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NEUROTROPHINS RECEPTORS: NEW AGGRESSIVENESS MARKERS IN GLIOBLASTOMA?

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Glioblastoma (GBM) is the worst brain tumor with therapeutic resistance and recurrence due to its strong cell heterogeneity, which relies on cancer stem-like cells' presence. Tumor aggressiveness is associated to cancer cell adaptation to their environment: autophagy process enhancement, the increase of growth factors signaling such as neurotrophins (TrkB/BNNF and TrkC/NT3), microenvironment modulation by mesenchymal stem cells (MSC). The high level of hypoxia commonly encountered in GBM is counterbalanced by the tumor autophagic capability and growth factors signaling activation. We demonstrated that an increase of autophagy precedes TrkC/NT3 pathway activation in GBM cells. Enhancement of both TrkC and NT-3 followed by the increase of p38MAPK phosphorylation, suggesting the occurrence of a survival loop that was also underlined in patient's tumors. However, the double inhibition of autophagy and TrkC signaling was the only one able to bring cells apoptosis. The ability of cancer cells, to shape tumor environment through exosomes release could explain the spreading of "therapeutic resistance" to neighboring cells. The "stemness" properties loss showed in YKL-40-silenced cells can be reversed by TrkB-containing exosomes provide by native cells. This process contributes to restore cell proliferation and to promote endothelial cell activation. In a xenograft model, TrkB-depleted exosomes from YKL-40-silenced cells inhibits tumor growth *in vivo*. Our recent works showed changes in MSC behavior "aggressiveness" by the GBM cell "secretion", following irradiations suggesting a putative link with neurotrophin receptor. Our data suggest that neurotrophin and their receptors could be considered as new relevant diagnosis biomarkers and potential therapeutic targets in glioblastoma.

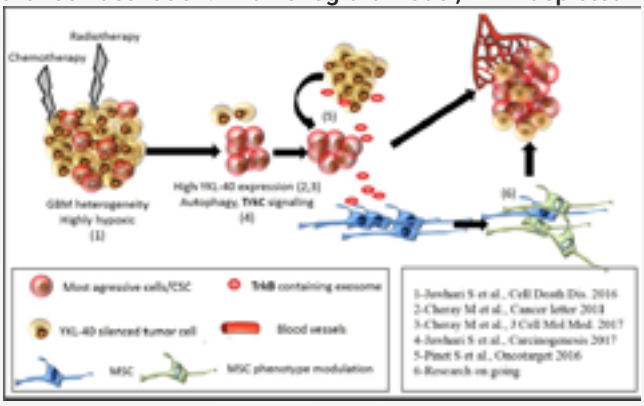

Figure: GBM aggressiveness modelization

BIOGRAPHY

Barbara Bessette received her PhD degree in Neuroscience and oncology from the University of Limoges, France in 2006. She worked one year in Paris on pediatric brain tumors and the characterization of cancer stem cells in these tumors. She followed her post-doctoral experience by collaborating and working for 3 years on GLIADYS project with IDD-Biotech (International Drug Development Biotech), specialized in monoclonal antibodies production in Lyon, France. The project consisted to develop new therapeutics for gliomas. During this project, she develops partner relationship with Oncomedics (CRO specialized in Individualized tumor response tests). She is currently a full-time assistant Professor at the University of Limoges in the Department of Physiology and she leads research into HCP-CAPTur team. Her current research activity focuses on cancer stem cells in glioblastoma and the role of neuropeptides in their therapeutic resistance capacity. One of the workpackages leaders in SUMCASTEC (H2020 European Project) she participates to determine cancer stem cell electromagnetic signature in glioblastoma and medulloblastoma.

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