Supplemental Materials

Molecular Biology of the Cell

Diedrichs et al.

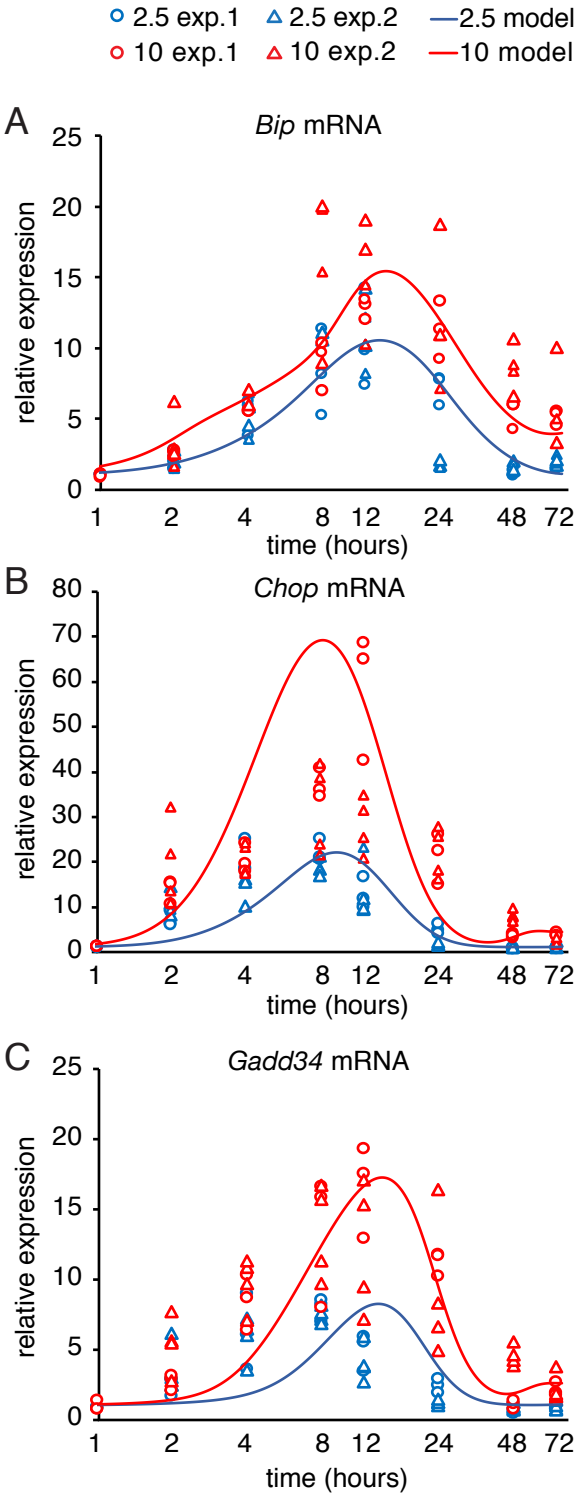

Figure S1. Comparison of model output against both the entrainment data set and a separate independent data set not used in entrainment.
(A-C) *Bip*, *Chop*, and *Gadd34* relative expression levels quantified by qRT-PCR from wild-type cells used to entrain the model (circles) and a second independent data set from a separate wild-type cell line (triangles), showing the intrinsic biological variability of the response. The x-axis (time) is shown on a log scale to enhance the presentation of early time points. Individual symbols represent biological replicates within an expeirment. A technical error prevented collection of 72h data from experiment 2, so a third experiment at only 72h was conducted to collect those data points (also depicted as triangles). Data at the 1h time point were collected in experiment 1, and shown in Figure 3, but not in experiment 2.

