Valproic Acid Negatively Regulated CD44 and BMI1 Expression in Stemâ€“like Cancer Cells

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Abstract

Cancer therapy is still very challenging since current modalities are not effective enough to eradicate chemoradiotherapy resistance and metastatic cancer cells. Valproic acid (VPA) is a short chain fatty acid with histone deacetylase-inhibiting effects that has been examined as an anticancer agent in several clinical trials. However, little is known about VPA effects on unique properties of cancer stem cell (CSCs). Therefore, the aim of present study was to investigate VPA effects on the expression of BMI1 and CD44, which have been introduced as CSC markers in gastrointestinal malignancies. In present study, KYSE30 cells, which are esophageal stem-like cancer cells positive for BMI1 and CD44, were treated with 2.5 and 5 mM VPA for 48 and 72h. Then, the total cellular RNA was extracted, and cDNAs were synthesized by M-MuLV reverse transcriptase. For quantitative RT-PCR, SYBR green master mix was used and PCR efficiencies were calculated for both BMI1 and CD44 primers. To note, normalized values were plotted as relative fold change over untreated cells, and fold change expression was calculated as 2(-Î”Î”CT). Quantitative RT-PCR results indicated that VPA significantly downregulated the expression of CSC markers in KYSE30 cells. Interestingly, in comparison with 5 mM VPA, treating cells with 2.5 mM VPA decreased the expression of BMI1 and CD44 to lower levels; after 48 and 72h, BMI1expression was calculated as 0.11 Â± 0.02 and 0.08 Â± 0.01, respectively, and CD44 expression decreased to 0.4 Â± 0.03 and 0.25 Â± 0.03, respectively. KYSE30 cells present a suitable model for studying effects of anticancer agents on stem-like cancer cells. Our results indicated that VPA has negative regulatory effects on the expression of CSC markers. However, more research is needed to understand whether VPA has similar effects on other CSC molecules, such as ALDH1, EpCAM and LGR5.

Keywords: Valproic Acid, Stem-like Cancer Cells, BMI1, CD44, Quantitative RT-PCR

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