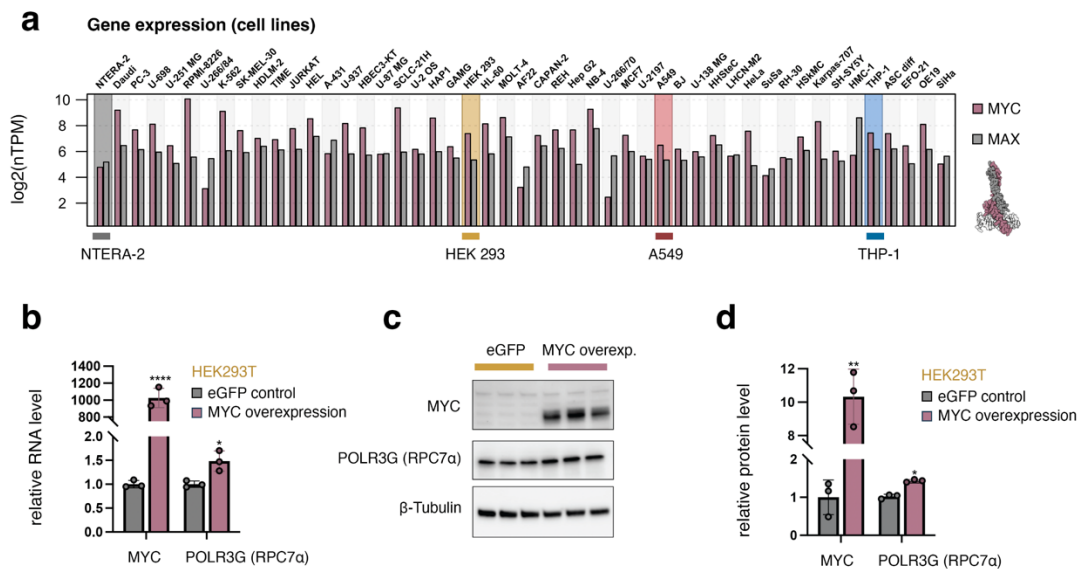
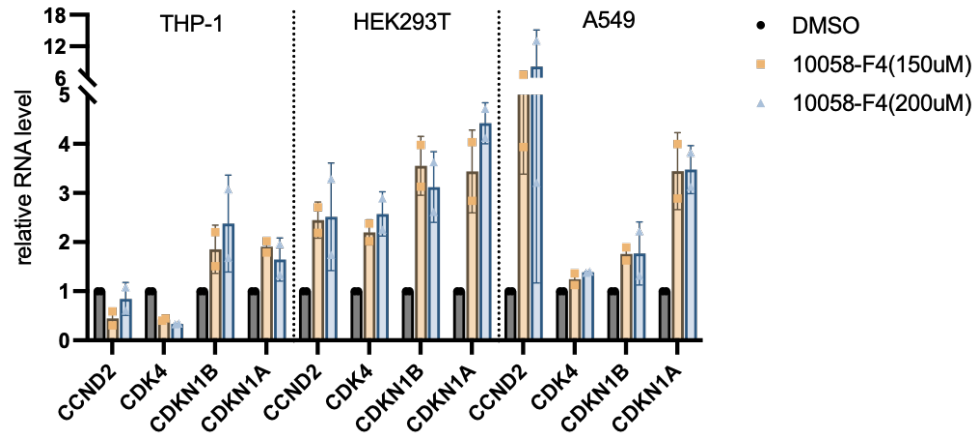


