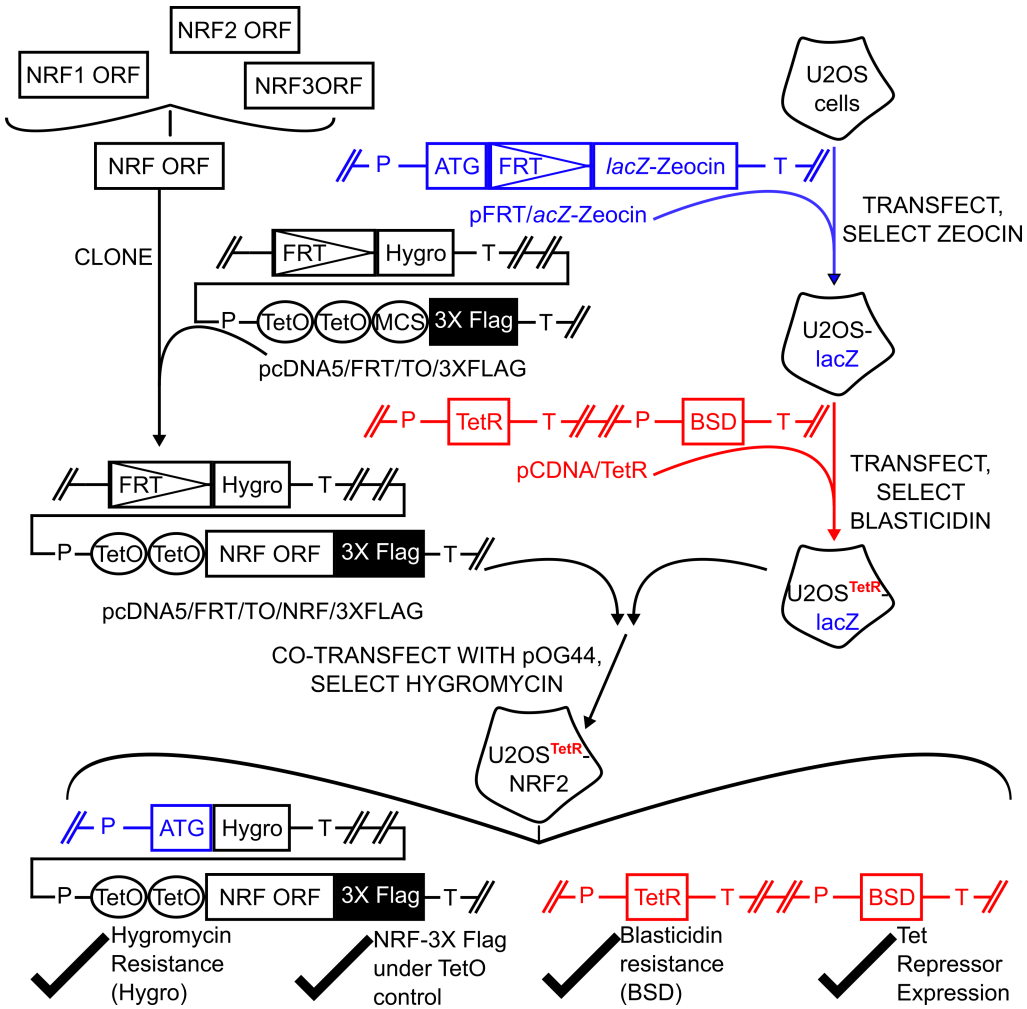

Figure S1. Schematic of NRF flp-in design. Related to Figure 1 and materials and methods section. U2OS cells were transfected with pFRT*lacZ*-Zeocin carrying a start codon ATG, Flp Recombination Target site (FRT), and *lacZ*-Zeocin open reading frame flanked by a constitutive promoter (P) and terminator (T) (blue). Cells with stable incorporation of this plasmid were selected for with zeocin and termed U2OS-lacZ. U2OS-lacZ cells were transfected with pCDNA/TetR carrying a TetR open reading frame and blasticidin resistance gene (Blasticidin-S-Deaminase, BSD) each under control of a constitutive promoter and terminator (red). Cells with stable incorporation of this plasmid were selected for with blasticidin and termed U2OS^{TetR}-lacZ. While U2OS^{TetR}-lacZ cells were being generated, the modified open reading frames (ORFs) of NRF members NRF1, NRF2, and NRF3 (collectively NRFX) were each cloned into pcDNA5/FRT/TO/3XFLAG vector (black, see **Figure 1B** for modifications to NRF ORFs). Each vector contained a FRT sequence followed by a hygromycin resistance gene and terminator, and a second cassette consisting of a promoter, two Tet operons, the NRF open reading frame joined in sequence to a triple FLAG sequence, and a terminator. The pcDNA5/FRT/TO/NRFX/3XFLAG vectors were co-transfected into U2OS^{TetR}-lacZ with pOG44, which encodes Flp recombinase, to generate U2OS^{TetR}-NRFX. U2OS^{TetR}-NRFX cells with proper incorporation of pcDNA5/FRT/TO/NRFX/3XFLAG at the FRT were selected for with hygromycin. U2OS^{TetR}-NRFX cells thus expressed hygromycin resistance gene, NRF member tagged with triple FLAG sequence under tet-operon control, blasticidin resistance gene, and Tet repressor.

