How NORE1A acts as a barrier to tumor growth

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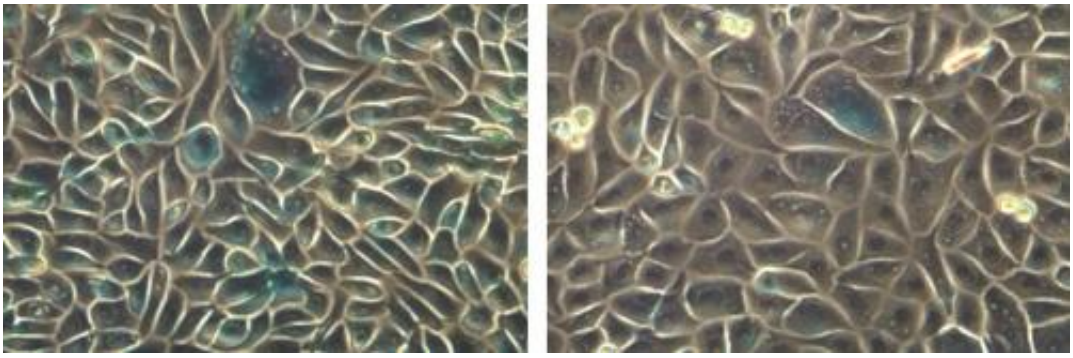

Activated Ras induces cell senescence (blue) are shown in the presence (left), but not the absence (right), of NORE1A. Credit: Clark Lab

Researchers reveal how cells protect themselves from a protein that is a key driver of cancer. The study appears in *The Journal of Cell Biology*.

Mutations that activate a protein called Ras drive excessive cell proliferation associated with cancer, but their ability to promote tumor growth is limited by the fact that they also induce cells to exit the cell cycle and become dormant, or senescent. How active Ras mutants induce senescence, and how this pathway is disrupted in cancer cells is still unclear.

Geoffrey Clark and colleagues from the University of Louisville examined the role of the tumor suppressor NORE1A, a protein that

binds to active Ras. Overexpressing NORE1A induced cell senescence, whereas removing the protein prevented senescence and enhanced the transformation of cells with cancer-promoting Ras mutations.

The researchers found that Ras enhanced NORE1A's association with a kinase called HIPK2, and that this interaction was required for cell senescence. NORE1A promoted HIPK2's association with p53, a tumor suppressor that plays a major role in restricting cancer development. HIPK2 is known to modify p53 in ways that cause either apoptosis, a kind of cell suicide, or senescence. Clark and colleagues found that NORE1A enhanced the senescence pathway.

The findings delineate how NORE1A allows Ras to modulate p53 function and induce cell senescence, and the loss of NORE1A may be a critical step in the growth of tumors.

More information: Donninger, H., et al. 2015. *J. Cell Biol*. DOI: 10.1083/jcb.201408087

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