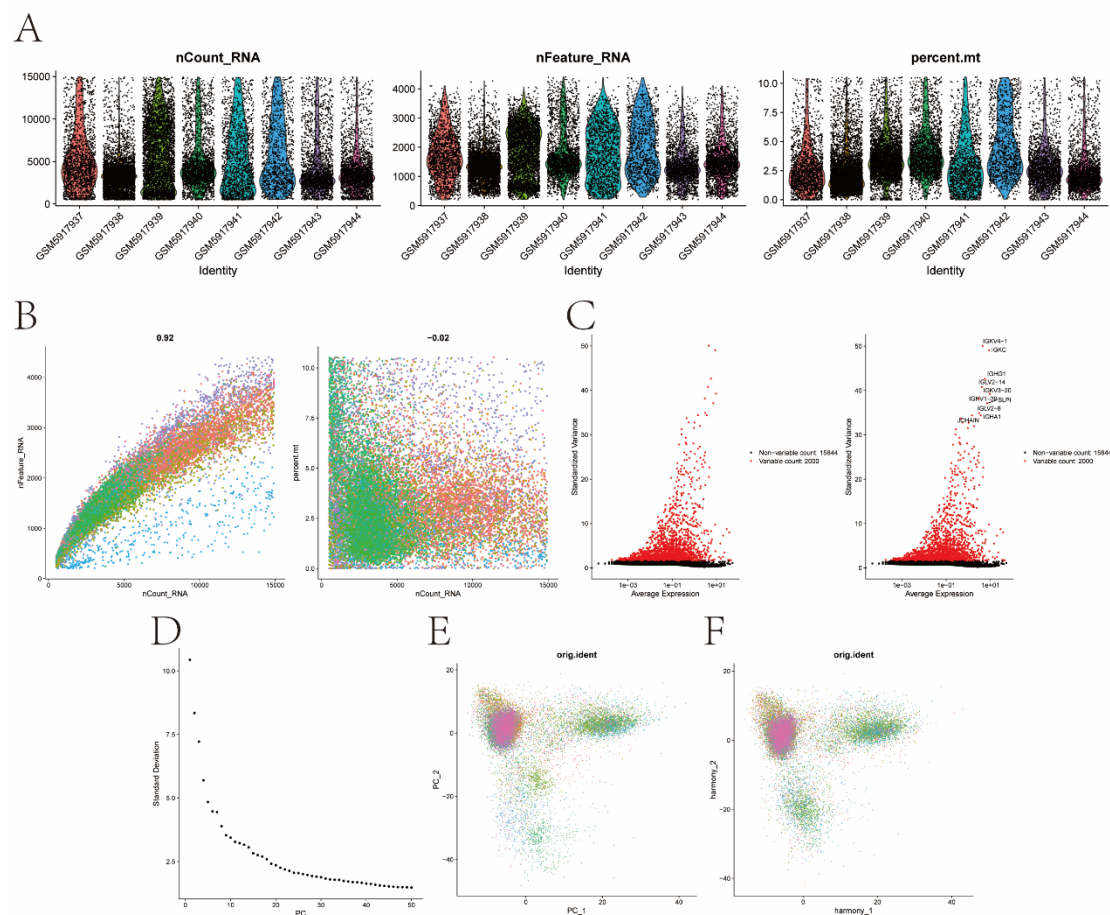
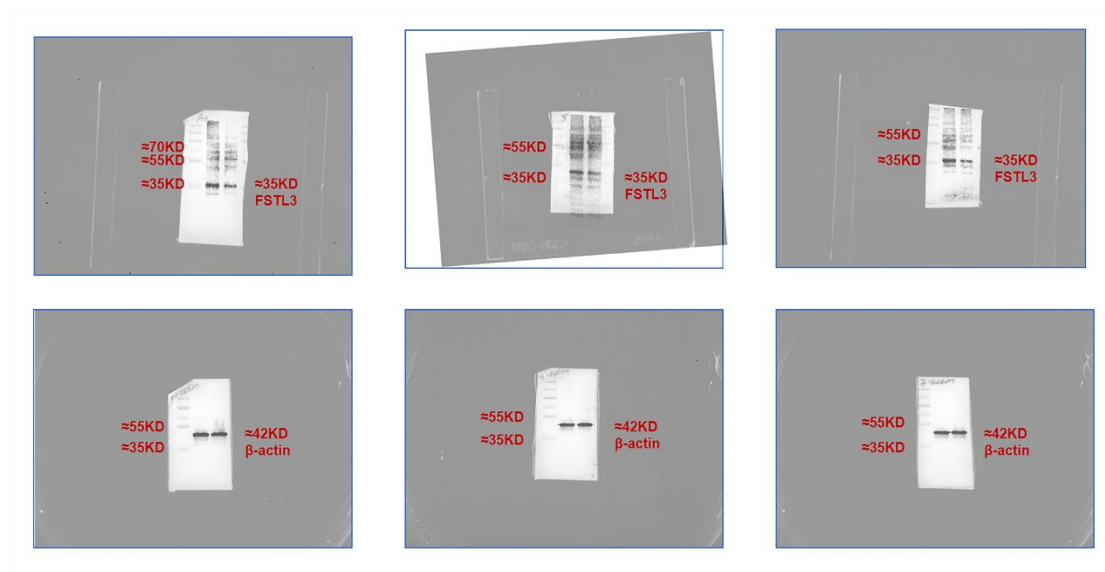


