

Title of the project: Experimental treatment of glioblastoma multiforme by thermoablation using superparamagnetic nanoparticles carrying doxorubicin

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Summary of 2018 results

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Glioblastoma multiforme (GBM) is the most common malignant primary brain tumour with a remarkably poor prognosis showing a 5-year survival rate of 4-5% despite combined therapy approach, so the new types of therapy are urgently needed.

In our project we introduced new method of the cultivation of glioblastoma cells obtained from patients who were operated at department of Neurosurgery in Hradec Kralove. We compared mechanic and enzymatic dissociation and characterize basic properties of thus derived cells, such as proliferation and migration, sensitivity to temozolomide or drug resistance. Cells obtained by enzymatic method of cultivation had significant changes in morphology with acquired mesenchymal phenotype, higher proliferation potential and increased cell migration. Furthermore, cells obtained by enzymatic dissociation were more susceptible to temozolomide treatment, while cells in the mechanic group had higher expression of markers related with drug resistance, such as MRP1, miR-21 and miR-125b.

After cultivation we implanted samples of both types of GBM cultivation into the four immunodeficient mice (Athymic nude Foxn1nu), but after 3 weeks we didn't find any signs of the tumour. Optimisation of this method will continue in the next year.

Recently we tested in vitro toxicity of doxorubicin conjugated with HPMA polymer and/or with HPMA-coated superparamagnetic nanoparticles. Toxicity was evaluated using the xCELLigence real-time monitoring. We investigated that proliferation of GBM cells was significantly decreased in the presence of doxorubicin conjugated with HPMA-coated magnetic nanoparticles. Moreover we tested in vitro viability of the GBM cells together with nanoparticles of maghemite after exposition to magnetic field (thermoablation). We chose human glioblastoma cell lines A172 and GaMG as well as glioblastoma cells acquired from operated patients. Results were analysed by xCELLigence system and we discovered partial changes in the cell adhesion and proliferation.

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