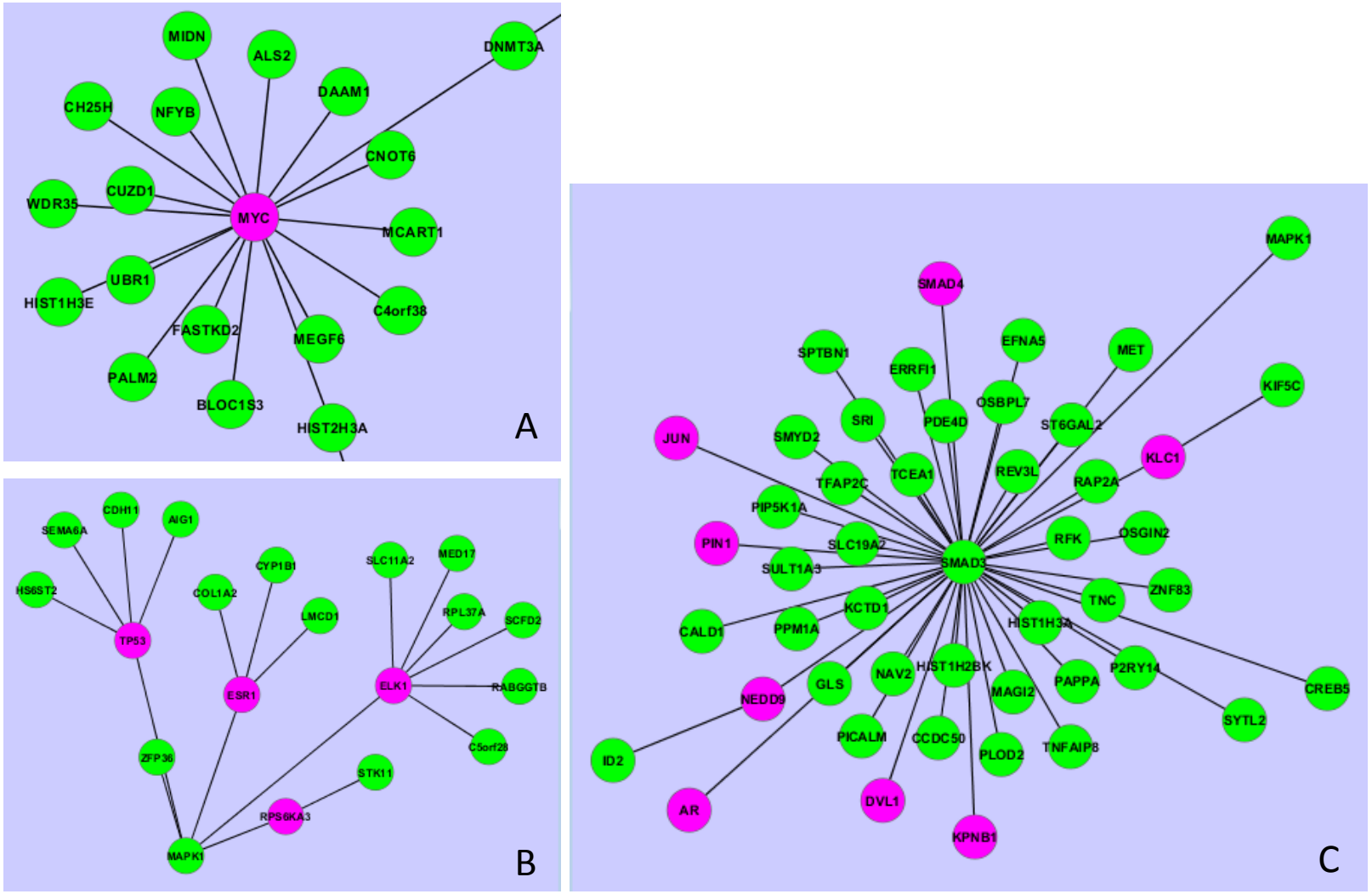


Fig. S1 Gene network analysis for dataset (GSE24182) indicates that several cancer-related pathways might be affected by RoR knockdown, including MYC (A), SMAD3 (B), and MAPK1 (C) pathways. Genes in red indicate alterations not reported in the dataset.

