Abstract

Anticancer Effects of the Potential BET Inhibitor CBL0137 on Breast Cancer Cells †

Valeriia Popova 1,2,*, Varvara Maksimova 1, Evgeniya Lylova 1, Anzhelika Bukina 1,2,3, Marianna Yakubovskaya 1,2 and Kirill Kirsanov 1,2

1 N.N. Blokhin National Medical Research Center of Oncology, 24 Kashirskoe Shosse, 115478 Moscow, Russia; lavarvar@gmail.com (V.M.); e.e.lylova@gmail.com (E.L.); aikaprus2000@gmail.com (A.B.); nnyakubovskaya@mail.ru (M.Y.); kkirsanov85@yandex.ru (K.K.)
2 Institute of Medicine, Peoples’ Friendship University of Russia (RUDN), 6 Miklukho-Maklaya Street, 117198 Moscow, Russia
3 Department of Biotechnology and Industrial Pharmacy, Russian Technological University (MIReA), 86 Vernadsky Avenue, 119571 Moscow, Russia
* Correspondence: nuarrbio@gmail.com
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Abstract: Breast cancer (BC) is a complex disease driven by a combination of genetic mutations and epigenetic modifications. In particular, the overexpression of BET family proteins (BETs) has emerged as a key epigenetic aberration contributing to BC pathogenesis. CBL0137 (CBL), a small-molecule compound, has shown promise as an inhibitor of BETs in HeLa TI cells. In this study, we aimed to assess the anticancer effects of CBL in vitro and evaluate its impact on the expression of BETs in BC cells. Cells of three subtypes of BC (MCF7, MDA-MB-231, SKBR3) were used in this study. Cytotoxic effects were analyzed using the MTT assay. Effects on cell cycle and apoptosis were assessed using FACS with PI and FITC-Annexin staining. The level of BETs (BRD2, BRD3, BRD4) was determined by Western blotting. CBL demonstrated a significant reduction in BC cell viability with an IC50 value of approximately 1 µM for all cell lines after 72h of exposure and 20 µM after 24h. CBL treatment resulted in an increase in cells in the G2/M phase in MCF7 and SKBR3 cells after 24h and 72h of action, as well as in MDA-MB-231 cells after 24h. In MCF7 cells, the influence of CBL led to apoptotic changes characterized by a slight elevation in the early apoptotic population. Treatment of MDA-MB-231 cells with CBL resulted in a decrease in the expression of BRD2, BRD3, and BRD4 proteins, while treatment of MCF7 cells led to a reduction in BRD2 and BRD4 protein levels. No significant changes in the amount of BET proteins were observed in SKBR3 cells. In conclusion, the presented data offer valuable insights into the mechanisms of action of CBL, providing a basis for further investigation into its therapeutic potential in BC treatment. This research was funded by the RSF (no. 21-75-10163).

Keywords: CBL0137; Breast cancer; BETs

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