



Research Project Proposal
Academic year 2015-2016

Project Nº 12
Title: Development of viral vectors able to express immunomodulatory antibodies for cancer gene therapy
Department/ Laboratory Department of Gene Therapy, CIMA
Director 1 Cristian Smerdou Contact: csmerdou@unav.es tel. 948194700 ext. 4027
Summary <p>In our laboratory we have extensively worked in cancer gene therapy using viral vectors to express immunostimulatory molecules, like cytokines.</p> <p>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.</p> <p>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 with antitumor properties.- Testing expression and functionality of the recombinant antibody 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> References <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.

- Quetglas J.I., Rodriguez-Madoz J.R., Bezunartea J., Ruiz-Guillen M., Casales E., Medina-Echeverz J., Prieto J., Berraondo P., Hervas-Stubbs S., Smerdou C. (2013). Eradication of liver-implanted tumors by Semliki Forest virus expressing IL-12 requires efficient long-term immune responses. *J. Immunology*. 190:2994-3004.

- 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.

POSSIBILITY OF PhD

YES*

* (PhD grant required)