Figure S1

DNA sequence of exon 10 to exon 12 of NCOR2
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CCCGGCGGCGGGCCAAGGAGAGCAAGGTGCGCGAGTACTACGAGAAGCAGTTCCCTGAGATCCGCAAGCAGCGCGA
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CCATGCTGTACGACGCTGACCAGCAGCGCATCAAGTTCATCAACATGAACGGGCTTATGGCCGACCCCATGAAGGTGTA
CAAAGACCGCCAGGTCATGAACATGTGGAGTGAGCAGGA**GAAGGAGACCTTCCGGGAGAA**

Red: exon 11 (91 bp)
Blue: target sites of NCOR2-BQ splicing forward and reverse primers
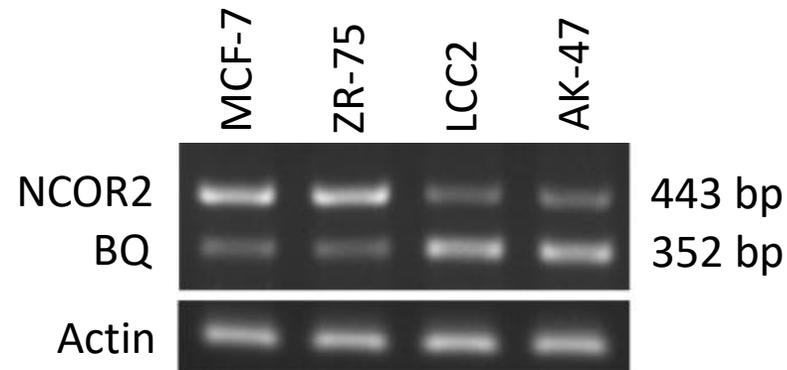
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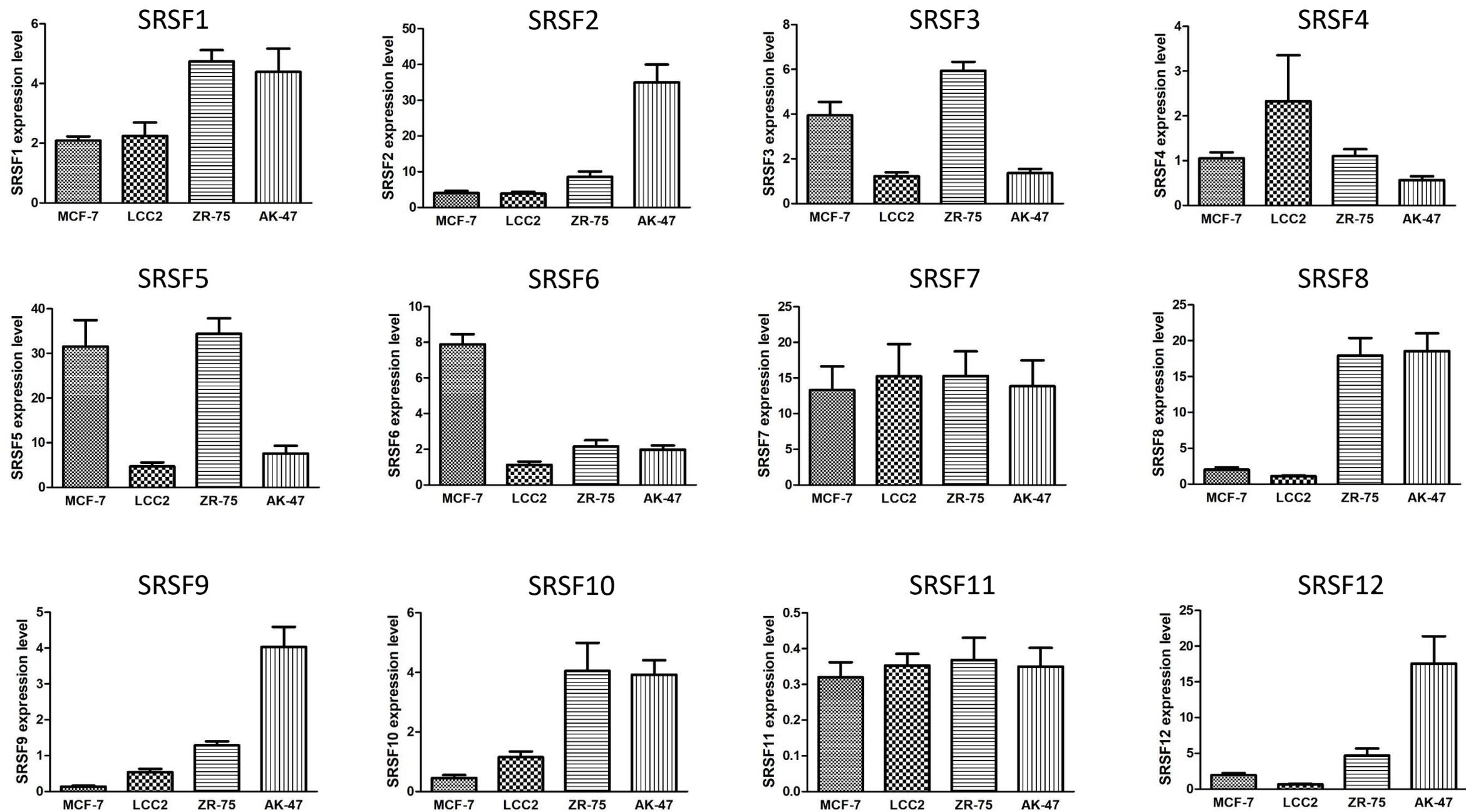
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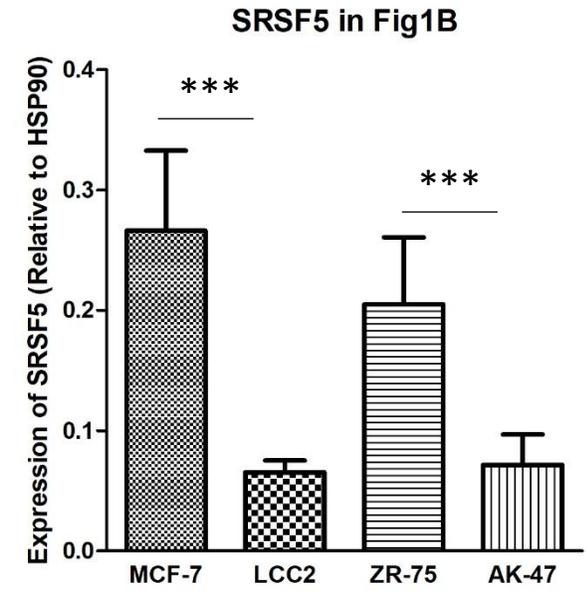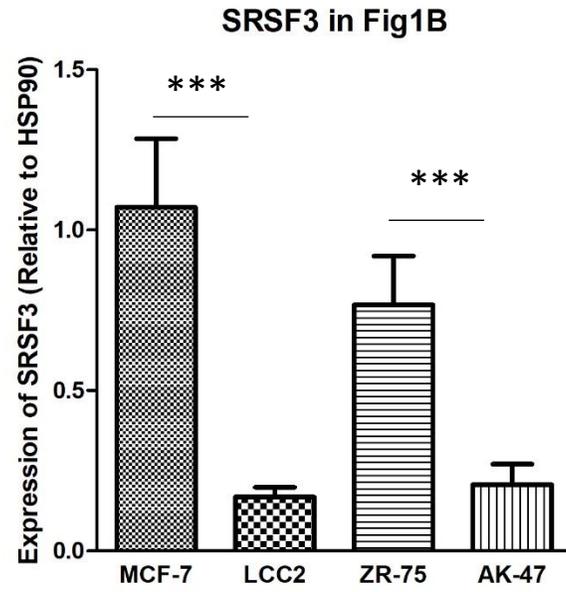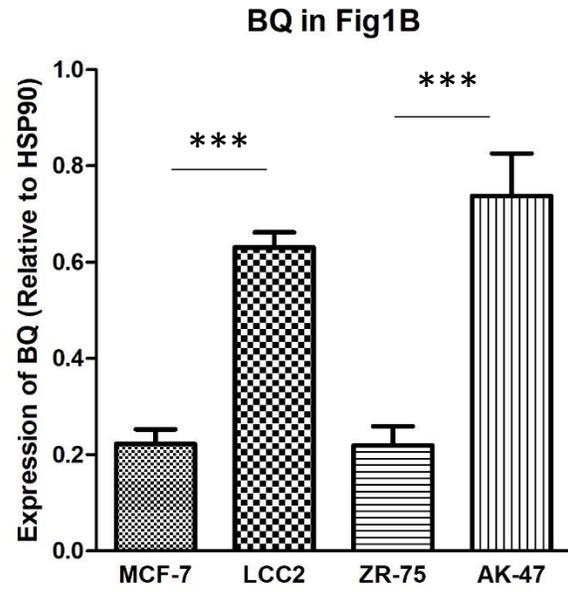
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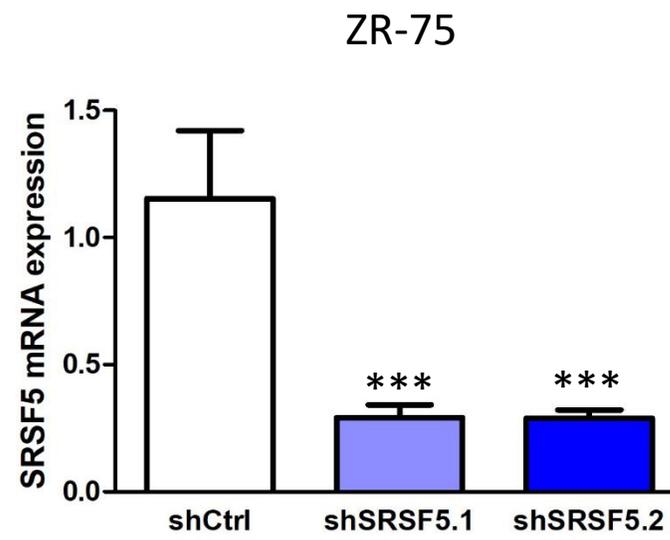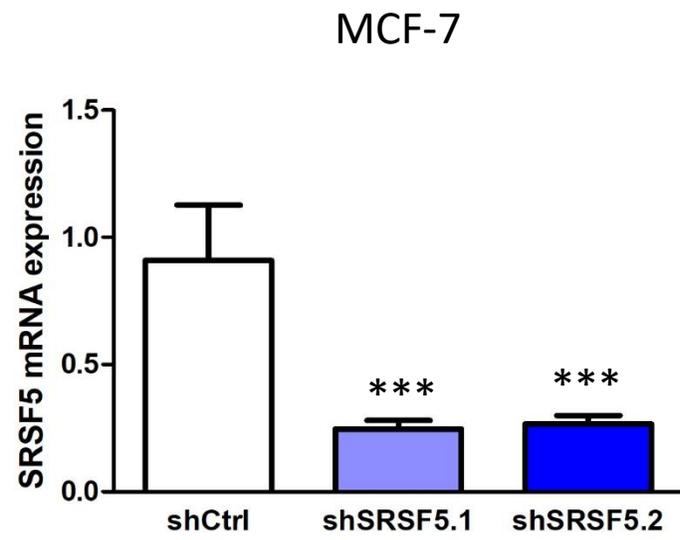
MCF-7

