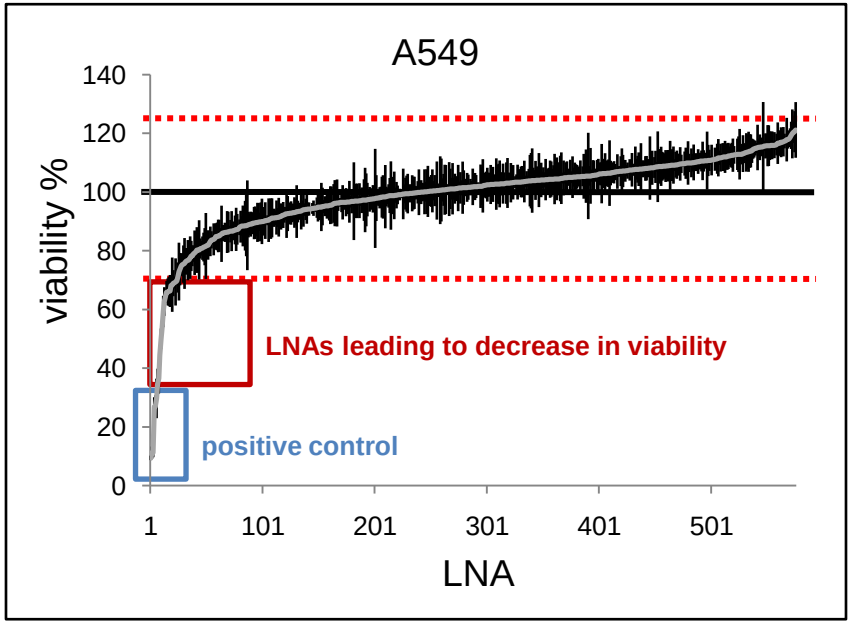
a)



b)

microRNA	viability %	st.dev.
133a/b	9.4	1.3
361-3p	11.3	3.6
512-5p	11.3	2.8
197	26.9	5.5
150	27.0	6.5
204	29.7	11.7
621	34.6	9.0
636	36.6	9.1
486-5p	44.5	2.9
326	50.0	6.1

***Figure* S1**- *Functional anti-miR screening in A549 cells* - **a)** Diagram showing results of LNA library (~600 LNAs) screening in A549 cells. The viable cell number was evaluated 72 hours after transfection by Cell Titer-Glo luminescent cell viability assay and normalized to the average of all samples, excluding controls. Values above and below two fold standard deviation (red dashed lines) were considered as significant. Reported is the mean ± s.e.m. of the screening performed in triplicate; each dot represents an individual LNA. **b)** Table showing 10 LNAs that resulted most effective in A549 cells and relative viability.

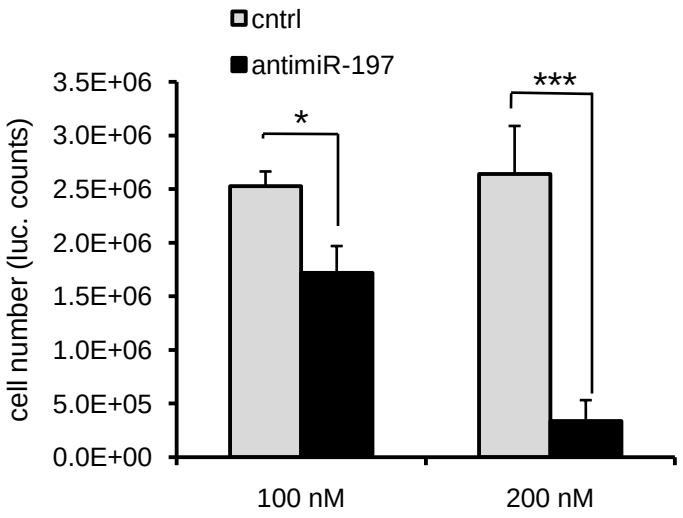


***Figure* S2-** *Inhibition of miR -197 by non LNA anti-miR* - Dose dependent effect on NIH-H460 lung cancer cells viability of a single-stranded, modified RNA oligonucleotide complementary to the miR-197 sequence (Qiagen).