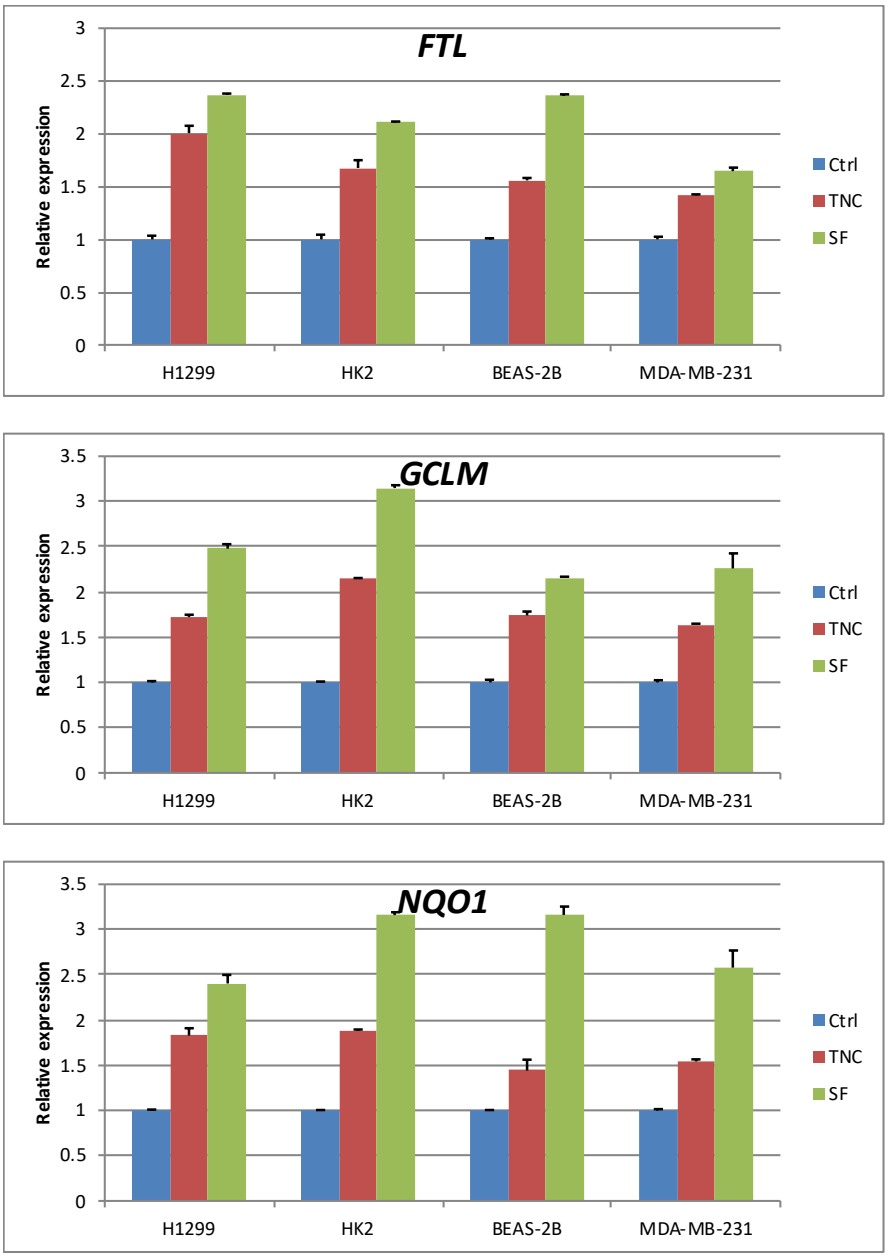

Figure S2. RT-qPCR of mRNA levels of *FTL*, *GCLM*, and *NQO1*. Total RNA was harvested after 16-hour treatment with either vehicle (Ctrl), 5 μg/mL tunicamycin (TNC), or 5 μM sulforaphane (SF) and prepared for qPCR analysis of transcript levels.