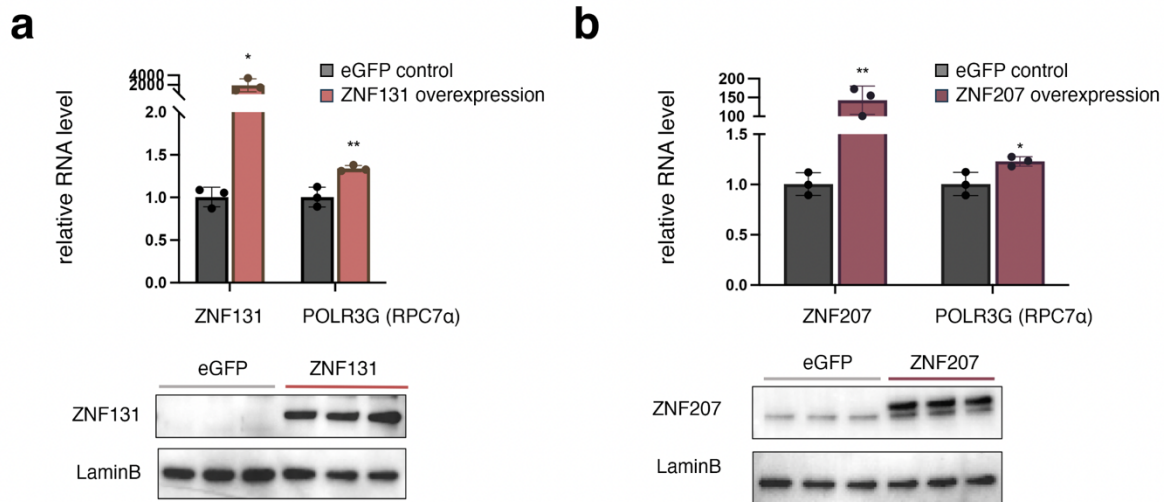
Supplemental Figure S3. A survey of *POLR3G* expression and *RPC7α* abundance across cell lines. **(a)** *POLR3G* and *POLR3GL* gene expression profiles across ~50 human cell lines (nTPM = normalized transcript per million; proteinatlas.org). Highlighted cell lines (NTERA-2, HEK293, A549, THP-1) relevant to cell lines in following *in vitro* experiments. **(b)** RT-qPCR analysis of *POLR3G* mRNA levels in H1-hESC, HEK293T, A549, and THP-1 cells. **(c, d)** Immunoblots and quantification of *RPC7α* (*POLR3G*), LaminB, and β -tubulin protein levels in H1-hESC, HEK293T, A549, and THP-1 cells. Protein abundances were calculated by normalizing to the average intensity of reference protein Lamin B2, β -tubulin and total protein.



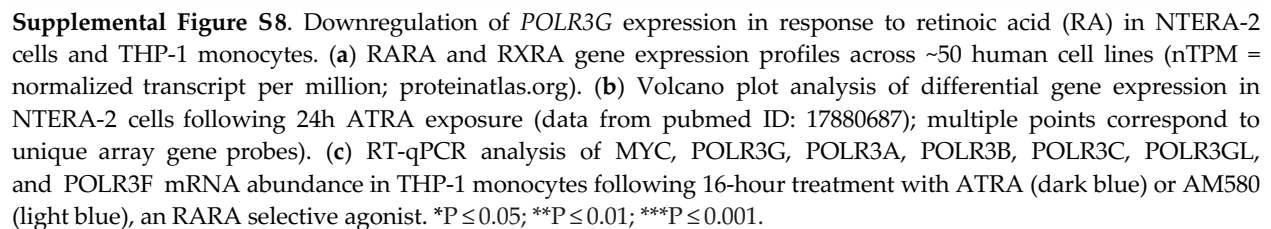
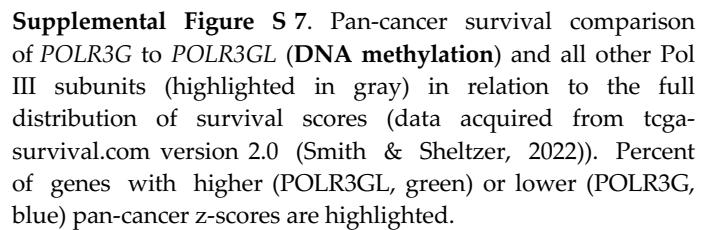
Supplemental Figure S4. Overexpression of MYC in HEK293T increases *POLR3G* expression and *RPC7α* abundance. **(a)** MYC and MAX gene expression profiles across ~50 human cell lines (nTPM = normalized transcript per million; proteinatlas.org). **(b)** RT-qPCR analysis of MYC and *POLR3G* mRNA levels in HEK293T following overexpression of MYC (pcDNA3.1) compared to GFP (pcDNA3.1; control). **(c, d)** Immunoblots and quantification of MYC and *RPC7α* (*POLR3G*) protein levels in HEK293T following overexpression of MYC (pcDNA3.1) compared to GFP (pcDNA3.1; control). * $P \leq 0.05$; ** $P \leq 0.01$; *** $P \leq 0.0001$.

