UNCONVENTIONAL ROLE OF VEGFC AND LYMPHATIC VESSELS ON MEDULLOBLASTOMA CELL FATE

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Medulloblastoma (MB) is the most common malignant cerebellar pediatric tumor. MB is a heterogeneous pathology composed of four molecular subgroups, with variable prognoses depending on the subgroup. MB treatment includes surgical resection of the tumor, craniospinal X-ray irradiation and adjuvant chemotherapy. Despite this treatment, 30% of the patients relapse. Their progression is marked by the fatal appearance of metastases within 5 years. The major actors of metastatic dissemination are the lymphatic vessel growth factor, VEGFC, and its receptor, VEGFR3. According to the current dogma, the lymphatic network is one of the main ways of tumor cell spreading. In this work, we meant to i) correlate VEGFC expression and MB aggressiveness; ii) determine the relevance of developing therapeutic strategies targeting the VEGFC / VEGFR3 axis. We showed that VEGFC mRNA expression is inversely correlated to cell aggressiveness. VEGFC decreased proliferation and migration of MB cell lines and promoted in vitro pseudo-vessel formation by MB cells. We generated irradiation-resistant cells and demonstrated that aggressive irradiation resistant-cells presented enhanced levels of VEGFC. Moreover, they acquired the ability to form vessel-like structures. Cells ectopically overexpressing VEGFC and irradiation-resistant cells formed smaller experimental tumors in nude mice. Opposite to the common dogma, our results give strong arguments to the role of VEGFC as a negative regulator of MB growth. However, VEGFC effect as for tumor dissemination might be MB subgroup dependent. Therefore, the use of VEGFC/VEGFR3 axis inhibitors to fight these tumors has to be considered with caution.

Abstracts should be submitted no later than 1st September 2018 at:

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