



**MASTER'S DEGREE IN BIOMEDICAL RESEARCH**  
**Research Project Proposal**  
Academic year 2023-2024

<b>Project Nº 49</b>		
<b>Title:</b> Modulation of the Integrated Stress Response as a therapeutic target for <i>Amyotrophic Lateral Sclerosis</i> treatment		
<b>Department/ Laboratory</b> CIMA, Gene Therapy and Regulation of Gene Expression (Neurosciences) (laboratories 2.05 and 4.03)		
<b>Director 1</b> <i>Montse Arrasate Iragui</i> <b>Contact:</b> <i>marrasatei@unav.es</i> <b>Codirector:</b> <i>Tomás Aragón Amonarriz</i> <b>Contact:</b> <i>taragon@unav.es</i>		
<b>Summary</b> <p>The development of effective treatments that delay or stop Amyotrophic Lateral Sclerosis (ALS) requires the identification of new therapeutic targets. To pursue that goal, our laboratory seeks to understand the specific molecular mechanisms underlying neuronal death. In this project we will focus in the role of the Integrated Stress Response (ISR) -a cellular pathway activated upon different stress conditions- in ALS.</p> <p>ALS is a neurodegenerative disease that affects motoneurons in the central nervous system. Although mostly sporadic, familial cases account for 5-10% of the cases. Mutations in SOD1 account for at least 20% of familial ALS. In our lab we work with neuronal and transgenic ALS models based on the expression of SOD1 mutant versions. The ISR is activated in those models and, importantly, closely correlates with neuronal death (<i>Bugallo et al, 2020, Cell Death and Disease</i>). The goal of this project is to analyse the ISR pharmacological modulation effect in the onset and progression of the disease in transgenic mouse models of ALS. Methodology: Automated microscopy and survival analysis, CRISPR/Cas9, transgenic ALS animal models, electrophysiological analysis (electromyography), clinical evaluation of the symptomatology, motor performance evaluation and immunohistochemistry analysis of brain and spinal cord tissues to address motoneuron survival.</p>		
<b>yes</b>	<input checked="" type="checkbox"/>	Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?
<b>no</b>	<input type="checkbox"/>	