DRAK1 suppresses inflammation-induced cervical cancer progression by targeting TRAF6 protein

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Introduction

Expression level of DRAK1 in human cancers and its binding protein, TRAF6

A

Disease Summary for STK17A

Analysis Type by Cancer	Cancer vs. Normal		Cancer vs. Cancer: Cancer Histology		Cancer vs. Cancer: Multi-cancer		Clinical Outcome	
Bladder Cancer								
Brain and CNS Cancer	7		1	1	2			
Breast Cancer		1						
Cervical Cancer	1							
Colorectal Cancer		9				3		
Esophageal Cancer					1			
Gastric Cancer								
Head and Neck Cancer	5				1			
Kidney Cancer	1	5	2	1	1			
Leukemia		5	1					
Liver Cancer	2							
Lung Cancer								
Lymphoma		5	1	1	4			
Melanoma								
Myeloma								
Other Cancer	2		1					
Ovarian Cancer								
Pancreatic Cancer								
Prostate Cancer								
Sarcoma	1		5	5				
Significant Unique Analyses	18	25	9	8	9	3		
Total Unique Analyses	430		713		260			

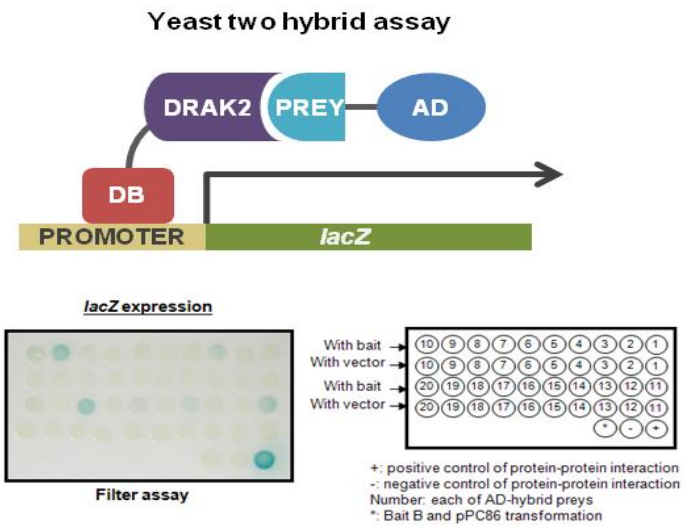
1 5 10 10 5 1

%

Cell color is determined by the best gene rank percentile for the analyses within the cell.

NOTE: An analysis may be counted in more than one cancer type.

B



Identify TRAF6 as DRAK1 binding protein from yeast two hybrid assay

Figure 1. DRAK1 decreases the stability of TRAF6 through its interaction with the TRAF domain