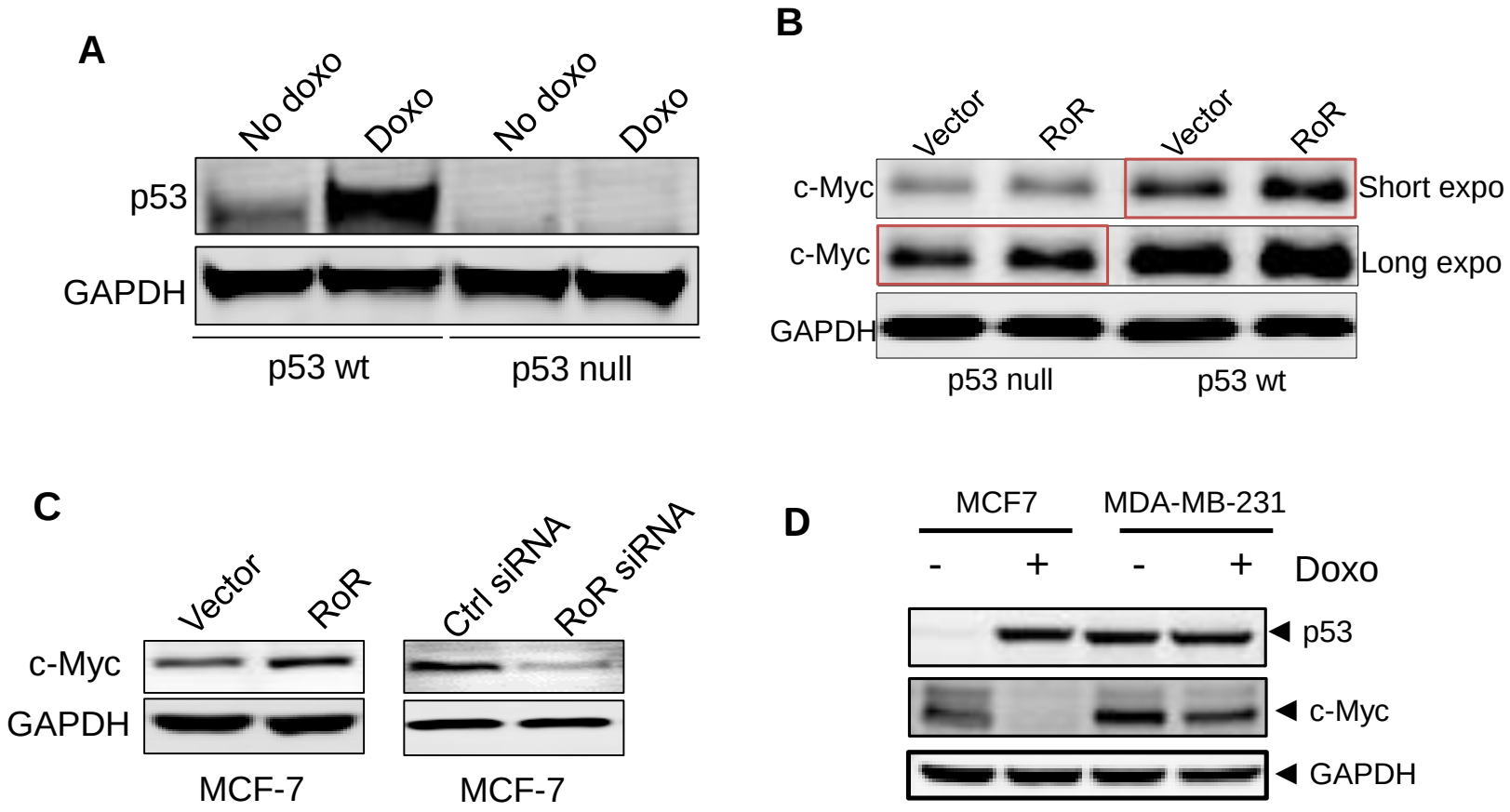


Fig. S2 Effect of Linc-RoR on c-Myc expression. A, Expression of p53 in HCT-116 p53 wt and p53 null cells in the presence or absence of doxorubicin (doxo). B, Effect of RoR on c-Myc expression. Areas with red marking were used in Fig. 1E. C, Effect of RoR on c-Myc expression in MCF-7 cells. D, Confirmation of negative regulation of c-Myc by p53. MCF-7 cells carry wild type p53, which is able to suppress c-Myc in the presence of doxo. In contrast, MDA-MB-231 cells carry mutant p53 which has little effect on c-Myc.

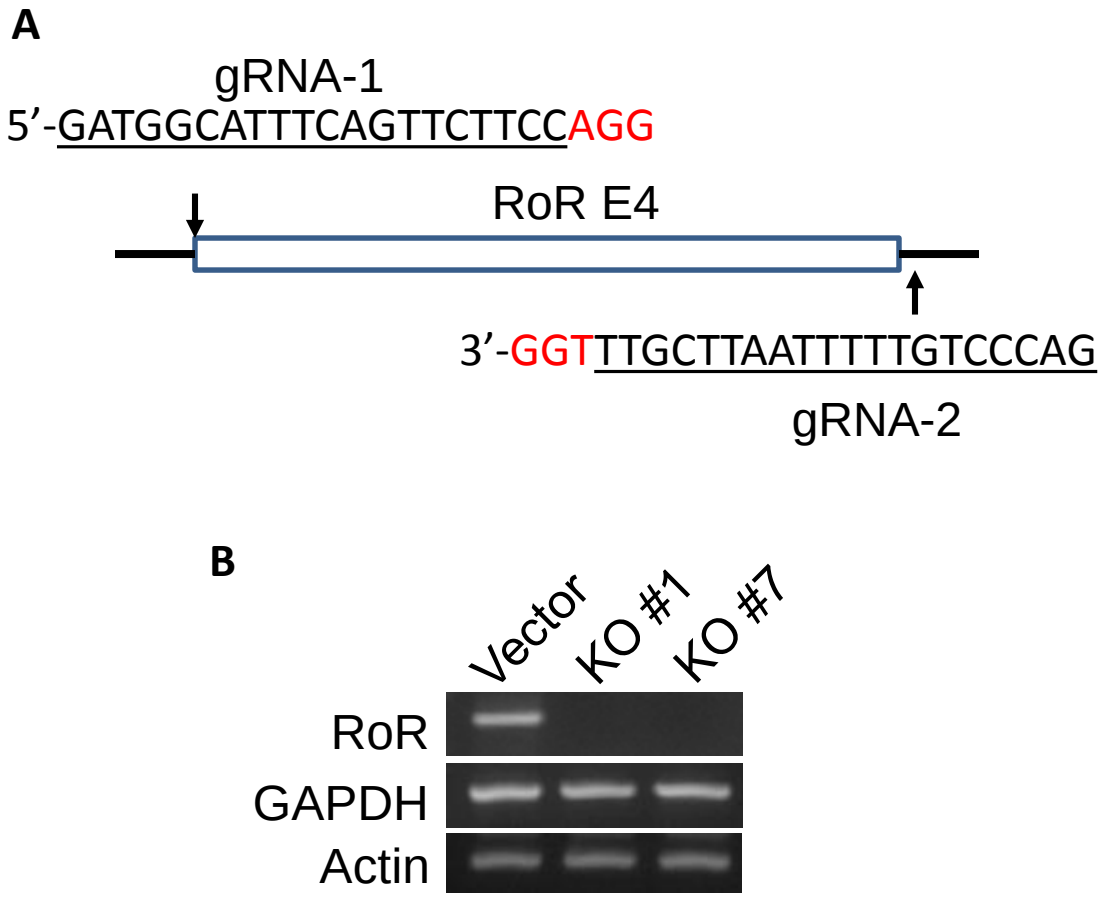


Fig S3. Knockout of Linc-RoR by CRISPR/Cas9. A, Relative location of two gRNAs outside of Linc-RoR exon 4 with sequences indicated. B, Identification of Linc-RoR E4 knockout in HCT-116 cells by genomic PCR using primers RoR-E4-RT-5.1A and RoR-E4-RT-3.1A, derived from the inside of exon 4.

