Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: Visualizing DNA Repair through live-Cell Microscopy

Proposal:
The Sergio Almeida lab at the Instituto de Medicina Molecular João Lobo Antunes (iMM-JLA) is offering a Master Thesis Project with a focus on advanced fluorescence confocal microscopy and super-resolution microscopy at the interface of biophysics and molecular biology. The master student candidate should have an interest in molecular biomedicine and in the application of advanced optical microscopy in live human cells and will learn to use state of the art microscopy equipment, image analysis and molecular biology assays to investigate open questions in the field of genomic instability.

Synopsis:
The Sergio Almeida lab has developed a novel fluorescent tool to visualize an uncommon form of nucleic acid structures called R-loops. These structures form mostly during transcription, when an RNA hybridizes with the complementary template DNA strand to form a DNA/RNA hybrid and thereby displacing the other single strand of DNA.
R-loops have both deleterious and beneficial roles in the cell, they are sources of DNA damage and genomic instability, but they also emerged as important regulators of cellular processes, such as gene expression, class-switch recombination, and telomere stability. Recent reports showed that R-loops not only cause DNA damage but supposedly form newly at sites of DNA damage and may have a role in the signalling and/or repair of DNA damage.
To investigate the role of R-loops in the cellular DNA damage response, the master student will use our new fluorescent sensor and advanced live-cell microscopy to look at R-loops at sites of DNA damage in different physiological settings.

Supervisor: *Robert M. Martin, Sergio de Almeida Lab, robertmartin@medicina.ulisboa.pt*
Co-Supervisor: *Sergio de Almeida, Sergio de Almeida Lab, sergioalmeida@medicina.ulisboa.pt*
Webpage of the group

Related literature:
1. Santos-Pereira, J. M. & Aguilera, A. R loops: new modulators of genome dynamics and function. Nat. Rev. Genet. 16, 583–597 (2015).
2. Crossley, M. P., Bocek, M. & Cimprich, K. A. R-Loops as Cellular Regulators and Genomic Threats. Mol. Cell 73, 398–411 (2019).
3. C. Ohle, et al., Transient RNA-DNA Hybrids Are Required for Efficient Double-Strand Break Repair. Cell 167 (2016).