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Insider News

Heterochromatin induction offers new target for cancer therapy

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by ecancer reporter Janet Fricker

Specialised regions of inactive DNA and protein complex may explain why defective cells are able to survive, and become cancerous, reports *Nature Cell Biology*. The Italian researchers believe their findings could eventually be used as a new approach in cancer therapy.

Damage to DNA triggers cells to die or to stop dividing, but to remain alive in a dormant state known as cellular senescence. Cellular senescence is induced by telomere shortening of dysfunction, DNA damaging agents or oncogene activation. Senescent cells are known to contain protein complexes, known as Senescence-associated heterochromatic foci (SAHF) that are formed following oncogene activation. SAHF are highly condensed and heterochromatic chromosomes that have been proposed to enforce cellular senescence by suppressing the transcription of genes involved in proliferation.

In the current study Fabrizio d'Adda di Fagagna and colleagues from the FIRC Institute of Molecular Oncology Foundation (Milan, Italy) investigated the interplay between SAHF and the DNA damage response pathway (DDR) that induces apoptosis in senescence and cancer.

When the team examined SAHF levels in lung, colon, and head and neck cancer samples, they found that levels were considerably higher than those found in normal tissue, and that the levels were independent of the proliferative index or stage of the tumours.

Furthermore, both pharmacological and genetic disturbances to SAHF in oncogene expressing cells increased DDR signalling and led to apoptosis. In an in vivo study, a histone deacetylase inhibitor (HDACi) caused heterochromatin relaxation, increased DDR, apoptosis and tumour regression.

"As heterochromatin induction is specifically associated with oncogenic events and is not lost during cancer progression, we reasoned that it could represent an attractive target for cancer therapy in that, by boosting DDR signalling pathways, heterochromatin perturbation may cause apoptosis of tumour cells," write the authors.