



**Research Project Proposal**  
Academic year 2020-2021

***Máster en Investigación Biomédica***

<b>Project Nº 36</b>	
<b>Title:</b> <i>Optimization of brain biodistribution of high-capacity adenoviral vectors</i>	
<b>Department/ Laboratory</b> Gene therapy and regulation of gene expression program. CIMA.	
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<b>Summary</b>  <p>Vectors derived from adenovirus are commonly used in gene therapy approaches, due to their efficacy for <i>in vivo</i> transduction, genomic stability and high cloning capacity. They are double-stranded DNA viruses with 100 nm, non-enveloped icosahedral capsids.</p> <p>When they are used for brain-directed gene therapy, one of their major drawbacks is their limited biodistribution across different brain structures.</p> <p>The objective of this project is to evaluate different routes of administration and capsid modifications, in order to obtain selective and widespread transduction of neurons <i>in vivo</i>.</p> <p>The vectors have been already produced. They express a reporter gene consisting of a fusion between luciferase and green fluorescence protein (GFP) coding sequences. Stereotaxic injection will be carried out in different brain coordinates of C57BL/6 mice. Intraparenchymal and intraventricular routes will be evaluated. Different methods to obtain transient disruption of the brain-blood barrier will be tested. The parameters studied will be the spread and intensity of transgene expression, as well as the identity of transduced cells (neurons, astrocytes, microglia).</p> <p>Surgeries will be performed by specialized members of the team. The student will be trained in basic animal handling procedures, brain anatomy, tissue processing, quantification of luciferase expression, histological techniques (including immunofluorescence), and microscopy.</p>	
yes	X
no	
<b>Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?</b>	