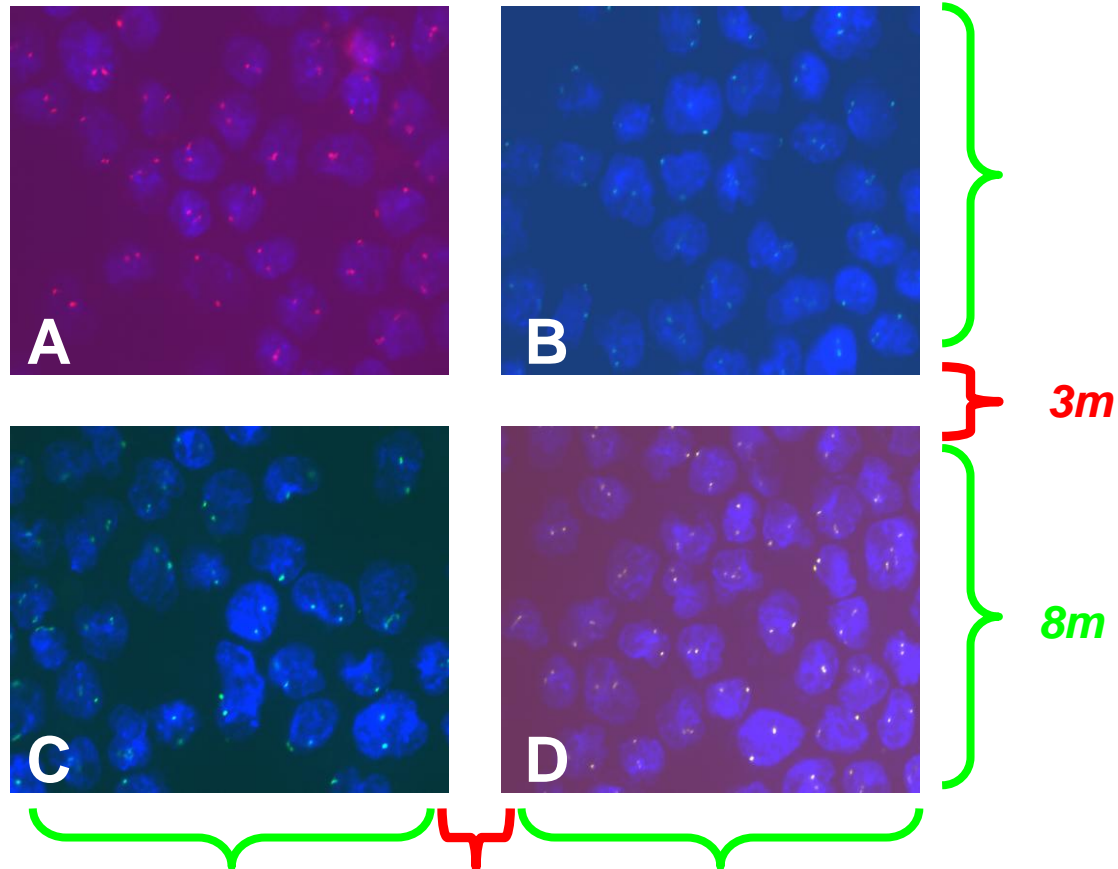Supplementary Fig. 1. Normal diploid cell population comprised two aqua, two green, two red, and two yellow signals.

When an in situ mini-chip containing only a one-color fluorescence-labeled probe in each element is applied to bronchial epitheliums obtained from sputum of an healthy individual, square A showed only two red signals, square B two green signals; and so on in each interphase of the specimen.

Supplementary table 1. Characteristics of an independent cohort of NSCLC and non-cancer individuals