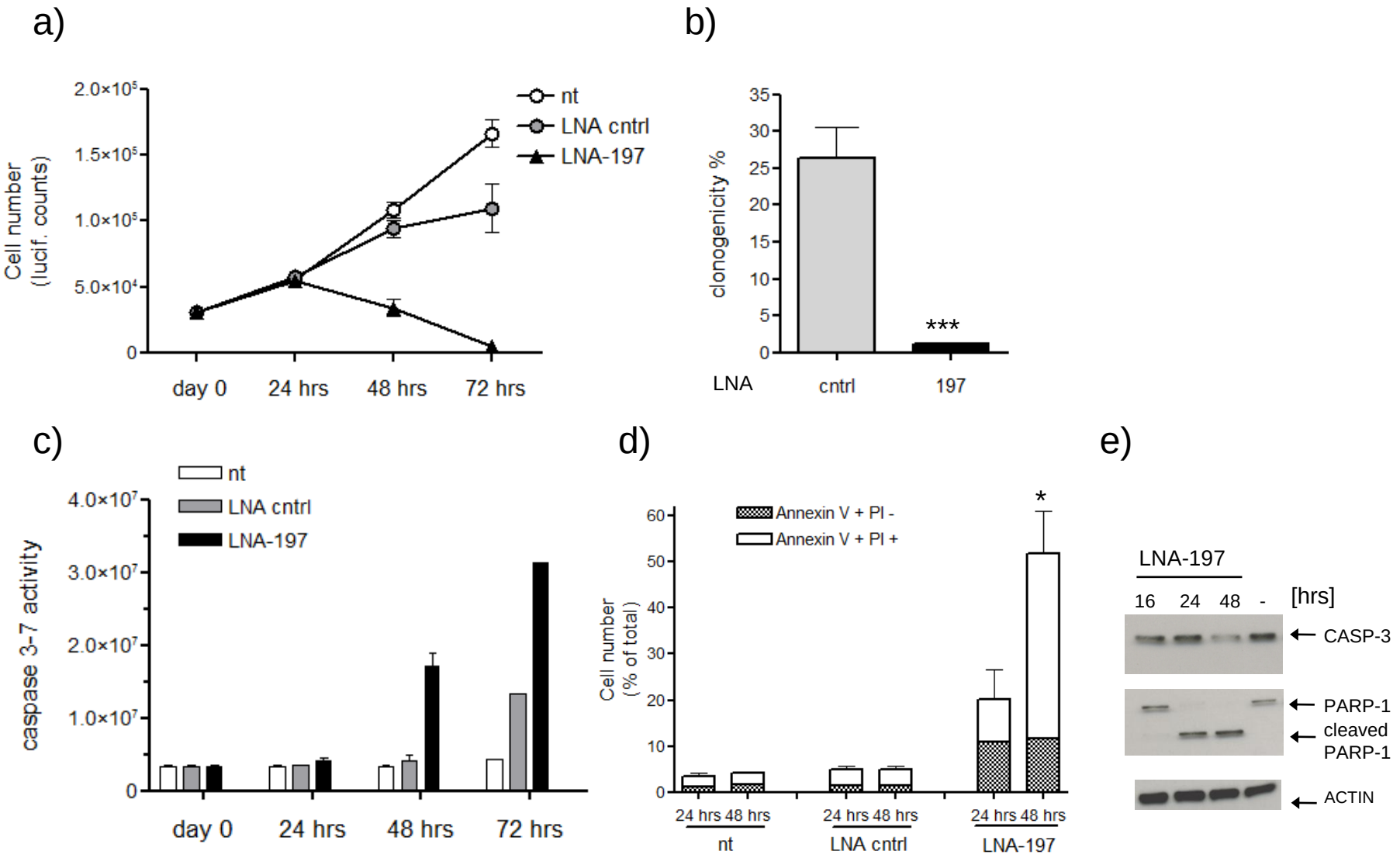


***Figure* S3-** *LNA-197 treatment impairs cell proliferation and induces apoptosis in A549 lung cancer cells* - **a)** Growth curve of A549 cells untreated (nt), transfected with control LNA or LNA-197 at 25nM; cell number was assessed by Cell Titer Glo assay at the indicated time points after transfection. **b)** Clonogenic capacity of A549 cells after anti-miR-197 treatment; the graph shows the percentage of plated cells that give rise to colonies. **c)** Activation of the apoptotic pathway after LNA-197 transfection is shown by CASPASE 3-7 activity, Annexin V staining **(d)** and immunoblot using the specified antibodies at the indicated time points **(e)**. ***p<0.001, **p<0.01, *p<0.05.

