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Identification of molecular markers in therapy-refractory glioblastoma

Nancy Berte and Ella L. Kim University Medical Center Mainz, Germany

Therapy resistance and inevitable post-treatment recurrence poses a persistant challenge for treating glioblastomas (GB). Recent advances in massively parallel sequencing have allowed to compare molecular landscapes between newly diagnosed and recurrent GBs. Previous studies have revealed that post-treatment recurrence in GBs is frequently accompanied by molecular drifts manifest by considerable differences in the levels and spectrum of genomic aberrations, gene expression patterns and epigenetic profiles. The emergence of this fundamental trait necessitates in-depth investigations into the mechanisms that underlie changes in molecular patterns after (or during) therapy. The proposed project aims to elucidate the role of glioma stem cells implicated as a key driver of post-treatment recurrence in gliomas and the most clinically relevant type of glioma cells possessing both an inherent and acquired cytotoxic resistance. Up till now, genome-wide comparisons between untreated and recurrent GB have been exclusively performed on heterogeneous GB tissues with undefined proportions of glioma stem cells. In this study, a comparative analysis of gene expression landscapes was conducted in glioma stem cells isolated from patient-matched newly diagnosed and recurrent GB or by using experimental models of radio/chemoresistant glioma stem cells. The main novelty of the proposed project lies in its focus on the specific contribution of glioma stem cells to GB recurrence under cytotoxic therapy. To our knowledge, this is the first study to address individual impacts of clinically relevant regimens of radiation and chemotherapy on gene expression patterns in glioma stem cells.

Nancy.Berte@unimedizin-mainz.de

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