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## TRIM28 prevents the export of retrotransposons

After completion of processing in the nucleus eukaryotic mRNAs are bound by the nuclear export factor NXF1 and are exported to the cytoplasm. For binding to mRNAs, NXF1 requires adapter proteins that recruit NXF1 to newly transcribed pre-mRNAs in a non-sequence-specific manner. To identify novel NXF1 adapter proteins for the selective export of specific transcript classes we developed a screen, which is based on their known characteristics: I) they bind in close proximity to NXF1 on the same RNA and II) the interaction is stabilized by the bound RNA. Our screen confirmed all known NXF1 adapter proteins, but also identified several chromatin-regulating proteins (CRPs) that were not known as NXF1 adapters or RNA binders. Interestingly, a lot of them are involved in retrotransposon silencing. We then focused on TRIM28 and tested whether it affects the export of retrotransposons via NXF1. TRIM28 is known to silence retrotransposons at the DNA level by interacting with KRAB zinc-finger proteins and recruiting the silencing machinery leading to heterochromatin formation. We confirmed that TRIM28 binds to RNA and iCLIP of NXF1 and TRIM28 showed that both proteins co-bind within retrotransposons (LTRs & non-LTRs), but also within protein coding transcripts and pseudogenes. Investigating whether TRIM28 acts as a novel NXF1 adapter for the export of mRNA we found that the depletion of TRIM28 does not affect the export of polyadenylated mRNA and it does not shuttle between nucleus and cytoplasm. Co-immunoprecipitations confirmed that NXF1 interacts with TRIM28 and with other proteins of the silencing machinery. Interestingly, TRIM28 also interacts with NXF1 but not with mRNA processing factors such as SRSF7 or PABPN1. This implies that NXF1 is present in different subcomplexes, either for bulk mRNA export or for retrotransposon silencing. A comparison of export targets derived from FRAC-Seq data after depletion of NXF1 and TRIM28 suggest that NXF1 binding is important for the export of retrotransposon and other foreign transcripts to the cytoplasm for translation and that TRIM28 normally prevents their export. This would represent a new layer of RNA-based mechanism for genome surveillance.

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