

INTRINSIC OR INDUCED AGGRESSIVENESS-LINKED REGULATION OF VEGFC IN MEDULLOBLASTOMA CELL LINES

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Medulloblastoma (MDB) is the most common pediatric malignant brain tumor. MDB is a very heterogeneous disease that consists of four subgroups, each of them with different molecular profiles, metastasis status and clinical outcomes. Treatment of MDB includes surgery, radiotherapy and chemotherapy. It cures 70% of the patients nevertheless with many side effects. Relapse is always fatal. Understanding the mechanisms of this relapse might lead to the development of new targeted treatments. VEGFC and lymphatic markers are the main actors of the metastatic process in many tumors. We thus meant to determine their role and regulation in MDB-derived cells.

We demonstrated that low-aggressiveness MDB-derived cells, DAOY, expressed high basal amounts of lymphatic marker mRNAs and proteins (VEGFC, PROX1, NRP2). Conversely, highly aggressive cells, HD-MB03, presented low amounts of these markers. Chemical treatment (etoposide, carboplatin, vincristine) or X-ray irradiation of the cells induced a rise in VEGFC, at the mRNA and protein levels. We thus questioned the regulation of lymphatic markers in MDB cells. We observed that in the highly aggressive HD-MB03 cells, VEGFC mRNA amount relies upon a very active NF- κ B-dependent promoter, but that the mRNA gets intensely degraded, hence the low level of VEGFC mRNA in these cells. Conversely, Daoy cells present low activity of VEGFC promoter and high stability of the synthesized mRNA. The promoter activity is independent from NF- κ B. Moreover, while VEGFC is secreted in Daoy cells, it is retained inside the cytoplasm of HD-MB03 cells.

Since VEGFC is so precisely regulated in MDB cells, it may play an important part in MDB aggressiveness.

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

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