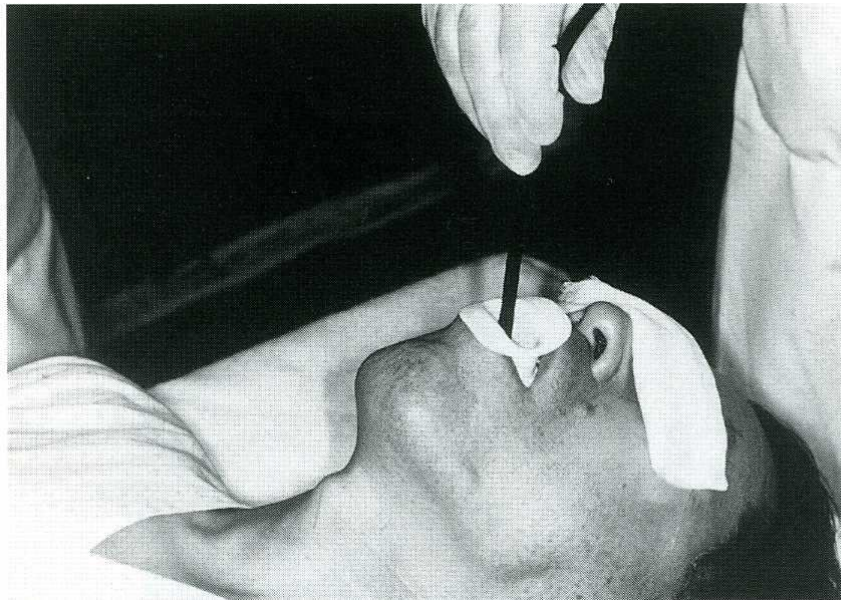
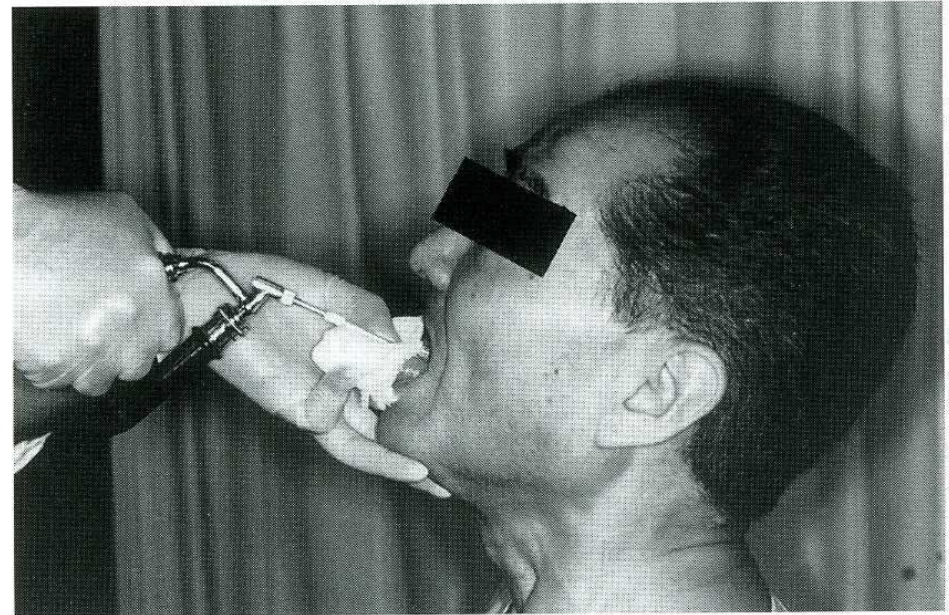
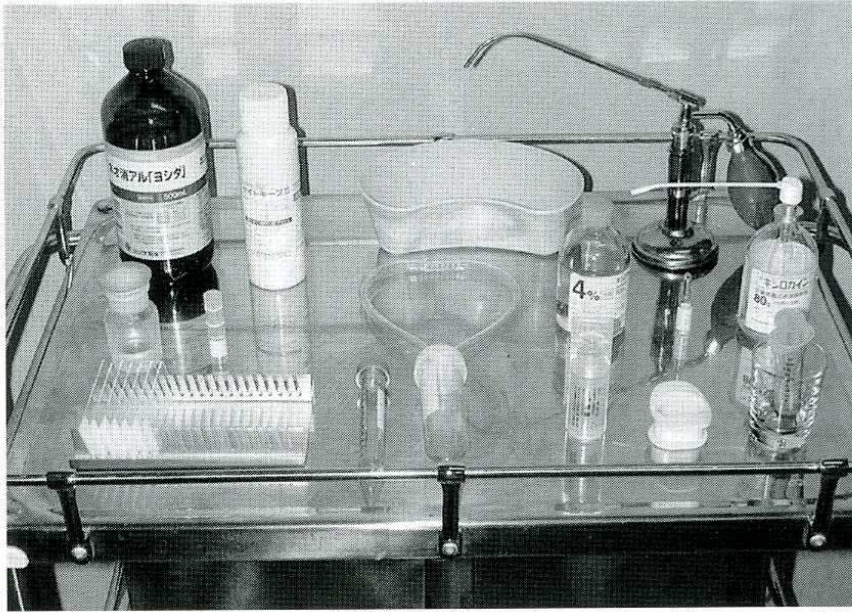


ゲノム解析を用いた肺癌の診断法 : 気管支鏡検査の正診率向上へ

Improvement of the diagnostic
performance of bronchoscopy

研修医 伊勢洋史
呼吸器外科 後藤太一郎

気管支鏡の準備



気管支鏡下生検(透視下)

