

## Supplemental tables

**Supplementary Table S1** Summary of microarray expression profiles of ESCC and normal esophagus for FGmRNA profiling.

Data source	Sample size of normal esophageal squamous epithelium	Sample size of ESCC
Kimchi ET et al., Cancer Research 2005. [37]	8	0
Stairs DB et al., Plos One 2008. [38]	7	0
Wang Q et al., BMC Cancer 2013. [39]	19	9
Lee JJ et al., Carcinogenesis 2010. [40]	5	5
Yu K et al., Plos Genetics 2008. [41]	13	16

Hyland PL et al., International Journal of Epidemiology 2016. [42]	53	53
Aoyagi K et al., Plos One 2011. [43]	0	20
Chen K et al., Plos One 2013. [44]	15	15
<b>Total</b>	120	118

**Supplementary Table S3** Literature search results of top 60 genes

RA NK	GEN E	Locat ion	Location (genecards)	Location (ICAN)	IHC esophagus	IHC GE	Carcinogen esis	Ima gin g	R ef.
1	PSM D2	IC,M	N, cytosol, EC	cytosolic proteasom e complex, DNA directed RNA polymeras e III complex	None	None	Matsuyama Y,et al [45].	Non e	[4 5]
2	GRE M1	S	EC	Proteinace ous extracellul	None	None	Davis H,et al [46]; van Vlodrop	Non e	[4 6- 47]

				ar matrix			IJ,et al [47].		]
3	BMP7	IC,S	EC	Extracellular matrix, synaptic membrane	Xu G, et al [48]	Motoyama K, et al. [49]	Alarmino EL, et al [50].	None	[48-50]
4	XCL1	S	EC	Not assigned	None	None	Wang T, et al. [51]	None	[51]
5	SLC33A1	M	M;endoplasmic reticulum; golgi apparatus	Side of membrane	None	None	None	None	
6	XCL2	S	EC	Not available	None	None	Kim M, et al [52]	None	[52]
7	SERP1	IC,M	Cytoskeleton; cytosol; endoplasmic reticulum	Not assigned	None	None	Not conclusive	None	
8	GSTP1	IC	Cytosol, EC, mitochondrion	Not assigned	Yamamoto Y, et al. [54] Allameh A,et al [55].	Zhang R, et al [56].	Louie SM, et al. [53]	Fujikawa Y, et al [57].	[53-57]
9	FXR1	IC,S	N,cytosol	CUL3 ring ubiquitin ligase complex	None	Jin X, et al. [58]	Qian J, et al. [59]	None	[58-59]
10	SPRR1B/cornifin B	IC	EC,M, cytosol	Cornified envelope, keratin filament	None.	None	Michifuri Y, et al [60].	None	[60]
11	COPB2	IC	Cytosol;golgi apparatus ;ER	COPI coated vesicle	None	None	Pu X, et al [61].	None	[61]

				membrane, golgi associated vesicle membrane					
12	FZD6	M	M	Apicolateral plasma membrane	None	Kim BK, et al [62].	Yan J, et al [63].	None	[62-63]
13	NDUFB5	IC,M,S	Mitochondrion;nucleus	Oxidoreductase complex, mitochondrial membrane part, cytochrome complex	None	None	None	None	
14	HOXD10	IC	Nucleus,cytosol	Proteinaceous extracellular matrix	None	None	Wang L, et al [64].	None	[64]
15	HOXD11	IC	nucleus	Ionotropic glutamate receptor complex	None	None	Not conclusive	None	
16	PKP1	IC	Cytoskeleton; EC;N;M	Intermediate filament, desmosome, cell cell junction, anchoring junction, cornified envelope	None	None	Lee P, et al. [65]	None	[65]