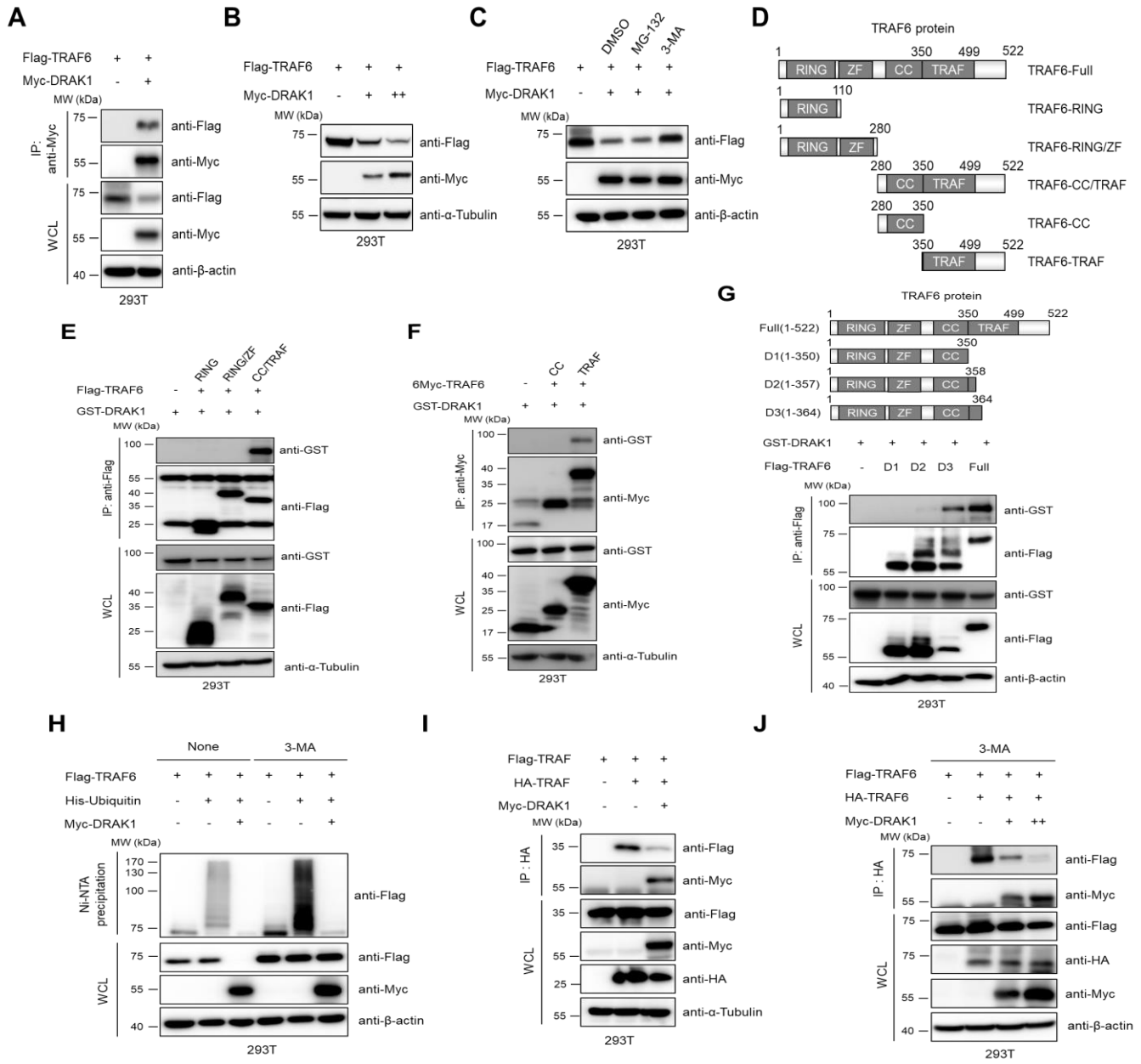


Figure 2. DRAK1 induces the autophagy-mediated degradation of TRAF6 in cervical cancer cells

