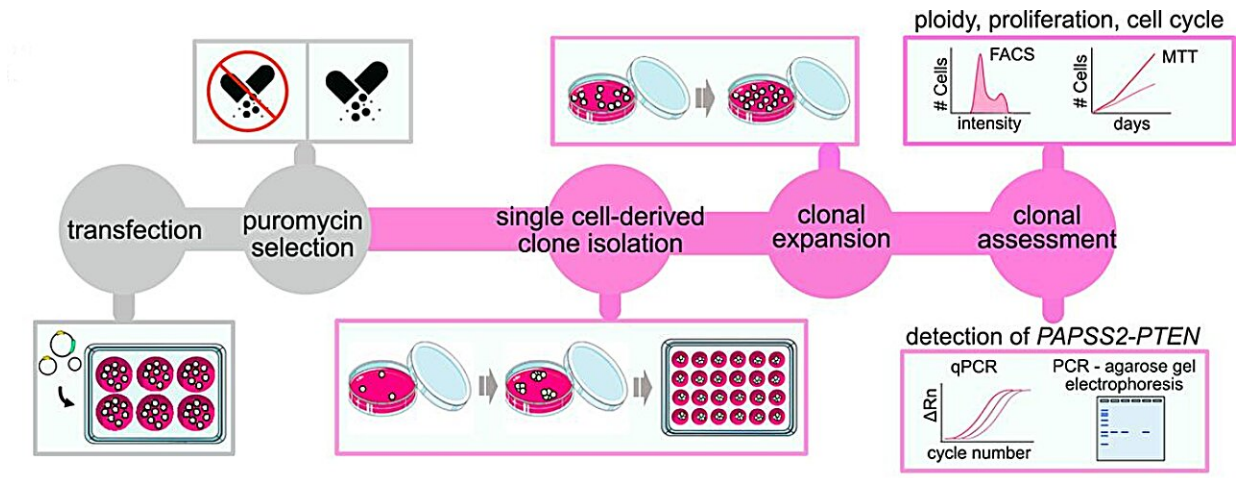
Medical Xpress

New study reveals unexpected consequences of CRISPR-Cas9 gene editing

November 21 2023



Schematic illustration displays the workflow for determining the frequency of the genomic deletion of the PAPSS2-PTEN locus and associated cellular consequences in single-cell–derived HAP1 clones. In some experiments, the transfection and puromycin selection steps (colored in gray) were omitted as part of the testing. Credit: *Life Science Alliance* (2023). DOI: 10.26508/lsa.202302128

A new study by Claudia Kutter's research group at the Department of Microbiology, Tumor and Cell Biology (MTC) has identified potential pitfalls in the use of the gene editing technique CRISPR-Cas9, a gene scissors that is used for cancer treatments.

The study has identified that a cancer cell line derived from leukemia removes a region that encodes a tumor-suppressing gene and genes that control cell growth. The findings are published in the journal *Life Science Alliance*.

"We found that this elimination often occurs when cancer cells are exposed to stress, such as when using CRISPR, gene scissors, or other treatments such as antibiotics. The elimination changes gene regulation in a unique way, which in turn affects basic biological processes such as DNA replication, cell cycle regulation, and DNA repair," says Claudia Kutter, research group leader at MTC, Karolinska Institutet.

This knowledge is important for researchers, clinicians, and biotechnologists to correctly interpret and apply gene editing results. The study also has clinical relevance, as the observed eliminations are in genes associated with cancer, which has implications for cancer research and treatment.

"Shockingly, this elimination has been unintentionally overlooked by many researchers who modify genes in cancer cells by CRISPR screenings. The elimination also occurred more frequently in patients who have undergone cancer treatment. The treated cancer cells had, due to the elimination, a selective advantage, which is bad for the patient's long-term survival as these cells remained after the treatment," says Claudia.

"The study mainly serves as a warning signal, but also opens doors for further research aimed at harnessing the potential of gene editing while minimizing unintended consequences," Claudia concludes.

More information: Keyi Geng et al, Intrinsic deletion at 10q23.31, including thePTENgene locus, is aggravated upon CRISPR-Cas9–mediated genome engineering in HAP1 cells mimicking cancer

profiles, *Life Science Alliance* (2023). DOI: 10.26508/lsa.202302128