Medical University of Graz

Establishment of autologous tumor models and definition of new biomarkers at the extracellular vesicles level

Summary

Core Facility Alternative Biomodels & Preclinical Imaging, Biomedical Research, Medical University of Graz, Austria

Supervisor:	Prof. Dr. Beate Rinner
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: Sarcomas are a heterogeneous, rare, and complex group of neoplasms of mesenchymal origin whose diagnosis and resulting medical treatment are challenging. Metastatic sarcomas in particular are often detectable late and rarely curable, so biomarkers are urgently sought[1-4]. One group of sarcomas are translocation-associated sarcomas[5,6] (TAS), which arise from specific gene fusions. In our group, we were able to isolate extracellular vesicles (EVs) from TAS and detect the fusion in released EVs. EVs play an important role in tumorigenesis, metastasis, and immune surveillance[7,8]. Their biological role in the context of TAS has not yet been fully elucidated and will be studied in detail in vitro and in vivo in this project. We assume, that sarcoma cell-derived EVs force reprogramming of tumour-associated stroma to promote tumour growth and metastasis and can be used as biomarkers to monitor the disease. The aim is to investigate the tumorigenesis potential of EVs by using autologous derived patient sarcoma models and patients samples.

Hypothesis and Objectives: Tumor-derived EVs force reprogramming of tumor-associated stroma to promote tumor growth and metastasis. Aim is to investigate the tumorigenesis potential of EVs by using autologous derived patient sarcoma models. Translationally: EVs derived from fusion-translated sarcomas will be identified in plasma of patients to investigate their biological and potential diagnostic significance.

Methodology:

We will employ basic and advanced cell culture techniques, with an emphasis on primary cell culture including isolation of cells by using human tumor dissociation technique and immortalization of cancer associated fibroblasts by using hTERT technique. Furthermore, established patient derived cell lines will be characterized in detail by using various well established molecular biological methods (Western Blot, PCR, immunohistochemistry, flow cytometry, STR analyses).

Release of EVs from cell culture models will be performed by using ultracentrifugation and/or NanoView technology. Analyses for EV characterization will be done according to MISEV2018-guidelines (Nanosight technology, flow cytometry, PCR, western blotting and NanoView). The content of EVs will be further characterized in terms of specific RNA-fusion transcripts. Release of EVs will be measured in complex in vitro models followed by xenograft mouse models. To transfer the obtained results on a translational level, EVs and their content in plasma from sarcoma patients will be investigated by using NanoView technology. The proximity to the clinic, the know-how of the comprehensive cancer centre and the available ethics application (ethic 31,457ex18/19) enables the establishment of new sarcoma models/cell lines as well as the investigation of plasma from sarcoma patients with regard to EV release.

References

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