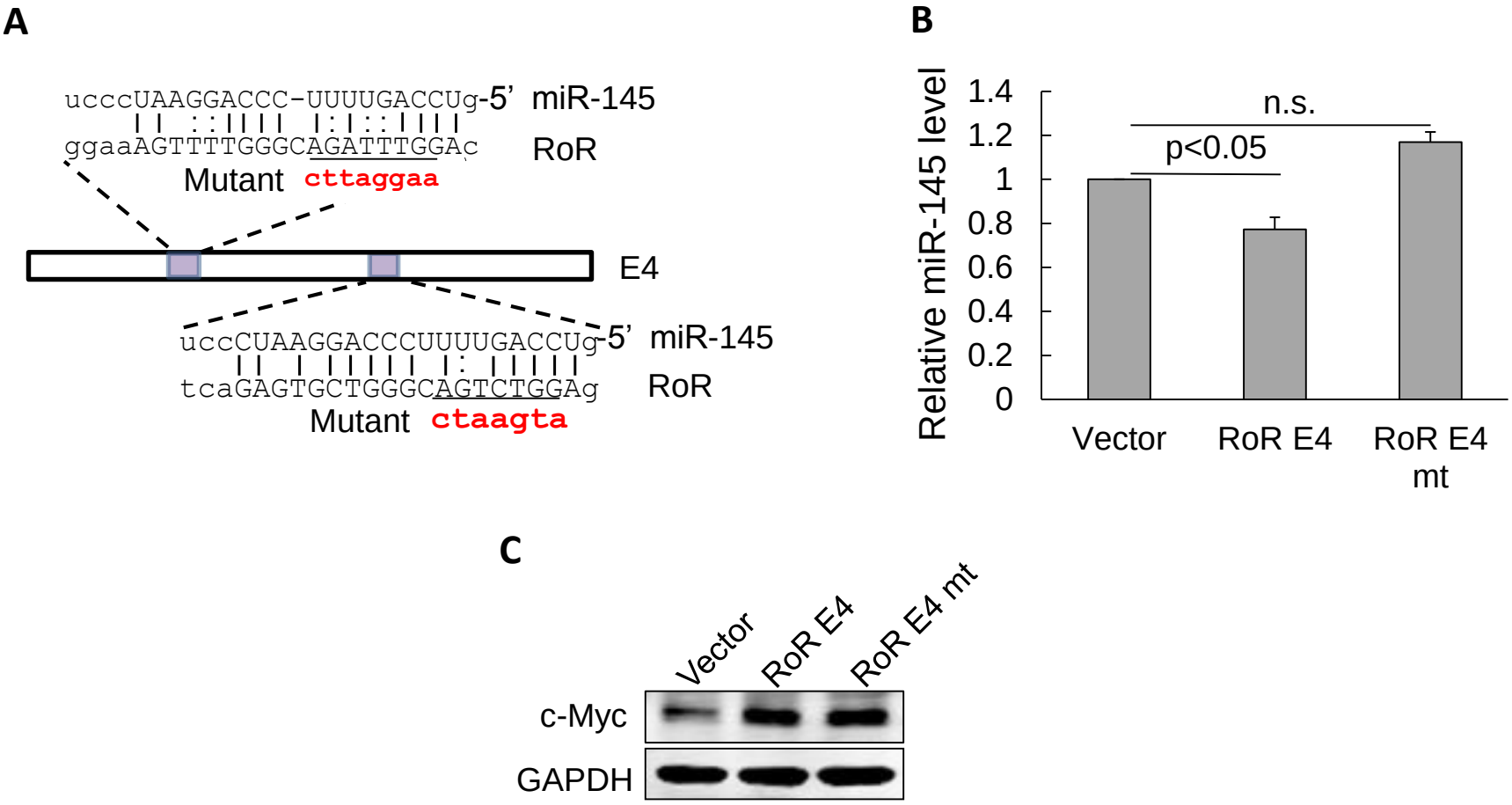


Fig. S4 Linc-RoR regulates c-Myc independent of miR-145. A, Two potential miR-145 binding sites in Linc-RoR E4 and mutant sequences. B, While Linc-RoR E4 suppresses miR-145, no such suppression effect is seen for Linc-RoR E4 mt in HCT-116 cells. C, Both wild type Linc-RoR E4 and mutant Linc-RoR E4 increase c-Myc protein level. Error bars represent S.E.M., n = 3.

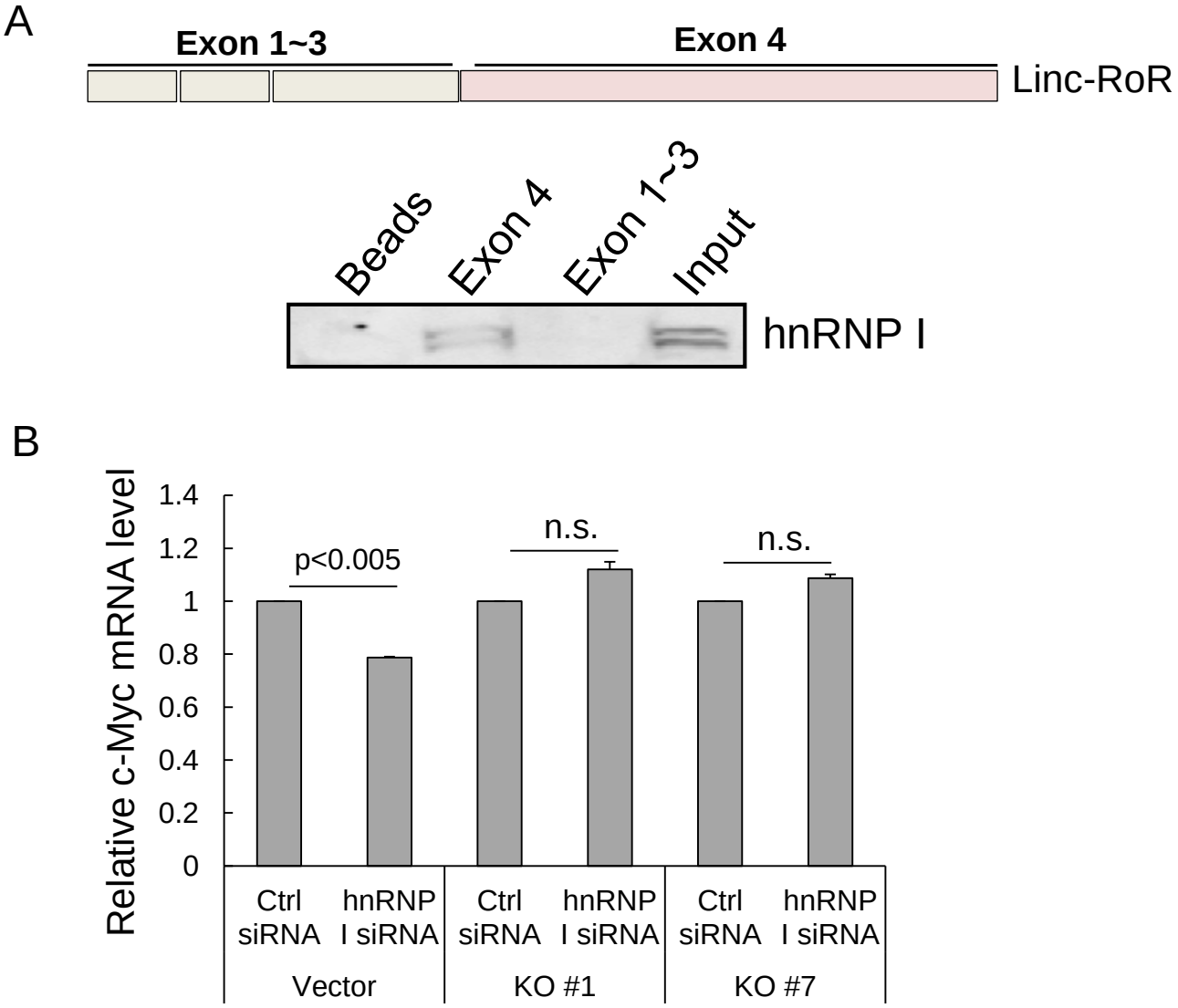


Fig. S5 Linc-RoR functionally interacts with hnRNP I. Pulldown of hnRNP I by Linc-RoR Exon 4 but not Exon 1~3. B, Suppression of hnRNP I by RNAi reduces c-Myc mRNA level in vector control cells, but not in Linc-RoR KO cells. Error bars represent S.E.M., n = 3.

