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| **Research Theme:** Molecular Biology |
| **PhD Research Project Title:**Regulation and artificial modulation of alternative splicing in human genetic diseases |
| **Principal Investigator/Supervisor:** Francesc Xavier Roca Castella |
| **Co-supervisor/ Collaborator(s) (if any):** NIL |
| **Project Description**1. **Background:**

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 and cancer. Our lab mainly focuses on splicing in human myeloid cells involved in innate immunity such as monocytes, macrophages and neutrophils, as well as in the splicing regulation of antiviral genes. We also study natural sequence variations affecting splicing in Asian genomes. 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.1. **Proposed work:**

In this project we aim to characterize general mechanisms of constitutive and alternative splicing in these human cells, as well as their alterations by mutations in affected splicing events or in other genes encoding splicing factors. We will also aim to modify splicing by splice-switching antisense oligonucleotides with therapeutic potential. The student will use mainly wet-lab biology in human cell lines, and some basic bioinformatics if needed. The wet-lab experiments include characterization of splicing events by minigenes followed by transfection and RT-PCR. The student will modify 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. The computational work will include analysing large amounts of splicing data in public databases or others, with due training provided by our group. Overall the student should become proficient with experimental and basic computational tests for the analysis of splicing, as highly relevant skills for transcriptomics or genomics in the context of either academic or biotech research.1. **Preferred skills:**

Experience in cell culture, standard molecular biology like cloning, transfection and RT-PCR, flowcytometry, fluorescent microscopy, RNA sequencing, bioinformatics analyses. |
| **Supervisor contact:****If you have questions regarding this project, please email the Principal Investigator:**xroca@ntu.edu.sg
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| **SBS contact and how to apply:**Associate Chair-Biological Sciences (Graduate Studies) : AC-SBS-GS@ntu.edu.sg
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| Please apply at the following: |

60 Nanyang Drive, Singapore 637551

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**Application portal:**

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<https://venus.wis.ntu.edu.sg/GOAL/OnlineApplicationModule/frmOnlineApplication.ASPX>

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