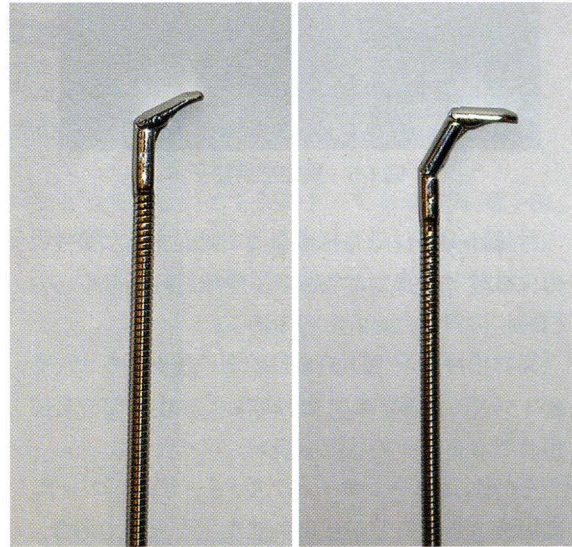
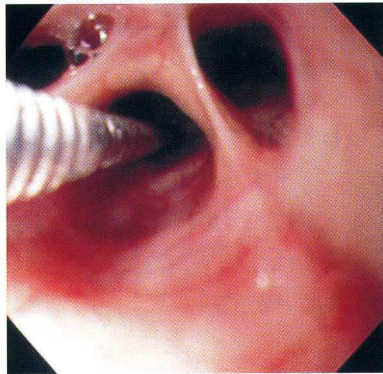
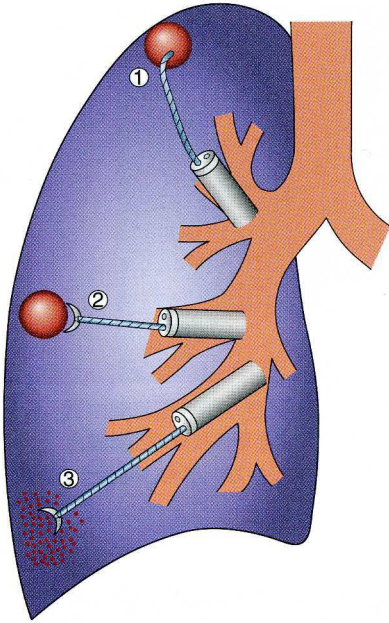
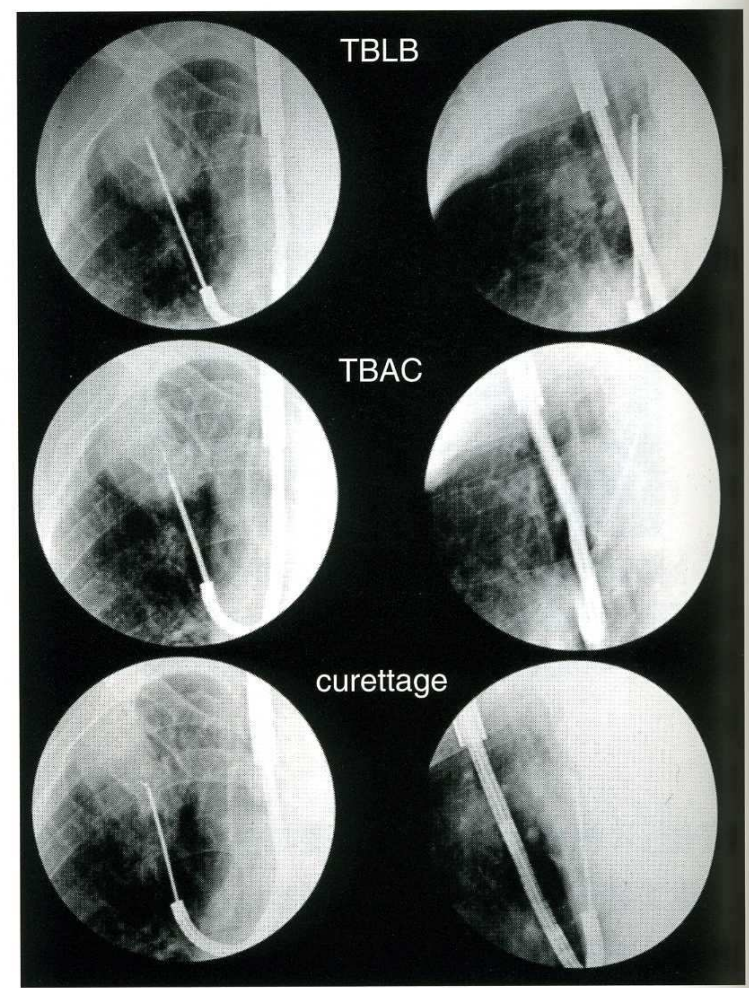
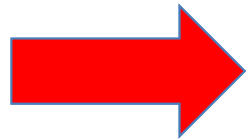


図 1-3 鋭匙 (キュレット) (単関節, 双関節)



肺癌診断のための気管支鏡検査における喀痰、気管支洗浄液の遺伝子変異解析



1. 喀痰での肺癌診断の可否
2. 気管支鏡検査の正診率向上
3. 気道内spreading DNAの証明

A Bronchial Genomic Classifier for the Diagnostic Evaluation of Lung Cancer

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Michael Elashoff, Ph.D., Kate Porta Smith, M.P.H., J. Scott Ferguson, M.D.,
Ed Parsons, Ph.D., Nandita Mitra, Ph.D., Jerome Brody, M.D., Marc E. Lenburg, Ph.D.,
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BACKGROUND

- ・肺癌疑いの患者に対して、通例、気管支鏡検査を行うが、
気管支鏡検査の正診率は低く、治療選択に難渋する症例が多い。
- ・気管支鏡検査の診断能を向上させるべく、気道上皮細胞の遺伝子発現分類を行い、診断における有効性について検証を行った。

METHODS

- Population
 - i) 21歳以上
 - ii) 現在・過去喫煙者
 - iii) 肺癌の既往のない者
 - iv) 肺癌疑いで気管支鏡検査を受ける者
- 28施設で実施した2つの前向き多施設共同研究 (AEGIS-1、AEGIS-2) に登録した。
- Intervention conventional BF vs Genomic classifier
- Primary endpoint sensitivity

