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Abstract

THE PROTEIN KINASE ATAXIA-TELANGIECTASIA AND RAD3-RELATED (ATR) IS AN IMPORTANT PLAYER TO GUARANTEE THE GENOME INTEGRITY IN *LEISHMANIA MAJOR*.

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The protein kinase Ataxia-Telangiectasia and Rad3-related (ATR) is a master regulator of the eukaryotic response to DNA injuries that is activated in response to the accumulation of single stranded DNA (ssDNA) and orchestrates checkpoint activation, cell cycle arrest, replication fork stabilization/restart, control of origin firing and telomeric stabilization providing genome maintenance and stability. However, little is known about ATR kinase functions in an organism with a remarkable plastic genome such as *Leishmania*. Using CRISPR/Cas9 editing tool we were able to generate cells expressing a N'terminal tagging (^{myc}ATR) that reveals the presence of the kinase at nuclear and kinetoplast. The deletion of ATR C'terminal region (^{myc}ATR$^{\Delta C}$), where the kinase domains are predicted, seems to affect the protein location, expression and/or stability. Those mutant ATR cells showed to be sensitive to replication stress: accumulating ssDNA, DNA damage markers (γH2A), and a disrupted cell cycle. The Marker Frequency Analysis (MFA-seq) showed that in ^{myc}ATR$^{\Delta C}$ the replication activation on the main origin is not affected with or without replication stress. However, under stress, those cells showed a significantly decrease of sub-telomeric replication signal. Those results suggest that ATR is important to genome maintenance guarantying the proper replication process after stress.