

**Research Project Proposal**  
Academic year 2017-2018

<b>Project Nº 20</b>
<b>Title: Development and validation of a lentiviral library for CRISPR-Cas9-based screening of the human miRNome role in cell biology</b>
<b>Department/ Laboratory</b> <b>Advanced Genomics Lab (1.04), Onco-Hematology Program, Center for Applied Medical Research (CIMA)</b>
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<p><b>Summary</b></p> <p>MiRNAs are small non-coding RNA molecules involved in RNA silencing and post-transcriptional regulation of gene expression. Numerous miRNAs have been shown to play major roles both in the normal physiology of the cell and in the pathological setting, including cancer. However, there is a lack of tools to study their role following a systematic approach. Recently, the CRISPR-Cas9 technology has opened new and more feasible avenues of genome editing, allowing researches to manipulate any given region of the genome in order to further our understanding of its function. To date, this tool has been used to study coding genes, transcription factor binding regions, or individual miRNAs. However, to the best of our knowledge, it has not yet been used to methodically study the role of miRNAs in the screening setting. <b>AIMS.</b> The aim of the present project is to develop and validate a lentiviral library for CRISPR-Cas9-based screening of the role of over 1800 different human miRNAs. This library will subsequently be used on different projects running within the Onco-Hematology Program. <b>METHODS.</b> The present project will involve both advanced molecular biology techniques (including genetic engineering and next generation sequencing, NGS) and regular cellular biology techniques (such as lentiviral vectors production, cell culture, and cell sorting).</p> <p><b>References</b></p> <p>Yoshino et al. microRNA-210-3p depletion by CRISPR/Cas9 promoted tumorigenesis through revival of TWIST1 in renal cell carcinoma. <i>Oncotarget</i>. <b>2017</b> Feb 1. PMID: 28152509</p> <p>Larrea &amp; Fernandez-Mercado et al. Follicular Lymphoma cases harbour recurrent mutations in miRNA binding sites of genes associated with lymphomagenesis. <b>2016</b> <i>European Journal of Cancer</i>. 61 - S1, pp. S11. 01/07/2016. doi: 10.1016/S0959-8049(16)61028-6</p> <p>Shalem et al. Genome-scale CRISPR-Cas9 knockout screening in human cells. <i>Science</i>. <b>2014</b> Jan</p>



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