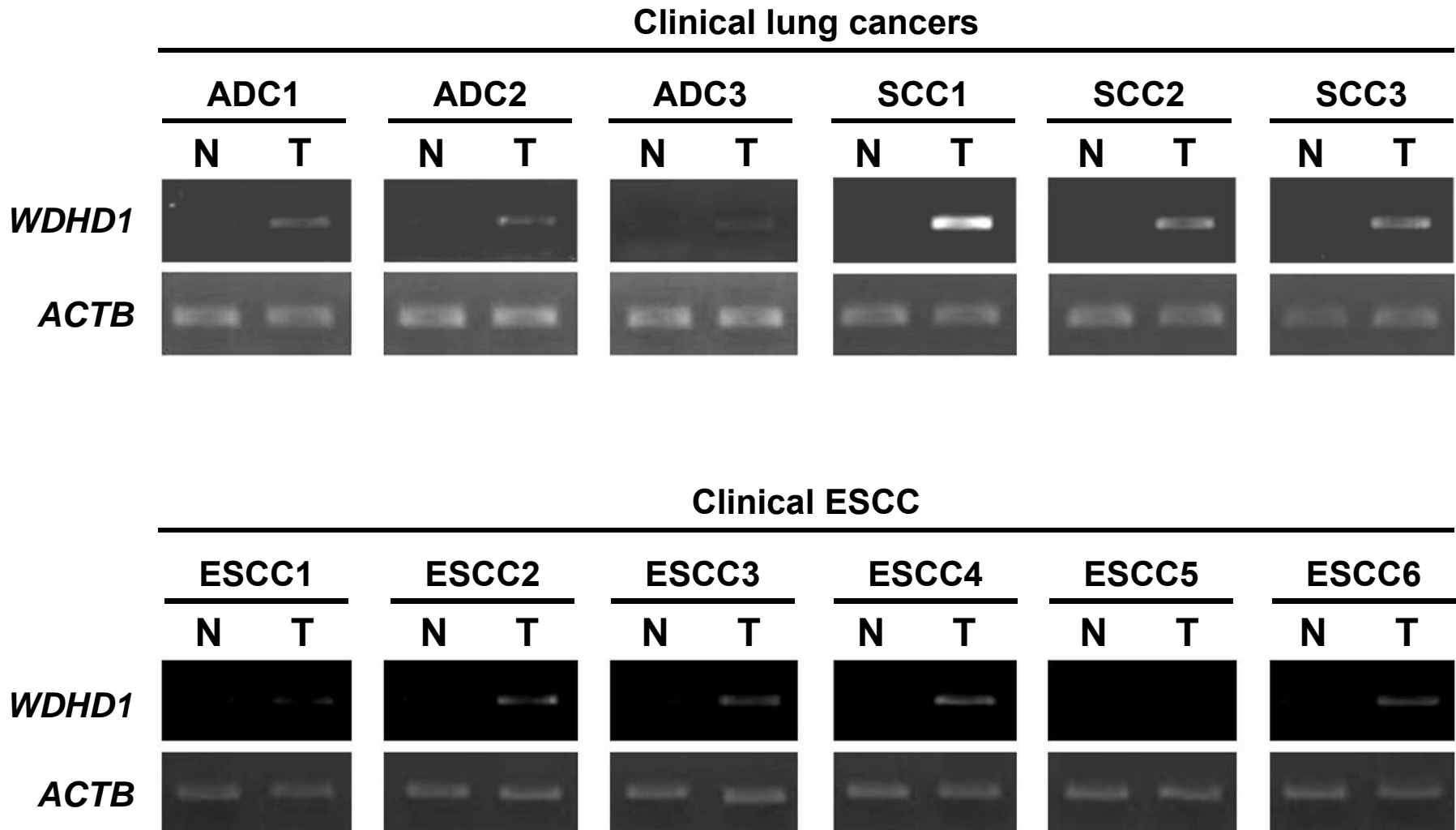


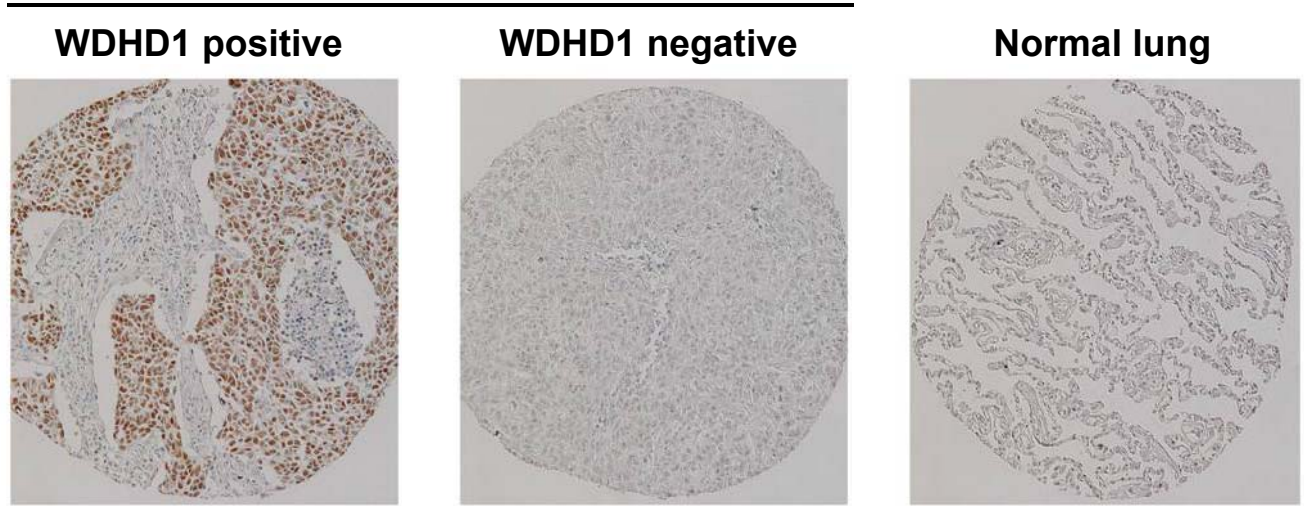
A



Supple Fig.1

B

