Researchers uncover new operations of cancer suppressor

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(Medical Xpress) -- Scientists at the University of Dundee studying an important tumour suppressor, which is involved in at least a quarter of all cancers, have uncovered new ways in which it works.

The research team at the College of Life Sciences at Dundee have been studying the tumour suppressor protein PTEN, which when 'turned off' or damaged drives the development of many cancers.

By studying brain tumour cells, the Dundee team led by Dr Nick Leslie found that some damaged PTEN proteins can still operate in many of their normal ways but importantly lose the ability to stop cancer cells invading the brain.

Brain tumours are particularly deadly, having a very poor prognosis, because although they rarely spread outside the brain, by the time they are diagnosed, some cancer cells have usually moved away from the original tumour and infiltrated the surrounding brain tissue. Therefore, when a surgeon removes the initial tumour, it is often not long before a second tumour grows from the few cancer cells in the surrounding brain tissue.

Dr Leslie's team set up experiments, using a 3D matrix similar to that found between cells in the brain, to investigate this process of how cancer cells invade from a tumour mass into healthy tissue. Their work, published in the journal Science Signalling, describes how PTEN controls the way these brain tumour cells grow, change their shape,

switch particular genes on and off and importantly how PTEN normally stops this invasion process.

"We know that PTEN has lots of effects on what cells do, but it has proved harder to be certain which of these effects are important in stopping cancer and therefore which ones we should develop drugs to target," said Dr Leslie.

"It is really important we understand the factors driving these cancers, which affect thousands of people every year in the UK."

Dr Leslie said a lot was already known about one way in which PTEN can stop cells growing and dividing, but there have been several hints in the past that there are other undiscovered ways in which PTEN may stop cancers developing.

"In our new work, we've used two similarly damaged versions of PTEN, one of which was found in a tumour, that we show can still do the best recognised things that PTEN does, just as well as normal PTEN protein. However, these damaged proteins have completely lost the ability to stop brain tumours cells invading through a 3D matrix. This implies that in some, and perhaps many, tumours it is not the best known things that PTEN does that explain why it gets damaged, but instead it must be these new ways that PTEN can work that we know much less about."

The work also identified a 'gene signature' (showing which genes are turned on and off in particular cells) that is controlled by PTEN, which links to its control of invasion, but not its best recognised ways of working.

"Interestingly this gene signature also seemed to be recognisable in almost all of a large set of human brain tumour samples that lack or have damaged PTEN, providing more evidence that this new way in which

PTEN works may be important in brain tumour development," said Dr Leslie.

"The key goals of future work in this area need to include understanding much more about these new ways in which PTEN can work and whether they show us new ways to develop drugs to treat brain and other tumours."

The work of Dr Leslie and the Dundee team has been supported by funding from the Medical Research Council and the Association for International Cancer Research.

Provided by University of Dundee