

<b>Research Theme:</b> Molecular Biology
<b>Research Project Title:</b> Splicing mechanisms and their alterations in human genetic diseases.
<b>Principal Investigator/Supervisor:</b> Francesc Xavier Roca Castella
<b>Co-supervisor/ Collaborator(s) (if any):</b>
<b>Project Description</b>
<p><b>a) Background:</b></p> <p>Pre-messenger RNA splicing is an essential step for the correct expression of over 90% of human protein-coding genes, and splicing alterations often cause genetic diseases, such as beta-thalassemia, cystic fibrosis and cancer. We aim to characterize general mechanisms of constitutive and alternative splicing in human cells, as well as their alterations by mutations in affected splicing events or in other genes encoding splicing factors. The main splicing element that we will study is the 5' splice site at the beginning of introns, which is recognized by the U1 small nuclear RNA, which was recently found to act as a cancer driver upon distinct mutations. For many years, our lab characterized the mechanisms of recognition of 5' splice sites by U1, and we propose to extend these studies and perhaps try pharmacological interventions. This project should contribute to our basic understanding of splicing mechanisms in human cells, with implications for the molecular diagnosis of splicing mutations and potentially for therapeutics.</p>
<p><b>b) Proposed work:</b></p> <p>The student will use mainly wet-lab biology in human cell lines and maybe some basic bioinformatics if needed. The wet-lab experiments include characterization of one or few splicing events by splicing minigenes cloned in plasmids and analysed by transfection and RT-PCR. The student will modify the action of certain splicing factors by RNA interference and/or CRISPR-mediated genome editing. The student might also apply high-throughput analyses of splicing by RNA sequencing to derive the splicing patterns of many genes at a time. The computational work will include a bit of script to analyse large amounts of splicing data in public databases or others, and due training will be provided by our group. Overall the student will become proficient with experimental and basic computational tests for the analysis of splicing, which are highly relevant skills for future transcriptomics or genomics projects, in the context of either academic or biotech research.</p>
<p><b>Supervisor contact:</b>  <b>If you have questions regarding this project, please email the Principal Investigator:</b> <a href="mailto:xroca@ntu.edu.sg">xroca@ntu.edu.sg</a></p>
<p><b>SBS contact and how to apply:</b>  Associate Chair-Biological Sciences (Graduate Studies) : <a href="mailto:AC-SBS-GS@ntu.edu.sg">AC-SBS-GS@ntu.edu.sg</a>  Please apply at the following:  <a href="http://admissions.ntu.edu.sg/graduate/R-Programs/R-WhenYouApply/Pages/R-ApplyOnline.aspx">http://admissions.ntu.edu.sg/graduate/R-Programs/R-WhenYouApply/Pages/R-ApplyOnline.aspx</a></p>