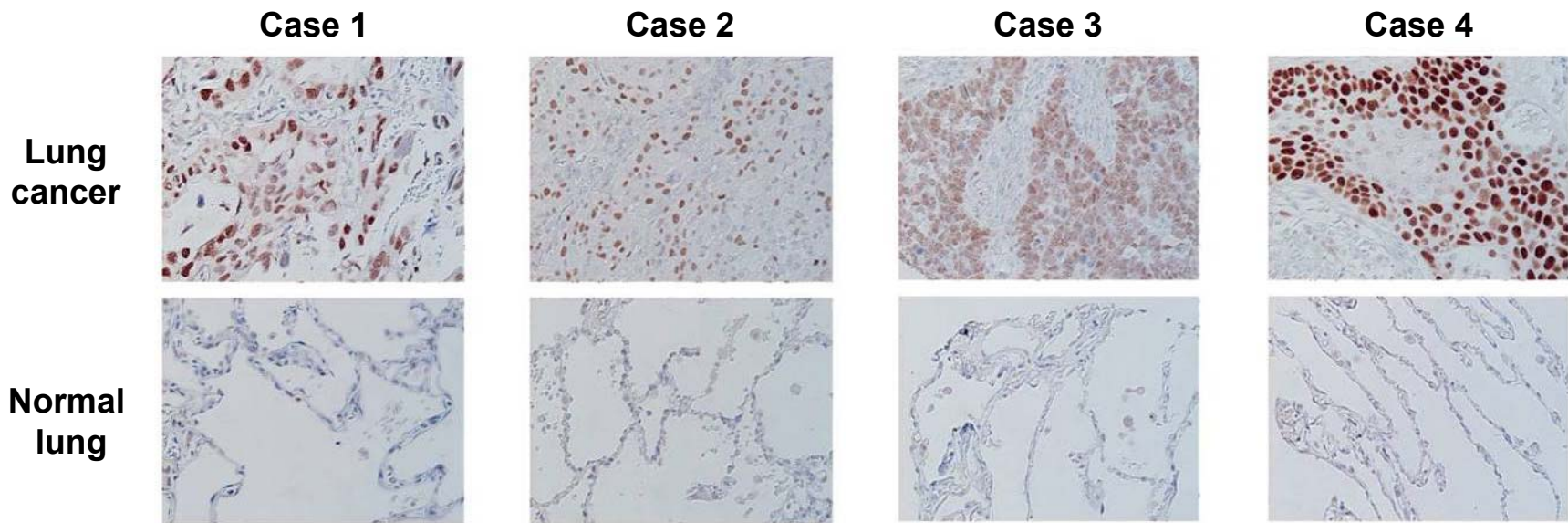
Lung SCC



C

Lung ADC

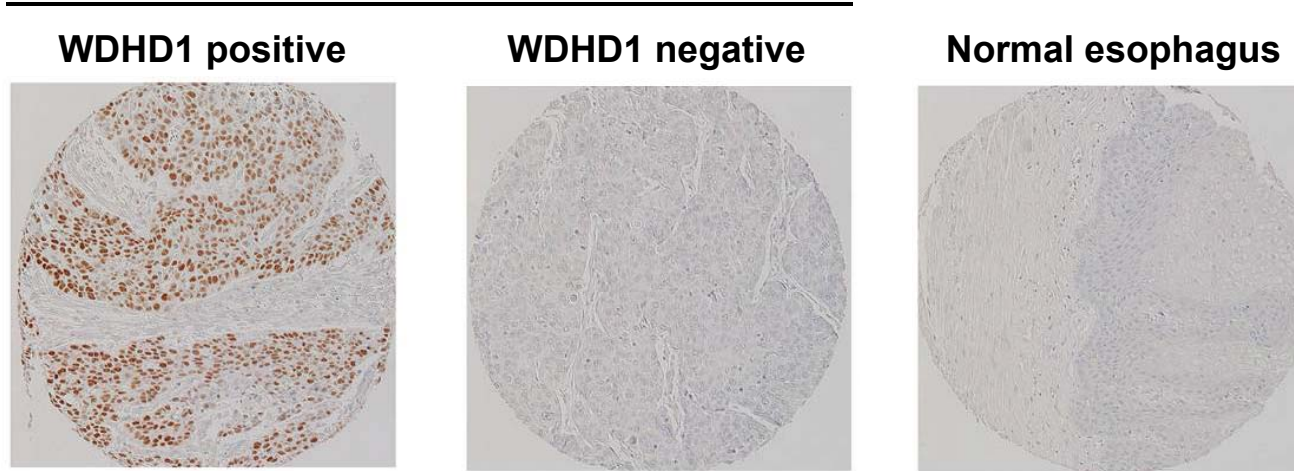
Lung SCC



Supple Fig.1

