Mitochondrial DNA depletion and its correlation with TFAM, TFB1M, TFB2M and POLG in human diffusely infiltrating astrocytomas

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Mitochondrial mass and mitochondrial DNA (mtDNA) copy number in individual cells vary according to tissue type, and are related to internal or external factors associated with ATP demand, such as exercise, hypoxia and hormone stimulation. A significant variation of mtDNA copy number was demonstrated in several types of cancer. In humans, mtDNA is transcribed by the mitochondrial polymerase catalytic subunit-γ (p140 or POLG) and two identical accessory subunits (p55 or POLG2), and mtDNA directed-RNA polymerase (POLMRT). POLMRT forms a complex with two other mitochondrial transcription B paralogue factors — TFB1M and TFB2M — which recognize the promoter at the D-loop region. We analyzed the mtDNA copy numbers in human astrocytomas and we found a marked decrease along with the increase in malignancy compared to non-neoplastic brain tissues, being mostly depleted in GBM. Although high relative gene expression levels of mtDNA replication regulators (mitochondrial polymerase catalytic subunit (POLG), transcription factors A (TFAM), B1 (TFB1M) and B2 (TFB2M)) were detected, it cannot successfully revert the mtDNA depletion observed in our samples. On the other hand, a strong correlation among the expression levels of mitochondrial transcription factors corroborates with the TFAM role in the direct control of TFB1M and TFB2M during initiation of mtDNA replication. POLG expression was related to decreased mtDNA copy number, and its overexpression associated with TFAM expression levels also have an impact on long-term survival among GBM patients, interpreted as a potential predictive factor for better prognosis.