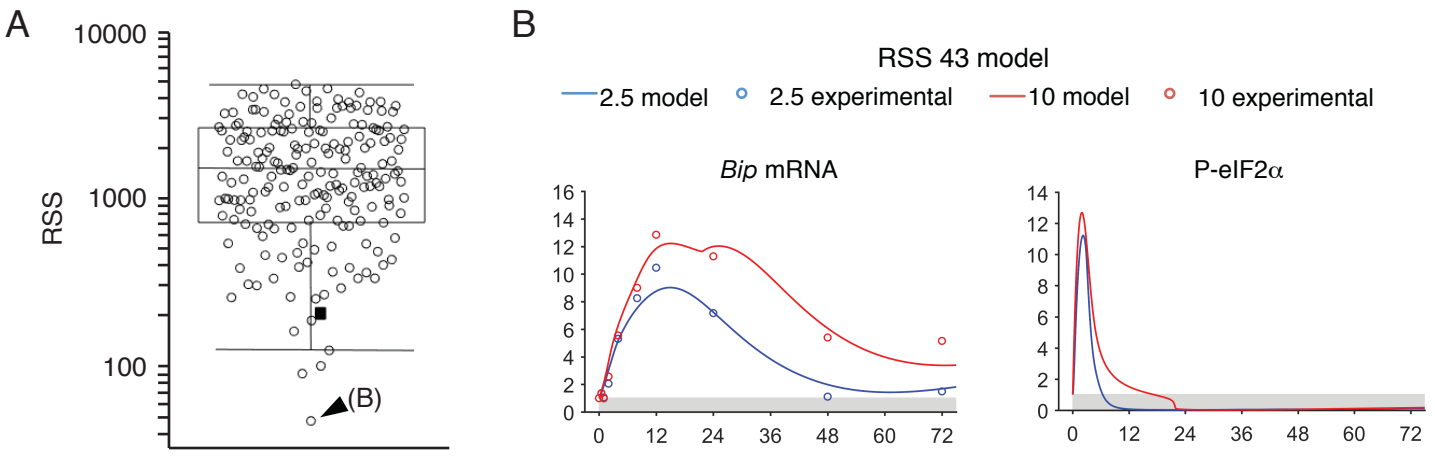

Figure S2. RSS optimization of model parameters
(A) Bee swarm plot of the distribution of RSS values between experimental measurements and model solution obtained by 200 random samples of parameter sets. The RSS of our optimum parameter set was 224 (square symbol), which puts it among the lowest three percent of RSS values among parameter sets.
(B) Model output files for a parameter set with a lower RSS than the model (arrowhead on bee swarm plot), showing good fit for *Bip* mRNA expression (left panel) but grossly incorrect output for eIF2α phosphorylation (right panel), since there is no evidence that eIF2α phosphorylation becomes quantitatively impaired during the recovery phase. Such discrepancies typified the few parameter sets with an RSS lower than the model's.

