

Table S1 Clinical and pathological parameters of HNSCC (n=528)

Clinical characteristics		n	Percent
Age	Mean (SD)	60.91 (11.93)	
	Median [IQR]	61.00 [53.00, 69.00]	
Gender	Female	142	26.9%
	Male	386	73.1%
LVI	No	232	43.9%
	Yes	124	23.5%
PNI	NA	172	32.6%
	No	198	37.5%
	Yes	172	32.6%
TNM stage	NA	158	29.9%
	I	22	4.2%
	II	101	19.1%
	III	114	21.6%
	IV	291	55.1%
OS	NA	0	0.0%
	Alive	358	67.8%
	Dead	170	32.2%
	Missing	0	0.0%

LVI, lymphovascular invasion; NA, not available; OS, overall survival; PNI, perineural invasion.

Table S2 The EETs-related genes

Gene	Name
<i>AGER</i>	Advanced Glycosylation End-Product Specific Receptor
<i>ACTB</i>	Actin Beta
<i>ACTN1</i>	Actinin Alpha 1
<i>ACTN4</i>	Actinin Alpha 4
<i>AKTs</i>	AKT Serine/Threonine Kinases
<i>ALDOA</i>	Aldolase A
<i>ANXA1</i>	Annexin A1
<i>ANXA5</i>	Annexin A5
<i>BCL6</i>	B-cell lymphoma 6
<i>C/EBP</i>	CCAAT/Enhancer Binding Protein
<i>C5</i>	Complement Component 5
<i>C5AR1</i>	Complement C5a Receptor 1
<i>C5AR2</i>	Complement C5a Receptor 2
<i>CAT</i>	Catalase
<i>CCDC25</i>	Coiled-Coil Domain Containing 25
<i>CCL11</i>	C-C Motif Chemokine Ligand 11
<i>CCL13</i>	C-C Motif Chemokine Ligand 13
<i>CCL22</i>	C-C Motif Chemokine Ligand 22
<i>CCL24</i>	C-C Motif Chemokine Ligand 24
<i>CCL26</i>	C-C Motif Chemokine Ligand 26
<i>CCL3</i>	C-C Motif Chemokine Ligand 3
<i>CCL4</i>	C-C Motif Chemokine Ligand 4
<i>CCL5</i>	C-C Motif Chemokine Ligand 5
<i>CCR1</i>	C-C Motif Chemokine Receptor 1
<i>CCR3</i>	C-C Motif Chemokine Receptor 3
<i>CD244</i>	Cluster of Differentiation 244
<i>CD274</i>	Cluster of Differentiation 274
<i>CD300A</i>	Cluster of Differentiation 300A
<i>CD40</i>	Cluster of Differentiation 40
<i>CD48</i>	Cluster of Differentiation 48
<i>CD58</i>	Cluster of Differentiation 58
<i>CD80</i>	Cluster of Differentiation 80
<i>CD84</i>	Cluster of Differentiation 84
<i>CD86</i>	Cluster of Differentiation 86
<i>CLC</i>	Charcot-Leyden crystal
<i>CLEC7A</i>	C-Type Lectin Receptor 7A
<i>CRLF2</i>	Cytokine Receptor-Like Factor 2
<i>CS</i>	Citrate Synthase
<i>CSF2</i>	Colony Stimulating Factor 2
<i>CXCL10</i>	C-X-C Motif Chemokine Ligand 10
<i>CXCL16</i>	C-X-C Motif Chemokine Ligand 16
<i>CXCL9</i>	C-X-C Motif Chemokine Ligand 9
<i>CXCR5</i>	C-X-C Motif Chemokine Receptor 5
<i>CYSLTR1</i>	Cysteinyl Leukotriene Receptor 1
<i>DEFA5</i>	Defensin Alpha Family
<i>ECP</i>	Eosinophil Cationic Protein
<i>EGF</i>	Epidermal Growth Factor
<i>EPX</i>	Eosinophil Peroxidase
<i>ERBB2</i>	Erb-B2 Receptor Tyrosine Kinase 2
<i>FGFs</i>	Fibroblast Growth Factors
<i>FLNA</i>	Filamin A
<i>FPR1</i>	Formyl Peptide Receptor 1
<i>FPR2</i>	Formyl Peptide Receptor 2
<i>GAPDH</i>	Glyceraldehyde-3-Phosphate Dehydrogenase
<i>GATA1</i>	GATA Binding Protein 1
<i>GATA2</i>	GATA Binding Protein 2
<i>GZMA</i>	Granzyme A
<i>GZMB</i>	Granzyme B
<i>H2AC11</i>	H2A Clustered Histone 11
<i>H2AC21</i>	H2A Clustered Histone 21
<i>H2AC6</i>	H2A Clustered Histone 6
<i>H3-7</i>	Histone Cluster 1 H3 Family Member G
<i>Histones</i>	Histone Proteins
<i>HMGB1</i>	High Mobility Group Box 1
<i>HSPA5</i>	Heat Shock Protein Family A Member 5
<i>ICAM1</i>	Intercellular Adhesion Molecule 1
<i>ICAM3</i>	Intercellular Adhesion Molecule 3
<i>ID2</i>	DNA Binding Inhibitor 2
<i>IDO1</i>	Indoleamine 2
<i>IDO2</i>	Indoleamine 2
<i>IFNG</i>	Interferon Gamma
<i>IFNGR1</i>	Interferon Gamma Receptor 1
<i>IFNGR2</i>	Interferon Gamma Receptor 2
<i>IL10</i>	Interleukin 10
