

MAMMALIAN RUVBL PROTEINS ARE ESSENTIAL FOR EFFECTIVE REPLICATION AND PROTECTION FROM REPLICATION STRESS

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The frequent occurrence of transcription and DNA replication in cells results in many encounters, and thus conflicts, between the transcription and replication machineries. These conflicts constitute a major intrinsic source of genome instability, which is a hallmark of cancer cells. The INO80 family members RUVBL1 and RUVBL2 are overexpressed in cancers from many different tissue types. They belong to a large family of ATPases known as AAA+ proteins (ATPases associated with diverse cellular activities) including nucleic acid-processing enzymes, chaperones, and proteases. Their functional diversity is likely due to participation in different cellular complexes or complex sub-assemblies, including INO80, TRRAP-TIP60 and SRCAP chromatin remodeling complexes. RUVBL proteins regulate the expression of p21 and interact with c-myc, RPA which could play a significant role in cancer cell growth. Previously, we have shown that the knock-down of Ino80 and Arp8 subunits of INO80 remodeler led to deficient replication elongation and destabilized stalled replication forks, implying a similar requirement for RUVBL proteins. In line with this expectation, knock-down of RUVBL1 like their overexpression slowed S-phase progression and led to reduced rate of replication elongation as found by DNA fiber labeling and analysis with EdU incorporation. Reduced levels of RUVBL proteins and their overexpression also lead to increased replication stress and genome instability. We hypothesize the possible involvement of RUVBL in resolution of transcription-replication conflicts in the nucleus

Biography

Rossitsa Hristova is PhD student in Institute of Molecular Biology, Bulgarian Academy of Sciences. She has completed her Master degree in Genetic and Cellular Engineering from Sofia University "St. Kliment Ohridsky". She is first Author in two scientific articles related with genome stability and DNA repair. She has received some awards for scientific excellence in recent three years.

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