

Valproic acid: Growth inhibition of head and neck cancer by induction of terminal differentiation and senescence

Abstract

Background: There are limited studies on the effects of drugs that modulate epigenetic regulation for head and neck squamous cell carcinoma (HNSCC). This study determined the effect of valproic acid (VPA) on HNSCC. Methods: Growth inhibition effects of VPA alone or in combination with 5-aza-2'deoxycytidine (5-aza-dC) or all-trans retinoic acid (ATRA) was evaluated with MTT and clonogenic assays on 5 HNSCC cell lines. The mechanism of growth inhibition was investigated by looking at markers of terminal differentiation and senescence. Results: Growth inhibition profiles of HNSCC cell lines varied in response to VPA. Inhibition of clonogenic survival in response to VPA was associated with an upregulation of p21, expression of terminal differentiation markers, and cellular senescence. Notably, a combination treatment of 5-Aza-dC-VPA-ATRA enhanced growth inhibition in cells resistant to VPA. Conclusion: VPA is a potent inhibitor of proliferation in some HNSCC cell lines, and may be used to treat HNSCC. © 2011 Wiley Periodicals, Inc.

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