ZR-75

Figure S5

BQ/GADPH MCF-7 Fig 1C
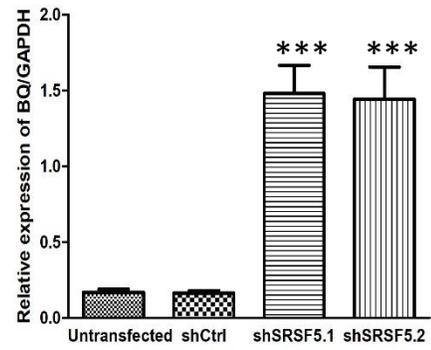
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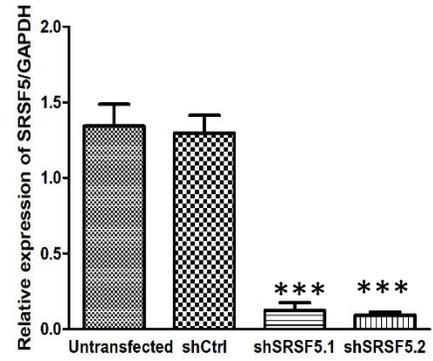
BQ/GADPH ZR-75 Fig 1C
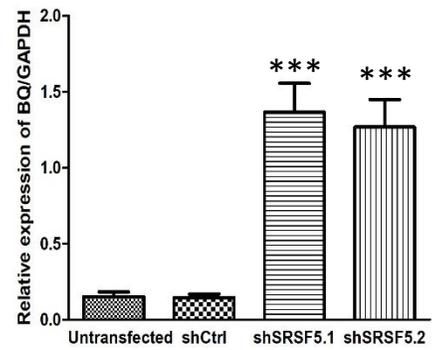
SRSF5/GADPH ZR-75 Fig 1C
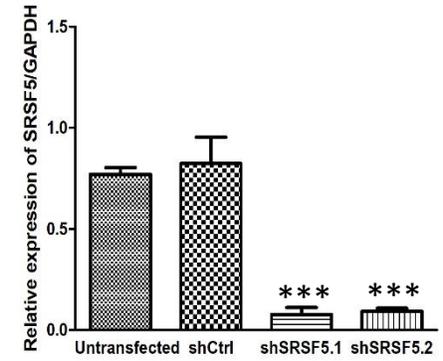
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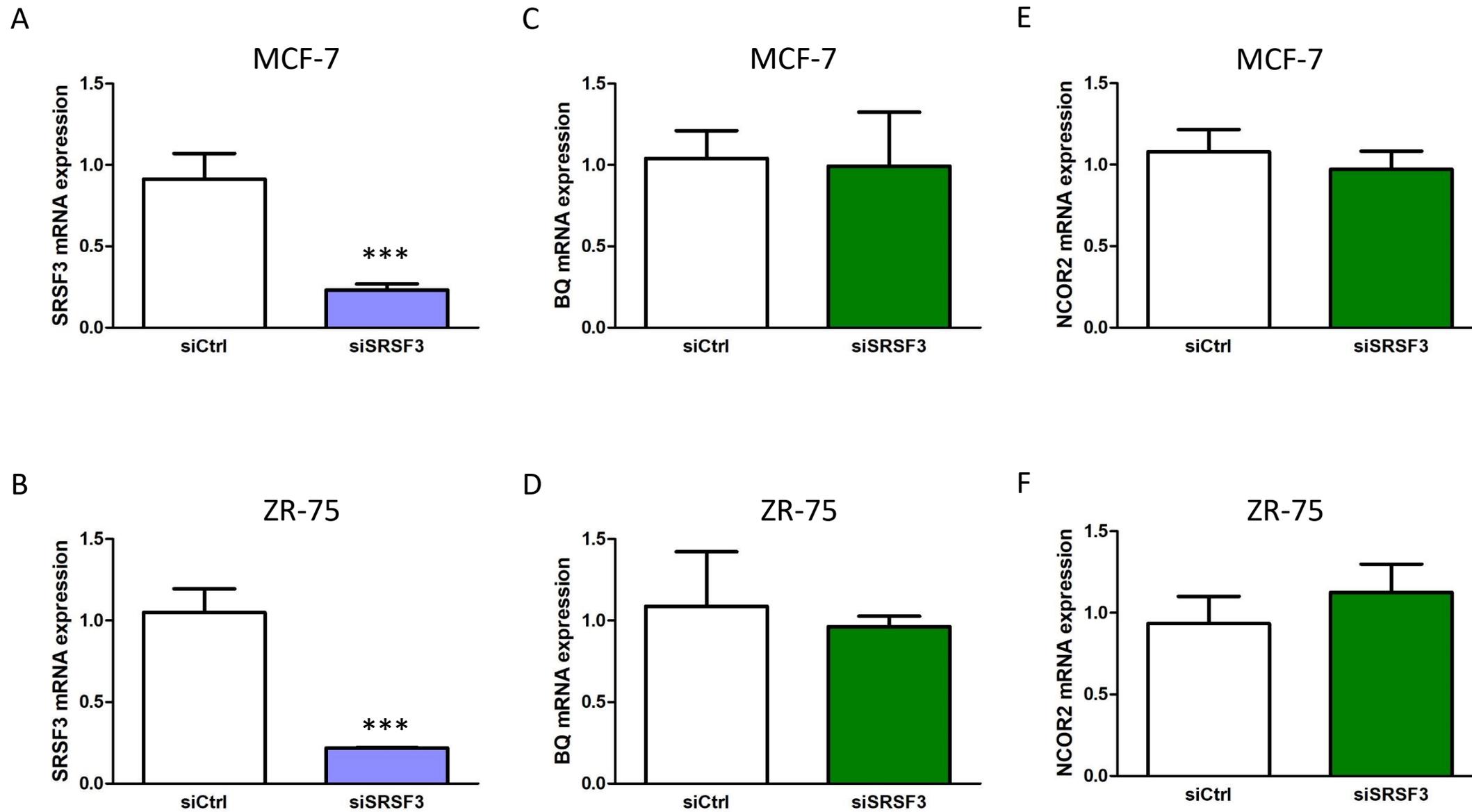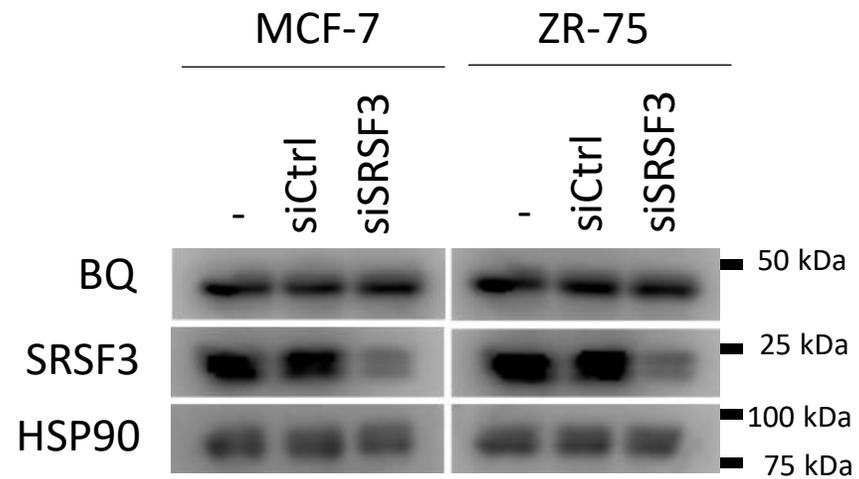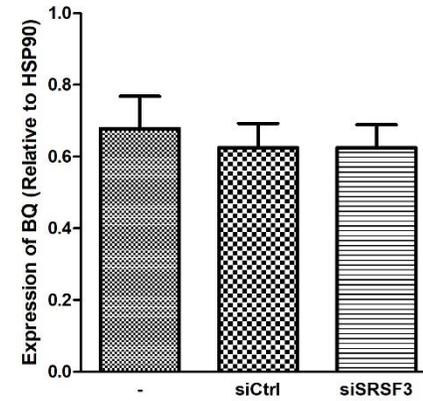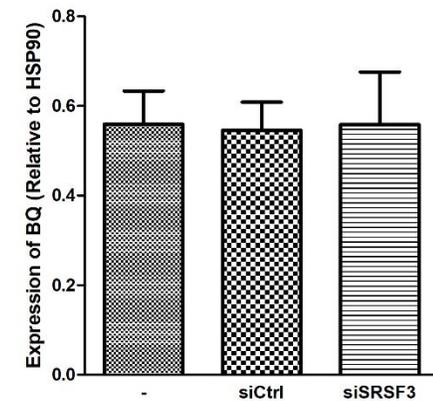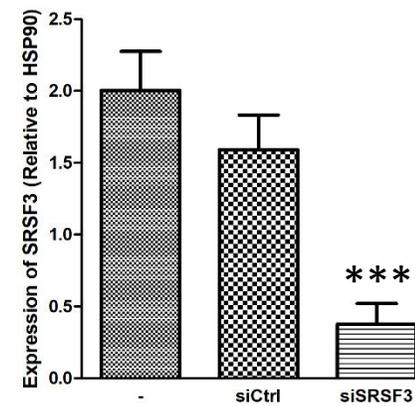
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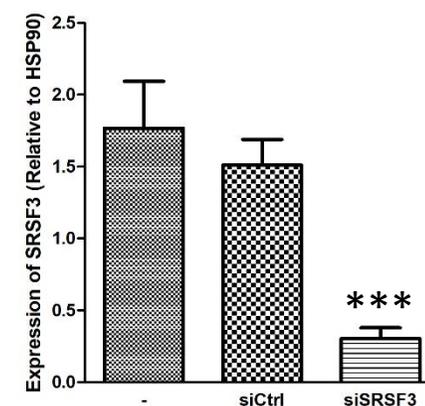
Figure S8

BQ/HSP90 LCC2 Fig 1D
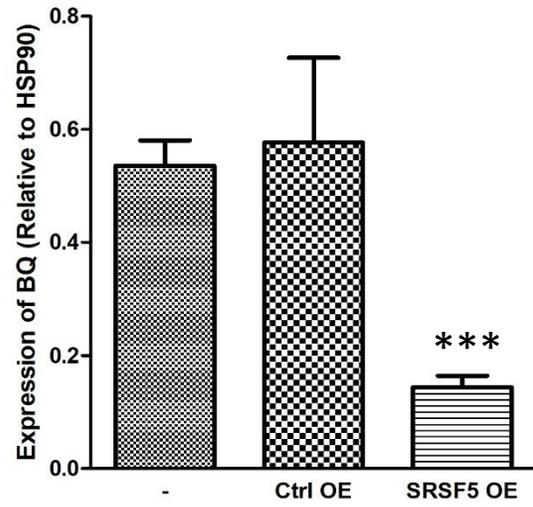
BQ/HSP90 AK-47 Fig 1D
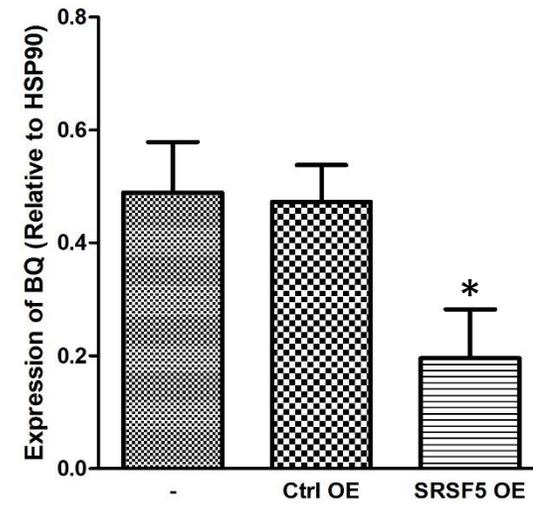
SRSF5/HSP90 LCC2 Fig 1D
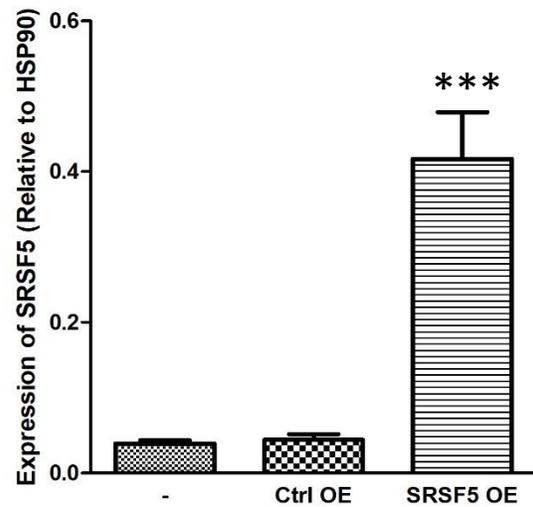
SRSF5/HSP90 AK-47 Fig 1D

