

**Supplementary Table 1. The iMYC signature.** Gene symbol and Entrez Gene ID of each gene in the iMYC signature is listed. Expression level and p-value of each result, categorized by iMYC cell line, are shown.

**Supplementary Table 2. Hypergeometric p-values of overlap among the iMYC gene sets.** The p-values show that overlap of any two iMYC signatures using the third iMYC signature as background is greater than expected by chance for both upregulated and down-regulated gene sets. The p-values also show that overlap of all three iMYC signatures is greater than expected by chance for both upregulated and down-regulated gene sets.

**Supplementary Figure 1. Major canonical network enrichment identified by Ingenuity Pathway Analysis among the down-regulated genes of the iMYC signature.** The p-value of the enrichment is indicated.

**Supplementary Figure 2. TGF $\beta$  pathway genes that are down-regulated in iMYC cells do not show similar expression pattern in another immortalized cell line.** Real-time quantitative PCR (qPCR) analysis of genes in the iMYC signature that are involved in TGF $\beta$  signaling, performed on normal HFFs, eMYC, a third iMYC line, and HFFs immortalized by hTERT (HFF-fhTERT). Results from analysis of iMYC 3 show that these genes are also down-regulated, relative to expression levels in eMYC, in a third iMYC cell line. In contrast, most of these genes are unchanged in HFFs and HFF-fhTERT cells, indicating that down-regulation of these genes is specific to iMYC and not a characteristic shared by human cells immortalized by a gene other than c-MYC.

Expression levels are normalized to GAPDH and shown relative to expression levels of eMYC cells set as “1.”



