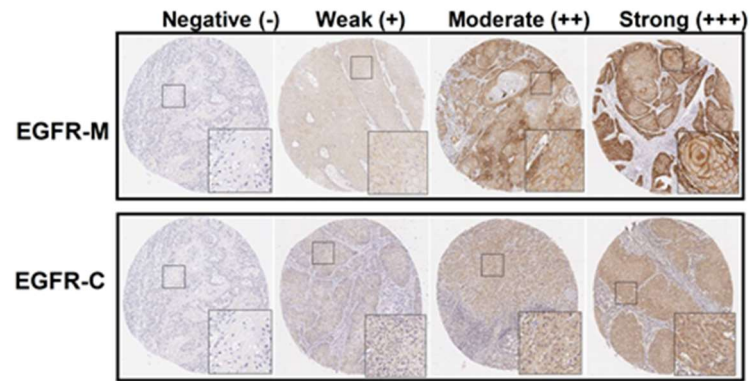


Supplementary materials

A



B

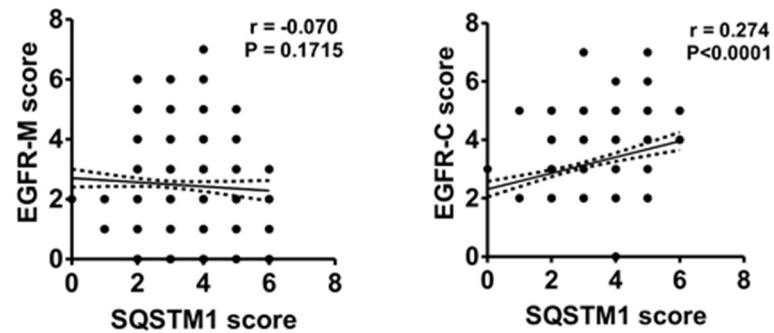


Figure S1. Expressions of EGFR-M and EGFR-C and their correlation with SQSTM1 in tumor tissues of OSCC patients. **(A)** Representative IHC images showing intensity scores of EGFR-M and EGFR-C staining as negative (-), weak (+), moderate (++), and strong (+++). **(B)** The correlation of EGFR-M and EGFR-C with SQSTM1 by the Pearson correlation analysis.

Table S1. The comparison of EGFR-M and EGFR-C expressions between corresponding tumor adjacent normal and normal tissues in OSCC patients.

Variables	No.	Tumor adjacent normal		Tumor		Z	p-value*
		Mean±SD	Median	Mean±SD	Median		
OSCC							
EGFR-M	348	1.48± 1.22	2.00	2.62± 1.16	3.00	10.542	<0.001
EGFR-C	348	2.51± 0.86	2.00	3.08± 1.10	3.00	8.296	<0.001
BMSCC							
EGFR-M	144	1.55± 1.27	2.00	2.54± 1.06	2.00	6.547	<0.001
EGFR-C	144	2.54± 0.95	2.00	3.06± 1.07	3.00	4.994	<0.001
TSCC							
EGFR-M	204	1.44± 1.17	2.00	2.68± 1.22	3.00	8.235	<0.001
EGFR-C	204	2.49± 0.80	2.00	3.09± 1.12	3.00	6.618	<0.001
Abbreviations: OSCC, oral squamous cell carcinoma; BMSCC, buccal mucosa squamous cell carcinoma; TSCC, tongue squamous cell carcinoma; SD, standard deviation.; M, membrane; C, cytoplasmic.							
*p-valueswere estimated by Wilcoxon signed-rank test.							

Table S2. The association of EGFR-M expression with clinicopathologic outcomes in OSCC patients.

