Pluridisciplinary characterization of DNA repair in yeast

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Abstract

The DNA damage response machinery plays a central role in ageing and oncogenesis. Large expansions of non-coding trinucleotide repeats on the DNA chain are responsible for a growing number of neurological and developmental human disorders. Gene editing (deleting or shortening to a non-pathological length) aforesaid sequences is an appealing therapeutic approach. Nonetheless, given the complexity of genetically manipulating human cells, model organisms have been used to comprehend this procedure. Indeed, recent assays allow the efficiency of DNA repair in *Saccharomyces cerevisiae* to be quantified *in vivo* with fluorescent protein reporters. In this work, we characterize the cellular consequences of such DNA repair with an interdisciplinary approach: Using microfluidics, we track in a time-resolved manner the growth of several cell populations starting from single yeast cells upon DNA-repair induction. Observing the dynamics of those monoclonal populations allows us to analyze the heterogeneity of cells with successful DNA-repair outcome: Their distinct time evolution gives us a deeper understanding of the individual cells' contributions to the global population scale and repair efficiency. Moreover, the detailed observation obtained with our approach provides access to infer the molecular steps that account for successful DNA repair in cells: Our experimental data are used to formulate a mathematical model of the observed DNA-repair process. Hence, with this investigation we aim to shed light on the mechanisms underlying successful DNA repair, refining our knowledge for gene editing therapies.

Keywords: yeast, DNA repair, time lapse microscopy, heterogeneity

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