Scientists discover that modifications to protein RUNX3 may promote cancer growth

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Scientists from the Cancer Science Institute of Singapore (CSI Singapore) at the National University of Singapore (NUS) have discovered that modifications to a protein called RUNX3 may promote cancer progression. The results of the study were published in the prestigious journal *Proceedings of the National Academy of Sciences* (*PNAS*) in June 2016.

The research team, led by Professor Yoshiaki Ito, Senior Principal Investigator at CSI Singapore, found that a modification called phosphorylation made to RUNX3 promotes cancer progression by allowing cell division. Uncontrolled cell division in the body is a process by which tumours form and hence is a hallmark of cancer. RUNX3 is a tumour suppressor gene that prevents the formation of tumours by binding to DNA.

The phosphorylation, or the addition of a phosphate group to a molecule, is carried out by an enzyme called Aurora Kinase, which has been observed to be present in unusually high levels in some cancers. Phosphorylation prevents the binding of RUNX3 to DNA, resulting in RUNX3 relocating to centrosomes, intracellular organelles that control the start of cell division.

"This study identifies a new post-translational modification to RUNX3, which provides RUNX3 with a novel role in the regulation of cell division. Our results suggest that frequent overexpression of Aurora Kinase in cancer may reduce RUNX3 transcription activity, leading to

cell division and formation of tumours. Understanding the molecular mechanisms underlying Aurora kinase-overexpressing tumours will help in the design of targeted and personalised cancer therapy," said Dr Linda Chuang, Senior Research Scientist at CSI Singapore, who is the first author of the study.

"Unlike other modifications which stem from changes to the RUNX3 DNA itself or how DNA is read, phosphorylation does not accompany any changes in the DNA and is hence undetectable at the genetic level. Given that modifications such as phosphorylation are likely to be impermanent and reversible, the clinical implications are far-ranging. Moving forward, the team is looking into ways to assess the feasibility of enhancing RUNX tumour suppression or inhibiting RUNX mitotic function to kill rapidly proliferating cancer cells," said Prof Ito.

More information: Linda Shyue Huey Chuang et al. Aurora kinase-induced phosphorylation excludes transcription factor RUNX from the chromatin to facilitate proper mitotic progression, *Proceedings of the National Academy of Sciences* (2016). DOI: 10.1073/pnas.1523157113

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