

Development of a microfluidic system for mutation monitoring in new DNA repair mechanisms coupled with transcription

Context

The integrity and expression of the genome are essential functions of the cell. Deregulation of transcription, the first step of gene expression, and defects in DNA repair lead to a number of serious diseases. Recently in our group, we discovered an unexpected link between transcription and DNA repair that could involve the phenomenon of transcription-associated mutagenesis. In this project we propose to develop a new monitoring system for spontaneous mutations accumulation in yeast Saccharomyces cerevisiae in order to analyze new DNA repair mechanisms coupled with transcription.

The project MutMonitor is based on the complementary skills of two laboratories in integrative biology, functional genomics and bioinformatics (J. Soutourina) and microfluidics and interface physics (F. Malloggi).

The project will allow us to evaluate the role of the components of the repair machinery coupled with transcription. The tool developed will allow us to use the technology derived from physics to answer important biological questions related to the expression and integrity of genomes and to better understand human pathologies such as cancer and rare diseases. It also presents a potential for using the tool developed to mimic the accumulation of mutations according to the genetic context in the digital patient or mutagen identification programs, or the innovative concepts connecting gene expression and DNA repair to propose potential therapeutic targets.

Mission

This project proposed the development of a microfluidic system for mutation monitoring. The system will allow the growth of yeast populations over 100 generations through population bottlenecks and the analysis of the mutation spectrum in different genetic contexts by high-throughput sequencing (NGS). The successful candidate will contribute to the design, the microfabrication, and the optimization of the microsystem, to the measurement campaigns and to the data analysis. The candidate will mainly works in the LIONS for the microsystem development but he/she will be in close collaboration with the biologists of the SBIGeM.

Profile

Applicants could be graduated from an engineer school or could have a Master degree or a PhD in Microfluidics/Engineering/Physics or related disciplines and will be motivated by challenges in a multidisciplinary team.

Applicants will have an experimentalist profile.

Applicants shall speak English or French, and have good communication skills.

Duration: 12 months **Starting date:** To be filled last trimester 2018

Localization: LIONS and SBIGeM at CEA/Saclay, Gif sur Yvette France

Contacts CV, motivation letter and recommendation letter should be sent to both contacts. Dr. Florent Malloggi : <u>florent.malloggi@cea.fr</u> Dr. Julie Soutourina : <u>julie.soutourina@cea.fr</u>