Table S1. Phosphorylation, Acetylation, and Ubiquitylation Sites Used for the Analysis, Related to Results

The data can be accessed via a website (http://ptmfunc.com). For each species we used PFAM annotations to count the number of PTMs that are found within globular protein domains. On average, ~75% of the phosphosites ~40% of acetylation and ~45% of ubiquitylation sites are found outside PFAM domains.

Species	PTM type	PTM total	Within PFAM domains	% Outside PFAM domain
H. sapiens	Phosphorylation	31165	11726	62.4
	Acetylation	8042	4604	42.8
	Ubiquitylation	22057	11079	49.7
M. musculus	Phosphorylation	24921	6825	72.6
	Acetylation	3384	2298	32.1
R. norvegicus	Phosphorylation	1885	913	51.6
X. laevis	Phosphorylation	470	149	68.3
C. elegans	Phosphorylation	6715	1074	84.0
D. melanogaster	Phosphorylation	17535	2081	88.1
	Acetylation	1707	858	49.7
S. pombe	Phosphorylation	2540	636	75.0
S. cerevisiae	Phosphorylation	15144	3747	75.3
	Acetylation	657	433	34.1
	Ubiquitylation	2499	1426	42.9
C. albicans	Phosphorylation	2910	532	81.7
A. thaliana	Phosphorylation	4527	648	85.7
O. sativa	Phosphorylation	3140	633	79.8

Table S2. Estimation of False Discovery Rate for the *S. cerevisiae* Phosphosite Data Set after Compilation of 12 Different Reported Experiments, Related to Results

Although individual proteomic experiments report false discovery rates (FDR) of peptide identification on the order of 2% or less, the accumulation of different independent datasets results in an increase of FDR. We collected 12 different phosphoproteomics studies for *S. cerevisiae* and used these to estimate an upper bound for this increase. Assuming a rate of 2% peptide FDR for each individual dataset and that no false-positive site is identified more than once, we estimate that the combined *S. cerevisiae* phosphoproteome has, at most, an FDR of ~4%. This suggests that even for species that have been extensively studied such as *S. cerevisiae* and *H. sapiens*, the fraction of incorrectly identified PTMs is likely to be low. For each study we estimated the total number of false positive phosphosites assuming a false-discovery rate (FDR) of 2%. We assumed, conservatively, that no false-positive phosphosite is observed more than once. Under these assumptions the total expected number of false positives would be equivalent to 4% of the compiled non-redundant *S. cerevisiae* phosphosites (836 out of 20658).

Pubmed ID	Phosphosites obtained from study	Projected false-positives (assuming 2% FDR)
19823750	2876	57.52
17563356	6489	129.78
19684113	4000	80
17287358	1154	23.08
19795423	3010	60.2
20377248	2526	50.52
15665377	591	11.82
19547744	3435	68.7
17330950	1386	27.72
21177495	3540	70.8
21298081	6071	121.42
19779198	6744	134.88
Sum	**41822**	**836.44**
Sum non-redundant	**20658**	**836.44**

Table S3 - Overlap of Different Posttranslational Modifications within the Same Proteins Does Not Depend on Protein Abundance, Related to Figure 2

We observed that proteins with different lysine modifications (acetylation, ubiquitylation and sumoylation) are also very likely to be phosphorylated. One possible explanation for this would be an experimental identification bias in MS experiment. Since MS experiments preferentially identify highly abundant proteins then the overlap could be due this bias. In order to control for this we used protein abundance estimates for human proteins (http://pax-db.org/). We excluded all human proteins with estimated abundance over half of the median such that there was no significant difference in the abundance levels of phosphorylated versus non-phosphorylated proteins (p-value=0.44 with a KS ranked test). After controlling for abundance we still see a very significant enrichment of phosphoproteins among the lysine modified proteins over random (using a Fisher's exact test).

Protein Subset	Total	Phosphoproteins (% from total)	Enrichment over random	p-value for enrichment
All proteins	3522	1526 (43%)	-	-
Ubiquitylated	816	539 (66%)	1.5	$<10^{-40}$
Acetylated	306	237 (77%)	1.8	$<10^{-33}$
Sumoylated	46	43 (93%)	2.1	$<10^{-12}$

Table S4. Domain Families Selected for Phosphopeptide Enrichment Analysis, Related to Results

We used PFAM annotations and the compilation of known phosphorylation sites for the 11 species considered in this study to count the total number of phosphorylation sites found for each PFAM domain. Among the domain families with higher number of total phosphosites across all the species we selected 10 that had an available representative structure deposited in the PDB for analysis. For each of these PFAM domains we provide here the total number of domain instances annotated across the 11 species as well as the total number of phosphosites found for each and the representative structure used for the enrichment analysis.

PFAM id	Domain name	Total phosphosites	Total number of domains	PDB ID of structure used
Pkinase	Protein kinase	1273	4269	1QMZ
Pkinase_Tyr	Protein tyrosine kinase	495	1427	1M14
HSP70	Heat shock proteins, Hsp70	313	195	1YUW
RRM_1	RNA recognition motif	253	2438	3BS9
UCH	Ubiquitin carboxyl-terminal hydrolase	200	390	3H0X
Ras	Ras domain	190	821	1EK0
HSP90	Heat shock proteins, Hsp90	145	78	2IOP
PH	Pleckstrin homology domain	144	856	1MAI
MFS_1	Major Facilitator Superfamily (MFS) transporters	120	723	2GFP
Mito_carr	Mitochondrial carrier	119	1434	2C3E

Table S5. Total 1-to-1 Orthoproteins and Phosphosites Used in Species to Human Comparative Analysis, Related to Experimental Procedures

We counted the total number of human to species 1-to-1 orthologs with an inparanoid score greater than 90%. We also detailed how many of these are phosphoproteins and how many phosphosites in total were used for the comparative studies throughout the paper.

Species	Total number of orthologs	Orthologs that are phosphoproteins	Number of phosphosites in orthologs
M.musculus	15982	5923	31317
R. norvegicus	14940	1059	2547
X.laevis	8261	279	394
C.elegans	4489	1445	4309
D.melanogaster	5346	2279	9264
S.pombe	2225	597	1382
S.cerevisiae	1992	1234	6413
C.albicans	2129	526	1481
A.thaliana	2888	476	1036
O.sativa	2872	464	989