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Supplementary Materials for

Protein Complex–Based Analysis Framework for High-Throughput Data Sets

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This PDF file includes:

Table S7. Comparison of protein complexes with GO and KEGG with respect to co-citation.
Table S8. Comparison of protein complexes with GO and KEGG with respect to protein colocalization.
Table S9. Comparison of protein complexes with GO and KEGG with respect to gene coexpression.
Table S10. Annotation of the protein complex resource.
Table S11. Gene or protein input identifiers supported by the COMPLEAT.
Table S20. Dynamic phosphosites changing in response to insulin treatment.

Other Supplementary Material for this manuscript includes the following:
(available at www.sciencesignaling.org/cgi/content/full/6/264/rs5/DC1)

Table S12 (Microsoft Excel format). Enriched protein complexes at baseline (mtDER-S2R+ cell line).
Table S13 (Microsoft Excel format). Enriched protein complexes at EGF stimulus (mtDER-S2R+ cell line).
Table S14 (Microsoft Excel format). Enriched protein complexes at baseline (S2R+ cell line).
Table S15 (Microsoft Excel format). Enriched protein complexes at insulin stimulus (S2R+ cell line).
Table S16 (Microsoft Excel format). Consistent protein complexes with respect to baseline versus EGF stimulus.
Table S17 (Microsoft Excel format). Dynamic protein complexes with respect to baseline versus EGF stimulus.
Table S18 (Microsoft Excel format). Consistent protein complexes with respect to baseline versus insulin stimulus.
Table S19 (Microsoft Excel format). Dynamic protein complexes with respect to baseline versus insulin stimulus.

Supplementary materials

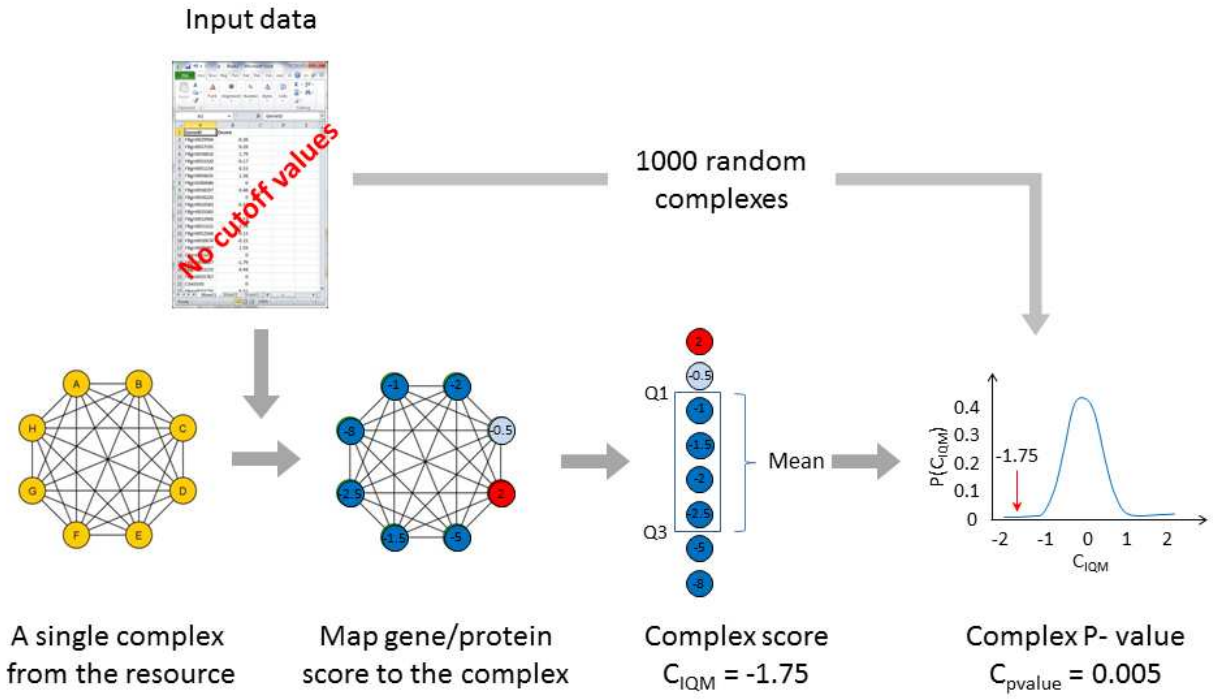


Figure S1: Schematic representation of protein complex scoring. In this model, the complex score and p-value calculation of a single complex is shown. First, the input data (without preselecting hits) is mapped to the protein complex. To calculate the interquartile mean (IQM), complex members are ordered based on the protein-score, and the mean value between first (Q1) and third (Q3) quartile is calculated. The p-value corresponding to the IQM is calculated by comparing it to the distribution of random IQM scores calculated based on the 1000 random complexes. Random complexes are generated either based on the input data or based on the complex resource, depending on the user specification.

