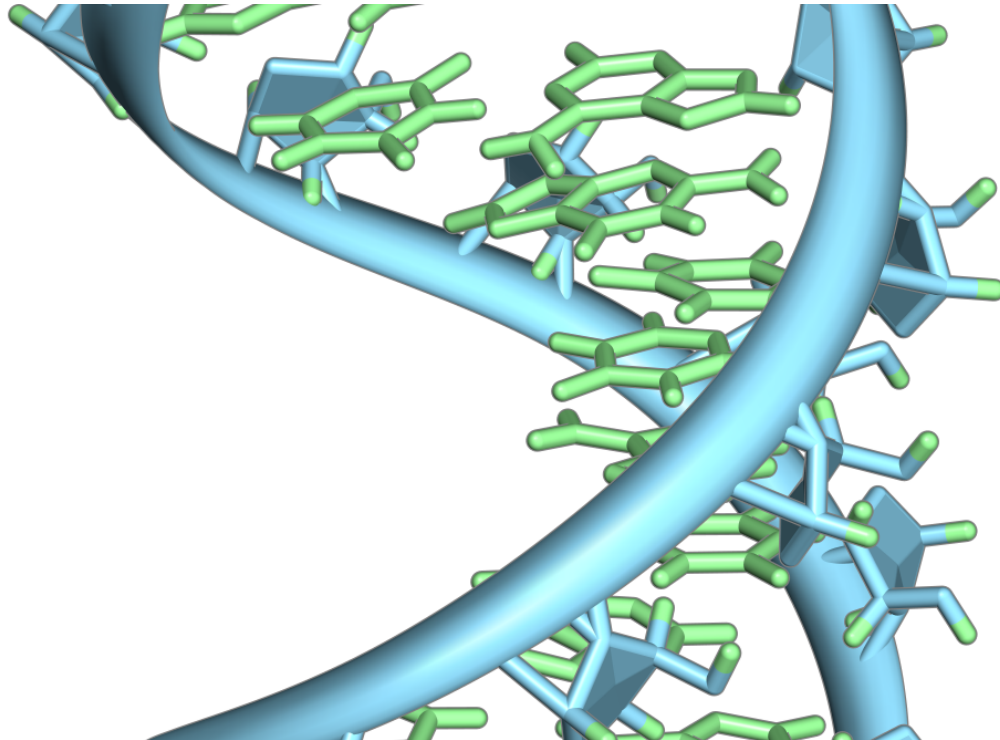


New RNA molecules may play a role in aging

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A hairpin loop from a pre-mRNA. Highlighted are the nucleobases (green) and the ribose-phosphate backbone (blue). Note that this is a single strand of RNA that folds back upon itself. Credit: Vossman/ Wikipedia

The genome is the master plan for all body parts, from toe nails to eyebrows. But it's not just the blueprint that determines what's built. All of the cellular players that draw instructions from the blueprint add their own interpretation to the design, and researchers are still discovering new players. Using new tools they developed, Thomas Jefferson

University researchers have found a sea of a new subtype of RNA molecules in the cell, and evidence suggesting they may play a role in aging processes.

"A lot of research has focused on the most famous short RNA—the microRNA," says senior author Yohei Kirino, Ph.D., associate professor in the Department of Biochemistry and Molecular Biology and Jefferson's Computational Medicine Center. "MicroRNA is powerful in that it can silence messenger RNA, essentially diverting the production of certain cellular elements encoded by the genome, and we can study them with established methods. We wanted to know what these other, more difficult to capture short RNA were doing in the cell. Our study begins to answer that question."

The research was published in *PLOS Genetics* on January 13th.

The subtype of RNA Dr. Kirino studied is called cyclic-phosphate containing RNA, or cP-RNA, for short. Although researchers knew this unusual form of phosphate existed on RNA molecules, they assumed it was just an intermediate form generated during RNA digestion. Current methods to track RNA, by amplifying and sequencing the molecule, fail to capture RNA with a cyclic phosphate tail. "The shape is problematic," says Dr. Kirino.

[Three years ago](#), however, Dr. Kirino's lab [developed a system](#) for targeting cP-RNAs so that they could be amplified and sequenced. Using this method, the research team was able to sequence all of the cP-RNAs present in the mouse tissues. "This is the first complete sequencing data for this RNA subtype," says Dr. Kirino.

The sequencing revealed several surprises. First, first author Megumi Shigematsu, a research associate in Dr. Kirino's lab, showed there was a lot more of the cP-RNA than expected. Numerous novel cP-RNA

species were identified to be generated from various types of cellular RNAs such as transfer RNAs, messenger RNAs, and ribosomal RNAs. This suggests that cyclic phosphates may be involved in the function of RNA with various roles in the cells.

And those cP-RNAs were very abundant—for example, just one cP-RNA from ribosomal RNA were 300-fold more abundant than all of the varieties of microRNA in the cell combined. cP-RNAs were also present throughout tissues of the body of a mouse, including the lung, muscle, spleen and thymus. Finally, the researchers saw that the abundance of cP-RNAs changed over time, decreasing in number as the mouse aged.

"We still have more questions about these molecules than we have answers," says Dr. Kirino. "But given their abundance, how ubiquitous they are in tissues throughout the body, and that their numbers change as tissues age, we know that this is an area that needs further exploration."

Dr. Kirino's lab is working to explore how cP-RNAs play a role in asthma, infectious disease and cancer.

More information: Megumi Shigematsu et al, Genome-wide identification of short 2',3'-cyclic phosphate-containing RNAs and their regulation in aging, *PLOS Genetics* (2019). [DOI: 10.1371/journal.pgen.1008469](https://doi.org/10.1371/journal.pgen.1008469)

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