17	HSP90AB1	IC	Cytosol;EC;N; mitochondrion	Ribosome	None	None	Hamamoto R,et al. [66]	Chan CT, et al. [67]	[66-67]
18	SPRR1A	IC	M, cytosol	Cornified envelope, keratin filament	None	None	Lau D, et al. [68]	None	[68]
19	PLAG1	IC	N	Pericentriolar material	None	Matsuyama A , et al. [69]	Declercq J, et al. [70]	None	[69-70]
20	PDCD10	IC	EC;M;cytosol; golgi apparatus	Chromosomal region	None	None	Lauenborg B, et al. [71]	None	[71]
21	SP140L	IC	N	Synaptic membrane	None	None	None	None	
22	POLR2H	IC	Cytosol;N	Nucleolar part, DNA-directed RNA polymerase III complex, DNA-directed RNA polymerase I complex, DNA directed RNA	None	None	None	None	

				polymerase II holoenzyme, nucleoid					
23	PPP1R13B	IC	Nucleus;M;cytosol	Centrosome	None	None	Wang Y, et al. [72]	None	[72]
24	ALG3	M	Endoplasmic reticulum	Ribosome	None	None	Not conclusive	None	
25	EXOSC4	IC	Cytosol;N;cytoskeleton	Organellar large ribosomal subunit	None	None	O'Byrne K, et al [73].	None	[73]
26	DVL3	IC	Cytosol;N	WNT signalosome, nuclear chromosome	Hasan R, et al. [74]	You XJ, et al. [75]	Zhao H, et al. [76]	None	[74-76]
27	SLC2A1/GLUT1	M, IC	M;EC;cytoskeleton	Cell cell junction, apical plasma membrane, cytoplasmic region, keratin filament	Ogane N, et al. [77]	Goos JA, et al. [78]	Wellberg EA, et al. [79]	Sohn CH, et al. [80]	[77-80]
28	SEN5	IC	nucleus	not assigned	None	None	Jin ZL, et al. [81]	None	[81]
29	ETNK2	IC	cytosol	not assigned	None	None	None	None	
30	FND C3B	IC,M	M;endoplasmic reticulum	Endoplasmic reticulum lumen	None	None	Chen CF, et al. [82]	None	[82]

31	PIK3R4	IC	Cytosol;endosome;cytoskeleton	Vesicle membrane, extrinsic component of membrane, endocytic vesicle, nuclear envelope, proteinaceous extracellular matrix	None	None	Not conclusive	None	
32	MCC C1	IC,S	Cytosol;mitochondrion	Mitochondrial matrix, vesicle membrane	None	None	None	None	
33	ABC C5/MRP5	IC,M	M	Not assigned	None	None	Mourskaia AA, et al. [83]	None	[83]
34	Septin9	IC,S	Cytoskeleton	Not assigned	None	Tóth K, et al [84]	Liu M, et al. [85]	None	[84-85]
35	ADIPOQ	S	EC;endoplasmic reticulum	Collagen trimer, proteinaceous extracellular matrix	None	None	Name N, et al. [86]	None	[86]
36	ENT PD1/CD39	M	EC;M	Side of membrane	None	Cai XY, et al. [87]	Cai XY, et al. [88]	None	[87-88]

37	CORO1C	IC	M; cytoskeleton	Plasma membrane protein complex, cell substrate junction, endoplasmic reticulum subcompartment	None	None	Luan SL, et al. [89]	None	[89]
38	DCUN1D1	IC	Nucleus, cytosol	PML body	None	None	Fu W, et al. [90]	None	[90]
39	EXT1	IC,M	Golgi apparatus;endoplasmic reticulum	Anchoring junction	None	None	de Andrea CE, et al. [91]	None	[91]
40	HIST3H2A	IC	EC;N	Not available	None	None	Aihara H,et al. [92]	Jullien D, et al. [93]	[92-93]
41	KRT6A	IC	EC; N; cytosol	Intermediate filament, keratin filament, intermediate filament cytoskeleton, cornified envelope	None	None	Hu J, et al. [94]	None	[94]
42	RNF7	IC	N; cytosol	Nuclear ubiquitin	None	None	Sun Y,et al [95]	None	[95]

