CYTOTOXIC AND ANTIMIGRATORY EFFECT OF THE INHIBITION OF SPlicing REGULATORY SRPKs IN SKIN METASTATIC MELANOMA CELLS

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The dysregulation in the pre-mRNA splicing machinery activity has been linked to the development of several diseases, including cancer. The serine arginine-rich protein kinases (SRPKs) regulate alternative splicing events by phosphorylating the splicing factors known as SR proteins, which, in turn, help to assemble the spliceosome complex and coordinate the selection of cleavage points in pre-mRNAs. Studies have been showing that the kinases SRPK1 and SRPK2 are overexpressed in several types of tumors, which promotes dysregulation in the pattern of SR proteins phosphorylation and fosters cell phenotypes related to cancer. Thus, here we investigated the cytotoxic and antimigratory effect of inhibiting SRPKs in skin metastatic melanoma cells B16F10. MTT assays were performed to evaluate the cytotoxicity and to estimate the IC\textsubscript{50} of the compounds evaluated. Furthermore, scratch assays were performed to assess the impact of SRPKs inhibition on cell migration process. Also, morphological changes due to the pharmacological treatments were analyzed by measuring the cells length and width. We observed that the SRPKs inhibition impaired cell migration, inhibiting this process in more than 70\%. Lastly, analyzing cellular length and width, it was possible to observe clear alterations in overall cell morphology, suggesting that SRPKs might be involved in signaling events responsible for cell shape definition. Therefore, our data point that SRPKs inhibition renders antimelanoma effect and impairs metastatic cancer cell migration and overall morphology. These findings certainly yield additional evidences supporting the use of SRPKs as target to develop novel anticancer therapies.

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