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## An architectural checkpoint for the licensing of spliced mRNAs for mRNA export.

Harsh Vinodkumar Oza, Marius Wegener, Timur Makarov\*, Jonas Busam, Kathi Zarnack# & Michaela Müller-McNicoll# A critical quality control step in gene expression is the coupling of pre-mRNA splicing to nuclear export, ensuring that only fully processed transcripts reach the cytoplasm. How splicing fidelity is monitored and translated into export competence, however, remains poorly understood. Here we show that the splicing factor SRSF3 establishes an architectural checkpoint that licenses spliced messenger ribonucleoprotein complexes (mRNPs) for nuclear export. Using mild splicing inhibition by isoginkgetin in pluripotent mouse P19 cells, we induce selective intron retention in otherwise normally processed, polyadenylated transcripts. These intron-containing mRNAs fail to be exported and accumulate transiently and reversibly in enlarged nuclear speckles. Within these structures, mRNPs adopt a striking spatial organization, with coding regions buried in the core and retained introns and poly(A) tails exposed at the periphery, forming a characteristic donut-like pattern. Mechanistically, we find that splicing inhibition stabilizes SRSF3 in a hyperphosphorylated state. Hyperphosphorylated SRSF3 remains bound to RNA but fails to recruit the nuclear export receptor NXF1 and the poly(A)-binding protein ZC3H14. ZC3H14 is identified as a splicing-sensitive SRSF3 interactor whose recruitment to mRNA depends on SRSF3 dephosphorylation. iCLIP analysis reveals that ZC3H14 binds CA-rich regions near transcript 3' ends in spliced mRNAs, while upon splicing inhibition it binds almost exclusively to poly(A) tails. Consistently, splicing inhibition selectively impairs nucleo-cytoplasmic shuttling of ZC3H14. Together, our findings identify an export-competency checkpoint that operates at the level of mRNP architecture. We propose that SRSF3-dependent recruitment of ZC3H14 enables poly(A)-tail internalization and mRNP compaction, allowing release from nuclear speckles and export, whereas failure of this process traps mis-spliced mRNPs in a reversible, pre-export state.

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