				ligase complex, secretory vesicle					
43	LEPR	M	M	Nuclear chromosome	Howard JM, et al. [97]	Milosevic VS,et al. [96]	Milosevic VS,et al. [96]	None	[96-97]
44	KRT16	IC	EC;N;cytoskeleton;cytosol	Intermediate filament, intermediate filament cytoskeleton, cornified envelope	None	None	Not conclusive	None	
45	SELENOT	M	Endoplasmic reticulum	Extracellular matrix	None	None	None	None	
46	JUP	IC	M; EC; N	Desmosome, apicolateral plasma membrane, intermediate filament cytoskeleton, cell cell junction	None; Downregulated [99]	Luque-García JL,et al. [98]	None	None	[98-99]
46	KRT17	IC	EC;cytoskeleton;cytosol	Intermediate filament, keratin filament cytoskeleton	None	Kim CY, et al. [100]	Hu H. et al. [101]		[100-101]
47	CEP63	IC	Cytoskeleton; cytosol	Centrosome, PML body	None	None	Not conclusive	None	

48	IFNG R1	IC,M, S	M	Side of membrane	None	Simpson JA, et al. [102]	Zhang C, et al.[103]	Non e	[1 02 - 10 3]
49	PTK2 /FAK	IC	N;M;cytoskele ton;cytosol	Cell cortex, cytoplasmic region, cytoplasmic side of membrane	Miyazaki T, et al. [104]	Cance WG, et al. [105]	Kessler BE, et al. [106]	Lia o X,et al. [10 7]	[1 04 - 10 7]
50	PITX 2	IC	nucleus	not assigned	Zhang JX, et al. [108]	None	Huang Y, et al. [109]	Non e	[1 08 - 10 9]
51	TFG	IC	Cytosol;EC;en doplasmic reticulum	Rough endoplasmic reticulum membrane	None	None	Kim AY,et al. [110]	Non e	[1 10 ]
52	CLIP 4	IC	Cytosol	Not assigned	None	None	Not conclusive	Non e	
53	PLN	M	Mitochondrion ;endoplasmic reticulum;	Sarcoplas m, transporter complex, sarcoplasmic reticulum membrane, cation transportin g atpase	None	None	None	Non e	

				complex, atpase complex, myosin filament					
54	IGF2 BP2	IC	N; cytoskeleton; cytosol	Not assigned	Barghash A,et al. [113]	Liu W, et al. [111]	Ye S, et al. [112]	Non e	[1 11 - 11 3]
55	ELF3 /ESE 1/ER T/ES X	IC	Nucleus;cytosol	Apical plasma membrane	None	None	Yachida S, et al. [114]	Non e	[1 14 ]
56	MMP 12	S	EC	Proteinace ous extracellul ar matrix	Ding Y, et al. [115]	Zheng J, et al. [116]	Xu J, et al. [117]	Non e	[1 15 - 11 7]
57	MRC 1	M	M; endosome	Endosomal part, endocytic vesicle	None	None	Not conclusive	Non e	
58	BGN	S	EC	EC, sarcolemm a, golgi lumen, lysosomal lumen, vacuolar lumen	Zhu YH, et al. [118]	Wang B, et al. [119]	Xing X, et al. [120]	Non e	[1 18 - 12 0]
59	SSFA 2	IC	N;M;cytosol	Side of membrane	None	None	Okayama A, et al. [121]	Non e	[1 21 ]

60	TP63	IC	Nucleus;cytosol	Chromatin, nuclear chromosome, cornified envelope	Hu H,et al. [122]	Song Y, et al. [123]	De Oliveria DH, et al. [124]	Schütz M, et al. [125]	[122 - 125]
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**Supplementary Table S4.** Immunohistochemistry (IHC) protocols for four targets proteins