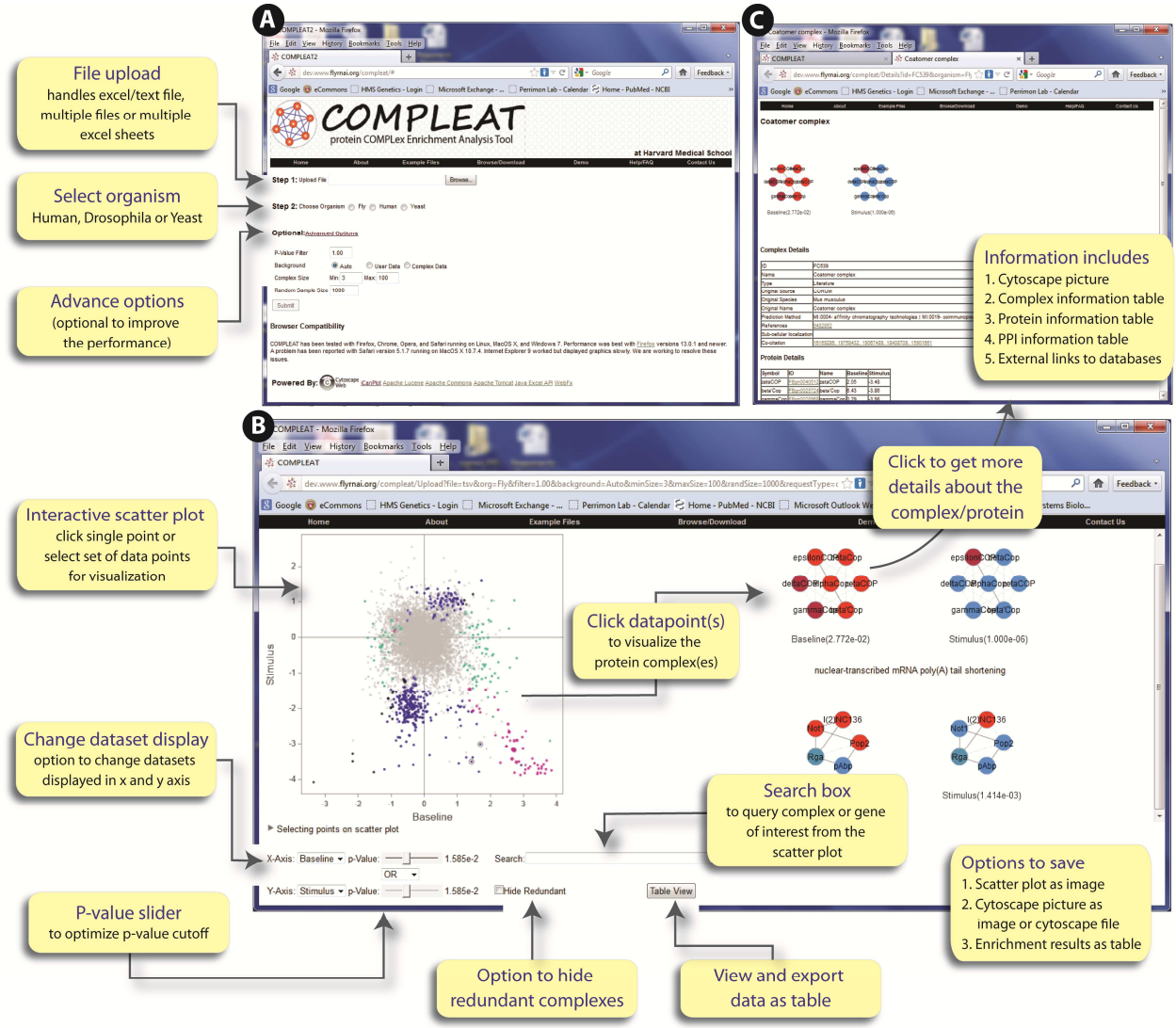


Figure S2: Snapshots of the COMPLEAT Web interface. (A) Input page for COMPLEAT with options to upload input file, choose organism and set advance parameters**.** (B) The COMPLEAT result page includes an interactive scatterplot where each point on the scatter plot represents a single complex whose position corresponds to the score. Size reflects the relative complex size, and color corresponds to the p-value. The user has the option to change the p-value threshold using p-value adjustment sliders. When a user selects the complex of interest from the scatter-plot, the network illustrations of the complexes are displayed on the Web Cytoscape panel (right panel of the same page). The node color in the network corresponds to the user input values, and the color-code ranges from blue to red (blue corresponds to the lowest value, and red is the maximum value). Note that the gray node represents a missing value, meaning that a particular gene or protein is present in the complex but missing in the user input data.