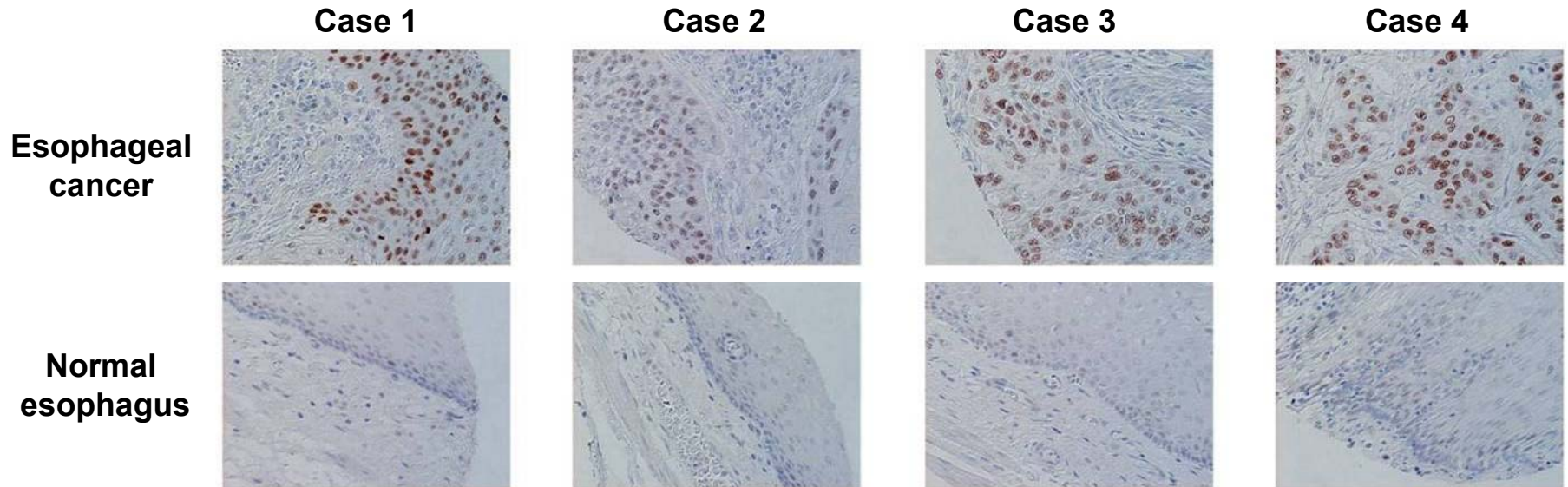
D

ESCC

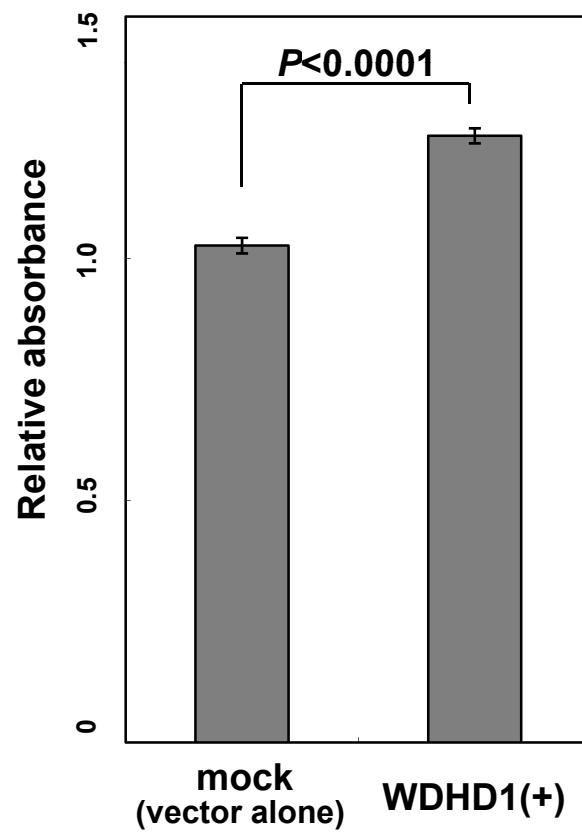
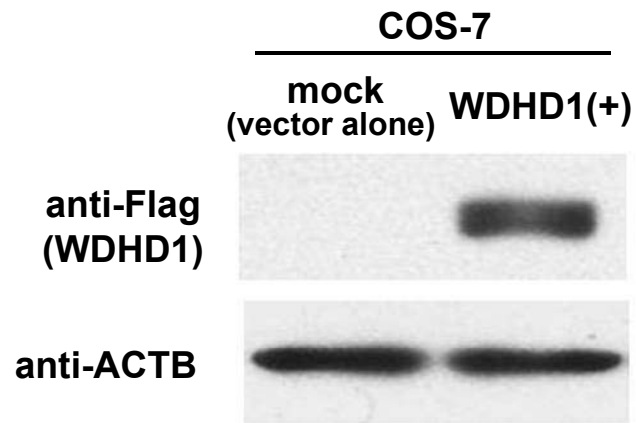


