Harnessing synthetic lethal interactions for personalized medicine

Grace S. Shieh1,2,3,4*

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1 Institute of Statistical Science, Academia Sinica, Taipei, TAIWAN; gshieh@stat.sinica.edu.tw

2 Bioinformatics Program, Taiwan International Graduate Program, Academia Sinica, Taipei, TAIWAN

3 Genome and Systems Biology Degree Program and 4 Data Science Degree Program, Academia Sinica and National Taiwan University, Taipei, TAIWAN

* Correspondence: gshieh@stat.sinica.edu.tw
Abstract

Two genes are said to have synthetic lethal (SL) interactions if the simultaneous mutations in a cell lead to lethality, but each individual mutation does not. Targeting SL partners of mutated cancer genes can kill cancer cells, but leave normal cells intact. The applicability of translating this concept into clinics has been demonstrated by three drugs that have been approved by the FDA to target PARP for tumors bearing mutations in BRCA1/2. This article reviews applications of the SL concept to translational cancer medicine over the past five years. Topics are (1) exploiting the SL concept for drug combinations to circumvent tumor resistance, (2) using synthetic lethality to identify prognostic and predictive biomarkers, (3) applying SL interactions to stratify patients for targeted and immunotherapy, and (4) discussions on challenges and future directions.

Keywords: biomarker; cancer; genetic interaction; precision medicine; synthetic lethal