Figure S9

MCF-7

ZR-75

MCF-7

ZR-75
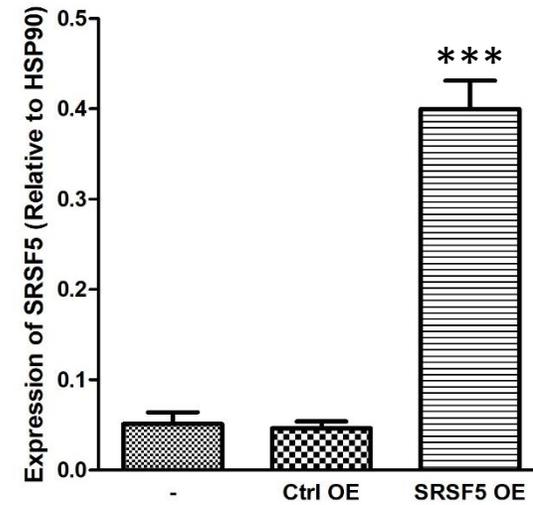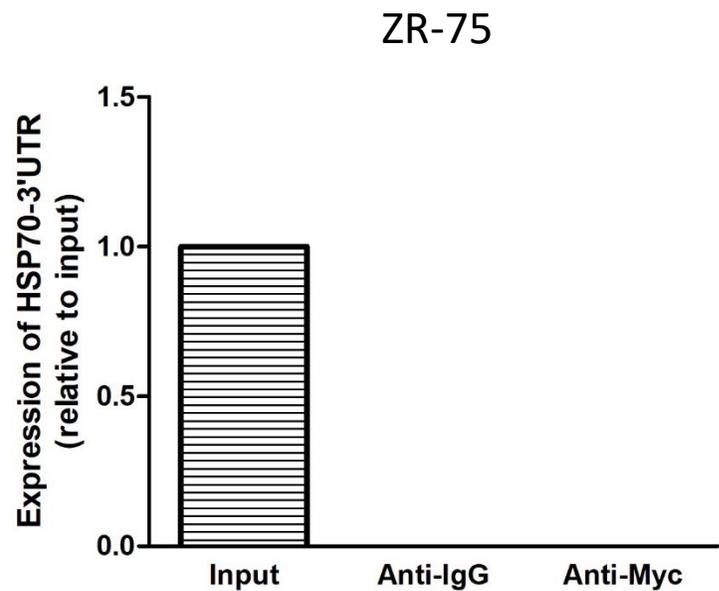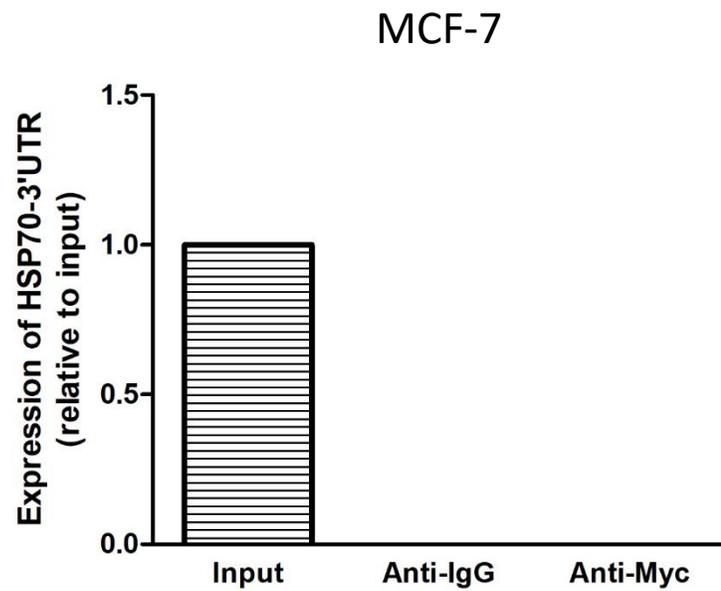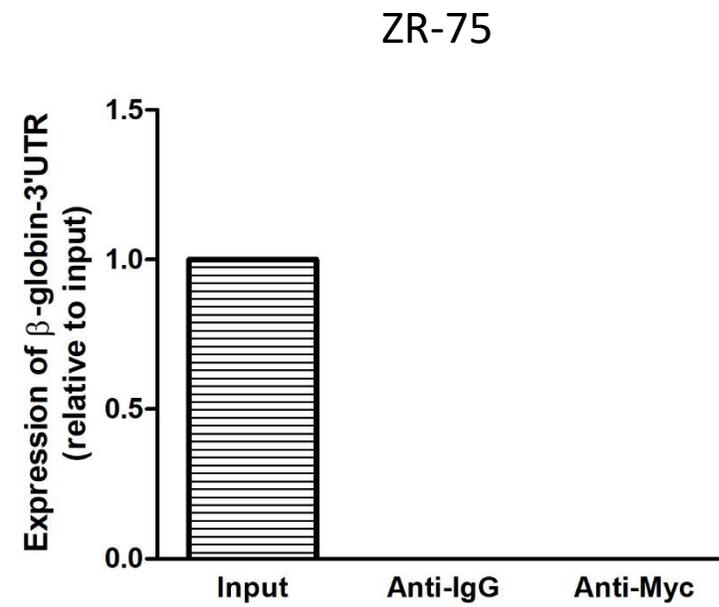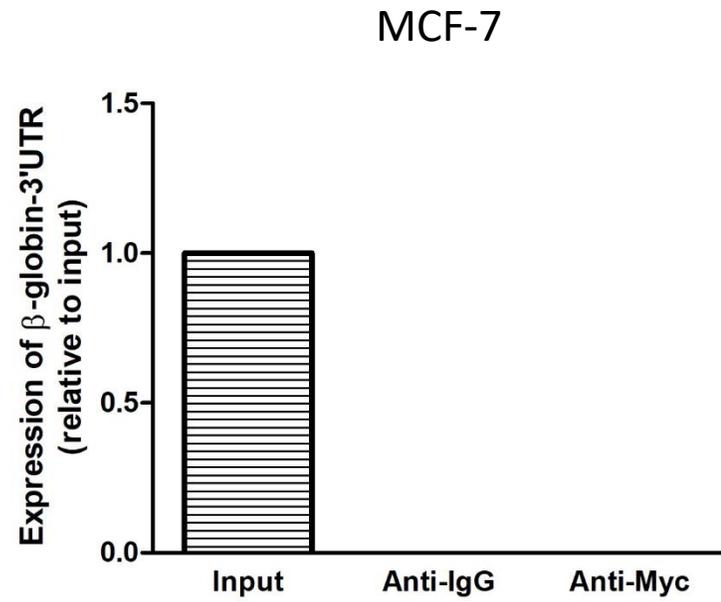
Figure S10

