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# Quiescent cells also mutate

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For almost a hundred years, geneticists have believed that the more a cell divides the more mutations it acquires. However, research by scientists at the Institut Pasteur shows that quiescent cells, which do not divide, also acquire a particular type of mutation - deletions (mutations through loss of nucleobases).

Geneticists study heredity or the transmission of characters between generations. The genetic information responsible for these characters is contained in the DNA molecule, which is replicated each time a cell divides and transmitted to the daughter cells. "DNA replication machinery is powerful enough to faithfully transmit genetic information, and flexible enough to allow it to evolve through variations that we call mutations", explains Benoît Arcangioli, Head of the Dynamics of the Genome Unit at the Institut Pasteur.

## What we currently know about mutations

Most mutations have a neutral effect, and positive or negative impacts on the characters of cells, individuals and species are rare. However, their build up, under the influence of natural selection, helps species to evolve.

In this context, and for close to one hundred years, geneticists have expressed mutations according to the number of cell divisions. "To keep it simple, the more a cell divides, the more mutations it acquires", explains Benoît Arcangioli. However, under natural conditions, cells spend relatively little time dividing and are often idle, or in the quiescent

state, for example in adult organisms. The question therefore is whether mutations appear in these quiescent cells.

## Quiescent cells also mutate

Benoît Arcangioli's team at the Institut Pasteur has shown that the DNA of quiescent cells also acquires mutations. "These mutations appear linearly over time and are different from those that appear during growth." During growth, mutations tends to increase the number of A/T (adenine/thymine) bases at the expense of C/G (cytosine/guanine) bases and insertions are more frequent than deletions. The situation is reversed in the quiescent state in the sense that changes between the A/T and G/C bases seem balanced and deletions prevail over insertions. As a consequence, "alternation between two mutating systems brings a dynamic balance to the composition and size of genomes in a given species". This also implies that quiescence, like growth, is subject to natural selection and will optimize the survival potential of cells when there is no division.

## A role in male/female gamete dimorphism

"In many species, ranging from plants to humans, male gametes divide constantly while the opposite is observed for female gametes, adds Benoît Arcangioli. The main implication of our article is therefore that male and female gametes, each with their different mutations, will gradually impact their genetic material differently." The combination of two mutating methods could therefore play a key role in male and female gamete dimorphism.

Furthermore, by providing proof that these different mutation methods occur at different moments in cell life (cells in the growth or quiescent state), the notion of time is introduced to the mutagenesis mechanism.

"This concept of mutations over time has two advantages, concludes the researcher. Firstly, it is consistent with the molecular clock theory used for evolution (and expressed in years) and, secondly, it gives an evolutionary force back to female gametes."

**More information:** Serge Gangloff et al, Quiescence unveils a novel mutational force in fission yeast, *eLife* (2017). DOI: 10.7554/eLife.27469

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