Structural Basis for Specific Recognition of the UsnRNP m_3G-cap by Snurportin1

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The small nuclear ribonucleoprotein particles (snRNPs) are the major components of the splicing machinery that removes introns from pre-mRNA. In metazoans, the snRNP biogenesis is an ordered process requiring both nuclear and cytoplasmic phases. After transcription, the snRNAs U1, U2, U4, and U5 are exported into the cytoplasm, where the assembly with seven Sm proteins occurs and the snRNA 5′-cap nucleotide is modified from a 7-methyl-guanosine (m^7G-) to a 2,2,7-trimethyl-guanosine (m_3G-) cap. The hyper-methylated m_3G-cap represents one of the two nuclear localisation signals of the snRNPs. As an import adaptor snurportin1 bridges the interaction between the m_3G-cap bearing snRNPs and the nuclear import receptor importin-β, which mediates the interaction with and translocation through the nuclear pore complex. Snurportin1 contains a N-terminal importin-β-binding (IBB) domain and a m_3G-cap-binding region, which shows no similarity to other known nuclear import factors. We have solved the crystal structure of the m_3G-cap binding domain of snurportin1 by means of MIRAS, and the structure was refined at 2.4 Å resolution. The crystal structure reveals an unexpected binding mode for the m_3G-cap, that significantly differs from other cap-binding proteins such as eIF4E and CBP20. The structural basis for the discrimination of m^7G-cap bearing RNAs by snurportin1 will be discussed.

Keywords: RNA-protein interactions, nuclear transport, MIRAS