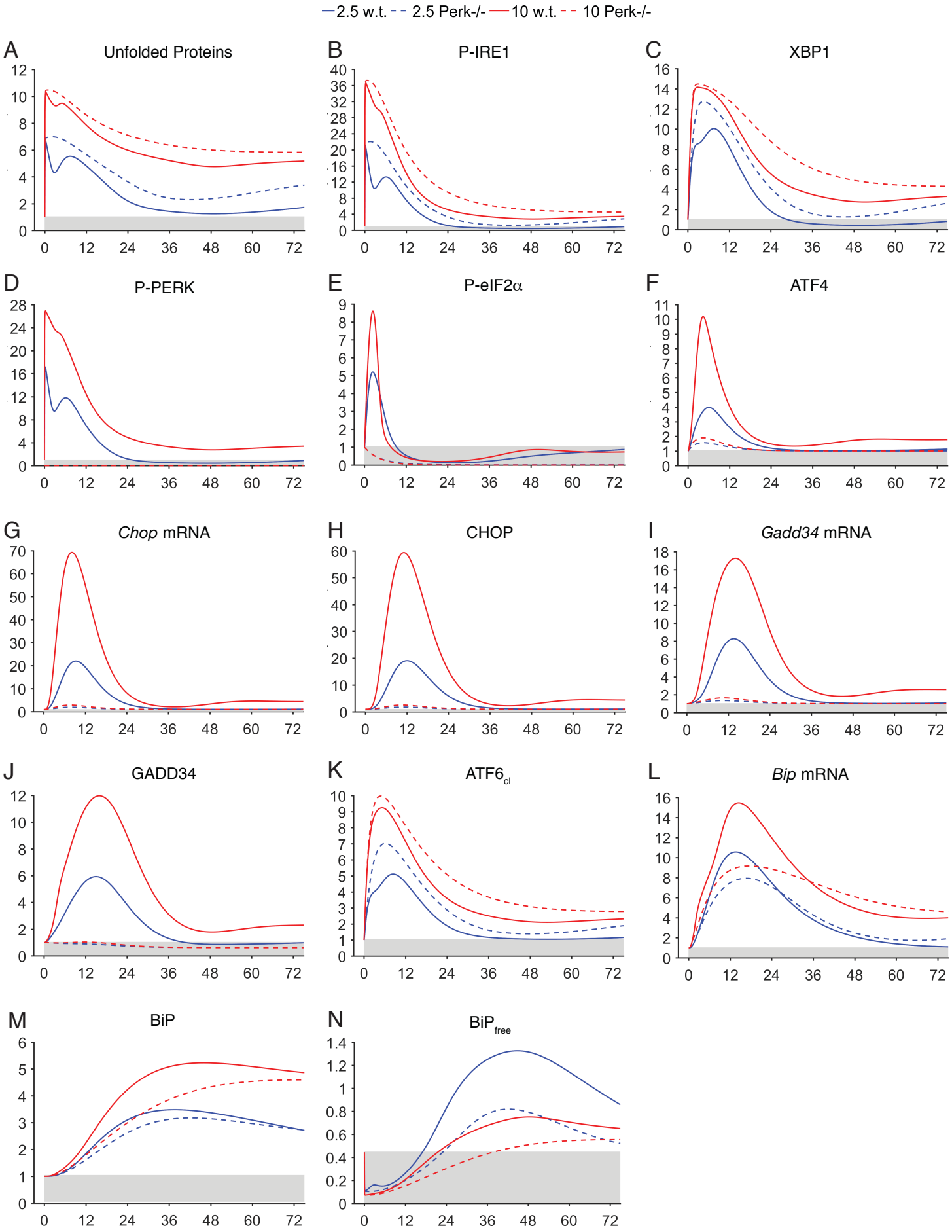

Figure S3: Wild-type versus *Perk*-/- cells.

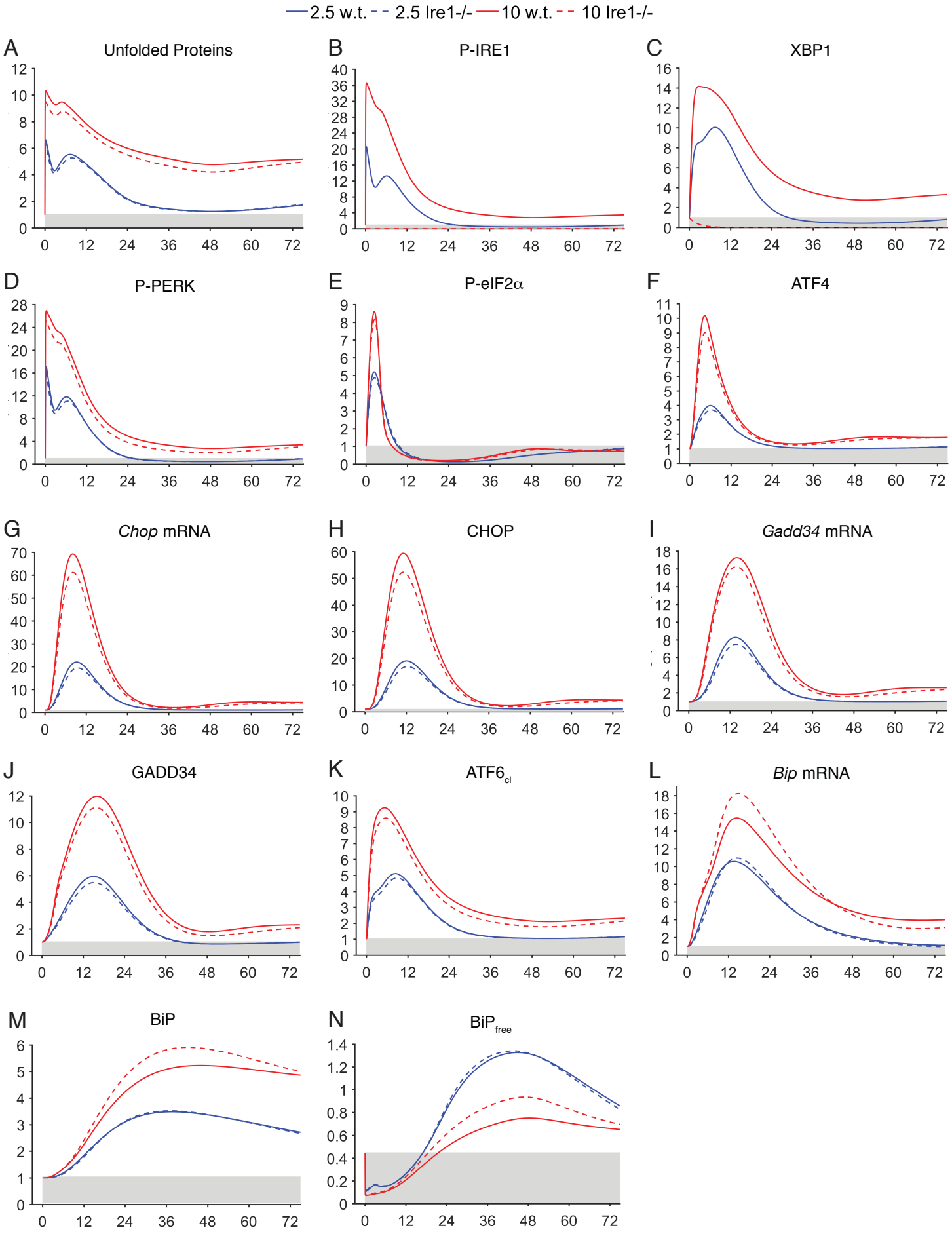

Figure S4: Wild-type versus *Ire1*-/- cells.

