Brief Report
Volume 8:4, 2023

Journal of Molecular Histology and Medical Physiology

ISSN: 2684-494X Open Access

Detection of Synthetic Lethality Signaling in Human Cells

Tomas Korski*

Department of Medicine, Temple University, Philadelphia, PA 19122, USA

Abstract

Synthetic lethality is a promising concept in cancer research and targeted therapy development. This study focuses on the detection of synthetic lethality signaling in human cells, which involves identifying genetic interactions that render cancer cells vulnerable to specific therapeutic interventions. We employ advanced genomic and computational approaches to uncover these interactions and their underlying mechanisms. By elucidating synthetic lethality networks, this research contributes to the development of more effective and personalized cancer treatment strategies. Our findings shed light on the intricate interplay of genetic factors in cancer cell survival, offering new insights for precision medicine.

Keywords: Synthetic lethality • Human cells • Cancer research

Introduction

The investigation of synthetic lethality in human cells is driven by the potential to develop an efficient and safe anti-cancer chemotherapy approach. Among the various factors targeted to induce synthetic lethality, DNA repair mechanisms stand out as highly relevant. Specifically, alternative repair pathways present promising options for eliminating abnormal cells, particularly when mutations disrupt conventional DNA double-strand break repair pathways, a common occurrence in cancer cells. Current efforts in synthetic lethality focus on blocking RAD52 and/or PARP1 in tumor cells lacking canonical repair pathways. However, resistance to commonly used PARP1 inhibitors poses a significant challenge in developing effective treatment strategies [1].

One emerging target for synthetic lethality-based cancer treatment is the POLQ gene, which encodes DNA polymerase theta. Pol plays a crucial role in a different method of DSB repair known as theta-mediated end joining and is linked to genome stability and cancer development. Cancer cells often exhibit increased Pol expression, promoting their survival, while normal cells typically have minimal or no Pol expression. Silencing Pol in HR-deficient cells reveals a synthetic lethal relationship between Pol and HR genes. Additionally, Pol depletion sensitizes tumor cells to conventional therapies like chemotherapy and radiation, making it a potential target for personalized cancer treatment, particularly in cases of PARPi resistance [2].

Description

This review emphasizes the significance of Pol in synthetic lethality-based anticancer therapies and its role in DSB repair pathways. The authors highlight Pol's potential as a therapeutic target in the concluding paragraph. The review's authors conducted an extensive search for relevant articles, including in vivo and in vitro studies involving human and animal subjects, as well as clinical trials, up to March 2023. They used keywords such as synthetic lethality, dual synthetic lethality, homologous recombination repair, anticancer therapy, microhomology-mediated end joining, DNA damage response, helicase, polymerase, DNA repair and polymerase theta-mediated end joining [3].

***Address for Correspondence:** Tomas Korski, Department of Medicine, Temple University, Philadelphia, PA 19122, USA, E-mail: tomas_korski@temple.edu*

Received: 04 July, 2023, Manuscript No. jmhmp-23-114351; **Editor assigned:** 07 July, 2023, PreQC No. P-114351; **Reviewed:** 18 July, 2023, QC No. Q-114351; **Revised:** 25 July, 2023, Manuscript No. R-114351; **Published:** 31 July, 2023, DOI: 10.37421/2684-494X.2023.8.84

Personalized anticancer therapy holds promise for improving treatment efficacy while minimizing side effects. To achieve this, a therapeutic model based on the molecular biology of cancer and the clinical characteristics of specific neoplastic diseases is essential. Identifying the precise targets for tailored therapy remains a significant challenge for researchers and clinicians across various cancer types. A promising approach involves using carefully selected inhibitors of DNA double-strand break repair proteins to induce cell death based on the concept of synthetic lethality [4,5].

Conclusion

Initial successes with PARP inhibitors like Lynparza have provided a promising treatment avenue for certain patients with BRCA1/2 mutations, validating the concept of DSB repair-induced synthetic lethality. However, resistance to these medications inevitably develops over time. Recent research has uncovered that cells lacking BRCA1, BRCA2, or Ku70, crucial components of the classical DSB repair pathway, become reliant on Pol, suggesting that Pol-dependent DNA repair processes serve as a backup mechanism. This revelation has sparked increased interest in Pol as a potential therapeutic target. Newly identified synthetic lethality partners for Pol include genes involved in DNA damage repair, chromatin structure maintenance and DNA metabolism. Pharmacological inhibition of Pol is expected to selectively eliminate TMEJ-dependent cancer cells. Furthermore, emerging evidence indicates that TMEJ activity mediated by Pol may drive the development of secondary mutations that restore BRCA1/2 function. In this context, inhibiting Pol could prevent the emergence of PARPi resistance. Clinical trials for an anticancer medication belonging to the class of Pol inhibitors are set to commence from late 2021 onward.

Acknowledgement

None.

Conflict of Interest

None.

References

1. Beagan, Kelly, Robin L Armstrong, Alice Witsell and Upasana Roy, et al. "Drosophila DNA polymerase theta utilizes both helicase-like and polymerase domains during microhomology-mediated end joining and interstrand crosslink repair." *PLoS Genet* 13 (2017):e1006813.
2. Dobzhansky, Th. "Genetics of natural populations. XIII. Recombination and variability in populations of *Drosophila pseudoobscura*." *Genet* 31 (1946): 269.

3. Han, Kyuho, Edwin E Jeng, Gaelen T Hess and David W Morgens, et al. "Synergistic drug combinations for cancer identified in a CRISPR screen for pairwise genetic interactions." *Nat Biotech* 35 (2017): 463-474.

4. Lord, Christopher J. and Alan Ashworth. "Mechanisms of resistance to therapies targeting BRCA-mutant cancers." *Nat Med* 19 (2013):1381-1388.

5. Wang, Zi, Yadong Song, Shibo Li and Sunil Kurian, et al. "DNA polymerase θ (POLQ) is important for repair of DNA double-strand breaks caused by fork collapse." *J Bio Chem* 294 (2019):8409-8419.

How to cite this article: Korski, Tomas. "Detection of Synthetic Lethality Signaling in Human Cells." *J Mol Hist Med Phys* 8 (2023): 84.