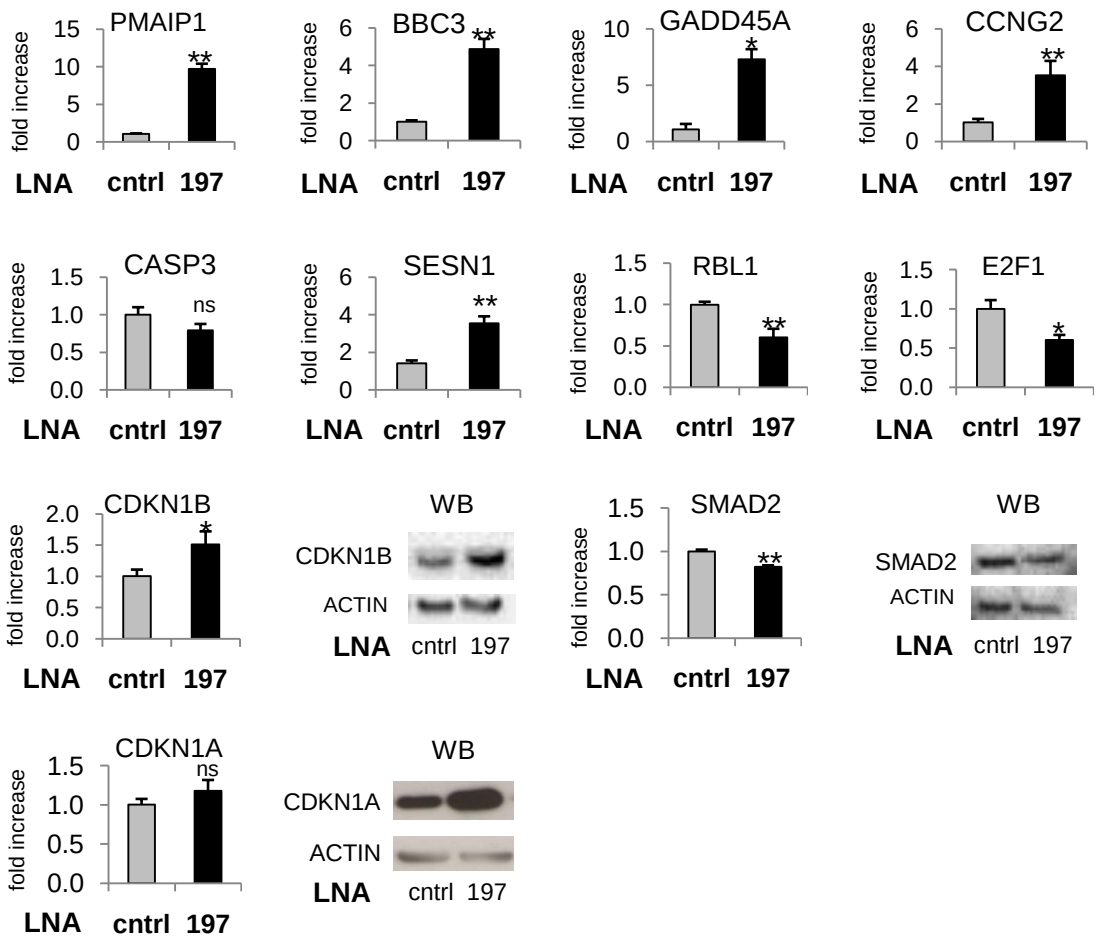


***Figure* S4-** Validation of gene arrays results by real time PCR and western blotting - Mean ± s.d.

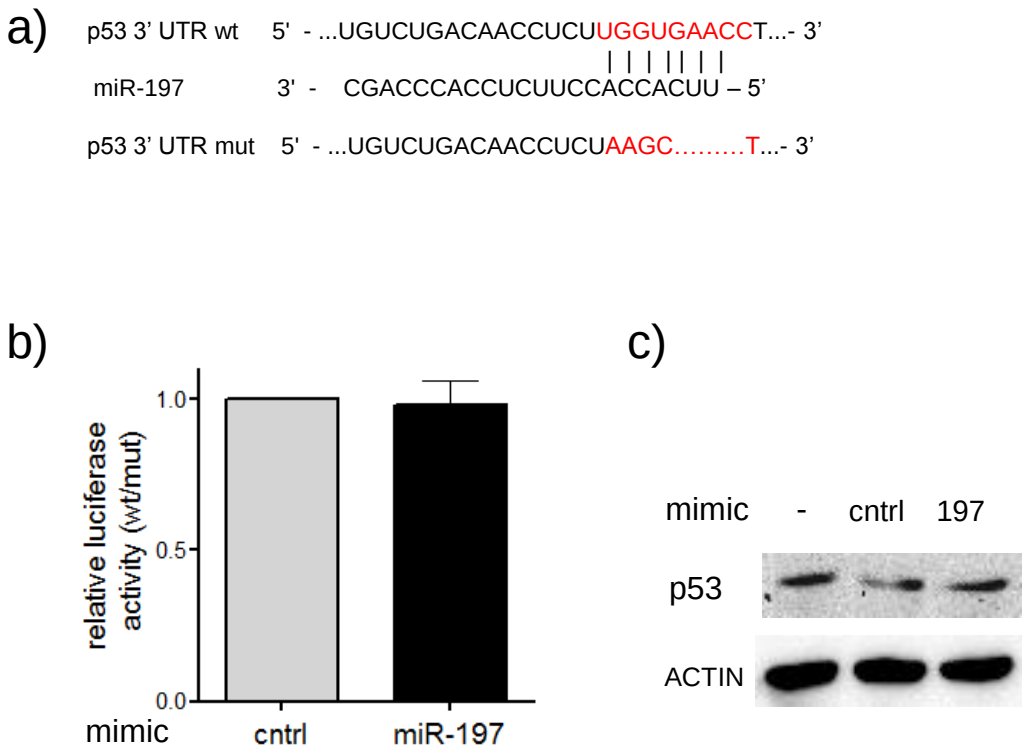


***Figure* S5-** *p53 is not a direct target of miR-197* - **a)** Predicted p53 3' UTR binding site for miR-197. The alignment of the seed region of miR-197 with p53 3' UTR is shown. The sites of target mutagenesis are indicated in red. **b)** Luciferase activity in NIH-H460 cells transfected with p53 UTR wt or mut in combination with a control or LNA-197. The ratio of normalized luciferase activity in cells transfected with p53 UTR wt versus mut is indicated - Mean ± s.e.m. **c)** Western blot showing p53 protein in NIH-H460 cells treated with a control or with miR-197 mimic. ACTIN was used as loading control.