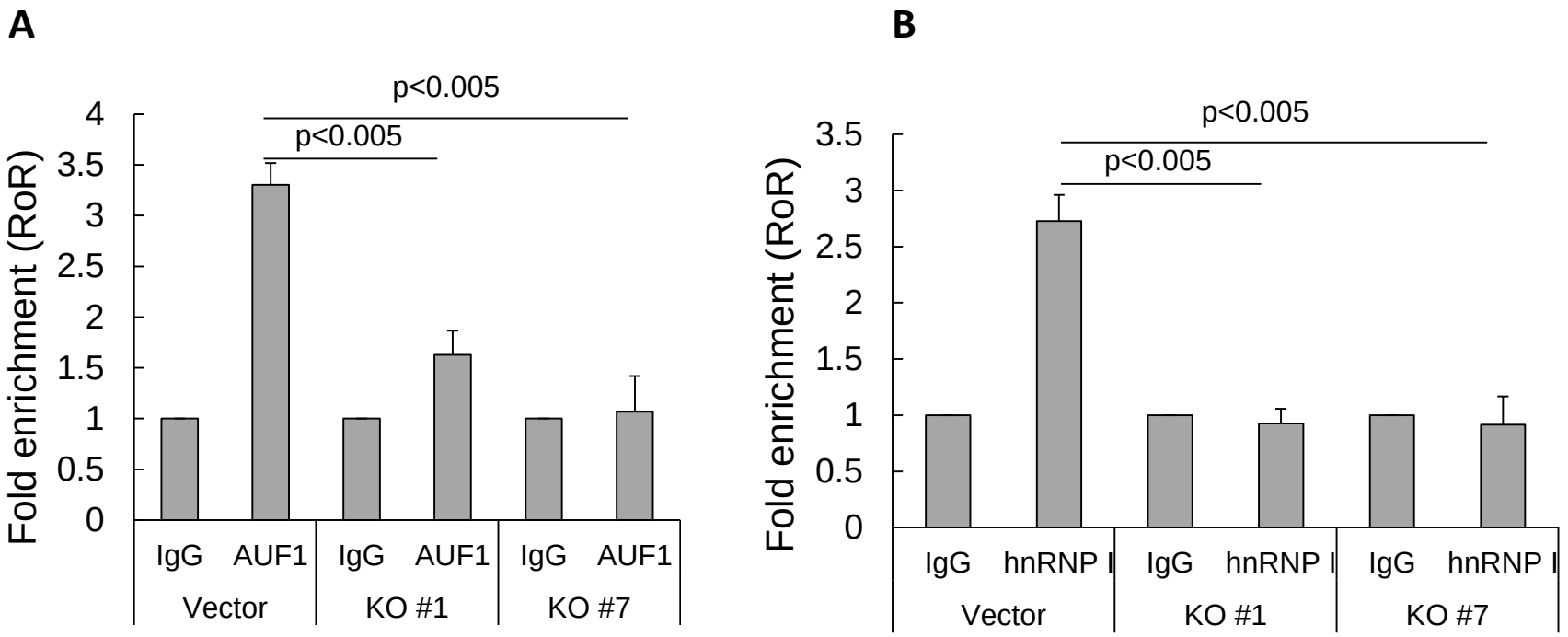


Fig. S6 Both AUF1 and hnRNP I interact with Linc-RoR, as detected by RIP assays using AUF1 or hnRNP I antibody. Error bars represent S.E.M., n = 3.

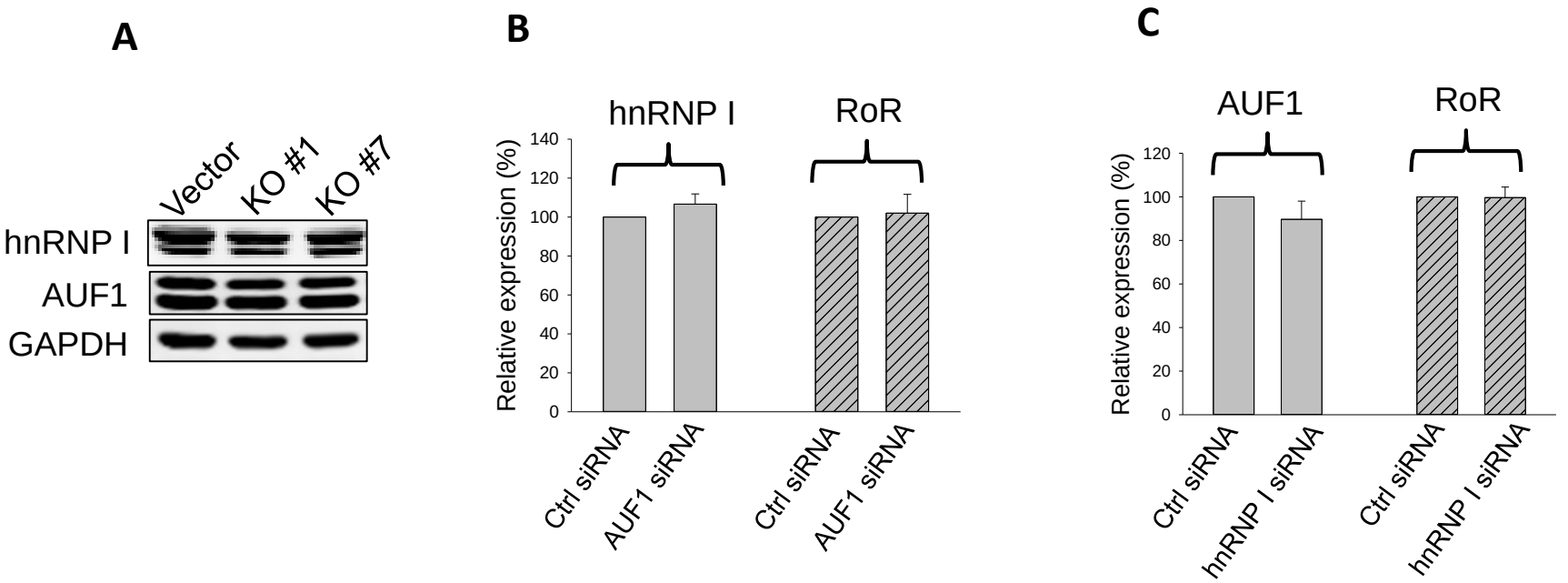


Fig. S7 A, Linc-RoR KO has no effect on expression of hnRNP I or AUF1, as detected by Western blot. B, Suppression of AUF1 by RNAi has no effect on hnRNP I or RoR levels, as detected by qRT-PCR. C, Suppression of hnRNP I by RNAi has no effect on AUF1 or RoR levels, as detected by qRT-PCR.