Variable	BMSCC (n=181)				TSCC (n=244)				OSCC (n=425)			
	%	Mean±SD	Median	p-value	%	Mean±SD	Median	p-value	%	Mean±SD	Median	p-value
Sex												
Female	2.2	1.50 ± 0.58	1.50	0.079*	11.9	2.34 ± 1.29	3.00	0.278*	7.8	2.24 ± 1.25	2.00	0.162*
Male	97.8	2.45 ± 1.07	2.00		88.1	2.61 ± 1.22	2.00		92.2	2.54 ± 1.16	2.00	
Age, y												
≤ 50	44.2	2.50 ± 1.09	2.00	0.442*	51.6	2.52 ± 1.20	2.00	0.479*	48.5	2.51 ± 1.15	2.00	0.990*
> 50	55.8	2.38 ± 1.06	2.00		48.4	2.64 ± 1.27	3.00		51.5	2.52 ± 1.18	2.00	
Cell differentiation												
Well	26.0	2.60 ± 1.06	2.00	0.176†	10.7	2.85 ± 1.08	3.00	0.164†	17.2	2.68 ± 1.07	3.00	0.052†
Moderate	69.1	2.41 ± 1.05	2.00		82.4	2.58 ± 1.23	3.00		76.7	2.52 ± 1.16	2.00	
Poor	5.0	1.89 ± 1.36	2.00		7.0	2.12 ± 1.41	2.00		6.1	2.04 ± 1.37	2.00	
AJCC pathological stage												
I, II	61.3	2.51 ± 0.96	2.00	0.192*	68.9	2.65 ± 1.27	3.00	0.181*	65.6	2.60 ± 1.16	3.00	0.051*
III, IV	38.7	2.30 ± 1.22	2.00		31.1	2.42 ± 1.12	2.00		34.4	2.36 ± 1.17	2.00	
T classification												
T1, T2	75.7	2.47 ± 1.09	2.00	0.336*	79.5	2.59 ± 1.30	3.00	0.911‡	77.9	2.54 ± 1.21	2.00	0.398*
T3, T4	24.3	2.30 ± 1.02	2.00		20.5	2.54 ± 0.93	2.00		22.1	2.43 ± 0.98	2.00	
N classification												
N0	75.1	2.53 ± 0.97	2.00	0.031*	79.9	2.63 ± 1.24	3.00	0.227*	77.9	2.54 ± 1.21	2.00	0.019*
N1, N2	24.9	2.13 ± 1.31	2.00		20.1	2.39 ± 1.19	2.00		22.1	2.43 ± 0.98	2.00	
Abbreviations: OSCC, oral squamous cell carcinoma; BMSCC, buccal mucosa squamous cell carcinoma; TSCC, tongue squamous cell carcinoma; AJCC, American Joint Committee on Cancer.												
*p values were estimated by student's t-test.												
†p values were estimated by one-way ANOVA test.												
‡p values was estimated by Mann-Whitney U test.												

Table S3. The association of EGFR-C expression with clinicopathologic outcomes in OSCC patients.

Variable	BMSCC (n=181)				TSCC (n=244)				OSCC (n=425)			
	%	Mean±SD	Median	p-value	%	Mean±SD	Median	p-value	%	Mean±SD	Median	p-value
Sex												
Female	2.2	2.50 ± 0.58	2.50	0.308*	11.9	3.03 ± 0.98	3.00	0.693*	7.8	2.97 ± 0.95	3.00	0.566*
Male	97.8	3.03 ± 1.04	3.00		88.1	3.12 ± 1.12	3.00		92.2	3.08 ± 1.08	3.00	
Age, y												
≤ 50	44.2	3.11 ± 1.04	3.00	0.296*	51.6	3.15 ± 1.09	3.00	0.558*	48.5	3.14 ± 1.07	3.00	0.241*
> 50	55.8	2.95 ± 1.02	3.00		48.4	3.07 ± 1.12	3.00		51.5	3.01 ± 1.08	3.00	
Cell differentiation												
Well	26.0	2.94 ± 0.87	3.00	0.745‡	10.7	3.00 ± 1.17	2.00	0.209‡	17.2	2.96 ± 0.98	3.00	0.162‡
Moderate	69.1	3.02 ± 1.04	3.00		82.4	3.08 ± 1.06	3.00		76.7	3.06 ± 1.05	3.00	
Poor	5.0	3.44 ± 1.59	3.00		7.0	3.65 ± 1.41	4.00		6.1	3.58 ± 1.45	4.00	
AJCC pathological stage												
I, II	61.3	2.94 ± 0.93	3.00	0.352†	68.9	2.93 ± 1.05	3.00	<0.001*	65.6	2.93 ± 1.00	3.00	<0.001†
III, IV	38.7	3.16 ± 1.18	3.00		31.1	3.51 ± 1.11	4.00		34.4	3.34 ± 1.15	3.00	
T classification												
T1, T2	75.7	2.99 ± 1.02	3.00	0.400*	79.5	3.01 ± 1.10	3.00	0.003*	77.9	3.00 ± 1.07	3.00	0.006*
T3, T4	24.3	3.14 ± 1.07	3.00		20.5	3.52 ± 1.01	4.00		22.1	3.34 ± 1.05	3.00	
N classification												
N0	75.1	2.95 ± 0.93	3.00	0.312†	79.9	3.02 ± 1.06	3.00	0.013†	77.9	2.99 ± 1.01	3.00	0.012†
N1, N2	24.9	3.24 ± 1.28	3.00		20.1	3.49 ± 1.21	3.00		22.1	3.37 ± 1.24	3.00	
Abbreviations: OSCC, oral squamous cell carcinoma; BMSCC, buccal mucosa squamous cell carcinoma; TSCC, tongue squamous cell carcinoma; AJCC, American Joint Committee on Cancer.												
*p values were estimated by student's t-test.												
† p values was estimated by Mann-Whitney U test.												
‡ p values were estimated by Kruskal-Wallis one-way ANOVA test.												