Genomic Classifier

正常に見える主気管支から採取した気管支上皮細胞で mRNA の発現パターンを評価した

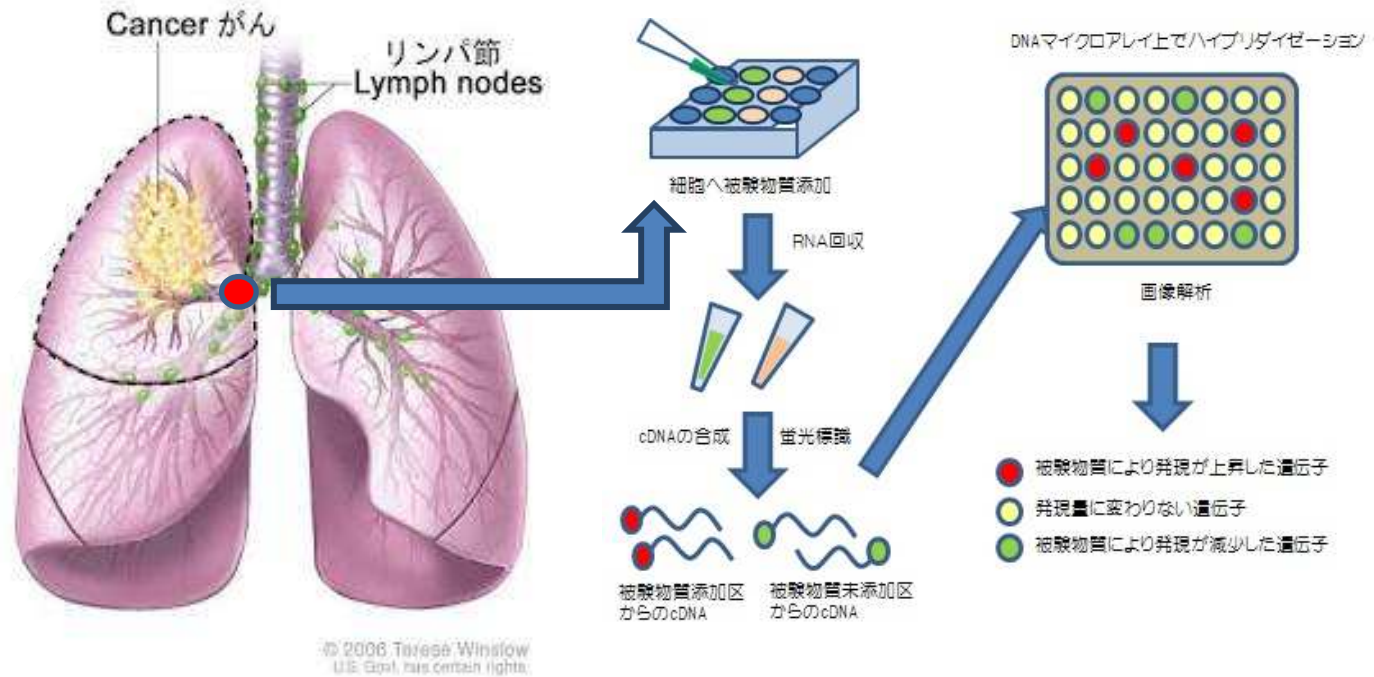


Table 1. Demographic and Clinical Characteristics of the Study Participants.*

Characteristic	AEGIS-1 (N = 298)	AEGIS-2 (N = 341)
Sex — no.†		
Female	125	106
Male	173	235
Median age (IQR) — yr†	62 (55–70)	64 (57–71)
Race — no.‡		
White	226	267
Black	55	66
Other	15	4
Unknown	2	4
Smoking status — no.		
Current	146	169
Former	152	172
Median cumulative tobacco use (IQR) — pack-yr	40 (24–60)	45 (25–63)
Lesion size — no.		
<2 cm	48	83
2 to 3 cm	41	39
>3 cm	155	188
Infiltrate§	32	28
Unknown	22	3

Table 1. Demographic and Clinical Characteristics of the Study Participants.*

Characteristic	AEGIS-1 (N = 298)	AEGIS-2 (N = 341)
Lesion location — no.		
Central	98	127
Peripheral	86	108
Central and peripheral	90	102
Unknown	24	4
Lung-cancer histologic type — no.¶	220	267
Small-cell	38	42
Non-small-cell	175	222
Adenocarcinoma	69	100
Squamous	72	81
Large-cell	8	8
Non-small-cell not otherwise specified	26	33
Unknown	7	3
Diagnosis of a benign condition — no.	78	74
Infection	18	14
Sarcoidosis	16	15
Resolution or stability	27	24
Other	17	21

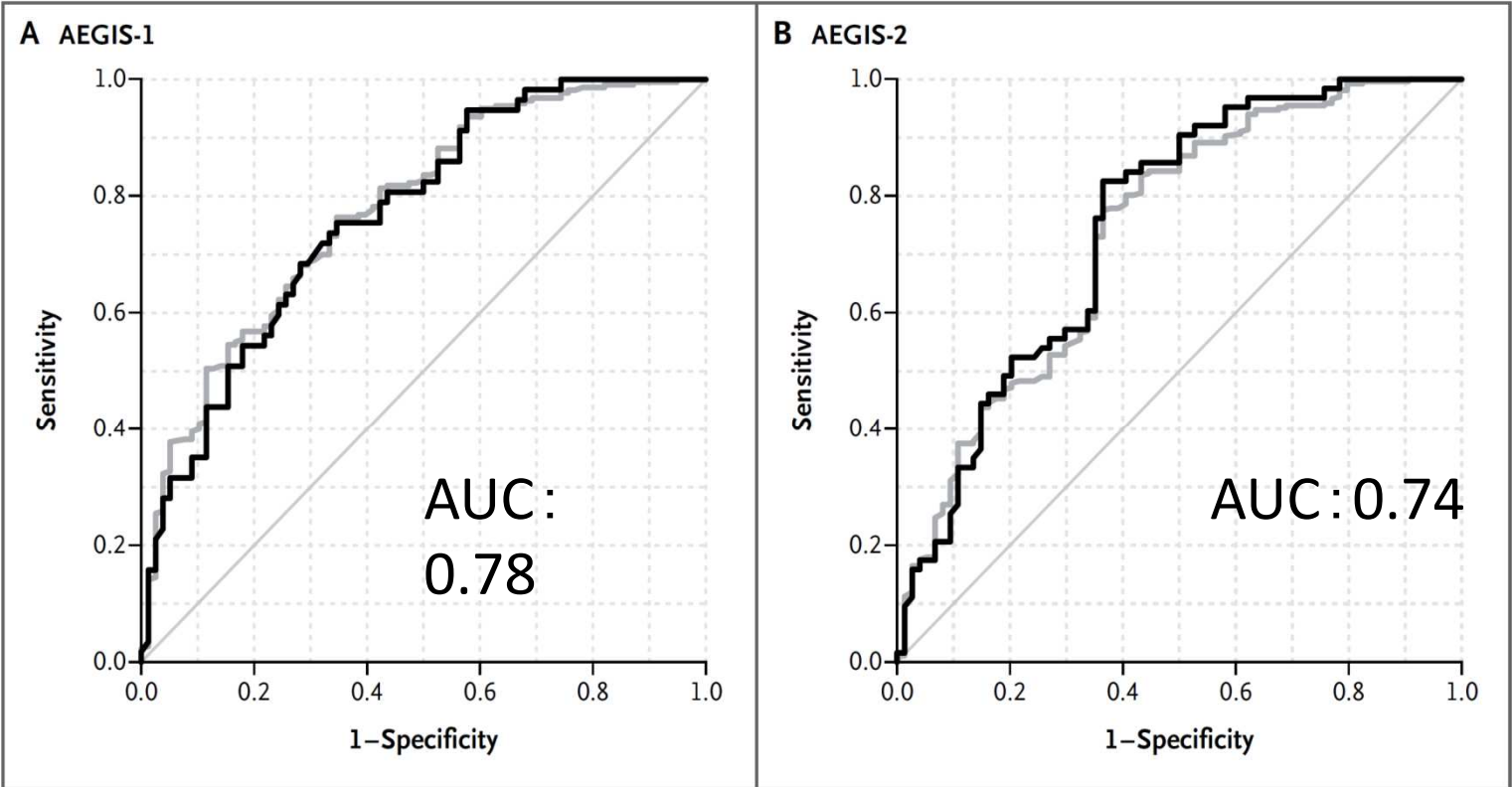


Figure 1. Classifier Performance in the AEGIS-1 and AEGIS-2 Studies.

Table 2. Sensitivity of the Classifier, Bronchoscopy, and the Combined Approaches, According to Radiologic Imaging Characteristics.

