Violacein Induces Specific Alterations in Hyaluronic Acid Metabolism in Chronic Myeloid Leukemias

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The abnormal production and degradation of hyaluronic acid (HA) by hyaluronidases have been shown to contribute to malignancy by signaling through its receptors, such as CD44. In some types of leukemias, the interaction of HA with its receptors reduces drug-induced apoptosis. Herein, the effects of the antileukemic agent violacein on hyaluronic acid synthases (HAS) and hyaluronidases (HYAL) gene expression, as well as in HYAL activity and HA production, in chronic myeloid leukemias (K562 and its MDR-resistant variant Lucena) were studied. HYAL activity and HA quantification were measured by an ELISA-like method. Gene expression was assessed by qPRC after violacein cell treatment. We observed an increased expression of HAS III in Lucena than in K562 cells. The same levels of HAS I were expressed by these cell lines, while HAS II was not detected. Violacein treatment decreased HAS I and II expression in both cells. Higher levels of HYAL II and III were demonstrated in Lucena cells, whereas HYAL I expression was lower when compared to K562. After treatment, HYAL I increased only in Lucena cells and the expression of HYAL II decreased in both cells. A higher activity of HYAL was observed in the conditioned medium of Lucena cells, which is consistent with the presence of HA only in the cellular fraction. Moreover, cellular HA decreased after treatment with violacein in both cell lines. Collectively, these results indicate that violacein treatment induces alterations in AH metabolism that may impact leukemogenesis.

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