Table S4. The co-expression of EGFR-M and SQSTM1 in disease-specific survival of OSCC patients.

Variable		No. (%)	CHR (95% CI)	<i>p</i> -value	AHR (95% CI)	<i>p</i> -value *
OSCC						
EGFR-M	Low (0-3)	363 (84.6)	1.00		1.00	
	High (4-7)	66 (15.4)	0.94 (0.61-1.43)	0.763	1.12 (0.73-1.72)	0.591
SQSTM1	Low (0-2)	239 (55.7)	1.00		1.00	
	High (3-7)	190 (44.3)	1.43 (1.07-1.93)	0.017	1.51 (1.12-2.04)	0.006
EGFR-M (L) SQSTM1 (L)		200 (46.6)	1		1	
either		202 (47.1)	1.25 (0.92-1.68)	0.143	1.30 (0.96-1.77)	0.093
EGFR-M (H) SQSTM1 (H)		27 (6.3)	1.25 (0.70-2.24)	0.460	1.43 (0.78-2.62)	0.255
BMSCC						
EGFR-M	Low (0-3)	157 (86.3)	1.00		1.00	
	High (4-7)	25 (13.7)	0.85 (0.42-1.70)	0.642	0.95 (0.47-1.93)	0.894
SQSTM1	Low (0-3)	96 (52.7)	1.00		1.00	
	High (4-7)	86 (47.3)	1.72 (1.09-2.71)	0.021	1.85 (1.16-2.94)	0.010
EGFR-M (L) SQSTM1 (L)		78 (42.9)	1		1	
either		97 (53.3)	1.81 (1.14-2.90)	0.013	1.80 (1.11-2.90)	0.017
EGFR-M (H) SQSTM1 (H)		7 (3.8)	0.63 (0.15-2.55)	0.514	0.88 (0.21-3.70)	0.858
TSCC						
EGFR-M	Low (0-2)	125 (50.6)	1.00		1.00	
	High (3-7)	122 (49.4)	0.88 (0.59-1.30)	0.517	1.11 (0.75-1.66)	0.598
SQSTM1	Low (0-2)	143 (57.9)	1.00		1.00	
	High (3-7)	104 (42.1)	1.26 (0.85-1.87)	0.252	1.34 (0.90-1.98)	0.150
EGFR-M (L) SQSTM1 (L)		73 (29.6)	1		1	
either		122 (49.4)	0.80 (0.54-1.18)	0.257	0.84 (0.54-1.32)	0.458
EGFR-M (H) SQSTM1 (H)		52 (21.1)	1.28 (0.80-2.03)	0.305	1.15 (0.67-1.97)	0.610
Abbreviations: OSCC, oral squamous cell carcinoma; BMSCC, buccal mucosa squamous cell carcinoma; TSCC, tongue squamous cell carcinoma; CHR, crude hazard ratio; CI, confidence interval; AHR, adjusted hazard ratio; H, high expression; L, low expression; M, membrane.						
* <i>p</i> -value were adjusted for cell differentiation (moderate+poor vs. well) and AJCC pathological stage (stage III+IV vs stage I+II) by multiple Cox's regression.						

Table S5. The co-expression of EGFR-C and SQSTM1 in disease-specific survival of OSCC patients.

