Abstract

Glioblastomas are the most common and the deadliest types of brain tumours. Due to their highly invasive behaviour, they are incurable by convencial therapeutical strategies. It was shown that some components of microtubules, namely class III β-tubulin, γ-tubulin and microtubule severing protein spastin are overexpressed in glioblastoma cell lines as well as glioblastomas. This diploma thesis is focused on the expression, subcellular distribution and function of katanin, another microtubule-severing enzyme, in gliobastoma cell lines. Katanin is formed by catalytic (p60) and regulatory (p80) subunits. Expression and cellular localization of both katanin subunits was studied in panel of human glioblastoma cell lines isolated form adults (T98G, U87MG, U118MG and U138 MG) and child (KNS42). Data presented in this thesis demonstrated that katanin subunits were overexpresed both on transcript and protein levels in T98G, U87MG and KNS42 cell lines, but not in U138MG and U118MG cell lines when compared to normal non-transformed human astrocytes. Immunofluorescence microscopy revealed that both katanin subunits were diffusively distributed in cytoplasm and concentrated on spindle poles of mitotic cells and on leading edges of migrating cells. Examination of cell motility revealed that velocities in glioblastoma cell lines corelated with protein levels of both katanin subunits. T98G and U87MG cells migrated significantly faster when compared to U118MG and U138 MG cells. Depletion of either p60 or p80 katanin subunits by siRNA in T98G and U87MG cells resulted in reduced cell motility. These results were in T98G cell supported by a radial cell migration assay. Moreover, proliferation in T98G and U87MG cells was inhibited in katanin-depleted cells.

Collectively, presented results indicate, for the first time, that enhanced expression of katanin in glioblastoma cells might be linked to tumour cell proliferation, migration, and invasion.