There are two types of edges: Solid edges correspond to known PPIs. Broken edges are interologs (proteins for which the ortholog gene pairs in another species are known to physically interact). The user has the options to zoom in or out in the network and save the network images. (C) Additional information about complexes or proteins can be obtained by clicking nodes or complexes. For example, clicking a node takes the user to the corresponding gene or protein database. Clicking a complex provides annotation regarding the complex, such as the original source, purification method or prediction algorithm, PubMed references (if available), sub-cellular locations and co-cited literature (see Materials and Methods for details).

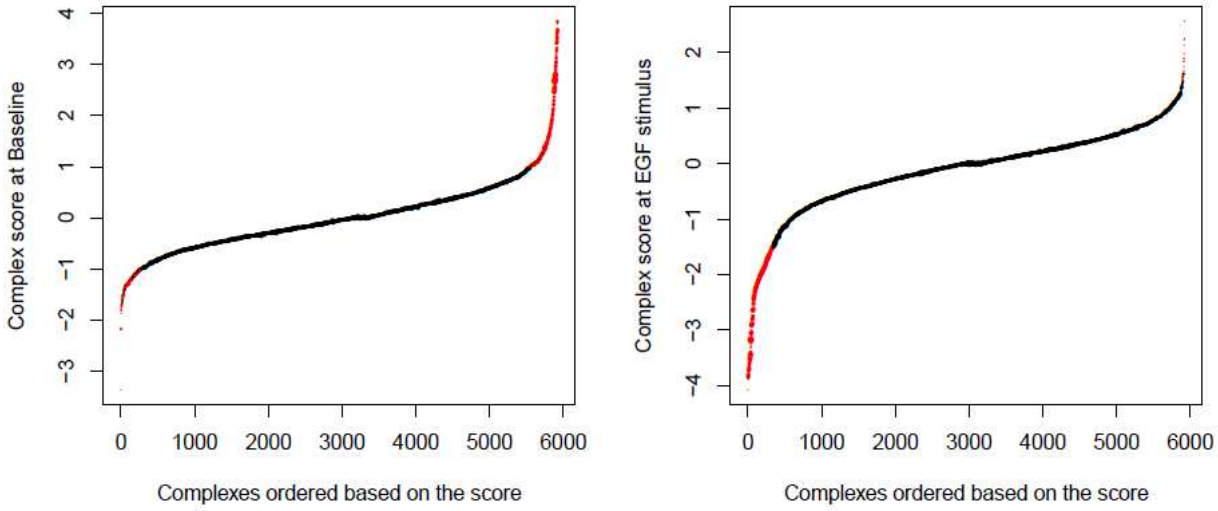


Figure S3: Complex enrichment results of baseline and EGF stimulus. (A) Distribution of complex scores from baseline data. Significant complexes are highlighted in red (p-value ≤ 0.01 and score ≥ 1 or ≤ -1). (B) Complex score distribution from EGF stimulus data. Significant complexes are shown in red (p-value ≤ 0.01 and the score ≥ 1.5 or ≤ -1.5). The point size is proportional to the complex size.

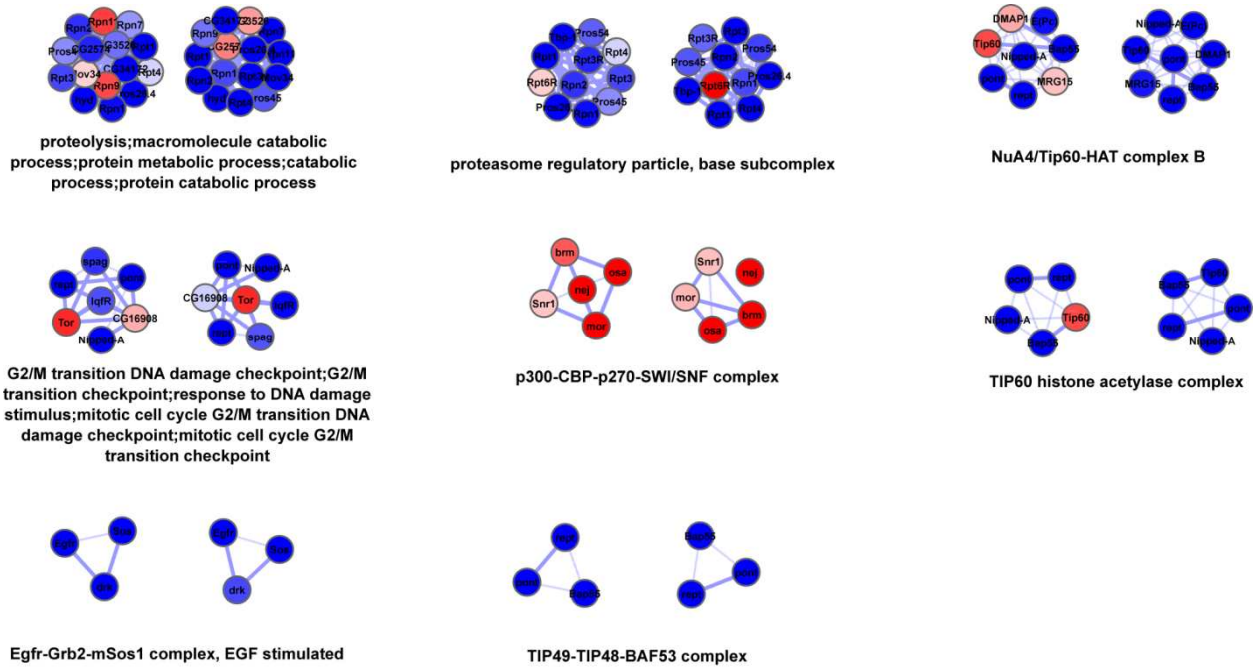
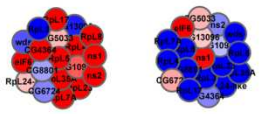
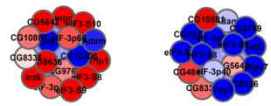


