New research describes key function of enzyme involved in RNA processing

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Researchers at the Case Western Reserve University School of Medicine have identified a cellular mechanism that is critical in maintaining normal cell function.

In their work, the researchers led by Eckhard Jankowsky, PhD, researcher and associate professor in the Center for RNA Molecular Biology at the Case Western Reserve University School of Medicine, examined the function of TRAMP, a protein complex involved in the processing of RNA or ribonucleic acid within the cell. They identified a key function for the protein Mtr4p in a process that initiates the degradation of select RNAs, a necessary step in preserving normal cell function.

The research findings appear in the June 9 issue of the journal *Cell* in a paper titled "The RNA Helicase Mtr4p Modulates Polyadenylation in the TRAMP Complex." Dr. Jankowsky is the senior author.

Cellular function requires a multitude of different types of RNA that need to be correctly processed and assembled into functional complexes.

"RNA that is improperly assembled, defective, or no longer needed, looks very similar to RNA that is being used," Dr. Jankowsky said. "So, improperly assembled, defective, or no longer needed RNA can readily interfere with ongoing processes. To avoid this, there are several very efficient RNA degradation pathways, and one of these is initiated by TRAMP."

The TRAMP complex identifies the RNAs slated for degradation and tags them with a stretch of adenosines, one of the four nucleotides of which RNA is made. The number of adenosines in the tag has to be limited, because RNAs with too many adenosines are no longer recognized as targets for degradation.

Dr. Jankowsky and the team of researchers that included Huijue Jia, a graduate student at the School of Medicine, and Jim Anderson, associate professor of Marquette University, a key collaborator and instrumental figure in the discovery of the TRAMP complex, studied the molecular mechanism how the TRAMP complex marks RNAs. TRAMP is comprised of the enzyme poly(A) polymerase Trf4p, the Zn-knuckle protein Air2p, and Mtr4p, a RNA helicase. Helicases unwind helices, but in TRAMP, the researchers found, the helicase Mtr4p controls the number of adenosines added.

In their paper, the researchers detail how the helicase controls the number of the adenosines that are appended. Mtr4p counts the number of adenosines (between four and five) that have been appended by the polymerase, and then adjusts the polymerase activity accordingly.

"Our work explains an important step in the mechanism by which cells mark RNAs for degradation in the nucleus," Dr. Jankowsky said. "Appropriate tagging is critical for cell function."

The research, which took place in Dr. Jankowsky's lab in the Center for RNA Molecular Biology at Case Western Reserve University School of Medicine, establishes a basis for future research to examine the steps between tagging RNA and the actual RNA degradation by other enzymes that are involved in this process.

Provided by Case Western Reserve University