The double-edge sword of CRISPR application for in vivo studies

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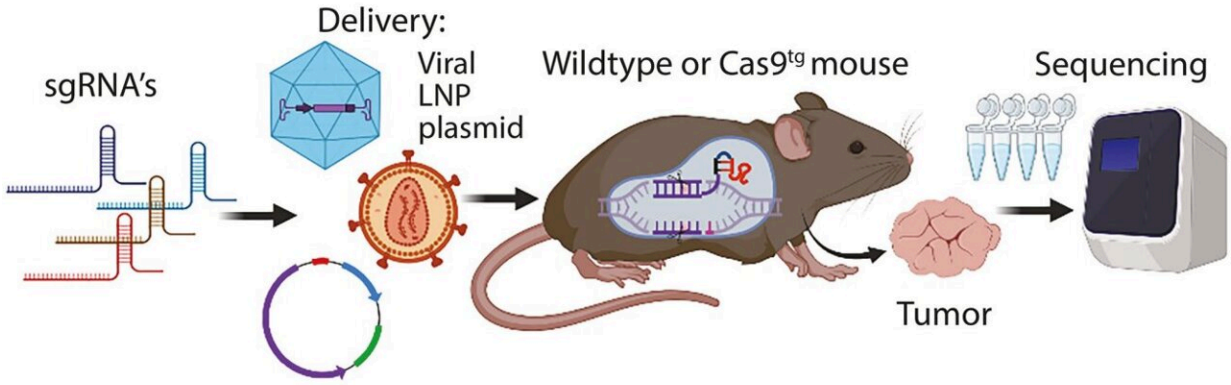

Workflow illustration. Credit: *Oncotarget* (2023). DOI: 10.18632/oncotarget.28459

A new editorial paper titled "The double-edge sword of CRISPR application for in vivo studies" has been published in*Oncotarget*.

In this new paper, researcher Martin K. Thomsen from Aarhus University begins his editorial by discussing a hallmark paper that was published a decade ago by Platt et al. on the in vivo application of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) to generate cancer in different organs of mice.

This hallmark paper outlines the advancement of delivering sgRNAs to

the target tissue to create loss or gain of function mutations without the need for timely intercrossing of genetic mouse strains. Furthermore, the study showed that multiplexing was possible, thereby enabling the method to target multiple sites simultaneously. It was foreseen that this technology would change the way mouse models of cancer were generated, but even after 10 years, only few studies have relied on this methodology.

"The double-edged sword of in vivo application of CRISPR is the imperfection of mutations generated in the target sequence," Thomsen writes.

As CRISPR introduces mutations, they do not always occur, resulting in cells being present without the desired mutation. This is further complicated by the different types of indels, which can result in a functional protein with only changes in a few amino acids, without the introduction of a premature stop codon. This introduces clone-to-clone variation and results in tumors with a different mutation profile. However, this is also an advantage of CRISPR for generating in vivo cancer models, as natural selection will occur, resulting in a cancer Darwinian evolution.

"Altogether, the in vivo application of CRISPR will become more common, even though the technique has challenges, it will only become more feasible in the future, allowing more researchers to apply this technology," concludes Thomsen.

More information: Martin K. Thomsen, The double-edge sword of CRISPR application for in vivo studies, *Oncotarget* (2023). DOI: 10.18632/oncotarget.28459