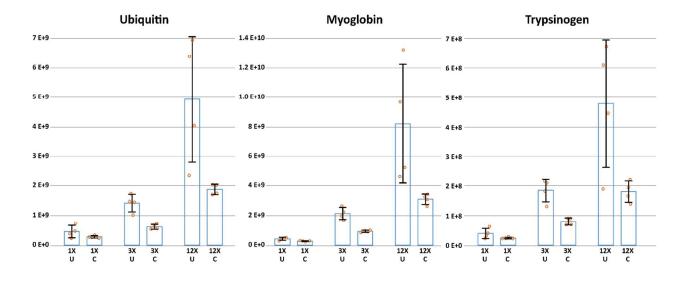
## Applying Label-Free Quantitation to Top Down Proteomics

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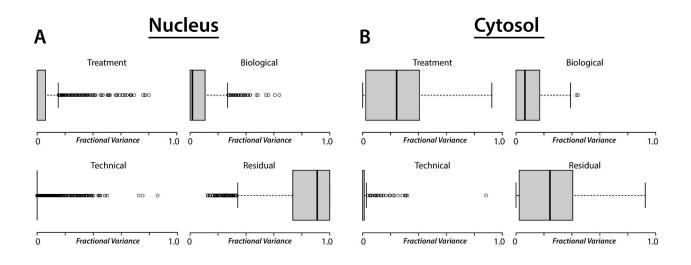
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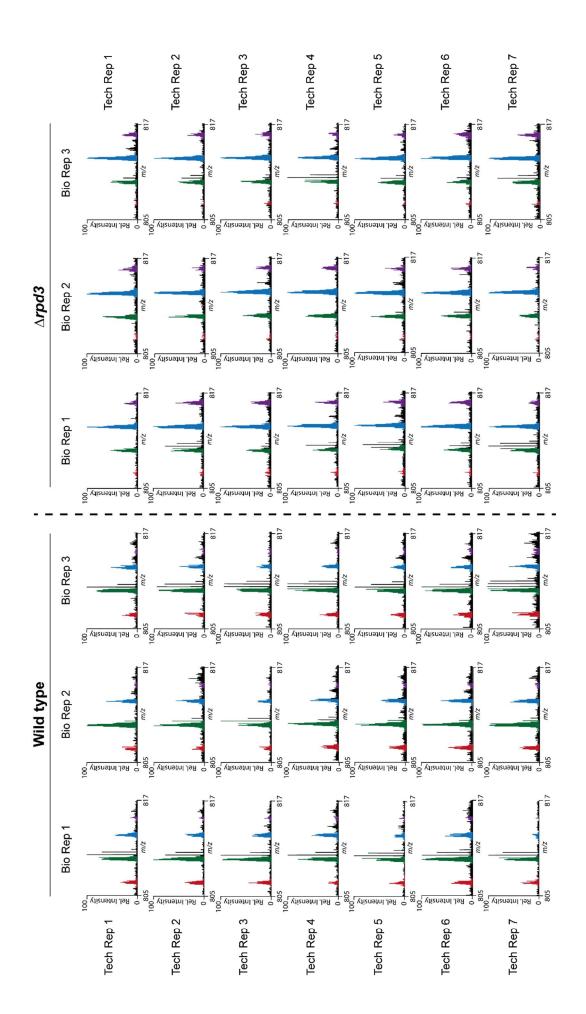
**Contents:** Figures S1-S3



**Figure S1.** Bar charts showing the effects of using raw data (U) versus data normalized to total ion counts across a LC-MS run (C) on the precision of intensity measurements for three protein standards spiked in complex yeast extracts at 3 different levels (1X, 3X, and 12X). Individual intensity measurements are shown as yellow circles; error bars indicate standard deviation of the intensities.



**Figure S2.** Box plots of the proportional variance partitioned to each of three different random effects (and residual variance) in (A) nuclear and (B) cytosolic fractions of WT vs.  $\Delta rpd3$  mutant yeast cells. The four categories and their definitions are as follows: "Treatment" effect, or the main point of the study, (WT vs. the  $\Delta rpd3$ ), "Biological", which refers to the fractional variance assigned to the biological replicates, the "Technical", or the fractional variance assigned to technical variation in the study, and the "Residual", or those sources of variation left unassigned by the hierarchical linear model. In these box and whisker plots, the box indicates the range where 75% of the variances fall and the whiskers indicate the range encompassing 95% of the measurements.



**Figure S3.** Mass spectrometric data from each of 42 technical replicates of histone H4. The effect is restricted to the treatment levels (Wild type vs  $\Delta rpd3$ ), and the relative ratios of proteoform intensities are consistent across biological and technical replicates. Monoacetyl, red; diacetyl, green; triacetyl, blue; tetraacetyl, purple.