

Supplementary Table 1. Clinical-pathological parameters of 13 ESCC patients

Case	Sex	Age	pTNM staging	Differentiation (Grade)	Smoking status	Drinking status
ESCC01	Female	66	pT3N0M0	Low (G3)	Never	Never
ESCC02	Female	76	pT3N1M0	Middle/Low (G2/G3)	Never	Never
ESCC03	Female	72	pT2N1M0	Middle (G2)	Never	Never
ESCC04	Male	66	pT3N0M0	High (G1)	Heavy (≥ 40 pack years)	Occasional
ESCC05	Male	30	pT2N1M0	Middle/Low (G2/G3)	Never	Never
ESCC06	Female	60	pT1bN1M0	Middle (G2)	Never	Never
ESCC07	Male	52	pT3N2M0	Middle (G2)	NA	NA
ESCC08	Male	69	pT3N1M0	Low (G3)	Heavy (≥ 40 pack years)	Everyday (500 ml/day, about 40 years)
ESCC09	Male	70	pT3N0M0	Middle (G2)	Moderate (20-40 pack years)	Regular (250 ml/time, about 40 years)
ESCC10	Male	51	pT2N1M0	Middle (G2)	Moderate (20-40 pack years)	Regular (100 ml/time, about 20 years)
ESCC11	Male	71	pT3N1M0	Middle (G2)	Heavy (≥ 40 pack years)	Everyday (250 ml/day, about 40 years)
ESCC12	Male	42	pT2N0M0	Low (G3)	Heavy (≥ 40 pack years)	Regular (500 ml/time, about 5 years)
ESCC13	Female	71	pT3N2M0	Low (G3)	Never	Never

Supplementary Table 5. Within-patient versus within-region mutational rate

Case	Number of mutations in patient (n = 13)	Number of mutations in regions (n = 51)			
		T1	T2	T3	T4
ESCC01	241	189	192	206	206
ESCC02	87	84	82	86	83
ESCC03	279	155	224	217	213
ESCC04	109	88	87	NA	85
ESCC05	84	58	58	57	60
ESCC06	208	195	194	192	190
ESCC07	170	150	155	120	134
ESCC08	147	123	82	119	121
ESCC09	196	153	154	145	156
ESCC10	117	106	103	100	102
ESCC11	148	127	111	113	123
ESCC12	98	70	84	84	84
ESCC13	294	280	289	281	234
Total number of mutations	2,178	7,104			
Mutational rate	168 (2,178/13)	139 (7,104/51)			

Supplementary Table 7. Immune cell fractions estimated from methylation profiles

Case	Region	Immune cell fractions
ESCC01	T1	1.1%
	T2	5.4%
	T3	14.1%
	T4	7.8%
ESCC03	T1	24.0%
	T2	1.4%
	T3	25.4%
	T4	29.8%
ESCC05	T1	31.4%
	T2	37.4%
	T3	23.0%
	T4	38.0%