

Figure	Classification here	Age	Sex	Smoking	Mutation	Size	Histology
4a, 4d, 4e	Lepidic	74	F	NS	EGFR L858R	3.2 cm	Invasive well-differentiated adenocarcinoma arising within a background of fibroelastosis, 60% acinar, 40% lepidic
4a, 4c, ED1b	Lepidic	73	M	50 PY	KRAS G12C, NF1, NF2	1.4 cm	Papillary and lepidic, mucinous and non-mucinous, additional foci of AAH
4a, 4e	Lepidic	77	F	NS	EGFR L858R, TP53, KDR	2.4 cm	Invasive, well-differentiated adenocarcinoma 75% acinar, 15% Papillary, 10% lepidic
4a	Lepidic	67	M	7.5 PY	EGFR Exon 19 del	2.0 cm	Invasive, well-differentiated adenocarcinoma 70% acinar, 15% micropapillary, 10% papillary, and 5% lepidic
4a, 4c	Lepidic	75	F	15 PY	EGFR Exon 19 del	2.7 cm	Invasive, well-differentiated adenocarcinoma 50% acinar, 30% papillary, 15% lepidic, and 5% micropapillary
ED3b	Lepidic	65	M	NS	EGFR L858R	2.0 cm	Invasive well differentiated adenocarcinoma, 55% lepidic and 45% acinar
4a	Non-Lepidic	67	M	35 PY	CDH1, STK11, TP53	1.8 cm	Invasive poorly differentiated adenocarcinoma
4a	Non-Lepidic	80	M	50 PY	NF1, TP53, MET	2.2 cm	Invasive poorly differentiated adenocarcinoma
4a	Non-Lepidic	74	M	50 PY	ARID1A, KEAP1, NF1, TP53	5.0 cm	moderately differentiated adenocarcinoma with papillary (50%), micropapillary, (10%), solid (20%) and acinar (20%) patterns
4a	Non-Lepidic	76	M	Yes	MAPK21	3.7 cm	Invasive adenocarcinoma, solid predominant
4a	Non-Lepidic	78	F	NS	EGFR exon19 deletion	4.5 cm	well-differentiated adenocarcinoma, 60% papillary, 20% micropapillary, 20% acinar
ED1b, ED3a	Non-Lepidic	77	M	75 PY	NF1, NKX2-1, PTEN	4.4 cm	mixed mucinous and pleomorphic/spindle cell carcinoma
ED3a	Non-Lepidic	75	M	NS	KRAS G12D, NKX2-1	6.9 cm	invasive mucinous adenocarcinoma

Strunz et al 2020	Kobayashi et al 2020	Choi et al 2020	Marjanovic et al 2020
Krt8+ Alveolar Differentiation Intermediate (Krt8+ ADI)	Pre-alveolar type-1 transition cell state (PATs)	Damage Associated Transient Progenitors (DATPs)	High Plasticity Cell State
Cldn4	Cldn4	Cldn4	Cldn4
Krt8	Lgals3	Krt8	Lgals3
Itgb6	Fn1	Sprr1a	Scl4a11
Sprr1a	Trp53	Tnip3	Epcam
Tnip3	Krt19	Cdkn1a	Cldn7
Cdkn1a	Sfn	Ly6a	Cars
Plaur	Ctgf	S100a14	Hmces
Hbegf	Sox4	Cxcl15	Dusp10
Areg		Ndr1	Lif
Edn1		Krt19	Tigit

Wnt related driver mutation data from Caso et al 2020.						
Accessed through www.cbioportal.org		"Lung Adenocarcinoma (MSK, J Thorac Oncol 2020)"				
Sample	Gene	Variant	OncoKB annotation	Net Wnt Effect	Predominant Histologic Subtype	Classification in this manuscript
P-0019612	CTNNB1	D32G	Gain-of-function	Augmentation	Papillary	Non-Lepidic
P-0022830	CTNNB1	D32N	Gain-of-function	Augmentation	Micropapillary	Non-Lepidic
P-0028486	CTNNB1	D32V	Likely Gain-of-function	Augmentation	Acinar	Non-Lepidic
P-0036267	CTNNB1	D32Y	Gain-of-function	Augmentation	Acinar	Non-Lepidic
P-0005198	CTNNB1	S33P	Likely Gain-of-function	Augmentation	Papillary	Non-Lepidic
P-0014502	CTNNB1	G34E	Likely Gain-of-function	Augmentation	Acinar	Non-Lepidic
P-0029396	CTNNB1	G34R	Likely Gain-of-function	Augmentation	Papillary	Non-Lepidic
P-0008957	CTNNB1	G34R	Likely Gain-of-function	Augmentation	Acinar	Non-Lepidic
P-0003489	CTNNB1	S37F	Gain-of-function	Augmentation	Acinar	Non-Lepidic
P-0017437	CTNNB1	S37F	Gain-of-function	Augmentation	Acinar	Non-Lepidic
P-0033508	CTNNB1	S37F	Gain-of-function	Augmentation	Acinar	Non-Lepidic
P-0036267	CTNNB1	S37F	Gain-of-function	Augmentation	Acinar	Non-Lepidic
P-0023153	CTNNB1	S45P	Gain-of-function	Augmentation	Micropapillary	Non-Lepidic
P-0014089	CTNNB1	S45P	Gain-of-function	Augmentation	Acinar	Non-Lepidic
P-0010507	CTNNB1	N387K	Gain-of-function	Augmentation	Acinar	Non-Lepidic
P-0029357	AMER1	R586*	Likely Loss-of-function	Augmentation	Acinar	Non-Lepidic
P-0007638	AMER1	W695_R696delins*	Likely Loss-of-function	Augmentation	Micropapillary	Non-Lepidic
P-0021718	AMER1	E702*	Likely Loss-of-function	Augmentation	Acinar	Non-Lepidic
P-0004860	AMER1	E752*	Likely Loss-of-function	Augmentation	Acinar	Non-Lepidic
P-0025918	AMER1	E920*	Likely Loss-of-function	Augmentation	Acinar	Non-Lepidic
P-0009312	APC	X278_splice	Likely Loss-of-function	Augmentation	Acinar	Non-Lepidic
P-0029294	APC	S1068*	Likely Loss-of-function	Augmentation	Acinar	Non-Lepidic
P-0029294	APC	E1097*	Likely Loss-of-function	Augmentation	Acinar	Non-Lepidic
P-0015862	APC	E1149*	Likely Loss-of-function	Augmentation	Solid	Non-Lepidic
P-0026187	APC	S1346*	Likely Loss-of-function	Augmentation	Solid	Non-Lepidic
P-0016172	APC	R1450*	Likely Loss-of-function	Augmentation	Acinar	Non-Lepidic
P-0016036	APC	S1465Wfs*3	Likely Loss-of-function	Augmentation	Acinar	Non-Lepidic
P-0022251	APC	P2094Lfs*18	Likely Loss-of-function	Augmentation	Solid	Non-Lepidic
P-0019612	AXIN1	Y237*	Likely Loss-of-function	Augmentation	Papillary	Non-Lepidic
P-0012540	AXIN2	X746_splice	Likely Loss-of-function	Augmentation	Solid	Non-Lepidic
P-0026688	AXIN2	K508lfs*181	Likely Loss-of-function	Augmentation	Papillary	Non-Lepidic