Direct binding of Ataxin-2 to distinct elements in 3' UTRs promotes mRNA stability and protein expression

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It has been proposed that Ataxin-2, a member of the LSm protein family, participates in the regulation of RNA metabolism through interaction with PABPC1. However, the exact biological mechanism and in vivo targets remain unknown. Here we report that Ataxin-2 binds directly to RNAs in a PABPC1-independent manner. High-throughput sequencing of Ataxin-2-bound RNAs prepared by PAR-CLIP revealed that Ataxin-2 binds predominantly to uridine-rich elements, including well-characterized cis-regulatory AU-rich elements, in the 3'UTRs of target mRNAs. Gene expression analysis after Ataxin-2 depletion or overexpression revealed that Ataxin-2 stabilizes target mRNAs and increases the abundance of corresponding proteins. A tethering assay demonstrated that Ataxin-2 elicits this effect by direct interaction with mRNAs. We also found that disease-associated polyglutamine expansion downregulates the physiological activity of Ataxin-2. These findings suggest that Ataxin-2 is an RNA-binding protein that targets cis-regulatory elements in 3'UTRs to stabilize a subset of mRNAs and increase protein expression.