E

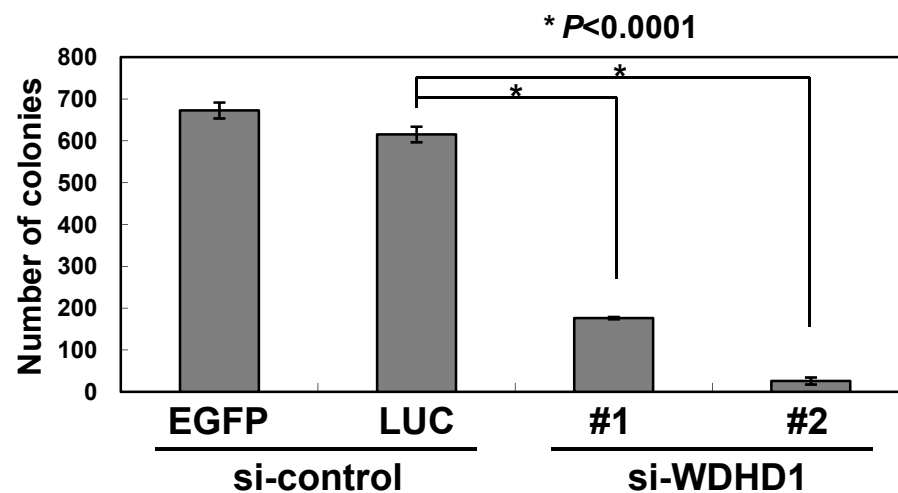
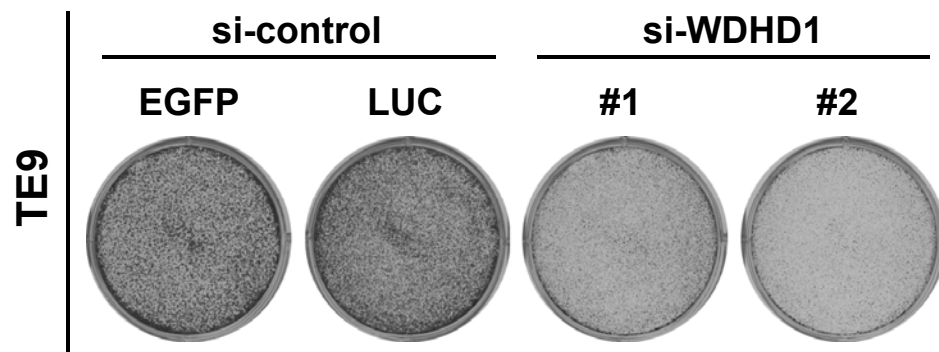
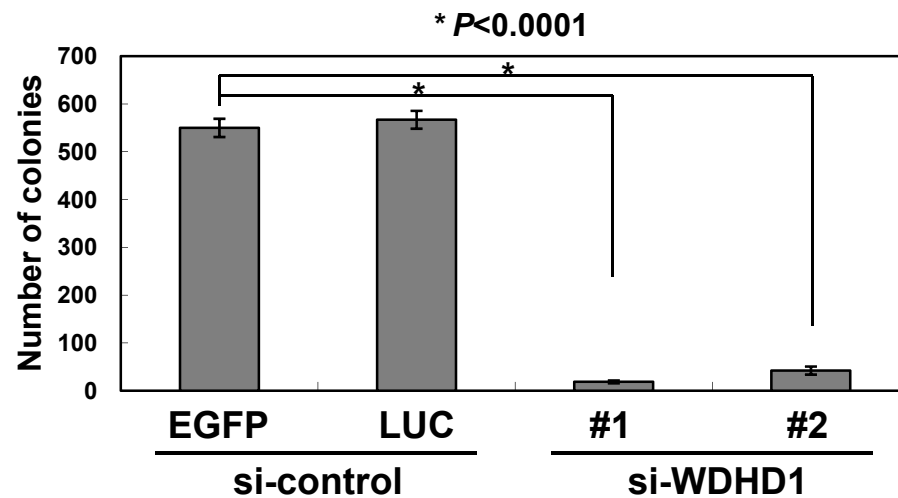
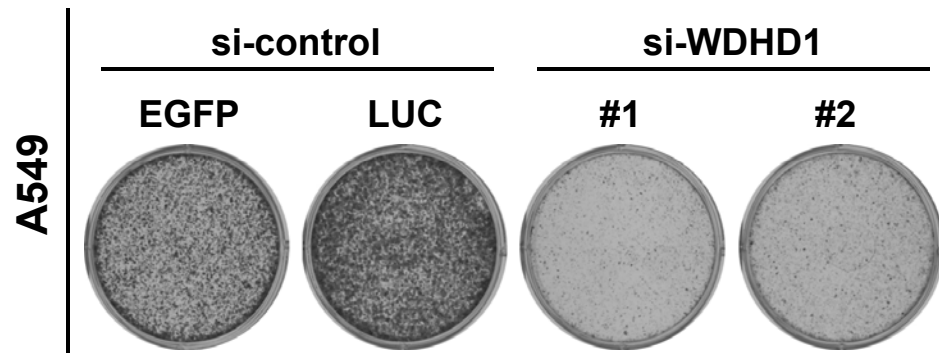
ESCC