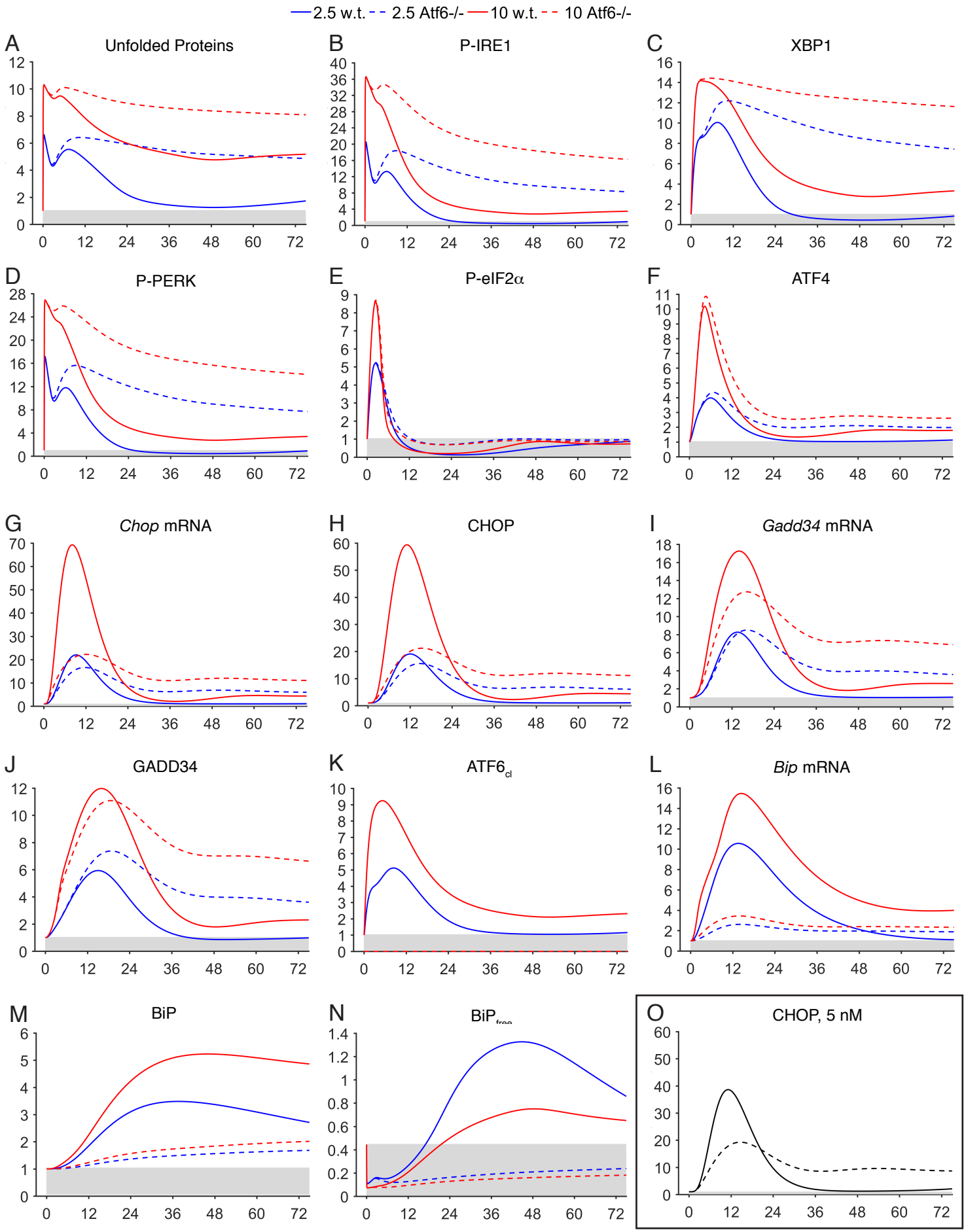

Figure S5: Wild-type versus *Atf6α-/-* cells. Panel (O) shows CHOP in wild-type (solid lines) and *Atf6-/-* (dashed lines) conditions for 5 nM treatment.