Figure S11

Figure S12

BQ/GAPDH Fig3D

Figure S13

BQ/GAPDH Fig4D

Figure S14

A

MCF-10A

B

LCC2 **LCC2**

AK-47 **AK-47**

C

LCC2 **AK-47**
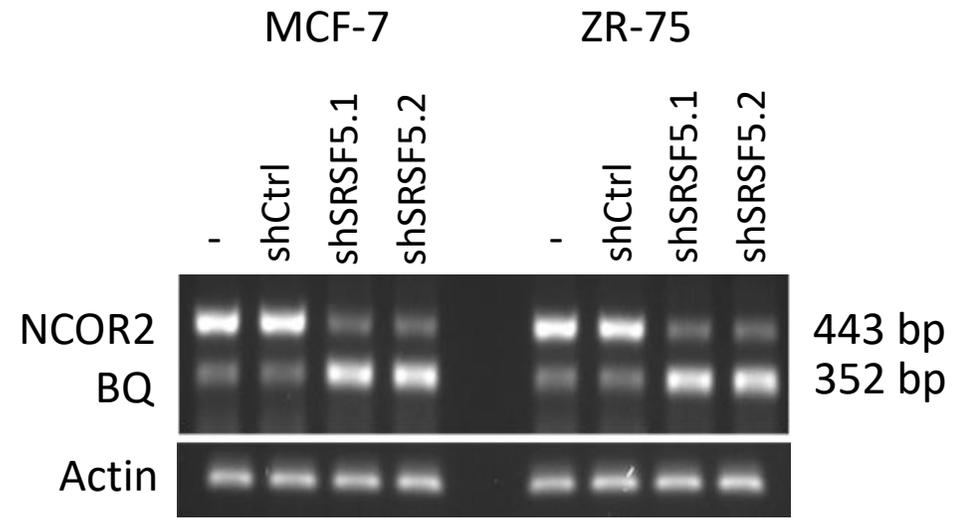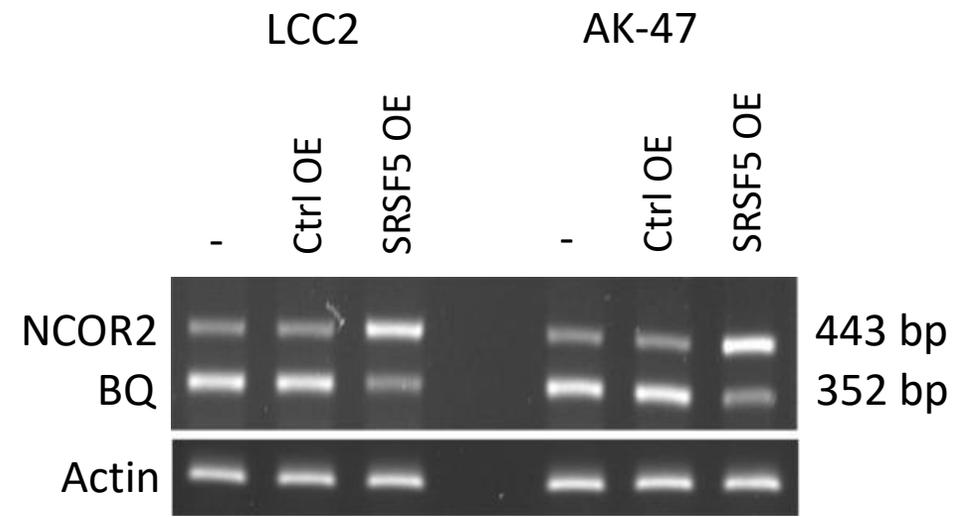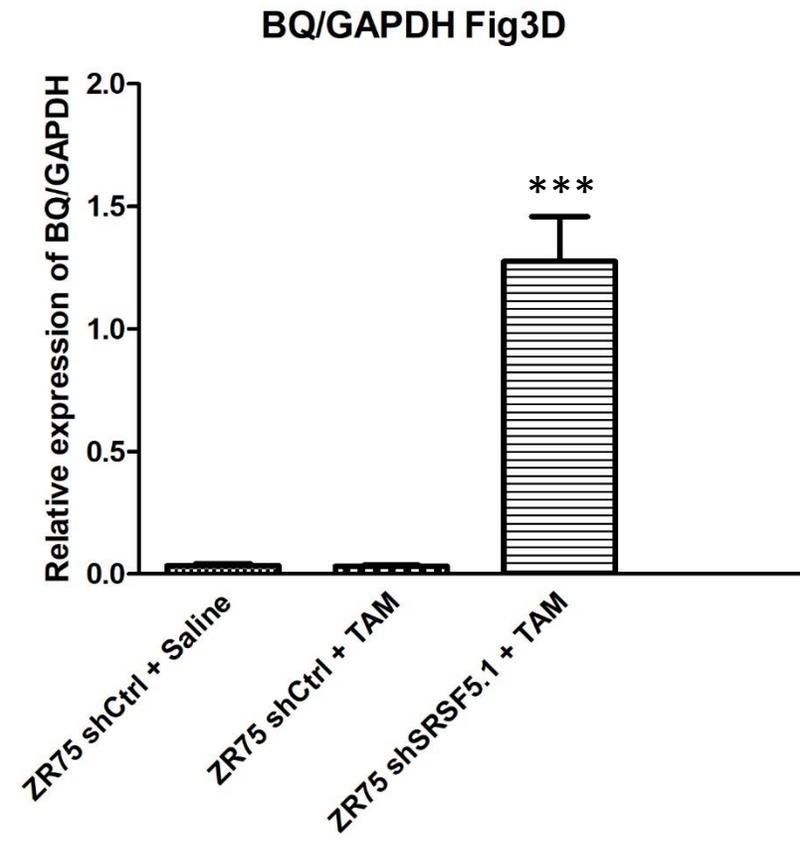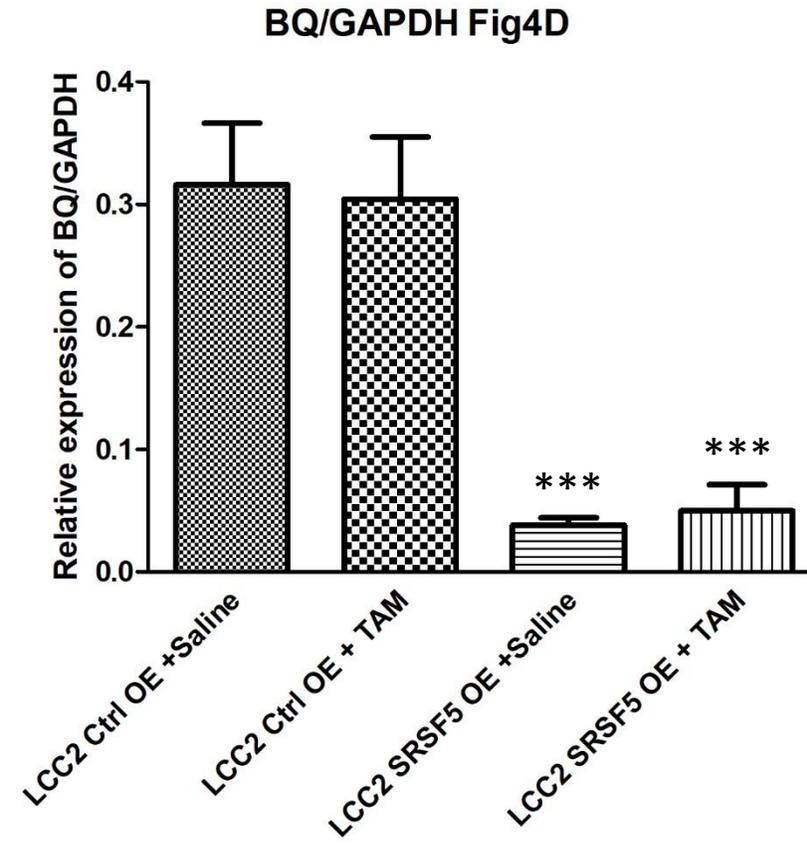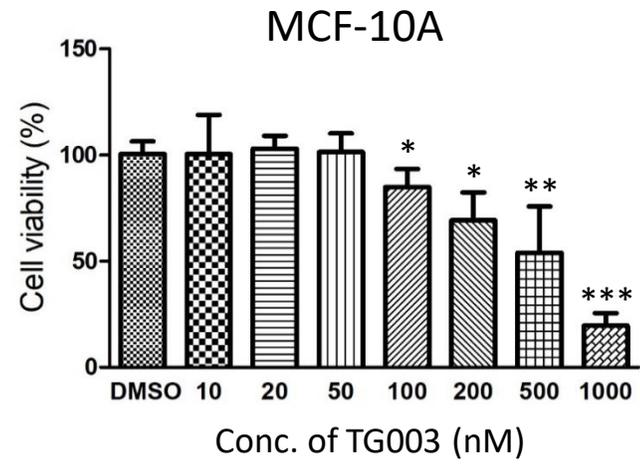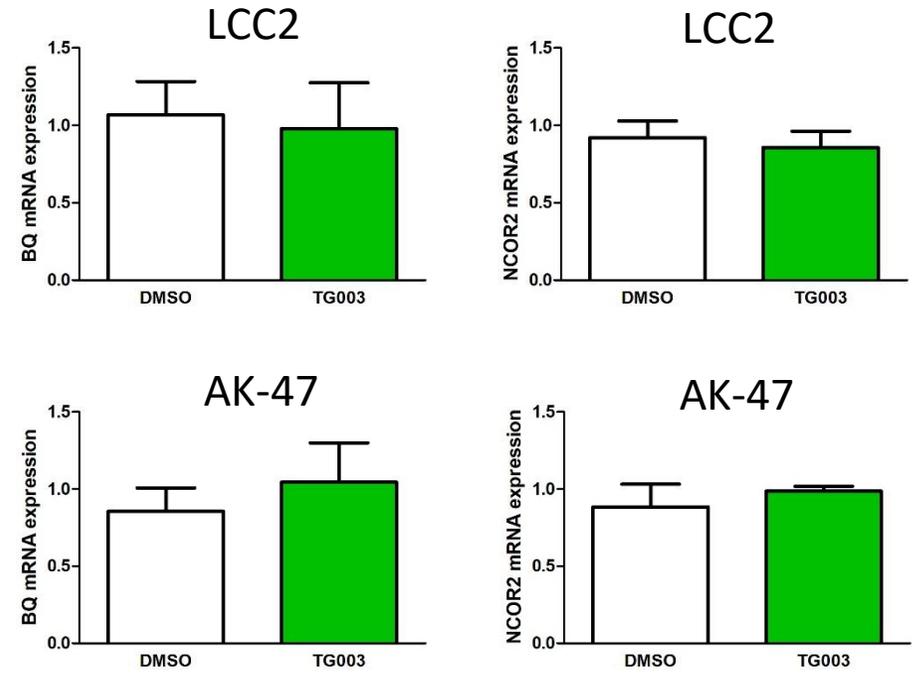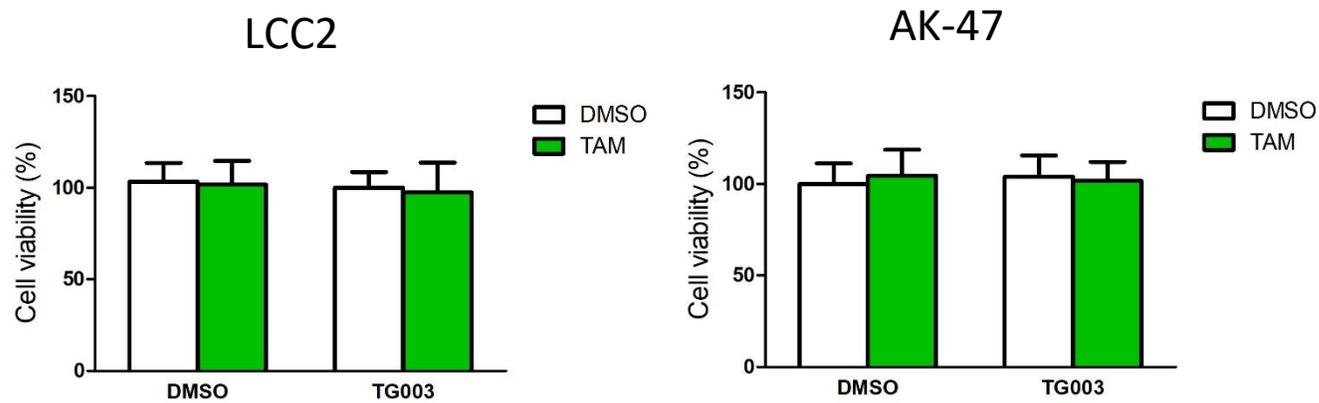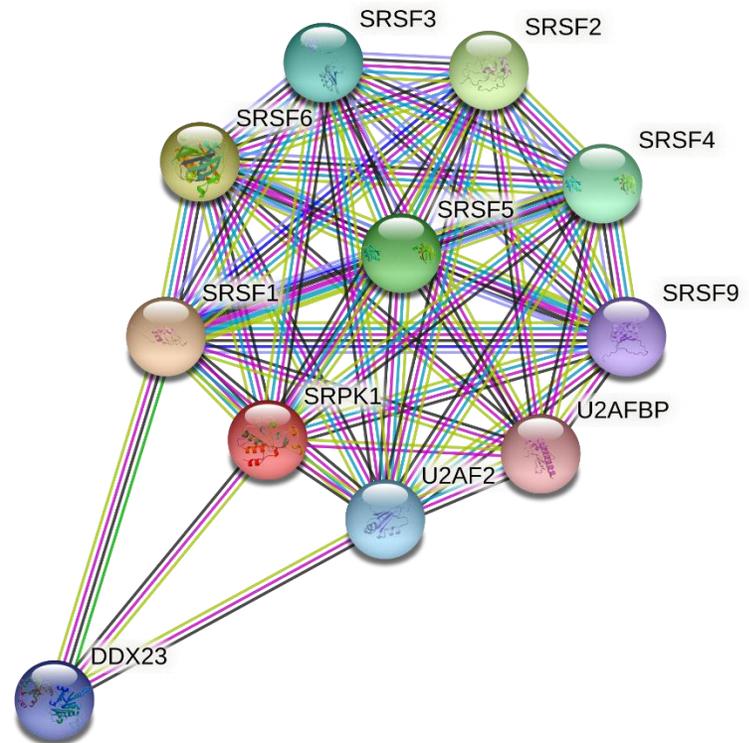
Figure S15

Figure S16
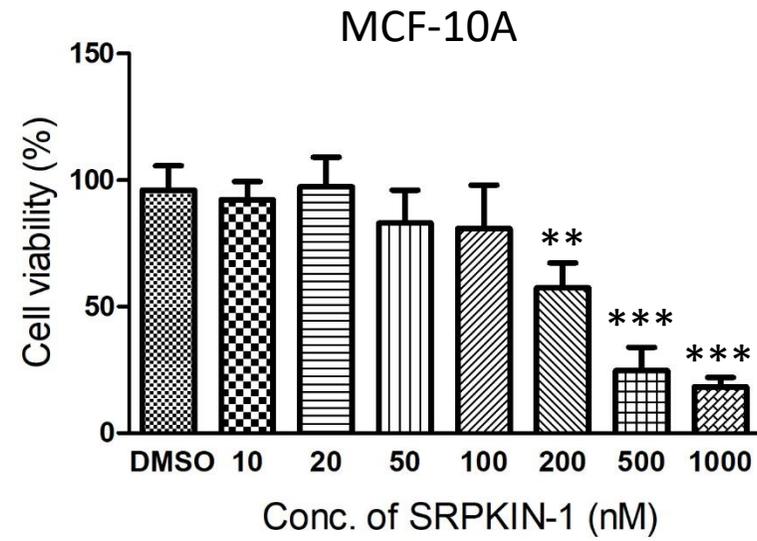
Figure S17

Figure S18

pSR/SRSF5 Fig6D
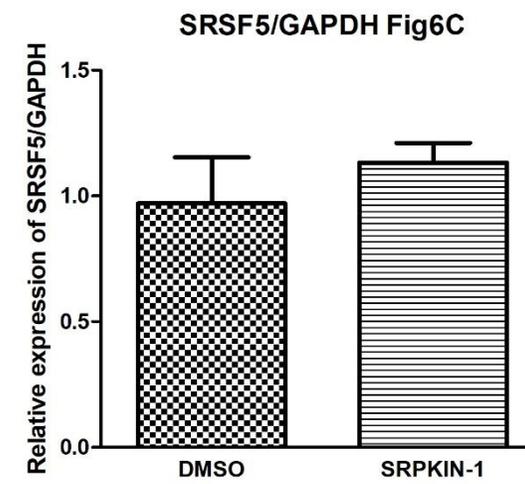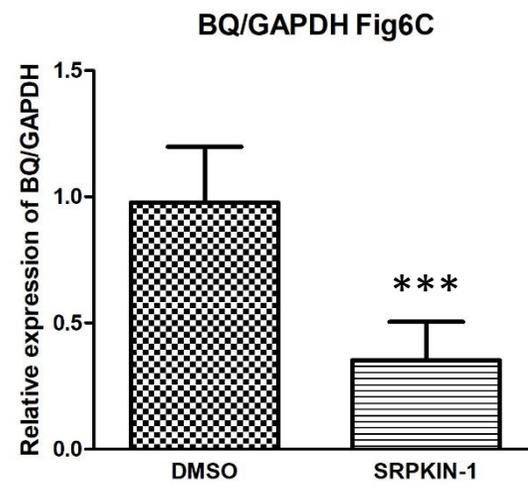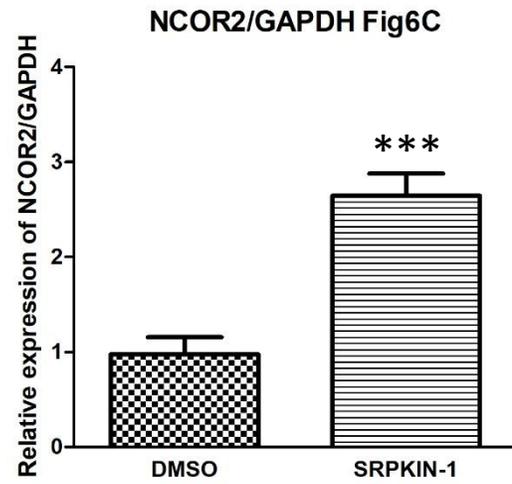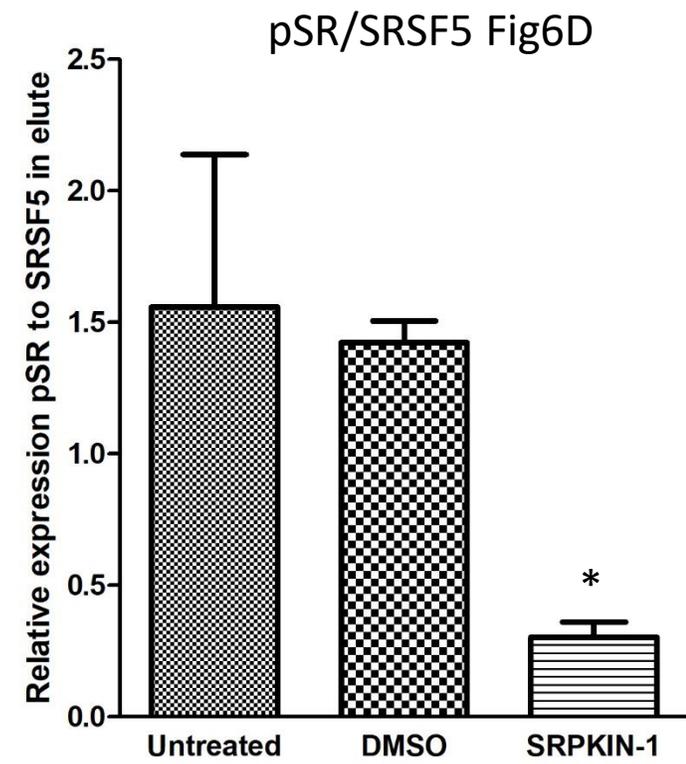
Figure 1B uncropped blots

