

Table S1. Complete list of protein interactors obtained from MS analysis of SL-let-7a-1 and SL-let-7g ARiBo pull-downs.^a

Results from MS analysis of ARiBo pull-downs							Previous studies		
Gene name	Protein name	Uniprot entry	SL-let-7a-1		SL-let-7g		RBP	7a-1	7g
			versus mock	versus dlet-7g	versus mock	versus dlet-7g			
ADAR	Double-stranded RNA-specific adenosine deaminase	P55265	○	○			•	3,4	
ATP5B	ATP synthase subunit beta, mitochondrial	P06576	○					4	
BTF3	Transcription factor BTF3	P20290	○				•		
BTF3L4	Transcription factor BTF3 homolog 4	Q96K17	○	○					
C7orf50	Uncharacterized protein C7orf50	Q9BRJ6	○	○	○	○	•		
CBR1	carbonyl reductase [NADPH] 1	P16152	○						
CD3EAP	DNA-directed RNA polymerase I subunit RPA34	O15446	○	○			•		
CNBP	Cellular nucleic acid-binding protein	P62633	○				•		
CSDAP1	Y-box-binding protein 3	P16989	○	○	○	○	•	4	
CSNK2A1	Casein kinase II subunit alpha	P68400	○	○	○	○			
DDX17	Probable ATP-dependent RNA helicase DDX17	Q92841			b	○	•	3	6
DDX5	Probable ATP-dependent RNA helicase DDX5	P17844	○	○	○	○	•	3,4	6
DXH9	ATP-dependent RNA helicase A	Q08211	○	○	○		•	1,3,4,5	6
DUS3L	tRNA-dihydrouridine(47) synthase [NAD(P)(+)]-like	Q96G46	○	○			•		
EEF1A1	Elongation factor 1-alpha 1	P68104	○				•		
EIF2AK2	Interferon-induced, double-stranded RNA-activated protein kinase	P19525	○	○			•		
EPB41	Protein 4.1	P11171	○	○					
FARSA	Phenylalanine--tRNA ligase alpha subunit	Q9Y285	○	○			•		
FAU	Ubiquitin-like protein FUBI	P35544			○	○	•		
G3BP1	Ras GTPase-activating protein-binding protein 1	Q13283		○			•		
GNL3	Guanine nucleotide-binding protein-like 3	Q9BVP2	○	○			•		
GRSF1	G-rich sequence factor 1	Q12849	○	○	○		•		
HMGAI	High mobility group protein HMG-I/HMG-Y	P17096	○		○				
HNRNPA0	Heterogeneous nuclear ribonucleoprotein A0	Q13151	○	○	○		•	1,3	
HNRNPA1	Heterogeneous nuclear ribonucleoprotein A1	P09651	○	○			•	2,3,4	6
HNRNPA2B1	Heterogeneous nuclear ribonucleoproteins A2/B1	P22626	○	○			•	3,4	6
HNRNPA3	Heterogeneous nuclear ribonucleoprotein A3	P51991	○	○	○	○	•	3,4	6
HNRNPAB	Heterogeneous nuclear ribonucleoprotein A/B	Q99729	○	○	○		•	4	6
HNRNPD	Heterogeneous nuclear ribonucleoprotein D0	Q14103	○	○	○		•	3	
HNRNPF	Heterogeneous nuclear ribonucleoprotein F	P52597	○	○			•	1,3,4	
HNRNPH1	Heterogeneous nuclear ribonucleoprotein H	P31943	○	○			•	1,3,4	6
HNRNPH3	Heterogeneous nuclear ribonucleoprotein H3	P31942	○	○			•	1,3	
HNRNPL	Heterogeneous nuclear ribonucleoprotein L	P14866	○	○			•	1,2,3,4	6
HNRNPM	Heterogeneous nuclear ribonucleoprotein M	P52272	○				•	3	
HNRNPR	Heterogeneous nuclear ribonucleoprotein R	O43390	○	○			•		
HNRNPU	Heterogeneous nuclear ribonucleoprotein U	Q00839	○	○	○		•	3,4	6
HNRNPUL1	Heterogeneous nuclear ribonucleoprotein U-like protein 1	Q9BUJ2	○	○	○		•	3,4	6
HSD17B10	3-hydroxyacyl-CoA dehydrogenase type-2	Q99714	○	○			•		
HSPE1	10 kDa heat shock protein, mitochondrial	P61604	○		○		•		
IGF2BP1	Insulin-like growth factor 2 mRNA-binding protein 1	Q9NZI8	○	○	○	○	•	3,4	6
IGF2BP2	Insulin-like growth factor 2 mRNA-binding protein 2	Q9Y6M1	○	○	○	○	•		
IGF2BP3	Insulin-like growth factor 2 mRNA-binding protein 3	O00425	○	○	○	○	•		
ILF2	Interleukin enhancer-binding factor 2	Q12905	○		○		•	3,4,5	6
ILF3	Interleukin enhancer-binding factor 3	Q12906	○		○		•	1,3,4,5	6
LIN28B	Protein lin-28 homolog B	Q6ZN17	○	○	○	○	•	1,4	6
MRPL12	39S ribosomal protein L22, mitochondrial	Q9NWU5	○	○			•		
NCL	Nucleolin	P19338	○	○	○	○	•	2,4,5	
NONO	Non-POU domain-containing octamer-binding protein	Q15233	○	○	○	○	•	4	6
NSUN2	tRNA (cytosine(34)-C(5))-methyltransferase	Q08J23	○	○	○		•		
PA2G4	Proliferation-associated protein 2G4	Q9UQ80		b		○	•		
PCBP2	Poly(rC)-binding protein 2	Q15366	○	○			•		
PRKRA	Interferon-inducible dsRNA-dependent protein kinase activator A	O75569	○	○			•		
PURA	Transcriptional activator protein Pur-alpha	Q00577	○	○			•		
PURB	Transcriptional activator protein Pur-beta	Q96QR8	○	○			•		6
PUS1	tRNA pseudouridine synthase A, mitochondrial	Q9Y606	○	○			•		
RPL22	60S ribosomal protein L22	P35268	○	○	○	○	•		
RPL22L1	60S ribosomal protein L22-like 1	Q6P5R6	○	○					