Group	All Patients	Patients with Cancer	Sensitivity*		
			Bronchoscopy	Classifier	Classifier plus Bronchoscopy
	<i>no. of patients</i>		<i>percent (95% confidence interval)</i>		
All patients	639	487	75 (71–79)	89 (82–94)	97 (95–99)
Lesion size					
<2 cm	131	73	55 (43–66)	91 (76–98)	96 (88–99)
2 to 3 cm	80	60	58 (45–71)	92 (74–99)	97 (88–100)
>3 cm	343	313	82 (78–86)	85 (74–93)	97 (95–99)
Infiltrate	60	25	84 (64–95)	100 (40–100)	100 (86–100)
Unknown	25	16	80 (54–96)	100 (29–100)	100 (79–100)
Lesion location					
Central	225	174	84 (78–89)	81 (62–94)	97 (93–99)
Peripheral	194	133	55 (46–63)	90 (79–96)	95 (90–98)
Central and peripheral	192	164	82 (75–87)	97 (82–100)	99 (96–100)
Unknown	28	16	81 (54–96)	67 (9–99)	94 (70–100)

Conclusion

従来の気管支鏡検査とBronchial Genomic Classifierを併用することで
肺癌の診断能が向上することが示された。

	sensitivity
Bronchoscopy only	75%
Bronchoscopy + genomic classifier	97%

当院での成績: 気管支鏡での肺癌診断の感度

Population:

- (i) 2014年1月から2015年10月までに当院で手術を行い、肺癌と病理診断された症例
- (ii) 肺癌を疑い、術前に当院で気管支鏡検査を施行した症例

Endpoint:

肺癌診断の感度

診断感度に影響を及ぼす因子の解析

(腫瘍の組織型、大きさ、部位、リンパ節転移)

Result 1

肺癌手術症例 164人

内、当院で術前にBFを施行した症例 95人

感度 65.3%

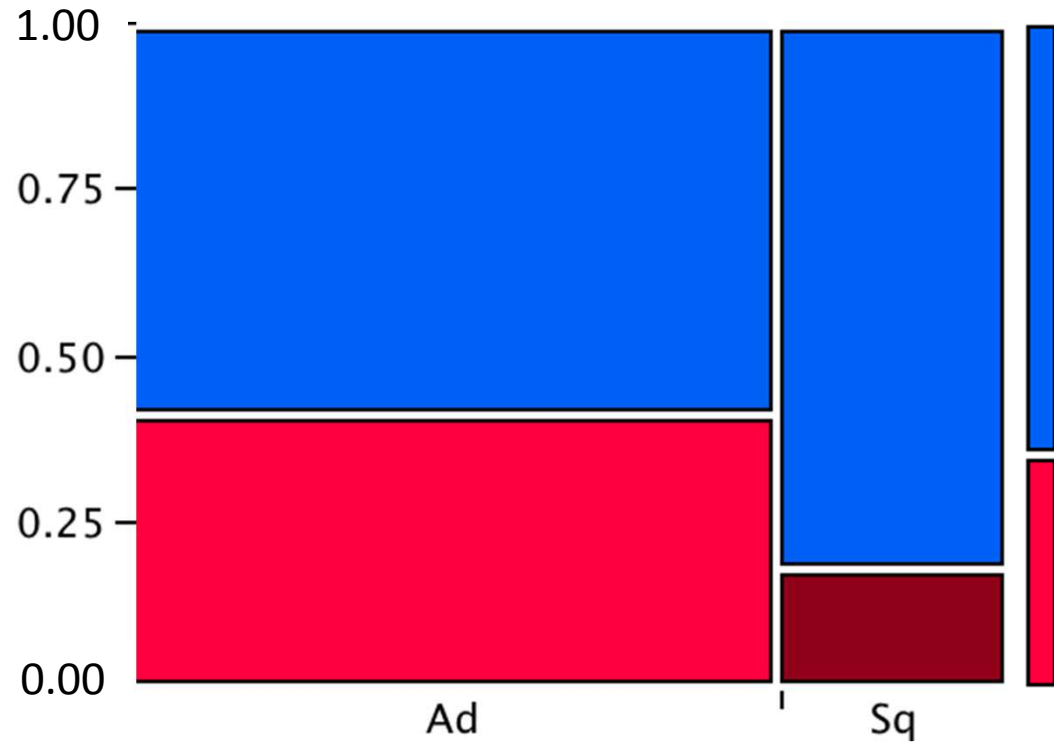
多変量解析結果

	<u><i>p</i> value</u>
組織型 (Ad, Sq, others)	<i>p</i> =0.45
size	<i>p</i> <0.05
location (C, P, CP)	<i>p</i> <0.05
リンパ節転移(n0-3)	<i>p</i> =0.17

