Mitochondrial DNA copy number as a minimally-invasive diagnostic biomarker of gliomas

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Background: More than a hundred histologically different classes of primary central nervous system tumors were revealed, among them, we study different types of gliomas, which are glial or precursor cell-originated tumors. The primarily researched glioblastoma (WHO grade 4) is the most common malignant tumor of the central nervous system, which is fatal mainly because of the invasiveness of the tumor. Liquid biopsy is a minimally invasive technique, which might redeem the gold standard tissue biopsy method as it can be easily repeated. In the biofluids, several nucleic acids might stand as potential biomarkers in cancer diagnostics as their expression levels can vary in cancer patients.

Methods: Our goal was to characterize the copy number of the mitochondrial DNA in tissue and plasma samples of glioma patients. Exosomes were isolated from plasma samples performing precipitation (Exosome Serum/Plasma Precipitation Solution, Macherery Nagel, Düren, Germany). DNA was isolated from tissue (Quick-DNA Miniprep Plus Kit, Zymo Research, Irvine, California), plasma, and exosome samples (QIAamp DNA Blood Mini Kit, Qiagen, Hilden, Germany), and the mitochondrial DNA copy number was determined by quantitative real-time PCR (Human Mitochondrial DNA Monitoring Kit, Takara, Shiga, Japan). The results were analyzed with GraphPad Prism Program using the Mann-Whitney test and ANOVA.

Results: Altered mitochondrial DNA copy numbers were revealed in the tissue samples of glioblastoma, astrocytoma grade 2 and grade 3, oligodendroglioma grade 2 and 3 and meningioma compared to the non-tumor samples. We compared the results of the gliomas to meningioma, to determine the difference between benign and malignant intracranial tumors. We found significant differences in mitochondrial DNA copy numbers between gliomas and meningioma ($p=0.0022$). We also found mitochondrial DNA alterations in case of the plasma and exosome samples.

Conclusion: The mitochondrial DNA copy numbers were altered between patients and controls, suggesting deregulation of energy production can be associated with cancer development. Differences in mitochondrial DNA copy numbers between different types of glioma have been revealed, thereby demonstrating the potential of using mitochondrial DNA copy numbers to confirm differential diagnosis.