BioISI - Biosystems & Integrative Sciences Institute

Regulation of HIV gene expression by small non-coding RNAs

Place of work: RNA Systems Biology Lab, Gene Expression and Regulation Group, BioISI, FCUL (Dept. of Chemistry and Biochemistry)

Supervisors: Margarida Gama-Carvalho

Contact: mhcarvalho@fc.ul.pt

Previous work from the lab has identified candidate viral and cellular encoded microRNAs that have the potential to regulate HIV replication by interfering either with viral or endogenous genes required for viral gene expression. The aim of this project is to investigate the functional impact of the expression of these molecules in this process. For this purpose, vectors encoding the miR-precursors will be expressed in different human cell lines and the corresponding functional impact on selected target gene expression or cellular phenotype will be assessed through the use of qRT-PCR and functional assays with fluorescent read-outs (either by FACS or microscopy), respectively. Candidate target genes will be selected based on bioinformatic prediction algorithms. Cell lines will include the JLat T cell line, which contains a stable, latent integration of a modified GFP-HIV-1 genome, allowing for the easy and safe evaluation of viral transcriptional processes. Candidate targets for regulation may be further validated through the use of a luciferase-reporter system in order to confirm the direct nature of the miR-target interaction process. The results will support the generation of a model for a regulatory network of virus-host molecular interactions through small-non-coding RNAs, potentially providing insights into new therapeutic targets for the modulation of viral replication.

Bibliography: Amaral AJ et al (2017). miRNA profiling of human naive CD4 T cells links miR-34c-5p to cell activation and HIV replication. EMBO J. 2017 Feb 1;36(3):346-360.