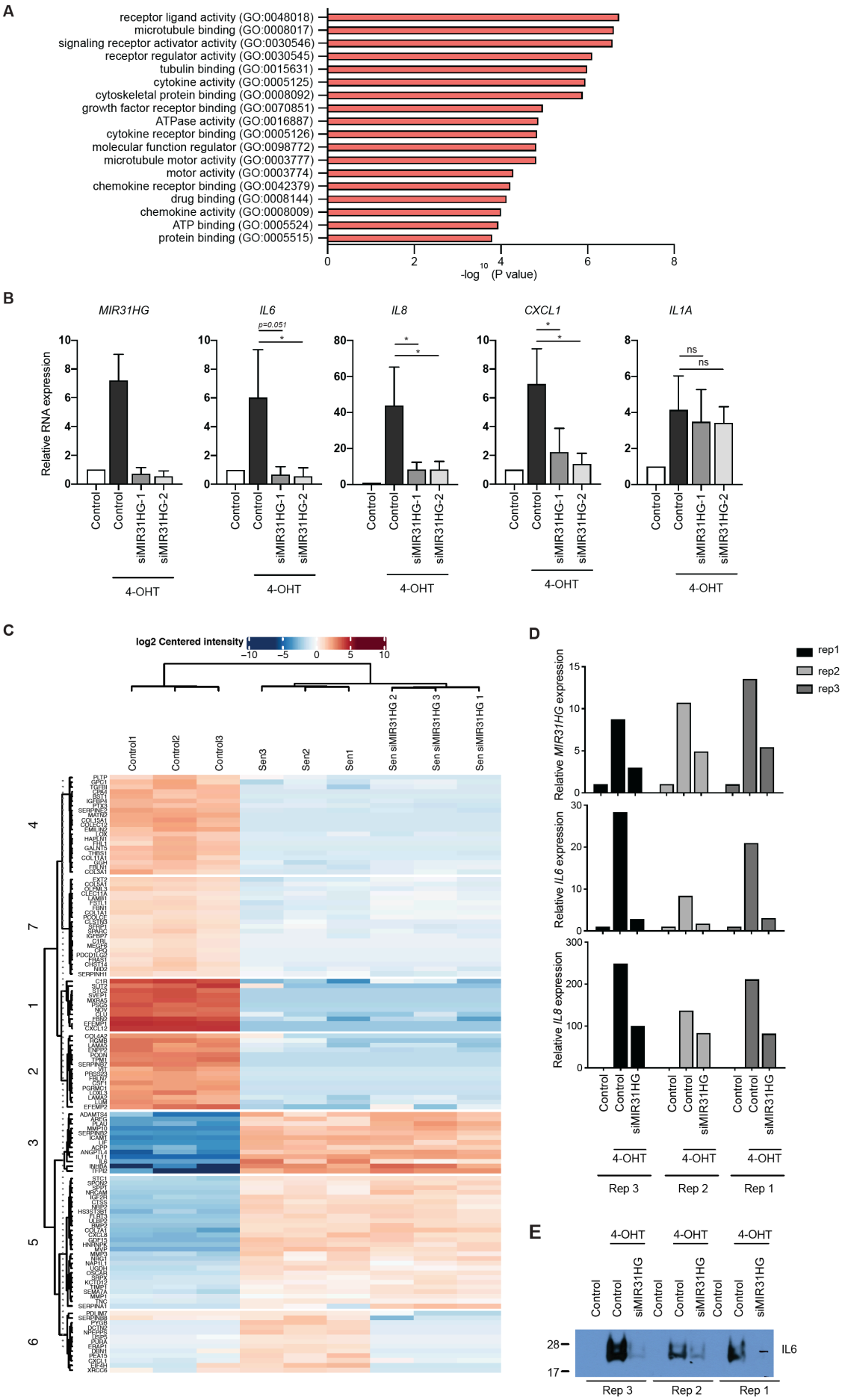
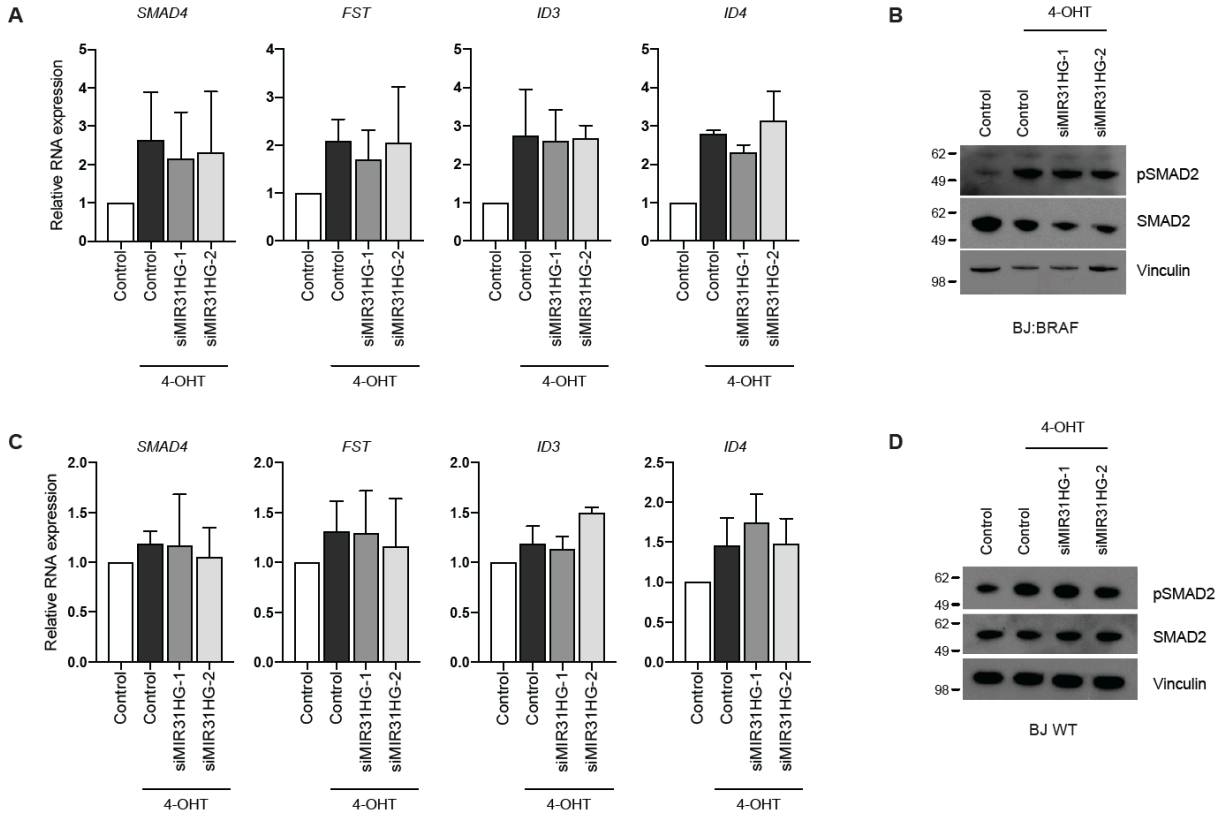
Supplementary Fig.1. Related to Figure 1.