SRSF5 in Figure 1B

50 kDa
37 kDa

25 kDa

20 kDa

15 kDa

SRSF3 in Figure 1B

50 kDa
37 kDa

25 kDa
20 kDa

15 kDa

BQ in Figure 1B

75 kDa

50 kDa

37 kDa

25 kDa

20 kDa

HSP90 in Figure 1B

150 kDa
100 kDa
75 kDa
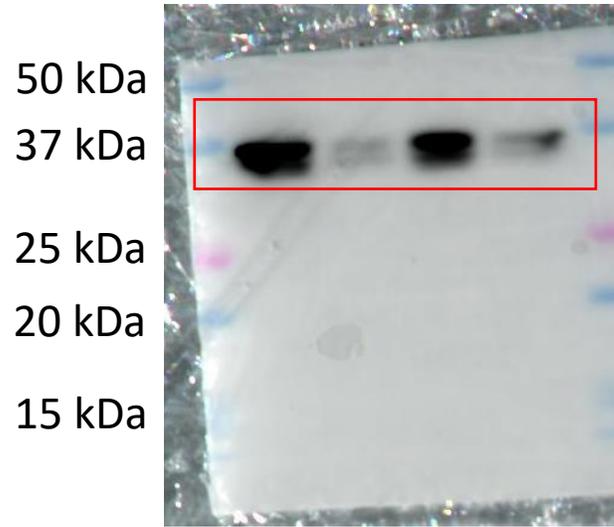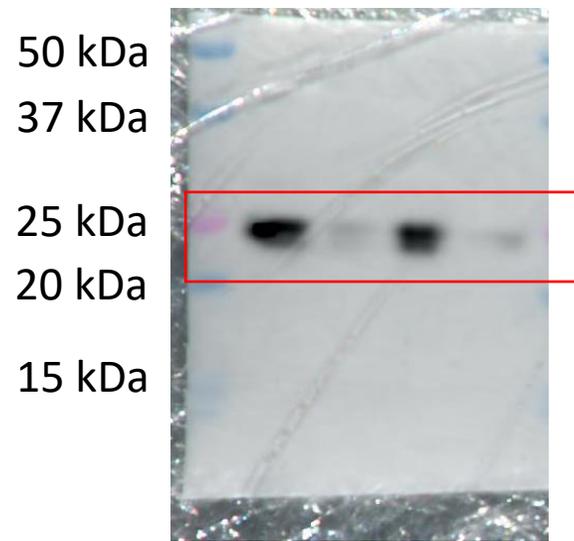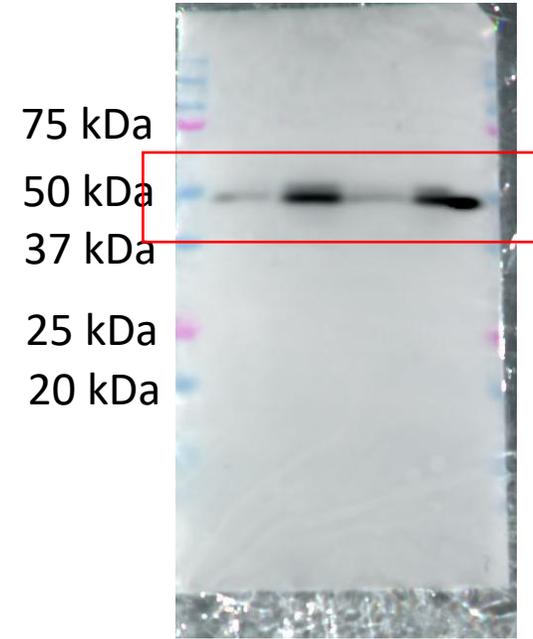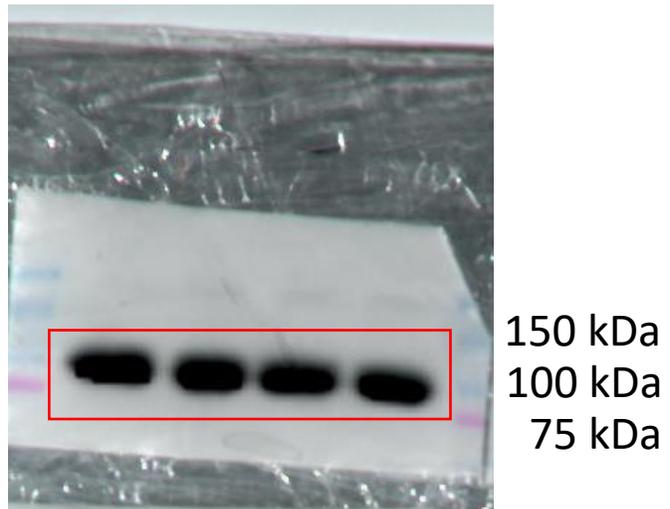
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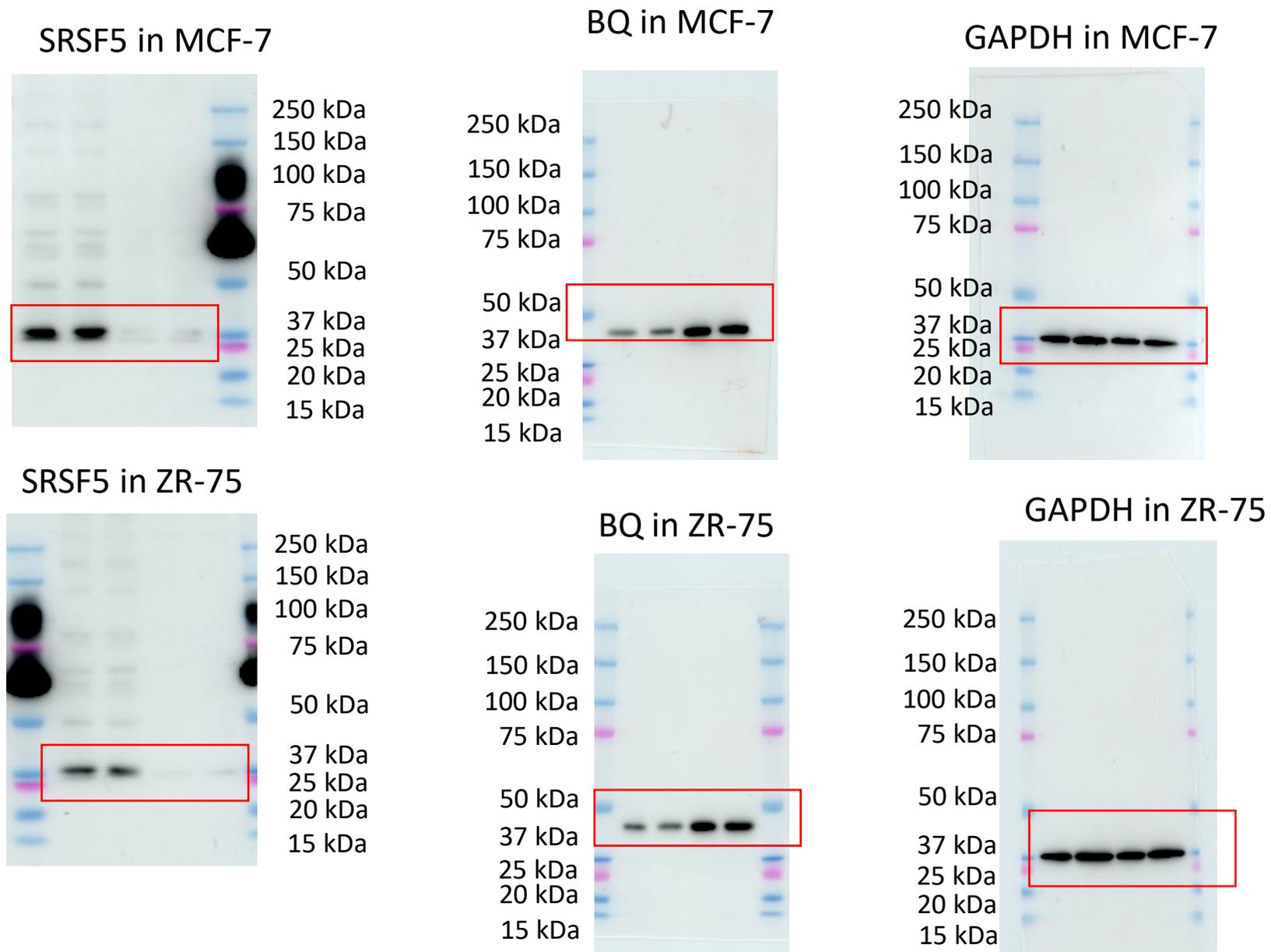
# Figure 1D uncropped blots

