**Assessment of enhancer RNA relevance in chronic kidney graft rejection**

Martin Morin, U1064 CRTI, Nantes

Kidney transplantation is currently the best treatment against end-stage kidney diseases. However, despite the improvement of 1-year survival rate in the past decades, the 10-year survival rate has remained stable. So far, very few genomic, epigenomic or transcriptomic strategies have been implemented to investigate chronic kidney graft loss and most of them had limited power. Overall, no clear molecular pathway for chronic graft rejection has been characterized. In this project, we propose to leverage the recent uprising of genomic annotation of regulatory elements through an innovative strategy to better pinpoint the molecular pathway(s) involved in chronic graft failure. In the past 20 years, the DIVAT cohort collected clinical and phenotypic dataset as well as biosamples (peripheral blood mononuclear cell or PBMC, and biopsies) from kidney-transplanted patients. We selected 167 PBMC samples from transplanted patients and aim to perform a total RNA sequencing (tRNA-seq) on these cells. Transcriptomic data from patients experiencing chronic rejection will be compared to stable patients not experiencing chronic rejection. The recent discovery of transcription occurring at enhancer regulatory elements will be instrumental to further characterize the molecular mechanisms of gene expression regulation. Using a recently published pipeline, we aim to provide a proof-of-concept of tRNA-seq potential in enhancer RNA detection on a subset of these samples. Our analysis will allow the building of gene regulatory networks (enhancers-genes) involved in the graft tolerance vs. chronic rejection balance. We then intend to further explore the identified gene regulatory networks in the entire cohort and to run the first multiomic study (combining genomics, transcriptomics and epigenomics) of chronic kidney graft rejection. Finally, we ambition to build a score based on multiomics to predict chronic graft rejection from a simple blood sample.