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**Structural Biology of Ribozymes**

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The National Synchrotron Light Source (NSLS) has been instrumental to the investigation of RNA molecular structures and interactions during the past year. Several crystal forms of the hepatitis delta virus ribozyme, a small self-cleaving RNA essential for viral replication, have been investigated at NSLS beamlines using multiwavelength anomalous diffraction (MAD) techniques. Ultimately, four structures will be determined using these data, revealing the pre-cleaved state of the ribozyme as well as the product form of the ribozyme found in a viral replication intermediate. These structures, at resolutions from 1.8 – 3.0 Å, will be essential to understanding the catalytic mechanism of the ribozyme and the structural similarities and differences between the two closely related forms found in the hepatitis delta virus pathogen.

We have also utilized the data collection time provided at the NSLS to solve crystal structures of key components of two different self-splicing intron classes. Recently-determined structures of three variants of the P4-P6 domain of the *Tetrahymena* group I intron provide important insights into the molecular basis for unusual stability of a ubiquitous RNA tertiary interaction called the A-minor motif. A-minor interactions are thought to be essential to the folding of numerous large RNAs, and also may be responsible for accuracy during decoding of messenger RNA templates on the ribosome. A structure of the catalytically essential domains 5 and 6 of a group II intron has been solved using MAD, revealing a totally unexpected structure around the “branchpoint” residue in domain 6 that explains why this particular nucleotide acts as the nucleophile during intron splicing.

Finally, a crystal structure of the hepatitis C internal ribosome entry site (IRES) RNA IIIabc domain reveals a complex molecular surface recognized by the host translational machinery during viral infection. This structure provides a basis for biochemical experiments to test the role of this RNA in recruiting and positioning ribosomes on viral messenger RNAs.