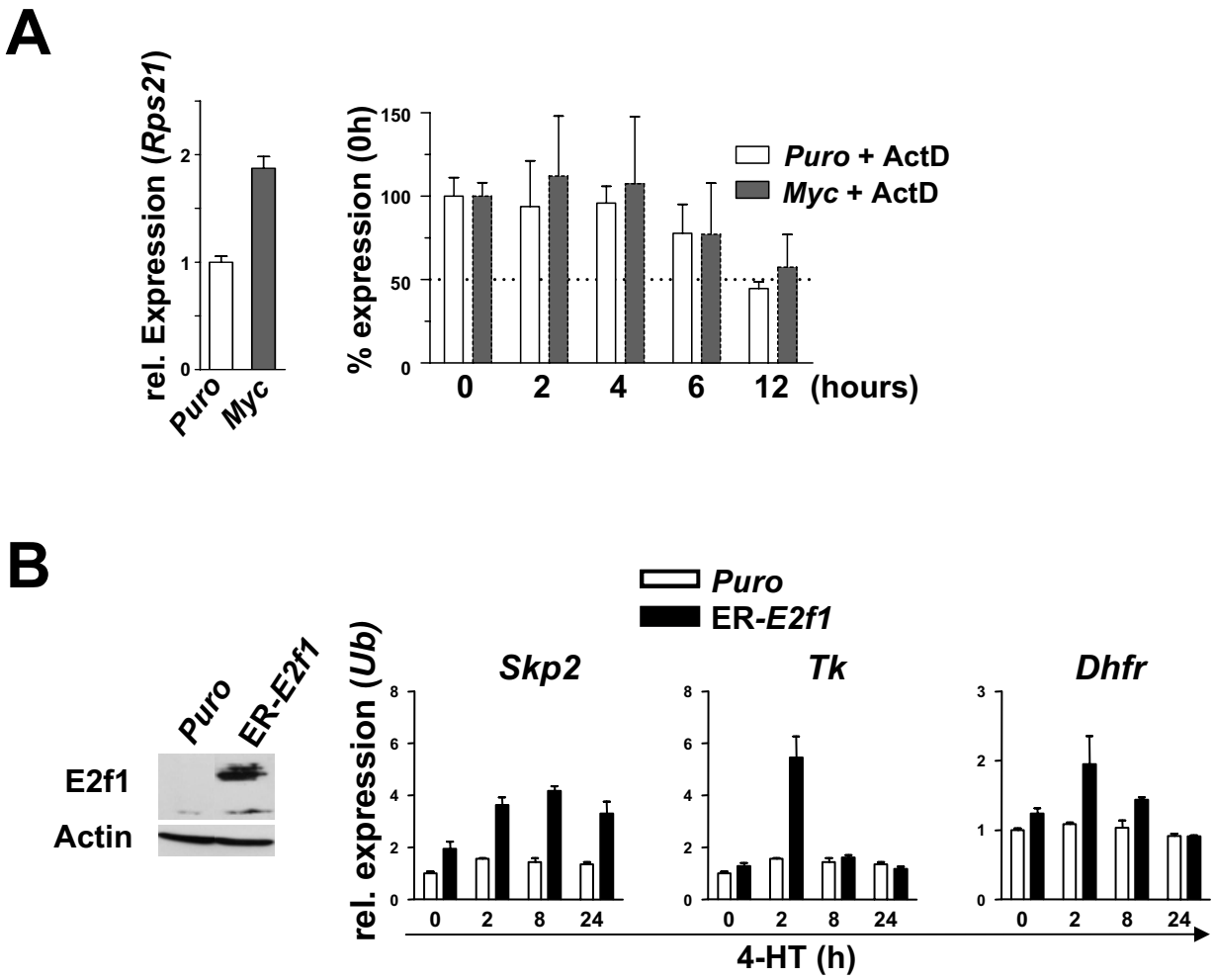
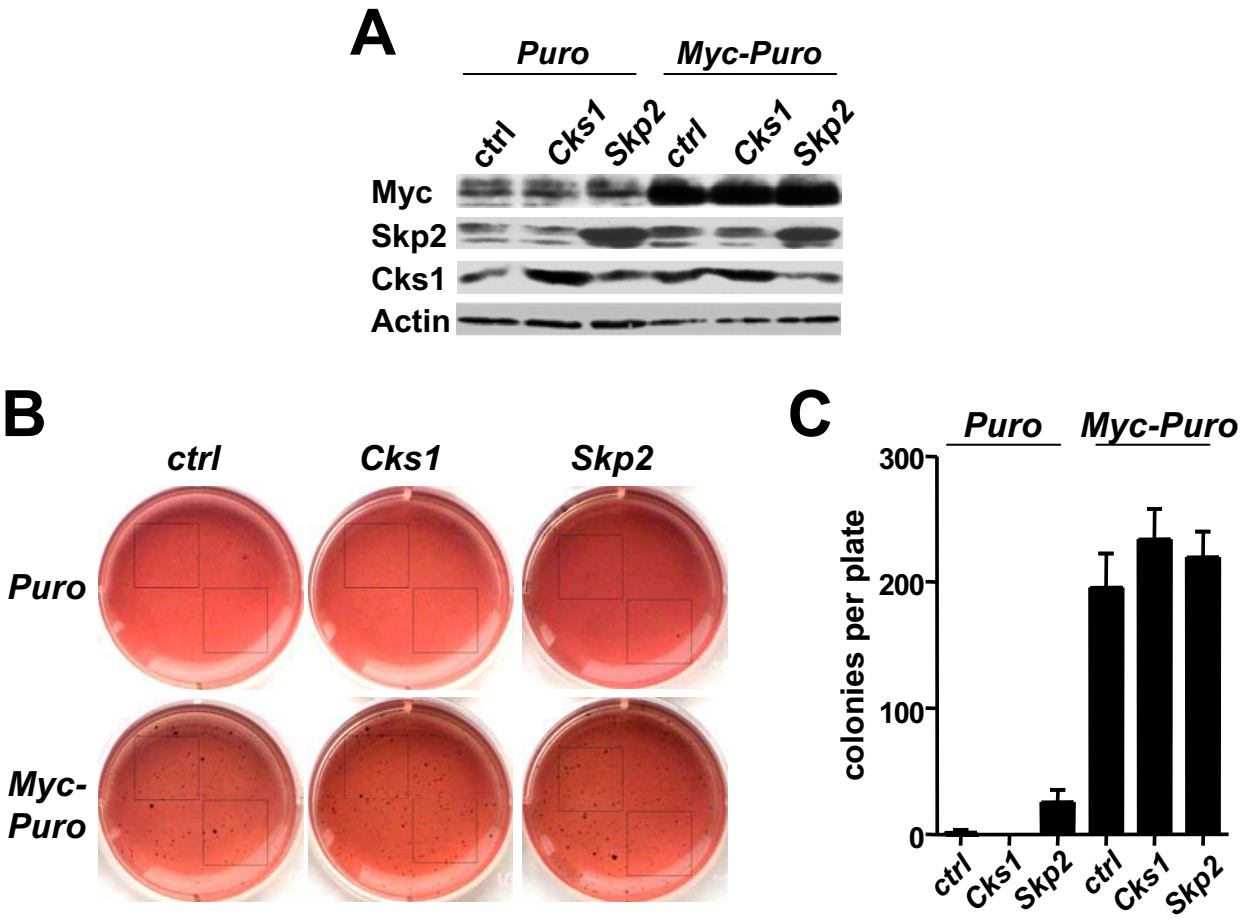