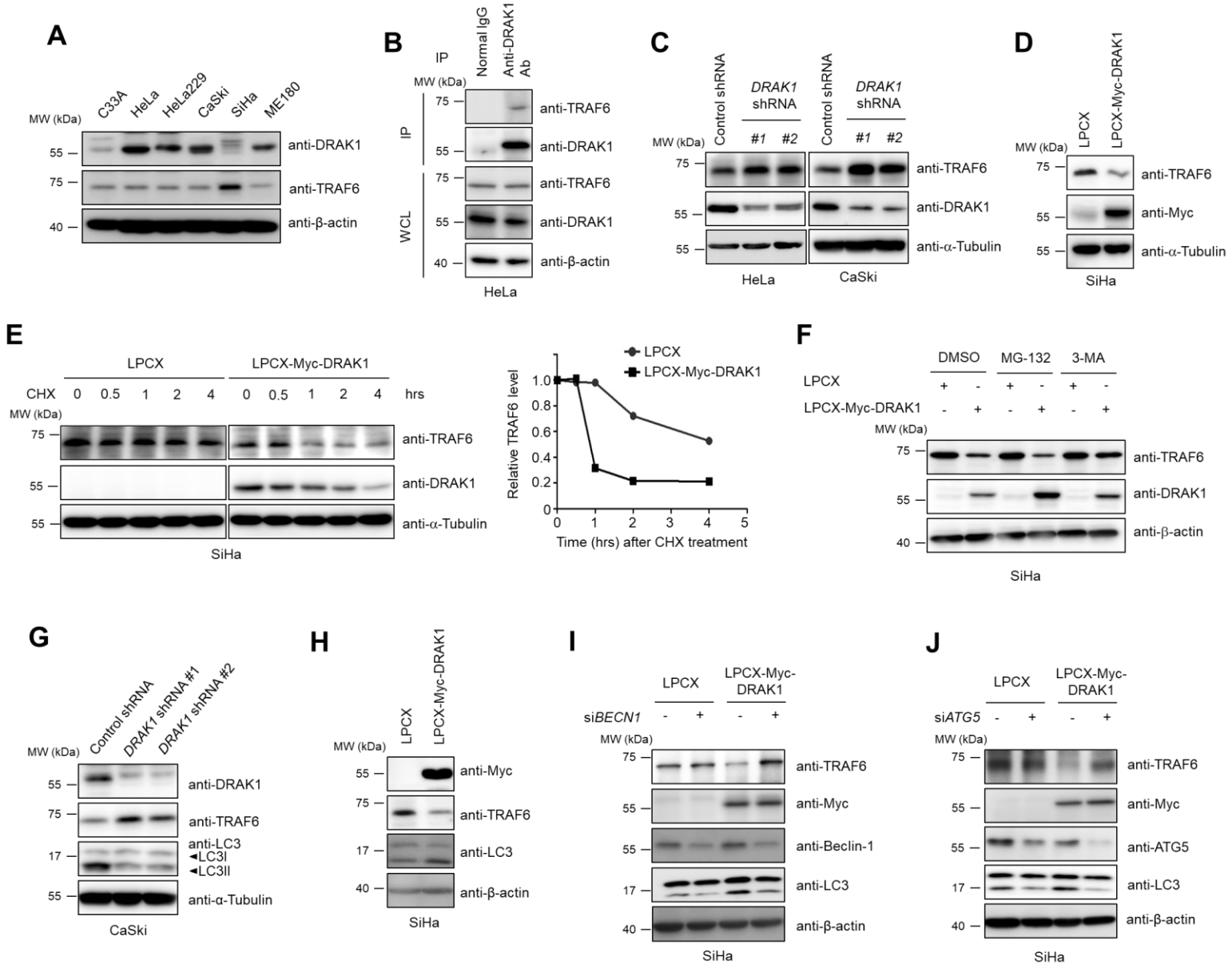


Figure 3. DRAK1 inhibits the TRAF6-mediated activation of NF-kB in cervical cancer cells

