## Figure Legend

**Figure 1**

Schematic of the EN-CODEC resource. The pink box summarizes data in top-tier cell lines associated our cancer associated encyclopedia and the yellow box demonstrates the focus of the main encyclopedia. Our resource includes both generalized (blue) and cell type (green) specific analyses.

**Figure 2**

BMR modeling and burden analysis. (A) improvement of BMR estimation by including multiple genomic features; (B) coefficient of remaining features after MCF-7 replicating timing is selected in breast cancer; (C) significantly burdened genes using coding regions, TSS, and extended genes; (D) expression of BCL6 is correlated with patient survival.

**Figure 3**

Integrate ENCODE networks with expression profiles from cancer patients. (A) heatmap of regulatory power for TF/RBPs to drive tumor-to-normal differential expression in multiple cancer types; (B) activity of MYC targets is associated with patient survival in breast cancer and target vs. non-target gene expression after MYC knockdown in MCF-7; (C) investigation of how MYC work with other TFs using TF network; (D) activity of SUB1 targets is associated with patient survival in lung cancer and target vs. non target gene expression after MYC knockdown in HepG2

**Figure 4**

Network hierarchy analyses of (A) generalized network. TFs in at top layers are enriched with cancer associated genes and demonstrate higher gene regulation power (B) cell type specific network. Rewiring of top layer TFs more significantly drives tumor-to-normal differential expression and bottom layer TFs are more often associated with burdened binding sites

**Figure 5**

Network rewiring analysis. (A) rewiring index of cell type specific network; (B) example of network rewiring; (C) genomic features associated with rewiring

**Figure 6**

(A) Schematic for stepwise prioritization scheme; (B) small scale validation results from luciferase assay; (C) an example for multiscale integrative analysis on sample 5