

## Research Project Proposal

Academic year 2019-2020

<b>Project Nº 40</b>		
<b>Title:</b> <i>In vivo visualization and optimization of tumor immunotherapy by use of photo-convertible mice</i>		
<b>Department/ Laboratory</b> Immunology and Immunotherapy. CIMA.		
<b>Director 1</b> Ana Rouzaut Subirá. <b>Contact:</b> <a href="mailto:arouzaut@unav.es">arouzaut@unav.es</a> <b>Codirector:</b> Álvaro Teijeira Sánchez <b>Contact:</b> <a href="mailto:ateijeiras@unav.es">ateijeiras@unav.es</a>		
<b>Summary.</b> <p><b>Background.</b> Melanoma is one of the most devastating cancer types. Recently, immunotherapy with modulators of the immune check point inhibitors has inspired hopes although there is ample room for improvement. Visualization of biological events <b>in vivo</b> directly using living mice is determinant to dissect immune responses in cancer. In this sense, <u>the study of immune cell movement from tumours to the lymph nodes</u> will help us to understand the biological roles of immune cells during immunotherapy.</p> <p><b>Objective.</b> In this project we will make use of the photoconvertible Kikume (CAG-KikGR) mice strain to study by in vivo confocal microscopy immune cell migration in models of melanoma in the context of immunotherapy.</p> <p><b>Methodology.</b> The transgenic CAC-KikGR mice express the photoconvertible and humanized protein kikume derived from corals. Fluorescence colour of KikGR mice changes irreversibly from green to red upon exposure to violet light, making possible to follow the migratory paths of illuminated cell populations.</p> <p>Concretely, we will establish subcutaneous tumors and illuminate them after being treated with combinations of anti-PD-1 and anti-CD137 mAb, in the presence or in the absence of anti-angiogenic therapies.</p> <p>Our endpoints will be:</p> <ul style="list-style-type: none"> <li>- Study of dendritic cell (DC) and cytotoxic and memory T cell migration from tumors to the lymph nodes.</li> <li>- Immune-cell contact at the tumor site: mainly. DC, CD8+T cell, neutrophil and NK cell</li> <li>- Transendothelial transit of leukocytes in the tumor microenvironment.</li> </ul> <p>Our <b>final goal</b> will be to ascertain whether immunotherapy improves immune cell movement in the tumor context and to dissect ways to improve their access to immune relevant organs.</p>		
<input checked="" type="checkbox"/> yes	<input type="checkbox"/> X	<b>Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?</b>
<input type="checkbox"/> no		