RPL30	60S ribosomal protein L30	P62888			○	○	•	
RPS17;RPS17L	40S ribosomal protein S17	P08708	○	○	○	○	•	
RPS3A	40S ribosomal protein S3a	P61247	○	○			•	3,4
RPS7	40S ribosomal protein S7	P62081	○	○	○	○	•	
SARS2	Serine-tRNA ligase, mitochondrial	Q9NP81			○	○	•	
SART3	Squamous cell carcinoma antigen recognized by T-cells 3	Q15020	○	○			•	
SFPQ	Splicing factor, proline- and glutamine-rich	P23246	○	○			•	3,4
SNRPA	U1 small nuclear ribonucleoprotein A	P09012	○	○			•	3
SNRPD3	Small nuclear ribonucleoprotein Sm D3	P62318	○	○			•	4
SON	Protein SON	P18583	○		○		•	
SOX2	Transcription factor SOX-2	P48431	○	○				
SRP14	Signal recognition particle 14 kDa protein	P37108	○	○	○	○	•	
SRSF1	Serine/arginine-rich splicing factor 1	Q07955	○	○	○	○	•	3
SRSF2	Serine/arginine-rich splicing factor 2	Q01130	○	○			•	
SRSF3	Serine/arginine-rich splicing factor 3	P84103	○	○			•	
SRSF9	Serine/arginine-rich splicing factor 9	Q13242	○	○	○	○	•	
SSB	Lupus La protein	P05455	○	○	○		•	3
STAU1	Double-stranded RNA-binding protein Staufen homolog 1	O95793	○		○		•	3,4
STRBP	Spermatid perinuclear RNA-binding protein	Q96S19	○	○	○	○	•	3,4
SUB1	Activated RNA polymerase II transcriptional coactivator p15	P53999	○	○	○	○	•	
SYNCRIP	Heterogeneous nuclear ribonucleoprotein Q	O60506	○	○	○	○	•	
TCOF1	Treacle protein	Q13428	○		○		•	
TFAM	Transcription factor A, mitochondrial	Q00059	○	○	○	○	•	
THOC4	THO complex subunit 4	Q86V81	○	○	○	○	•	
TKT	Transketolase	P29401				○		
TRIM28	Transcription intermediary factor 1-beta	Q13263	○				•	
TRIM71	E3 ubiquitin-protein ligase TRIM71	Q2Q1W2	○	○			•	
TRMT1L	TRMT1-like protein	Q7Z2T5				○	○	•
TRMT61A	tRNA (adenine(58)-N(1))-methyltransferase catalytic subunit	Q96FX7	○	○	○	○		
XRCC5	X-ray repair cross-complementing protein 5	P13010			○	○	•	
XRCC6	X-ray repair cross-complementing protein 6	P12956	○	○	○	○	•	
YBX1	Nuclease-sensitive element-binding protein 1	P67809	b	○	b	○	•	4
ZC3H4	Zinc finger CCCH domain-containing protein 4	Q9UPT8	○	○			•	
ZC3HAV1	Zinc finger CCCH-type antiviral protein 1	Q7Z2W4	○	○	○	○	•	
ZFR	Zinc finger RNA-binding protein	Q96KR1	○	○			•	
ZNF346	Zinc finger protein 346	Q9UL40	○	○			•	3,4
ZNF787	Zinc finger protein 787	Q6DD87	○	○				

^aPositive identification of a protein interactor (open circle) from the SL-let-7a-1 and SL-let-7g pull-downs is based on a SAINTexpress score ≥ 0.65 . Results are listed using either the mock or the dlet-7g ARiBo pull-down as the negative control. RNA-binding proteins (RBP; black dot) are inferred based on recent genome-wide AP-MS studies of mRNA-binding proteins (Baltz *et al.* 2012; Castello *et al.* 2012; Kwon *et al.* 2013; Beckmann *et al.* 2015). Results from previous AP-MS studies are provided for let-7a-1 stem-loops [7a-1; **1**: WCE from Huh7 cells (Heo *et al.* 2008); **2**: with nuclear extract from HeLa cells (Michlewski *et al.* 2008; Michlewski and Caceres 2010); **3**: WCE from Lin28A-transfected HEK203T cells (Heo *et al.* 2009); **4**: WCE from P9 cells (Chang *et al.* 2013); and **5**: WCE from HeLa and NT2 cells (Lee *et al.* 2013)] and a let-7g stem-loop [7g; **6**: with P19 cells (Viswanathan *et al.* 2008)].

^bThe SAINTexpress scores are just below the cutoff ($0.65 > \text{score} \geq 0.60$).