Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2017-2018

Project Nº 40

Title: ***Strategies of transient gene engineering with mRNA of antitumor T-cells***

Department/ Laboratory: ***Program of Immunology and Immunotherapy, Laboratory 3.04, CIMA***

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Summary

The project will consist in antitumoral injections in mouse tumor models of mRNA engineered antitumor T cells to transiently express IL-12 and CD137L. On going work in our laboratory about efficacy, safety and mechanistic studies upon intratumoral delivery in mouse tumor models of T-cell cultures with anti-tumor specificity transiently electroporated with optimized synthetic mRNA to confer expression of single-chain interleukin-12 has so far shown significant anti-tumor efficacy with no toxicity. The anti-tumor efficacy of the transiently engineered adoptive T cell therapy is futher enhanced by local administration of 1D8, a mouse antiCD137 agonist monoclonal antibody, thus obtaining systemic effect and eradicating stabishled B16OVA tumors. The main objective of the project will be to evaluate anti-tumor efficacy of electroporating tumor specific CD8+ T cells with IL12 mRNA and CD137L mRNA.

Therapeutic efficacy and immunobiology functions will be assessed.

References

Quetglas JI, Dubrot J, Bezunartea J, Sanmamed MF, Hervas-Stubbs S, Smerdou C, Melero I. Immunotherapeutic synergy between anti-CD137 mAb and intratumoral administration of a cytopathic semliki forest virus encoding IL-12. Mol Ther. 2012 .

Kerkar SP, Goldszmid RS, Muranski P, Chinnasamy D, Yu Z, et al. IL-12 triggers a programmatic change in dysfunctional myeloid-derived cells within mouse tumors. J Clin Invest. 2011.

Velasquez MP, Szoor A, Vaidya A, Thakkar A, Nguyen P, Wu M-F, et al. CD28 and 41BB costimulation enhances the effector function of CD19-specific engager T cells. Cancer Immunol Res. 2017.

POSSIBILITY OF PhD

YES*

* (PhD grant required)