

CRISPR screening

CRISPR screening is a large-scale **experimental** approach used to screen a **population** of mutant cells to discover genes involved in a specific **phenotype**. Instead of repressing genes at the post-transcriptional level, CRISPR introduces mutations to genes that render them nonfunctional.

Immunotherapy has transformed **cancer treatments**; however, a large fraction of **patients** encounter **resistance**. Such resistance is mediated by complex factors, often involving interactions between multiple **genes**. Thus, it is crucially important to identify genetic interactions between genes that are significantly mutated in cancer patients and those involved in **immune responses**, ideally the ones that currently have chemical compounds for direct targeting. To systematically interrogate such genetic interactions that mediate cancer cells' response to **T cell** killing, Park et al. designed an asymmetric dual perturbation **library** targeting the matched combinations between significantly mutated **tumor suppressors** and immune resistance genes. They performed a combinatorial double **knockout** screen on 1159 gene pairs and identified those where joint loss-of-function renders altered cellular response to **T cell cytotoxicity**. They also performed comparative transcriptomics-based analyses on tumor and normal samples from TCGA and GTEx cohorts, mutational profiling analyses, and **survival analysis** to further characterize the significance of identified hits in clinical patients. Interactions between significantly mutated tumor suppressors and potentially druggable **immune resistance** genes may offer insights on potential new concepts of how to target clinically relevant cancer mutations with currently available agents ¹⁾

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Park JJ, Codina A, Ye L, Lam S, Guo J, Clark P, Zhou X, Peng L, Chen S. Double knockout CRISPR screen for cancer resistance to T cell **cytotoxicity**. J Hematol Oncol. 2022 Dec 1;15(1):172. doi: 10.1186/s13045-022-01389-y. PMID: 36456981.

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