SRSF5 in LCC2

50 kDa
37 kDa
25 kDa
20 kDa
15 kDa

BQ in LCC2

75 kDa
50 kDa
37 kDa
25 kDa
20 kDa

HSP90 in LCC2

150 kDa
100 kDa
75 kDa

SRSF5 in AK-47

50 kDa
37 kDa
25 kDa
20 kDa
15 kDa

BQ in AK-47

75 kDa
50 kDa
37 kDa
25 kDa
20 kDa

HSP90 in AK47

150 kDa
100 kDa
75 kDa
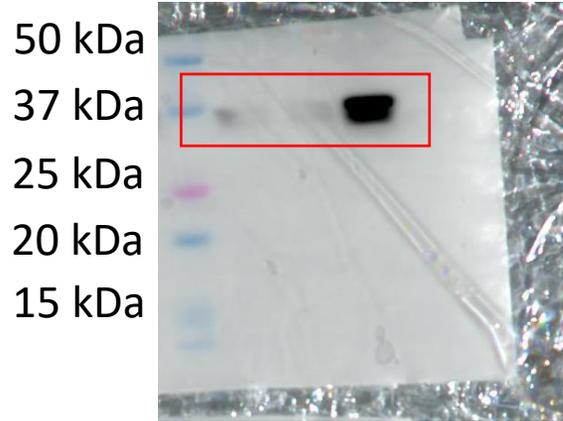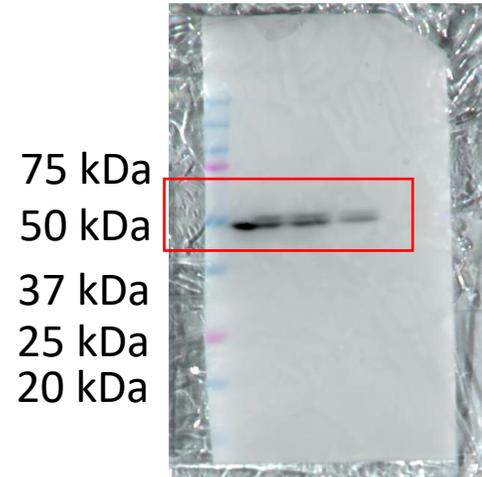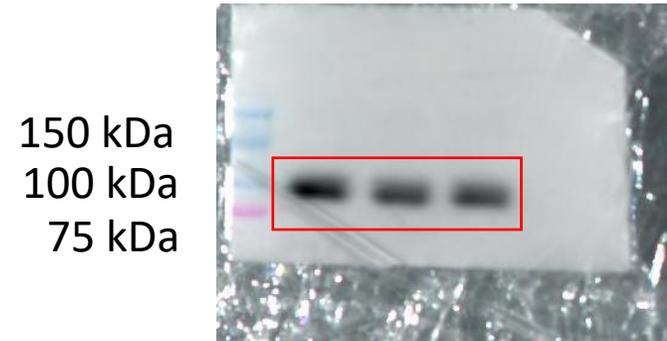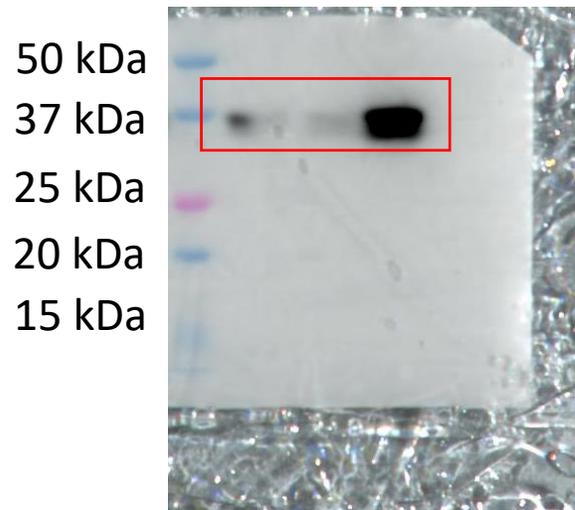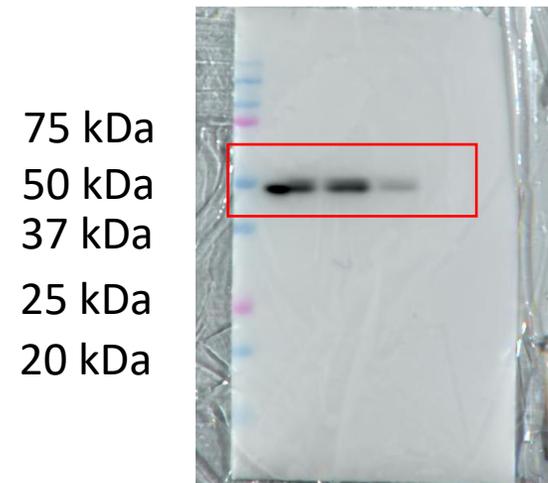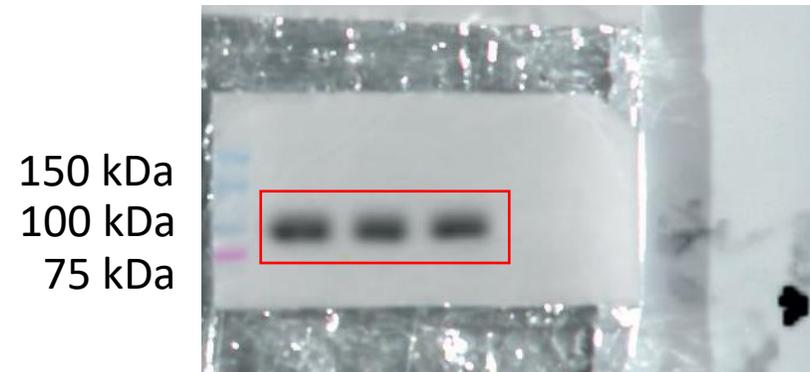
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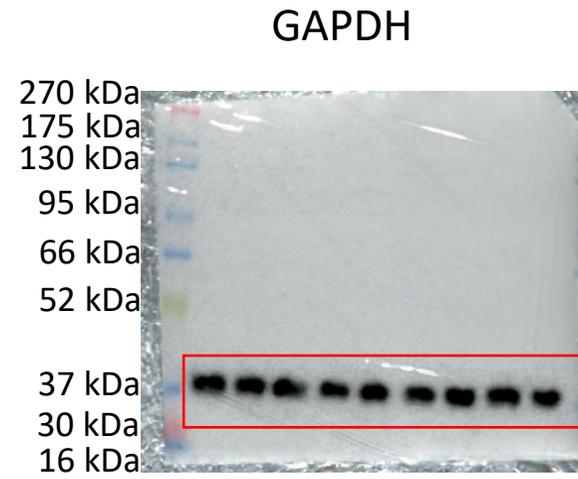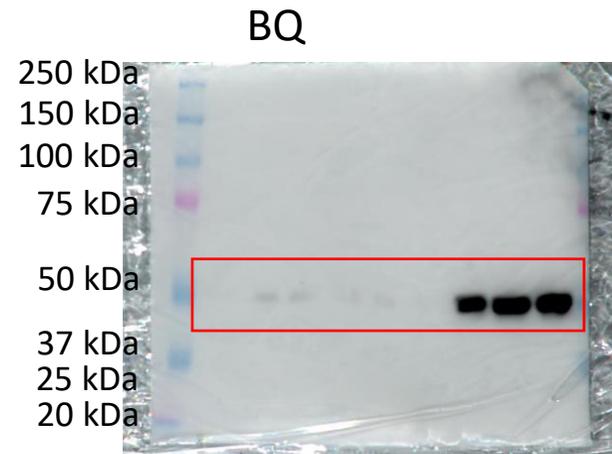
Figure 4D uncropped blots

BQ
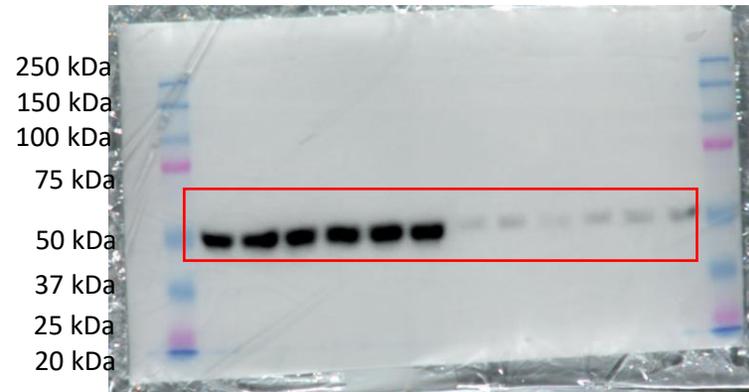
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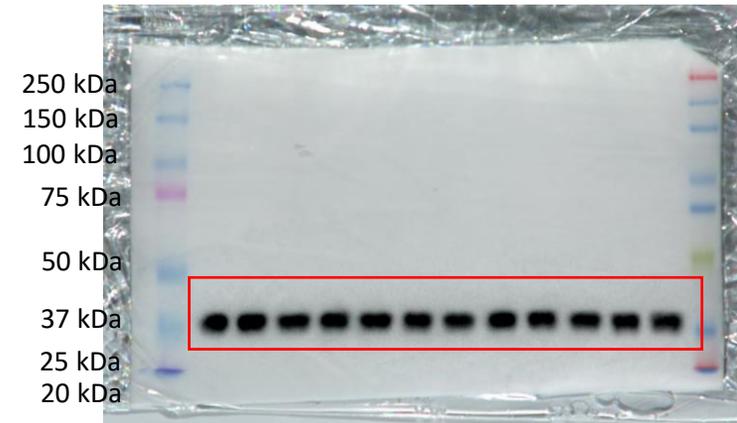
Figure 6A uncropped blots

LCC2 SRPK1 input

270 kDa
175 kDa
130 kDa
95 kDa
66 kDa
52 kDa
37 kDa
30 kDa
16 kDa

LCC2 SRSF5 input

75 kDa
50 kDa
37 kDa
25 kDa

LCC2 SRPK1 elute

270 kDa
175 kDa
130 kDa
95 kDa
66 kDa
52 kDa
37 kDa

LCC2 SRSF5 elute

270 kDa
175 kDa
130 kDa
95 kDa
66 kDa
52 kDa
37 kDa
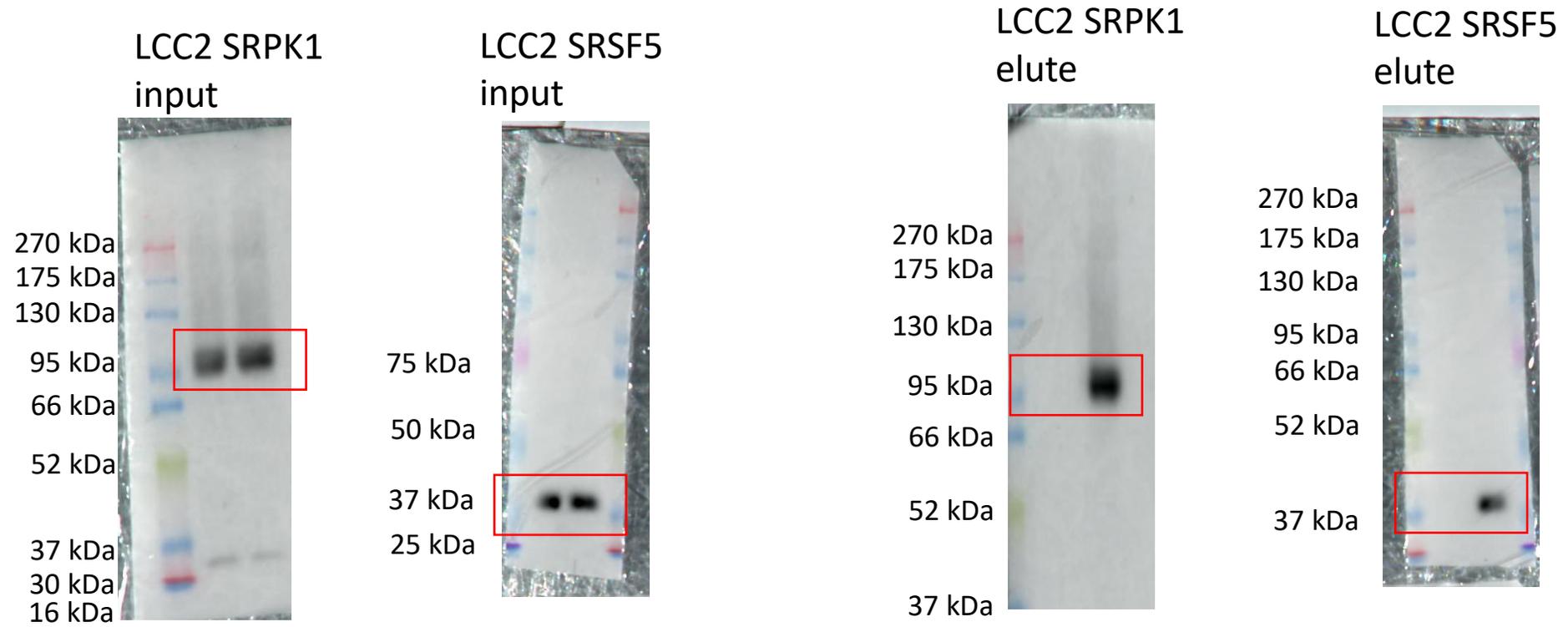
Figure 6C uncropped blots
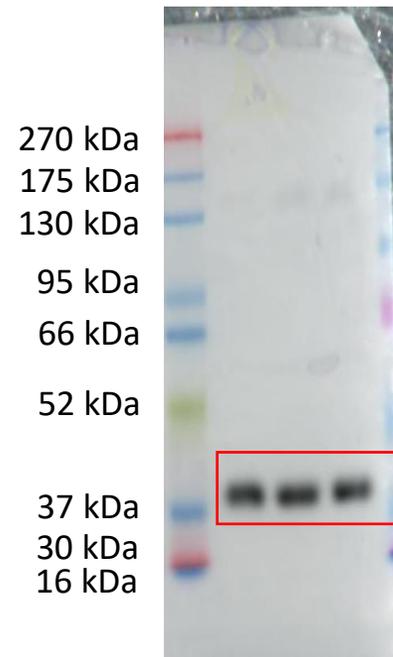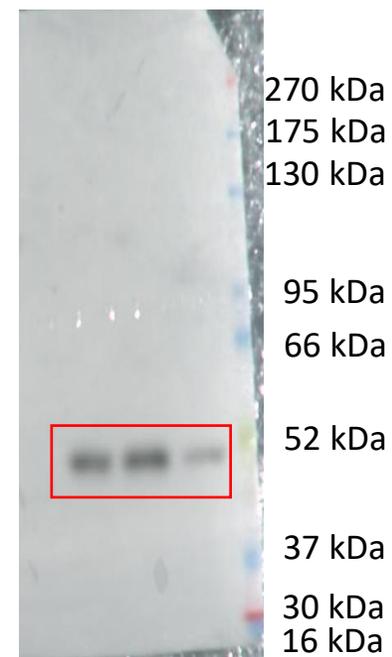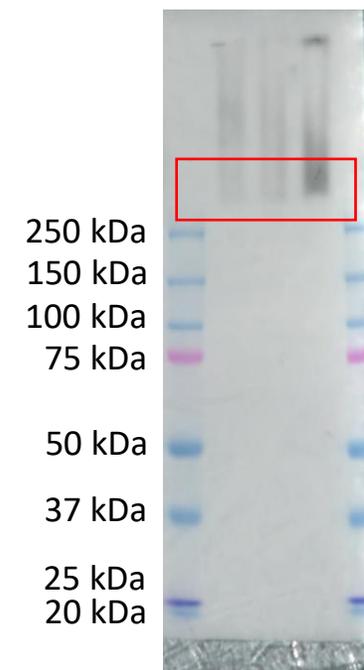
Figure 6D uncropped blots