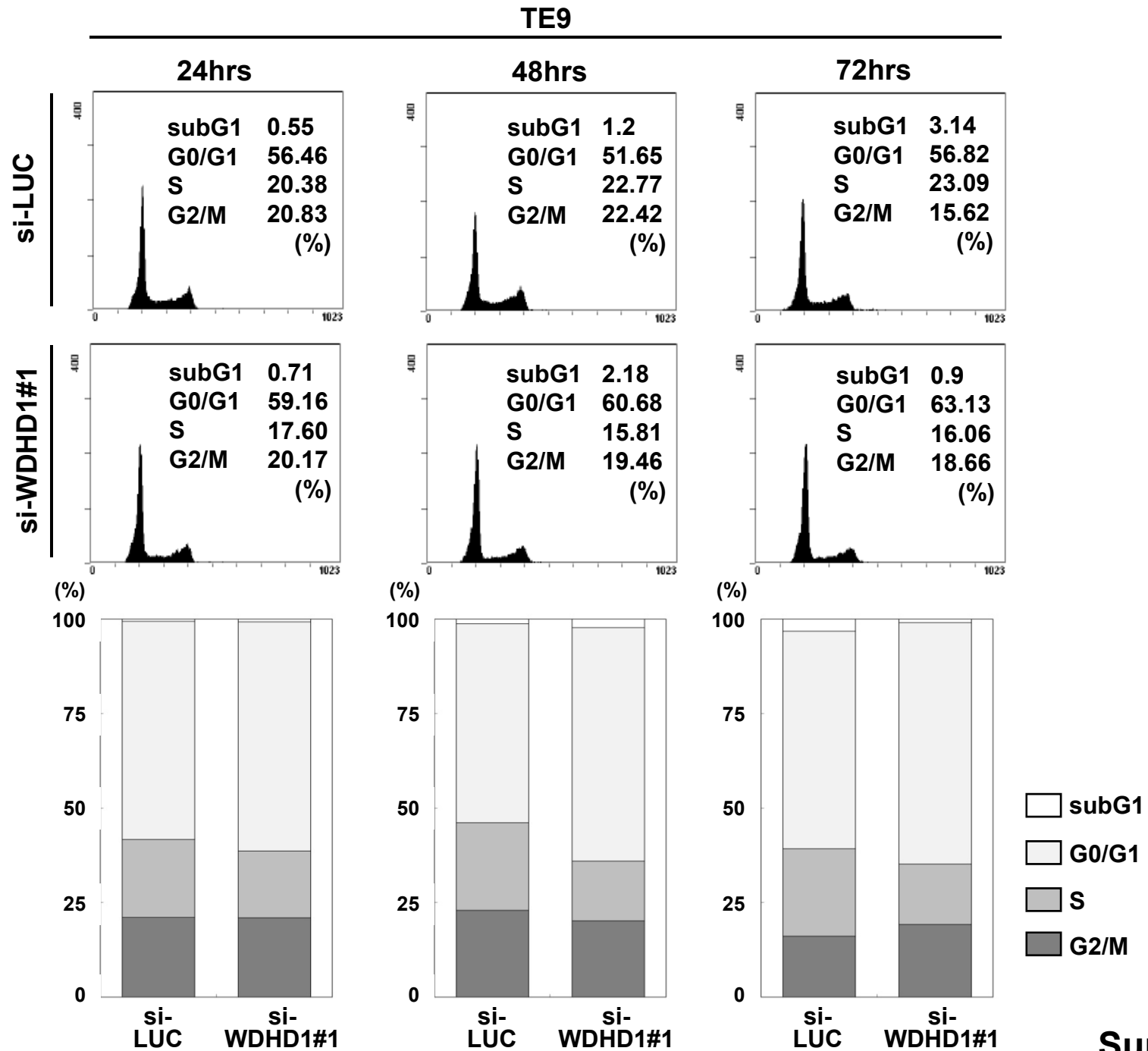
Supple Fig.1

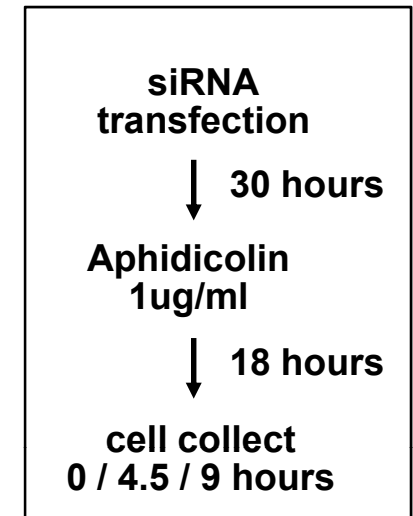
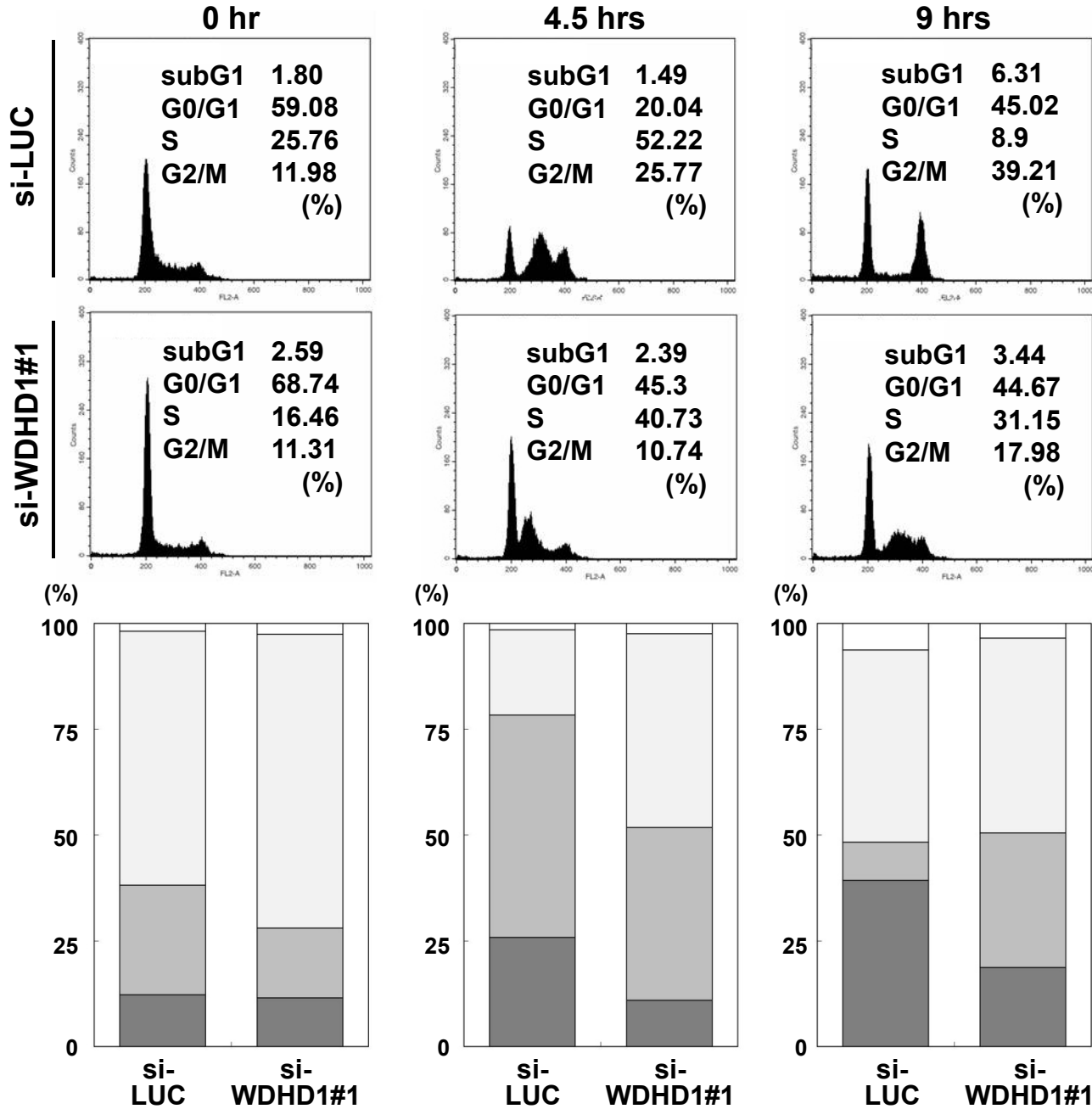


