

Title

Base Editor Scanning to Identify Functionally Essential Amino Acids in 'Undruggable' Anti-Cancer Phosphatases

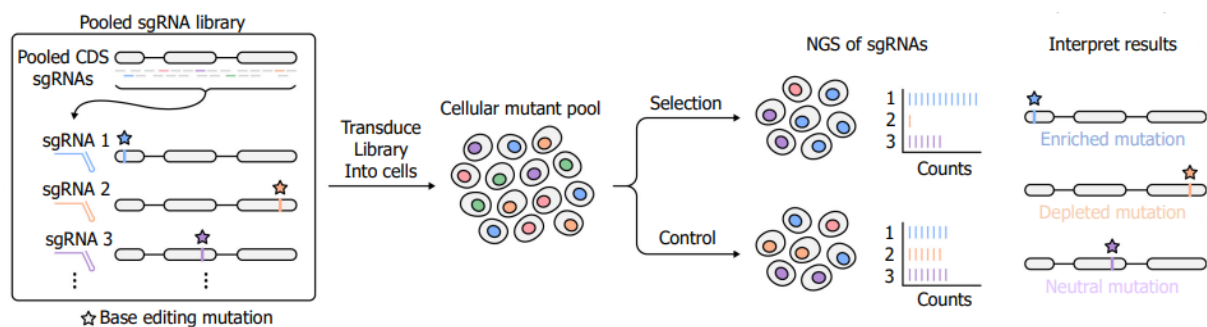
Authors

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Poster presentation

CRISPR/Cas9 knock-out (KO) screens are instrumental to determine protein-disease relationships but lack resolution beyond protein level to dissect sequence-function relationships within proteins of interest. CRISPR/Cas9 base editing has emerged as powerful gene editing tool with the ability to induce targeted and predictable point mutations with high efficiency and scalability. Recent work has shown that base editors can be readily used in pooled genetic screens, mutationally scanning over proteins of interest with amino acid-level resolution. Here, we propose to employ base editor scanning to identify functionally essential amino acids in 'undruggable' anti-cancer phosphatases, providing rational starting points for the development of drugs with an innovative mode of action.

Figure



References

1. Lue, N.Z., et al., *Base editor screens for in situ mutational scanning at scale*. *Molecular Cell*, 2023. **83**(13): p. 2167-2187.
2. Garcia, E. M., et al., *Base editor scanning reveals activating mutations of DNMT3A*. *ACS chemical biology*, 2023. **18**(9): p. 2030-2038.
3. Li, H., et al., *Assigning functionality to cysteines by base editing of cancer dependency genes*. *Nature chemical biology*, 2023. **19**(11): p. 1320-1330.