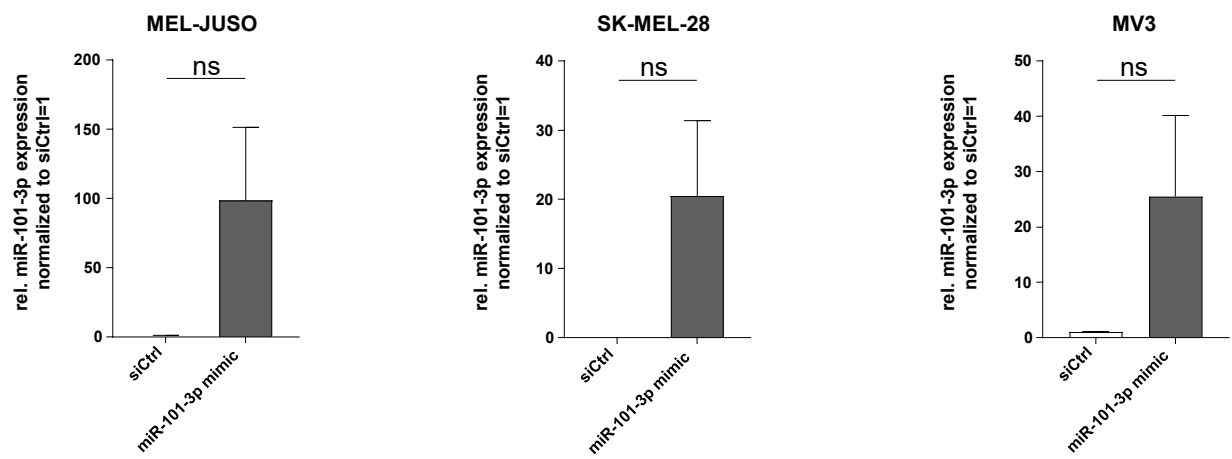
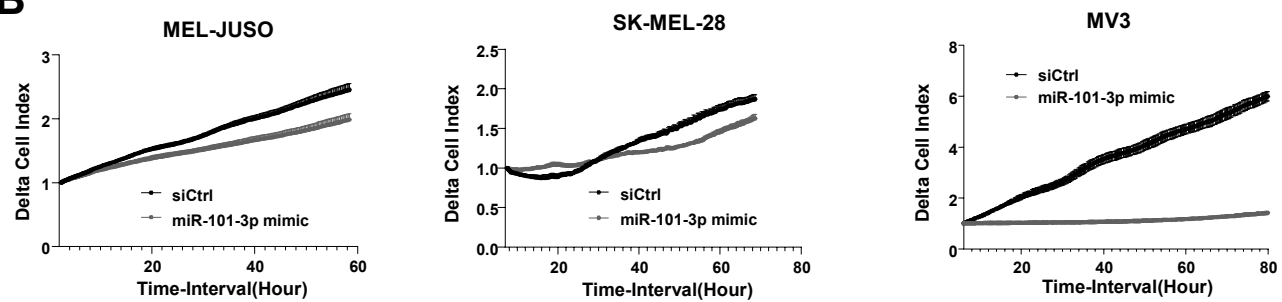


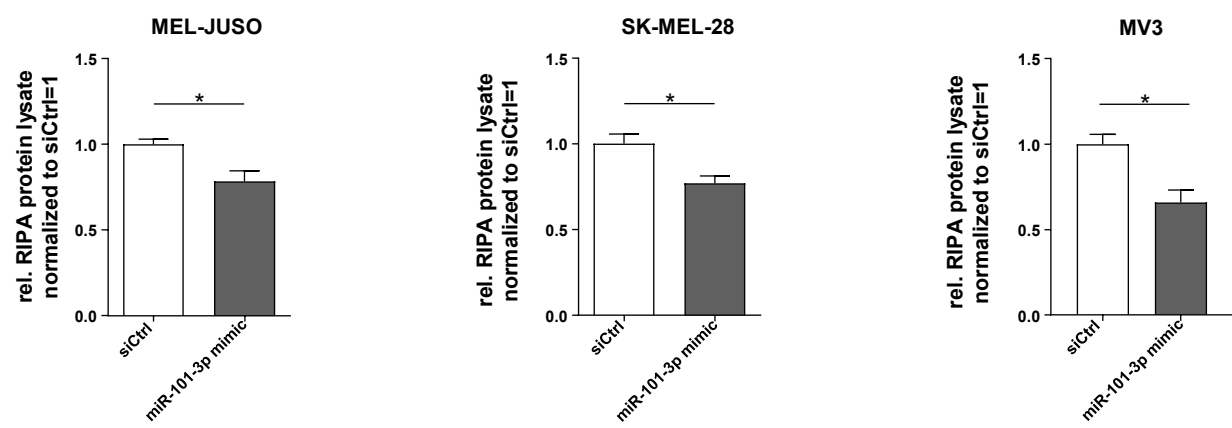
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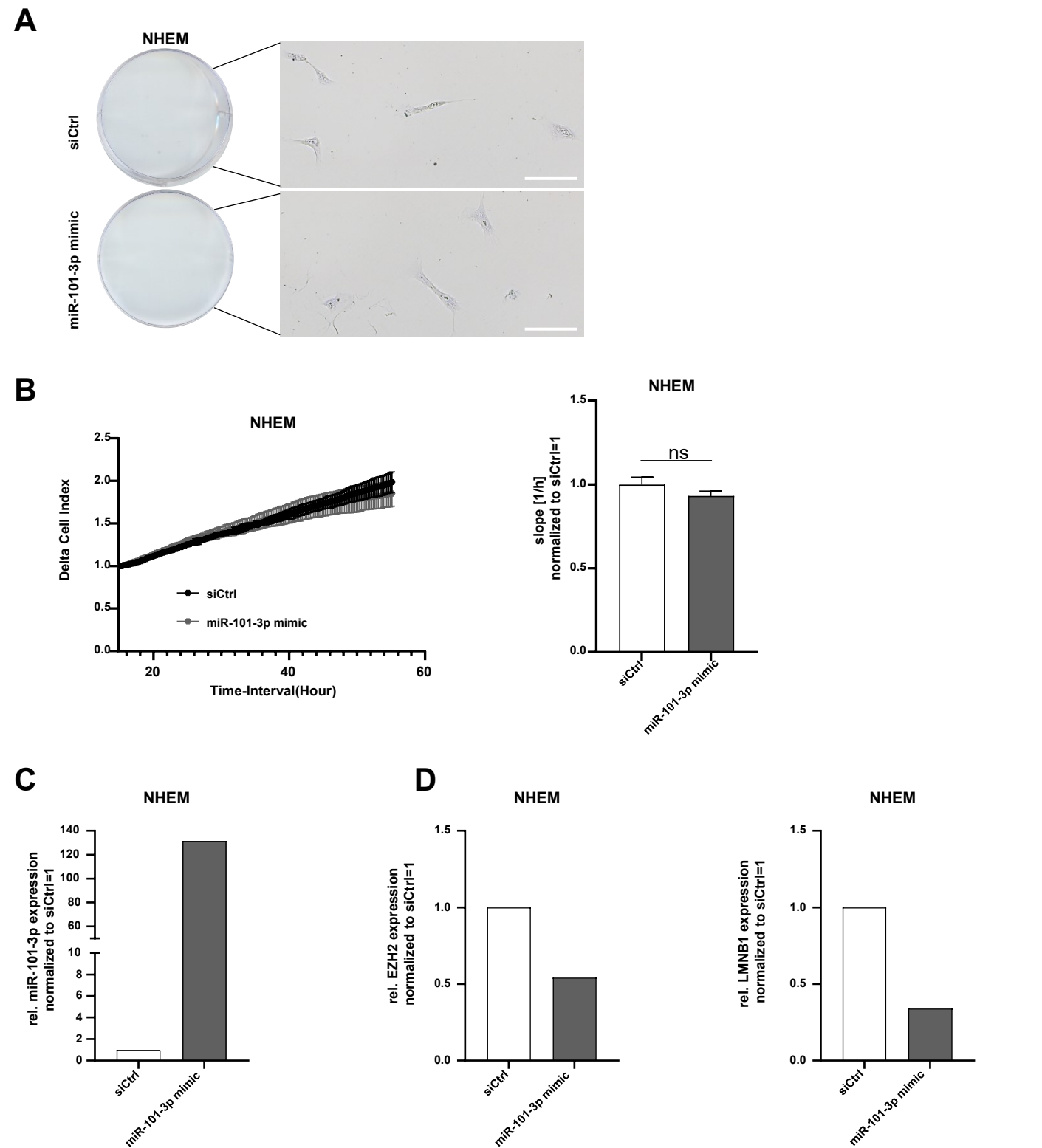
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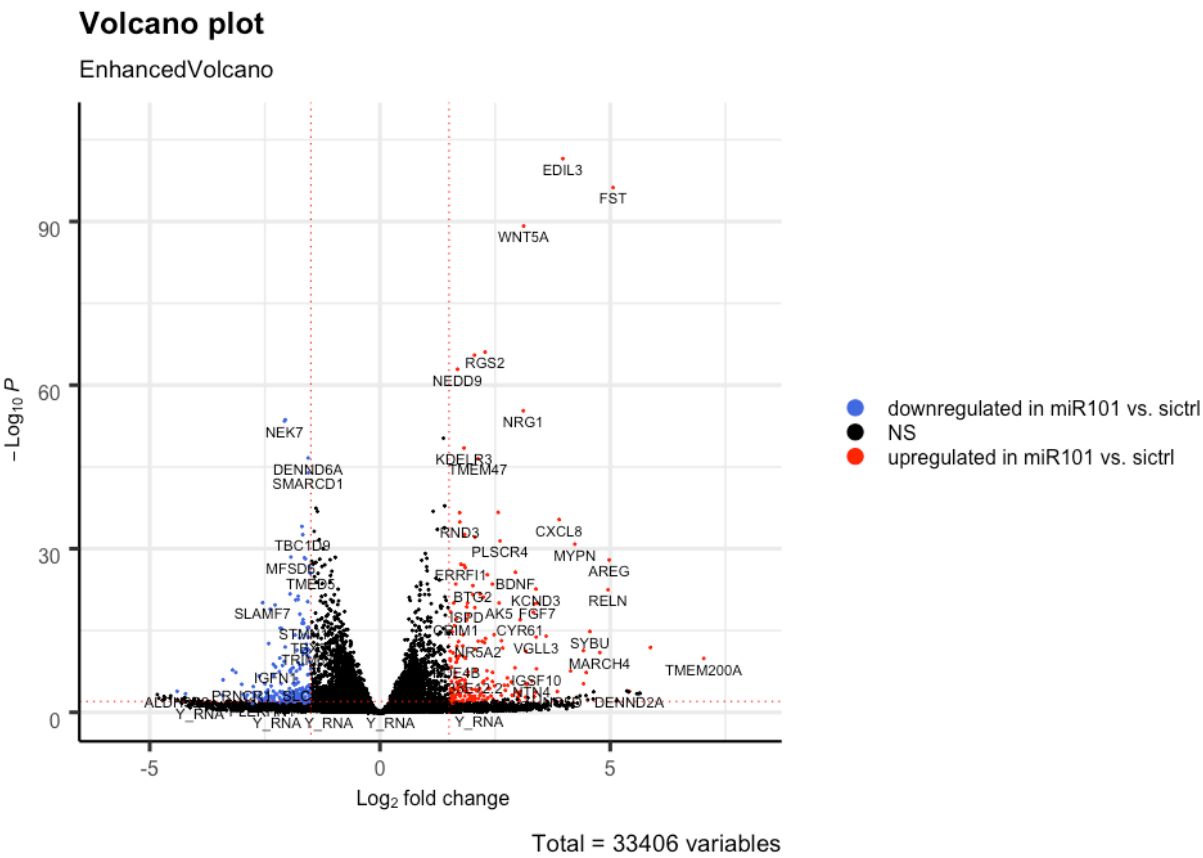
C



SupplFigure 1: (A) Quantitative real-time PCR analysis of miRNA expression of miR-101-3p in MEL-JUSO, SK-MEL-28 and MV3 after miR-101-3p mimic transfection compared to siCtrl (72 h) (Student's *t*-test). (B) Proliferation Curves of real time cell analysis in dependency of impedance measurement of MEL-JUSO, SK-MEL-28 and MV3 treated with miR-101-3p Mimic (72 h) and respective siCtrl (Student's *t*-test). (C) Total protein lysate after RIPA of MEL-JUSO, SK-MEL-28 and MV3 transfected with miR-101-3p mimic and siCtrl (72 h) (Student's *t*-test). Bars represent the means ± SEM (* = $p \leq 0.05$, ns = not significant).

