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# Nanobyte

With all the excitement around the promise of the CRISPR-Cas9 genome editing tool, and justifiably, the rush to move ahead with it in the clinic, it comes as no surprise that things are not as simple as one would have imagined. CRISPR-Cas9 induces a p53 response, as was recently reported in back-to-back research papers published in Nature Medicine.[1,2] The involvement of an all-too-familiar molecule, p53, makes the CRISPR story even more fascinating. The molecular oncology community has studied p53 meticulously since its initial discovery in 1979 when it was thought to actually be an oncogene.[3] A decade later, following an observation of loss of p53 from a chromosome of Li-Fraumeni syndrome patients, its' function as a tumor suppressor was identified, and numerous subsequent studies have uncovered its' mechanism and involvement across cell and molecular biology.[4] Thus, to a molecular oncologist, the involvement of p53 in curtailing the apparent meddling by a gene-editing system such as CRISPR-Cas9 would be consistent with the natural history of p53 in the management of cell death and survival. The recent report by Haapaniemi *et al*.[1] shows that p53 is upregulated in immortalized retinal pigment epithelial cells that have been subjected to CRISPR-Cas9 genome editing, provoking a DNA damage response, and cell cycle arrest. Cells that manage to be successfully edited may either contain endogenous defective p53 or thrive under suppression of p53 function. However, concerns have been raised that cells with compromised p53, even temporarily, could now pose a risk of developing cancer in the future owing to increased vulnerability to mutations. The second research report by Ihry *et al*. in the same issue of Nature Medicine showed that genome engineering of human pluripotent stem cells was inefficient owing to a toxicity of engineered cells and that this toxicity was p53 dependent.[2] Clearly, more research is warranted to find a way for this powerful technology to be used safely in the clinic. As with most serendipitous observations and unintended consequences, there may be a silver lining. Gene editing provoking a DNA damage response might be a line of research to be carried further in the field of cancer therapeutics. In an age when rapid solutions and instantaneous cures are coveted and valued over slower and time-tested research methodology and carefully designed clinical studies, such setbacks will not be uncommon. In the meantime, we await more detailed molecular mechanisms and watch as the gene therapy story unfolds. CRISPR-Cas9 will undoubtedly continue to remain a powerful *in vitro* diagnostic and research tool for molecular oncologists.[5]

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## References

1. Haapaniemi E, Botla S, Persson J, Schmierer B, Taipale J. CRISPR-cas9 genome editing induces a p53-mediated DNA damage response. Nat Med 2018. DOI: 10.1038/s41591-018-0049-z.
2. Ihry RJ, Worringer KA, Salick MR, Frias E, Ho D, Theriault K, *et al.* P53 inhibits CRISPR-cas9 engineering in human pluripotent stem cells. Nat Med 2018. DOI: 10.1038/s41591-018-0050-6.
3. Lane DP. Crawford LV. T antigen is bound to a host protein in SV40-transformed cells. Nature 1979;278:261-3.
4. Marcel V, Van Long F, Diaz JJ. 40 years of research Put p53 in translation. Cancers 2018;10:152.
5. Vaishnav RA. The emerging role of CRISPR-Cas9 in molecular oncology. Int J Mol Immuno Oncol 2017;2:45-6.

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