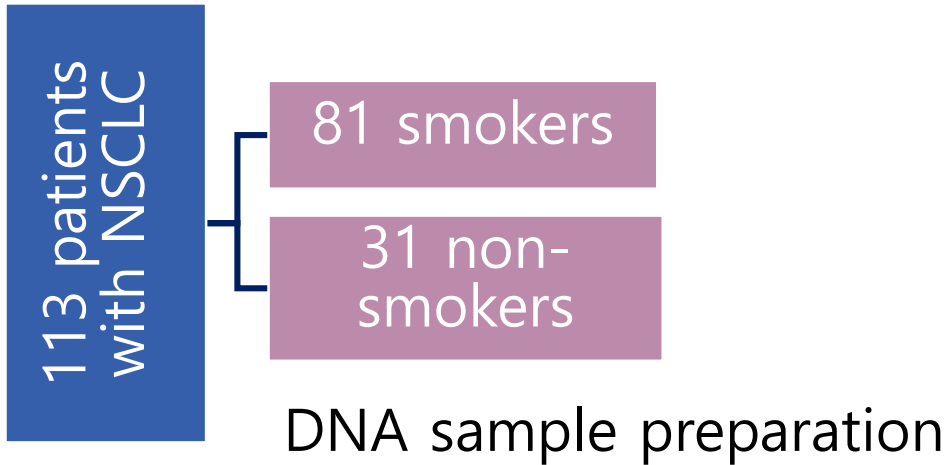
methylation features of the genes

- *HOXA9*
- *MARCH11*
- *PTGDR*
- *UNCX*

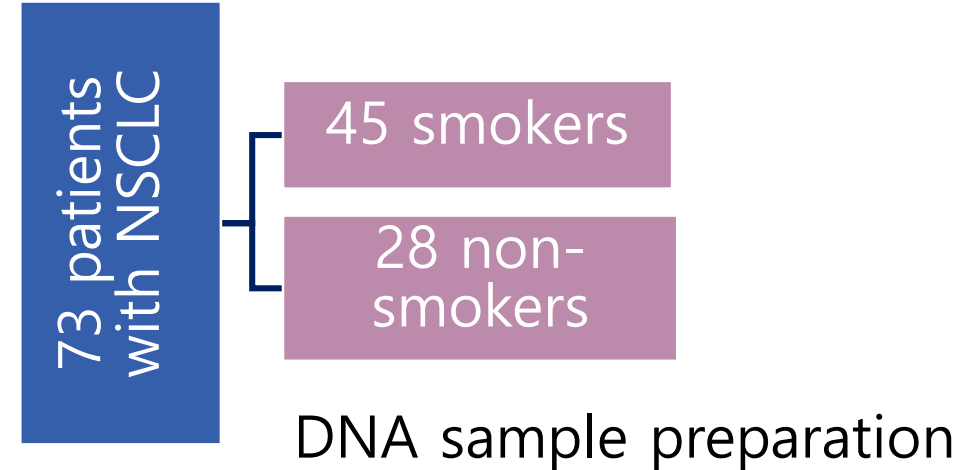


# Methods

For investigating the mutational burden:




Analysis of methylation:



TruSeq Amplicon Cancer Panel kit (Illumina, USA)  
and  
AmpliSeq for Illumina Cancer HotSpot Panel v2 kit

quantitative methylation-specific PCR  
of the promoter regions of the *HOXA9*,  
*MARCH11*, *PTGDR*, and *UNCX* genes

Bioinformatics analysis



The relative methylation level was defined  
as the ratio of the fluorescence level of  
the studied gene to the fluorescence level  
of the beta-actin gene