Supplementary Fig.1



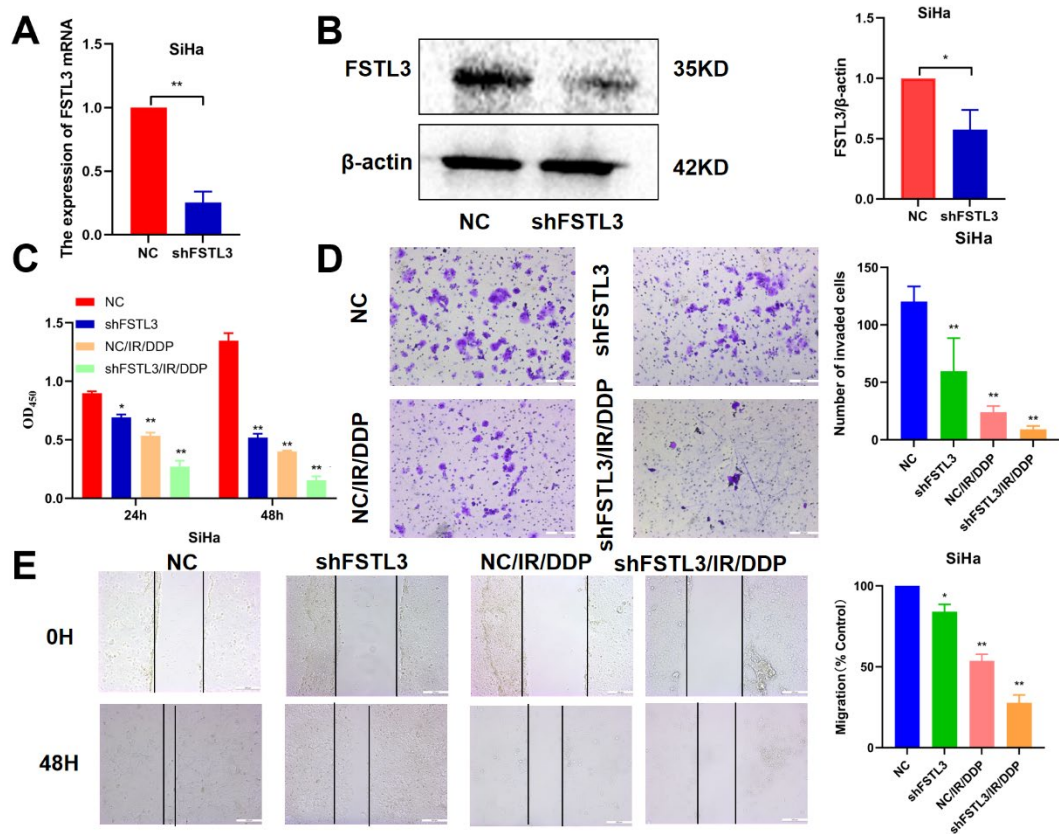
Supplementary Fig. 1. Quality control and batch correction of single-cell RNA sequencing data. (A-B) Violin plots and scatter plots showing the filtering results of single-cell RNA sequencing (scRNA-seq) data from the GEO dataset GSE197461 (8 cervical cancer tumor tissue samples from 8 patients). Cells were filtered based on quality control metrics: outliers and cells with <200 detected genes were excluded, and doublets were removed using the DoubletFinder package, resulting in 21,518 high-quality cells for downstream analysis; (C) Top 10 genes with the highest standard deviation in the filtered dataset; (D) Elbow plot indicating the optimal number of principal components (PCs = 20) for dimensionality reduction; (E-F) Principal component analysis (PCA) plots before (E) and after (F) batch correction using the Harmony algorithm; batch effects among samples were effectively mitigated post-correction.