Supple Fig.2



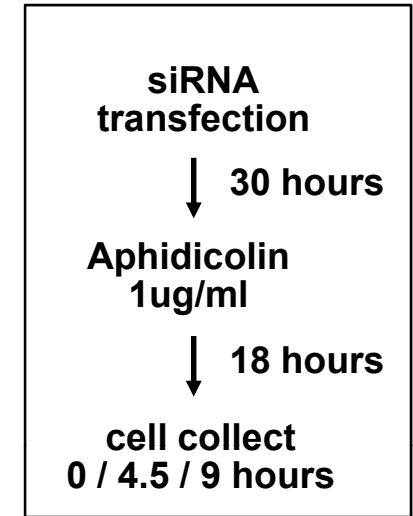
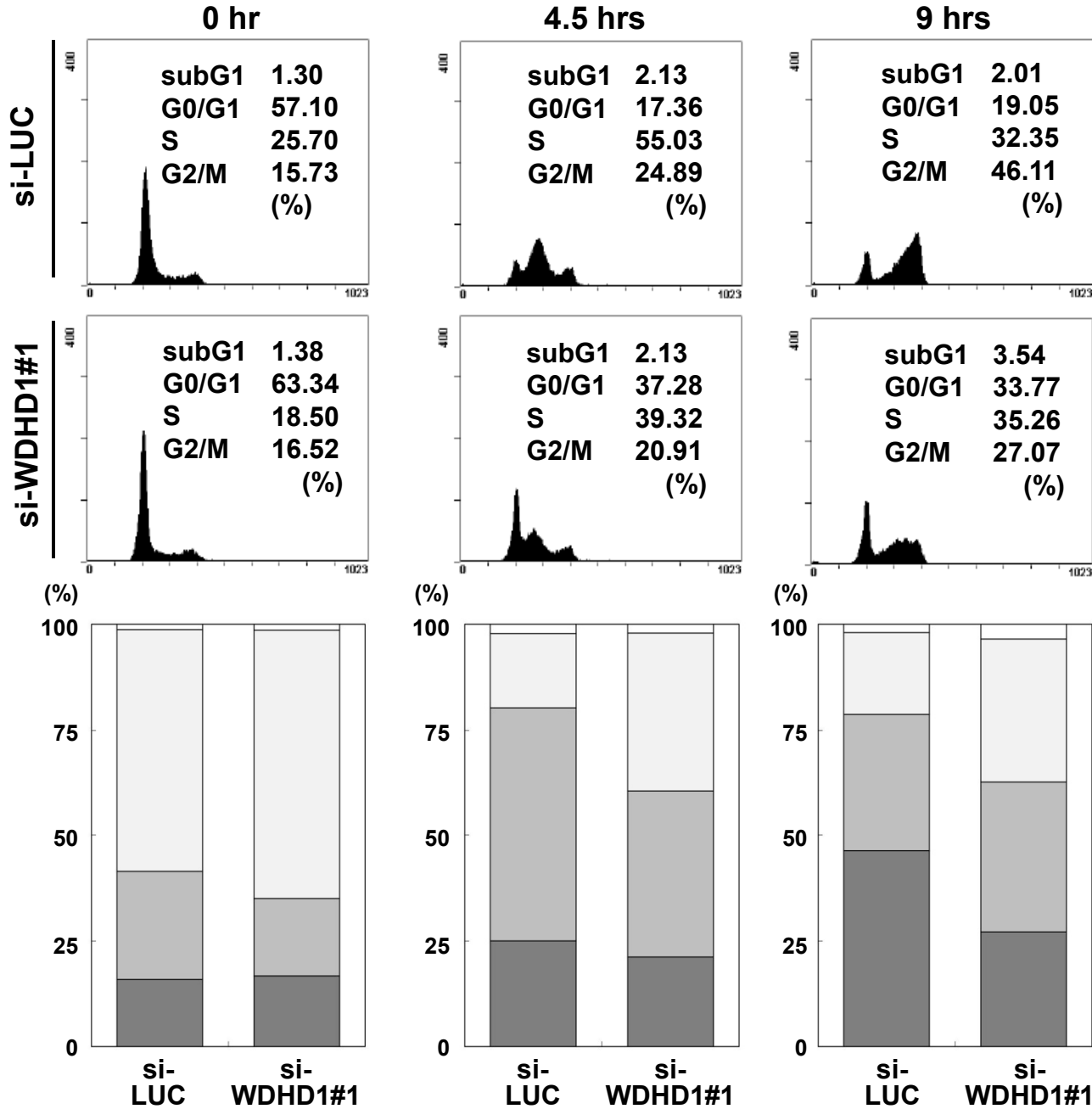
Supple Fig.3