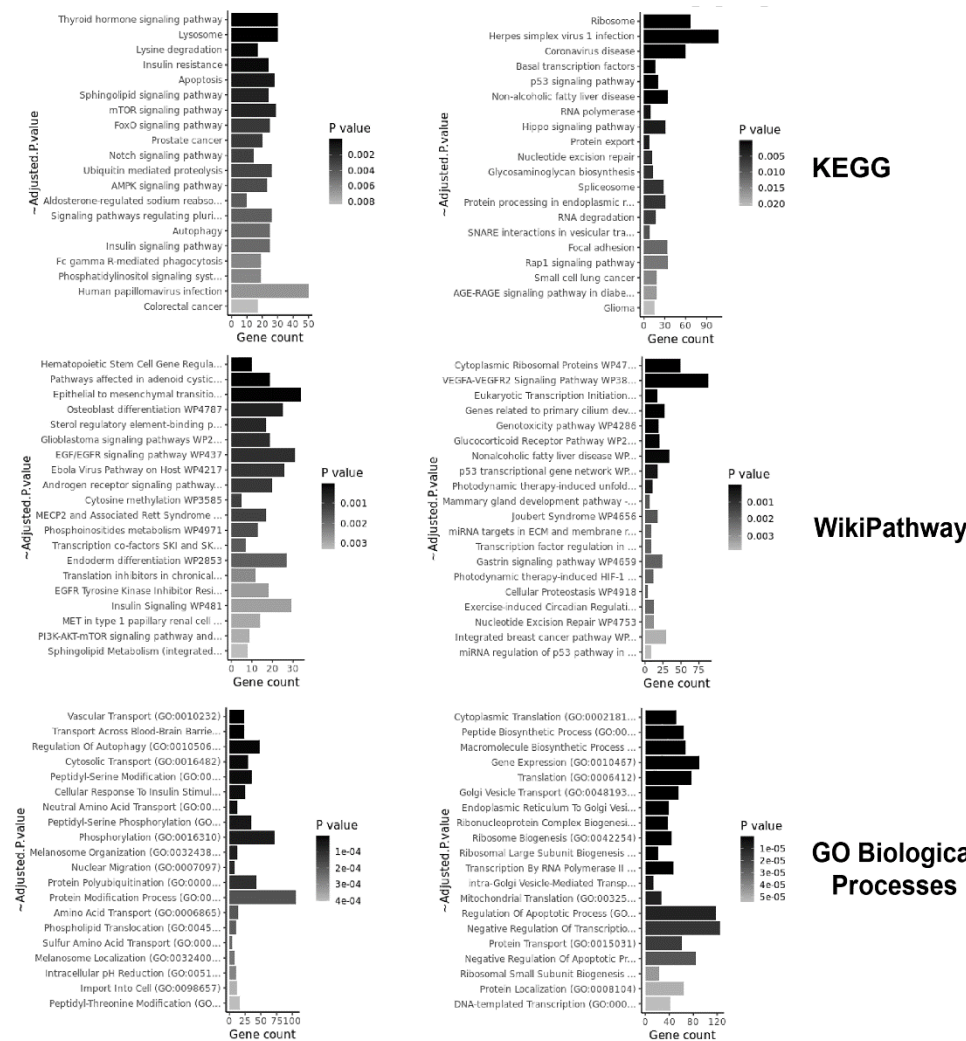


SupplFigure 2: (A) Clonogenic assay with NHEM treated with miR-101-3p mimic (18 h) and respective siCtrl (n=1). Representative images of NHEM stained with crystal violet, treated with miR-101-3p mimic and siCtrl. Scale bars equal 100 μ m. (B) Proliferation Curves of real time cell analysis in dependency of impedance measurement of NHEM treated with miR-101-3p Mimic (18 h) and respective siCtrl (n=1,) (Student's *t*-test). (C) Quantitative real-time PCR analysis of miRNA expression of miR-101-3p in NHEM after miR-101-3p mimic transfection compared to siCtrl (18 h, n=1). (D) Quantitative real-time PCR analysis of RNA expression of EZH2 and LMNB1 in NHEM after miR-101-3p mimic transfection compared to siCtrl (18 h, n=1).