Supplementary Fig. 2



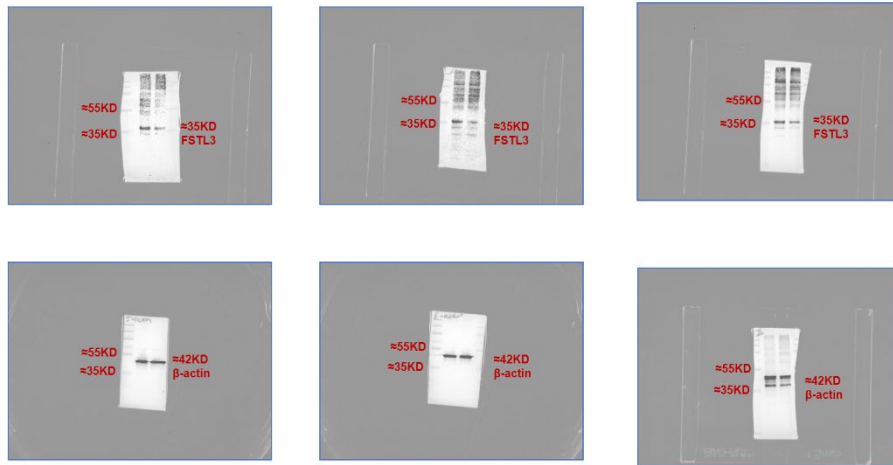
Supplementary Fig. 2. Original full membrane image of western blot for Fig. 8B. Full uncropped membranes for FSTL3 and β -actin from three independent biological replicates are shown. Parallel membranes were processed simultaneously under identical loading and transfer conditions due to the close molecular weights of FSTL3 (~35 kDa) and β -actin (~42 kDa). Densitometric quantification normalized to β -actin is provided in Supplementary Table S3.

Supplementary Fig. 3



Supplementary Fig. 3. In vitro functional exploration of *FSTL3* in SiHa cells. (A) qRT-PCR analysis of relative *FSTL3* mRNA levels in SiHa cells transfected with either negative control shRNA (NC) or *FSTL3* knockdown shRNA (*shFSTL3*) constructs. (B) Representative Western blotting images and corresponding quantification of *FSTL3* protein expression, with β -actin serving as the internal reference. (C) CCK-8 cell proliferation assay demonstrating cell viability at 24 h and 48 h across four experimental groups (NC, *shFSTL3*, NC/IR/DDP, *shFSTL3*/IR/DDP). (D) Representative Transwell invasion staining images and corresponding quantification of invasive cell numbers in each group. (E) Wound healing assay micrographs and corresponding quantification of cell migratory capacity, normalized to the NC group. * $P < 0.05$, ** $P < 0.01$; NC, negative control shRNA; IR, irradiation; DDP, cisplatin treatment.

