Medical University of Graz

Targeted Drug Delivery by an Iontronic Implant for Tunable Chemoimmunotherapy

Summary

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Supervisors:	PD Dr. Rainer Schindl Dr. Linda Waldherr
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between August 03, 2022 00:00 and September 20, 2022 23:59 (Europe/Zurich)

Description

Background: Chemo- and immunotherapy are two powerful therapeutic interventions to fight cancer. However, synergetic effects between these two cancer therapies are largely hampered by the fact that classical systemic chemotherapy not only targets tumor cells, but often interferes with the alarmed immune system. To synergize these two therapeutic strategies, local chemotherapy is a powerful tool to increase both cytotoxic effects in a confined target area and to boost immunotherapy, while the systemic burden is kept low. This is especially of importance for therapeutically exhausted cancer patients or those suffering cachexia, as they are either resistant to- or cannot pursue classic anticancer treatment.

We have recently established, a worldwide unique, free-standing electronically controlled device prototype for the long-time administration of the potent and immune-augmenting chemotherapeutic gemcitabine (Gem)[1] that will be further developed for an implantable and remotely controllable local chemotherapy. Our next aim is now to establish an electrically triggered implant based on this iontronic technology[2] for the administration of chemotherapeutic drugs into the immediate vicinity of *in vivo* tumors to achieve greater efficacy than systemic drug application and reduce adverse effects. Furthermore, we aim to combine iontronic therapy with immunological checkpoint inhibitors in an *in vivo* mouse flank tumor xenograft model.

Objectives and hypothesis: We aim to compose a tunable “multi-level” chemo-immuno-treatment regime. By developing a personalized multi-level treatment tool for chemo-tuned immunotherapy, we aim to potentiate the efficacy of both approaches and to reduce cytotoxic- and immune-related side effects. In the long run we foresee an iontronic implant for finely-tunable, chronic chemoimmunotherapy that can be used for treatment of therapeutically-exhausted patients.

The goal of this PhD thesis is to operate iontronic implants on tumors in the flank of mice. We will focus on the evaluation of synergetic treatment of iontronic chemotherapy and immunotherapy in Lewis lung carcinoma and pancreatic adenocarcinoma. This will comprise the monitoring of *in vivo* pharmacodynamics and immune cell infiltration, cell viability, cell cycle arrest, as well as tumor size and overall survival of mice.

Methodology: The PhD student should be motivated to engage beyond the field of tumor biology and immunology with project related sciences, such as Chemistry, (Bio)Physics and material science. The work of the PhD student will include cell culture, animal experiments in rodents, immunohistochemistry and imaging techniques, flow cytometry and sample preparation for mass spectrometry. Prospective students should be able to plan experiments independently and like to work in an interdisciplinary research team. Strength of the research team is intense collaboration with leading laboratories ranging of organic chemistry, computer simulations to clinical oncology. Experiments will be performed at the Division of Medical Physics and Biophysics, and with collaboration partners within the Medical University of Graz.

References:

1. Waldherr, L. *et al.* Targeted Chemotherapy: Targeted Chemotherapy of Glioblastoma Spheroids with an Iontronic Pump (Adv. Mater. Technol. 5/2021). *Advanced Materials Technologies* **6**, 2170026 (2021).

2. Simon, D. T. *et al.* Organic electronics for precise delivery of neurotransmitters to modulate mammalian sensory function. *Nat Mater* **8**, 742–746 (2009).