	NSCLC cases		Non-cancer individuals	
	35 SCC patients	34 AC patients	26 healthy smokers	39 COPD patients
Age	69 (SD 13.1)	68 (SD 12.2)	65 (SD 11.8)	69 (SD 11.6)
Sex				
Female	11 (31.4%)	11 (32.3%)	8 (30.8%)	12 (30.8%)
Male	24 (68.6%)	23 (67.7%)	18 (69.2%)	27 (69.2%)
Race				
White	28 (80.0%)	27 (79.4%)	21 (80.8%)	31 (79.5%)
African American	7 (20.0%)	7 (20.6%)	5 (19.2%)	8 (20.5%)
Smoking status				
Pack-years	32.6 (SD 22.3)	31.6 (SD 21.7)	32.7 (SD 23.2)	30.5 (SD 23.1)
Stage				
I	10 (28.6%)	11 (32.4%)		
II	12 (34.3%)	10 (29.4%)		
III-IV	13 (37.1%)	13 (38.2%)		
Location of tumor				
Central	30 (85.7%)	3 (8.8%)		
Peripheral	5 (14.3%)	31 (91.2%)		

Abbreviations: NSCLC, non-small-cell lung cancer; SCC, squamous cell carcinoma; AC, adenocarcinoma; COPD, chronic obstructive pulmonary disease; SD, standard deviation.

Supplementary table 2. Genomic copy number changes of 15 genes represented by PPC in 26 healthy smokers, 39 COPD patients, and 69 NSCLC patients

Genes	Mean (SD) in healthy smokers	Mean (SD) in COPD patients	Mean (SD) in NSCLC patients
ENO1	6.2 (1.7)	8.2 (1.5) *	10.3 (2.6) [†]
SKP2	6.8 (1.9)	7.6 (1.5)	12.5 (2.9) [†]
NME2	3.3 (1.3)	5.2 (1.6) *	6.4 (2.5) [†]
S100A1	4.6 (1.2)	7.3 (1.3) *	8.3 (2.7) [†]
POLR	5.5 (1.3)	6.6 (1.3)	8.8 (2.5) [†]
14-3-3-zeta	5.3 (1.6)	6.7 (1.8)	13.6 (2.7) [†]
EEF1A2	6.5 (1.2)	8.8 (1.2) *	11.6 (2.3) [†]
FGF4	5.7 (1.1)	6.3 (1.7)	8.6 (1.9) [†]
hTERT	4.9 (1.1)	5.7 (1.1)	7.6 (2.8) [†]
FHIT	6.4 (1.5)	6.2 (1.9)	13.3 2.8) [†]
TGFBR	5.1 (1.9)	6.8 (1.7) *	8.7 (2.2) [†]
HYAL2	7.6 (1.9)	8.4 (2.2)	12.6 (3.2) [†]
CD74	5.1 (1.3)	8.6 (1.2) *	11.3 (2.5) [†]
P16	4.0 (1.6)	5.8 (1.7) *	9.2 (2.6) [†]
SP-A	2.6 (1.3)	3.9 (1.7) *	8.9 (2.7) [†]

Abbreviations: PPC, percentage of the positive cells with genetic changes; COPD, chronic obstructive pulmonary disease; NSCLC, non-small-cell lung cancer; SD, standard deviation.
*Comparison of COPD patients and healthy subjects with P <0.05.
[†]Comparison of cancer patients with both healthy subjects and COPD patient for PPCs, all P values <0.05.

Supplementary Table 3. ROC and AUC analysis of the 15 genes to determine their sensitivity and specificity in distinguishing cancer patients from healthy smokers and COPD individuals

Genes	Distinguishing cancer patients from healthy smokers				Distinguishing cancer patients from COPD patients			
	AUC (SE)	Thresholds[*]	Sensitivity (%)	Specificity (%)	AUC (SE)	Thresholds[*]	Sensitivity (%)	Specificity (%)
ENO1	0.625 (0.026)	8.26	63.5	75.7	0.617 (0.022)	9.65	62.8	75.2
SKP2	0.668 (0.029)	9.25	62.7	75.8	0.656 (0.028)	10.25	62.6	76.3
NME2	0.656 (0.023)	4.35	62.6	75.9	0.632 (0.013)	5.91	62.2	76.1
S100A1	0.623 (0.025)	6.55	61.2	73.2	0.614 (0.021)	7.95	59.2	75.6
POLR	0.659 (0.022)	7.05	57.2	78.6	0.652 (0.017)	7.82	60.3	77.9
14-3-3-zeta	0.678 (0.019)	9.25	79.8	61.5	0.664 (0.015)	10.35	78.3	58.7
EEF1A2	0.646 (0.033)	9.15	63.6	77.6	0.635 (0.012)	10.77	58.7	76.8
FGF4	0.643 (0.029)	7.25	58.9	77.2	0.638 (0.025)	7.55	60.3	76.5
hTERT	0.667 (0.025)	6.35	63.2	75.3	0.663 (0.018)	6.85	61.5	74.8
FHIT	0.658 (0.019)	9.95	77.5	60.8	0.645 (0.031)	9.75	73.1	62.2
TGFBR	0.667 (0.031)	6.82	58.8	79.4	0.659 (0.026)	7.95	59.2	76.6
HYAL2	0.652 (0.015)	10.30	60.3	76.1	0.658 (0.026)	10.43	58.2	72.7
CD74	0.643 (0.026)	8.65	63.4	72.2	0.648 (0.017)	9.97	58.6	73.9
P16	0.669 (0.022)	6.78	76.7	59.1	0.667 (0.012)	7.85	73.6	61.2
SP-A	0.657 (0.023)	5.73	62.8	73.6	0.660 (0.018)	6.51	61.3	75.5

