

**P018** The Connection between Histone pre-mRNA Processing Factors and Cell Cycle

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The replication-dependent histone mRNAs lack a 3' polyA tail, but rather end with an evolutionarily conserved stem loop (SL). Formation of these unique 3' termini is cell-cycle regulated, occurring only in S phase to coordinate histone and DNA synthesis. Processing is mediated by both the U7snRNP and the Stem Loop Binding Protein (SLBP). We previously identified a zinc finger protein (ZFP100), a component of U7 snRNP, which interacts with SLBP only in the presence of the SL.

Here we report that Lsm11, a core U7 snRNP protein, interacts with ZFP100 through its N-terminal region that is conserved only in vertebrates. ZFP100 requires its C-terminal zinc fingers to bind to Lsm11, whereas its internal zinc fingers are required for SLBP/SL interaction. RNAi of ZFP100 or Lsm11 reduces SLBP levels and arrests cells in G1; revealing an unanticipated link between these proteins and G1 checkpoint machinery. RNAi of SLBP does not result in G1 arrest but rather an accumulation of cells in S phase. This suggests that the U7 snRNP components are essential to process histone pre-mRNA but SLBP may be essential for the efficient maintenance of the processed message but perhaps not for processing.

We also show that ZFP100 localizes to Cajal bodies. The zinc fingers required for Lsm11 binding are also required for Cajal body localization. ZFP100 localization to Cajal bodies is dependent on Lsm11 expression but independent of SLBP expression. These data suggest that the ZFP100/Lsm11 interaction is functionally upstream of ZFP100/SLBP in the metabolism of histone message.