# Results

Variants of great clinical significance

for smoking patients

for non-smokers

*PIK3CA*  
(0.81%)

p.Glu545Lys

*EGFR*  
(0.52%)

p.Glu746\_Ala750del

p.His773dup

*KRAS*  
(0.25%)

p.Gly13Val

p.Gly13Asp

p.Gly12Val

p.Gly12Asp

p.Gly12Cys

*KIT*  
(0.04%)

p.Phe591Leu

*STK11*  
(0.01%)

p.Tyr36Ser

p.Arg40Cys

p.Tyr60Cys

p.Ser69Thr

p.Ser69Ter

p.Thr71Ala

p.Leu80His

*KRAS*  
(0.04%)

p.Gly12Ala

p.Gly12Cys

*EGFR*  
(0.37%)

p.Asn771dup

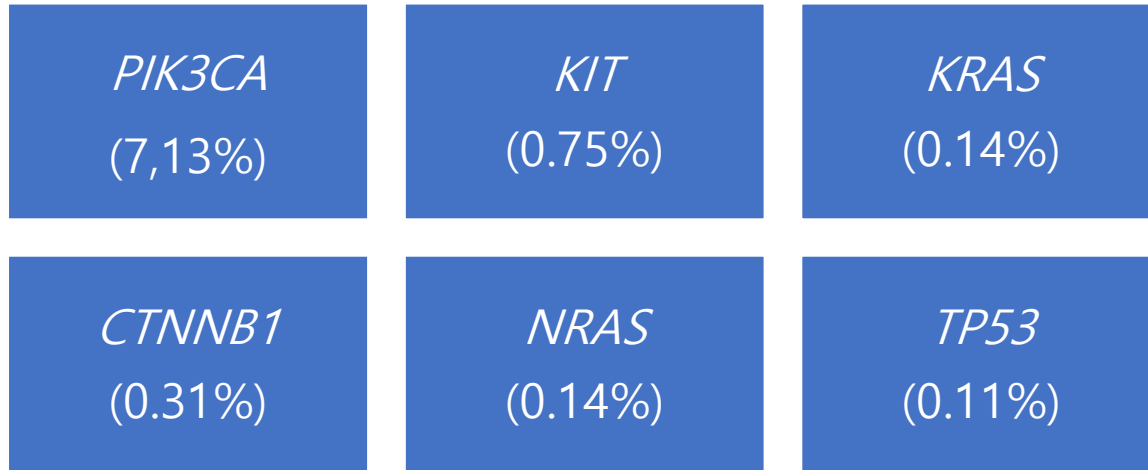
p.Glu746\_Ala750del

p.Leu747\_Pro753delinsSer

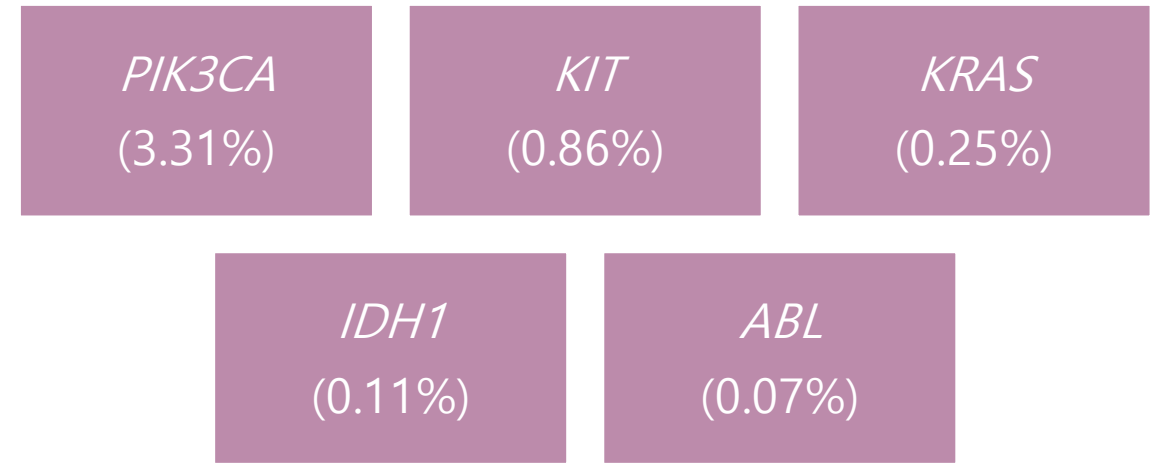
p.His773\_Val774insThrHis

# Results

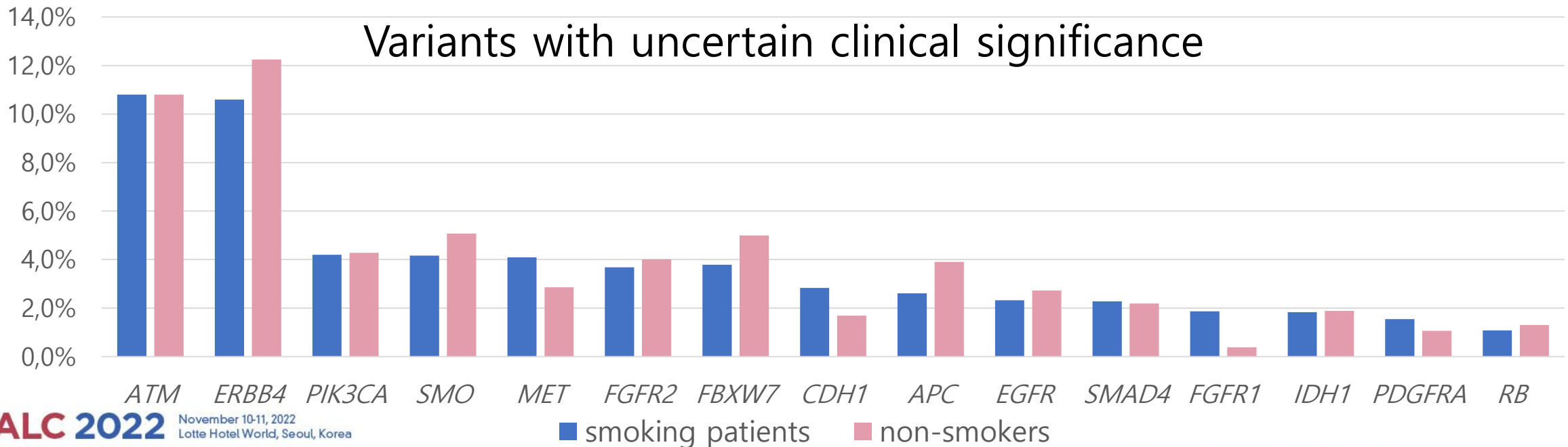
Variants with potential clinical significance  
for smoking patients



for non-smokers



Variants with uncertain clinical significance



# Results

The relative level of methylation of four rare markers in tumor and non-tumor tissues of patients with NSCLC

Gene	<i>HOXA9</i>		<i>MARCH11</i>		<i>UNCX</i>		<i>PTGDR</i>	
Tissue type	tumor	non-tumor	tumor	non-tumor	tumor	non-tumor	tumor	non-tumor
Number of samples	61	61	59	59	62	62	50	50
Mean	97.60	49.63	43.04	26.95	52.99	35.37	47.13	23.42
SD	40.72	37.89	19.36	13.90	34.87	17.05	36.28	25.38