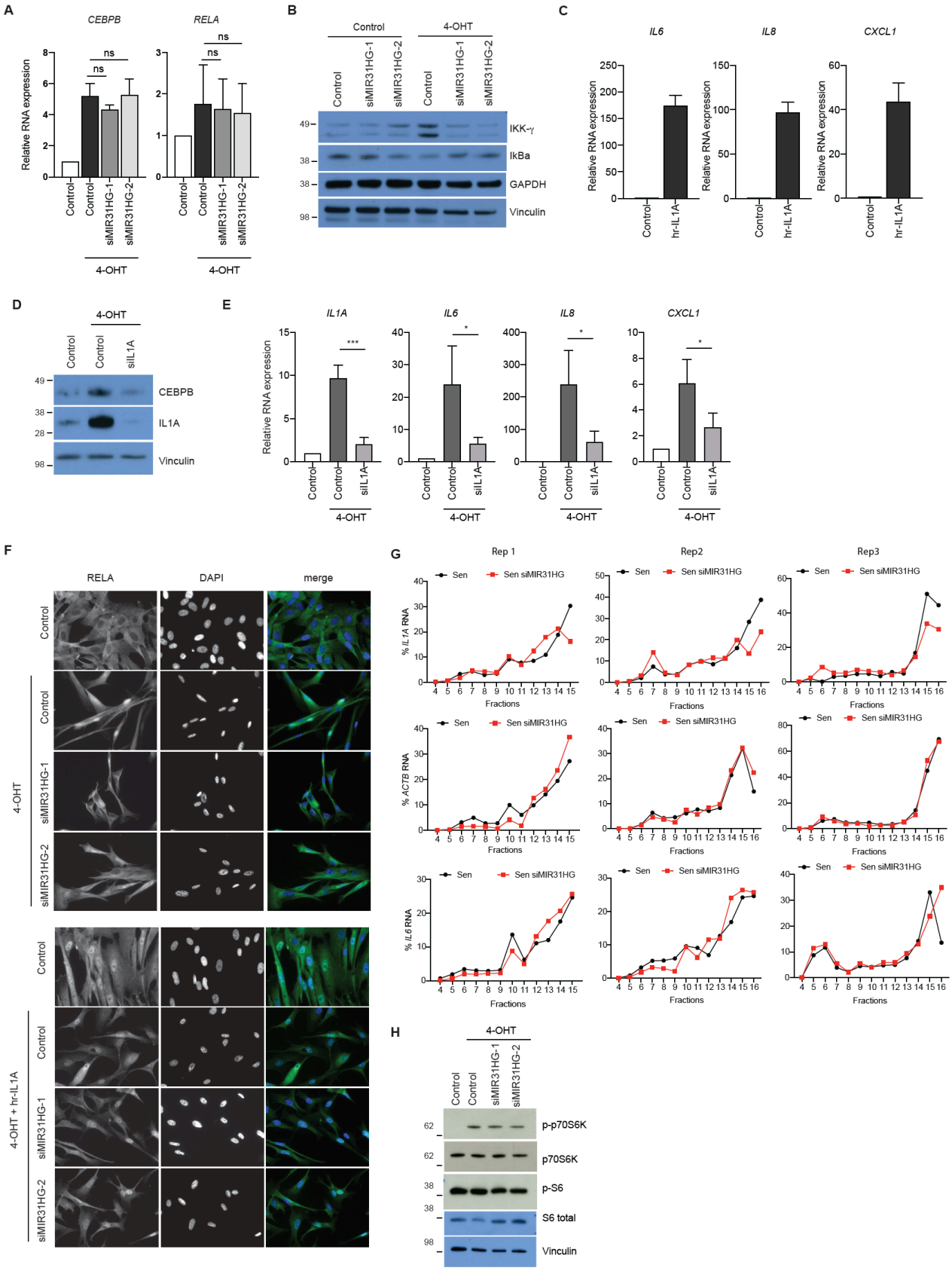
Supplementary Fig. 1 (a) GO enrichment analysis for the significant downregulated genes in BJ ER:BRAF senescent *MIR31HG* knock-down cells compared to control knock-down senescent cells treated with 1μM 4-OHT for 48h. The graph displays the molecular function of the significant categories. **(b)** qRT–PCR analysis of selected components of the SASP normalized to housekeeping genes (*HPRT1* and *RPLP0*) in TIG3 ER:BRAF cells transfected with the indicated siRNAs (Control or siMIR31HG1-2), treated with ethanol (Control) or 1μM 4-OHT for 48h. The graphs show results compared to control ethanol-treated set to 1 (n=3). **(c)** The heat map represents the intensity of all the proteins identified by mass spectrometry described in Fig. 1c. The heat map shows BJ ER:BRAF ethanol treated cells (Control 1-3), BJ ER:BRAF transfected with control siRNA (Sen 1-3) or siMIR31HG (Sen siMIR31HG 1-3) treated with 1μM 4-OHT for 72h. **(d)** qRT–PCR analysis of total RNA extracted from the cells that were subjected to mass spectrometry described in Fig. 1c. **(e)** Western blot analysis for IL6 secretion from precipitated protein from the CM that was subjected to mass spectrometry described in Fig. 1c. Molecular weight marker is shown in KDa. All error bars represent means ± s.d.