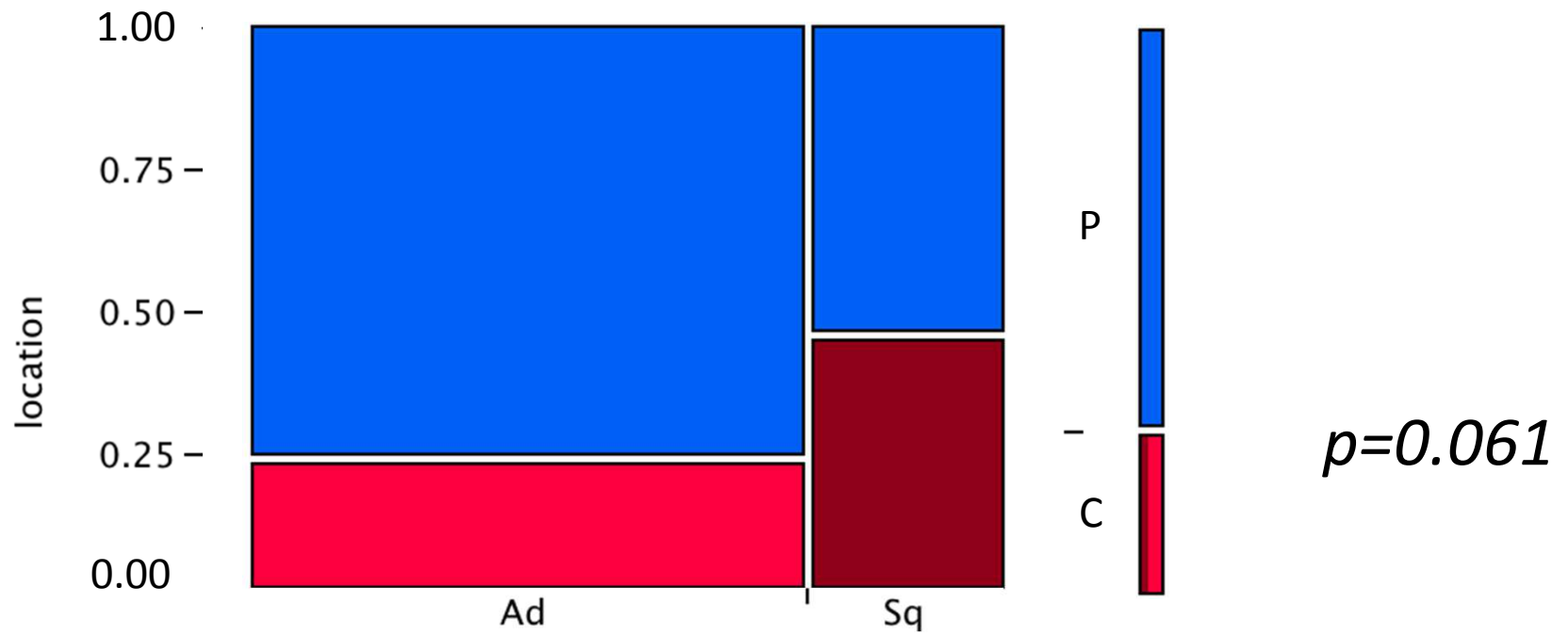
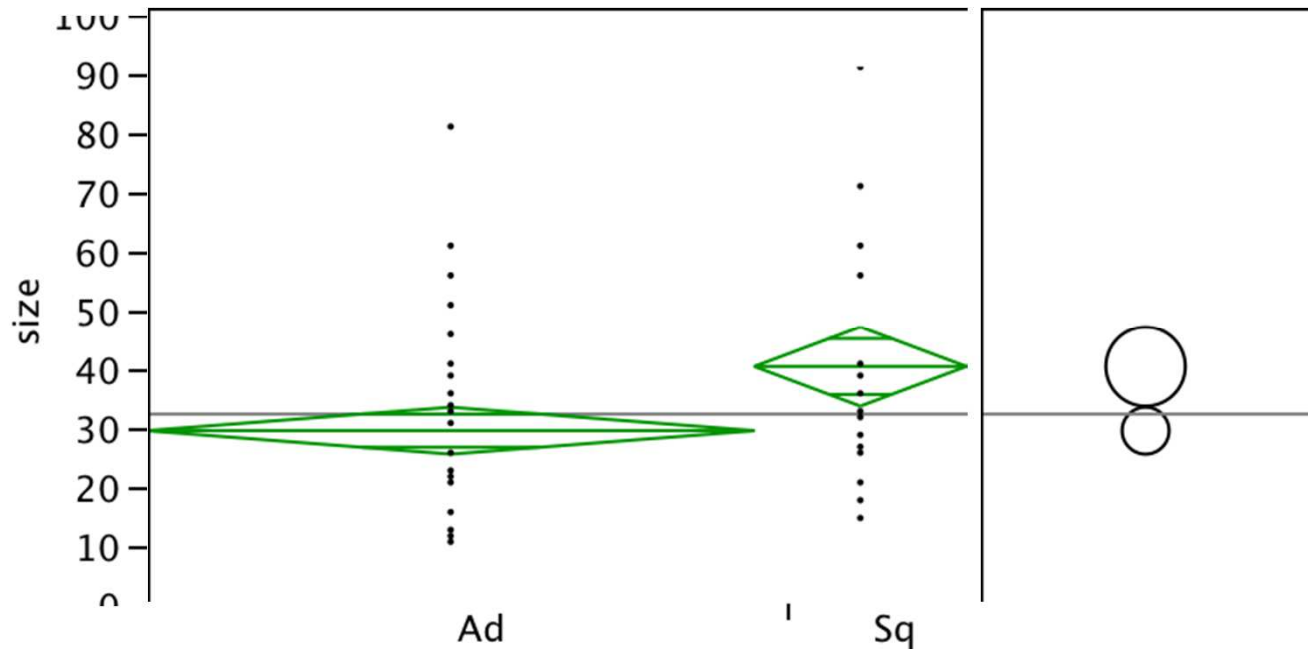
Result 2

	All patients	Patients with Cancer	Sensitivity of the bronchoscopy
All patients	95	62	65.3
Lesion size			
<2 cm	20	7	35
2 to 3 cm	34	20	58.8
>3 cm	41	35	85.4
Lesion location			
Central	16	13	81.3
C and P	13	12	92.3
Peripheral	66	37	56.1

