**Figure 4. Proteome-wide analysis of intrinsic disorder among CDK substrates and dynamic phosphoproteins**

a. Circle plots presenting enrichment of homologues of human CDK substrates among *Xenopus* phosphoproteins detected *in vivo* and those with dynamic phospohosites.

b. Diagrams of IUPred scores over the length of CDC6, MCM4, RIF1, and ELYS proteins in Xenopus. Regions with scores >0.5 (red) are considered to be disordered, and <0.5 (grey) structured. Blue vertical lines indicate Ser and Thr residues; yellow circles, phosphorylated sites; green circles, phosphorylations showing a dynamic behavior throughout the cell cycle.

c. Scheme illustrating potential enrichment of phosphorylation in disordered regions when taking into account amino acid compositional bias.

d. Scatter plot of expected vs observed number of phosphorylated Ser/Thr for each protein of human and *Xenopus* phosphoprotein datasets. Statistical significance was calculated with the binomial test and corrected for multiple hypothesis testing by calculating the false discovery rate (FDR). FDR thresholds of 5% and 1% are marked in yellow and red, respectively. Crosses represent proteins with at least one dynamic phosphorylation in *Xenopus*,or human CDK1 subfamily substrates, respectively.

e. Boxplots showing expected vs observed phosphorylated serines and threonines among all phosphoproteins detected (left), phosphoproteins with at least one dynamic phosphosite (middle), and dynamic phosphoproteins also detected as CDK1 subfamily targets in humans (right). Distributions were compared with the Wilcoxon signed-rank test.

f. Violin and box plots showing the distribution of the percentage of disordered residues per protein for CDK targets vs the rest of the phosphoproteome for human and yeast, and dynamic phosphoproteins vs the rest of the phosphoproteome for *Xenopus*. Intrinsic disorder was calculated with three different predictors (IUPred, SPOT, and VSL2b). Statistical significance was evaluated with the Wilcoxon–Mann–Whitney test.

g. Plot showing the -log10(p-value) vs the log10(common Odds Ratio) calculated with the

Cochran–Mantel–Haenszel test for stratified contingency tables to evaluate enrichment in IDRs of CDK-mediated phosphorylation (or dynamic phosphorylation in *Xenopus*). For all organisms, the disordered regions were calculated with three different disorder predictors. The disordered fraction is shown with a colour scale.

h. Human CDK1 subfamily targets, *Xenopus* dynamic phosphoproteins, and the intersection of both sets, that are present in our manually curated proteome of membraneless organelles.