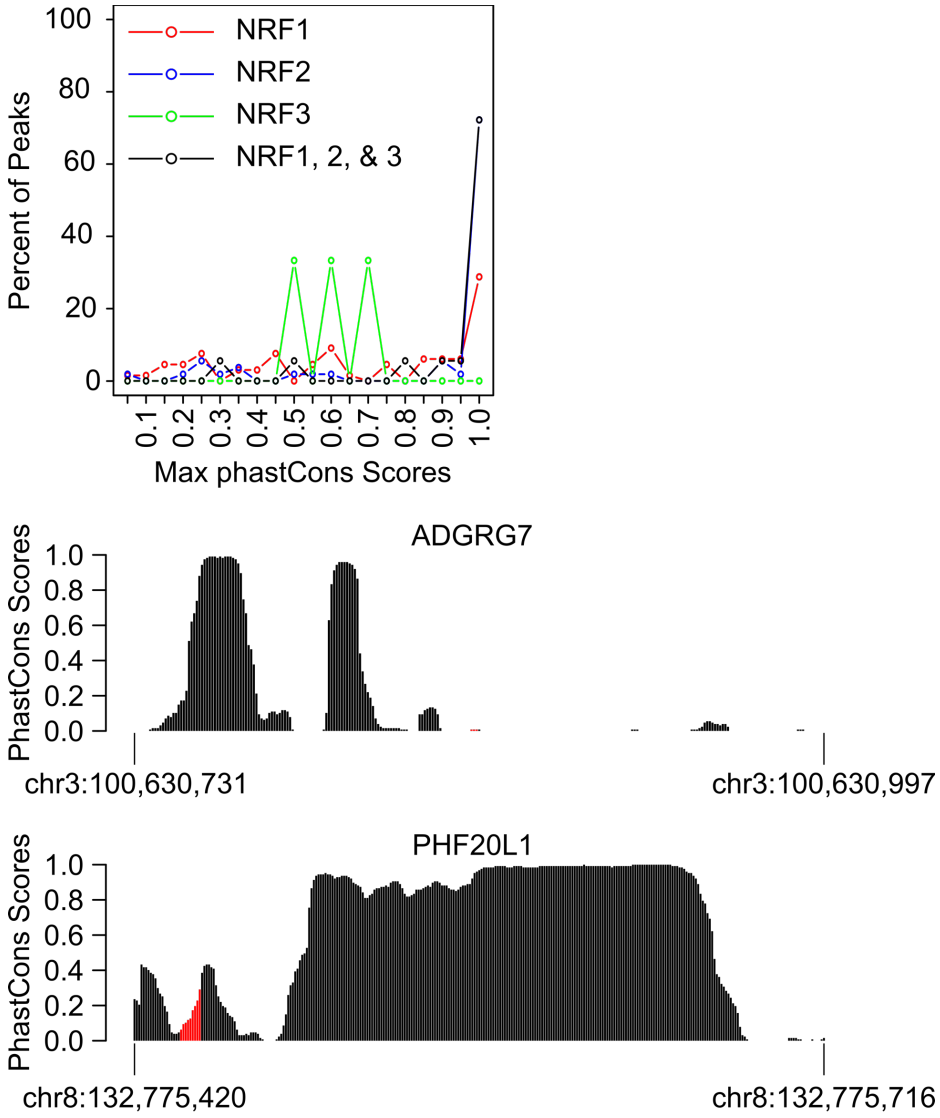

Figure S3. Sequence conservation of ChIP peaks across vertebrates. Analyzed vertebrates include human, chimp, rhesus, mouse, rat, dog, and opossum. Red colored bars in PhastCons plots represent ARE bases.