Supplementary Fig.2. Related to Figure 2.



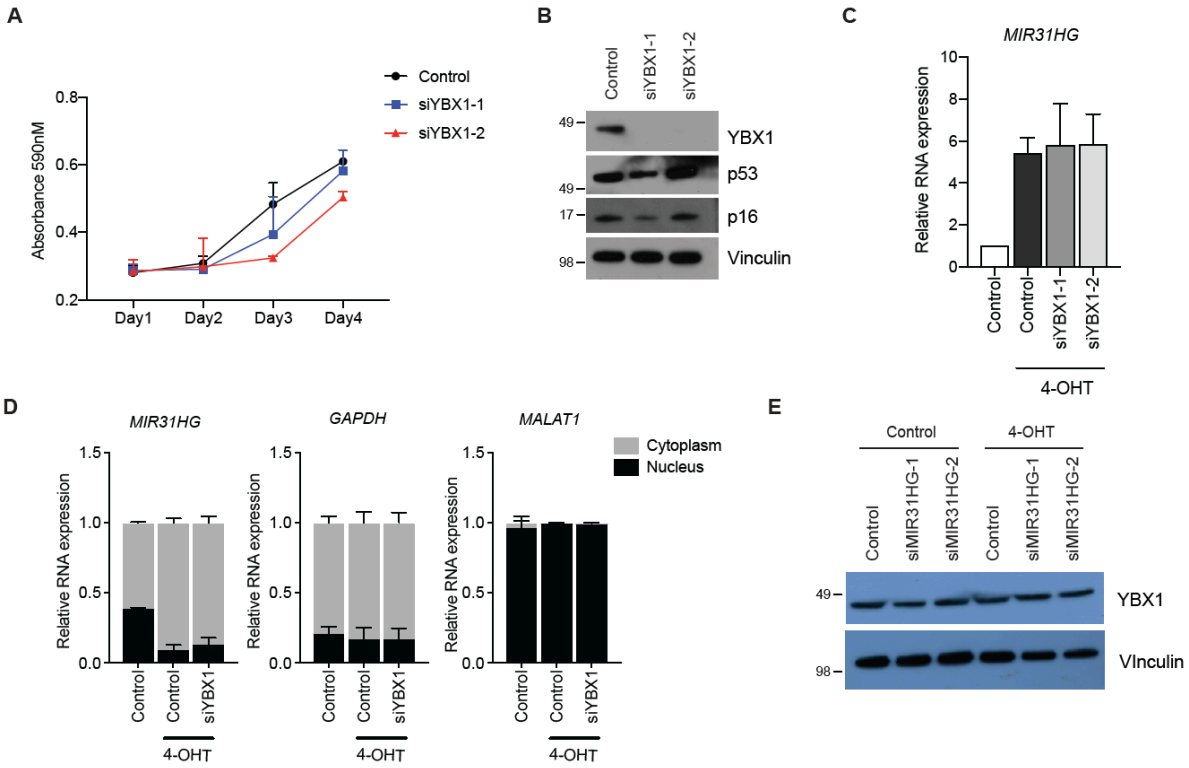
Supplementary Fig. 2 (a) qRT–PCR analysis of selected TGFβ target genes relative to housekeeping genes (*HPRT1* and *RPLP0*) in BJ ER:BRAF cells transfected with the indicated siRNAs (Control or siMIR31HG1-2), treated with ethanol (Control) or 1μM 4-OHT for 48h. The graph shows results compared to control ethanol-treated set to 1 (n=2). **(b)** Western blot for p-SMAD and total SMAD in the cells described in (b). Vinculin was used as loading control. Molecular weight marker is shown in KDa (n=2). **(c)** qRT–PCR analysis of selected TGFβ target genes relative to housekeeping genes (*HPRT1* and *RPLP0*) in BJ wild type (BJ WT) cells that have been incubated with the CM from cells described in (a) for 72h (n=2). **(d)** Western blot for p-SMAD and total SMAD in the cells described in (c). Vinculin was used as loading control. Molecular weight marker is shown in KDa (n=2). All error bars represent means ± s.d.