SRSF5-myc input
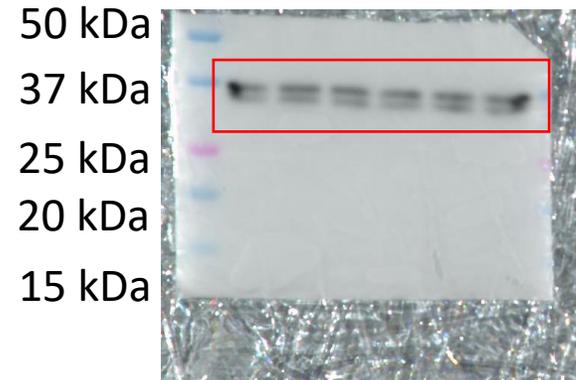
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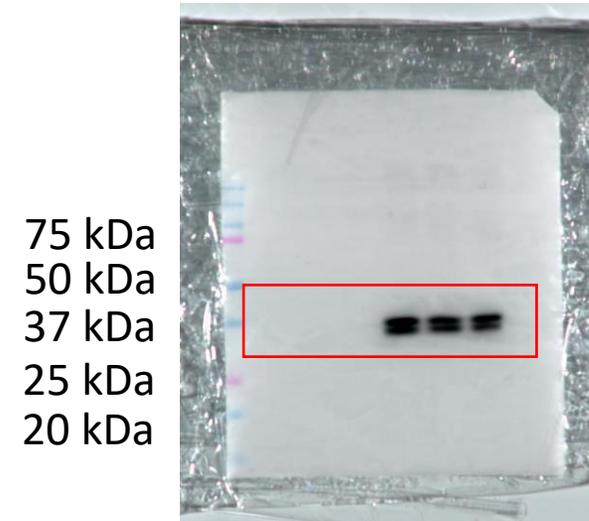
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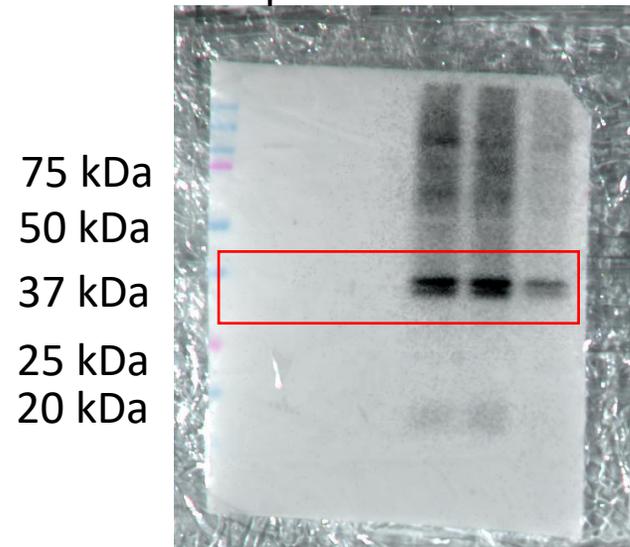
Figure S7 uncropped blots

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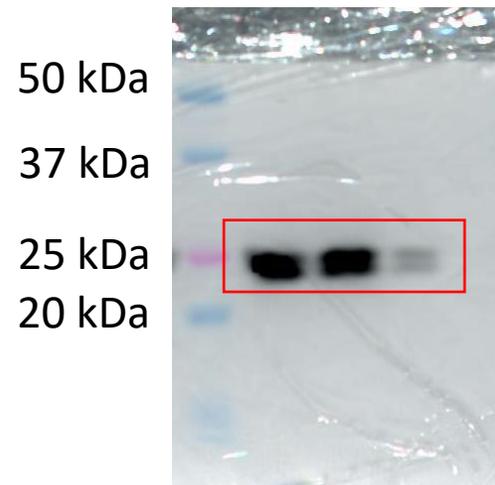
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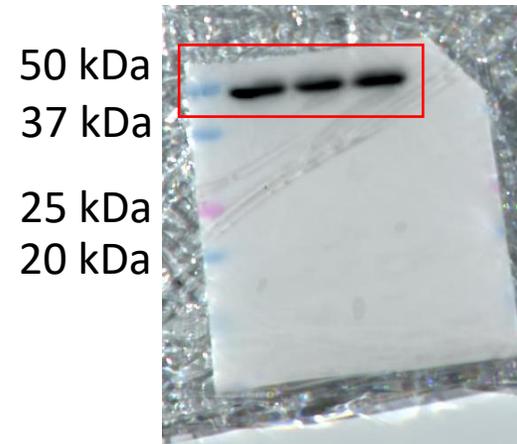
HSP90 MCF7
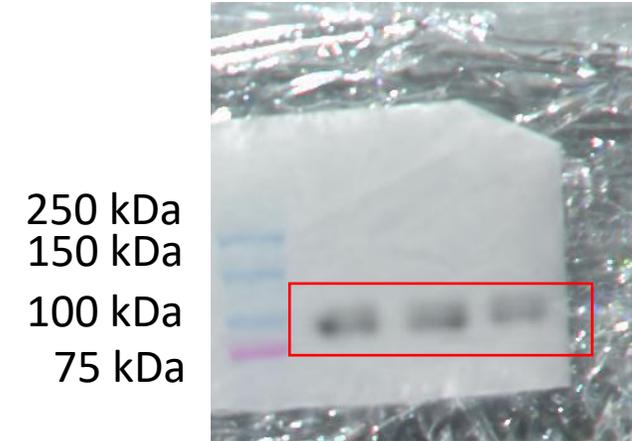
SRSF3 ZR75
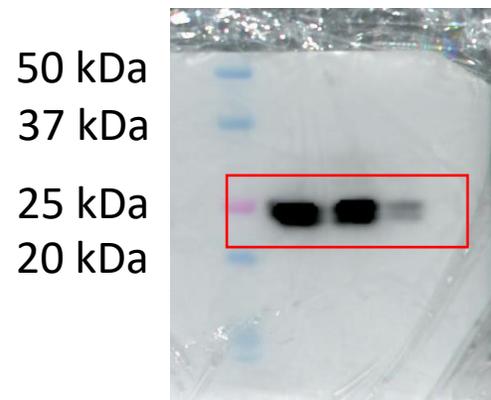
ZR75 ZR75
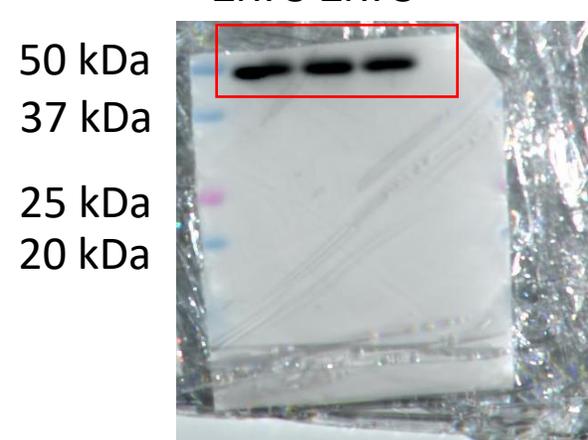
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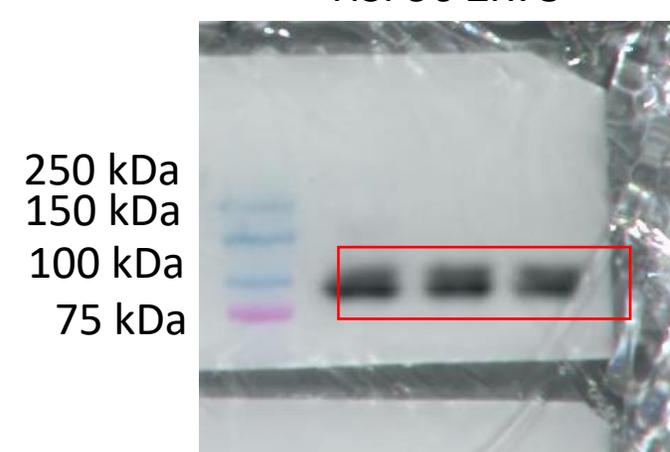
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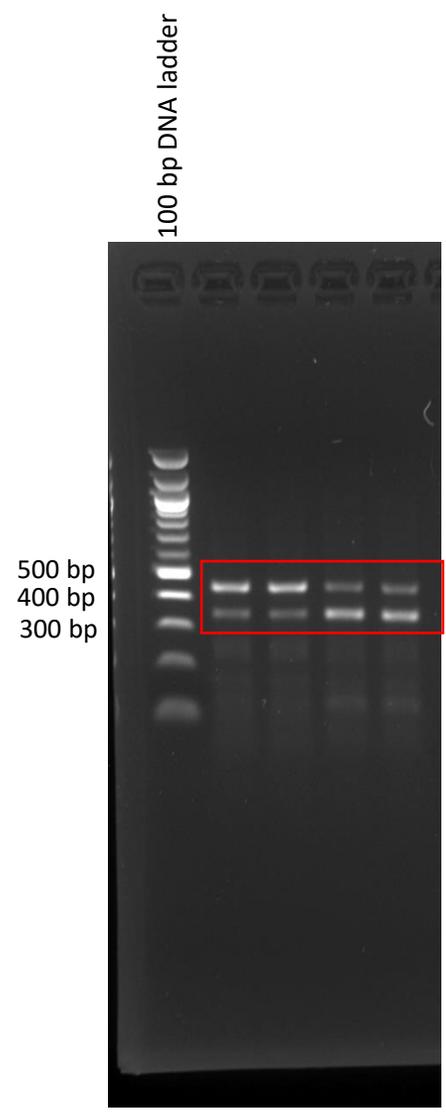
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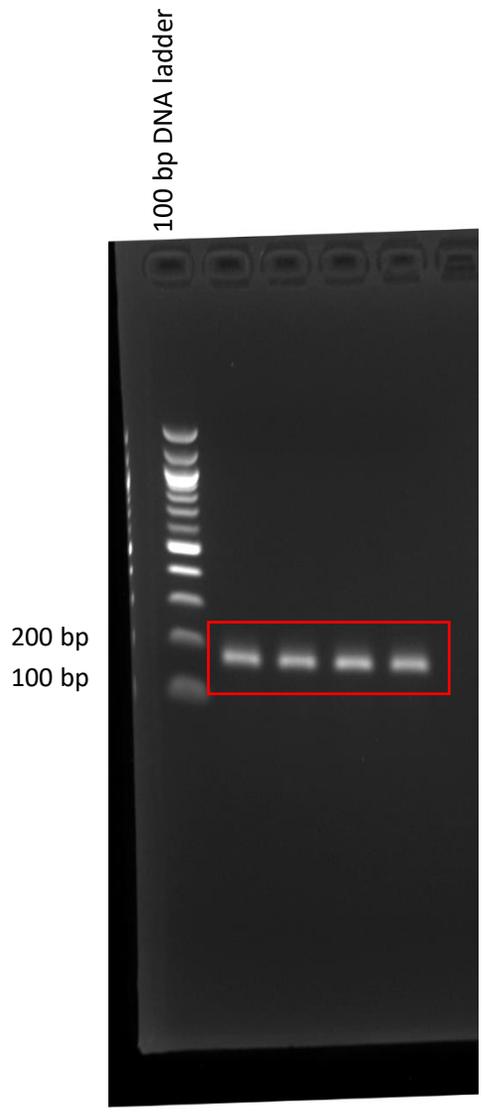
Actin

