

Abstract (English)

snRNPs are key components of the spliceosome. During their life, they are found in the cytoplasm and also in the nucleus, where carry out their function. There are five major snRNPs named according to RNA they contain U1, U2, U4, U5 and U6. Each snRNP consists from RNA, ring of seven Sm or LSm proteins and additional proteins specific for each snRNP. Their biogenesis starts in the nucleus, where they are transcribed. Then they are transported into the cytoplasm. During their cytoplasmic phase, the SMN complex forms the Sm ring around the specific sequence on snRNA and cap is trimethylated. These two modifications are the signals for reimport of snRNA into the nucleus, where they accumulate in the nuclear structures called Cajal bodies (CBs), where the final maturation steps occur.

There are several quality control points during snRNP biogenesis that ensure that only fully assembled particles reach the spliceosome. The first checkpoint is in the nucleus immediately after the transcription, when the export complex is formed. The second checkpoint is in the cytoplasm and proofreads Sm ring assembly. If the Sm ring formation fails, the defective snRNPs are degraded in the cytoplasm by Xrn1 exonuclease. However, it is still unclear, how the cell distinguishes between normal and defective snRNAs. The last checkpoint occurs in CBs. However, signals that target and retain snRNPs in CBs have yet to be described.

In this work, I analyzed the main role of Sm ring in the quality control of snRNA in the nucleus and the cytoplasm.

First, we identified Sm protein motifs important for targeting of snRNPs into CBs and proposed a model, where Sm proteins play an important role in quality control in CBs.

Second, we explored a role of the component of the SMN complex, Gemin3, in the Sm ring assembly. My data suggest that Gemin3 is involved in unwinding of the secondary structure of snRNA prior to Sm ring formation.

Finally, we investigated the defective snRNAs which failed to acquire the Sm ring in the cytoplasm. We found that immature snRNAs are localized in P bodies and identified a new role for the LSm1 protein in snRNA degradation.