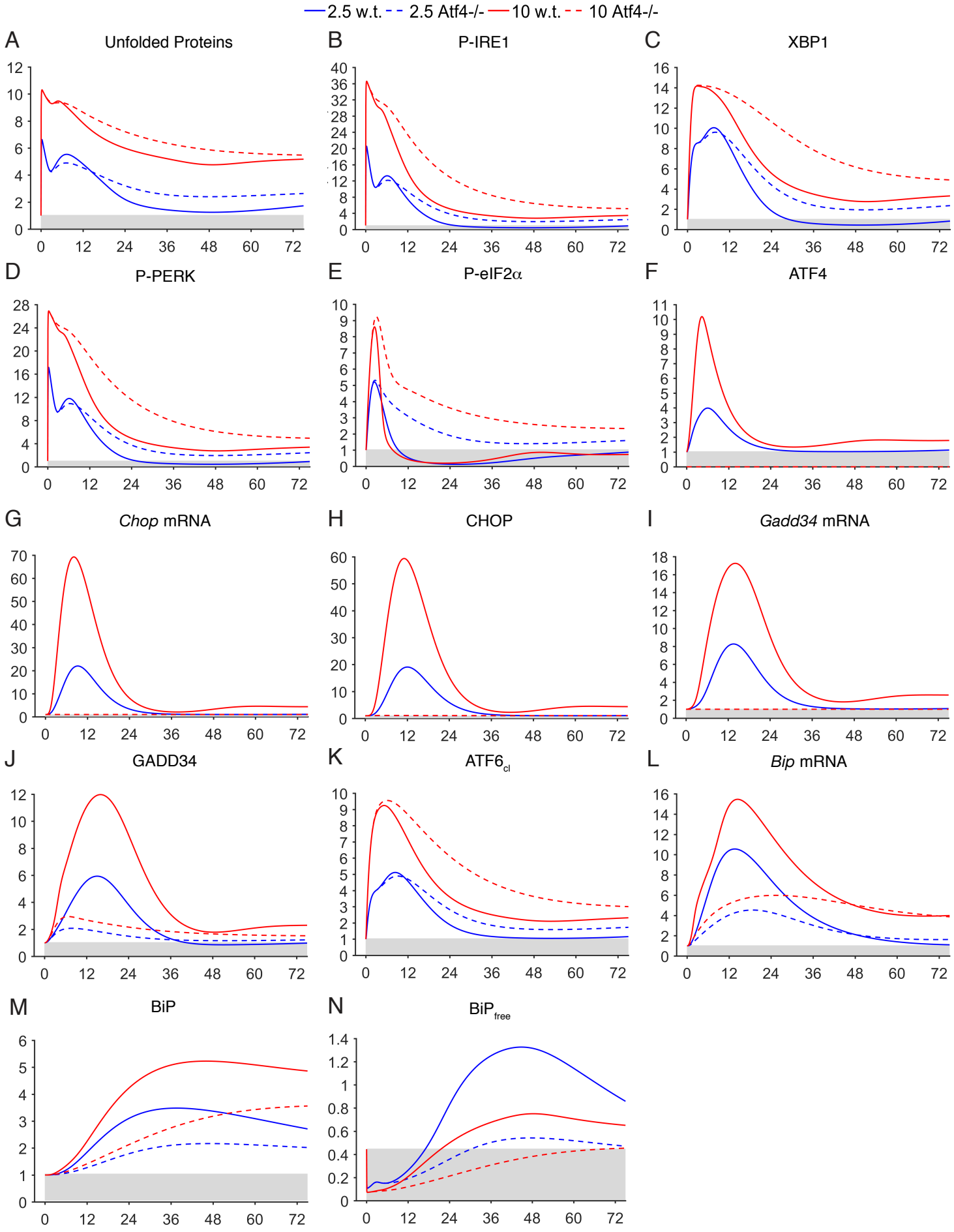

Figure S6: Wild-type versus *Atf4*-/- cells.