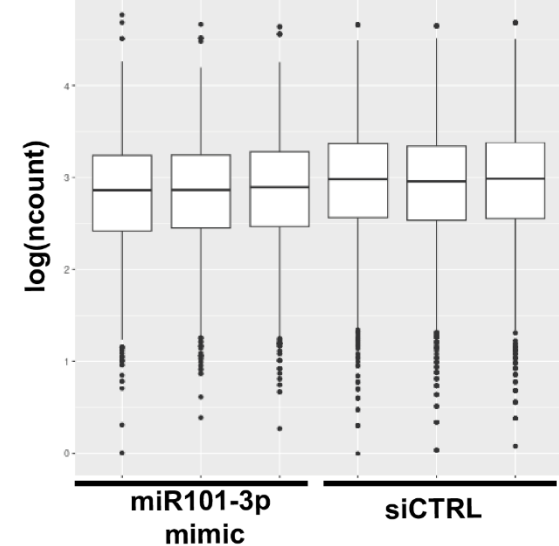


SupplFigure 3: Volcano Plot of differentially expressed genes in miR-101-3p mimic transfected cells compared to siCtrl-transfected cells analyzed by RNA-Seq. Significantly ($p\text{-value} < 0.1$) and strongly ($\log_2$ FoldChange > 1.5 or < -1.5 respectively) upregulated genes are marked in red and downregulated genes in blue.

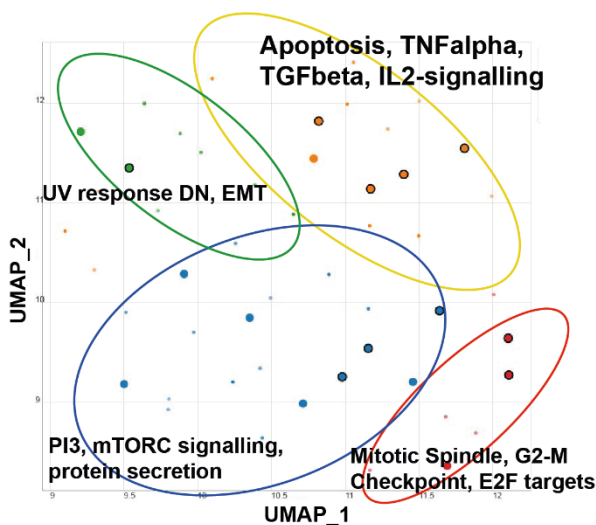
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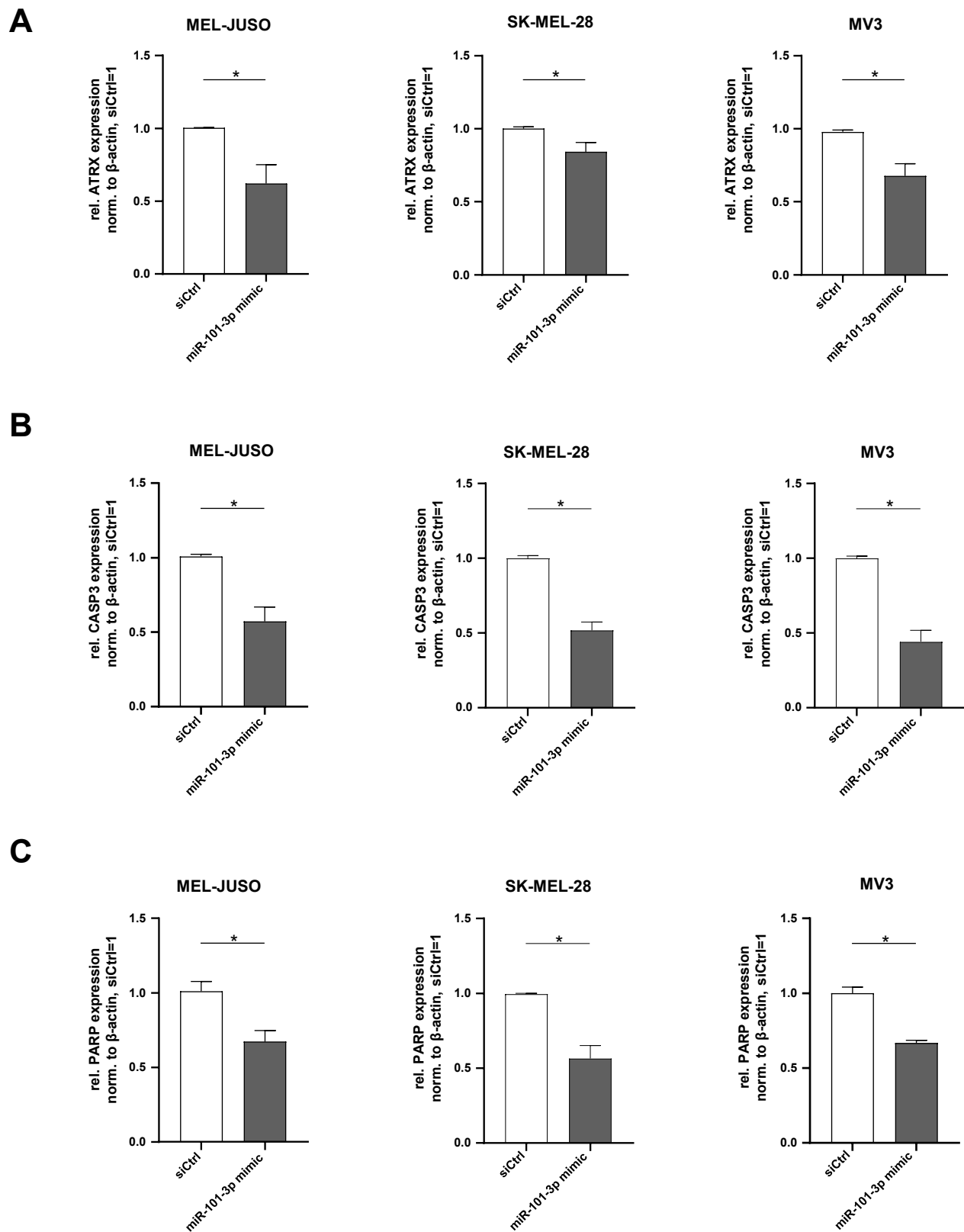
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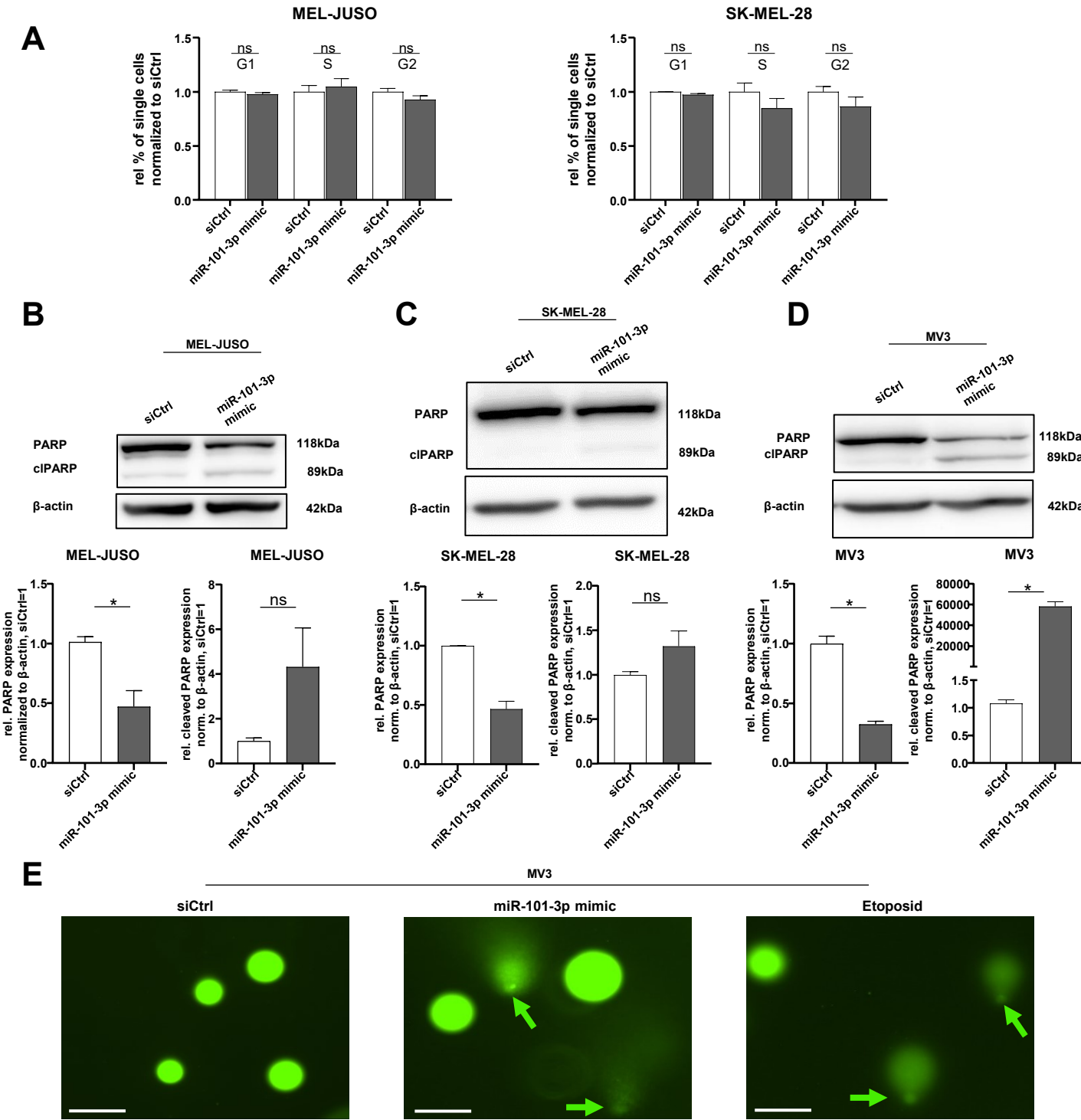


SupplFigure 4: (A) EnrichR analysis of significant regulated genes after miR-101-3p transfection by using different bioinformatical databases: KEGG, WikiPathway, GO Biological Processes (genes with padj < 0.1). **(B)** Distribution of