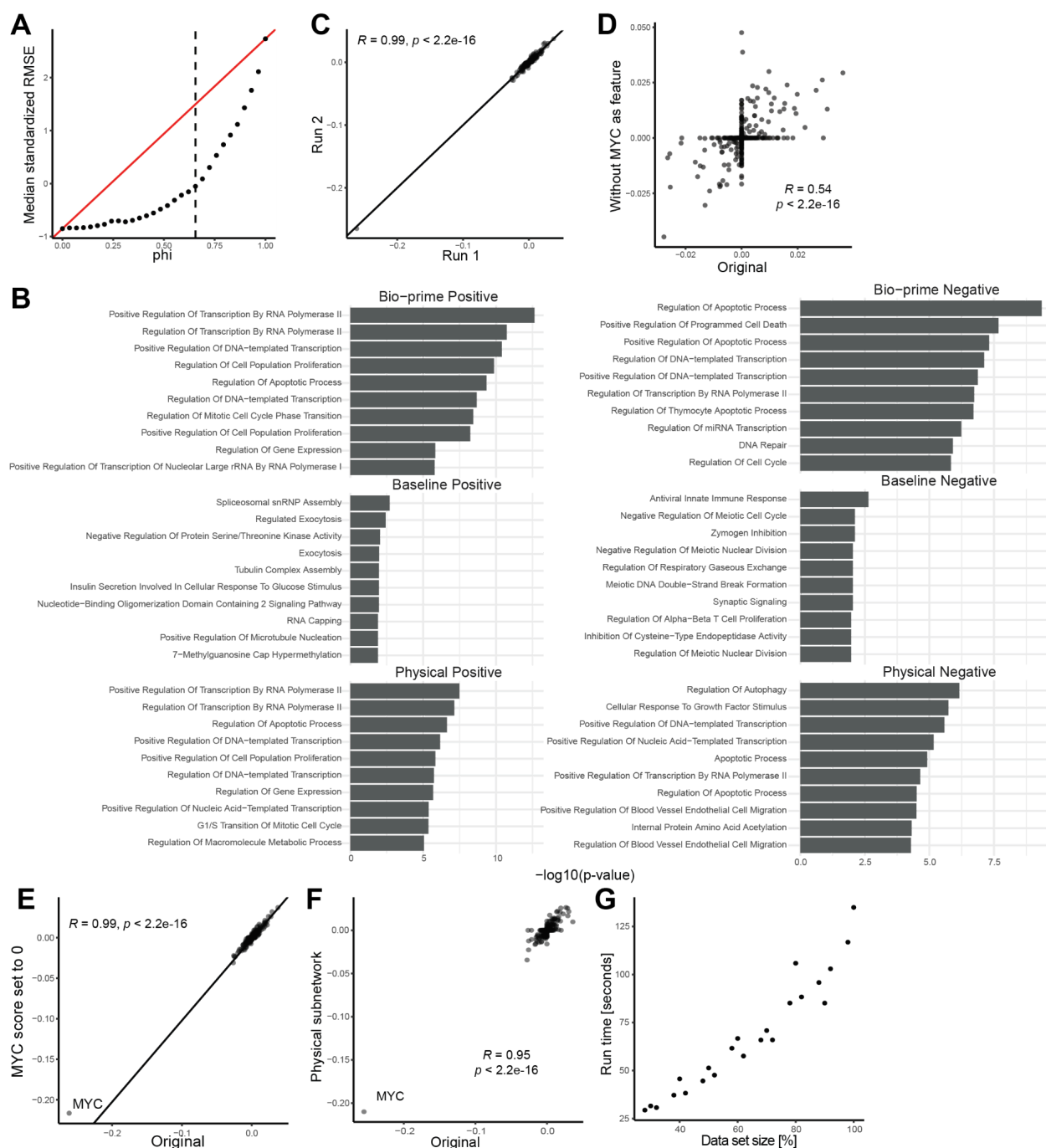
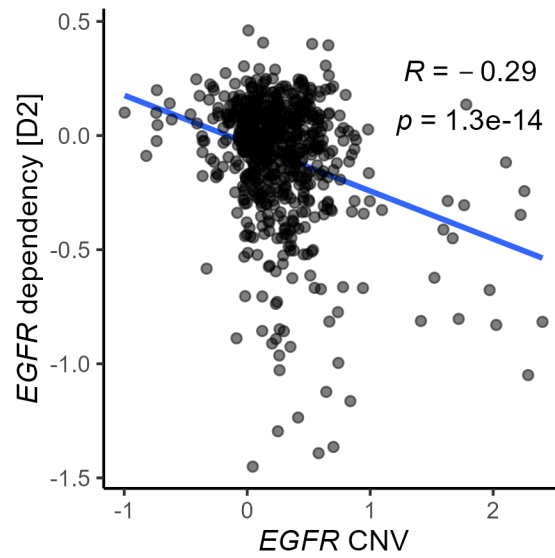


Supplementary Table 1. Results from systematic prediction of copy number biomarkers for 431 highly selective dependencies. Columns in table list the target gene dependency, the CNV biomarker, the biomarker's chromosome, the biomarker's start position on the chromosome, the correlation between the biomarker and target dependency, and the resulting beta coefficients for the baseline and bio-primed LASSO.