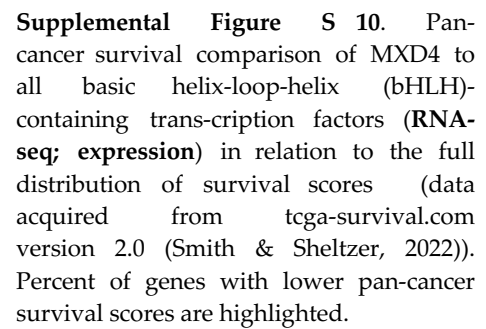


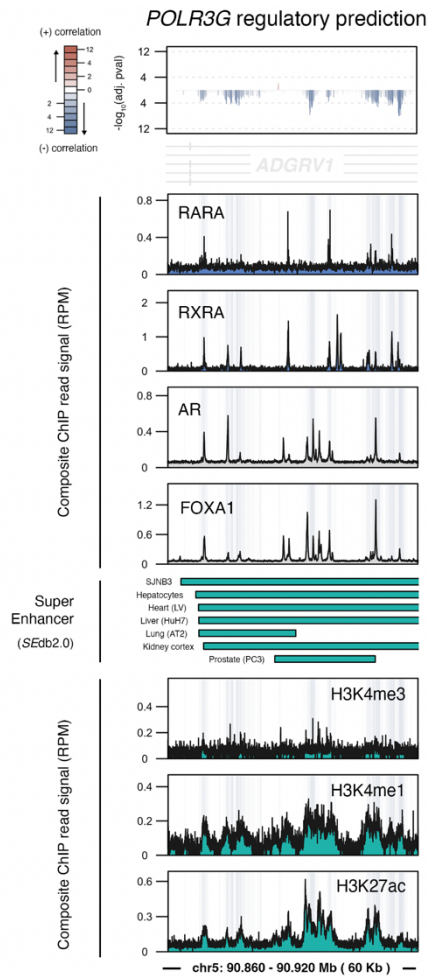
Supplemental Figure S5. MYC/MAX dimerization inhibitor 10058-F4 disrupts canonical MYC target genes in THP-1 monocytes, however alternate patterns are observed in HEK293T and A549. RT-qPCR analysis of canonical MYC target genes (CCND2 and CDK4) and genes negatively regulated by MYC (CDKN1A, CDKN1B) following exposure to 10058-F4 (150uM, orange; 200 uM; blue), compared with DMSO control (gray). CCND2 and CDK4 are downregulated following MYC/MAX dimerization in THP-1; this canonical effect is not observed in HEK293T and A549 cell lines.



Supplemental Figure S6. Overexpression of Zinc finger proteins ZNF131 and ZNF207 increase *POLR3G* mRNA abundance in HEK293T cells. (a) RT-qPCR analysis of ZNF131 and *POLR3G* mRNA abundance in HEK293T cells overexpressing ZNF131 (pcDNA3.1) compared with eGFP (pcDNA3.1; control). Bottom: immunoblot validation of ZNF131 overexpression. (b) RT-qPCR analysis of ZNF207 and *POLR3G* mRNA abundance in HEK293T cells overexpressing ZNF207 (pcDNA3.1) compared with eGFP (pcDNA3.1; control). Bottom: immunoblot validation of ZNF207 overexpression. * $P \leq 0.05$; ** $P \leq 0.01$.

