

Research Project Proposal
Academic year 2016-2017

Project Nº 35
Title: Development of viral vectors able to express immunomodulatory antibodies for cancer gene therapy
Department/ Laboratory Department of Gene Therapy, Center for Applied Medical research, Center for Applied Medical research, CIMA
Director: Dr. Cristian Smerdou Contact: csmerdou@unav.es
<p>Summary In our laboratory we have extensively worked in cancer gene therapy using viral vectors to express immunostimulatory molecules, like cytokines. Recently it has been shown that the immune system can be modulated by using antibodies able to either stimulate activators of immune responses or block inhibitors of immune responses. These antibodies have been successfully used in clinical trials involving many cancer patients. However, the systemic delivery of these antibodies has also resulted in non-desired toxic effects in many of the patients. To avoid this toxicity we propose a new approach based on expressing these therapeutic antibodies locally in vivo using viral vectors that can be administered directly into the tumors.</p> <p>For that purpose the following partial objectives are proposed:</p> <ul style="list-style-type: none"> - Construction and production of a viral vector able to express a monoclonal antibody or an immunocytokine (fusion of an antibody and a cytokine) with antitumor properties. - Testing expression and functionality of the recombinant antibody (or immunocytokine) in vitro. - Testing the antitumoral activity of this vector in an animal model of cancer. <p>The project will involve the use of many different techniques, including Molecular Biology, cell culture, virus production, analysis of protein expression, immunological techniques, animal models of cancer etc.</p> <p>References</p> <ul style="list-style-type: none"> - Quetglas J.I., Dubrot J., Bezunartea J., Sanmamed M.F., Hervas-Stubbs S., Smerdou



C.*, Melero I.* (2012) Immunotherapeutic synergy between anti-CD137 mAb and intratumoral administration of a cytopathic Semliki Forest virus encoding IL-12. *Molecular Therapy*. 20(9):1664-1675.

- Rodriguez-Madoz J.R., Zabala M., Alfaro M., Prieto J., Kramer M.G., Smerdou C. (2014). Short-term intra-tumoral IL-12 expressed from an alphaviral vector is sufficient to induce an efficient anti-tumoral response against spontaneous hepatocellular carcinomas. *Human Gene Therapy*. 25(2): 132-143.

- Quetglas J.I., Labiano S., Aznar M.A., Bolaños E., Azpilikueta A., Rodriguez I., Casales E., Sánchez-Paulete A.R., Segura V., Smerdou C., Melero I. (2015). Virotherapy with a Semliki Forest Virus-based Vector encoding IL-12 synergizes with PD-1/PD-L1 Blockade. *Cancer Immunology Research*. 3(5):449-454.

POSSIBILITY OF PhD

YES*

* (PhD grant required)