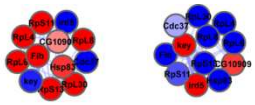
Figure S4: Baseline compared with EGF stimulus common complexes. Non-redundant complexes corresponding to table S16 are shown. Each complex is represented twice; the complex on the left corresponds to baseline, and that to the right represents the stimulus condition. The network picture was generated using Cytoscape software (www.cytoscape.org/). The node color ranges from dark blue to dark red, where the lowest value correspond to dark blue (negative Z-score) and highest score corresponds to dark red (positive z-scores). Solid edges correspond to known PPI and broken edges correspond to interolog.



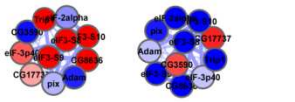
Yph1-L



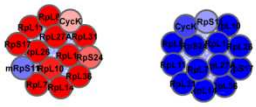
eIF3 complex (EIF3S6, EIF3S5, EIF3S4, EIF3S3, EIF3S6IP, EIF3S2, EIF3S9, EIF3S12, EIF3S10, EIF3S8, EIF3S1, EIF3S7, PCID1)



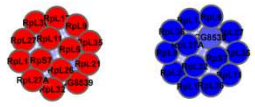
TNF-alpha/NF-kappa B signaling complex 6



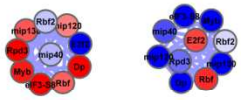
cellular macromolecule biosynthetic process;cellular protein metabolic process;translational initiation;translation;macromolecule biosynthetic process



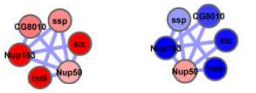
centrosome organization;mitotic spindle organization;centrosome cycle;centrosome duplication;mitotic spindle elongation



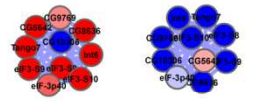
centrosome organization;mitotic spindle organization;centrosome cycle;centrosome duplication;mitotic spindle elongation



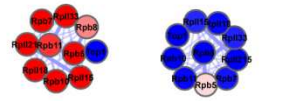
eggshell chorion assembly;negative regulation of transcription from RNA polymerase II promoter;eggshell chorion gene amplification;negative regulation of transcription, DNA-dependent;regulation of transcription from RNA polymerase II promoter



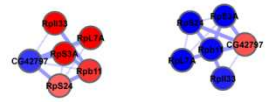
transmembrane receptor protein serine/threonine kinase signaling pathway;protein targeting;nuclear import;protein import into nucleus;SMAD protein import into nucleus



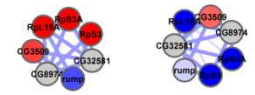
cellular biosynthetic process;cellular macromolecule biosynthetic process;cellular protein metabolic process;translational initiation;translation



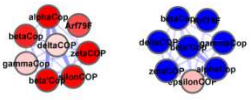
DNA-directed RNA polymerase II, core complex



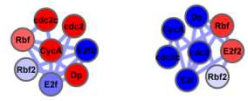
cellular biosynthetic process;cellular macromolecule biosynthetic process;cellular macromolecule metabolic process;gene expression;macromolecule biosynthetic process



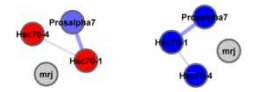
cellular component organization at cellular level;mitotic cell cycle;cell cycle phase;organelle organization;M phase