Target protein	Protein location	Antigen retrieval	Concentration	1 <sup>st</sup> antibody	Company	Mono/poly-clonal	Dye
GLUT-1	membrane	Tris/EDTA (pH 9.0)	1:250 for TMA slices; 1:500 for biopsies.	Ab115730, RRID: AB_10903230	Abcam, Cambridge, UK	Monoclonal	AEC and DAB
ENTPD1	Membranous+cytoplasm	Tris/EDTA (pH 9.0)	1:1000	Ab223842	Abcam, Cambridge, UK	Monoclonal	DAB
LEPR	Mainly cytoplasm, with some nucleus staining	Citrate buffer (10mM, pH 6.0)	1:100	Ab60042, RRID:AB_943984	Abcam, Cambridge, UK	Polyclonal	DAB
LEPR	cytoplasm	Citrate buffer	1:10	Ab2143,	Abcam,	Monoclonal	DAB

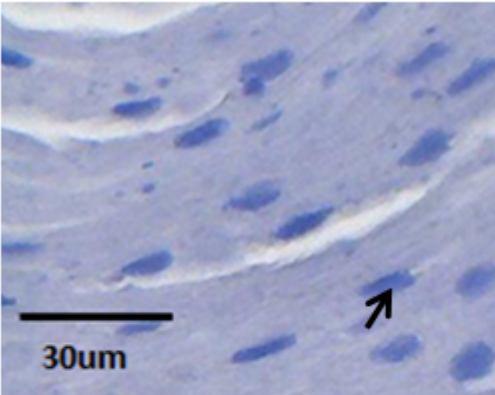
		(10mM, pH 6.0)		RRID:AB_302860	Cambridge, UK		
LEPR	cytoplasm	Tris/EDTA (pH 9.0)	1:200	Sc8391, RRID:AB_627882	Santa Cruz Biotechnology, Dallas, Texas, USA	Monoclonal	DAB
IFNGR1	cytoplasm	Tris/EDTA (pH 9.0)	1:50	Sc28363, RRID:AB_673491	Santa Cruz Biotechnology, Dallas, Texas, USA	Monoclonal	DAB
IFNGR1	cytoplasm	Citrate buffer (10mM, pH 6.0)	1:100	Ab134070	Abcam, Cambridge, UK	Monoclonal	DAB

# Supplemental figure

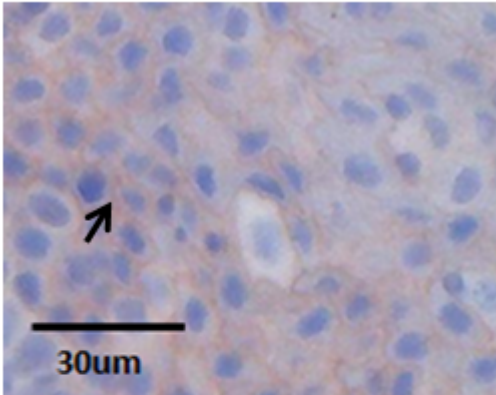
**Supplementary Fig. S1** The IHC staining intensity score of esophagus epithelial cells. No IHC positive staining is scored as 0. Score 1 means weak IHC staining. Score 2

means moderate staining intensity. Score 3 means strong staining intensity.

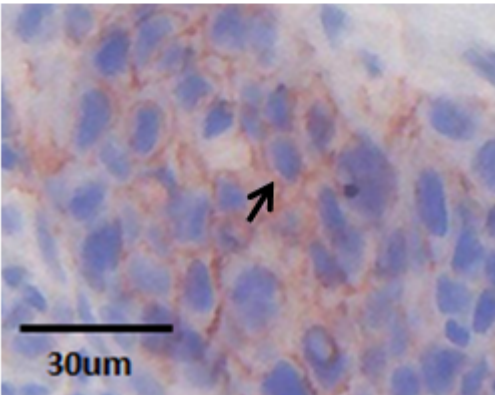
H-Score 0



H-Score 1



H-Score 2



H-Score 3

