PROPOSITION DE STAGE
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Équipe de recherche : Biophysics of growth and division control
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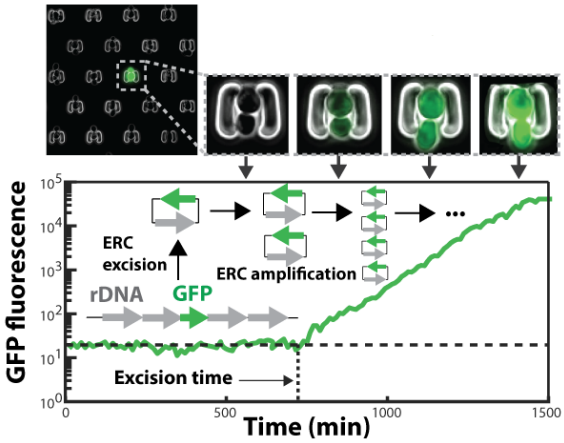
Titre du stage: Building a high-throughput single cell imaging device to monitor rDNA genomic instability during entry into senescence in budding yeast

Background

Aging is a ubiquitous feature of living organisms, yet its fundamental origin still remains to be deciphered. Over the last twenty years, budding yeast has emerged as a simple yet powerful simple model to identify and characterize the molecular mechanisms that drive age-associated physiological declines: indeed, following an asymmetrical pattern of division, mother cells can generate a limited number of daughter cells (typically 25) before entering senescence and eventually dying. Our group and others have pioneered the development of longitudinal live cell imaging approaches to monitor the successive divisions of living cells from birth to death under the microscope, in order to characterize the dynamics of entry into senescence with single cell resolution. Our recent results suggest a model in which rDNA genomic instability constitutes the Achilles's heel of cellular lifespan.



Aims

The project aims at investigating further the role of rDNA instability by using a high-throughput device to detect rare recombination events in single dividing cells, which lead to the formation of extrachromosomal rDNA circles (ERCs). ERCs accumulate within mother cells (see figure) and our long term goal is to determine how this process is regulated and whether and how it is deleterious to cellular function.

Internship specific objectives

We have started to developed a methodology that let us monitor thousands of individual dividing cells under the microscope to detect the rare excision of ERC molecules in aging cells. The goal of this internship will be to establish the proof of principle of this technique by recording excision events in various genetic contexts and following specific environmental perturbations. The student will acquire knowledge in microfluidics, image acquisition and processing, yeast genetics, and instrumentation.

Environment

The group of Gilles Charvin has a long-standing interest in the development of single cell imaging techniques to address fundamental questions related to the control of cell proliferation budding yeast, including oxidative stress response, cell cycle regulation and replicative aging. Please contact Gilles Charvin (charvin@igbmc.fr) or visit our website for further information:
http://charvin.igbmc.science

Ref :, Morlot S[1], Song J[2], Léger-Silvestre I[3], Matifas A[2], Gadal O[3], Charvin G[4], Cell Rep. 2019 Jul 9;28(2):408-422.e4