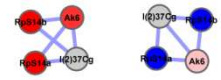
Coatomer-Arf1 complex



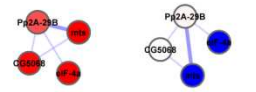
S-phase-specific E2F-p107 complex



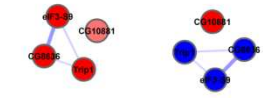
DNAJB2-HSPA8-PSMA3 complex



cellular macromolecule biosynthetic process;cellular macromolecule metabolic process;gene expression;macromolecule biosynthetic process



PPP2R1A-PPP2R1B-PPP2CA-PPME1-EIF4A1 complex



EIF3 complex (EIF3B, EIF3G, EIF3I)

nuclear-transcribed mRNA catabolic process, deadenylation-dependent decay;nuclear-transcribed mRNA catabolic process;G2/M transition DNA damage checkpoint;nuclear-transcribed mRNA poly(A) tail shortening;mitotic cell cycle G2/M transition DNA damage checkpoint

Ccna2-Cdk2 complex;CDC2-CCNA2-CDK2 complex;CDK2-CCNA2 complex;CyclinA2-Cdk2 complex

Malpighian tubule morphogenesis;centrosome cycle;centrosome duplication;mitotic sister chromatid separation;mitotic sister chromatid segregation

Figure S5: continued…

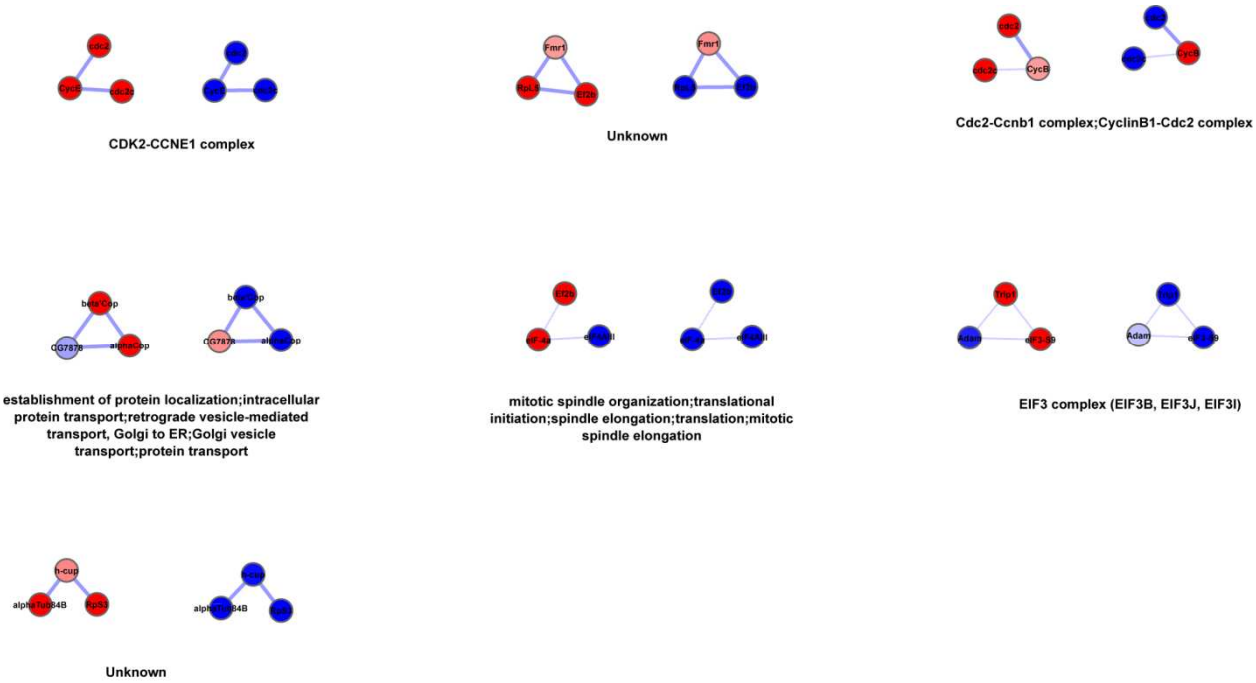


Figure S5: Baseline compared with EGF stimulus dynamic complexes: opposing effects. Non-redundant complexes corresponding to table S17 are shown. Node color and edge style are as described in figure S4.

