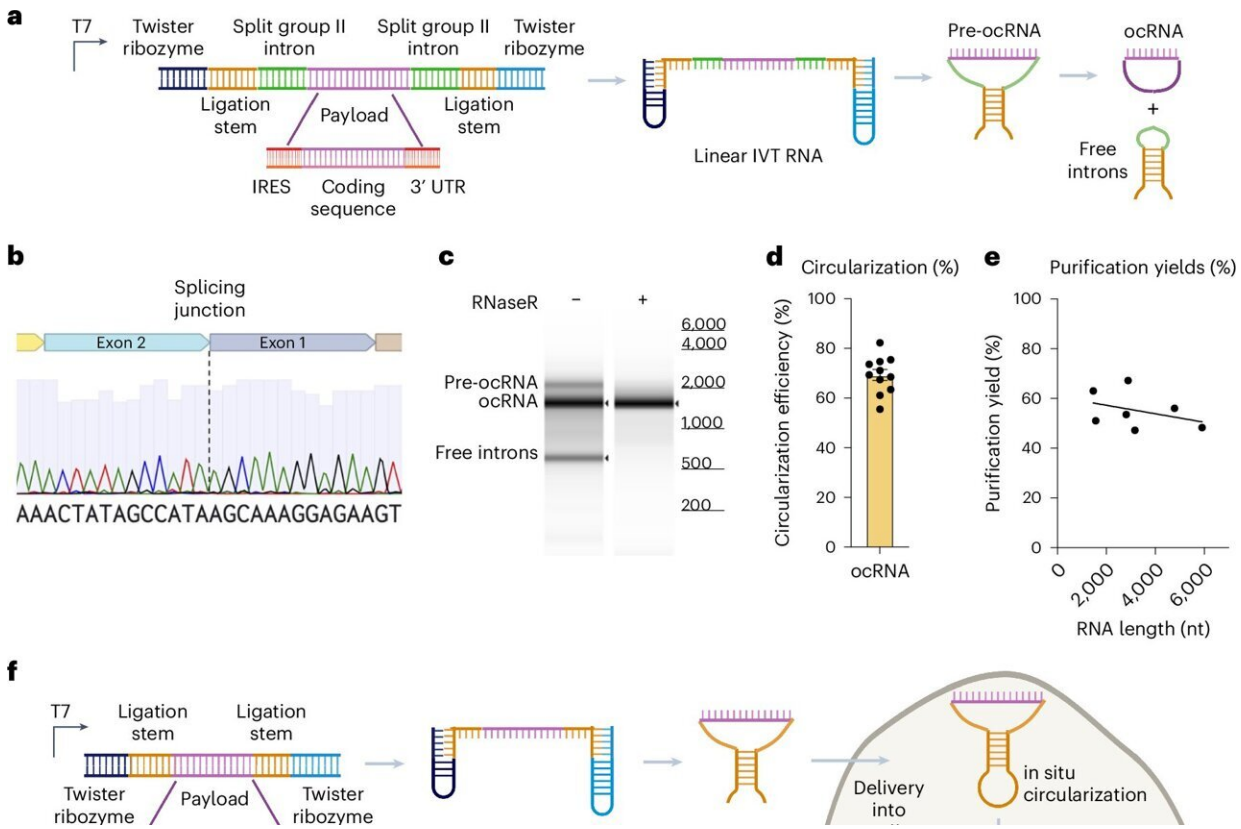
Closing the RNA loop holds promise for more stable, effective RNA therapies

August 26 2024, by Liezel Labios



Engineering ocRNAs and icRNAs. Credit: *Nature Biomedical Engineering* (2024). DOI: 10.1038/s41551-024-01245-z

New methods to shape RNA molecules into circles could lead to more effective and long-lasting therapies, shows a study by researchers at the

University of California San Diego. The advance holds promise for a range of diseases, offering a more enduring alternative to existing RNA therapies, which often suffer from short-lived effectiveness in the body.

The work is published in *Nature Biomedical Engineering*.

RNA molecules have emerged as powerful tools in modern medicine. They can silence genes through small interfering RNAs (siRNAs) or serve as templates for making therapeutic proteins, as seen with messenger RNAs (mRNAs). Unlike gene editing technologies, which make permanent changes to DNA, RNA therapies offer a temporary but highly targeted approach.

However, one major challenge is that RNAs do not last long in the body, which limits their effectiveness. The concept of circular RNAs (cRNAs) has gained traction as a solution to this challenge. Circular RNAs, unlike their linear counterparts, have a closed-loop structure that renders them more resistant to degradation. The problem is that existing methods for creating circular RNAs are complex and inefficient.

To overcome these hurdles, researchers led by Prashant Mali, a professor in the Shu Chien-Gene Lay Department of Bioengineering at UC San Diego, developed two new methods for producing circular RNAs that are simple and scalable. One method occurs inside cells using a naturally occurring protein called RtcB, to splice RNA strands into loops. The other method, in contrast, uses a type of bacterial enzyme known as group II introns to form circular RNAs outside of cells.

The researchers also developed simple purification steps that significantly boost the yield of circular RNAs. These advancements mean that circular RNAs can be produced with greater ease and quantities than previously possible.

The circular RNAs were tested in heart muscle cells and neurons. They displayed enhanced stability and biological activity, outperforming traditional linear RNAs in both cell types. These findings suggest that circular RNAs could be beneficial in treating conditions that affect the heart and nervous system.

Next, researchers are working to extend these studies into additional in vivo settings.

More information: Michael Tong et al, Robust genome and cell engineering via in vitro and in situ circularized RNAs, *Nature Biomedical Engineering* (2024). DOI: 10.1038/s41551-024-01245-z

Provided by University of California - San Diego