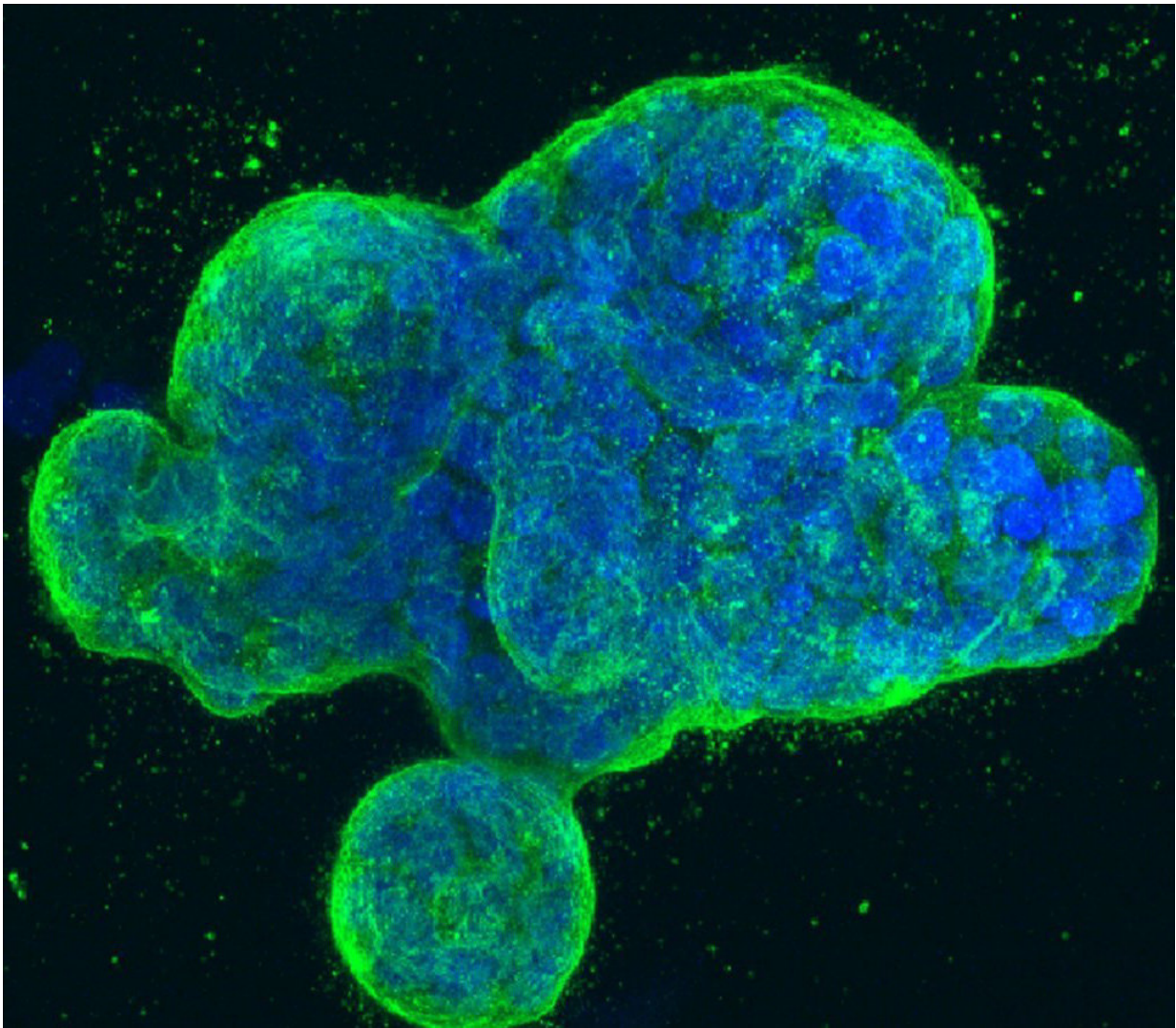


An errant editing enzyme promotes tumor suppressor loss and leukemia propagation

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Three-dimensional culture of human breast cancer cells, with DNA stained blue and a protein in the cell surface membrane stained green. Credit: National Institutes of Health

Writing in the January 3 issue of *Cancer Cell*, researchers at University of California San Diego School of Medicine report that detection of "copy editing" by a stem cell enzyme called ADAR1, which is active in more than 20 tumor types, may provide a kind of molecular radar for early detection of malignancies and represent a new therapeutic target for preventing cancer cell resistance to chemotherapy and radiation.

Adenosine deaminases are a family of three enzymes encoded by the ADAR genes, which stand for adenosine deaminase acting on RNA. They regulate [gene expression](#) by modifying nucleotides within double stranded RNA molecules, serving as fundamental editors in the development of new stem cells.

The enzyme, however, is also activated in cancers as diverse as liver, breast and leukemia. A [research team](#) led by senior author Catriona Jamieson, MD, Ph.D., deputy director of the Sanford Stem Cell Clinical Center and deputy director of the UC San Diego Moores Cancer Center, found that the normal functions of the ADAR1 enzyme are hijacked by pre-[malignant cells](#), leading to a cascade of molecular consequences that promote malignant transformation, dormant cancer stem cell generation and resistance to treatment.

"We were able to illuminate the abilities of ADAR1 to 'hyper-mutate' tumor suppressor RNAs in leukemia and, at the same time, edit the microRNA aimed at targeting the tumor suppressor RNA. This enzyme turns on cancer resistance via a [domino effect](#) on RNA instead of DNA," said first author Qingfei Jiang, Ph.D., assistant project scientist in Jamieson's lab.

Jamieson characterized RNA editing as tweaking basic genetic blueprints, not fundamentally rewriting them. Nonetheless, the results

might be dramatic. "One result of detection of malignant RNA editing could be exposing dormant cancer stem cells that often escape therapies that target dividing cells, which leads to therapeutic resistance and disease relapse, and also highlight ADAR as a potentially tractable target for cancer stem cell elimination," said Jamieson.

More information: Hyper-Editing of Cell-Cycle Regulatory and Tumor Suppressor RNA Promotes Malignant Progenitor Propagation, *Cancer Cell* (2019). [DOI: 10.1016/j.ccell.2018.11.017](https://doi.org/10.1016/j.ccell.2018.11.017) , [www.cell.com/cancer-cell/fullt... 1535-6108\(18\)30538-5](http://www.cell.com/cancer-cell/fulltext/S1535-6108(18)30538-5)

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