Supplementary Fig. 4



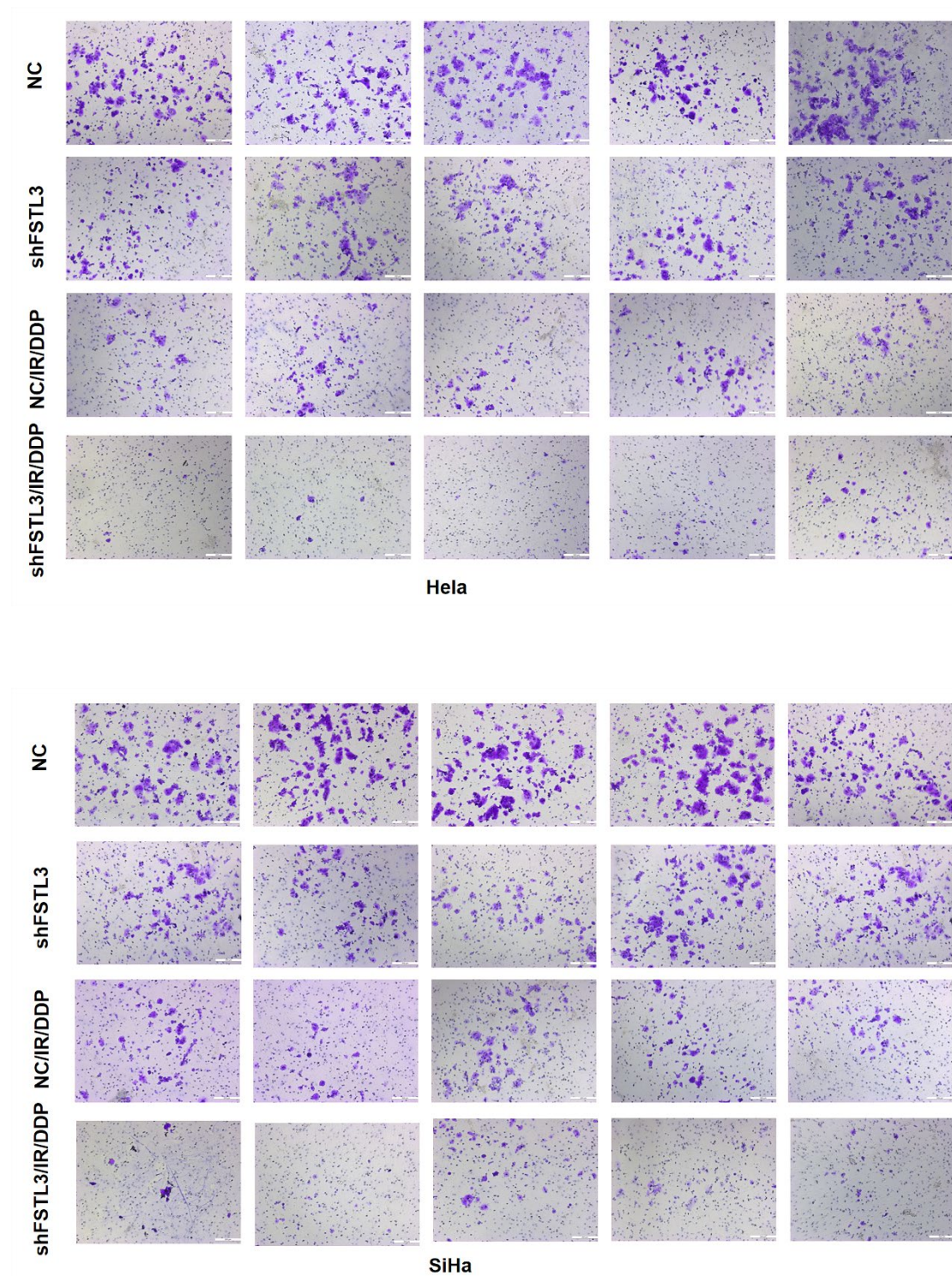
Supplementary Fig. 4. Original full membrane image of western blot for Supplementary Fig. 3B. Full uncropped membranes for FSTL3 and β -actin from three independent biological replicates are shown. Parallel membranes were processed simultaneously under identical loading and transfer conditions due to the close molecular weights of FSTL3 (~35 kDa) and β -actin (~42 kDa). Densitometric quantification normalized to β -actin is provided in Supplementary Table S3.

