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Psychiatry and Neuroscience Seminar Series 2023

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(Host G Van Niel)
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Glioblastoma cells walk the line with brain vessels

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Room D Levy, 102-108 rue de la santé - 75014 Paris

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On the ground of our interests for molecular piracy exerted by tumor cells to survive, adapt and remodel their environment, we explore the signaling mechanisms involved in non-oncogene addiction and loss of vascular homeostasis. Glioblastoma multiforme (GBM) is a rare, yet devastating, primary brain tumor in adults. Current treatments remain generally ineffective and GBM almost invariably recurs, resulting in median survival of 15 months. Within GBM, exists a population of self-sustaining transformed cells with stem-like properties (GSCs), which are thought to be responsible for tumor initiation, growth, and invasion, as well as recurrence. In the tumor microenvironment, GSCs might be found in the vicinity of brain endothelial cells, which provide a protective habitat. Herein, we established an ex vivo model to explore GSC invasive behavior. We found that patient-derived cells massively invade the collagen matrix. In addition, we described that the glycoprotein Neuropilin-1 (NRP1) contributes to GSC spreading and invasion. Indeed, both RNA interference-mediated silencing and CRISPR-mediated gene editing deletion of NRP1 strongly impaired the 3D invasive properties of patient-derived GSCs and their close localization to the brain blood vessels. Of note, other typical features of GSCs, such as expansion and self-renewal were maintained. From a mechanistic standpoint, this biological effect might rely on the expression of the β3 subunit integrin cell-extracellular matrix adhesive receptor. Our data, therefore, propose a reliable approach to explore invasive properties of patient glioma cells ex vivo and identify NRP1 as a mediator in this malignant process.

Keywords:

Extracellular Vesicle, Intracellular Signaling, Trafficking, Tumor Cells

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