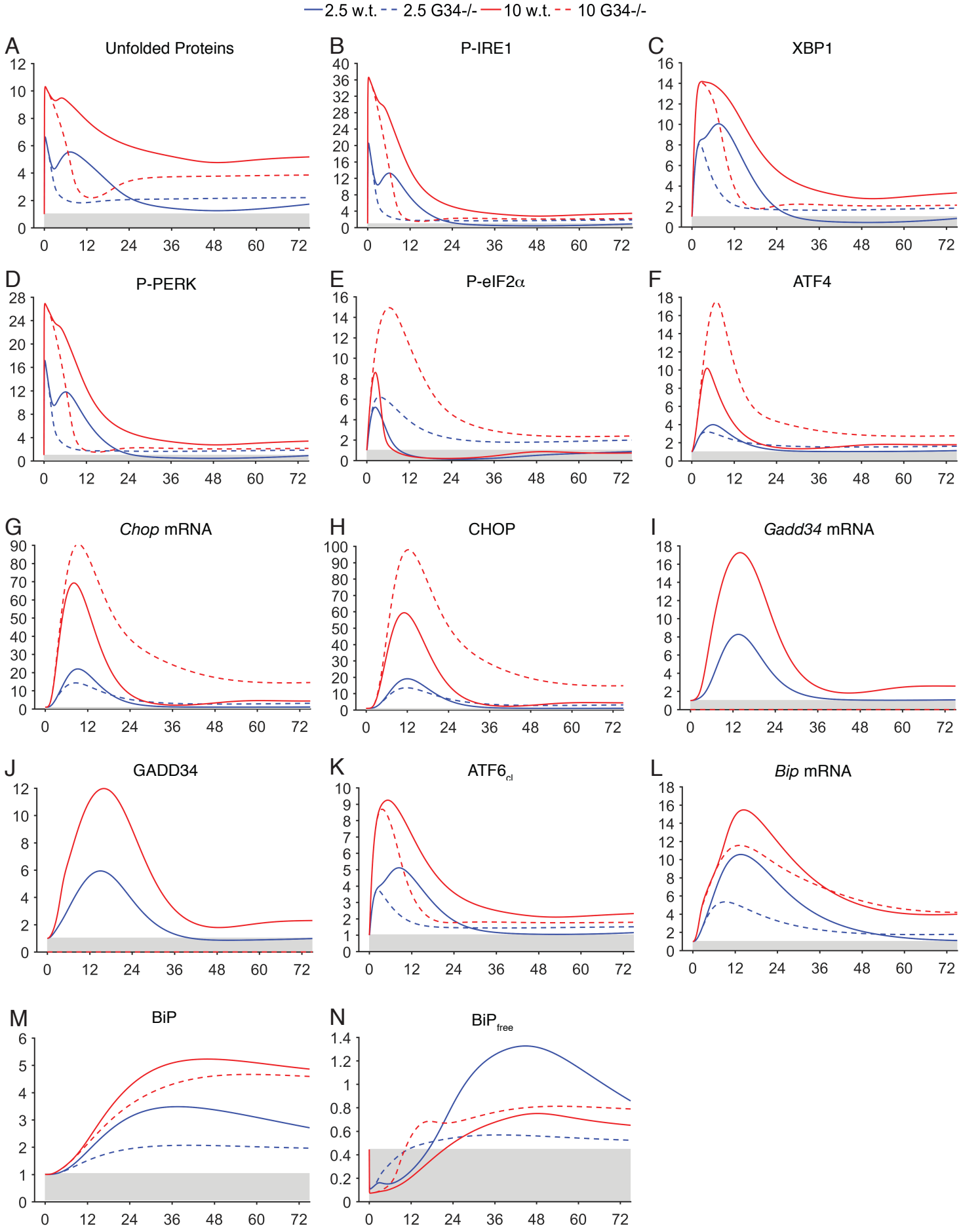

Figure S7: Wild-type versus *Gadd34*-/- cells.

