

Innovative technique developed to destroy cancerous kidney cells

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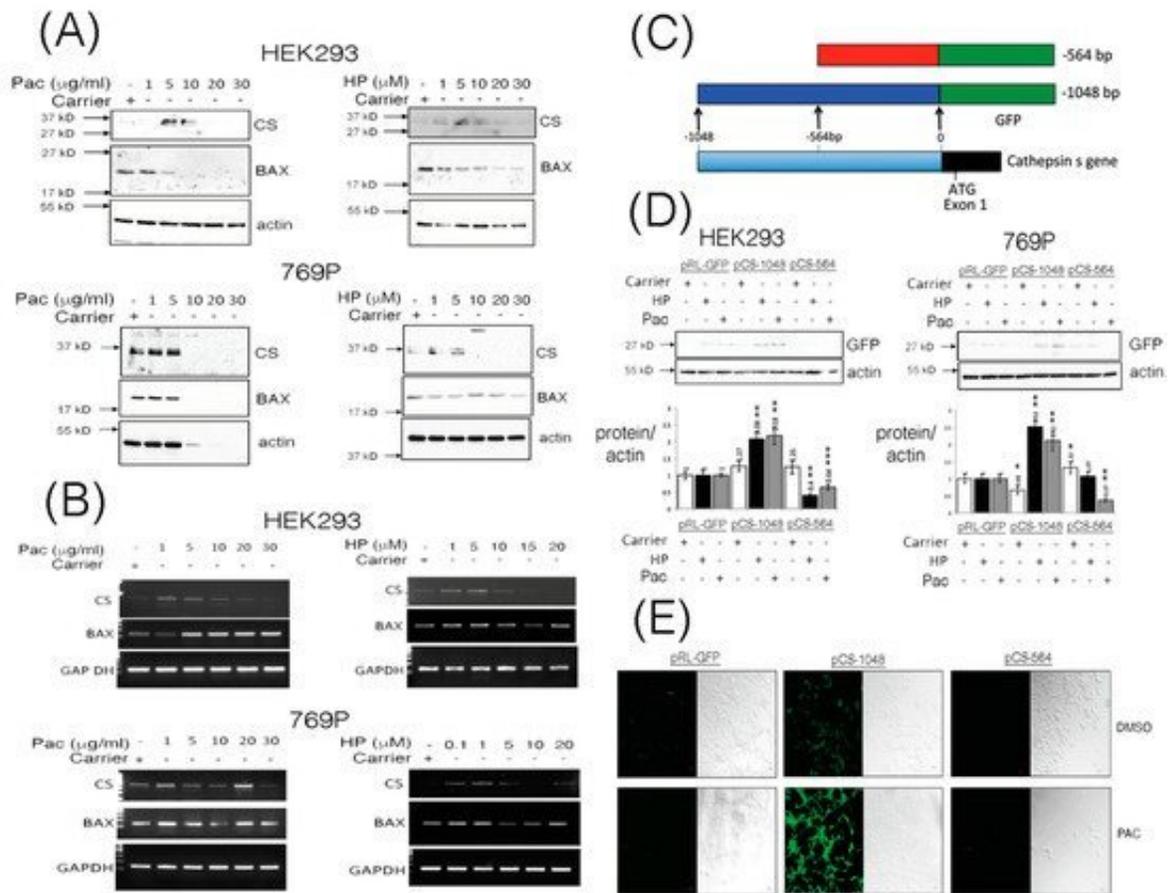


Figure 1 Cathepsin S (CS) protein expression levels are induced through the -1048 promoter fragment from the CTTS gene upon Paclitaxel or hydrogen peroxide stimulation. HEK293 and 769P cells were stimulated with increasing doses of Paclitaxel (Pac) and hydrogen peroxide (HP) and soluble lysates prepared after 24 h and equal volumes analyzed by Western blotting for cathepsin S (CS), BAX and actin expression (Panel A). Similarly, total RNA was isolated from cells stimulated for 24 h with increasing doses of Pac or HP and

equal quantities of template cDNA analyzed for transcriptional expression of CS, BAX and Glyceraldehyde-3-phosphate dehydrogenase (GAP-DH, Panel B). Promoter fragments, derived from the transcriptional start site of the CTTS gene to -1048 and -564, were PCR cloned and fused to a promoter-less GFP encoding plasmid (Panel C) and evaluated for GFP expression in equal volumes of HEK293 and 769P cleared whole cell lysates (WCLs) under Pac (10 $\mu\text{g}/\text{mL}$ and 5 $\mu\text{g}/\text{mL}$, respectively) or HP (5 μM) stimulatory conditions. GFP expression was also quantified, standardized and corrected against GFP expression from cells stimulated with carrier alone and is shown as a fold change over basal GFP expression (Panel D). HEK293 cells transfected with pCS-1048 or pCS-564 and stimulated with Pac (5 $\mu\text{g}/\text{mL}$) for 24 h were also fixed and visualized for GFP expression using laser scanning confocal microscopy (Panel E). The red bar indicates 1 micron. Quantified data are presented as the mean \pm SEM and its significance (where p

An innovative new technique that encourages cancer cells in the kidneys to self-destruct could revolutionize the treatment of the disease, a new study in the journal *Pharmaceutics* reports.

During this unique study, researchers from the University of Surrey and Sechenov First Moscow State Medical University in Russia investigated whether certain naturally occurring proteins within the body can be used to treat cancer.

Focusing on cathepsin S, a member of the lysosomal cathepsin proteins that are known to affect [cancer](#) progression, and p21 BAX, a [protein](#) that can stimulate cell destruction, researchers found that both can be deployed simultaneously to fight [cancer cells](#) in a two-pronged 'attack.' They act firstly by stopping the mechanism that makes certain treatments of the disease ineffective, and secondly by effectively encouraging cancerous [cells](#) to self-destruct.

This revolutionary approach targets two converging regulatory pathways that can sometimes be resistant to chemotherapy, and has led to the development of a potential ground-breaking therapy using a novel peptide, CS-PEP1. Researchers found that this peptide inhibits both cathepsin S and its ability to break down the p21 BAX protein, resulting in the accumulation of p21 BAX, which encourages

the death of cancer cells in the kidneys. The twin-track effect of this peptide can also override the molecular resistance often found during conventional chemotherapy treatment and offers a novel and effective approach in treating cancer.

An increased focus on therapeutic cancer treatments has signaled a move away from traditional methods such as chemotherapy and radiotherapy, as therapeutic treatments have been found to cause less harm to normal cells and fewer side effects for patients.

Professor Paul Townsend, principal investigator, pro-vice-chancellor, and executive dean of the Faculty of Health and Medical Sciences at the University of Surrey, said: "Kidney cancer is a very difficult type of cancer to cure; there is an increased need to think innovatively to develop new techniques. We have now discovered that proteins already in the body can be manipulated to encourage cancerous cells to die. This is an extraordinary breakthrough and insight, and can be used to potentially inform the treatment of other types of aggressive cancers, such as cancers of the breast and prostate."

More information: Surinder M. Soond et al. Cathepsin S Cleaves BAX as a Novel and Therapeutically Important Regulatory Mechanism for Apoptosis, *Pharmaceutics* (2021). [DOI: 10.3390/pharmaceutics13030339](https://doi.org/10.3390/pharmaceutics13030339)

Provided by University of Surrey

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