

Supplementary Table 6. Mutation frequency of 50 LUAD related genes in our cohort and the TCGA cohort

Gene	Young Never-smokers(n=36) # silent mutations	Young Never-smokers(n=36) # missense mutations	Young Never-smokers(n=36) # nonsense mutations	Young Never-smokers(n=36) # splice site mutations	Young Never-smokers(n=36) # indels
TP53	0	6	3	0	2
EGFR	0	7	0	0	3
KRAS	0	4	0	0	0
RB1	0	0	2	1	0
NF1	0	1	0	1	0
CDKN2A	0	2	0	0	0
SETD2	0	2	1	0	1
PTEN	0	0	0	1	1
U2AF1	0	1	0	0	0
MGA	0	1	0	0	0
ERBB2	0	0	0	0	1
RUFY2	0	1	0	0	0
SKIV2L2	0	1	0	0	0
TBC1D14	0	1	0	0	0
APC	0	0	0	1	0
STK11	0	0	0	0	0
PIK3CA	0	0	0	0	0
ATM	0	0	0	0	0
MLEC	0	0	0	0	0
NCKAP1L	1	0	0	0	0
CRISPLD1	0	0	0	0	0
NSUN3	0	0	0	0	0
RBM10	0	0	0	0	0
KEAP1	0	0	0	0	0
BRAF	0	0	0	0	0
SMARCA4	0	0	0	0	0
MET	0	0	0	0	0
ARID1A	0	0	0	0	0
RIT1	0	0	0	0	0
HAX1	0	0	0	0	0
CDC27	0	0	0	0	0
CLIP1	0	0	0	0	0
ATF7IP	0	0	0	0	0
C7orf45	0	0	0	0	0
KIAA0907	0	0	0	0	0
CSF3R	0	0	0	0	0
ZNF223	0	0	0	0	0

RPL5	0	0	0	0	0	0
IL32	0	0	0	0	0	0
KLF5	0	0	0	0	0	0
PAPD7	0	0	0	0	0	0
DBR1	0	0	0	0	0	0
DOT1L	0	0	0	0	0	0
SAPS1	0	0	0	0	0	0
MAP1B	0	0	0	0	0	0
SNX9	0	0	0	0	0	0
CD40LG	0	0	0	0	0	0
SFRS18	0	0	0	0	0	0
UBAP2	0	0	0	0	0	0
COL9A2	0	0	0	0	0	0

Young Never-smokers(n=36) # mutated patients	Young Never-smokers(n=36) # mutated sites	Nature Samples (n=412) # silent mutations	Nature Samples (n=412) # missense mutations	Nature Samples (n=412) # nonsense mutations	Nature Samples (n=412) # splice site mutations
10	11	6	132	42	10
9	5	3	56	1	0
4	2	1	115	1	0
3	3	0	4	1	3
2	2	11	21	11	6
2	2	1	6	4	2
2	4	2	13	10	3
2	2	1	2	3	1
1	1	1	13	0	0
1	1	4	11	11	1
1	1	2	2	1	1
1	1	0	7	1	1
1	1	1	13	1	1
1	1	0	2	3	0
1	1	1	11	1	3
0	0	1	18	19	9
0	0	3	23	0	0
0	0	4	26	13	3
0	0	0	2	0	0
0	0	3	20	2	0
0	0	2	14	2	1
0	0	0	3	0	3
0	0	1	8	8	5
0	0	0	49	3	2
0	0	0	34	1	3
0	0	3	18	12	2
0	0	3	16	1	4
0	0	4	17	15	0
0	0	1	8	0	0
0	0	1	1	0	0
0	0	1	8	1	0
0	0	3	6	0	0
0	0	1	9	3	3
0	0	1	7	1	0
0	0	0	5	0	0
0	0	0	4	0	2
0	0	2	8	1	0

0	0	0	1	1	2
0	0	1	2	0	0
0	0	1	10	0	0
0	0	2	7	0	0
0	0	0	1	0	0
0	0	1	4	5	1
0	0	0	6	3	2
0	0	6	9	0	0
0	0	0	7	3	0
0	0	1	8	1	1
0	0	0	5	2	0
0	0	1	8	0	0
0	0	0	4	1	1

Nature Samples (n=412) # indels	Nature Samples (n=412) # mutated patients	Nature Samples (n=412) # mutated sites	Young Never- smokers percentage	Nature Percentage	P Value
26	196	139	27.78%	47.57%	0.024
24	64	40	25.00%	15.53%	0.157
0	115	9	11.11%	27.91%	0.030
8	16	16	8.33%	3.88%	0.189
14	45	52	5.56%	10.92%	0.407
6	18	16	5.56%	4.37%	0.670
11	29	37	5.56%	7.04%	1.000
1	7	7	5.56%	1.70%	0.158
0	13	2	2.78%	3.16%	1.000
6	25	29	2.78%	6.07%	0.711
6	10	7	2.78%	2.43%	0.606
1	10	9	2.78%	2.43%	0.606
1	16	15	2.78%	3.88%	1.000
1	6	5	2.78%	1.46%	0.446
4	19	19	2.78%	4.61%	1.000
20	64	53	0.00%	15.53%	0.005
0	23	13	0.00%	5.58%	0.241
5	41	45	0.00%	9.95%	0.063
3	5	3	0.00%	1.21%	1.000
1	21	23	0.00%	5.10%	0.398
1	18	17	0.00%	4.37%	0.383
0	6	5	0.00%	1.46%	1.000
9	30	29	0.00%	7.28%	0.156
7	61	58	0.00%	14.81%	0.009
0	36	22	0.00%	8.74%	0.100
3	33	34	0.00%	8.01%	0.096
3	24	22	0.00%	5.83%	0.243
3	31	34	0.00%	7.52%	0.159
2	10	8	0.00%	2.43%	1.000
5	6	3	0.00%	1.46%	1.000
4	13	10	0.00%	3.16%	0.612
1	7	3	0.00%	1.70%	1.000
4	18	19	0.00%	4.37%	0.383
2	10	10	0.00%	2.43%	1.000
4	9	6	0.00%	2.18%	1.000
2	8	7	0.00%	1.94%	1.000
0	9	6	0.00%	2.18%	1.000

4	8	8	0.00%	1.94%	1.000
4	6	3	0.00%	1.46%	1.000
0	10	7	0.00%	2.43%	1.000
3	10	8	0.00%	2.43%	1.000
4	5	3	0.00%	1.21%	1.000
3	12	13	0.00%	2.91%	0.611
1	12	12	0.00%	2.91%	0.611
3	12	11	0.00%	2.91%	0.611
0	10	10	0.00%	2.43%	1.000
0	10	10	0.00%	2.43%	1.000
2	9	7	0.00%	2.18%	1.000
2	9	8	0.00%	2.18%	1.000
1	7	7	0.00%	1.70%	1.000