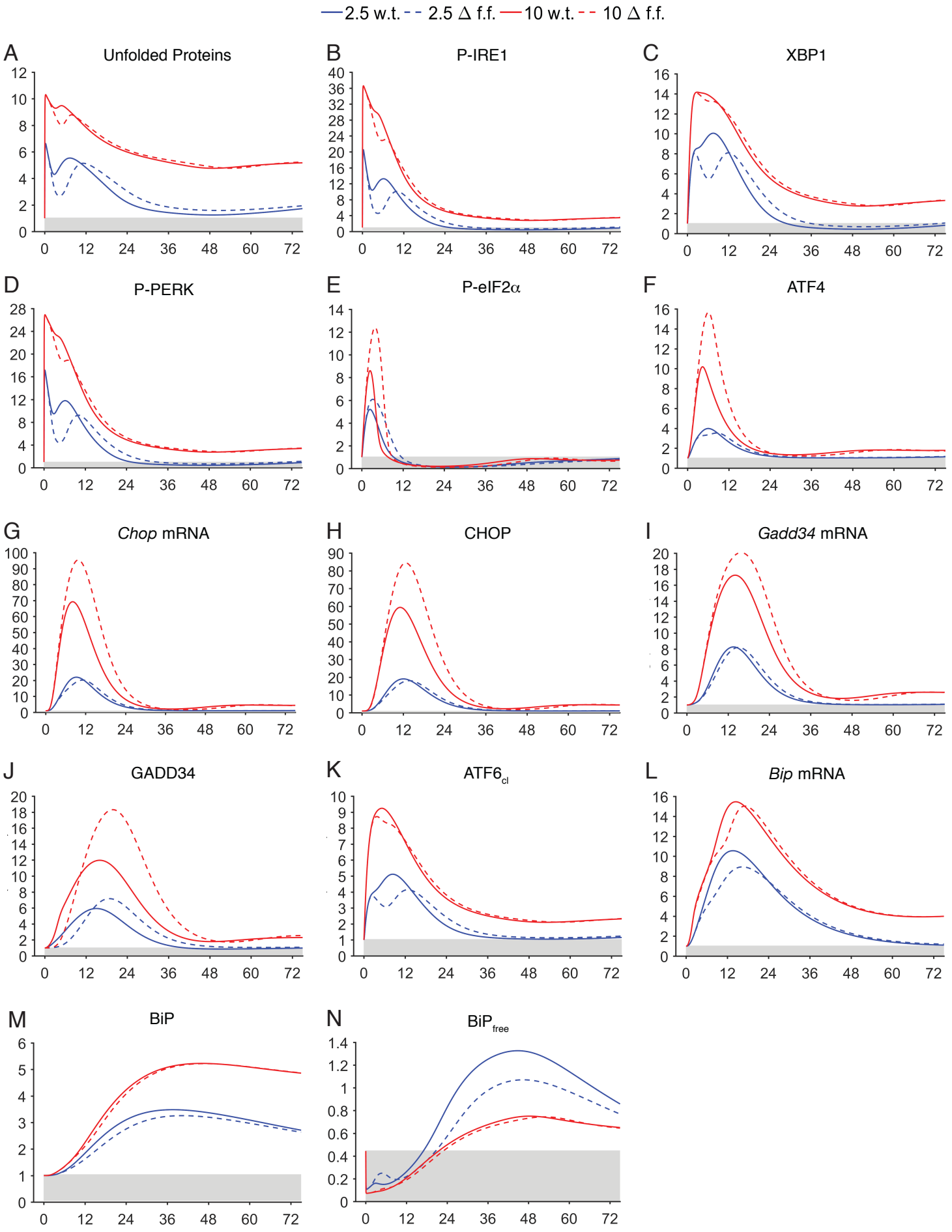

Figure S8: Wild-type cells versus cells in which eIF2α phosphorylation regulates only *Atf4* translation but not translation of *Chop* or *Gadd34* (Δf.f.).

