

Deciphering the DNA replication stress response choreography and nuclear architecture with high resolution quantitative imaging

Interference with the DNA replication process – also known as replication stress (RS) – is a hallmark of hyper-proliferation and tumorigenesis and at the same time a central strategy for cancer chemotherapy. Hence, understanding the mechanistic peculiarities of cancer onset and improving available cancer therapy regimens require in-depth molecular insight into the RS response. Our lab and others rigorously used classical molecular and cellular biology approaches, coupled with single-molecule assays, revealing different modes of replication fork plasticity upon genotoxic stress. Recent studies – pioneered by our lab and few others – have shown that these local fork transactions in face of obstacles are assisted by key components of nuclear architecture. How they are rapidly and transiently integrated into a global response within the nucleus remains unknown.

In this project, we aim to exploit new probes, super-resolution imaging and quantification to explore how replication centers react to genotoxic stress, recruiting specialised fork plasticity factors and take contact with key components of nuclear architecture. Capitalising on recent promising evidence from our lab (references below), the aim is to visualize how the ATR kinase, nuclear F-actin, lamin A and cohesin orchestrate replication fork plasticity throughout intact nuclei. Moreover, we aim to resolve the RS response and nuclear architecture dynamics from local transactions at DNA lesions sites to a global nuclear response beyond DNA lesions.

The Lopes Lab is internationally well-recognized in the field of DNA replication stress and cancer biology. With this PhD project, you will support the lab's transition towards higher resolution quantitative imaging approaches. You will be part of an international, stimulating and social research group, embedded in the Institute of Molecular Cancer Research (IMCR) at the University of Zurich. We recently moved to a brand-new building on the beautiful Irchel Campus and are situated in proximity to a fully-equipped and supportive microscopy facility. This project will surely profit from a deep interest and fascination towards microscopy, image processing and mechanistic studies. Previous experience on these aspects will be much valued.

The position is being filled via our international PhD program (<https://www.mls-phd.uzh.ch/en.html>, deadline May 1st, 2025), aiming for a start in late 2025. **Spontaneous direct applications** may be exceptionally considered in parallel, if submitted **via e-mail by July 1st**. Please send a detailed CV, a motivation letter and the contact details of at least two references to lopes@imcr.uzh.ch and krietsch@imcr.uzh.ch.

- Lopes Lab: <https://www.imcr.uzh.ch/en/research/lopes.html>; @lopeslab.bsky.social
- IMCR: <https://www.imcr.uzh.ch/en.html>
- Center for Microscopy and Image Analysis: <https://www.zmb.uzh.ch/en.html>
- González-Acosta and Lopes, Chromosoma 2023, PMID: 38055079
- Palumbieri MD et al., Nat Commun. 2023, PMID: 38016948
- Mutreja K et al., Cell Rep. 2018, PMID: 30184498
- Cherdyntseva V et al., <https://www.biorxiv.org/content/10.1101/2025.01.18.633737v1>