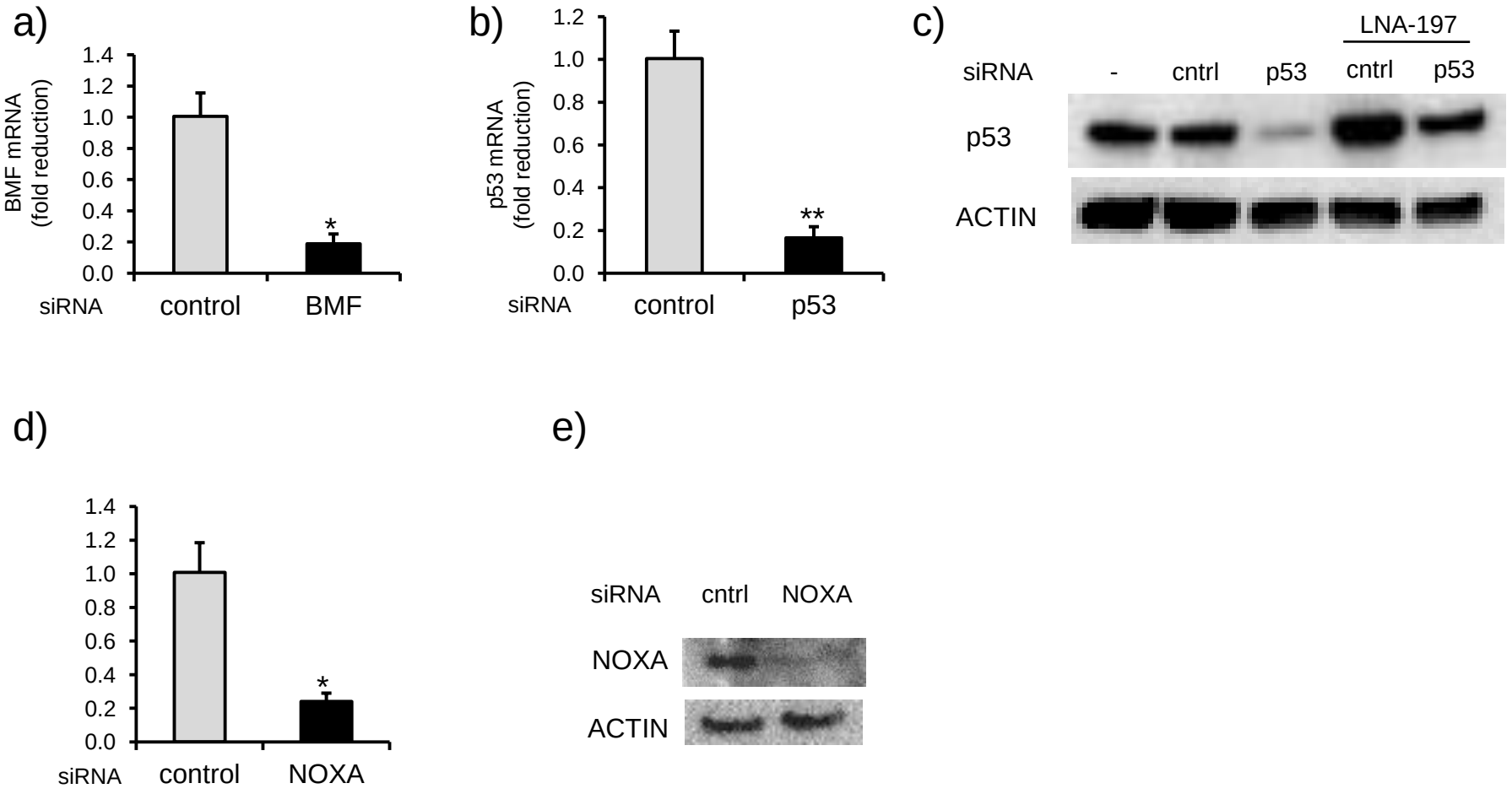


***Figure* S6-** *siRNAs validation* - **a)** BMF mRNA levels were evaluated by q-RT-PCR 48 hours after siRNA transfection. **b-c)** Q-RT-PCR and Western blotting showing p53 down-modulation in NIH-H460 cells treated with a control or anti p53 siRNA (Qiagen). Double transfection of anti p53 siRNA together with LNA-197 restores p53 levels of control cells, counteracting LNA-mediated p53 