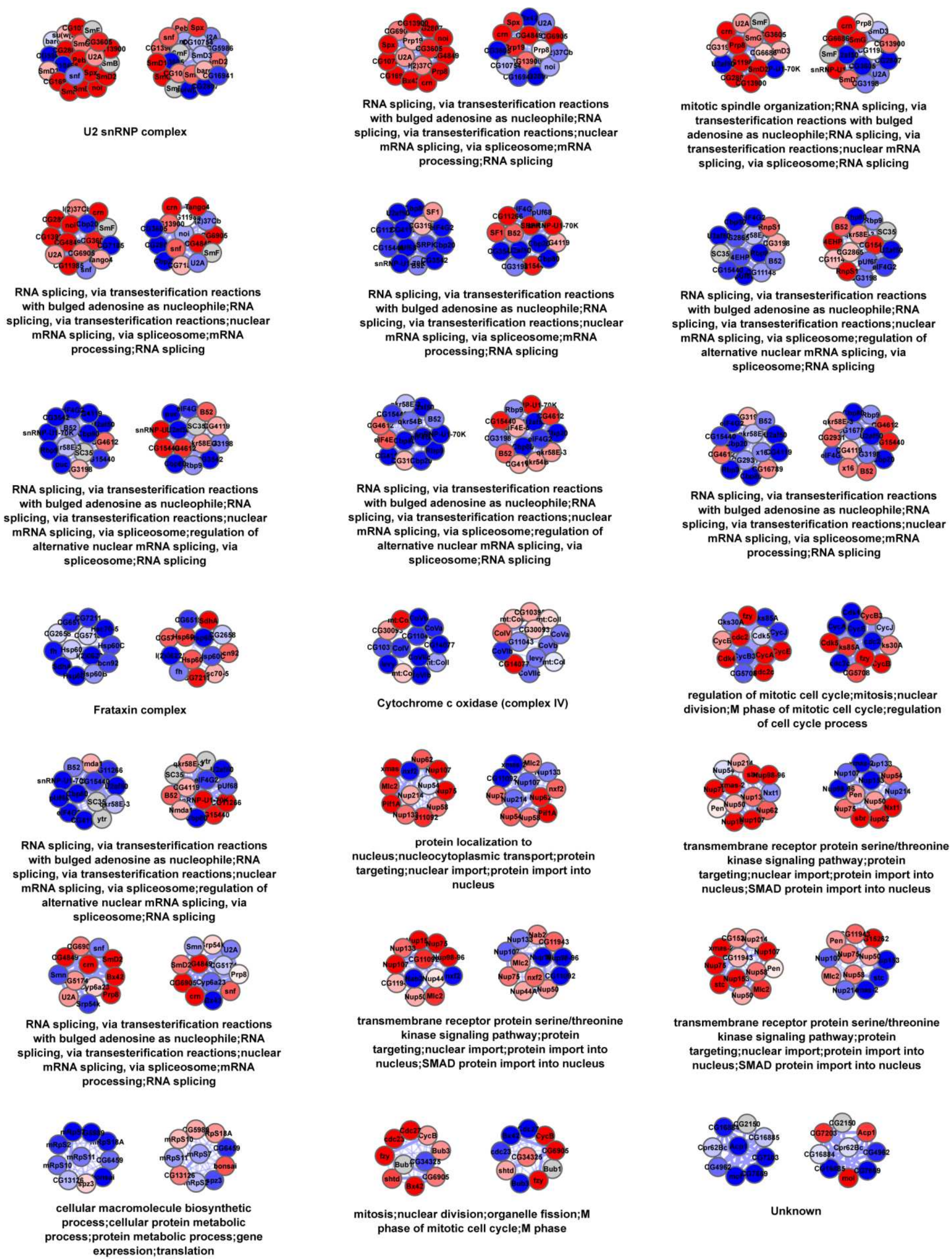
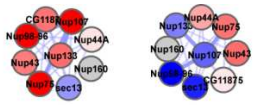
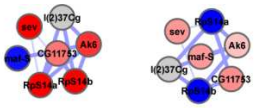


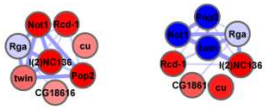
Figure S6: Continued…



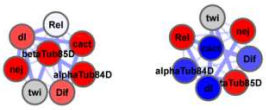
Nup 107-160 subcomplex



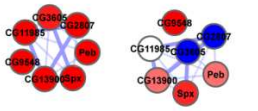
cellular macromolecule metabolic process;macromolecule metabolic process



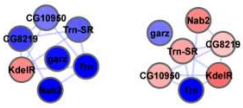
CCR4-NOT complex



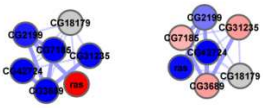
positive regulation of transcription, DNA-dependent;regulation of RNA biosynthetic process;regulation of transcription, DNA-dependent;regulation of transcription from RNA polymerase II promoter;positive regulation of transcription from RNA polymerase II promoter



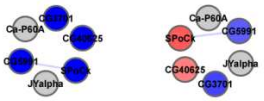
SF3b complex



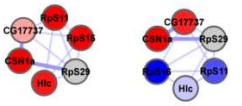
intracellular protein transport;nucleocytoplasmic transport;protein targeting;nuclear import;protein import into nucleus



