Medical University of Graz

Targeted Drug Delivery to Brain Tumors (Glioblastoma multiforme) by an Iontronic implant

Summary

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Supervisor:	PD Dr. Rainer Schindl
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between February 10, 2020 00:00 and March 30, 2020 23:59 (Europe/Zurich)

Description

Background: Despite therapeutic interventions, the mean survival time of Glioblastoma multiforme (GBM) patients is less than one year due to a considerable infiltration potential, in particular within 2 cm margin of the primary resection site in 90% of all patients. To tackle the reoccurring tumours and to gain life quality for GBM and glioma patients, more specific treatment approaches, alternative chemotherapeutic drugs and adjunctive therapies are necessary. We aim to establish a fundamental new-targeted administration of chemotherapeutic drugs into the immediate vicinity of tumours to achieve greater efficacy than systemic drug application and reduce adverse effects. To achieve optimized spatial restriction of the chemotherapeutic treatment of GBM, we aim at the development of a gemcitabine (Gem) based novel implant, based on the technology of Organic Electronic Ionic Pumps, named GemIPs (OEIPs). OIEPs were filled with approved chemotherapeutics and potent drugs as gemcitabine, which is a very effective radio sensitizer as well. Gem, on the other hand, can barely cross the blood brain barrier and is, therefore, generally of limited applicability to brain tumours. Hence, GemIPs will be optimized for local application via precise electronic controllability of dosing and timing using Glioblastoma cell lines and patient-derived glioblastoma cells and tissue.

Hypothesis and Objectives: The goal of this PhD thesis is to investigate the efficiency of GemIPs *in vitro*. In view of the marked genetic heterogeneity of GBM, a panel of four GBM cell lines with different levels of MGMT expression and variable p53 mutation status was selected to prove the impact of GemIPs on 2D cell monolayers and 3D generated tumorspheres. Moreover, patients derived Glioblastoma tumorspheres should be generated and analysed to gain insight in treatment efficiancy. Experiments will include coordinated chemo- and radiation therapy in time and dosing to assure the potentizing effect of radiation in response to Germ exposure.

Methodology: The PhD student should be motivated to engage beyond the field of neuroscience and tumorbiology with project related sciences, such as Chemistry, (Bio)Physics and material science. The work of the PhD student will include fluorescence imaging (Immunohistochemistry), cell culture, FACS and human tissue preparation. Prospective students should be able to plan experiments independently and like to work in an interdisciplinary research team. PhD candidates with a background in neuroscience/cancer biology and/or the required methods are preferred. Strength of the research team is intense collaboration with leading laboratories ranging of organic chemistry, computer simulations to neurosurgery. Experiments will be performed at the institute for Biophysics/Neurosurgery/Experimental Neurotraumatology and with collaboration partners within the Medical University of Graz.

References: Organic electronics for precise delivery of neurotransmitters to modulate mammalian sensory function. Simon DT, Kurup S, Larsson KC, Hori R, Tybrandt K, Goiny M, Jager EW, Berggren M, Canlon B, Richter-Dahlfors A. Nat Mater. 2009 Sep;8(9):742-6. doi: 10.1038/nmat2494.

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