Median	107.58	44.02	48,49	30.47	46.66	35.61	37.78	13.07
Minimum	18.49	0.43	0.73	0.44	5.03	0.58	1.58	0,01
25th percentile	71.11	27,62	27.06	17.39	22.83	23.50	19.40	8.20
75th percentile	127.90	61.46	54.90	36.95	78.48	43.11	63.33	31.29
Maximum	167.68	273.01	82.66	59.06	172.54	82.05	139.49	99.56
Wilcoxon Matched Pairs Test	5.46 $p=4.89 \times 10^{-8}$		4.69 $p=2.67 \times 10^{-6}$		3.64 $p=2.70 \times 10^{-4}$		5.38 $p=7.38 \times 10^{-8}$	

For smoking and non-smoking patients, the accurate significance of the relative methylation level was identified only in the *HOXA9* gene: the standardized indicator of the Mann-Whitney Utest was 1.96 ( $p=0.049$ ).



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## Conclusion

Thus, as a result of the study performed, the data on the spectrum of mutations and their clinical significance for smoking and non-smoking patients with NSCLC were obtained, and the relative methylation level of the genes *HOXA9*, *MARCH11*, *PTGDR*, and *UNCX* was determined, which will allow taking into account molecular genetic and epigenetic features of the tumor in the course of diagnosing, selecting of medications and prognosing the course of the disease.

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