Researchers show Myc protein is cancer's 'volume control'

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(Medical Xpress)—A protein called Myc, commonly found at high levels inside cancer cells, fuels the disease by allowing cells to override their in-built self-destruct mechanisms, according to two new studies by US scientists.

It does this by indiscriminately boosting the activity of any genes that are already active in the cell, rather than switching on particular target genes, as previously thought.

The researchers - from the Whitehead Institute and the National Institutes of Health - say their findings explain the wide range effects the Myc protein has been linked to. And they suggest that altering this amplification effect could lead to new ways to treat cancer.

Tumours that have increased levels of Myc have long been linked to poor clinical outcomes such as cancer spreading, or coming back after treatment.

Under normal circumstances, if levels of Myc get too high, cells immediately 'commit suicide' through a process called apoptosis. But cancer cells find a way to side-step the self-destruct process to survive.

In the new studies, researchers artificially increased the levels of Myc inside different types of cells, and then analysed the cells' DNA to find out where it 'stuck' - in other words which genes it had switched on.

They found that Myc was able to bind to DNA at a wide variety of sites across the genome, and that where it bound was determined by which genes were already active.

Dr Victoria Cowling, a Cancer Research UK-funded expert on Myc from the University of Dundee, said: "Myc increases the rate at which cells grow and divide, and when Myc levels increase it contributes to the development of almost all human tumour types.

"This comprehensive work confirms what other research has hinted at - that there may be a unifying explanation for the many effects Myc has in cancer cells."

Professor Richard Young from the Whitehead Institute said Myc was a "key driver" in a majority of cancers, but had so far proved difficult to target with drugs.

He added: "Now that we know the mechanism by which Myc acts, we can go after the components of that mechanism as potential drug targets. This research creates an even stronger impetus to find a way to drug the thing."

Dr Keji Zhao from National Institutes of Health, who worked on the second study, said their work shows that Myc is not a "power switch" but more "like the volume control of a music player".

Cancer Research UK's Dr Cowling said: "Rather than switching a specific set of gene targets on or off, Myc could be more like a volume control that amplifies the levels of all genes that are already active in cells."

She said the new research is likely to focus attention back on potential therapies that block Myc itself rather than its targets.

The results from both research projects are published in the journal *Cell*.

More information: Lin, C., Lovén, J., Rahl, P., Paranal, R., Burge, C., Bradner, J., Lee, T. & Young, R. (2012). Transcriptional Amplification in Tumor Cells with Elevated c-Myc, *Cell*, 151 (1) 67. DOI: 10.1016/j.cell.2012.08.026