induction. **d-e)** Q-RT-PCR and Western blotting showing NOXA down-modulation in NIH-H460 cells treated with a control or anti NOXA siRNA (Qiagen). GAPDH was used for PCR normalization; ACTIN was used as protein loading control.

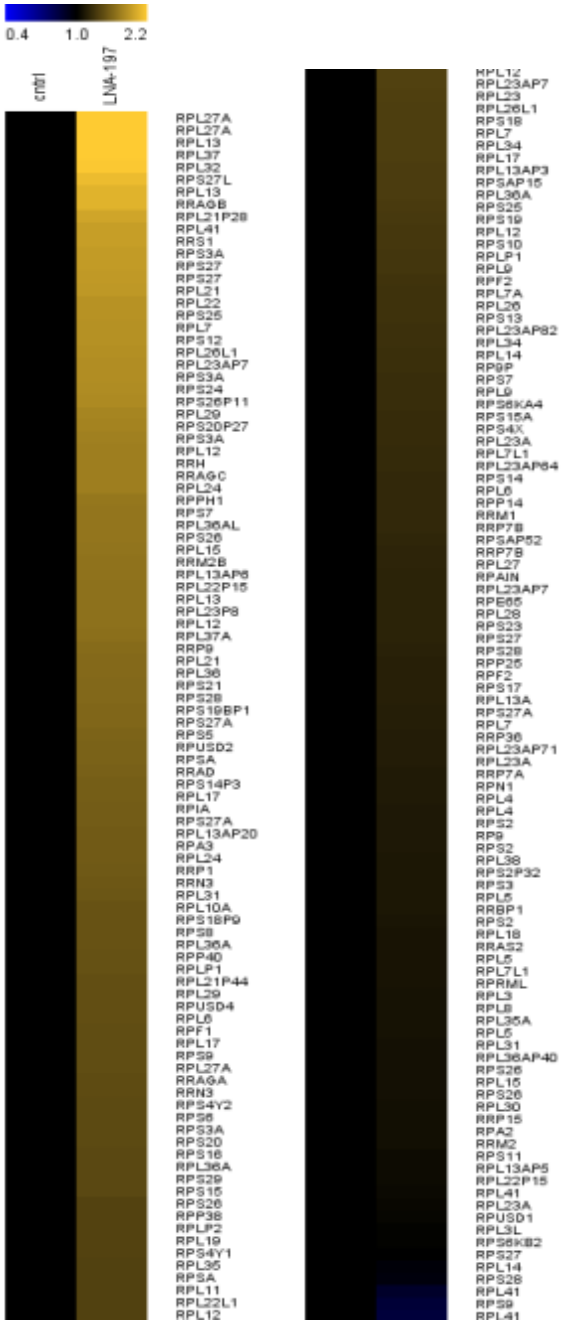


***Figure* S7-** Heatmap showing global up-regulation of ribosomal components in NIH-H460 cells transfected with LNA-197, as observed by gene array analysis.