Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2015-2016

Project Nº 28
Title: Inhibition of T regulatory cell activity as a therapeutic strategy against cancer
Department/ Laboratory Programa de Inmunología e InmunoterapiaCentro de Investigación Médica Aplicada, CIMA
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Summary One of the most important functions of the immune system is identifying and eliminating cancerous and/or precancerous cells. The ability of cancer cells to evade the immunoprotective network is due largely to their capacity to subvert the immune response by induction and recruitment of T regulatory cells (Tregs) –lymphocytic cells endowed with immunosuppressive activity– into the tumor microenvironment. Strategies proposed to improve antitumor immunity by depleting Tregs generally lack specificity, eliminate both effector T cells and Tregs, and raise the possibility of autoimmunity. Therefore, we propose to control Tregs by their functional inactivation rather than depletion. Tregs are characterized by expression of the FOXP3 transcription factor, which is considered their "master regulator". Its interaction with DNA is assisted primarily by its interaction with other transcription factors. We are conducting a drug discovery program by comprehensive pharmacophore-based virtual screening of a database of drug-like molecules to bind Foxp3. We have developed a panel of molecules able disrupt Foxp3 interactions with other factors and inhibit Treg activity in vitro. **In this project we are planning to characterize in vitro the mechanism of action of these molecules and evaluate their antitumor potential in vivo in different tumor models.** **References** References could be added (no more than three) 1. Matsoukas M, Aranguren-Ibáñez A, Lozano T, et al. Science Signaling 2015; In press. 2. Lozano T, Casares N, Lasarte JJ.. Front Oncol 2013; 3: 294. 3. Casares N, Rudilla F, Arribillaga L, et al. J Immunol 2010; 185: 5150-9.

POSSIBILITY OF PhD

YES, (PhD grant required)