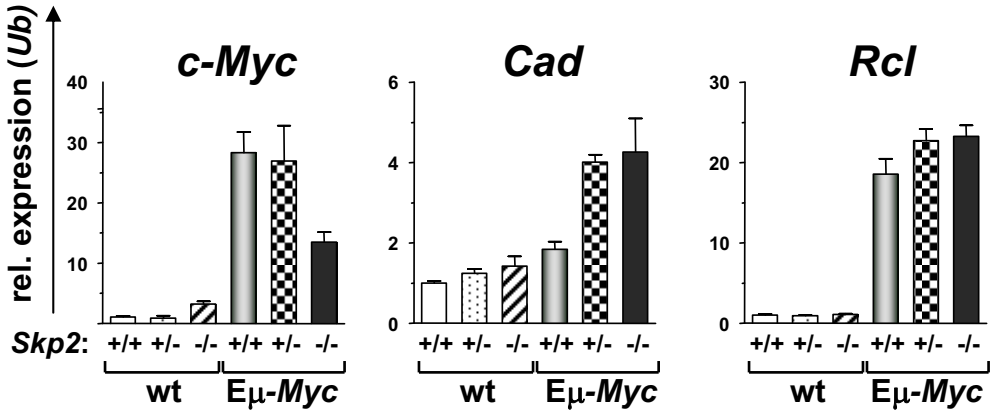
Supplemental Figure S1, Old *et al*.



