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The RNA world

This issue of *Nature Structural & Molecular Biology* presents studies investigating RNA processing, including mechanisms of splicing, biogenesis of the splicing machinery, decoding of mRNA by the ribosome, and deadenylation of mRNA for degradation. We are also delighted to be publishing News & Views and Comment pieces that reflect on these exciting advances in the field.

RNA is a remarkable molecule that, by virtue of its chemical composition and reactive nature, bridges two worlds of molecular function; like DNA, it can hold and transmit genetic information, and, like proteins, it can accelerate many of the central chemical reactions that constitute life. This month, *Nature Structural & Molecular Biology* (NSMB) features several papers where RNA and RNA-driven molecular machines take center stage. In these RNA-driven molecular machines, such as the spliceosome and the ribosome, RNA carries out these two molecular functions simultaneously as both subject and object.

The spliceosome is a remarkable eukaryotic RNA-driven molecular machine that catalyzes the removal of introns from nuclear pre-mRNA. In an insightful News & Views, Pleiss and colleagues observe that "…the spliceosome, which, like its ancestral cousin the ribosome, functions as an RNA–protein complex in which the RNA elements are thought to constitute the catalytic active site and the proteins have evolved to facilitate speed and fidelity within the process. Similar to the ribosome, which must readily distinguish between cognate and non- or near-cognate transfer RNA (tRNA) substrates in protein synthesis, the spliceosome must properly identify the 'cognate' splice site signals in a substrate among a background of near- and non-cognate sites."

In this issue, we observe several instances of these RNA-driven molecular machines as they work on their RNA substrates with such an exquisite level of chemical discernment. Suzuki and colleagues and Ryback and Gagnon detail the molecular underpinnings of the decoding capability of the bacterial ribosome, as it assesses matches between mRNA codons and tRNA anticodons, and the mechanisms by which it avoids imperfect matches, by capturing these transient states and imaging them with cryo-electron microscopy. Shi and colleagues show how this level of discernment reemerges in the process of branch site proofreading by the human spliceosome as it prepares to remove non-coding introns from pre-mRNA to generate mature translatable mRNAs. The accompanying News & Views from Pleiss and colleagues puts forth a fascinating conceptual synthesis of the parallels between this process and group II self-splicing introns, which carry out a similar reaction without the help of a *trans*-acting spliceosome, by contrasting with the structures of group II intron lariat formation by Toor and colleagues (D. B. Haack et al., *Nat. Struct. Mol. Biol.* **31**, 179–189; 2024) published in our January issue.

Before the human spliceosome can operate on its pre-mRNA substrate, it needs to be assembled from its component parts. Galej and colleagues and Plaschka and colleagues structurally detail the biogenesis and recycling of the 'heart' of the human spliceosome, the U5 small nuclear ribonucleoprotein particle (snRNP), with the help of protein chaperones. Zhang elegantly summarizes the findings from these two papers in an accompanying News & Views.

As a tribute to this impressive collection of papers investigating various aspects of RNA processing, our cover this month depicts a film being spliced. Moreover, in continuation of our series of articles commemorating NSMB's 30th anniversary, a Comment by Passmore and Zhang provides insights into RNA synthesis, splicing and maturation and how technological improvements have paved the way for increased experimental acuity. Valkov, Kim and colleagues further detail the kinetics of the stability of mRNAs and its dependence on the sequence and composition of their poly(A) tails.

We would be remiss to overlook the other molecular effectors that bring about cellular functions in this issue — DNA and proteins. Tachibana et al. look at how DNA packaged in chromatin can be opened by the pioneering factor NR5A2, and Rhodes writes an illuminating historical Perspective on how the chromatin remodeler INO80 alters chromatin in light of new and old studies. Eichman, Chazin and colleagues progress our conceptual understanding of DNA replication initiation mechanisms by the DNA polymerase α–primase, whereas O'Sullivan and colleagues demonstrate the unexpected regulation of telomere replication and stability by DNA, not protein, ADP-ribosylation, with an accompanying News & Views by Doksani and Lottersberger that contextualizes these findings. Finally, Aggarwal and colleagues solve the mechanism of activation of the bacterial self-killing Cap5 CBASS (cyclic oligonucleotide-based antiphage signaling system) immune defense system, and Moores, Way and colleagues investigate the structure and function of contractin at actin filament branches, a protein that helps with cellular motility, with an associated News & Views by Rottner and Bieling.

We hope you enjoy reading this issue of NSMB that delves into the wonderfully complex world of RNA and other molecular machines as much as we enjoyed putting it together.

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