



MÁSTER EN INVESTIGACIÓN BIOMÉDICA

Research Project Proposal

Academic year 2023

Project Nº 54 ASIGNADO

Title: Evaluation of the antitumor effect of Paxalisib in combination with the oncolytic adenovirus Delta-24-RGD for pediatric brain tumors

Department/ Laboratory *Laboratorio 2.03; Terapias Biológicas para Tumores Sólidos Infantiles*

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Summary *Short summary of the project with a maximum extension of 250 words, including the goals and the methodology that will be used*

Among pediatric solid tumors, brain cancer causes the highest mortality. Although the survival rates for some of them have improved in recent years, the overall prognosis remains poor. In addition, the long-term survivors suffer severe cognitive and psychological sequels due to the treatments used. Thus, searching for new therapies that not only cure the patients but also produce lower toxicities is essential. Combining drugs that have shown good therapeutic results as single agents is a common approach to obtain superior treatments. Delta-24-RGD is a replication-competent oncolytic adenovirus, which has shown effectiveness and a safe profile in the clinic. Paxalisib is a dual PI3K/mTOR inhibitor, which has been tolerated fairly well in dose escalation clinical trials. Here, we evaluated whether its combination cause improved antitumor effects *in vitro* and *in vivo*. Our results showed a synergistic response between both drugs decreasing cell viability *in vitro*. Treatment effects in apoptosis and cell cycle remain unclear and experiments need to be repeated to elucidate them. *In vivo*, combination treatment led to significant reduction cell proliferation and increased DNA damage in an orthotopic pediatric brain tumor model. From the therapeutic standpoint, combination therapy did not improve overall survival of treated mice. Nevertheless, since Paxalisib schedule was not fully given due to technical issues, this prevents from making definitive conclusions. In conclusion, combination of Paxalisib and Delta-24-RGD has shown potential as a treatment for brain tumors, but further studies are still required to assess properly its therapeutic response

yes	X
no	

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?