Supplementary Fig.3. Related to Figure 3.



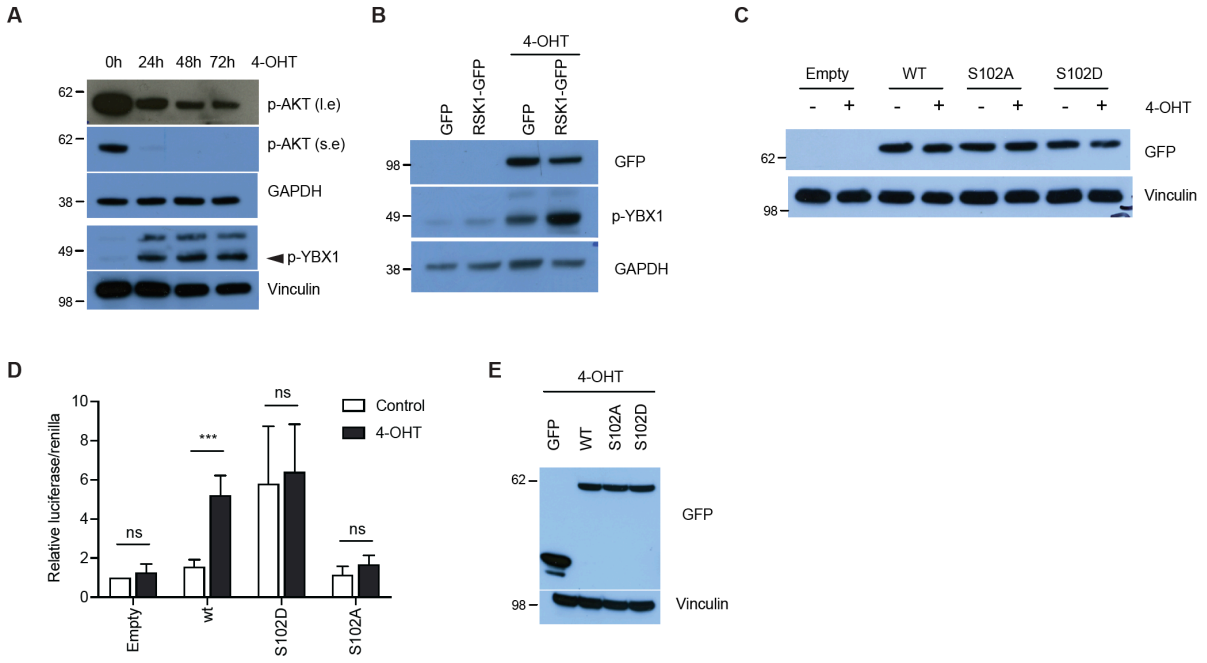
Supplementary Fig. 3 (a) qRT-PCR analysis of *CEBPB* and *RELA* mRNA normalized to the housekeeping genes (HPRT1 and RPLP0) in BJ ER:BRAF cells (Control or siMIR31HG1-2) treated with ethanol (Control) or 1μM 4-OHT for 48h. The graph shows relative RNA expression to control untreated cells set to 1 (n=3). **(b)** BJ ER:BRAF cells transfected with the indicated siRNAs (Control or siMIR31HG1-2), treated with ethanol (Control) or 1μM 4-OHT for 72h were analysed by western blot for p-RELA, CEBPB, IKK-γ and IKBa. Vinculin is shown as loading control. Molecular weight marker is shown in KDa (n=2). **(c)** qRT-PCR analysis of a subset of SASP components in BJ ER:BRAF cells untreated or treated with 10ng/ml of human recombinant IL1A (hr-IL1A) for 2h. **(d)** BJ ER:BRAF (Control or siIL1A) treated with ethanol (Control) or 1μM 4-OHT for 72h were analysed by western blot for CEBPB, IL1A and Vinculin. Molecular weight marker is shown in KDa (n=3). **(e)** qRT-PCR analysis of a subset of SASP components in the conditions described in (c) (n=5). (**f**) Immunofluorescence for RELA and DAPI staining (n=2) in BJ ER:BRAF cells transfected with the indicated siRNAs (Control or siMIR31HG1-2), treated with ethanol (Control) or 1μM 4-OHT for 48h, in the absence or presence of 10ng/ml for 24h before fixation. **(g)** Distribution of *ILA*, *ACTB* and *IL6* mRNA in the three polysome fractionations performed by sucrose gradient in BJ ER:BRAF control cells (Sen, black) or siMIR31HG cells (Sen MIR31HG KD, red) treated with 1μM 4-OHT for 72h. **(h)** BJ ER:BRAF cells transfected with the indicated siRNAs (Control or siMIR31HG1-2), treated with ethanol (Control) or 1μM 4-OHT for 72h were analysed by western blot for p-p70S6K, p70S6K, p-S6, S6 and Vinculin. Molecular weight marker is shown in KDa (n=3). Statistical significances were calculated using two-tailed Student t-tests, $****P < 0.0001$; $**P < 0.01$; $*P < 0.05$; ns, non-significant. All error bars represent means ± s.d.

Supplementary Fig. 4. Related to Figure 4.



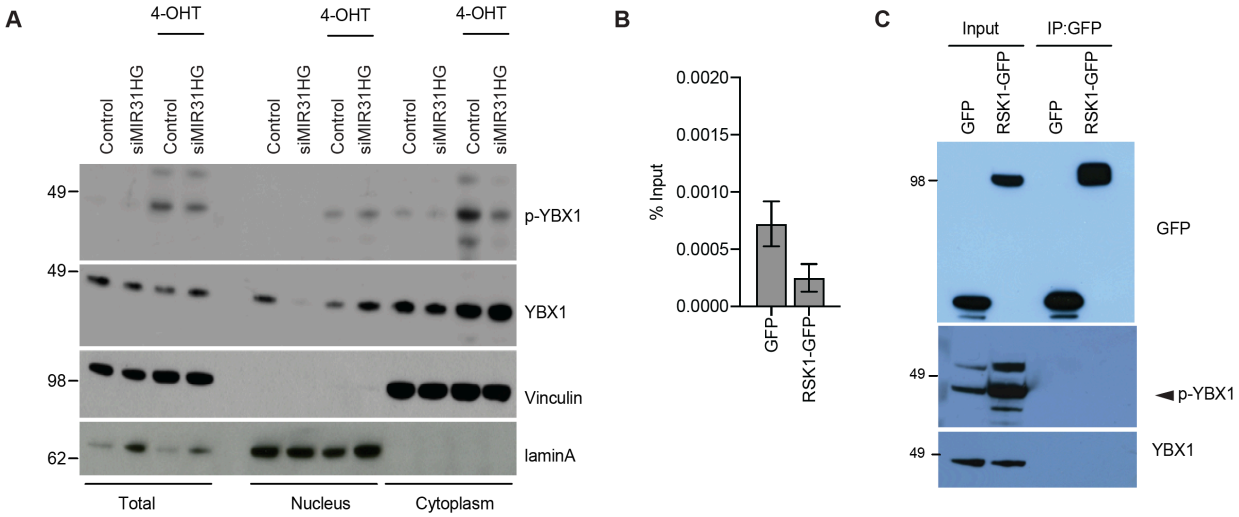
Supplementary Fig. 4 (a) BJ ER:BRAF (control or siYBX1-1-2) were stained with crystal violet staining (see materials and methods) to address the cell growth at the indicated days post-transfection. The graph shows the absorbance (590nM) measured after dissolving the crystal violet in 10% acetic acid (n=2). **(b)** BJ ER:BRAF (control or siYBX1-1-2) were analysed for western blot 72h post-transfection for YBX1, p53, p16 and Vinculin. Molecular weight marker is shown in KDa (n=2). **(c)** BJ ER:BRAF cells transfected with the indicated siRNAs (control or siYBX1-1-2), treated with ethanol (Control) or 1μM 4-OHT for 48h were analysed by qRT–PCR for *MIR31HG* mRNA relative expression normalized to housekeeping genes (HPRT1 and RPLP0) and represented relative to untreated control cells (n=4). **(d)** BJ ER:BRAF (control or siYBX1) treated with ethanol (Control) or 1μM 4-OHT for 48h were fractionated and the RNA was extracted. Distribution of *MIR31HG*, *GAPDH* and *MALAT1* (nuclear (grey), cytoplasmic (black)) was analysed by qRT-PCR. The graph shows the percentage of transcript relative to the input (n=2). **(f)** BJ ER:BRAF cells transfected with the indicated siRNAs (Control or siMIR31HG1-2), treated with ethanol (Control) or 1μM 4-OHT for 72h were analysed by western blot for YBX1 total levels. All error bars represent means ± s.d.