Abbreviations: ROC, receiver-operator characteristic curve; AUC, the area under ROC curve (AUC); COPD, chronic obstructive pulmonary disease;
SD, standard deviation; SE, standard error.
[*] Thresholds were represented by percentages of the positive cells with genetic changes. Optimal thresholds were set up by using constructed ROC curves and the associated AUC values, by which maximum sensitivity and specificity levels of the genes were determined in distinguishing cancer patients from healthy and COPD subjects, respectively.

Supplementary Table 4. Association of the changes of the six genes the with clinical and demographic characteristics of the NSCLC patients

	Genes, OR (95% CI), P[*]					
Characteristics	*ENO1*	*FHIT*	*SKP2*	*14-3-3-zeta*	*HYAL2*	*P16*
Age	0.46 (0.29 to 1.78), 0.46	0.69 (0.51 to 2.25), 0.69	0.45 (0.20 to 1.67). 036	0.69 (0.28 to 1.67), 0.25	0.68 (0.26 to 1.68). 027	0.65 (0.24 to 1.19), 0.23
Gender	1.57 (0.48 to 3.56), 0.21	1.67 (0.88 to 3.35), 0.25	1.24 (0.66 to 3.74), 0.58	1.68 (0.75 to 2.67), 0.58	1.73 (0.45 to 3.63), 0.46	1.78 (0.65 to 2.96), 0.34
Ethnic group	1.25 (0.37 to 2.85), 0.26	1.56 (0.35 to 3.68), 0 63	1.67 (0.46 to 3.85), 0.35	1.56 (0.46 to 2.78), 0.53	1.56 (0.35 to 3.77), 0.52	1.56 (0.75 to 249), 0.26
Smoking status	2.36 (0.57 to 5.56), **0.02**	2.34 (1.15 to 5.23), 0.02	2.46 (1.56 to 4.48), **0.02**	2.46 (1.03 to 4.88), **0.02**	2.36 (0.98 to 4.25), **0.03**	2.78 (1.13 to 4.56), **0.01**
Tumor location	2.45 (1.27 to 5.46), **0.01**	2.49 (1.56 to 5.35), **0.03**	2.37 (0.89 to 4.93), **0.01**	2.45 (1.66 to 5.07), **0.02**	2.78 (0.99 to 4.69), **0.05**	2.56 (1.88 to 4.86), **0.04**
Histological type	2.57 (1.58 to 6.36), **0.04**	2.36 (1.51 to 5.38), **0.05**	2.49 (0.12 to 5.98), **0.03**	2.56 (1.46 to 4.99), **0.01**	2.36 (0.12 to 5.49), **0.02**	2.26 (1.20 to 4.98), **0.05**
Stage	2.95 (0.92 to 5.08), **0.03**	2.67 (0.13 to 4.29), **0.02**	2.39 (0.98 to 4.79), **0.01**	2.68 (1.09 to 4.78), **0.05**	2.78 (0.99 to 4.38), **0.01**	2.69 (0.99 to 4.87), **0.03**

Abbreviations: NSCLC, non-small cell lung cancer; OR = odds ratio; CI = confidence interval.
[*] Uunivariate analysis. All P values are two-sided, and P≤0.05 was considered statistically significant and given in bold type.