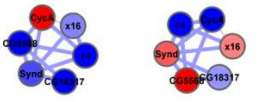
nucleic acid phosphodiester bond hydrolysis;mRNA metabolic process;mRNA cleavage;mRNA processing;RNA processing



purine ribonucleotide biosynthetic process;purine ribonucleoside triphosphate metabolic process;ATP metabolic process;purine ribonucleoside triphosphate biosynthetic process;ATP biosynthetic process



cellular macromolecule biosynthetic process;spindle elongation;gene expression;translation;mitotic spindle elongation



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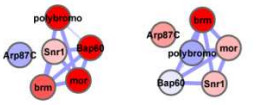
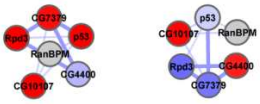
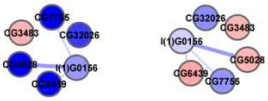


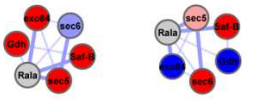
RSC complex



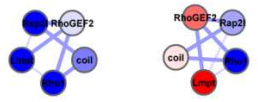
regulation of neuron differentiation



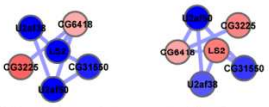
Isocitrate dehydrogenase



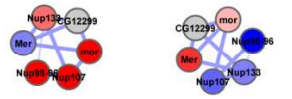
synaptic vesicle docking involved in exocytosis;border follicle cell migration;synaptic vesicle exocytosis;ovarian follicle cell migration;synaptic vesicle targeting



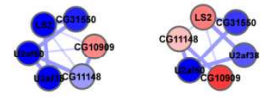
cell elongation involved in imaginal disc-derived wing morphogenesis;posterior midgut invagination;regulation of neuron projection development;germ-band extension;regulation of axonogenesis



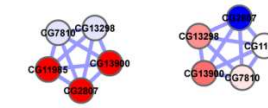
RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;regulation of alternative nuclear mRNA splicing, via spliceosome;mRNA processing



protein localization to nucleus;transmembrane receptor protein serine/threonine kinase signaling pathway;nuclear import;protein import into nucleus;SMAD protein import into nucleus



RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;regulation of alternative nuclear mRNA splicing, via spliceosome;mRNA processing



mitotic spindle organization;RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;RNA splicing

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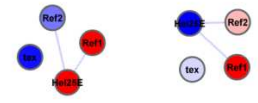
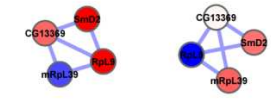
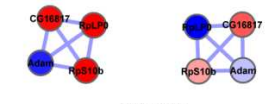


transcription export complex



mitotic spindle organization

ING1-p300-PCNA complex



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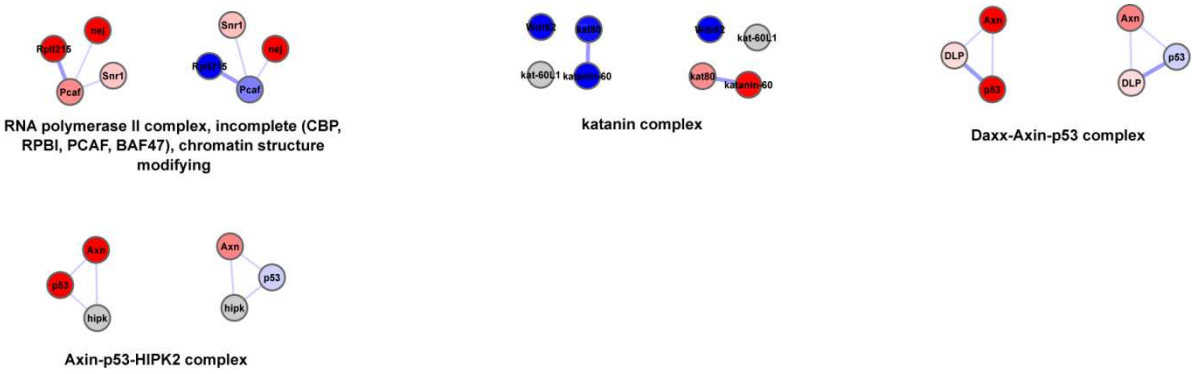
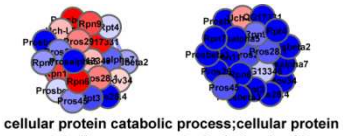
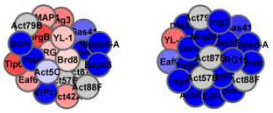


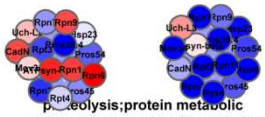
Figure S6: Baseline compared with EGF stimulus: baseline-specific dynamic complexes. Non-redundant complexes corresponding to table S17 are shown. Node color and edge style are as described in figure S4.



