Proposal of Master Research Project / Trabajo fin de Master for the academic year 2022-23

Group name: **Cell Plasticity in Development and Disease**
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Group web: **https://in.umh-csic.es/en/grupos/cell-plasticity-in-development-and-disease/**

Title of the MRP/TFM:

Contribution of neuroinflammation to brain metastases

Summary of the Project:

Effective treatments for brain metastases (BMs) constitute an urgent unmet clinical need. Clinical evidence shows that brain metastases differ from metastases in other organs as they respond differently to treatment. Several studies have suggested that tumor cells that metastasize to the brain may harbor specific intrinsic characteristics, but the unique microenvironment of the brain also contributes to these differences. A deeper understanding of the interplay of tumour cells with the brain microenvironment and how this reacts to the treatments is essential for the successful development and implementation of therapeutic strategies for patients with BMs. Glial cells constitute the majority of brain cells and play a key role in brain homeostasis We have identified neuroinflammation and different glial populations as regulators of BMs progression and potential modulators of responses to therapies, however the underlying mechanisms and the best strategy to target these populations to block BMs warrants further investigation. The general objective of this project is to investigate in detail the contribution of these microenvironmental regulators to BMs progression and responses to therapies.

Methods and technology involved in the MRP/TFM Project:

The methodology to be used in this project includes (but it is not restricted) to the following sections:

1. Cell cultures: maintenance of tumour cell lines (melanoma and/or breast cancer) and establishment of primary microglia/oligodendroglia cell lines from transgenic mice expressing green fluorescent protein YFP in microglia (Cx3cr1-CreERT2-YFP) or tdTomato in oligodendroglia (Plp-CreERT2-tdTomato) to perform co-culture.
2. Organotypic Cultures: Culture of BMs-harboring brain slices and treatment with candidate drugs to assess BMs growth.
3. Cellular and Molecular Biology: RT-qPCR techniques will be used to detect the expression of specific genes and flow cytometry (FACS) to isolate cell populations. In addition, “Live-imaging” of co-cultures of microglia/oligodendroglia and melanoma cells will be performed.
4. Histological and marker analysis by immunofluorescence and immunocytochemistry.

Member/s of the lab who will act as tutor/co-tutor of the project (if different from the group IP):

Dr. Francisco Rodríguez

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