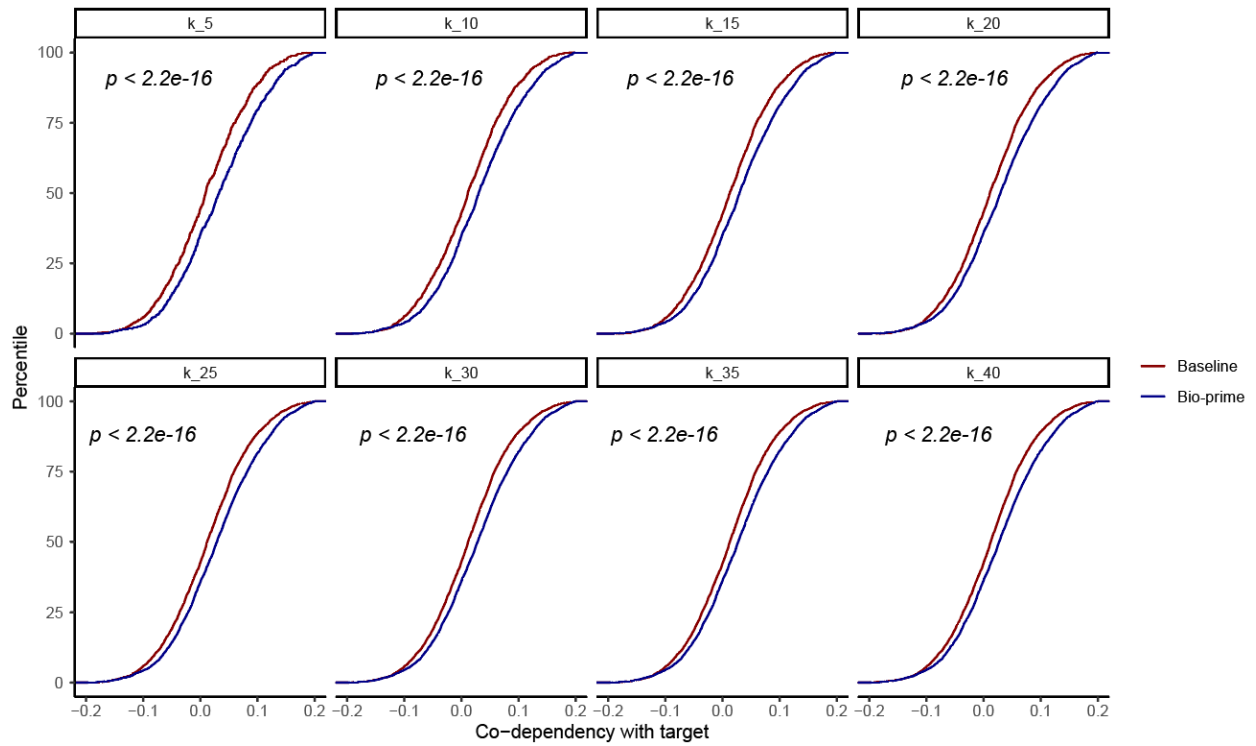


Supplementary Figure 1. Repeatability, performance, and robustness to noise. **A)** Scatter plot shows the median standardized root mean squared error (y-axis) across a range of Φ values (x-axis). Vertical dashed line represents the inflection point, identified as the optimal Φ . **B)** Barplots show the $-\log_{10}(p\text{-value})$ (x-axis) of enriched terms (y-axis) across genes exclusively identified in various models. First and second columns contain the enrichment results for genes with positive and negative coefficients. Rows correspond to genes exclusively identified in the following models from top to bottom: bio-prime, baseline and bio-prime restricted to physical

interaction subnetwork. **C)** Scatter plot shows high correlation between bio-prime coefficients derived from two independent runs. **D)** Scatter plot shows high correlation between bio-prime coefficients derived from the original model (x-axis) and the model without *MYC* RNA in the input features (y-axis). **E)** Scatter plot shows high correlation between bio-prime coefficients derived from the original model (x-axis) and the model where interaction score for *MYC* RNA was set to zero (y-axis). **F)** Scatter plot shows high correlation between bio-prime coefficients derived from the original model (x-axis) and the model restricted to physical interaction subnetwork (y-axis). **G)** Scatter plot shows the runtime (y-axis) across multiple models run with varying sample size (x-axis).



Supplementary Figure 2. Scatter plot with associated Pearson correlation coefficient and p-value shows *EGFR* log2 transformed CN (x-axis) and *EGFR* dependency (y-axis).



Supplementary Figure 3. Empirical cumulative density plot shows increased co-dependency between target gene and biomarkers derived from the bio-primed (blue) compared to the baseline (red) models across range of top k values.