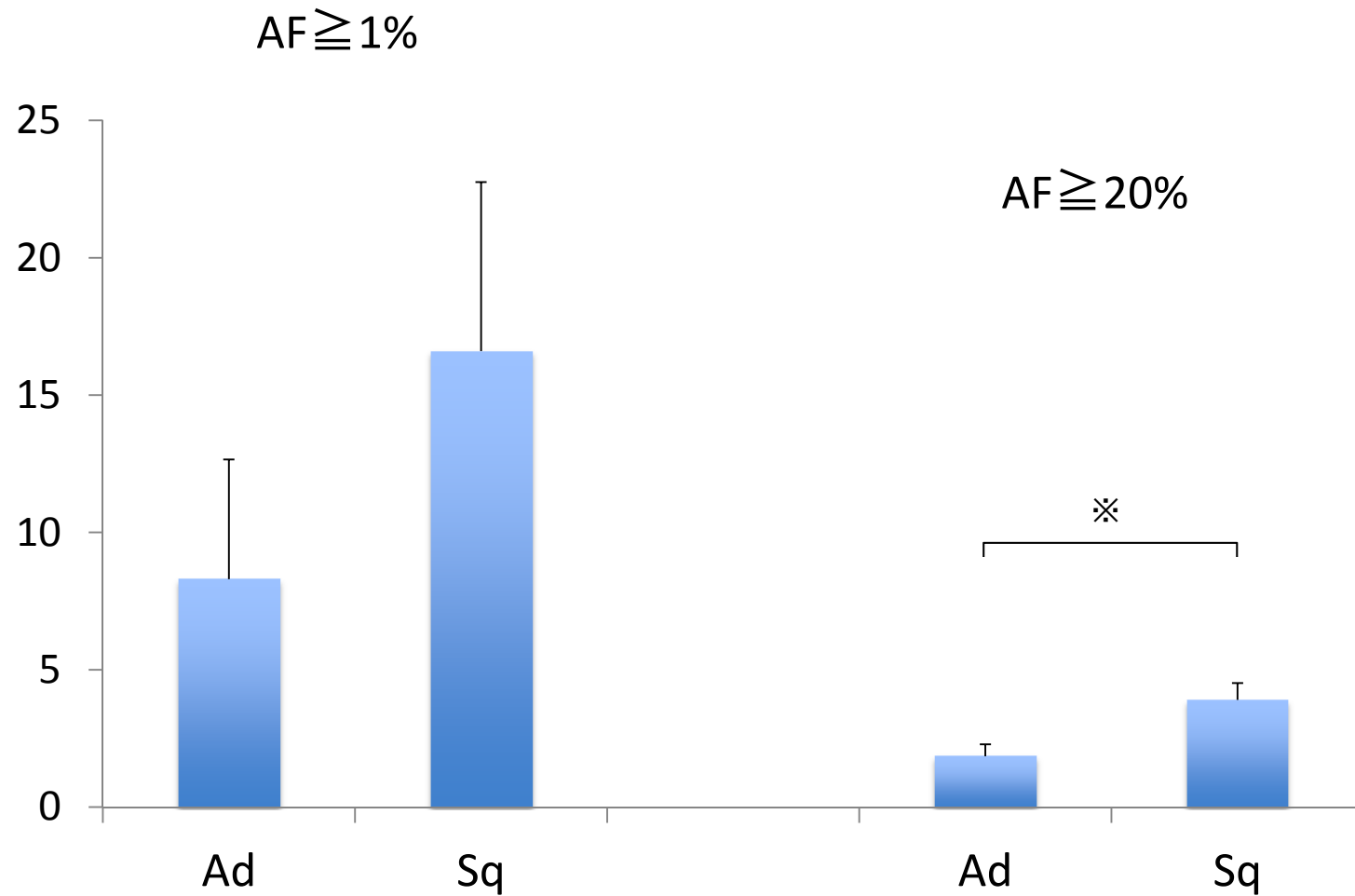
Result 3



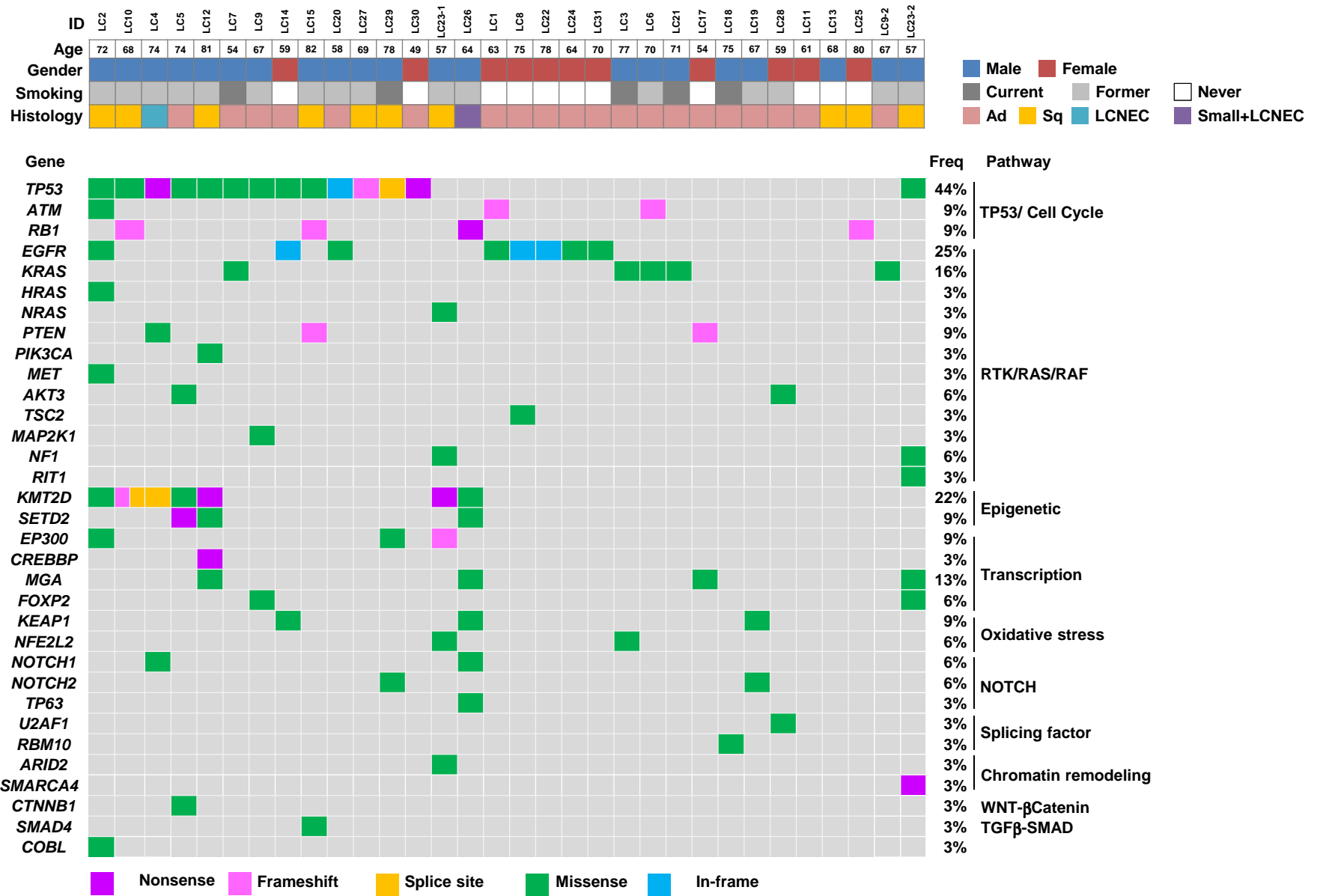
$p < 0.05$



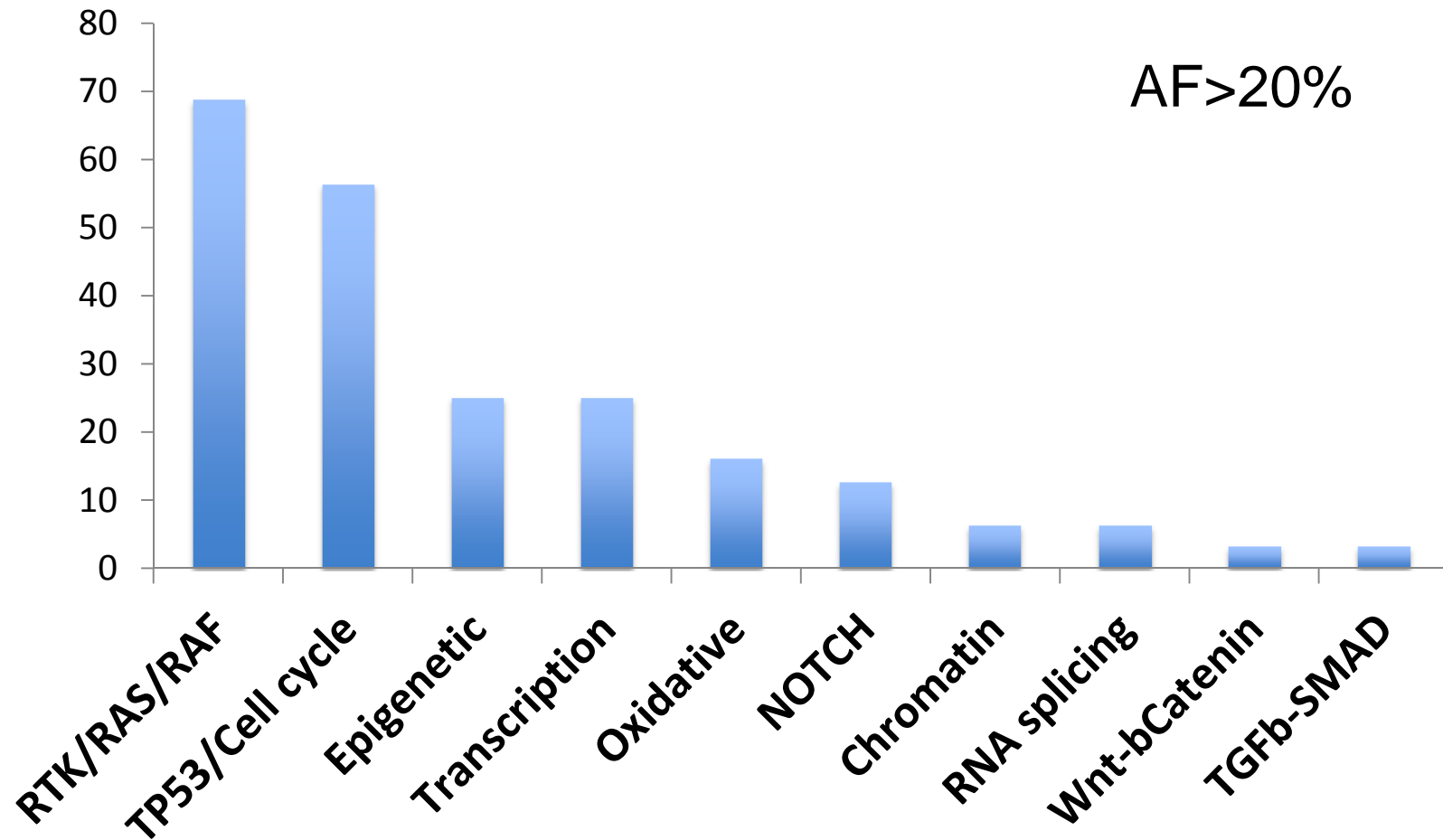
Number of Mutations in Lung Cancer