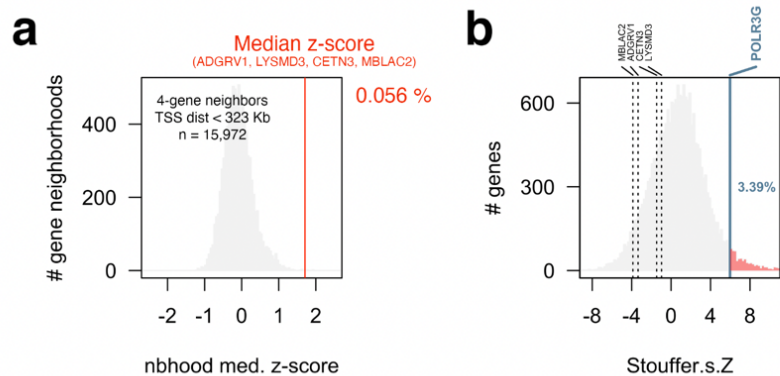




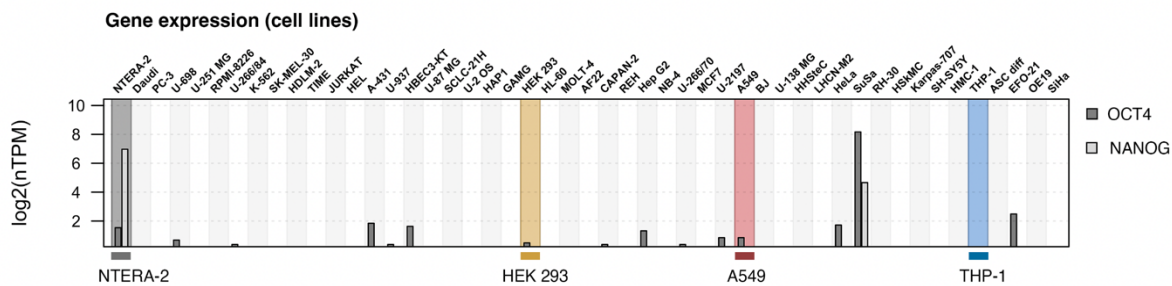
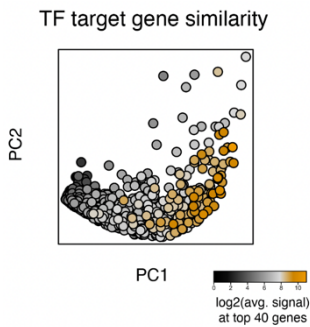


Supplemental Figure S11. Examination of the strongest negative chromatin correlates with *POLR3G* expression in cancer (top). ChIP-seq profiles for overlapping factors, including RARA, RXRA, Androgen Receptor (AR), FOXA1, histone marks (H3K4me3, H3K4me1, H3K27ac), and annotated super enhancers (SEdb2.0).

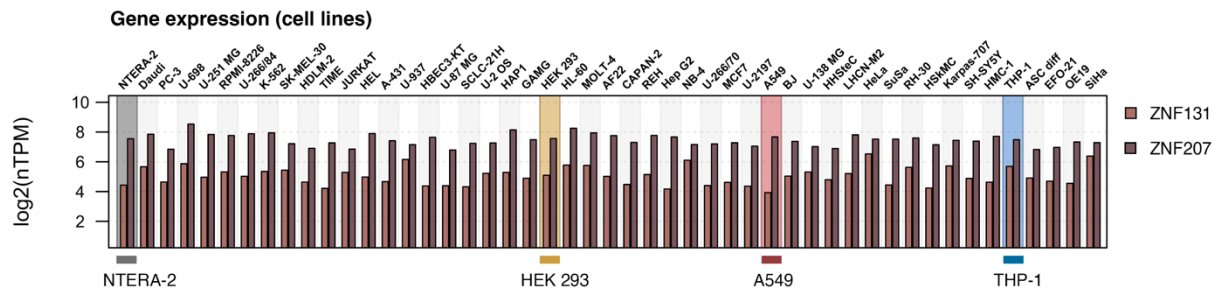
Supplemental Figure S 12. *POLR3G* neighboring genes, *CETN3*, *MBLAC2*, *LYSMD3*, and *ADGRV1*, correlate with *POLR3G* expression in cancer. (a) Distribution of median z-scores for 4-gene sets with maximum TSS distance equivalent to *CETN3*, *MBLAC2*, *LYSMD3*, and *ADGRV1*. (b) Pan-cancer survival comparison of *POLR3G* with neighboring genes, *CETN3*, *MBLAC2*, *LYSMD3*, and *ADGRV1*. (data acquired from tcga-survival.com version 2.0 (Smith & Sheltzer, 2022)).



Supplemental Figure S13. Visualization of transcription factor gene set similarity, as defined by the presence or absence at the promoter (+/- 1 Kb) of 19,022 target genes. Color represents the average ChIP-signal across the top 40 (top 1 bin) genes with highest similarity to *POLR3G*.



Supplemental Figure S14. Expression of Pluripotency factors OCT4 and NANOG is largely restricted to a limited number of cell lines. OCT4 and NANOG gene expression profiles across ~50 human cell lines (nTPM = normalized transcript per million; proteinatlas.org).



Supplemental Figure S15. Expression of pluripotency-related Zinc finger proteins ZNF131 and ZNF207 is generally ubiquitous across most cell lines. ZNF131 and ZNF207 gene expression profiles across ~50 human cell lines (nTPM = normalized transcript per million; proteinatlas.org).