Supplementary Fig. 5



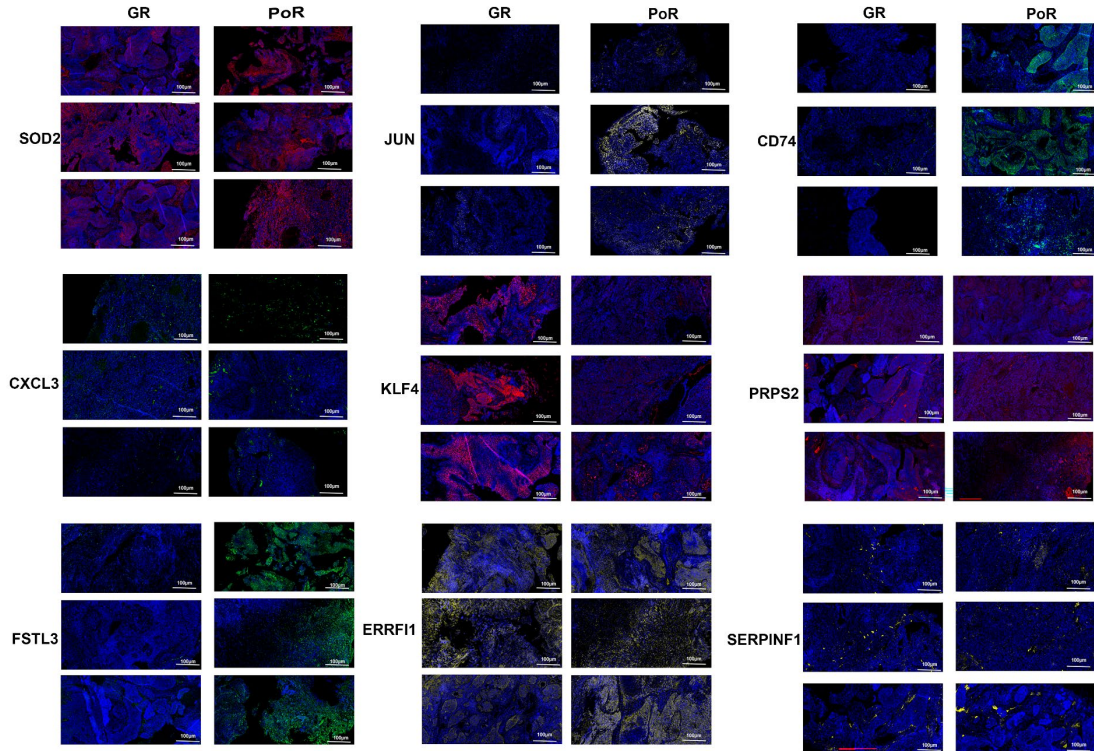
Supplementary Fig. 5. Original microscopy images of wound healing for Fig. 8E and Supplementary Fig. 3E. Representative original microscopy images from three independent biological replicates are shown for HeLa cells (upper panels) and SiHa cells (lower panels) across the four experimental groups at 0 h and 48 h post-scratching. Scale bar = 200 μm.

Supplementary Fig. 6



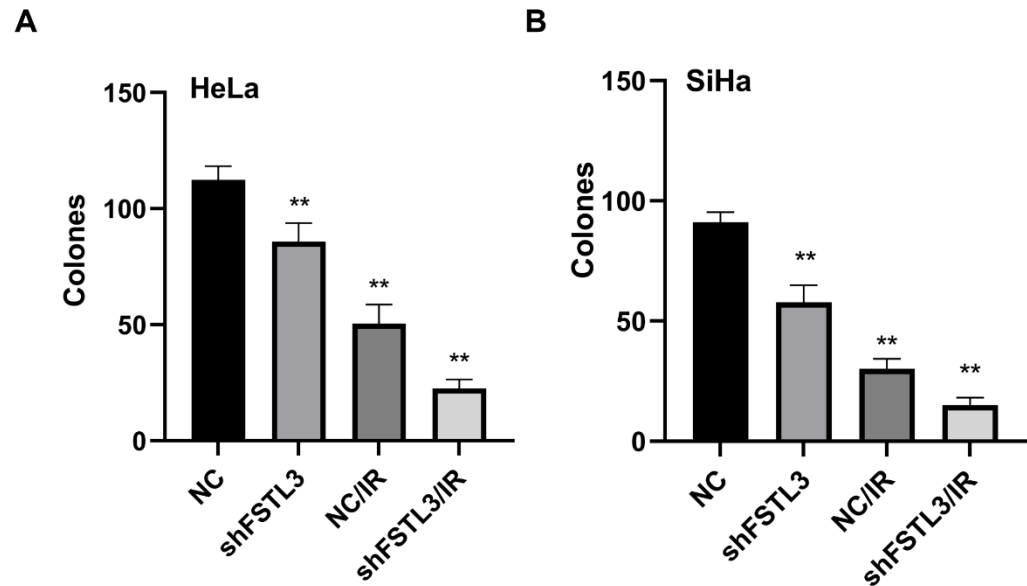
Supplementary Fig. 6. Original microscopy images of Transwell migration assays for Fig. 8D and Supplementary Fig. 3D. Representative original microscopy images from three independent biological replicates are shown for HeLa cells (upper panels) and SiHa cells (lower panels) across the four experimental groups. Scale bar = 200 μ m.

