MRC London Institute of Medical Sciences

XPO7 crucial to establish senescence and block tumour progression

19 February 2021 Research News

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Senescence is a cellular stress response that results in the stable growth arrest of old and damaged cells. This process is a key barrier to stopping these impaired cells transforming into cancerous cells. Yet, cancer is an increasingly common disease, so tumours must have found a way to bypass this process so that they can grow.

Research from the Cell Proliferation group at the LMS published on 18 February in the journal *Genes and Development* starts to unravel how cells escape senescence and gain all the properties of a tumour, and identify a gene that acts as a tumour suppressor and is essential for cells to establish senescence.

DNA damage is common to many types of senescence. So, the researchers used a DNA damage model to screen for genes that are essential for senescence to happen. One of the genes identified is called XPO7 and was found to be key to many types of senescence, including crucially so-called oncogene-induced senescence (OIS). This is a type of growth arrest that happens in cells where oncogenes, or 'cancer-promoting' genes, have been switched on.

XPO7 is a transport protein and shuttles cargo protein between the nucleus and the cytoplasm of the cell. In this study, the team found that XPO7 is involved in regulating a chain of events involving the protein TCF3, that results in altered levels p21, which regulates cell growth.

XPO7 is often deleted in many different types of cancer. When it was removed in a mouse model of liver cancer, it affected p21 and senescence induction, resulting in accelerated cancer progression.

Andrew Innes, first author on this paper, discussed next steps for the research:

"Now we know that XPO7 is essential for establishing senescence, and that without it, cells can bypass senescence and undergo cancer transformation. Understanding whether tumours lacking XPO7 present liabilities that we can target as a potential future treatment option is the logical next step. XPO7 is most relevant for prostate, colon and ovarian cancers, but other tumour types are likely to have alterations in other shuttling proteins that could have a similar role."

'XPO7 is a tumour suppressor regulating $p21^{CIP1}$-dependent senescence' was published on 18 February in the journal *Genes and Development*. Read the full article at http://genesdev.cshlp.org/content/early/2021/02/17/gad.343269.