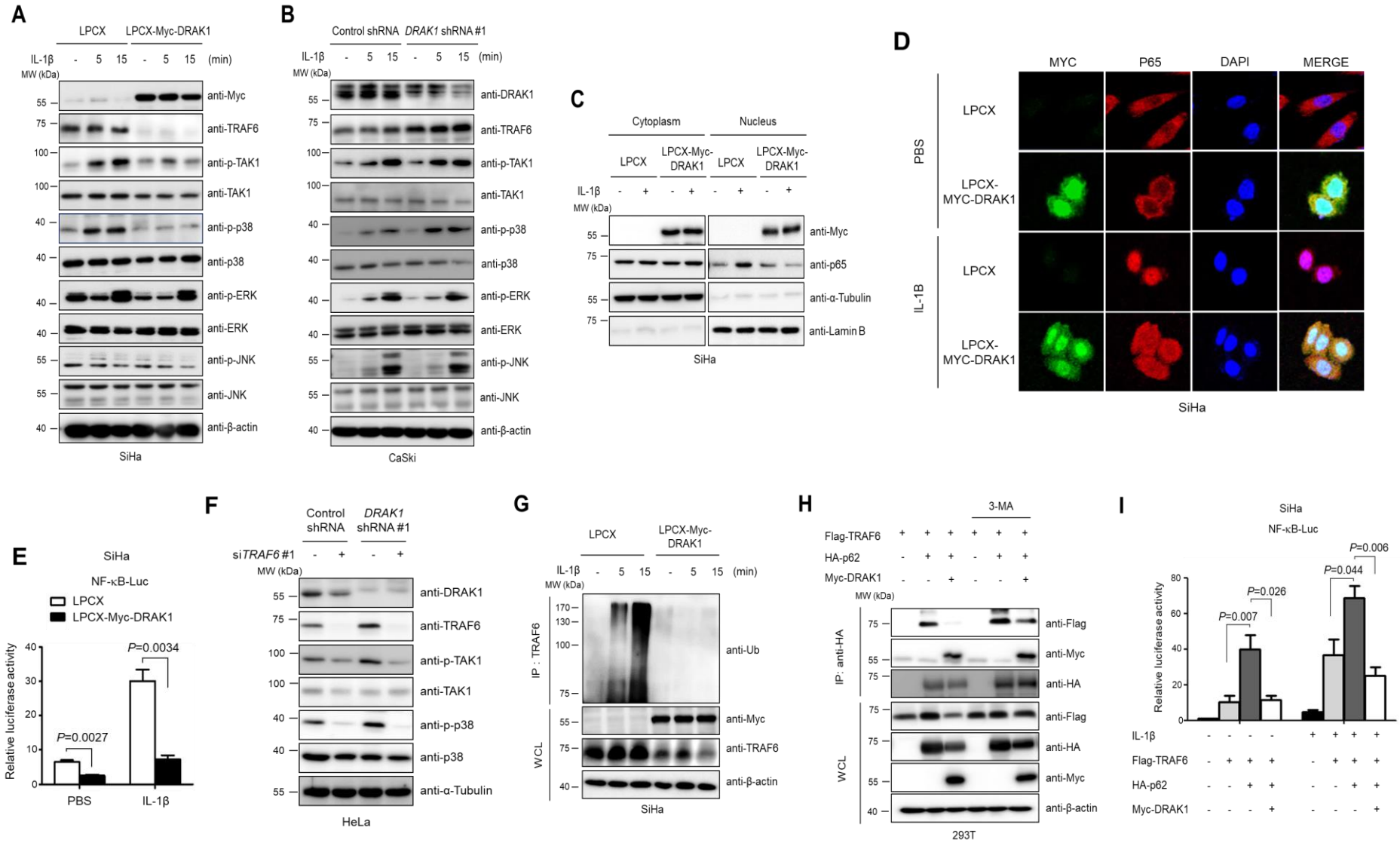


Figure 4. 11R-DRAK1 peptide suppresses inflammatory signaling activation through destabilization of TRAF6 protein