Supplementary Fig. 7



Supplementary Fig. 7. Original multiplex immunofluorescence images of the nine candidate genes in all 30 cervical cancer patients. Protein expression of KLF4, SERPINF1, CD74, PRPS2, ERFF1, FSTL3, SOD2, JUN, and CXCL3 was detected by multiplex immunofluorescence (mIHC) in tumor tissues from 30 cervical cancer patients. Representative whole-field original images from three patients in the GR group (n = 15) and three patients in the PoR group (n = 15) are shown. For each patient, one complete tissue field is presented, comprehensively displaying the spatial distribution and expression characteristics of each marker. Original images were not cropped or non-linearly processed, and retain the full tissue field of view. Images were acquired using a multispectral imaging system with identical exposure time and gain settings for each channel. All image acquisition and quantitative analyses were performed in a blinded manner. Quantitative data were derived from all 30 patients and are presented as mean $\pm$ SD. Comparisons between groups were performed using the Mann-Whitney U test. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; ns, not significant.

Supplementary Fig. 8



Supplementary Fig. 8. Effect of *FSTL3* knockdown on clonogenic survival of HeLa and SiHa cells. (A) Representative images of crystal violet-stained colonies formed by HeLa cells stably transfected with NC or *shFSTL3* vectors, cultured for 12 days following exposure to 0 Gy or 6 Gy irradiation. (B) Representative images of crystal violet-stained colonies formed by SiHa cells under the same experimental conditions. Quantification of survival fractions is shown as mean $\pm$ SD from three independent biological replicates. *P < 0.05, **P < 0.01; NC, negative control shRNA; IR, irradiation.

Supplementary Table 1. Algorithm-wise ranking of ketone-body metabolic activity across major cell types.

Algorithm	Top-ranked cell type	Second-ranked	Third-ranked
AUCell	Fibroblasts	Macrophages	CD8+ T cells
UCell	Fibroblasts	CD8+ T cells	Macrophages
singscore	Fibroblasts	Macrophages	CD4+ T cells
ssGSEA	Fibroblasts	Macrophages	B cells
AddModuleScore	Fibroblasts	CD8+ T cells	Macrophages

Supplementary Table 2. Basic characteristics of the patients

Characteristic	good response (n=15)	poor response (n=15)	<i>p</i> value
Age, median (range)	50 (23–65)	50 (24–68)	0.715
Pathologic type			
Squamous cell carcinoma	15	15	—
2018 FIGO staging			0.782
IIB	1	2	
IIIA	2	2	
IIIB	5	4	
IIIC	6	5	
IVA	1	2	
Tumour size			1.000
<5cm	4	5	
≥5cm	11	10	
Lymph-node status			1.000
Negative	9	8	
Pelvic node positive	4	5	
Para-aortic node positive	2	2	
Radiotherapy technique			1.000
3D-CRT	5	5	
IMRT/VMAT	10	10	
Cisplatin regimen			1.000
Weekly cisplatin concurrent CRT	2	3	
3-weekly cisplatin regimen	13	12	
Follow-up duration, median (range), months	28 (8-46)	22 (3-42)	0.106
Recurrence & survival endpoints			
Tumor recurrence, n (%)	2 (13.3)	8 (53.3)	0.027
Median DFS (months)	40	12	0.009
Median OS (months)	36	22	0.011

Supplementary Table 3. Densitometric quantification of FSTL3 protein expression normalized to β -actin in HeLa and SiHa cells.

