Proceedings International
Platinum Open Access Journal (ISSN 2668-6384)

Proceedings, Abstract
Volume 5, Issue 1, 2023, 37
https://doi.org/10.33263/Proceedings51.037

The Effect of *In vitro* Procaine Treatment on Histone Lysine Demethylases Profile †

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† Presented at 2nd Edition of the OncoHub Conference – Connecting Scientists and Physicians for Next Generation Cancer Management, Poiana Brașov, Brașov, 21-23 September 2022

Received: 10.12.2022; Accepted: 20.12.2022; Published: 5.01.2023

Abstract: Cervical cancer is one of the most significant women's health problems worldwide, with 99.7% of cervical cancer cases being caused by persistent genital high-risk human papillomavirus (hrHPV) infection. Several epigenetic changes were identified during HPV infection in both virus and host cell genomes, including DNA methylation and histone modifications. Inhibitors targeting DNA-modifying enzymes, particularly histone-modifying ones, may represent a potential cancer treatment. This study aimed to investigate the *in vitro* impact of procaine, as an epigenetic inhibitor, on the expression pattern of 7 histone lysine demethylases (KDMs). For this study CaSki cell line (HPV16 positive) was treated with c1=0.1 mM and c2=0.5 mM procaine for 24 hours, respectively 48 hours. RNA was isolated and reverse-transcribed. The cDNA obtained was used for Real-Time PCR to quantify the expression levels of KDM1B, KDM2B, KDM3C, KDM4C, KDM5A, KDM5C, and KDM6A. β-actin was used as a housekeeping gene, and the experiment was performed in triplicate. For statistical analysis, GraphPad Prism 5.0 software was used. Analysis of histone lysine demethylase expression in procaine treatment revealed its influence in both concentrations on all studied genes, leading to a significant increase in expression compared to the untreated cells at 24 hours (KDM1B: p1=0.0001; p2=0.0001). The same trend was displayed when the higher concentration was used at 48 hours (KDM1B: p2=0.0344). For the lower concentration, after 48 hours, there was no difference in expression levels between treated and untreated cells. The balance of epigenetic enzymes could be restored in cervical cancer using epigenetic drugs. Thus, a new therapeutic approach in cervical cancer therapy could be the modulation of investigated gene expression.

Keywords: cervical cancer; procaine; KDMs.

Funding

The study was partially supported by UEFISCDI, Grant 39 TE/ 2020.

Acknowledgments

This research has no acknowledgment.

Conflicts of Interest

The authors declare no conflict of interest.