New function discovered for ADAR1 in protecting stressed cells from apoptotic death

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The RNA editing protein ADAR1 was first discovered several decades ago. Now, scientists at The Wistar Institute have identified a new function for the protein: It stops cells that have been exposed to stressors such as ultraviolet (UV) radiation from dying. Study results were published recently in *Nature Structural & Molecular Biology*.

There are two forms of the ADAR1 protein, ADAR1p110 and ADAR1p150. Several biological functions for ADAR1p150 have been revealed, but little is known about the role of ADAR1p110 in vivo. The new research shows that ADAR1p110 regulates the response of cells to certain stressors, including UV radiation, by protecting them from dying as a result of a process called apoptosis, a form of programmed cell death.

"Before we started this work, we knew very little about the function of ADAR1p110 in vivo," said Kazuko Nishikura, Ph.D., professor in the Gene Expression and Regulation Program at The Wistar Institute and senior author of the study. "We knew that it could edit RNA, a polymeric molecule key for decoding the genetic material in a cell, but we did not know if this was important for its biological function."

"We were surprised to find that ADAR1p110 has an important biological role as a stress-response protein, and that this function is independent of its ability to edit RNA," she added.

To identify the functions of ADAR1p110, Nishikura and colleagues

reasoned that the cellular location of the protein must be linked to its function. They found that when cells were exposed to stressors such as UV radiation, ADAR1p110 transiently moved from its normal location in the nucleoplasm and nucleoli of a cell into the cytoplasm.

The researchers then characterized the pathway controlling this change in cellular distribution, finding that it involved a protein called MAP kinase p38, which was already known to have a role in regulating death or survival of stressed cells.

Once in the cytoplasm, Nishikura and colleagues showed that ADAR1p110 protects a defined set of mRNAs from degradation. Many of these mRNAs decode genes involved in preventing apoptotic cell death, leading the researchers to conclude that ADAR1p110 protects cells from stress-induced apoptosis by protecting anti-apoptotic mRNAs from degradation.

"Now that we have a well-defined function for ADAR1p110, we can work to understand its role in postnatal development and disease, in a particular cancer," added Nishikura.

More information: Masayuki Sakurai et al, ADAR1 controls apoptosis of stressed cells by inhibiting Staufen1-mediated mRNA decay, *Nature Structural & Molecular Biology* (2017). DOI: 10.1038/nsmb.3403

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