Researchers uncover biochemical rules between RNA-protein interactions and expressions

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A team of Case Western Reserve University researchers has found a way to measure key characteristics of proteins that bind to RNA in cells—a discovery that could improve our understanding of how gene function is disturbed in cancer, neurodegenerative disorders or infections.

RNA—short for ribonucleic acid—carries genetic instructions within the body. RNA-binding proteins play an important role in the regulation of gene expression. Scientists already knew that the way these proteins function depends on their "binding kinetics," a term that describes how frequently they latch on to a site in an RNA, and how long they stay there.

Until now, researchers could not measure the kinetics of RNA-binding proteins in cells. But the Case Western Reserve researchers answered this longstanding question in RNA biology. The findings open the door to a biochemical understanding of RNA protein interactions in cells.

By understanding the kinetics, researchers can quantitatively predict how an RNA binding protein regulates the expression of thousands of genes, which is critical for developing strategies that target RNA protein interactions for therapeutic purposes.

"The study marks a major step toward understanding how gene function is regulated and how to devise ways to correct errors in this regulation in diseases such as cancer, neurodegenerative disorders or infections," said Eckhard Jankowsky, the study's principal author and a professor of biochemistry at the university's School of Medicine and director of the

school's Center for RNA Science and Therapeutics .

Their study, "The kinetic landscape of an RNA binding protein in cells," was published Feb. 10 in *Nature*. Funding from the National Institute of General Medical Sciences and the National Science Foundation supported the research.

The co-authors, all from Case Western Reserve, are: research associate Deepak Sharma; graduate students Leah Zagore, Matthew Brister and Xuan Ye; Carlos Crespo-Hernández, a chemistry professor; and Donny Licatalosi, an associate professor of biochemistry and member of the Center for RNA Science and Therapeutics.

To measure the kinetics of RNA binding proteins, the researchers used a laser that sends out extremely short (femtosecond) pulses of ultraviolet light to cross-link the RNA-binding protein known as DAZL to its several thousand binding sites in RNAs. (DAZL, short for Deleted in Azoospermia-Like, is involved in germ cell development.) They then used high throughput sequencing to measure the change of the crosslinked RNA over time and determined the binding kinetics of DAZL at thousands of binding sites.

The resulting "kinetic landscape" allowed the researchers to decode the link between DAZL binding and its effects on RNAs.

More information: Sharma, D. et al. Dynamics of RNA–protein interactions studied in living cells, *Nature*
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