

Supplementary Materials

Data availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Computer Code and Software: The computer code that support the findings of this study are available from the corresponding author upon reasonable request. Correspondence and requests for materials should be addressed to ahnsyeon@snuh.org, chungjh@snu.ac.kr.

S1 Table. Patient characteristics and sample preparations

Patient	Age (yr)	Sex	Smoking (PY)	Lesions ^{a)}	WES (P=3, n=22)	Targeted seq (P=16, n=78)	RNA seq (P=9, n=44)
P1	64	M	CS (20)	LN	LN	LN	RNA LN ^{b)}
				AAH	AAH1, AAH2	AAH1, AAH2	RNA AAH2, RNA AAH4 ^{b)}
				AAH	AAH3	AAH3	RNA AAH3
				AIS	AIS	AIS	RNA AIS
				MIA	MIA1	MIA1	RNA MIA1
				MIA	MIA2	MIA2	RNA MIA2
				ADC-L	ADC1	ADC1	RNA ADC1
				ADC	ADC2	ADC2	RNA ADC2
P2	75	M	ES (35)	NT	NT ^{b)}		RNA NT
				LN	-	LN ^{b)}	RNA LN ^{b)}
				AAH		AAH ^{b)}	RNA AAH ^{b)}
				AIS		AIS ^{b)}	RNA AIS ^{b)}
				ADC-L		ADC1 ^{b)}	RNA ADC1 ^{b)}
P3	66	M	ES (10)	ADC		ADC2 ^{b)}	RNA ADC2 ^{b)}
				NT			RNA NT
				LN	-	LN ^{b)}	
				AAH		AAH1 ^{b)}	RNA AAH1 ^{b)}
				AAH		AAH2 ^{b)}	RNA AAH2 ^{b)}
P4	55	F	NS (0)	ADC		ADC*	RNA ADC ^{b)}
				NT			RNA NT ^{b)}
				LN	-	LN ^{b)}	
				AAH		AAH ^{b)}	RNA AAH ^{b)}
				AIS		AIS ^{b)}	
P5	53	F	NS (0)	ADC-L		ADC1 ^{b)}	
				ADC		ADC2 ^{b)}	RNA ADC ^{b)}
				NT			RNA NT ^{b)}
				LN	LN	LN	
				AAH	AAH1	AAH1	RNA AAH1
P6	68	F	NS (0)	AAH		AAH2	RNA AAH2 ^{b)}
				AIS	AIS	AIS	
				MIA	MIA	MIA	
				ADC	ADC	ADC	RNA ADC
				NT	NT ^{b)}		RNA NT
				LN	-	LN ^{b)}	-

P7	80	F	NS (0)	AIS	-	AIS ^{b)}	-
				MIA		MIA ^{b)}	
				ADC		ADC ^{b)}	
				LN		LN ^{b)}	
P8	69	M	ES (30)	AAH	LN AAH6	AAH ^{b)}	RNA AAH1 ^{b)} , RNA AAH6 RNA AAH2 ^{b)} RNA AAH3 ^{b)} , RNA AAH4 ^{b)}
				AIS		AIS ^{b)}	
				ADC		ADC ^{b)}	
				LN		LN	
P9	70	F	NS (0)	AAH	AIS MIA ADC NT ^{b)}	AAH ^{b)}	RNA ADC RNA NT
				ADC		ADC ^{b)}	
				NT		NT ^{b)}	
				LN		LN ^{b)}	
P10	72	M	CS (50)	AAH	-	AAH ^{b)}	RNA AAH ^{b)}
				ADC-L		ADC1 ^{b)}	
				ADC		ADC2 ^{b)}	
				NT		NT ^{b)}	
P11	51	M	ES (12)	AAH	-	AAH1 ^{b)}	RNA AAH1 ^{b)} RNA AAH2 ^{b)}
				AAH		AAH2 ^{b)}	
				ADC-L		ADC1 ^{b)}	
				ADC		ADC2 ^{b)}	
P12	70	M	ES (10)	NT	-	NT ^{b)}	RNA ADC ^{b)} RNA NT ^{b)}
				LN		LN ^{b)}	
				AIS		AIS ^{b)}	
				ADC-L		ADC1 ^{b)}	
P13	55	F	NS (0)	ADC	-	ADC2 ^{b)}	-
				LN		LN ^{b)}	
				AIS		AIS ^{b)}	
				ADC-L		ADC1 ^{b)}	
P14	72	F	NS (0)	ADC	-	ADC2 ^{b)}	-
				LN		LN ^{b)}	
				AIS		AIS ^{b)}	
				ADC-L		ADC1 ^{b)}	
P15	78	F	NS (0)	ADC	-	ADC2 ^{b)}	-
				LN		LN ^{b)}	
				MIA		MIA ^{b)}	
				ADC-L		ADC1 ^{b)}	
P16	61	F	NS (0)	ADC	-	ADC2 ^{b)}	-
				LN		LN ^{b)}	
				MIA		MIA ^{b)}	
				ADC-L		ADC1 ^{b)}	

ADC

ADC2^{b)}

WES, whole exome sequencing; RNA-seq, RNA sequencing; CS, current smoker; ES, ex-smoker; NS, never smoker; AAH, atypical adenomatous hyperplasia; ADC, adenocarcinoma; AIS, adenocarcinoma *in situ*; MIA, minimally invasive adenocarcinoma; LN, lymph node; NT, non-tumorous; PY, pack-year. ^{a)}Multiple independent lesions are shown in the separate rows, ^{b)}Samples excluded from the analysis.