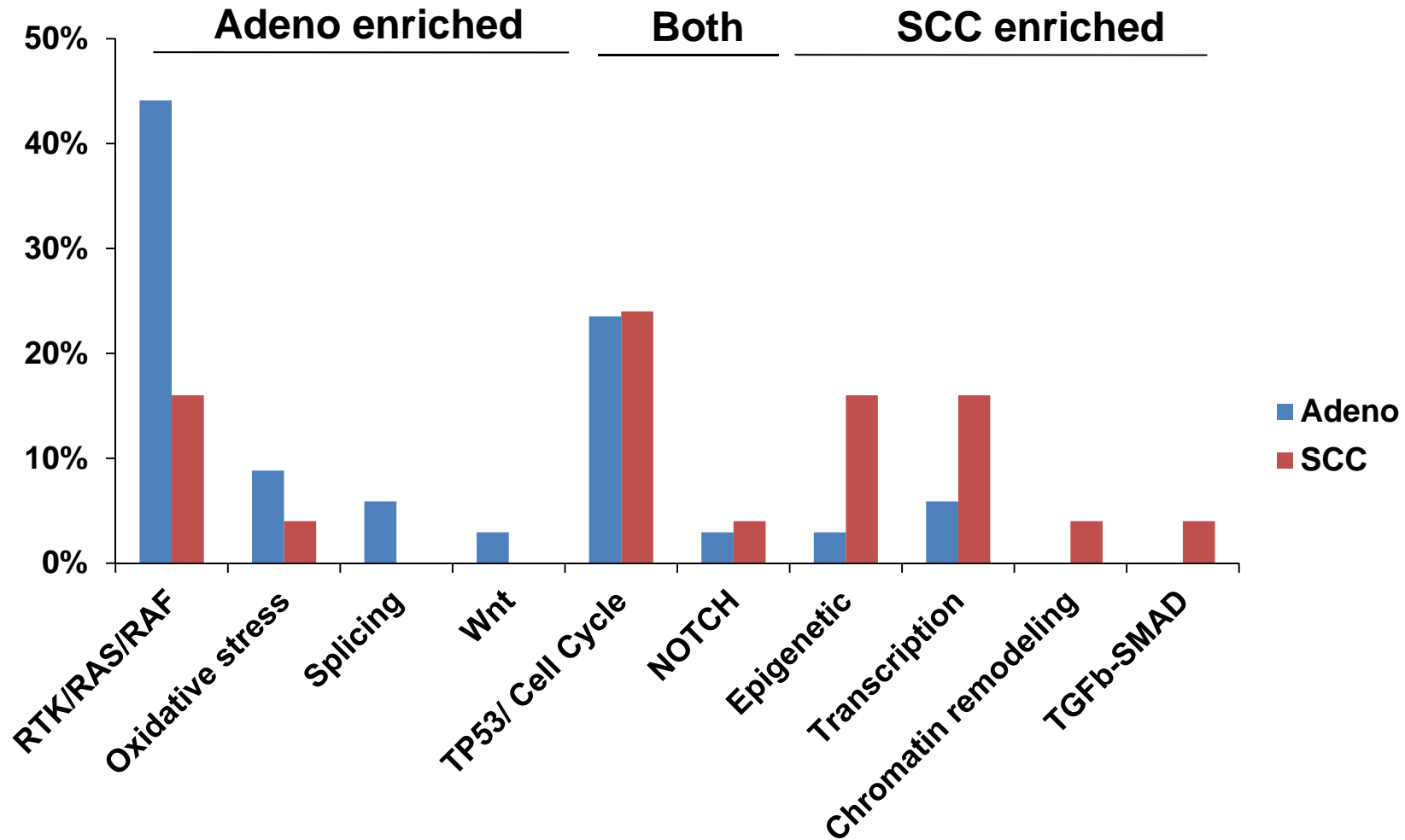
※, $p < 0.05$



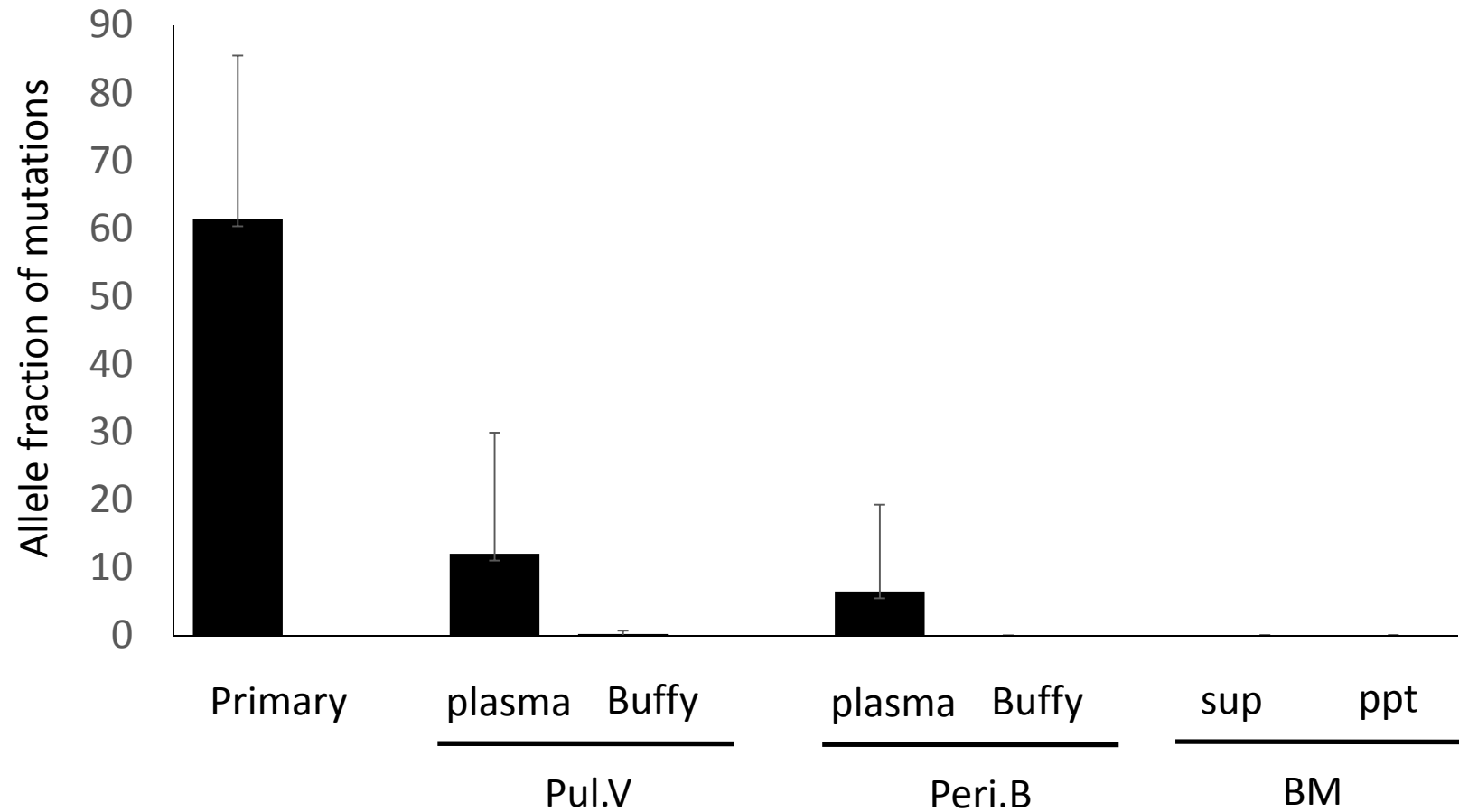
Aberrant Pathways in Lung Cancer



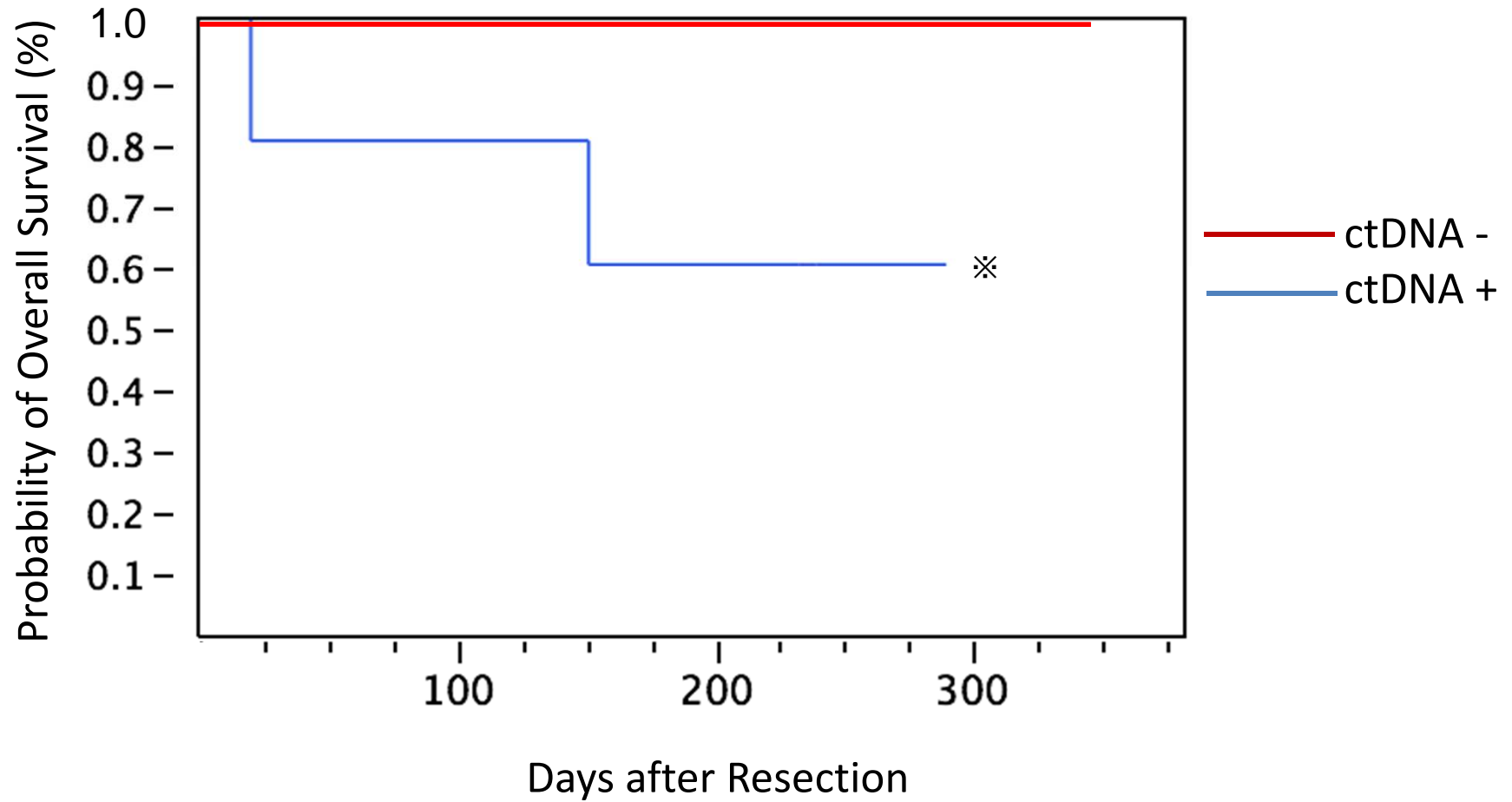
Aberrant Pathways in Lung Cancer



Distribution of ctDNA



Survival Curve



※, $p < 0.05$

当院の気管支鏡検体に対するゲノム解析に関しては、データ解析中

Our method

NEJM論文の方法より、直接的証明であり、正診率が高くなる可能性あり

Cancerのcharacterization可能
気道内DNAはnovel idea