Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2015-2016

Project Nº 1 ASIGNADO

Title: Optimizing cancer immunotherapy: stimulation of T cell migration across lymphatic vessels

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Summary

Our work is performed as part of the research of the group of Cancer Immunotherapy directed by Dr. Ignacio Melero in the center for Applied Medical Research (CIMA), University of Navarra in Pamplona, Spain.

Immunotherapy has emerged as a promising therapy to fight solid carcinomas. The main restrictions of this therapy emerge from the limited amount of T lymphocytes able to access the tumor stroma and draining lymph nodes. DC, effector and memory T cells use the lymphatic vessels (LVs) as conduits to egress from tissue and reach the lymph nodes and for recirculation. The propensity of leukocyte migration into the LVs is conditioned by the inflammatory context; in fact we have recently described how dendritic cells switch from an integrin independent to an integrin dependent mode when they have to transit across inflamed LVs.

In this project, funded by the Spanish Ministry of Health (FIS Project), we want to study the molecular mechanisms involved in T cell transit across lymphatic vessels in malignant tissue in the context of immunotherapy. For this purpose, the candidate will contribute to the study the associations between lymphatic vessel adhesive structures, inflammatory infiltrate and T cell migration in spontaneous and transplanted mouse tumor models as well as in clinical samples. Ex vivo and in vitro experiments will offer confocal microscopy-based evidences on the intervention of integrin ligands in this process, the subset of memory lymphocytes involved and the peculiarities of afferent lymphatic vessels in human and mouse tumors.
To sum up, we use mouse models of skin, lung and breast cancer to study whether the

lymphatic endothelium modulates the trafficking of T cells from the tumor to lymph nodes. We are especially interested in conditions of inflammation and in the context of immunotherapy.

References

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POSSIBILITY OF PhD

YES*

* (PhD grant required)