Design & Application of Innovative Locoregional Treatments in Glioblastoma: Vectorization versus interventionnal tumor traps

Multidisciplinary approaches on the design and application of innovative local treatments may pave the way in understanding and overcoming resistance to treatments in solid tumors, among which glioblastoma (GB) represent a unmet medical need. Through the development of micro-nanomedicines and investigations on GB models (in vitro, ex-vivo and in vivo syngeneic or xenogeneic human to mouse & rat models), two main approaches targeting GB tumor cells infiltrated into the central nervous system are studied. i) The first combines nano-vectorised internal radiation therapy with in situ radio-sensitization. ii) The second focus on the intraoperative implantation of bio-interactive traps for the control of fate & elimination of cancer cells. We developed ^{188}Re-labelled lipid nanocpasules (^{188}Re-LNC), demonstrated their preclinical efficacy through convection-enhanced delivery, and the interest of their functionalization for targeted therapy. Automation of their syntheses, infusion in the dog model and a GLP study in rat completed the work toward appication in human. Therapeutic combinations studies allowed to assess the interest of nanovectorized RNAi interference as well as to reveal the occurrence of certains gene fusions thus providing new targeting options. With a goal to exert homing of tumor cells in a controlled and confined area before elimination through biopolymer implants, we also develop and evaluate in GB intracavitary models, in vitro 3D models and organotypic slices, interventional micro-nano traps notably releasing chemoattractant molecules. Hence, several biomedical and technological bolts concerning the in vivo behavior of new particulate vectors and the targeting of key tumor entities in GB are unlocked. New strategies to eliminate radiation-resistant cell contingents are proposed.