Antitumor Impact Associated to Serine Arginine Protein Kinases (SRPKs) Pharmacological Inhibition in Metastatic Melanoma

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Serine/arginine-rich protein kinases (SRPKs) controls alternative splicing events by phosphorylating SR proteins, which in turn coordinate the selection of cleavage points on pre-mRNAs and help spliceosome complex assembly. Several studies have been demonstrating that SRPK1 and SRPK2 kinases are overexpressed in several tumours, which promotes deregulation on splicing pattern and leads to the development of cellular phenotypes related to carcinogenic processes. Recently, SRPK1 has been observed overexpressed in melanoma, which has been correlated to increased tumour maintenance, proliferation and aggressiveness. Then, we sought to evaluate the effects of SRPKs pharmacological inhibition in melanoma cells in vitro and in vivo. Proliferation tests with murine metastatic melanoma B16F10 cells were carried out using trypan blue in 24, 48 and 72 hours of treatment with the inhibitor SRPIN340, known to selectively inhibit SRPK1 and SRPK2. Cellular proliferation was reduced in more than 50% in these tests. Also, SRPIN340 substantially affected cell migration, adhesion and invasion of B16F10. Finally, we evaluated the effect of this inhibitor in a mouse model of metastatic melanoma. We observed that pharmacological SRPKs inhibition efficiently impacted lung metastasis in vivo. Together, these results reinforce that SRPKs would be an important therapeutic target for restraining growth and aggressiveness of metastatic melanoma.

Keywords: SRPK, melanoma, metastasis, pre-mRNA splicing, drug discovery.
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