Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2016-2017

Project Nº 27

Title: Study of the tumoral exosomes as inducer of myeloid-derived suppressor cells and messengers transporting immunosuppressive molecules

Department/ Laboratory Laboratory of Biochemistry. Clínica Universidad de Navarra

Director: Dr. Álvaro González Hernández
Contact: agonzaleh@unav.es

Codirector: Dra. Estibaliz Alegre Martínez
Contact: ealegre@unav.es

Summary

In this project we will study the mechanisms implicated in the accumulation of the Myeloid-derived suppressor cells (MDSCs) induced by the exosomas derived from neoplasic cells. We will also study the role of the suppressor molecules PD-L1 and HLA-G expressed by the malignant cells producing distant effects by being transported in exosomas. We will characterize the exosomes obtained from culture of tumor cell lines and from patients' samples (both serum and ascitic or pleural fluid). We will focus specially in the role of PD-L1, TGF-ß and HLA-G mediating the suppression induced by exosomes and we will use monoclonal antibodies and other compounds as therapeutic tools against these pathogenic mechanisms. We will study the role of PD-L1 and HLAG as tumor markes in patients with melanoma, lung, urologic and colon cancer. We will analyze the function of MDSCs in spleen and bone marrow obtained from immunodeficient mice xenotransplanted with a human cell line and/or injected with their corresponding exosomes. To carry out this project we have cell lines and a collection of samples obtained from patients with cancer. We also have the methodology to obtain and analysis exosomes and the corresponding models to study both in vivo and in vitro the induction and function of MDSCs.

References

Burke M, Choksawangkarn W, Edwards N, Ostrand-Rosenberg S, Fenselau C. Exosomes from myeloid-derived suppressor cells carry biologically active proteins. J Proteome Res 2014; 13:836-843.

Kumar V, Patel S, Tcyganov E, Gabrilovich DI. The Nature of Myeloid-Derived

Suppressor Cells in the Tumor Microenvironment. Trends Immunol. 2016;37:208-20.

Whiteside, T. L.Tumor-Derived Exosomes and Their Role in Cancer Progression.Adv Clin Chem 2016; 74: 103-41

POSSIBILITY OF PhD

YES*

* (PhD grant required)