log(norm counts) of the expressed genes in miR-101-3p mimic and siCtrl, determining that miR-101-3p target genes show lower expression overall in mimic transfected cells compared to siCtrl. **(C)** Enriched hallmark gene sets which cluster in 4 clusters based on the overrepresentation analysis of significantly downregulated miR-101-3p target genes via EnrichR against expressed genes of the RNA-Seq.



SupplFigure 5: (A, B, C) qRT-PCR analysis of potential target genes ATRX, CASP3 and PARP determined by EnrichR analysis using clustergram (Overlap of 40 enriched miR101-3p target genes within the top 20 overrepresented gene sets) (Student's *t*-test). Bars represent the means $\pm$ SEM (* = $p \leq 0.05$, ns = not significant).

SupplFig6



SupplFigure 6: (A) Flow cytometry with the fluorescent dye propidium iodide for cell cycle staining of G1, S and G2 phase. MEL-JUSO and SK-MEL-28 transfected with miR-101-3p mimic (72 h) and siCtrl respectively (two-way ANOVA and subsequent Fisher's LSD multiple comparison test). (B, C, D) Western blot analysis of full-length PARP and cleaved PARP following treatment 72 h with miR-101-3p mimic and siCtrl in MEL-JUSO,SK-MEL-28 and MV3 using β - actin as housekeeper. Representative images of PARP Western blots in MEL-JUSO, SK-MEL-28 and MV3 (Student's *t*-test). (E) Representative Comet-Assay images from fluorescence microscopy at 10x magnification showing the fragmented DNA migration from the nucleoid body which forms a comet tail in MV3 transfected with miR-101-3p mimic (72h) and siCtrl. The cytostatic etoposide was used as positive control respectively. Bars represent the means $\pm$ SEM (* = $p \leq 0.05$, ns = not significant).