

**Mip6 binds directly to the Mex67 UBA domain to maintain low levels of Msn2/4 stress dependent mRNAs**

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RNA-binding proteins (RBPs) participate in all steps of gene expression, underscoring their potential as regulators of RNA homeostasis. We structurally and functionally characterize Mip6, a four-RNA recognition motif (RRM)-containing RBP, as a functional and physical interactor of the export factor Mex67. Mip6-RRM4 directly interacts with the ubiquitin-associated (UBA) domain of Mex67 through a loop containing tryptophan 442. Mip6 shuttles between the nucleus and the cytoplasm in a Mex67-dependent manner and concentrates in cytoplasmic foci under stress. Photoactivatable ribonucleoside-enhanced crosslinking and immunoprecipitation experiments show preferential binding of Mip6 to mRNAs regulated by the stress-response Msn2/4 transcription factors. Consistent with this binding, MIP6 deletion affects their export and expression levels. Additionally, Mip6 interacts physically and/or functionally with proteins with a role in mRNA metabolism and transcription such as Rrp6, Xrn1, Sgf73, and Rpb1. These results reveal a novel role for Mip6 in the homeostasis of Msn2/4-dependent transcripts through its direct interaction with the Mex67 UBA domain.