Supplementary Fig.5. Related to Figure 5.



Supplementary Fig. 5 **(a)** Western blot for p-AKT long exposure (l.e) or short exposure (s.e) and pYBX1 (arrow) in BJ ER:BRAF cells treated with 4-OHT for the indicated time. GAPDH and Vinculin were used as loading control. Molecular weight marker is shown in KDa (n=2). **(b)** Western blot analysis for GFP, p-YBX and YBX1 in empty-GFP BJ ER:BRAF or RSK1-GFP BJ ER:BRAF induced with doxycycline (empty:20ng/ml, RSK1: 100ng/ml) untreated or treated with 1μM 4-OHT for 72h. **(c)** Western blot analysis to control the expression of the GFP-tagged proteins from experiment in Fig. 5e. **(d)** Response to 4-OHT of the different YBX1 cell lines from the data presented in Fig. 5e. **(e)** Western blot analysis for GFP to control the expression of the GFP-tagged proteins from experiment in Fig. 5f.

Supplementary Fig.6. Related to Figure 6.



Supplementary Fig. 6 (a) BJ ER:BRAF cells (Control or siMIR31HG1-2) were treated with ethanol (Control) or 1μM 4-OHT for 72h. After cellular fractionation p-YBX1 and YBX1in the total, nuclear and cytoplasmic fractions were analysed by western blot. Vinculin and laminA were used as cytoplasmic and nuclear controls respectively. **(b)**Native RNA-IP experiment of empty-GFP BJ ER:BRAF or RSK1-GFP BJ ER:BRAF induced with doxycycline (empty:20ng/ml, RSK1: 100ng/ml) and treated with 1μM 4-OHT for 72h. The graph shows the percentage of the input of *MIR31HG* bound to RSK (n=3). **(c)** Western blot analysis for GFP, p-YBX and YBX1 to control the IP efficiency in (b).