Cell line	Group	Replicate 1	Replicate 2	Replicate 3	Mean $\pm$ SD	P value*
HeLa	NC	1.00	1.00	1.00	1 $\pm$ 0	0.006
	shFSTL3	0.58	0.75	0.50	0.61 $\pm$ 0.13	
SiHa	NC	1.00	1.00	1.00	1 $\pm$ 0	0.011
	shFSTL3	0.44	0.52	0.76	0.57 $\pm$ 0.17	

*P value versus corresponding NC group (unpaired two-tailed Student's *t*-test).

Supplementary Table 4. The sequences of primers for qRT-PCR.

Gene	Forward Primer (5'→3')	Reverse Primer (5'→3')
<i>β-actin</i>	AGCGAGCATCCCCCAAAGTT	GGGCACGAAGGCTCATCATT
<i>KLF4</i>	CGGACATCAACGACGTGAG	GACGCCTTCAGCAGAACT
<i>SERPINF1</i>	GGAAATTCCCGATGAGATCAGC	AGTCAAACCTTTGTTACCCACTGC
<i>CD74</i>	GCTGGACAAACTGACAGTCAC	CAGGTGCATCACATGGTCCT
<i>PRPS2</i>	GGAGATTGGTGAAAGCGTGAG	AGGTTGTCGTTAATTTCCCCG
<i>ERRFI1</i>	GACCCACCGAAGATTAAGAAGG	GGTCTAGGAGGTATGGGAACCTCT
<i>FSTL3</i>	GTGCCTCCGGCAACATTGA	GCACGAATCTTTGCAGGGA
<i>SOD2</i>	TTTCAATAAGGAACGGGGACAC	GTGCTCCCACACATCAATCC
<i>JUN</i>	TGAGTGACCGCGACTTTTCA	TTTCTCTAAGAGCGCACGCA
<i>CXCL3</i>	GAGCACCAACTGACAGGAGA	AGTCCTTTCCAGCTGTCCCTA

Supplementary Table 5. Comparison of positive cell percentages for the nine signature proteins between good response (GR) and poor response (PoR) groups.

Protein	GR Group (% mean $\pm$ SD, n = 15)	PoR Group (% mean $\pm$ SD, n = 15)	P value*
KLF4	93.25 $\pm$ 1.77	69.17 $\pm$ 3.31	<0.0001
SERPINF1	57.49 $\pm$ 3.29	57.22 $\pm$ 2.70	0.81
CD74	17.83 $\pm$ 4.45	54.49 $\pm$ 5.98	<0.0001
PRPS2	45.57 $\pm$ 4.17	43.04 $\pm$ 3.19	0.07
ERRFI1	76.40 $\pm$ 2.07	76.01 $\pm$ 2.10	0.62
FSTL3	21.01 $\pm$ 1.40	54.73 $\pm$ 4.88	<0.0001
SOD2	45.26 $\pm$ 3.13	87.05 $\pm$ 2.67	<0.0001
JUN	18.23 $\pm$ 2.93	48.34 $\pm$ 2.51	<0.0001
CXCL3	29.76 $\pm$ 2.10	67.30 $\pm$ 2.77	<0.0001

Supplementary Table 6. Patient-level correlation between mRNA expression (qRT-PCR) and protein expression (mIHC) for the nine signature genes.

Gene	Spearman r	P value*
<i>KLF4</i>	0.7405	<0.0001
<i>SERPINF1</i>	-0.1451	0.4443
<i>CD74</i>	0.7666	<0.0001
<i>PRPS2</i>	-0.09437	0.6199
<i>ERRFI1</i>	0.2147	0.2546
<i>FSTL3</i>	0.8317	<0.0001
<i>SOD2</i>	0.8505	<0.0001
<i>JUN</i>	0.3998	0.0288
<i>CXCL3</i>	0.7370	<0.0001

*P value determined by Spearman rank correlation test.

