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Functional Genomics to Guide Cancer Therapy
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TITLE: Functional genomics to guide cancer therapy

ABSTRACT: The benefit of cancer therapeutics is frequently limited to small groups of patients. Moreover, this benefit is often short-lived, due to the rapid development of resistance to drug action. Thus, understanding resistance mechanisms will help to optimize treatment options for patients to overcome drug resistance. Using unbiased genetic tools that allow us to manipulate the expression of many different genes in cancer cells, we aim to systematically uncover the molecular pathways that confer resistance to targeted cancer therapies.

Genotype-directed anticancer drugs often target the gain-of-function oncogenic mutations. Since loss of tumour suppressors is not directly targetable, “synthetic lethality” is often employed to derive cancer-specific therapies that have minimal side effects in normal tissue. In this context, we use customized druggable gene-family shRNA/CRISPR libraries and compound collections to identify actionable targets whose inhibition is synthetic lethal with the driver mutations in the cancer types of interests. Our goals are to provide effective treatment strategies and result in clinical benefit for cancer patients.

Our examples of using different functional genomic tools to study cancer-relevant pathways will be discussed.