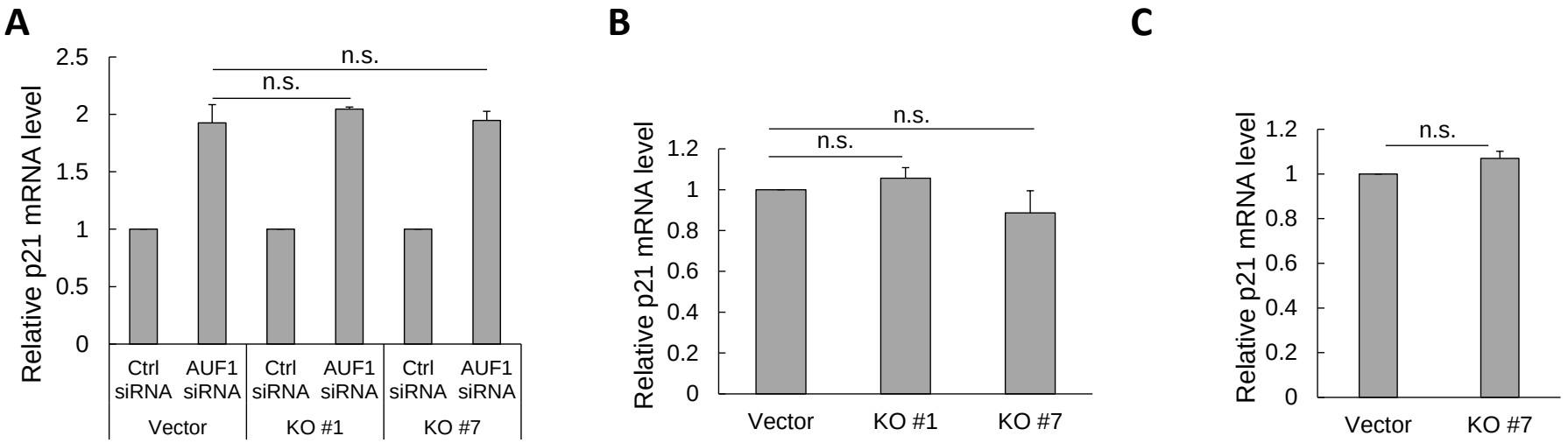
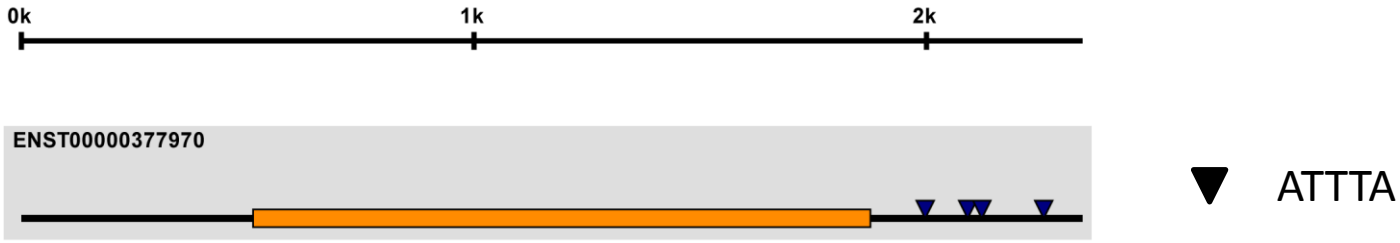


Fig. S8 Linc-RoR has no effect on p21, another AUF1 target. A, Detection of p21 mRNA levels in vector control or Linc-RoR KO cells after treatment with AUF1 siRNA. B, Detection of p21 mRNA levels in vector control or Linc-RoR KO cells with AUF1 siRNA. C, Detection of p21 mRNA levels in xenograft tumors derived from vector control or Linc-RoR KO cells. Error bars represent S.E.M., n = 3.



http://rna.tbi.univie.ac.at/cgi-bin/AREsite.cgi?t=ENSG00000136997&id=ckjh3BBoXJ&AUUUA=on&species=hg&representativeonly=on

C-Myc 3'-UTR sequence (489 nt)

```
   GGAAAAGTAAGGAAAACGATTCCTTCTAACAGAAATGTCCTGAGCAATCACCTATGAACTTGTTTCAAATGCATGATCAAATGCAACCTCACAACCTTGG
 1 ---------+---------+---------+---------+---------+---------+---------+---------+---------+---------+ 1
   CCTTTTCATTCCTTTTGCTAAGGAAGATTGTCTTTACAGGACTCGTTAGTGGATACTTGAACAAAGTTTACGTACTAGTTTACGTTGGAGTGTTGGAACC

   CTGAGTCTTGAGACTGAAAGATTTAGCCATAATGTAAACTGCCTCAAATTGGACTTTGGGCATAAAAGAACTTTTTTATGCTTACCATCTTTTTTTTTTC
101 ---------+---------+---------+---------+---------+---------+---------+---------+---------+---------+ 200
   GACTCAGAACTCTGACTTTCTAAATCGGTATTACATTTGACGGAGTTTAACCTGAAACCCGTATTTTCTTGAAAAAATACGAATGGTAGAAAAAAAAAAG

   TTTAACAGATTTGTATTTAAGAATTGTTTTTTAAAAAATTTTAAGATTTACACAATGTTTCTCTGTAAATATTGCCATTAAATGTAAATAACTTTAATAAA
201 ---------+---------+---------+---------+---------+---------+---------+---------+---------+---------+ 300
   AAATTGTCTAAACATAAATTCTTAACAAAAATTTTTTAAAATTCTAAATGTGTTACAAAGAGACATTTATAACGGTAATTTACATTTATTGAAATTATTT

   ACGTTTATAGCAGTTACACAGAATTTCAATCCTAGTATATAGTACCTAGTATTATAGGTACTATAAACCCTAATTTTTTTTATTTAAGTACATTTTGCTT
301 ---------+---------+---------+---------+---------+---------+---------+---------+---------+---------+ 400
   TGCAAATATCGTCAATGTGTCTTAAAGTTAGGATCATATATCATGGATCATAATATCCATGATATTTGGGATTAAAAAAAATAAATTCATGTAAAACGAA

   TTTAAAGTTGATTTTTTTCTATTGTTTTTAGAAAAAATAAAATAACTGGCAAATATATCATTGAGCCAAATCTTAAAAAAAAAAAAAAA
401 ---------+---------+---------+---------+---------+---------+---------+---------+---------+--------- 489
   AAATTTCAACTAAAAAAAGATAACAAAAATCTTTTTTATTTTATTGACCGTTTATATAGTAACTCGGTTTAGAATTTTTTTTTTTTTTT
```

Fig. S9 The c-Myc 3'-UTR carries several A-U rich elements (AREs); four AUUUA (ATTTA) elements are highlighted in blue. Two 11 nt sequences complementary to Linc-RoR are highlighted in red.