Variable		No. (%)	CHR (95% CI)	<i>p</i> -value	AHR (95% CI)	<i>p</i> -value *
OSCC						
EGFR-C	Low (0-3)	285 (75.5)	1.00		1.00	
	High (4-7)	144 (24.5)	1.21 (0.89-1.64)	0.230	1.06 (0.78-1.44)	0.718
SQSTM1	Low (0-2)	239 (55.7)	1.00		1.00	
	High (3-7)	190 (44.3)	1.43 (1.07-1.93)	0.017	1.51 (1.12-2.04)	0.006
EGFR-C (L) SQSTM1 (L)		174 (40.6)	1		1	
either		176 (41.0)	1.21 (0.90-1.63)	0.217	1.40 (1.00-1.95)	0.051
EGFR-C (H) SQSTM1 (H)		79 (18.4)	1.32 (0.92-1.90)	0.130	1.57 (1.05-2.36)	0.030
BMSCC						
EGFR-C	Low (0-3)	132 (72.5)	1.00		1.00	
	High (4-7)	50 (27.5)	1.37 (0.84-2.21)	0.204	1.19 (0.73-1.92)	0.492
SQSTM1	Low (0-2)	96 (52.7)	1.00		1.00	
	High (3-7)	86 (47.3)	1.72 (1.09-2.71)	0.021	1.85 (1.16-2.94)	0.010
EGFR-C (L) SQSTM1 (L)		76 (41.8)	1		1	
either		76 (41.8)	1.15 (0.73-1.81)	0.552	1.46 (0.87-2.46)	0.152
EGFR-C (H) SQSTM1 (H)		30 (16.5)	1.74 (1.01-2.99)	0.045	2.12 (1.15-3.94)	0.017
TSCC						
EGFR-C	Low (0-2)	99 (40.1)	1.00		1.00	
	High (3-7)	148 (59.9)	0.97 (0.65-1.44)	0.880	0.72 (0.48-1.08)	0.111
SQSTM1	Low (0-2)	143 (57.9)	1.00		1.00	
	High (3-7)	104 (42.1)	1.26 (0.85-1.87)	0.252	1.34 (0.90-1.98)	0.150
EGFR-C (L) SQSTM1 (L)		68 (27.5)	1		1	
either		106 (42.9)	1.07 (0.72-1.58)	0.754	1.16 (0.72-1.87)	0.543
EGFR-C (H) SQSTM1 (H)		73 (29.6)	1.08 (0.71-1.66)	0.713	1.19 (0.70-1.99)	0.523
Abbreviations: OSCC, oral squamous cell carcinoma; BMSCC, buccal mucosa squamous cell carcinoma; TSCC, tongue squamous cell carcinoma; CHR, crude hazard ratio; CI, confidence interval; AHR, adjusted hazard ratio; H, high expression; L, low expression; C, cytoplasmic.						
* <i>p</i> -value were adjusted for cell differentiation (moderate+poor vs. well) and AJCC pathological stage (stage III+IV vs stage I+II) by multiple Cox's regression.						

Table S6. The co-expression of EGFR-M and SQSTM1 in disease-free survival of OSCC patients.

Variable		No. (%)	CHR (95% CI)	<i>p</i> -value	AHR (95% CI)	<i>p</i> -value *
OSCC						
EGFR-M	Low (0-3)	363 (84.6)	1.00		1.00	
	High (4-7)	66 (15.4)	0.94 (0.63-1.42)	0.776	1.05 (0.69-1.58)	0.825
SQSTM1	Low (0-2)	239 (55.7)	1.00		1.00	
	High (3-7)	190 (44.3)	1.31 (0.98-1.76)	0.070	1.27 (0.95-1.71)	0.109
EGFR-M (L) SQSTM1 (L)		200 (46.6)	1		1	
either		202 (47.1)	1.28 (0.95-1.72)	0.100	1.30 (0.96-1.76)	0.093
EGFR-M (H) SQSTM1 (H)		27 (6.3)	0.98 (0.53-1.81)	0.956	1.12 (0.60-2.12)	0.717
BMSCC						
EGFR-M	Low (0-3)	157 (86.3)	1.00		1.00	
	High (4-7)	25 (13.7)	1.05 (0.57-1.94)	0.880	1.19 (0.64-2.22)	0.585
SQSTM1	Low (0-2)	96 (52.7)	1.00		1.00	
	High (4-7)	86 (47.3)	1.21 (0.78-1.88)	0.392	1.16 (0.74-1.81)	0.519
EGFR-M (L) SQSTM1 (L)		114 (62.6)	1		1	
either		62 (34.1)	1.49 (0.95-2.34)	0.079	1.44 (0.91-2.28)	0.117
EGFR-M (H) SQSTM1 (H)		6 (3.3)	0.51 (0.13-2.09)	0.353	0.63 (0.15-2.65)	0.531
TSCC						
EGFR-M	Low (0-2)	125 (50.6)	1.00		1.00	
	High (3-7)	122 (49.4)	0.87 (0.58-1.29)	0.479	0.92 (0.62-1.37)	0.680
SQSTM1	Low (0-2)	143 (57.9)	1.00		1.00	
	High (3-7)	104 (42.1)	1.38 (0.93-2.04)	0.112	1.35 (0.91-2.00)	0.138
EGFR-M (L) SQSTM1 (L)		73 (29.6)	1		1	
either		122 (49.4)	0.62 (0.42-0.93)	0.021	0.69 (0.43-1.09)	0.112
EGFR (H) SQSTM1 (H)		52 (21.1)	1.57 (1.01-2.45)	0.046	1.25 (0.75-2.09)	0.389
Abbreviations: OSCC, oral squamous cell carcinoma; BMSCC, buccal mucosa squamous cell carcinoma; TSCC, tongue squamous cell carcinoma; CHR, crude hazard ratio; CI, confidence interval; AHR, adjusted hazard ratio; H, high expression; L, low expression; M, membrane.						
* <i>p</i> -value were adjusted for cell differentiation(moderate+poor vs. well) and AJCC pathological stage (stage III+IV vs stage I+II) by multiple Cox's regression.						