Supplemental Figure S2, Old *et al*.



Supplemental Figure S3, Old *et al*.



SUPPLEMENTARY FIGURE S1. E2f1 induces *Skp2*. **A.** Primary early passage MEFs were infected with MSCV-IRES-Puro (*Puro*) or MSCV-*Myc*-IRES-Puro (*Myc*) retroviruses and Puromycin-selected. The left panel shows increased *Skp2* RNA levels in Myc over-expressing MEFs (relative expression as compared to *Rps21* levels; *Rps21* is not significantly regulated by Myc) assessed by quantitative real-time PCR. The right panel shows *Skp2* transcript levels in MEFs treated with Actinomycin D (ActD, 1µg/ml) for the indicated time. The levels of the *Skp2* transcripts were normalized to *Rps21* expression and set to 100 percent (0h). Shown is the percent expression after the indicated time of ActD treatment. **B.** Primary early passage MEFs were infected with pBabe-*Puro* (*Puro*) or pBabe-ER-*E2f1*-*Puro* (ER-*E2f1*) retroviruses. Puromycin-resistant cells were treated for the indicated times with 4-HT to activate ER-E2f1 and assessed for changes in the expression of *Skp2*, and the E2f1 targets *thymidine kinase* (*Tk*) and *dihydrofolate reductase* (*Dhfr*), by real-time PCR. Levels of RNA were standardized to the expression of *Ubiquitin* (*Ub*). **C.** NIH-3T3 cells were co-transfected with a *Skp2* promoter-reporter construct (*firefly* luciferase, (63)) and either *E2f1*, *c-Myc* or control (ctrl) expression plasmids. Luciferase activity was determined according to the manufacturer's instruction (Promega, Madison, WI). Relative luciferase activity was determined by calculating the ratio of *firefly* to co-transfected *renilla* luciferase activity. Note that E2f1, but not c-Myc, activated the *Skp2* promoter.

SUPPLEMENTARY FIGURE S2. Skp2 or Cks1 do not cooperate with Myc in the transformation of immortal fibroblasts. **A.** Immunoblot analysis of the indicated proteins in BALB/c-3T3 fibroblasts transfected with pBabe-*Puromycin* (*Puro*) or pBabe-*Myc*-

Puromycin (*Myc-Puro*) expression plasmids +/- Cks1 or Skp2 expression (which were expressed in MSCV-IRES-*GFP* expression plasmids; ctrl: MSCV-IRES-*GFP*). Transfected cells were selected for growth in puromycin-containing medium (6µg/ml) for 48 hr and were sorted for GFP by FACS. **B.** Soft-agar colony formation. 500 cells were plated per well in 6-well plates and grown for 14 days. Colonies were then stained with MTT. **C.** Quantification of colony formation. Shown is a representative experiment performed in duplicate.

SUPPLEMENTARY FIGURE S3. Analysis of Myc target gene expression in non-transgenic (wt) and Eµ-*Myc* B cells of the indicated *Skp2* genotypes. SYBR-green real-time PCR analysis of *c-myc*, *Cad*, and *Rcl* mRNA levels was performed on splenic $B220^{+}$ B cells from 4 week-old pre-cancerous Eµ-*Myc*;$Skp2^{+/+}$, Eµ-*Myc*;$Skp2^{+/-}$, and Eµ-*Myc*;$Skp2^{-/-}$ mice and compared to their expression in B cells from a wild type (wt) littermate. Levels of mRNAs were standardized to the expression of *Ubiquitin* (*Ub*).