A

RoR-wild type (WT)

CCACCTTATATTGATTAGGAAGACTGCTATAAAAATAGTAAACAAACAAACAAACAAAGTAAGTCTTGGGG
AGGATGCAGAGAAATTAAAATTTTTGTGCACTGTTAGTGGGAATGTAAAATGGTGCAGCTGTTACGGGAAA
CGGTATGACAGTTCCTCAAAAAATAAAA

RoR-mutant (mt)

CCACCTTATATTGATTAGGAAGttgaggctgacAATAGTAAACAAACAAACAAACAAAGTAAGTCTTGGGG
AGGATGCAGAGAAAggcaggtagctGTGCACTGTTAGTGGGAATGTAAAATGGTGCAGCTGTTACGGGAAA
CGGTATGACAGTTCCTCAAAAAATAAAA

B

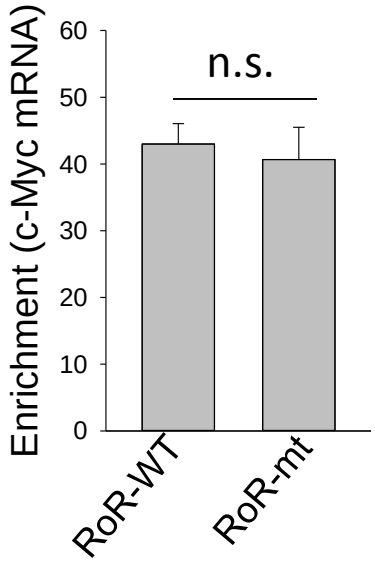
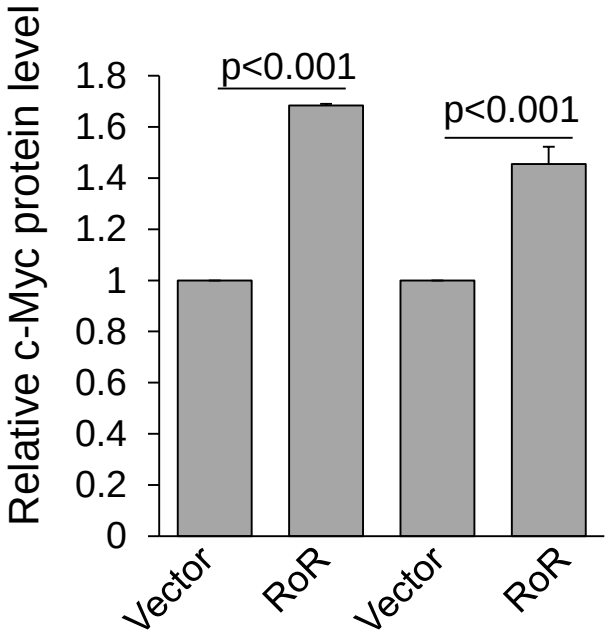


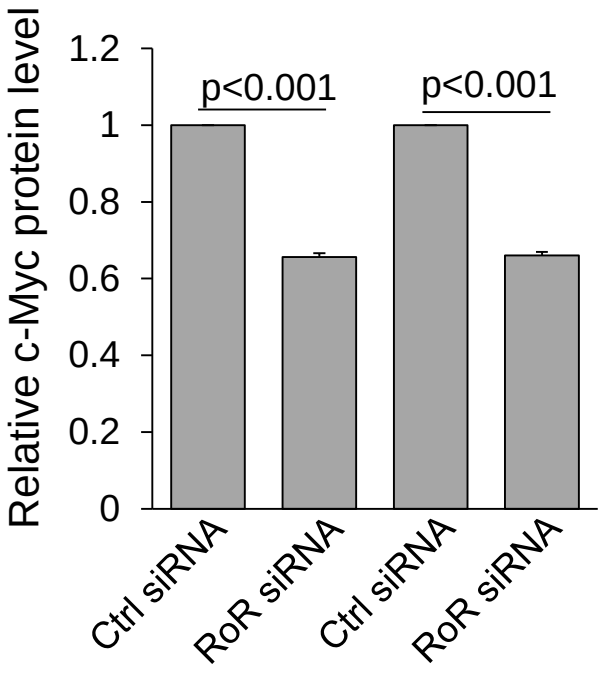
Fig. S10 Two 11 nt sequences of Linc-RoR complementary to c-Myc are not important to the binding of hnRNP I to c-Myc mRNA. A, Only the 3' end of Linc-RoR E4 was shown here. The mutated sites were highlighted in red. B, The Linc-RoR KO cells were transfected with RoR-WT or mutant and then RIP assay was performed using hRNP I antibody. The enrichment of c-Myc mRNA level was detected by qRT-PCR of the precipitates as compared to IgG control as 1.

Additional supplementary materials

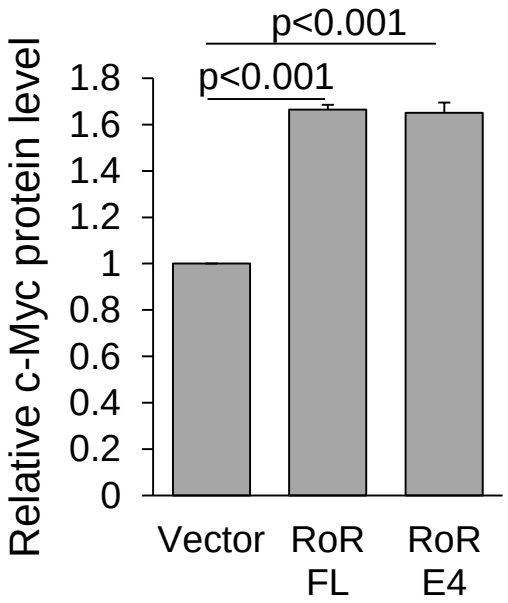
Quantification of western blot gel signals



