

Research Project Proposal
Academic year 2017-2018

Project Nº 5
Title: Dissection of new targets to block loco-regional failure post-brachytherapy
Department/ Laboratory Division of Oncology. Solid Tumors and Biomarkers, Center for Applied Medical Research (CIMA)
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Summary <p>Loco-regional failure (LRF) represents a frequent event that occurs after surgery with brachytherapy in a variety of tumors leading to a dismal prognosis with reduced therapeutic options. Yet, the molecular mechanisms directing this process are poorly understood. We have set up a novel animal model of murine breast cancer of loco-regional failure that recapitulates this process. Based on preliminary results, we have identified a transcriptomic signature critically involved in LRF after radiation. In preliminary results, using CRISPR/Cas9 technology we have knocked-out several of these mediators. The goal of this project will be to functionally validate their role in radio-resistance, survival in 3D cultures, and angiogenesis. We will also assess in vitro migration, invasiveness and cell growth kinetics by cutting-edge Real-Time Cell Analysis (xCELLigence). The in vitro findings will help dissect their contribution to the acquisition of the recurrent radio-resistant phenotype evaluated in relevant animal breast cancer model of LRF. We will also validate these findings in a retrospective cohort of breast cancer patients. The translation of this knowledge to the clinical setting will probably introduce new treatment strategies increasing patient survival.</p>
References : <ol style="list-style-type: none">1. Martinez-Monge R et al. Brachytherapy 2014;13:400-404.2. Martinez-Monge R et al. Brachytherapy 2015;14:565-570.3. Luis-Ravelo, (...) F Lecanda. Oncogene 2013; 23;33(43):5090-9