

Towards the mechanochemical characterization of the human mitochondrial replisome

P01-20

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Mitochondria are eukaryotic organelles, responsible for cellular energy generation. Besides their role in energy production, mitochondria are essential for cellular activity regulation, e.g. cell signaling and cell death. Mitochondria have their own DNA (mtDNA) and, in general, human cells contain thousands of mtDNA copies. A reduction in the number of mitochondrial DNA molecules or accumulation of mtDNA mutations may cause so-called ‘mitochondrial diseases’ that, in humans, affect tissues highly dependent on mitochondrial metabolism, such as brain, heart, liver, skeletal muscles and kidney tissues [1]. Therefore, mitochondrial dysfunction and, partly, mitochondrial diseases occurrence, in some measure, depend on effectiveness and accuracy of mtDNA replication.

The mitochondrial DNA replication machinery is much simpler than its nuclear DNA equivalents. The ‘minimal replisome’, that is capable of processive DNA synthesis, can be reconstituted *in vitro* with just three proteins: the TWINKLE DNA helicase, the single-stranded DNA binding protein (mtSSB) and the mitochondrial DNA polymerase γ [2].

The mechanism of human mtDNA replication has not yet been fully characterized. It is unclear how the proteins, involved in mtDNA replication, act at the replication fork. In present work, we aimed to detect and characterize the human mitochondrial DNA helicase activity at a single molecule level.

References

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