A**Supple Fig.4**

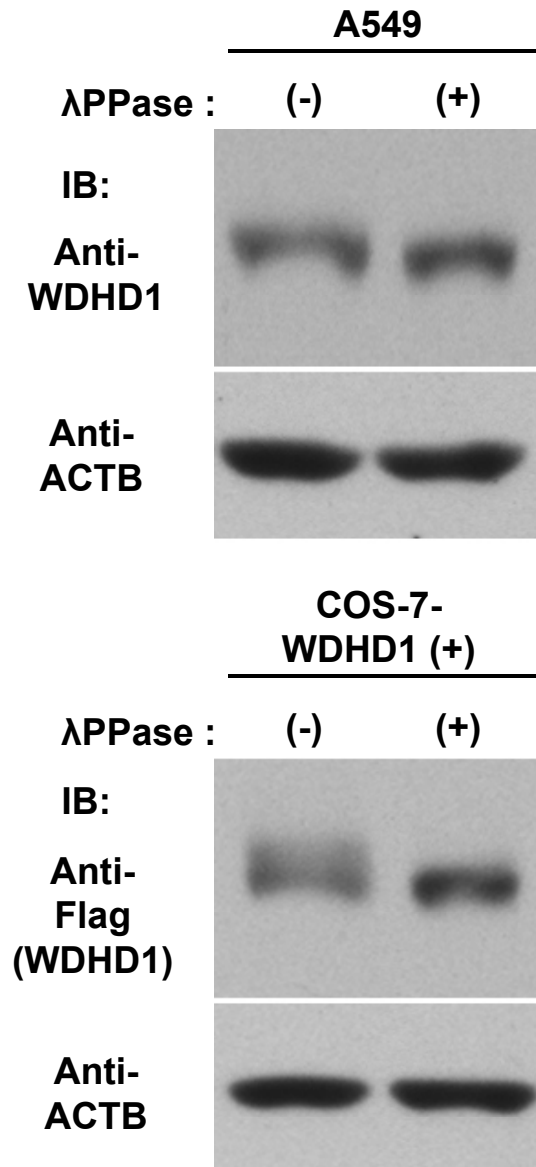
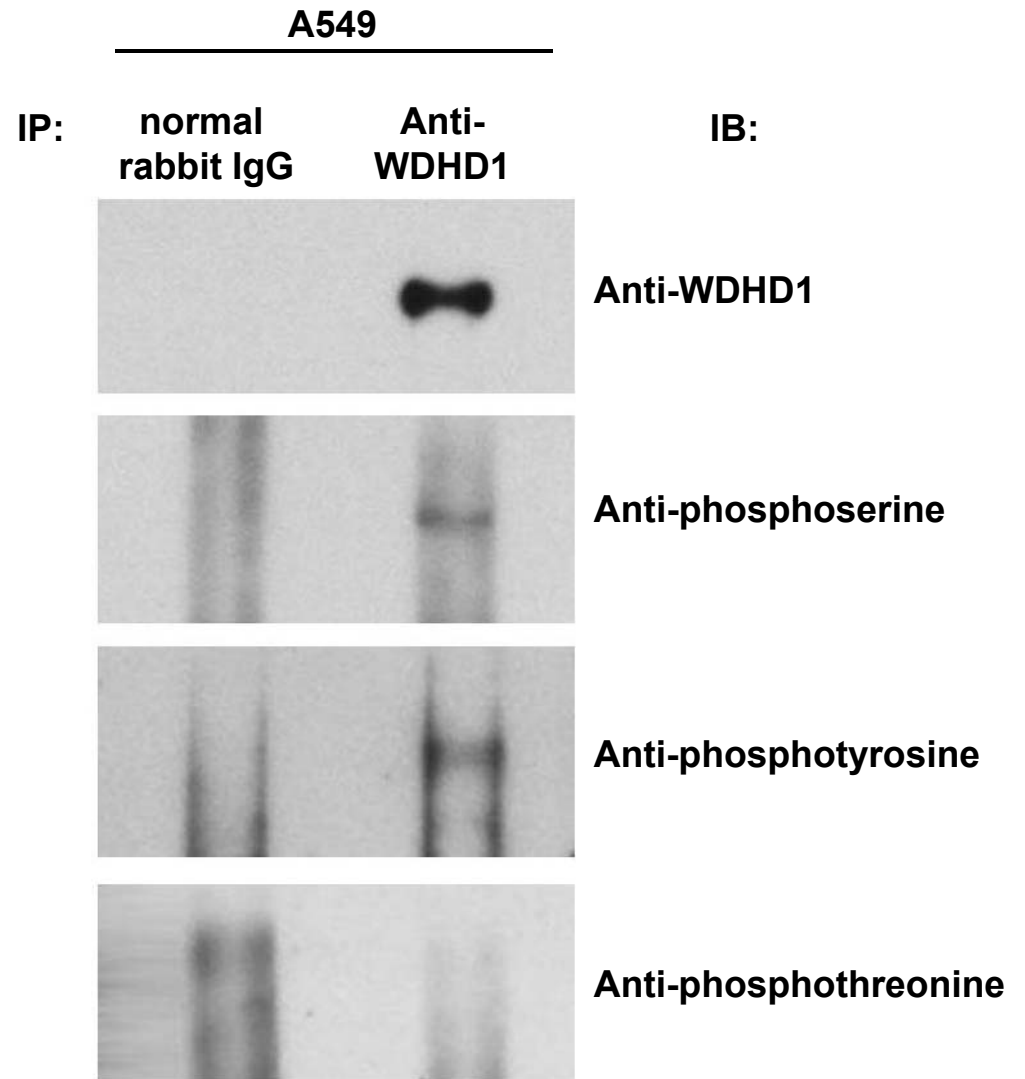
B**A549****Supple Fig.4**

C

TE9



Supple Fig.4

A**B****Supple Fig.5**

Supplementary Figure legend

Supplementary Figure 1. Expression of WDHD1 in lung and esophageal cancers and their adjacent normal tissues. **A**, Expression of *WDHD1* in 12 lung and esophageal cancer tissues (T; 6 NSCLCs and 6 ESCCs) and corresponding normal tissues (N), examined by semi-quantitative RT-PCR. **B**, Examples for positive and negative staining of WDHD1 protein expression in lung SCC tissues. **C**, Immunohistochemical staining of WDHD1 protein using anti-WDHD1 antibody in four representative paired NSCLCs and adjacent normal lung tissues (X 100). **D**, Examples for positive and negative staining of WDHD1 protein expression in ESCC tissues. **E**, Immunohistochemical staining of WDHD1 protein in four representative paired ESCCs and adjacent normal lung tissues (X 100).

