Putting the brakes on cancer

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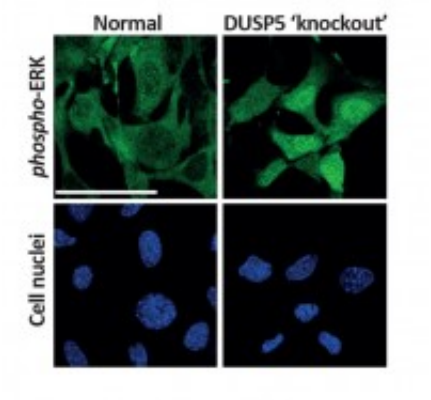

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A study led by the University of Dundee, in collaboration with researchers at our University, has uncovered an important role played by a tumour suppressor gene, helping scientists to better understand how it combats the effects of mutations which drive cancer development.

The research, published in *Proceedings of the National Academy of Sciences* (*PNAS*), shows how an enzyme called Dual-specificity phosphatase 5 (DUSP5) supresses tumour formation by 'switching off' another enzyme called ERK, which is involved in driving cell proliferation and survival.

The abnormal cell growth seen in cancers is often caused by mutations in

so-called 'oncogenes'. One of the most important of these is called 'Ras' and once mutated and activated, it can send powerful signals through ERK to drive tumour formation. The new study shows that DUSP5, by 'switching off' ERK, can act as a tumour suppressor and put the brakes on cancer development.

The University of Dundee's Professor Stephen Keyse, head of the Cancer Research UK Stress Response Laboratory at Ninewells Hospital, explained: "We know quite a lot about the way cancer-causing genes get switched on and drive the abnormal growth seen in tumours, but far less about the ways that our cells can react to this and try and suppress the dangerous signals that oncogenes propagate.

"Our work reveals that DUSP5 has an important role in protecting cells against the cancer causing effects of Ras mutations. It does this by switching off ERK in the cell nucleus and preventing the expression of other genes, which act to change cellular behaviour and promote tumour growth"

The team at Bath used a newly installed robotic microscope, which was funded by the Faculty of Science along with charitable donations from the University's Alumni fund. This equipment enabled the researchers to image and analyse hundreds to thousands of individual cells in repeated experiments to look in detail at how proteins are regulated in different locations of the cell.

Dr Jim Caunt, Lecturer in Cell Biology in the Department of Biology & Biochemistry, added, "To put this in context, doing comparable experiments using conventional microscopy with the same rigour would take years. It is great that these powerful new approaches are opening up new areas of cell biology to us."

Moving forward, this work will form the basis of future studies of

DUSP5 and help determine whether it can also suppress Ras-induced tumours in lung, pancreas and intestine, all common sites of human cancer.

"It will also be vital to study the expression of DUSP5 in human tumours to see if its expression is lost as part of the mechanism by which tumours progress," added Professor Keyse.

"Overall, the more we know about the 'wiring' of cancer cells and can unravel the complex interactions that occur in the way that cancer causing signals are processed, the better placed we will be to try and design new interventions and treatments."

More information: "Dual-specificity phosphatase 5 regulates nuclear ERK activity and suppresses skin cancer by inhibiting mutant Harvey-Ras ($HRas^{Q61L}$)-driven SerpinB2 expression." *PNAS* 2014 ; published ahead of print December 8, 2014, DOI: 10.1073/pnas.1420159112

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