New role assigned to a human protein in transcription and genome stability

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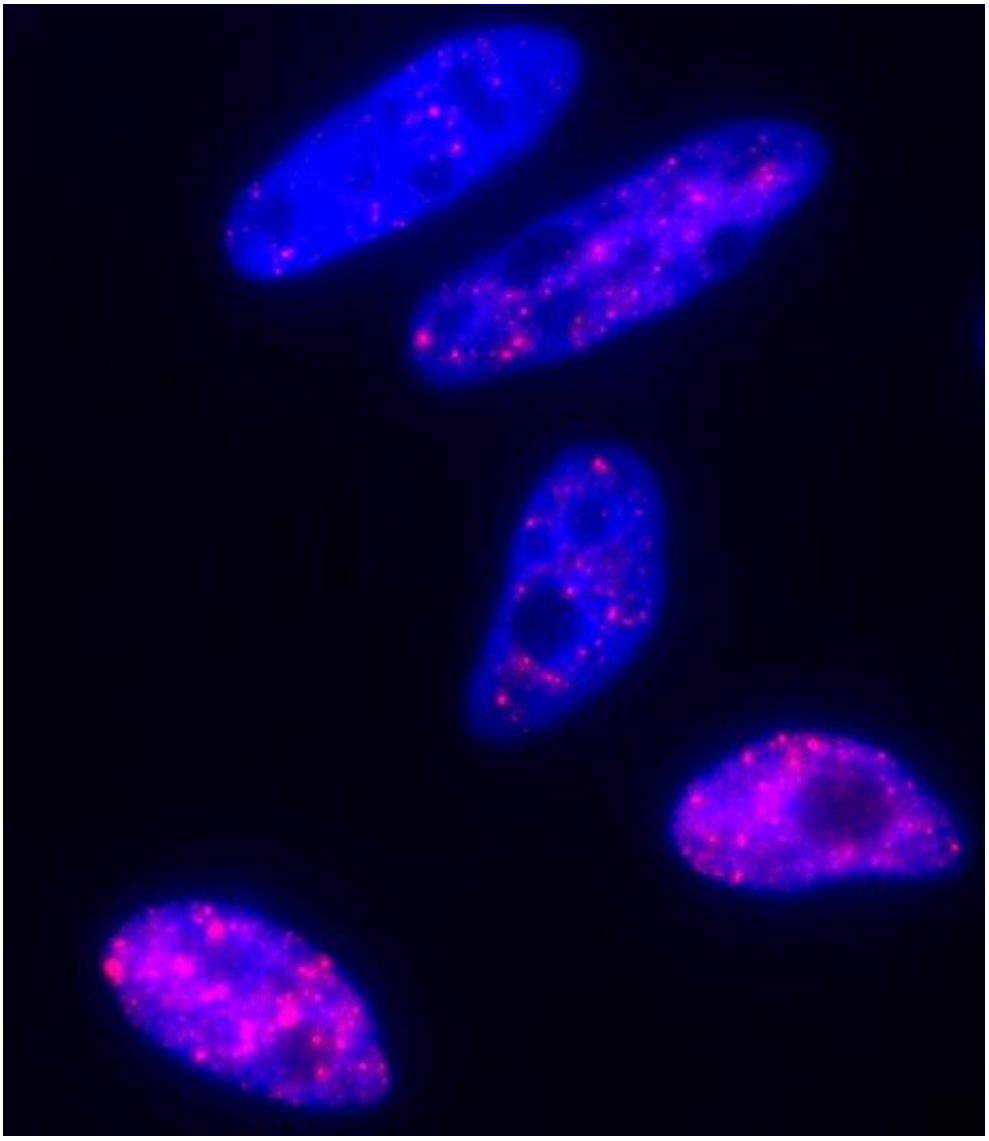

Credit: Universidad de Sevilla

Transcription of genetic information is a fundamental process for life. If it does not work correctly, the consequences for the organism range from lethality to defects during development, genetic diseases, insufficient response to infections and stresses or propensity to develop cancer, given its pleiotropic effect. For this reason, it is important to know in depth the process by which this 'DNA copy' is obtained and what elements are involved.

Along these lines, experts from the University of Seville and the Andalusian Center for Molecular Biology and Regenerative Medicine (Cabimer), in collaboration with the research group of Professor Patrick Sung from Yale University (USA), have published a new research article in which they show for the first time, the crucial role that the protein UAP56/DDX39B plays for a correct transcription of the genetic material and the integrity of the genome.

"DNA-RNA hybrids, or R loops, are structures that generate genomic instability, a common feature of tumor cells. In this article we have discovered that the human protein UAP56/DDX39B has a key role in the elimination of DNA-RNA hybrids that are accidentally generated during transcription, guaranteeing the integrity of the genome, as well as a correct gene expression," explains Andrés Aguilera, professor at the University of Seville and director of Cabimer.

UAP56/DDX39B is a protein found in the nucleus of mammalian cells. It is conserved in all eukaryotes and plays an essential role in the transcription and processing of RNAs. Organisms cannot live without this protein, its inactivation produces defects in the expression of genes and in the stability of genomes, which is why it is important to know its functions.

On the other hand, unscheduled R loops are DNA-RNA hybrids that are accidentally generated between the nascent RNA and its template DNA

during transcription. They form spontaneously, thanks to the pairing capacity of the nucleic acid chains, and for this reason cells have developed machineries to prevent and eliminate R loops, thus avoiding their negative consequences.

This work is part of the Ph.D. thesis of Dr. Carmen Pérez Calero, defended in February 2020 at the University of Seville, and is part of the ERC Advanced research project of the European Research Council obtained in 2015, funded of 2.35 million euros.

More information: Carmen Pérez-Calero et al, UAP56/DDX39B is a major cotranscriptional RNA–DNA helicase that unwinds harmful R loops genome-wide, *Genes & Development* (2020). DOI: 10.1101/gad.336024.119

Provided by University of Seville

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