Full agarose gel image for figure 10

NCOR2 BQ splicing
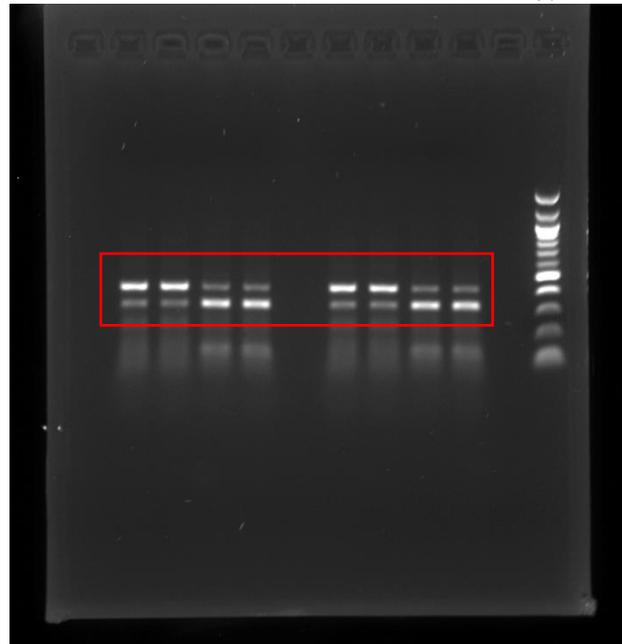
100 bp DNA ladder

500 bp
400 bp
300 bp

Actin
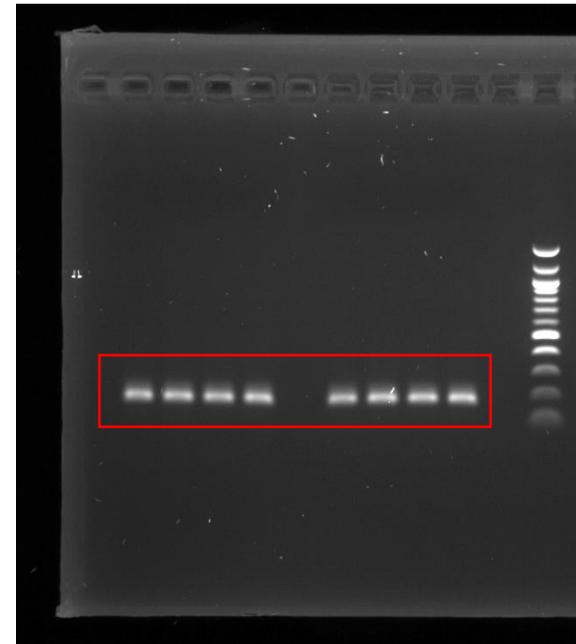
100 bp DNA ladder

200 bp
100 bp

Full agarose gel image for figure S11
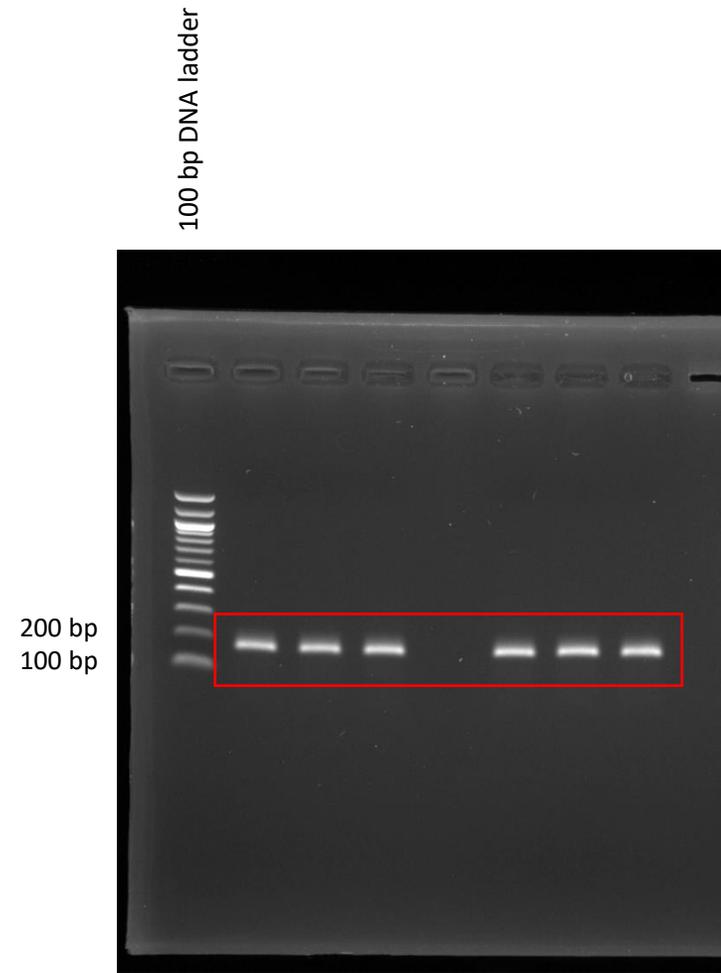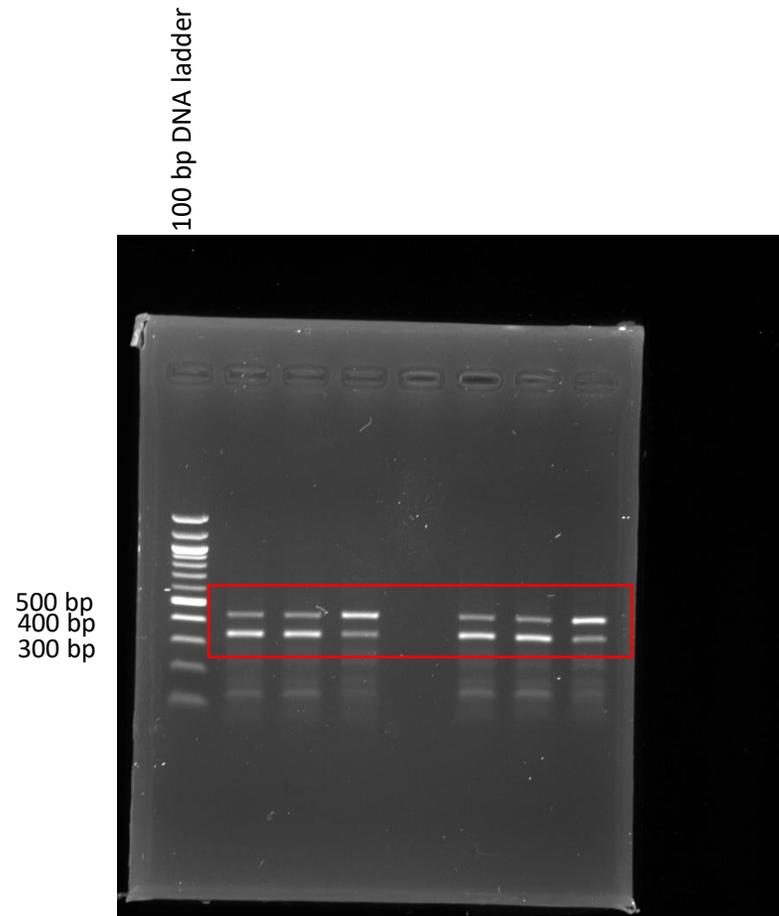
Supplementary figure legends

Figure S1 PCR-based splicing assay of NCOR2 and BQ. The DNA sequence of exons 10-12 of NCOR2 is shown. Using NCOR2-BQ splicing forward and reverse primers would yield two different PCR products with different product sizes, 443 bp and 352 bp for NCOR2 and BQ amplicons, respectively. Actin was the loading control.

Figure S2 Expression levels of SRSF1-12. qPCR was performed. ΔΔCT method was used and MCF-10A was used as the reference. Actin was used as the internal control. Results were shown as mean ± sd from three independent experiments.

Figure S3 Quantification of western blot results in Figure 1B. Results were shown as mean ± SD from four independent experiments. Students' t-test was employed for statistical analysis. *** represents $p < 0.001$.

Figure S4 Knockdown efficiency of shRNA targeting SRSF5. qPCR was employed to determine the expression of SRSF5. Actin was employed as the internal control. ΔΔCT method was used to evaluate the relative gene expression level. Results were shown as mean ± SD from three independent experiments. One-way ANOVA with Bonferroni post hoc test was used to determine the statistical significance between shCtrl and shSRSF5.1 or shSRSF5.2 groups. *** represents $p < 0.001$.

Figure S5 Quantification of western blot results in Figure 1C. Results were shown as mean ± SD from four independent experiments. One-way ANOVA with Bonferroni post hoc test was used to determine the statistical significance between shCtrl and shSRSF5.1 or shSRSF5.2 groups. *** represents $p < 0.001$.

Figure S6 The effect of SRSF3 siRNA. SRSF3 expression in A) MCF-7 and B) ZR-75. BQ expression in C) MCF-7 and D) ZR-75. NCOR2 expression in E) MCF-7 and F) ZR-75. 25 nM of siSRSF3 and siCtrl was employed. qPCR was performed 48 hours post-transfection. Actin was employed as the internal control. ΔΔCT method was used to evaluate the relative gene expression level. Results were shown as mean ± SD from four independent experiments. Students' t-test was employed for statistical analysis. *** represents $p < 0.001$.

Figure S7 SRSF3 knockdown could not affect BQ expression. 25 nM of siSRSF3 and siCtrl was employed. Western blot was performed 48 hours post-transfection. HSP90 was the loading control. The bar charts are the quantification of the western blots. Results were shown as mean ± SD from four independent experiments. Students' t-test was employed for statistical analysis. *** represents $p < 0.001$.

Figure S8 Quantification of western blot results in Figure 1D. Results were shown as mean ± SD from four independent experiments. One-way ANOVA with Bonferroni post hoc test was used to determine the statistical significance between untransfected and SRSF5 OE groups. *, and *** represent $p < 0.05$ and $p < 0.001$, respectively.

Figure S9 SRSF5 could not bind to 3'-UTR of HSP70 and β-globin. MCF-7 and ZR-75 were transfected and overexpressed with myc-tagged SRSF5. Immunoprecipitation was performed using anti-SRSF5 or anti-IgG. RNA associated with SRSF5 was extracted by Trizol reagent. RT-qPCR was performed to detect the expression of 3'-UTR of HSP70 and β-globin. The expression of these candidates in the input fraction was used as reference. 3'-UTR of HSP70 and β-globin were absent in the immunoprecipitants. Results were shown as mean ± SD from three independent experiments.

Figure S10 Knockdown of SRSF5 could enhance BQ expression but reduce NCOR2 expression. PCR-based splicing assay was performed on the control (shCtrl) and SRSF5 knockdown (shSRSF5.1 or shSRSF5.2). Actin was the loading control.

Figure S11 Overexpression of SRSF5 could reduce BQ expression but enhance NCOR2 expression. PCR-based splicing assay was performed on LCC2 and AK-47 stably transfected with pCMV-Myc-SRSF5 (SRSF5 OE) or pCMV (Ctrl OE). Actin was the loading control.

Figure S12 Quantification of western blot results in Figure 3D. Results were shown as mean ± SD from three independent tumours. One-way ANOVA with Bonferroni post hoc test was used to determine the statistical significance compared with the control (ZR-75 shCtrl + Saline).. *** represents $p < 0.001$.

Figure S13 Quantification of western blot results in Figure 4D. Results were shown as mean ± SD from three independent tumours. One-way ANOVA with Bonferroni post hoc test was used to determine the statistical significance compared with the control (LCC2 Ctrl OE + Saline). *** represents $p < 0.001$.

Figure S14 TG003 could not affect BQ expression and TAM resistance. A) the dose-dependent effect of CLK1 inhibitor TG003. MCF-10A was treated with different concentrations of TG003 for 96 hours. Cell viability assay was performed. Results were shown as mean ± SD from four independent experiments. One-way ANOVA with Bonferroni post hoc test was used to determine the statistical significance between DMSO and treatment groups. B) the effect of TG003 on BQ and NCOR mRNA expressions in LCC2 and AK-47. The cells were treated with 50 nM of TG003 for 72 hours. qPCR was performed. Results were shown as mean ± SD from four independent experiments. Students' t-test was employed for statistical analysis. C) TG003 could not reverse TAM resistance. LCC2 and AK-47 were treated with 50 nM of TG003 and 5 µM of TAM for 96 hours. Cell viability assay was performed. Results were shown as mean ± SD from four

independent experiments. Two-way ANOVA with Bonferroni post hoc test was used to determine the statistical significance. *, **, and *** represents $p < 0.05$, $p < 0.01$ and $p < 0.001$, respectively.

Figure S15 Protein-protein interaction network of SRPK1. The information was obtained from STRING database.

Figure S16 The dose-dependent effect of SRPK1 inhibitor SRPKIN-1. MCF-10A was treated with different concentrations of SRPKIN-1 for 96 hours. Cell viability assay was performed. Results were shown as mean ± SD from four independent experiments. One-way ANOVA with Bonferroni post hoc test was used to determine the statistical significance between DMSO and treatment groups. ** and *** represents $p < 0.01$ and $p < 0.001$, respectively.

Figure S17 Quantification of western blot results in Figure 6C. Results were shown as mean ± SD from three independent experiments. Students' t-test was employed for statistical analysis. *** represents $p < 0.001$.

Figure S18 Quantification of western blot results in Figure 6D. SRSF5-Myc and pSR from elute fraction were normalised using SRSF5-Myc from input fraction. The relative expression of normalised SRSF5-Myc and pSR was determined. Results were shown as mean ± SD from three independent experiments. One-way ANOVA with Bonferroni post hoc test was used to determine the statistical significance between untreated and SRPKIN-1 groups. * represents $p < 0.05$.