

# The Answer within the microEnvironment: pleural Mesothelioma resistance to Old and NEW drugs-ANEMONE

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## Summary

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Luka Brcic, Diagnostic and Research Institute of Pathology, Medical University of Graz

Supervisor: Dr. Luka Brcic  
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

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(International project financed in a TRANSCAN-3, ERA-NET Sustained collaboration of national and regional programmes in cancer research. Joint Transnational Call for Proposals 2021 (JTC 2021) co-funded by the European Commission/DG Research and Innovation: "Next generation cancer immunotherapy: Targeting the tumour microenvironment")

**Background:** Pleural mesothelioma (PM) is an intrathoracic neoplasia with an unfavourable prognosis. Although rare, a high peak in incidence is expected in 2020-2025. The most important risk factor is asbestos exposure that leads to a protracted immune response, making PM a candidate for immunotherapeutic approaches. However, to date, the overall response rates to treatment with immune checkpoint inhibitors (ICI) remain 10-20%.

**Hypothesis and Objectives:** Tumour microenvironment (TME), especially tumor immune microenvironment, plays a crucial role in the development and progression of PM, affecting the survival of mesothelial cells and evasion of the immunosurveillance.

*The main goal of the project is a precise characterization of TME in clinical samples, the evaluation of genetic alterations and gene/protein expression modulation on TME, and the identification of predictive biomarkers of ICI response by correlating pathological/molecular findings with clinical/radiological (radiomics) data using machine learning algorithms, in vitro and in vivo models.*

### Methodology:

*The research will be done on 360 chemo-naïve pleural biopsies from PM patients that will undergo neoadjuvant chemotherapy followed by surgery or palliative systemic treatment (platinum-based chemotherapy or immunotherapy). A subset of patient samples will be investigated before and after treatment. The research will be based on a multidisciplinary and interdisciplinary approach. Data from immunohistochemistry, radiomics, and high-throughput molecular assays will be integrated through advanced statistical methods to identify the most discriminative predictive features for the ICI treatment response. Experimental models (in vitro and in vivo) for functional studies will also be performed.*

*Specifically, at Med Uni Graz whole genome sequencing evaluation of collected samples and transcriptomic analysis (RNA-sequencing) will be performed. With TU Vienna collaboration high-performance liquid chromatography-mass spectrometry will be performed in a subset of samples. In all these analysis PhD student will be involved.*



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