TOXICOLOGY AND FORENSIC MEDICINE

Openventio PUBLISHERS

ISSN 2474-8978 Open Journal http://dx.doi.org/10.17140/TFMOJ-1-e005

Editorial

Corresponding author
Rehan Khan, MSc, PhD
Scientist-B
Institute of Nano Science and Technology (INST)
Habitat Centre, Phase X
Mohali-160062, Punjab, India
E-mail: rehankhan@inst.ac.in

Volume 1 : Issue 1
Article Ref. #: 1000TFMOJ1e005

Article History
Received: August 24th, 2016
Accepted: August 24th, 2016
Published: August 24th, 2016

Citation
Gupta A, Ahmad A, Dar AQ, Bhatt A, Khan R. Selective targeting of cancer cells using personalized nanomedicine. *Toxicol Forensic Med Open J*. 2016; 1(1): e12-e13. doi: 10.17140/TFMOJ-1-e005

Selective Targeting of Cancer Cells using Personalized Nanomedicine

Anuradha Gupta, PhD; Anas Ahmad, MS (Pharm); Aqib Iqbal Dar, MSc; Aashish Bhatt, MSc; Rehan Khan, MSc, PhD*

Institute of Nano Science and Technology (INST), Habitat Centre, Phase X, Mohali-160062, Punjab, India

Cancer is mostly caused by genetic alteration in either of gain of function and/or loss of function in response to mutagens, ionizing radiations etc. Synthetic lethality raised as an exciting new avenue to kill cancer cells by identifying potential druggable targets. Synthetic lethality define as a lethal interaction between two separate viable mutations when present together within a cell results in cell death, while mutation is only in either of the genes alone, cell remains viable.[1] Therefore, synthetic lethality is a new pragmatic strategy for the selective killing of cancer cells by exploring and targeting the synthetic lethal interactors of cancer cell's specific vulnerabilities like chromosomal instability (CIN) phenotype. Mutation in CIN genes leads chromosomal aberrations (aneuploidy by gene amplification, chromosomal translocation) and deoxyribonucleic acid (DNA) mutations leads to single/double strand break that are repaired by non-homologous end joining (NHEJ) resulting in accumulation of errors, leads to genomic instability, the hallmark of cancer.[2]

The sequencing of first human genome in 2000 gave a new track to understand the differences arises among individuals in response to harmful agent's exposure and in treatment outcome called as Pharmacogenetics and Pharmacogenomics.[3,4] Personalized medicine is the tailored treatment based on genetic constitution of a person responsible for individual variably in drug response and treatment outcome.[5] Nanotechnology based approaches helped in delivering drugs emerged based on synthetic lethal interaction. Nanotechnology offered the advantage of targeted drug delivery, reducing drug dose and dosage frequency and reducing systemic drug exposure thus limiting side effects and overcoming drug resistance.[6,7] The major breakthrough in the development of personalized medicine is the application of nano-approach to synthetic lethality to target mutated cancer cells with no harm to normal cells. This approach will help in increasing the effectiveness of treatment, preventing the development of metastasis of cancer cells and reducing adverse effects to healthy tissues.

To effectively kill the cancer cell, there is a need to refine and combine various therapeutic choices for the development of a personalized combination regimen depending upon the need of individual patient. To improve the clinical activity of dasatinib (tyrosine kinase inhibitor of src-family kinases) for epithelial ovarian cancer (EOC) it was given in combination with CX-4945 (CDK2 inhibitor) and increased apoptosis with reduced cell proliferation was observed across multiple EOC cell lines.[8] Three different block co-polymers, polycaprolactone, polyethylene glycol and poly-2-aminoethyl ethylene phosphate, self-assembled to formed nano-micelles for carrying PLK-1 siRNA (siPLK1) and paclitaxel and was given systemically to MDA-MB-435 induced tumor xenograft bearing mice for synergistic cancer cell killing requiring 1000-fold less paclitaxel compared to paclitaxel monotherapy, with no side effects.[9]

Synthetic lethal interactions mediated cancer cell killing is very promising and flourishing treatment strategy that exploits the tumor cell's vulnerabilities. Poor bioavailability, toxicity issues, emergence of drug resistant cases, and the presence of multiple survival pathways are the multi-factors that are leading to introduction of nanotechnology for synthetic lethal application and will lead to success as a targeted therapies. Identifying synergistic killing potential of SL interaction with radiotherapy and theranostics is also under progress. Overall,

ISSN 2474-8978 Open Journal http://dx.doi.org/10.17140/TFMOJ-1-e005

nanoformulations mediated synthetic lethal killing of cancer cells with siRNA or chemical inhibitor will lead to a way towards personalized nanomedicine with great success.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. van Pel DM, Barrett IJ, Shimizu Y, et al. An evolutionarily conserved synthetic lethal interaction network identifies FEN1 as a broad-spectrum target for anticancer therapeutic development. *PLoS Genet.* 2013; 9(1): e1003254. doi: 10.1371/journal.pgen.1003254

2. Bakhoum SF, Compton DA. Chromosomal instability and cancer: A complex relationship with therapeutic potential. *J Clin Invest.* 2012; 122(4): 1138-1143. doi: 10.1172/JCI59954

3. Ansari M, Krajinovic M. Pharmacogenomics in cancer treatment defining genetic bases for inter-individual differences in responses to chemotherapy. *Curr Opin Pediatr.* 2007; 19(1): 15-22. doi: 10.1097/MOP.0b013e3280140613

4. Weng L, Zhang L, Peng Y, Huang RS. Pharmacogenetics and pharmacogenomics: A bridge to individualized cancer therapy. *Pharmacogenomics*. 2013; 14(3): 315-324. doi: 10.2217/pgs.12.213

5. Cho S-H, Jeon J, Kim SI. Personalized medicine in breast cancer: A systematic review. *J Breast Cancer.* 2012; 15(3): 265-272. doi: 10.4048/jbc.2012.15.3.265

6. Minko T, Rodriguez-Rodriguez L, Pozharov V. Nanotechnology approaches for personalized treatment of multidrug resistant cancers. *Adv Drug Deliv Rev*. 2013; 65(13): 1880-1895. doi: 10.1016/j.addr.2013.09.017

7. Markman JL, Rekechenetskiy A, Holler E, Ljubimova JY. Nanomedicine therapeutic approaches to overcome cancer drug resistance. *Adv Drug Deliv Rev.* 2013; 65(13): 1866-1879. doi: 10.1016/j.addr.2013.09.019

8. Pathak HB, Zhou Y, Sethi G, et al. A synthetic lethality screen using a focused siRNA library to identify sensitizers to dasatinib therapy for the treatment of epithelial ovarian cancer. *PLoS One.* 2015; 10(12): e0144126. doi: 10.1371/journal.pone.0144126

9. Sun T-M, Du JZ, Yao YD, et al. Simultaneous delivery of siRNA and paclitaxel via a "two-in-one" micelleplex promotes synergistic tumor suppression. *ACS Nano.* 2011; 5(2): 1483-1494. doi: 10.1021/nn103349h