Short Communication

iMedPub Journals
www.imedpub.com

British Biomedical Bulletin
ISSN 2347-5447

2021
Vol. 9 No. 3:14

Hydralazine and Panobinostat Attenuate Malignant Properties of Prostate Cancer Cell Lines

Yashika Jindal*

Department of Biotechnology, Meerut Institute of Engineering and Technology, Meerut, U.P, India

*Corresponding author: Yashika Jindal

jindalyashika59@gmail.com

Department of Biotechnology, Meerut Institute of Engineering and Technology, Meerut, U.P, India.

Citation: Jindal Y (2021) Hydralazine and Panobinostat Attenuate Malignant Properties of Prostate Cancer Cell Lines. Br Biomed Bull Vol.9 No.3: 14.

Received: June 05, 2021, Accepted: June 15, 2021, Published: June 25, 2021

Introduction

Prostate Cancer (PCa) is the second most common cancer among men and the fifth greatest cause of cancer related mortality globally. More than 80% of PCa cases are currently diagnosed as localised disease, but up to a third of these patients will later recur and develop. Because androgens and Androgen Receptor (AR) signalling are so critical in normal prostate development and PCa progression, Androgen Deprivation Therapy (ADT) is the most common treatment for advanced PCa. Despite an initial response to ADT, individuals frequently develop resistant and advance to an aggressive disease state known as Castration-Resistant Pca (CRPC) between 12 to 30 months. Despite the fact that treatment with next generation androgen signalling inhibitors has improved the outcome, these patients still lack curative medicines, necessitating the urgent development of novel therapeutic techniques [1].

The molecular pathways that lead to the development of CRPC are numerous and intricate. Epigenetic dysregulation has been widely proven as a major component in PCa, as it has been in other cancer forms. DNA Methyltransferases Inhibitors (DNMTis) may re-sensitize malignant cells to antineoplastic drugs by preventing gene silencing, which contributes to ADT resistance. Changes in specific histone marks, on the other hand, define the epigenetic profile of PCa, affecting essential signalling pathways and transcriptional control, and contributing to prostate cancer [2]. In prostate cells, Histone Deacetylases (HDAC) controls a number of genes, including AR. Furthermore, HDAC Inhibitors (HDACis) prevent histone deacetylation, resulting in a more open chromatin structure, allowing for DNA access and, as a result, the reversal of epigenetically silenced genes by DNMTis.

As a result of their impact on histone alterations, HDACis are being studied in CRPC and chemotherapy-resistant PCa patients. Although the intrinsic toxicity of DNMTis and HDACis in clinical studies did not justify their use as single agents for the treatment of CRPC, results in pancreatic, lung, and breast cancer models suggest that utilising both epidrugs at the same time is more effective than using each epidrug separately.

The Food and Drug Administration (FDA) has approved two epigenetic medications that target DNA Methyltransferases (DNMT) and four epigenetic treatments that target HDAC so far. Recently, cedazuridine, a combination of a DNMTi and a cytidine deaminase inhibitor, was licenced for the treatment of myelodysplastic syndromes and chronic myelomonocytic leukaemia. Although DNMTis and HDACis are only licenced for haematological malignancies, multiple solid tumour clinical trials are now underway. 5-azacytidine (5-Aza-CR) and (5-Aza-CdR), both FDA-approved DNMT inhibitors, are nucleoside analogues that are integrated into DNA and demethylate DNMTs by covalently sequestering them [3]. However, because this inclusion is dependent on DNA replication, it has a stronger effect in proliferative tumours than indolent tumours. PCa fits into the second type, which could explain why clinical trials utilising 5-Aza-CR for CRPC found no substantial patient benefit.

Hydralazine hydrochloride, a medicine licenced by the FDA for the treatment of severe hypertension and heart failure, has been studied as a cancer treatment. In cancer cell lines and real tumours, several *in vitro* investigations showed that hydralazine has DNMTi capabilities and can restore the expression of Tumour Suppressor Genes (TSG) repressed by promoter hypermethylation without causing significant cytotoxicity. Hydralazine is a non-nucleoside analogue that targets the catalytic region of DNMT1A and DNMT3A/3B without incorporating itself into DNA. The efficacy of hydralazine has already been proven in clinical trials for solid tumours such as cervical, breast, lung, and ovarian cancer. Almost all of the clinical trials described earlier used hydralazine in combination with valproic acid, a treatment method that boosted therapy efficacy *in vitro* while also causing TSG reactivation. Valproic acid is an antiepileptic medicine that is also used to treat bipolar disorder. It is a short chain fatty acid inhibitor.

In addition, HDAC inhibition has been demonstrated to impact critical pathways including as cell cycle arrest, apoptosis, angiogenesis, and senescence in both *in vitro* and *in vivo* PCa models. Panobinostat is a panHDACi that has shown anti-tumor activity in many cell lines and xenograft models. It is approved for the treatment of multiple myeloma. Panobinostat's ability to be used at low and manageable doses makes it an appealing candidate for usage in combination with other anti-tumor drugs. As DNMTs are known to be elevated in PCa, we predicted that epidrugs could be an effective treatment for advanced PCa patients. The DNMTi hydralazine (Hydra), as well as the HDACis panobinostat (Pano) and valproic acid, were the focus of the research As a result, we wanted to see how effective these epigenetic medicines could be on their own or in combination with other treatments in PCa cell lines. To the best of our knowledge, this is the first study to look at the effects of hydralazine and panobinostat together in human PCa cells [4].

References

1. Sung, H, Ferlay, J, Siegel RL, Laversanne M, Soerjomataram I, et al. (2021) Global Cancer Statistics 2020: GLOBOCAN Estimates of incidence and mortality worldwide for 36 Cancers in 185 Countries. CA Cancer J. Clin. 71, 209-249.
2. Ceder Y, Bjartell A, Culig Z, Rubin MA, Tomlins S, et al. (2016) The molecular evolution of castration-resistant prostate cancer. Eur. Urol. Focus 2, 506-513.
3. Graça I, Sousa EJ, Costa Pinheiro P, Vieira FQ, Torres Ferreira J, et al. (2014) Anti-neoplastic properties of hydralazine in prostate cancer. Oncotarget 5, 5950-5964.
4. Yegnasubramanian S, De Marzo AM, Nelson WG (2019) Prostate cancer epigenetics: From basic mechanisms to clinical implications. Cold Spring Harb. Perspect. Med. 9, a030445.