Temozolomide affects Extracellular Vesicles Released by Glioblastoma Cells.

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Glioblastoma multiforme (GBM) is the most aggressive primary tumour within the brain as well as the most common and lethal cerebral cancer, mainly because of treatment failure. Indeed, tumour recurrence is inevitable and fatal in a short period of time. Glioblastoma stem-like cells (GSCs) are thought to participate in tumour initiation, expansion, resistance to treatments, including to the alkylating chemotherapeutic agent temozolomide, and relapse. Here, we assessed whether extracellular vesicles (EVs) released by GSCs could disseminate factors involved in resistance mechanisms. We first characterized EVs either circulating in peripheral blood from newly diagnosed patients or released by patient-derived temozolomide-resistant GSCs. We found that EVs from both sources were mainly composed of particles homogeneous in size (50-100 nm), while they were more abundant in liquid biopsies from GBM patients, as compared to healthy donors. Further, mass spectrometry analysis from GSC-derived EVs unveiled that particles from control and temozolomide-treated cells share core components of EVs, as well as ribosome- and proteasome-associated networks. More strikingly, temozolomide treatment led to the enrichment of EVs with cargoes dedicated to cell adhesion processes. Thus, while relatively inefficient in killing GSCs in vitro, temozolomide could instead increase the release of pro-tumoral information.

KEYWORDS: Brain tumour; Exosome; Glioma; Proteomics; Temozolomide; Vesicle

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