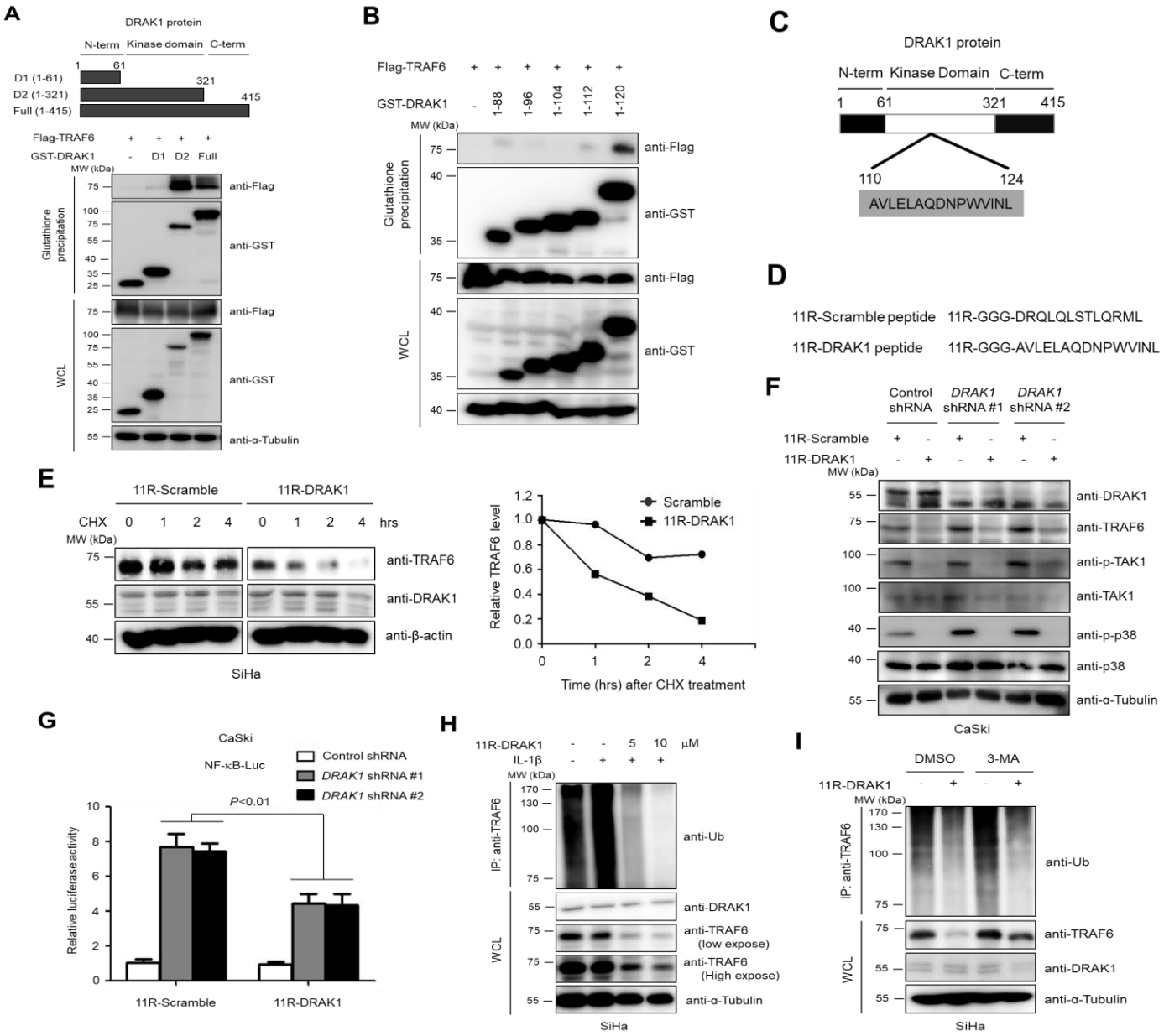


Figure 5. DRAK1 negatively regulates the TRAF6-mediated inflammatory gene network in cervical cancer cells

