| Cluster | RBPs | RNA categories | Function/References |
| --- | --- | --- | --- |
| c1 | XPO5, AGO1, AGO2, AGO3, AGO4 | miRNA + 3’UTR | XPO5, is a dsRNA-specific pre-miRNA and mRNA nucleocytosolic transporter (1) (2).  Four RBPs, AGO1, AGO2- AGO3, AGO4, are members of the AGO1 family, which crosslinked to microRNAs (miRNAs) and mature target mRNAs(3) (4). |
| c2 | NONO, TP53 | rRNA | Not known to specifically bind rRNA (reference library was depleted of rRNA and these libraries were shallow) |
| c3 | EIF3B, EIF3G, EIF3A, EIF3D, CPSF3, CPSF4, RBM10, NCBP3, DIS3, ALKBH5, LIN28A | Mixture (weak mRNA):  No distinct RNA annotation or positional binding preference | EIF3A, EIF3B, EIF3D, and EIF3G are involved in translational initiation and immunoprecipitated together {Lee:2015he} and showed a positional binding preference within the middle of the 5’ UTR, between the 5’ cap and the annotated start codon of the main open reading frame.  CPSF3 and CPSF4 are established cleavage and polyadenylation factors.  RBM10 is a splicing factor and exhibited preference for binding to both CDS and intron, particularly focused binding to 5’ and 3’ splice sites.  NCBP3 is a nuclear cap-binding protein.  DIS3 is the catalytic component of the nuclear RNA exosome and exhibited positional binding preference for the 5’ cap position.  ALKBH5 is an RNA demethylase.  LIN28A has been implicated in many aspects of RNA metabolism including splicing, translation, and miRNA biogenesis (5-8) (9). |
| c4 | SSB, DICER1 | tRNA | SSB has an established role in tRNA processing (10). Although DICER1 is not a canonical tRNA processing factor, it has been reported to bind to tRNAs (11, 12). |
| c5 | PAPD5, FBL, NOP58, NOP56, SRRM4 | snoRNA + snRNA | PAPD5 oligoadenylates specific snoRNAs (13).  FBL, NOP56, NO58 have established roles in snoRNA biogenesis (14, 15).  SRRM4 is known to co-IP with SNRNP70, U2AF1, U2AF2, SF3B1(16) and localize to splicing speckles (17) |
| c6 | FIP1L1, CPSF6, CPSF1, CPSF7, CSTF2, CSTF2T, MBNL1, HNRNPC, HNRNPD, FUS, ELAVL1, TARDBP | intron + 3’UTR | Predominantly nuclear proteins.  FIP1L1, CPSF6, CPSF1, CPSF7, CSTF2, CSTF2T regulate cleavage and polyadenylation (15). With the exception of CPSF1, these RBPs exhibited highly focused positional binding flanking the end of the 3’ UTR.  MBNL, FUS, and HNRNPC are involved in alternative splicing and polyadenylation (18, 19))(20, 21).  FUS exhibited positional binding preference for upstream of the end of 3’ UTR.  HNRNPC exhibited strong positional binding preference downstream of the 3’ UTR cleavage site.  ELAVL1, HNRNPD, FUS, and TARDBP are involved in many steps of RNA metabolism, including splicing, nuclear stability, and polyadenylation and mRNA stability and translation in the cytoplasm(22, 23) (24-27)).  ELAVL1 exhibited positional binding flanking the end of the 3’ UTR and for 5’ and 3’ splice sites.  TARDBP exhibited positional binding flanking the end of the 3’ UTR. |
| c7 | RBPMS, CAPRIN1, UPF1, IGF2BP1, LIN28B, FXR1, FXR2, FMR1iso1, FMR1iso7, RBM20, NUDT21, QKI, RTCB | CDS + 3’UTR | Mostly regulate translation, transport and localization of mature mRNAs in the cytoplasm. They exhibited variable levels of binding to both CDS and 3’ UTR.  RBPMS homolog Hermes is involved in germ plasm RNA localization in zebrafish and *Xenopus* oocytes (28-30) and exhibited preferential binding to the distal end of the 3’ UTR.  CAPRIN1 is involved in stress granule assembly (31).  UPF1 is an importer regulator of nonsense-mediated decay (32, 33).  IGF2BP1 is involved in mRNA stability, transport, and translation (34)and exhibited preferential binding to the distal end of the 3’ UTR.  LIN28B, like LIN28A has been implicated in many aspects of RNA metabolism and exhibited preferential binding to the distal end of the 3’ UTR.  FMR1 isoform 1 and isoform 7, FXR1, and FXR2 regulate transport and translation in many tissues including neurons (35, 36).  NUDT21 is involved in alternative polyadenylation (37).  QKI and RBM20 are primarily splicing factors, but also have been implicated in regulating stability and translation (38) (39). |
| c8 | ORF1, LINE1, TAF15, EWSR1, ZFP36, ZC3H7B, IGF2BP2, IGF2BP3, MOV10, ELAVL2, ELAVL3, ELAVL4, PUM2, DND1 | 3’UTR | ZFP36, ELAVL2, ELAVL2, ELAVL3, ELAVL4, and ZC3H7B are AU-rich element binding proteins that regulate mRNA stability and translation through the 3’ UTR (40, 41) (42).  PUM2, IGF2BP2 and IGF2BP3, PUM2, and DND1 regulate regulation of mRNA stability, localization and translation through 3’ UTR interaction (43) (3, 44) (45, 46).  Although TAF15 and EWSR1 are predominantly nuclear, regulation of RNA stability in the cytoplasm has been shown for TAF15 and FUS and might also be relevant for EWSR1 given nucleocytoplasmic shuttling (47).  MOV10 regulates mRNA stability and translation (48, 49) and has an established role in suppressing L1 elements (50), which encode ORF1 and LINE1.  MOV10 and UPF1 are prominent interactors of L1 RNPs (51). |

**Supplemental Table 1.**

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