Structures of Lsm rings from S. pombe

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Recruitment of U6 snRNA into spliceosomes is highly regulated by numerous protein chaperones. One such chaperone is the Lsm2-8 ring, which associates with the 3' end of U6 and stimulates intermolecular base-pairing between U6 and U4 snRNAs. The 3' end of U6 is itself a regulatory locus for spliceosome assembly, as RNA processing enzymes can alter the length of the RNA and install terminal phosphate groups, thereby masking the 3' cis diol group found on unprocessed U6 RNA.

Using the model system S. cerevisiae, we previously determined how the Lsm2-8 ring recognizes the unique non-cyclic phosphate group found in that species. However, S. cerevisiae is an evolutionary outlier in that the 3' ends of other eukaryotic orthologs of U6 (including humans) typically terminate with 2',3'-cyclic phosphate group. We now show that the S. pombe Lsm2-8 ring exhibits RNA binding properties that mirror the known properties of metazoan rings,
with a binding preference for RNA with a 2',3'-cyclic phosphate moiety. High resolution crystal structures of S. pombe Lsm2-8 bound to small fragments of U6 RNA show that Lsm2-8 ring does not specifically recognize the 3' cis diol moiety of nascent U6, while the cyclic phosphate (commonly denoted as ">p") on mature U6 RNA is recognized by contacts with highly conserved residues Lsm3-Arg27 and the C-terminus of Lsm8.