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# Researchers find new target deep within cancer cells

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Investigators reporting in the July issue of the journal *Cancer Cell* have found that blocking a fundamental process deep within cancer cells can selectively kill them and spare normal cells.

For more than a century, clinicians have known that abnormalities of the nucleolus—a small, rounded mass within the cell nucleus—can be diagnostic for cancer. The nucleolus is where certain genes are read to form the components of ribosomes, the cellular machines that make proteins. While abnormalities in the nucleolus are known to be diagnostic for cancer, researchers have wondered whether they are required for cells to become malignant.

Now investigators have provided definitive evidence that accelerated reading of ribosomal genes is responsible for causing abnormal nucleoli and is necessary for the survival of cancer cells. They also show that blocking this accelerated reading in mice can set off a cascade of events that cause lymphoma and leukemia cells to die while sparing normal cells.

"The work in this study demonstrates that cancer cells are far more dependent on their ability to make ribosomes than normal cells. Critically, we demonstrate that selective inhibition of the enzyme, RNA polymerase I, that's responsible for synthesizing the major ribosomal components can be used to selectively kill cancer cells while leaving normal cells untouched," says senior author Dr. Ross Hannan, of the Peter MacCallum Cancer Centre in Australia. Previously, it was assumed

that the ability to make ribosomes would be equally important to normal and cancer cells.

The findings suggest that selective inhibitors of RNA polymerase I may be effective therapeutics for the treatment of human cancers. Based on the findings in this study, investigators will study one such inhibitor, Cylene Pharmaceuticals' CX-5461, in clinical trials at the Peter MacCallum Cancer Centre later this year.

**More information:** Bywater et al.: "Inhibition of RNA Polymerase I as a Therapeutic Strategy to Promote Cancer-Specific Activation of p53." *Cancer Cell*. dx.doi.org/10.1016/j.ccr.2012.05.019

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