<i>IL12A</i>	Interleukin 12A
<i>IL12B</i>	Interleukin 12B
<i>IL13</i>	Interleukin 13
<i>IL18</i>	Interleukin 18
<i>IL1RAP</i>	Interleukin 1 Receptor Accessory Protein
<i>IL2</i>	Interleukin 2
<i>IL21</i>	Interleukin 21
<i>IL25</i>	Interleukin 25
<i>IL3</i>	Interleukin 3
<i>IL33</i>	Interleukin 33
<i>IL4</i>	Interleukin 4
<i>IL5</i>	Interleukin 5
<i>IL5RA</i>	Interleukin 5 Receptor Alpha
<i>IL6</i>	Interleukin 6
<i>IL7R</i>	Interleukin 7 Receptor
<i>CXCL8</i>	C-X-C Motif Chemokine Ligand 8
<i>IRF8</i>	Interferon Regulatory Factor 8
<i>ITGAL</i>	Integrin Subunit Alpha L
<i>ITGAM</i>	Integrin Subunit Alpha M
<i>ITGB2</i>	Integrin Subunit Beta 2
<i>KLRA1P</i>	Killer Cell Lectin-Like Receptor Subfamily A Member 1 Pseudogene
<i>KLRK1</i>	Killer Cell Lectin-Like Receptor Subfamily K Member 1
<i>LAMP2</i>	Lysosomal Associated Membrane Protein 2
<i>LCP1</i>	Lymphocyte Cytosolic Protein 1
<i>MBP</i>	major basic protein
<i>MHC-I</i>	Major Histocompatibility Complex Class I
<i>MHC-II</i>	Major Histocompatibility Complex Class II
<i>MMP2</i>	Matrix Metalloproteinase 2
<i>MMP9</i>	Matrix Metalloproteinase 9
<i>MNDA</i>	Myeloid Cell Nuclear Differentiation Antigen
<i>MSN</i>	Moesin
<i>MT-ATP6</i>	Mitochondrially Encoded ATP Synthase 6
<i>MT-CO1</i>	Mitochondrially Encoded Cytochrome C Oxidase I
<i>MT-ND1</i>	Mitochondrially Encoded NADH:Ubiquinone Oxidoreductase Core Subunit 1
<i>MYH9</i>	Myosin Heavy Chain 9
<i>NGF</i>	Nerve Growth Factor
<i>NOXs/DUOXs</i>	NADPH Oxidase Family / Dual Oxidase Family
<i>P2RY10</i>	Purinergic Receptor P2Y10
<i>PADI4</i>	Peptidyl Arginine Deiminase Type 4
<i>PAR2</i>	Protease-activated Receptor 2
<i>PDCCD1</i>	Programmed Cell Death 1
<i>PDGFs</i>	Platelet-Derived Growth Factors
<i>PDI3</i>	Protein Disulfide Isomerase Family A Member 3
<i>p-ERK</i>	Phospho-extracellular signal-related kinase
<i>PGD</i>	Phosphogluconate Dehydrogenase
<i>PGK1</i>	Phosphoglycerate Kinase 1
<i>PIK3CD</i>	Phosphatidylinositol-4
<i>PPIB</i>	Peptidylprolyl Isomerase B
<i>PRG2</i>	Proteoglycan 2
<i>PRG3</i>	Proteoglycan 3
<i>RNASE2</i>	Ribonuclease A Family 2
<i>RNASE3</i>	Ribonuclease A Family 3
<i>S100A6</i>	S100 Calcium Binding Protein A6
<i>S100A8</i>	S100 Calcium Binding Protein A8
<i>S100A9</i>	S100 Calcium Binding Protein A9
<i>SFTPD</i>	Surfactant Protein D
<i>SIGLEC8</i>	Sialic Acid Binding Ig-Like Lectin 8
<i>SLAMF6</i>	Signaling Lymphocytic Activation Molecule Family Member 6
<i>SPI1</i>	Spi-1 Proto-Oncogene
<i>SPINK5</i>	Serine Peptidase Inhibitor Kazal Type 5
<i>Srcs</i>	Src Family Kinases
<i>ST2</i>	Growth stimulation expressed gene 2
<i>SYK</i>	Spleen Tyrosine Kinase
<i>TALDO1</i>	Transaldolase 1
<i>TAP2</i>	Transporter 2
<i>TAPBP</i>	TAP Binding Protein
<i>TGFB1</i>	Transforming Growth Factor Beta 1
<i>TLN1</i>	Talin 1
<i>TLR2</i>	Toll-Like Receptor 2
<i>TLR4</i>	Toll-Like Receptor 4
<i>TNF</i>	Tumor Necrosis Factor
<i>TNFRs</i>	Tumor Necrosis Factor Receptors
<i>TPI1</i>	Triosephosphate Isomerase 1
<i>TSLP</i>	Thymic Stromal Lymphopoietin
<i>VCAM1</i>	Vascular Cell Adhesion Molecule 1
<i>VEGFA</i>	Vascular Endothelial Growth Factor A
<i>VIRMA</i>	Vir like m6A methyltransferase associated
<i>XBP1</i>	X-Box Binding Protein 1
<i>YWHAE</i>	Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Epsilon
<i>ZAP70</i>	Zeta Chain of T Cell Receptor Associated Protein Kinase 70
<i>ZFPM1</i>	Zinc Finger Protein, FOG Family-Like 1