For Fig. 1E

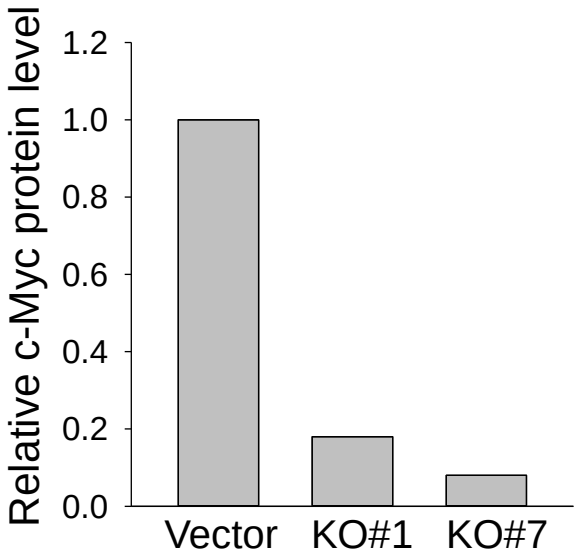


For Fig. 1F

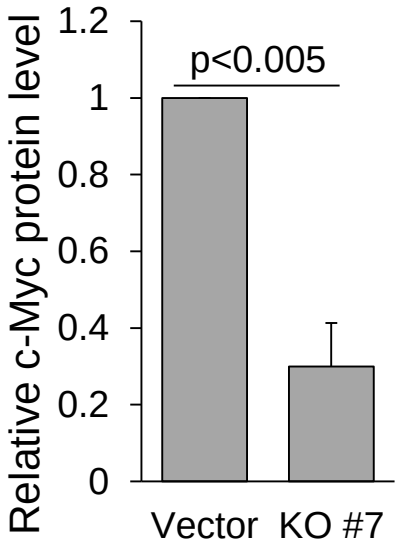


For Fig. 2A

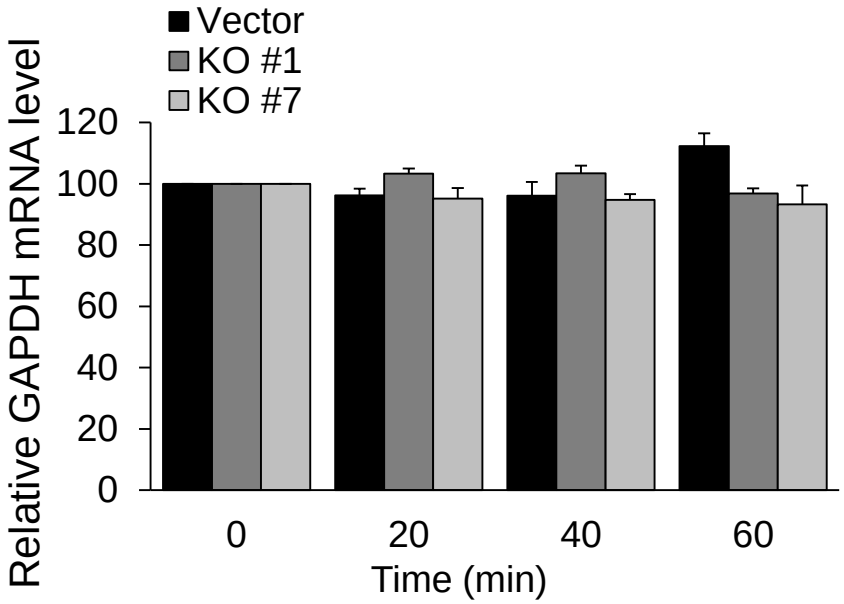
From one gel



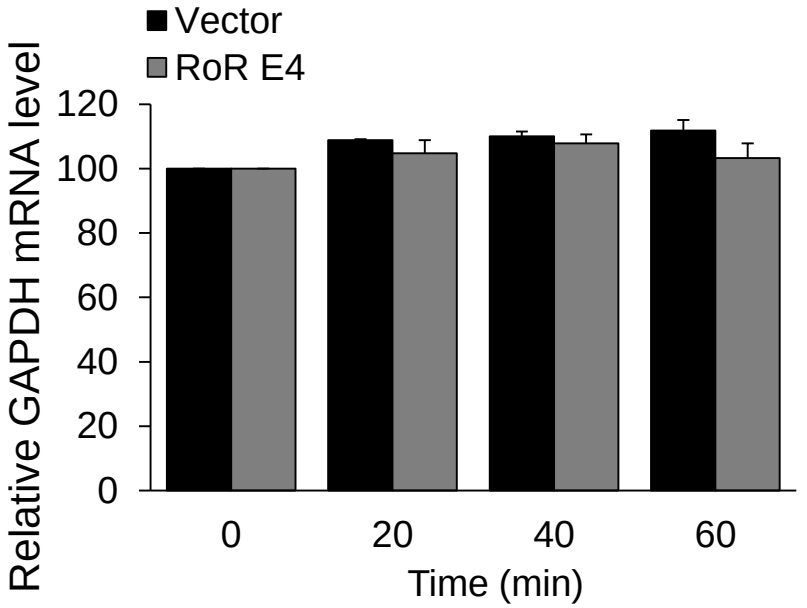
For Fig. 2E


Relative c-Myc protein level
1.2
1
0.8
0.6
0.4
0.2
0
p<0.005
Vector
KO #7

For Fig. 3D



For Fig. 4C



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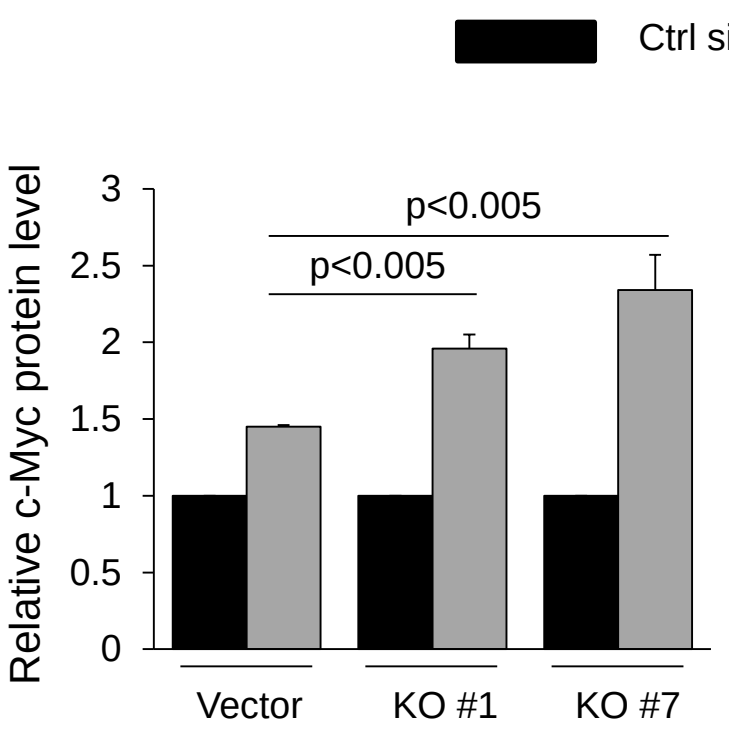