Supplementary Figure 2. Enhanced growth of mammalian cells transiently transfected with WDHD1-expressing plasmids. MTT assay showing the higher growth activity of COS-7 cells after transfection with expression plasmids for WDHD1, compared with mock-vector transfected COS-7 cells.

Supplementary Figure 3. Colony formation assays of A549 and TE9 cells transfected with si-WDHD1s or control siRNAs. The number of colonies was counted by Giemsa staining and colony-counting software (ImageJ software 1.42) at 7 days after transfection. *Columns*, averaged colony numbers of triplicate assays; *bars*, SD.

Supplementary Figure 4. Flow cytometric analysis of lung cancer cells transfected with si-WDHD1. **A**, TE9 cells were transfected with si-WDHD1-#1 or si-LUC, and collected at 24, 48, and 72 hours after transfection for flow cytometry. The numbers besides the panels indicate the percentage of cells at each phase. **B**, **C**, Flow cytometric analysis of lung cancer cells treated with si-WDHD1. A549 (**B**) and TE9 (**C**) cells transfected with si-WDHD1-#1 or si-LUC were synchronized in G0/G1 phase and collected for flow cytometric analysis at 0, 4.5, and 9 hours after the cell cycle release. The numbers besides the panels indicate the percentage of cells at each phase.

Supplementary Figure 5. Phosphorylation of WDHD1 at serine and tyrosine residues. **A**, Dephosphorylation of endogenous WDHD1 protein in A549 cells (**top panels**) and exogenous WDHD1 protein in COS-7 cells transfected with WDHD1-expressing plasmid (**bottom panels**) by treatment with λ -phosphatase. **B**, Phosphorylation of endogenous WDHD1 at its serine and tyrosine residues in A549 cells was indicated by immunoprecipitation with anti-WDHD1 antibody followed by immunoblotting with pan-phospho-specific antibodies.

Supplementary Table 1. Resource and histological type of lung cancer cell lines

Cell line	Resource Distributor	Histology
NCI-H1781	ATCC (American Type Culture Collection)	adenocarcinoma
NCI-H1373	ATCC (American Type Culture Collection)	adenocarcinoma
LC319	Aichi Cancer Center	adenocarcinoma
A549	ATCC (American Type Culture Collection)	adenocarcinoma
PC14	RIKEN BRC (BioResource Center)	adenocarcinoma
SK-MES-1	ATCC (American Type Culture Collection)	squamous cell carcinoma
NCI-H2170	ATCC (American Type Culture Collection)	squamous cell carcinoma
NCI-H520	ATCC (American Type Culture Collection)	squamous cell carcinoma
NCI-H1703	ATCC (American Type Culture Collection)	squamous cell carcinoma
LU61	Central Institute for Experimental Animals	squamous cell carcinoma
LX1	Central Institute for Experimental Animals	large cell carcinoma
SBC-3	JCRB (Japanese Collection of Research Bioresources)	small cell carcinoma
SBC-5	JCRB (Japanese Collection of Research Bioresources)	small cell carcinoma
DMS273	ECACC (European Collection of Animal Cell Cultures)	small cell carcinoma
DMS114	ATCC (American Type Culture Collection)	small cell carcinoma

Supplementary Table 2A. Summary of 267 NSCLC patients

	total
Patients recruited (n)	267
Median (range) age at diagnosis (y)	65 (26-84)
Sex (female) (%)	89 (33.3)
Current or ex-smoker (%)	179 (67.0)
Histological type (n)	
adenocarcinoma (%)	157 (58.8)
squamous carcinoma (%)	90 (33.7)
adenosquamous carcinoma (%)	4 (1.5)
large cell carcinoma (%)	16 (6.0)
Tumor size (n)	
pT1 (%)	114 (42.7)
pT2 (%)	125 (46.8)
pT3 (%)	28 (10.5)
Lymph node status (n)	
pN0 (%)	208 (77.9)
pN1 (%)	23 (8.6)
pN2 (%)	36 (13.5)

Supplementary Table 2B. Summary of 283 ESCC patients

	total
Patients recruited (n) (%)	283
Median (range) age at diagnosis (y)	62 (42-82)
Sex (female) (%)	27 (9.541)
Tumor size (n)	
pT1 (%)	73 (25.8)
pT2 (%)	47 (16.61)
pT3 (%)	163 (57.6)
Lymph node status (n)	
pN0 (%)	91 (32.16)
pN1 (%)	189 (66.78)
pN2 (%)	3 (1.06)

Supplementary Table 3A. Numbers at risk in NSCLC patients (n)

	total	WDHD1 positive	WDHD1 negative
1 year	220	108	112
2 year	144	68	76
3 year	92	43	49
4 year	78	34	44
5 year	55	25	30

Supplementary Table 3B. Numbers at risk in ESCC patients (n)

	total	WDHD1 positive	WDHD1 negative
1 year	201	119	82
2 year	139	81	58
3 year	108	61	47
4 year	76	42	34
5 year	51	28	23