Table S7. The co-expression of EGFR-C and SQSTM1 in disease-free survival of OSCC patients.

Variable		No. (%)	CHR (95% CI)	<i>p</i> -value	AHR (95% CI)	<i>p</i> -value *
OSCC						
EGFR-C	Low (0-3)	285 (75.5)	1.00		1.00	
	High (4-7)	144 (24.5)	0.90 (0.65-1.23)	0.509	0.87 (0.63-1.20)	0.383
SQSTM1	Low (0-2)	239 (55.7)	1.00		1.00	
	High (3-7)	190 (44.3)	1.31 (0.98-1.76)	0.070	1.27 (0.95-1.71)	0.109
EGFR-C (L) SQSTM1 (L)		174 (40.6)	1		1	
either		176 (41.0)	1.16 (0.86-1.56)	0.330	1.20 (0.87-1.66)	0.266
EGFR-C (H) SQSTM1 (H)		79 (18.4)	1.03 (0.70-1.51)	0.887	1.13 (0.74-1.72)	0.571
BMSCC						
EGFR-C	Low (0-3)	132 (72.5)	1.00		1.00	
	High (4-7)	50 (27.5)	0.68 (0.40-1.17)	0.163	0.65 (0.38-1.12)	0.122
SQSTM1	Low (0-2)	96 (52.7)	1.00		1.00	
	High (3-7)	86 (47.3)	1.21 (0.78-1.88)	0.392	1.16 (0.74-1.81)	0.519
EGFR-C (L) SQSTM1 (L)		76 (41.8)	1		1	
either		76 (41.8)	0.95 (0.61-1.47)	0.802	0.93 (0.58-1.49)	0.754
EGFR-C (H) SQSTM1 (H)		30 (16.5)	0.97 (0.52-1.78)	0.909	0.93 (0.48-1.79)	0.826
TSCC						
EGFR-C	Low (0-2)	99 (40.1)	1.00		1.00	
	High (3-7)	148 (59.9)	0.98 (0.66-1.46)	0.919	0.91 (0.60-1.37)	0.638
SQSTM1	Low (0-2)	143 (57.9)	1.00		1.00	
	High (3-7)	104 (42.1)	1.38 (0.93-2.04)	0.112	1.35 (0.91-2.00)	0.138
EGFR-C (L) SQSTM1 (L)		68 (27.5)	1		1	
either		106 (42.9)	1.03 (0.69-1.53)	0.900	1.17 (0.72-1.92)	0.523
EGFR-C (H) SQSTM1 (H)		73 (29.6)	1.18 (0.77-1.80)	0.458	1.30 (0.77-2.20)	0.334

Abbreviations: OSCC, oral squamous cell carcinoma; BMSCC, buccal mucosa squamous cell carcinoma; TSCC, tongue squamous cell carcinoma; CHR, crude hazard ratio; CI, confidence interval; AHR, adjusted hazard ratio; H, high expression; L, low expression; C, cytoplasmic.

**p*-value were adjusted for cell differentiation(moderate+poor vs. well) and AJCC pathological stage (stage III+IV vs stage I+II) by multiple Cox's regression.