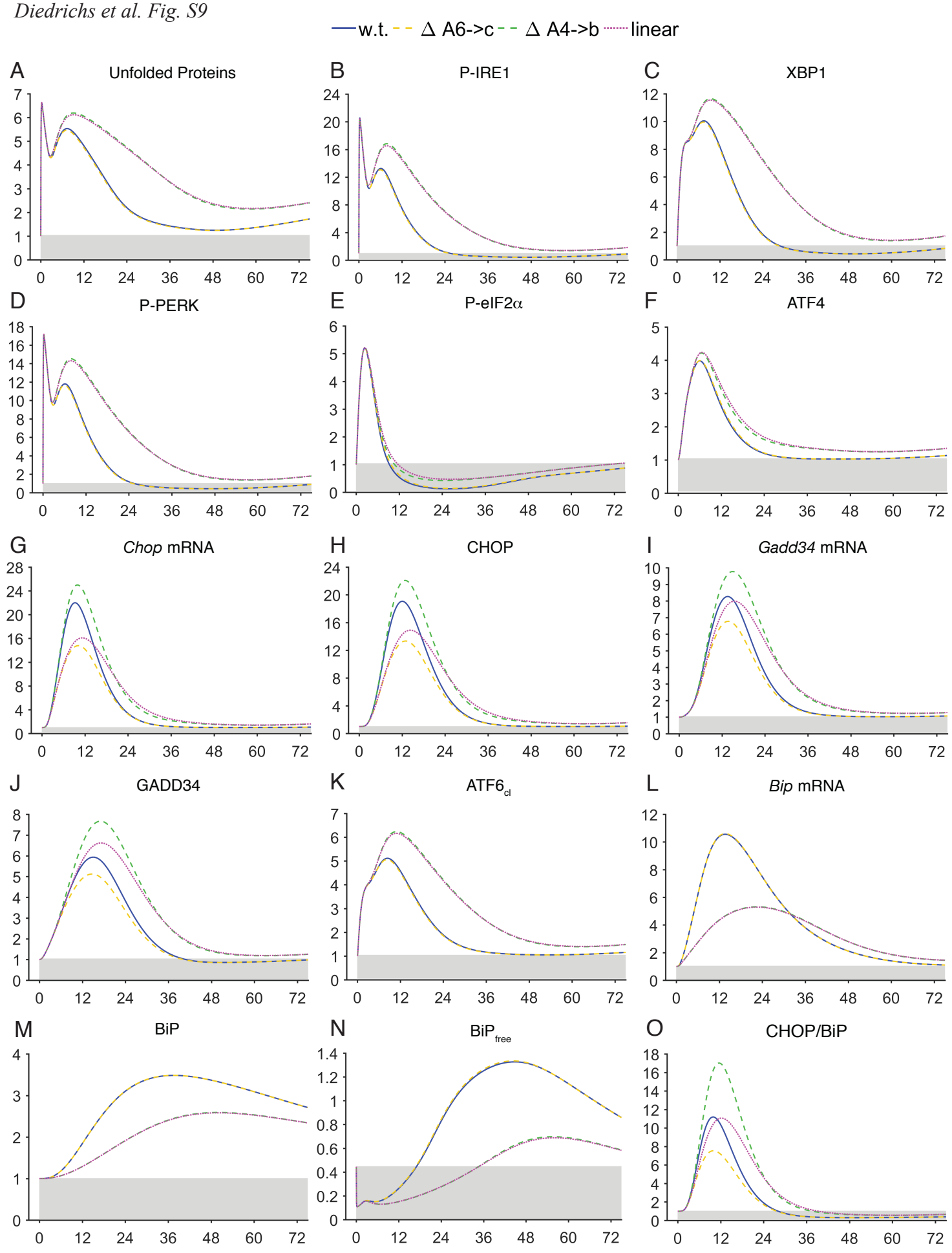

Figure S9: Wild-type cells versus cells in which the contribution of ATF6α to Chop (ΔA6->c) or of ATF4 to Bip (ΔA4->b), or both (linear) have been removed, under the 2.5 nM condition.

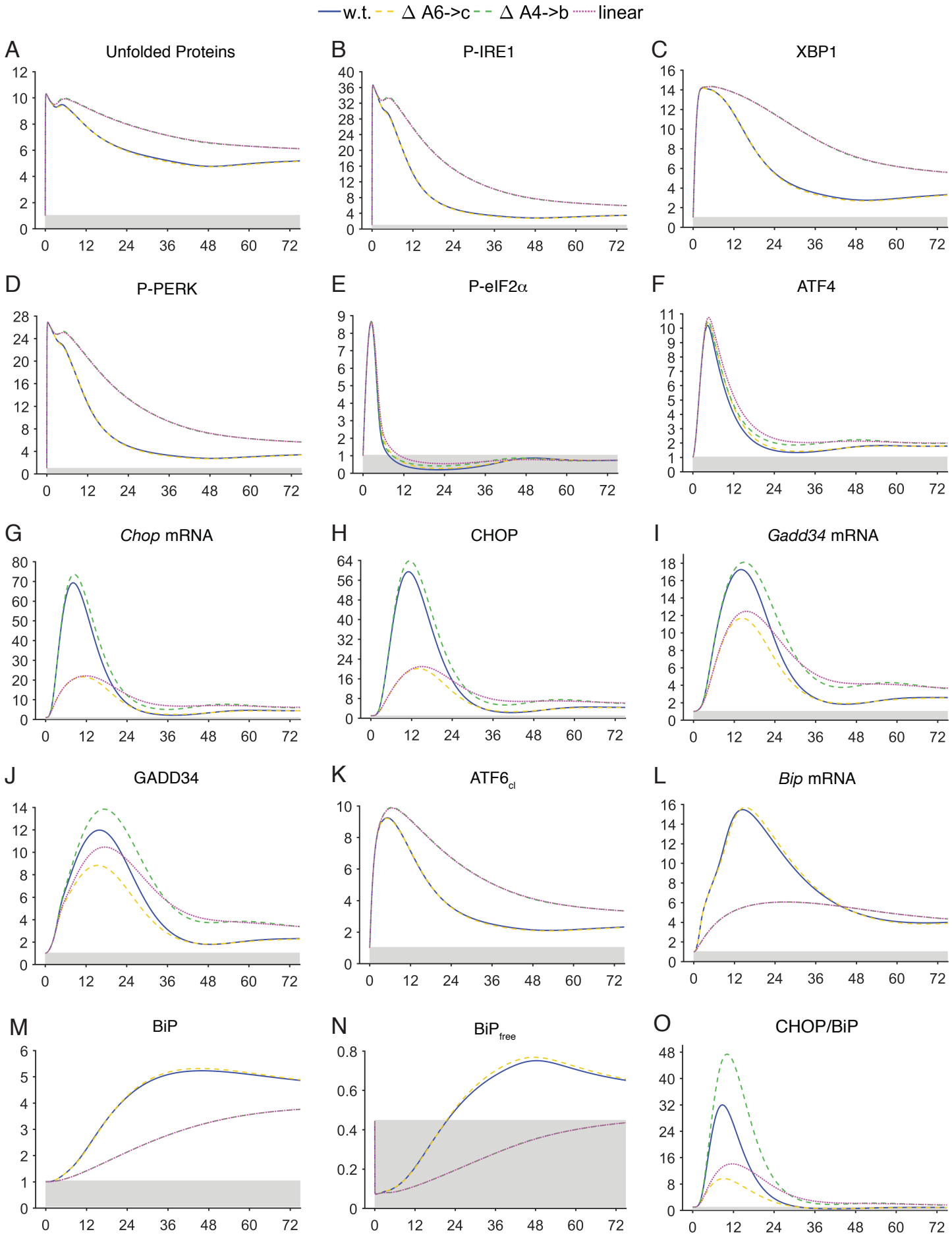

Figure S10: Wild-type cells versus cells in which the contribution of ATF6α to Chop (ΔA6->c) or of ATF4 to Bip (ΔA4->b), or both (linear) have been removed, under the 10 nM condition.