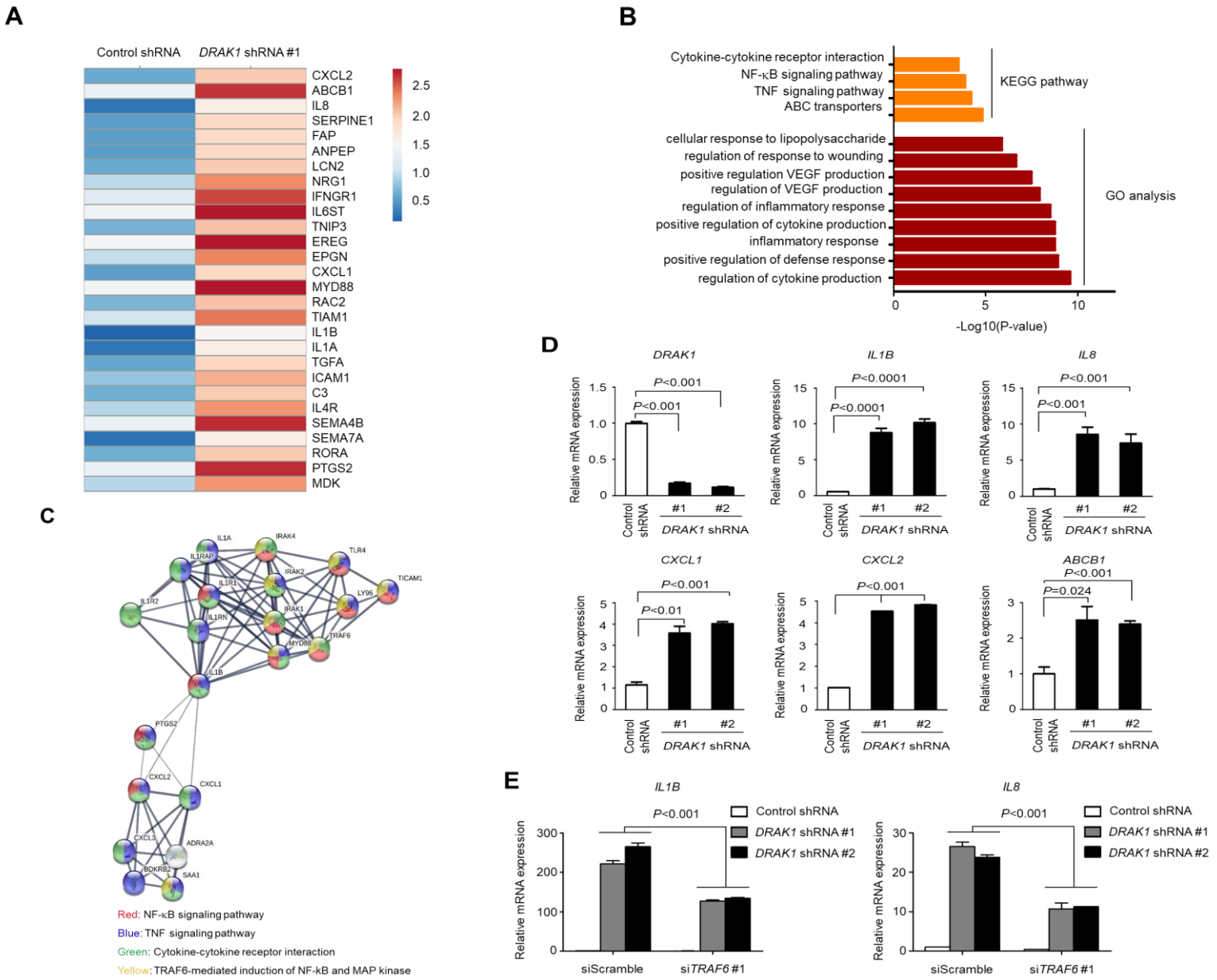


Figure 6. DRAK1 suppresses tumor growth and metastasis in cervical cancer cells

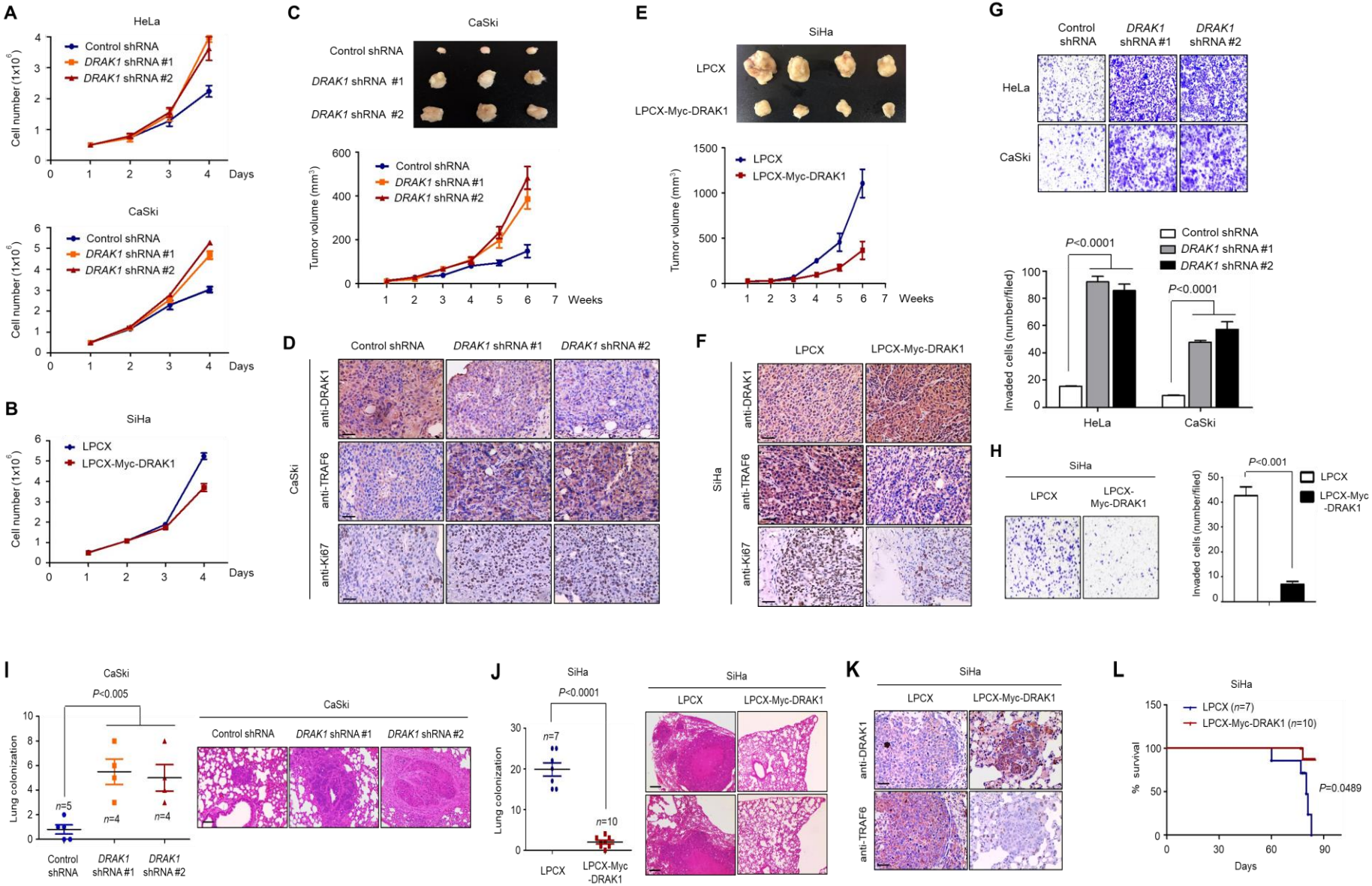
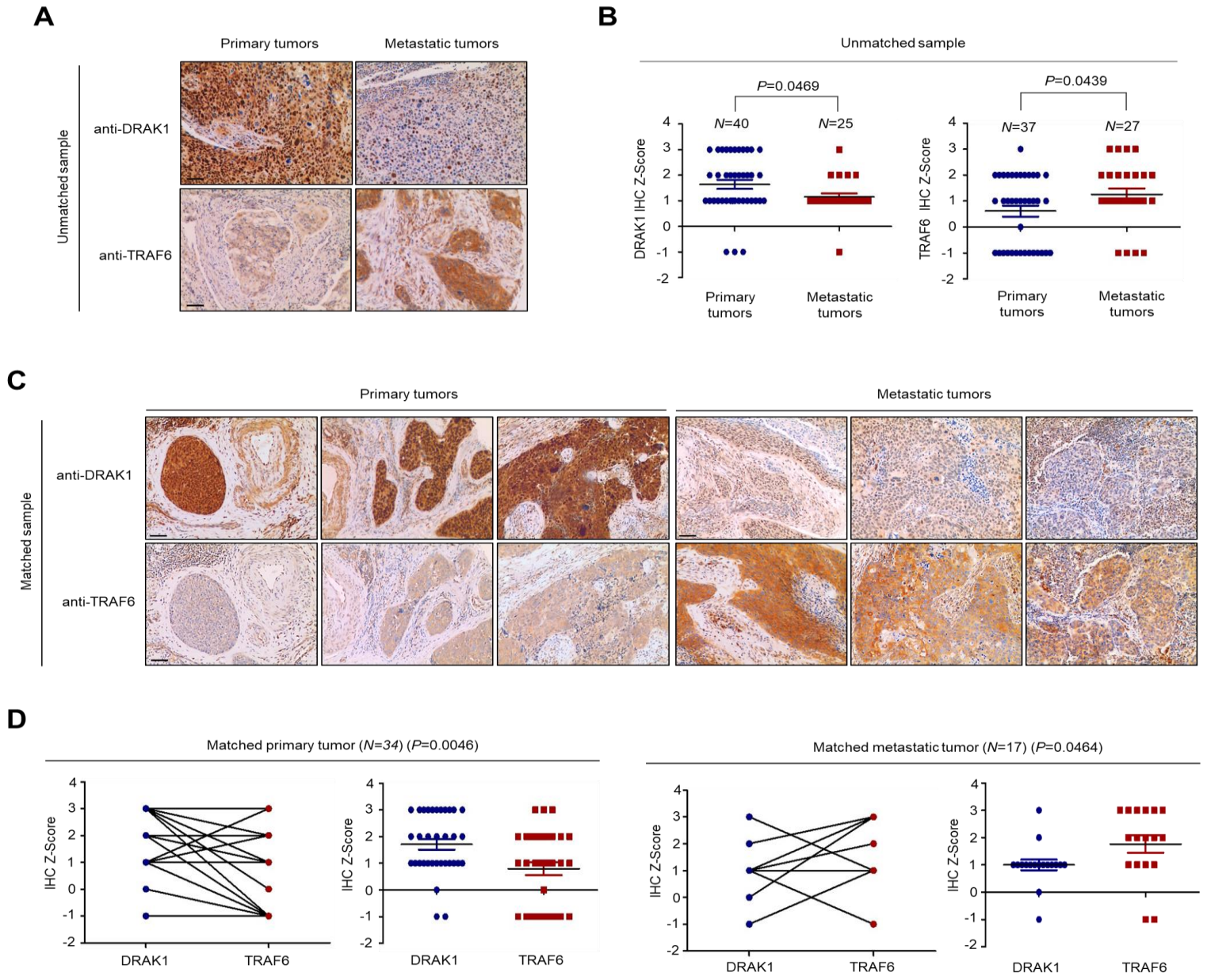


Figure 7. Expression levels of DRAK1 and TRAF6 are inversely correlated in patients with cervical cancer



Summary and Conclusions

- DRAK1 destabilize TRAF6 protein via an autophagy-mediated degradation pathway by interfering its autoubiquitination and homo-oligomerization
- DRAK1 decreases the TRAF6-activated NF-κB signaling pathway
- DRAK1 peptide suppresses the TRAF6-mediated signaling pathway via TRAF6 protein degradation
- DRAK1 negatively regulates the TRAF6-mediated inflammatory gene network
- DRAK suppresses tumor growth and metastasis in cervical cancer cells

Our findings highlight DRAK1 as a potential biomarker and therapeutic target for treatment of TRAF6-associated advanced cervical cancers as well as inflammation diseases.