Table S3 The EETs-related genes in patients with HNSCC

Gene	Name
<i>AGER</i>	Advanced Glycosylation End-Product Specific Receptor
<i>ACTN1</i>	Actinin Alpha 1
<i>ANXA1</i>	Annexin A1
<i>ANXA5</i>	Annexin A5
<i>CCL11</i>	C-C Motif Chemokine Ligand 11
<i>CCL26</i>	C-C Motif Chemokine Ligand 26
<i>CCL3</i>	C-C Motif Chemokine Ligand 3
<i>CCL4</i>	C-C Motif Chemokine Ligand 4
<i>CCL5</i>	C-C Motif Chemokine Ligand 5
<i>CCR1</i>	C-C Motif Chemokine Receptor 1
<i>CD274</i>	Cluster of Differentiation 274
<i>CD40</i>	Cluster of Differentiation 40
<i>CD80</i>	Cluster of Differentiation 80
<i>CD84</i>	Cluster of Differentiation 84
<i>CD86</i>	Cluster of Differentiation 86
<i>CLEC7A</i>	C-Type Lectin Receptor 7A
<i>CSF2</i>	Colony Stimulating Factor 2
<i>CXCL10</i>	C-X-C Motif Chemokine Ligand 10
<i>CXCL8</i>	C-X-C Motif Chemokine Ligand 8
<i>CXCL9</i>	C-X-C Motif Chemokine Ligand 9
<i>CYSLTR1</i>	Cysteinyl Leukotriene Receptor 1
<i>EGF</i>	Epidermal Growth Factor
<i>FLNA</i>	Filamin A
<i>FPR2</i>	Formyl Peptide Receptor 2
<i>GZMA</i>	Granzyme A
<i>GZMB</i>	Granzyme B
<i>H2AC11</i>	H2A Clustered Histone 11
<i>ICAM1</i>	Intercellular Adhesion Molecule 1
<i>IDO1</i>	Indoleamine 2,3-Dioxygenase 1
<i>IFNG</i>	Interferon Gamma
<i>IL1RAP</i>	Interleukin 1 Receptor Accessory Protein
<i>IL33</i>	Interleukin 33
<i>IL7R</i>	Interleukin 7 Receptor
<i>ITGAL</i>	Integrin Subunit Alpha L
<i>ITGAM</i>	Integrin Subunit Alpha M
<i>ITGB2</i>	Integrin Subunit Beta 2
<i>LCP1</i>	Lymphocyte Cytosolic Protein 1
<i>MMP2</i>	Matrix Metalloproteinase 2
<i>MMP9</i>	Matrix Metalloproteinase 9
<i>MSN</i>	Moesin
<i>MYH9</i>	Myosin Heavy Chain 9
<i>NGF</i>	Nerve Growth Factor
<i>P2RY10</i>	Purinergic Receptor P2Y10
<i>PDIA3</i>	Protein Disulfide Isomerase Family A Member 3
<i>PIK3CD</i>	Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Delta
<i>RNASE2</i>	Ribonuclease A Family 2
<i>S100A8</i>	S100 Calcium Binding Protein A8
<i>S100A9</i>	S100 Calcium Binding Protein A9
<i>SLAMF6</i>	Signaling Lymphocytic Activation Molecule Family Member 6
<i>SPINK5</i>	Serine Peptidase Inhibitor Kazal Type 5
<i>TAP2</i>	Transporter 1, ATP Binding Cassette Subfamily B Member
<i>TAPBP</i>	TAP Binding Protein
<i>TGFB1</i>	Transforming Growth Factor Beta 1
<i>TNF</i>	Tumor Necrosis Factor
<i>VCAM1</i>	Vascular Cell Adhesion Molecule 1
<i>VEGFA</i>	Vascular Endothelial Growth Factor A
<i>ZAP70</i>	Zeta Chain of T Cell Receptor Associated Protein Kinase 70

Table S4 Univariate and multivariate Cox regression analyses

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	1.016 (1.002–1.030)	0.028	1.016 (1.002–1.030)	0.022
Gender	0.943 (0.667–1.335)	0.742		
Risk score	1.436 (1.287–1.603)	<0.001	1.439 (1.290–1.605)	<0.001
Stage	1.067 (0.896–1.270)	0.465		