

<b>Research Theme:</b> Molecular Biology
<b>Research Project Title:</b> Analysis of alternative splicing events and factors in human myeloid immune cells
<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>We aim to characterize the global patterns of alternative splicing in human myeloid cells, focusing on new studies in neutrophils and continuing existing projects in monocytes and macrophages. Alternative splicing is the regulatory process by which exons are connected in different patterns from primary transcripts, generating different RNA and protein isoforms, thus expanding the human transcriptome and proteome. We previously performed high depth RNA sequencing (RNA-seq) of human primary monocytes and differentiated pro-inflammatory and wound healing (anti-inflammatory) macrophages, also upon their immune activation with different stimuli. Analogous experiments were done with the monocytic THP-1 cell line with much easier access, scaling up and manipulation, and now more myeloid cell lines are being introduced such as HL-60, which will be the major focus of this PhD project. The RNA-seq data revealed general changes in gene expression, and detailed alternative splicing profiles which were completely new, as published in Nucleic Acids Research in 2018.</p>
<p><b>b) Proposed work:</b></p> <p>This project addresses the basic functions of human immune myeloid cells, whose dysregulation causes multiple pathologies, including immunodeficiencies, autoimmunity and cancer. By studying alternative splicing, we aim to identify biomarkers and/or therapeutic targets that determine myeloid functions at the RNA level. The PhD student should continue characterizing the roles of alternative splicing events and factors in monocytes/macrophages by using molecular biology and RNA sequencing, with downstream bioinformatics analysis. Student will work on existing RNA sequencing data and also generate her/his own, by working with new human myeloid cell lines like HL-60 and perhaps also primary cells, such as neutrophils purified from blood donated by healthy individuals. Down the line, we will connect these splicing analyses to monocyte/macrophage and/or neutrophil-related diseases.</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>
<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>