Regulation of HIV latency by miR-34c-5p

Place of work/: RNA Systems Biology Lab - Gene Expression and Regulation Group, BioISI - FCUL

Supervisors: Margarida Gama Carvalho

Contact: mhcarvalho@fc.ul.pt

Abstract / MSc thesis project proposal

MicroRNAs are important regulators of gene expression, functioning as determinants of several biological processes, including the cellular response to viral infections. Using next-generation sequencing technologies, the host laboratory recently identified miR-34c-5p microRNA as a regulator of activation of CD4+ T lymphocytes, the main targets of HIV-1 infection (Amaral et al, EMBO J 2017). Representing the biggest epidemic today, the infection by this virus remains difficult to eradicate due to the possibility of latent integration in the genome of CD4+ T cells for several years. Our results show that this microRNA is a positive regulator of the viral replication process but, in a contradictory way, it seems to inhibit the reactivation of latent viruses.
The present project aims to dissect the molecular pathways by which miR-34c-5p regulates HIV-1 reactivation, using as a model the human lymphocytic cell line JLat, which contains a latent integration of a modified (and non-infectious) HIV genome. The work plan involves the investigation of different cellular pathways essential for HIV reactivation, and their interaction with predicted and known targets of miR-34c-5p in order to understand the mechanisms of action underlying its inhibitory role. The methodologies to be used will cover a set of standard techniques in the field of Molecular and Cell Biology, namely: PCR-based methods, cell culture techniques, fluorescence microscopy, transfection, RNA isolation and reverse transcription, Western-blotting, methodologies of molecular cloning and assays with luciferase reporter genes.