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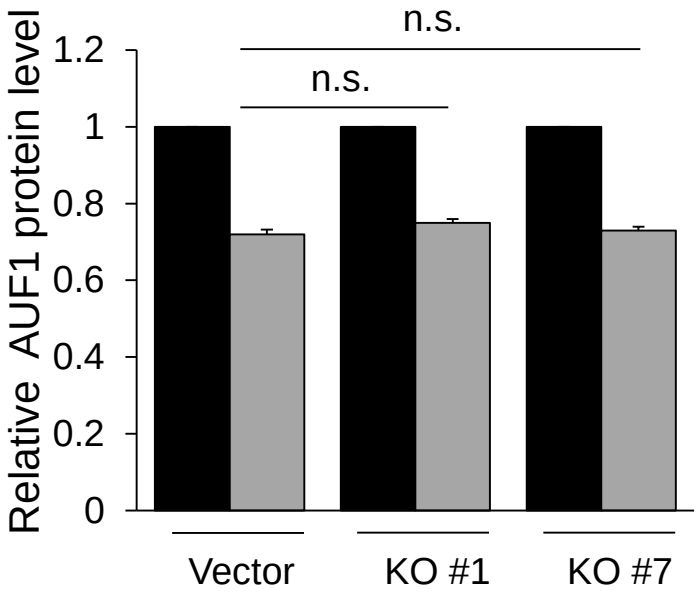
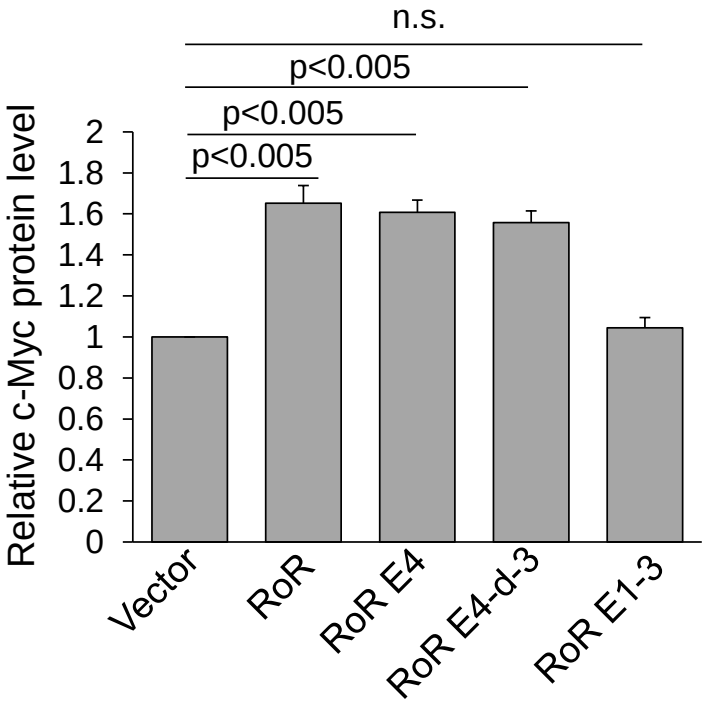


For Fig. 4F



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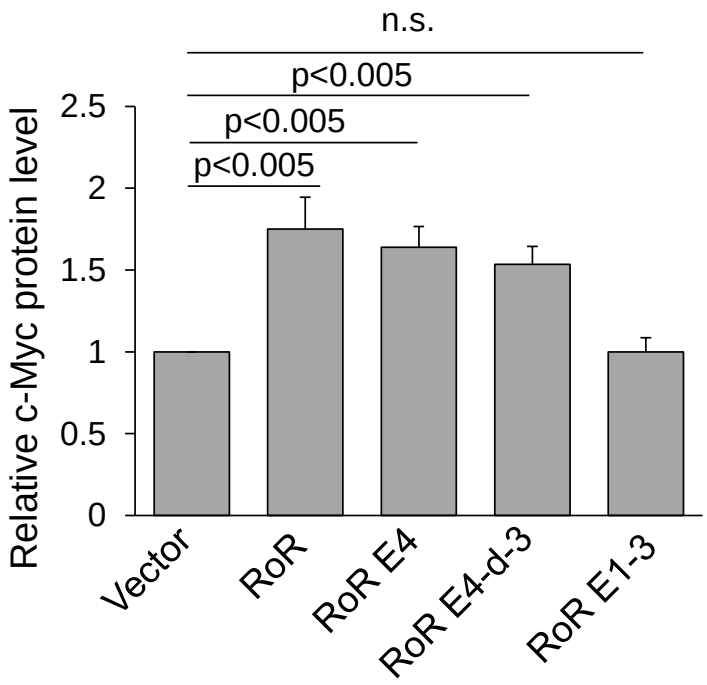
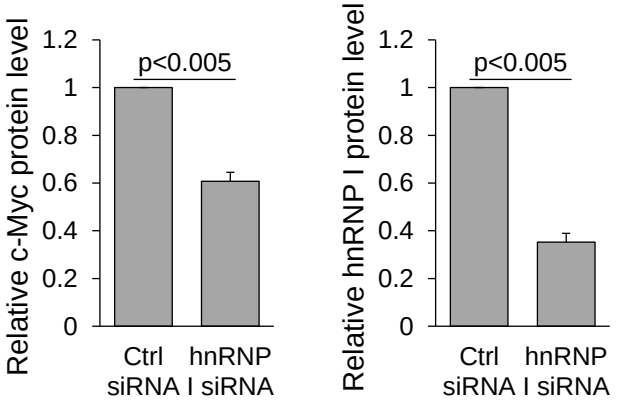
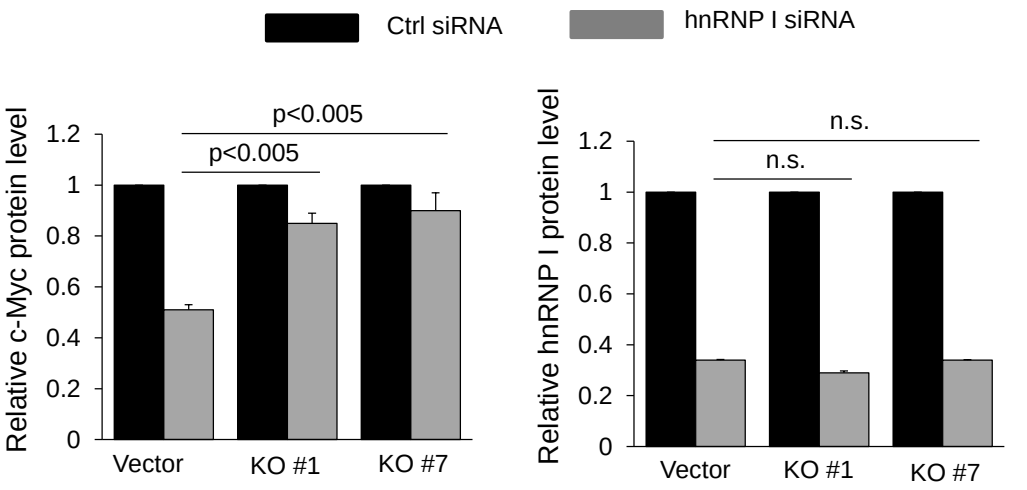


For Fig.5C



For Fig.5E



For Fig.5F