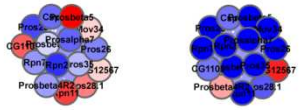
cellular protein catabolic process;cellular protein metabolic process;proteolysis involved in cellular protein catabolic process;cellular macromolecule catabolic process;protein catabolic process



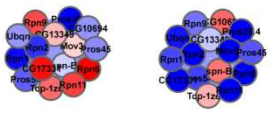
TRRAP/TIP60



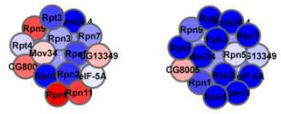
proteolysis;protein metabolic process;macromolecule catabolic process;primary metabolic process;protein catabolic process



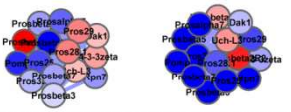
cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;modification-dependent protein catabolic process;modification-dependent macromolecule catabolic process;ubiquitin-dependent protein catabolic process



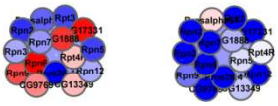
cellular response to stress;proteolysis;protein metabolic process;cellular macromolecule metabolic process;response to DNA damage stimulus



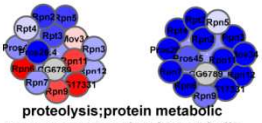
proteolysis;protein metabolic process;macromolecule metabolic process;primary metabolic process;metabolic process



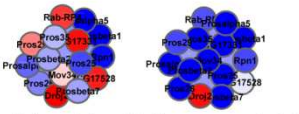
cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;modification-dependent protein catabolic process;modification-dependent macromolecule catabolic process;ubiquitin-dependent protein catabolic process



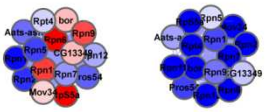
proteolysis;protein metabolic process;macromolecule metabolic process;primary metabolic process;metabolic process



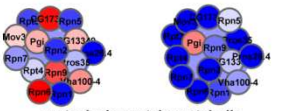
proteolysis;protein metabolic process;macromolecule metabolic process;primary metabolic process;metabolic process



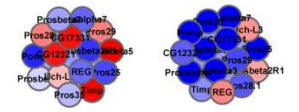
cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;modification-dependent protein catabolic process;modification-dependent macromolecule catabolic process;ubiquitin-dependent protein catabolic process



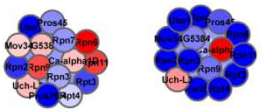
proteolysis;protein metabolic process;macromolecule metabolic process;primary metabolic process;metabolic process



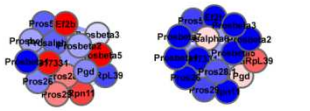
proteolysis;protein metabolic process;macromolecule metabolic process;catabolic process;primary metabolic process



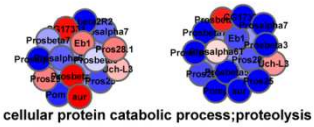
cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;modification-dependent protein catabolic process;modification-dependent macromolecule catabolic process;ubiquitin-dependent protein catabolic process



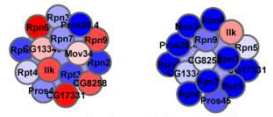
proteolysis;protein metabolic process;macromolecule catabolic process;catabolic process;protein catabolic process



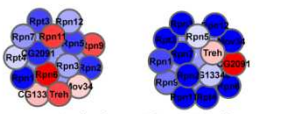
proteolysis;cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;cellular macromolecule catabolic process;protein catabolic process



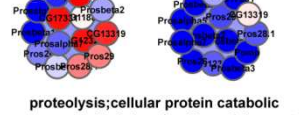
cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;modification-dependent protein catabolic process;modification-dependent macromolecule catabolic process;ubiquitin-dependent protein catabolic process



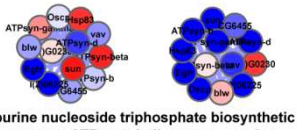
proteolysis;protein metabolic process;macromolecule metabolic process;primary metabolic process;metabolic process



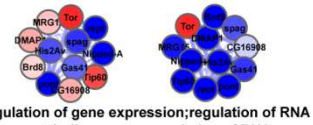
proteolysis;protein metabolic process;macromolecule metabolic process;primary metabolic process;metabolic process



proteolysis;cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;cellular macromolecule catabolic process;protein catabolic process



purine nucleoside triphosphate biosynthetic process;ATP metabolic process;purine ribonucleoside triphosphate biosynthetic process;ATP biosynthetic process;ATP synthesis coupled proton transport



regulation of gene expression;regulation of RNA metabolic process;regulation of RNA biosynthetic process;regulation of cellular macromolecule biosynthetic process;regulation of transcription, DNA-dependent

Figure S7: Continued…

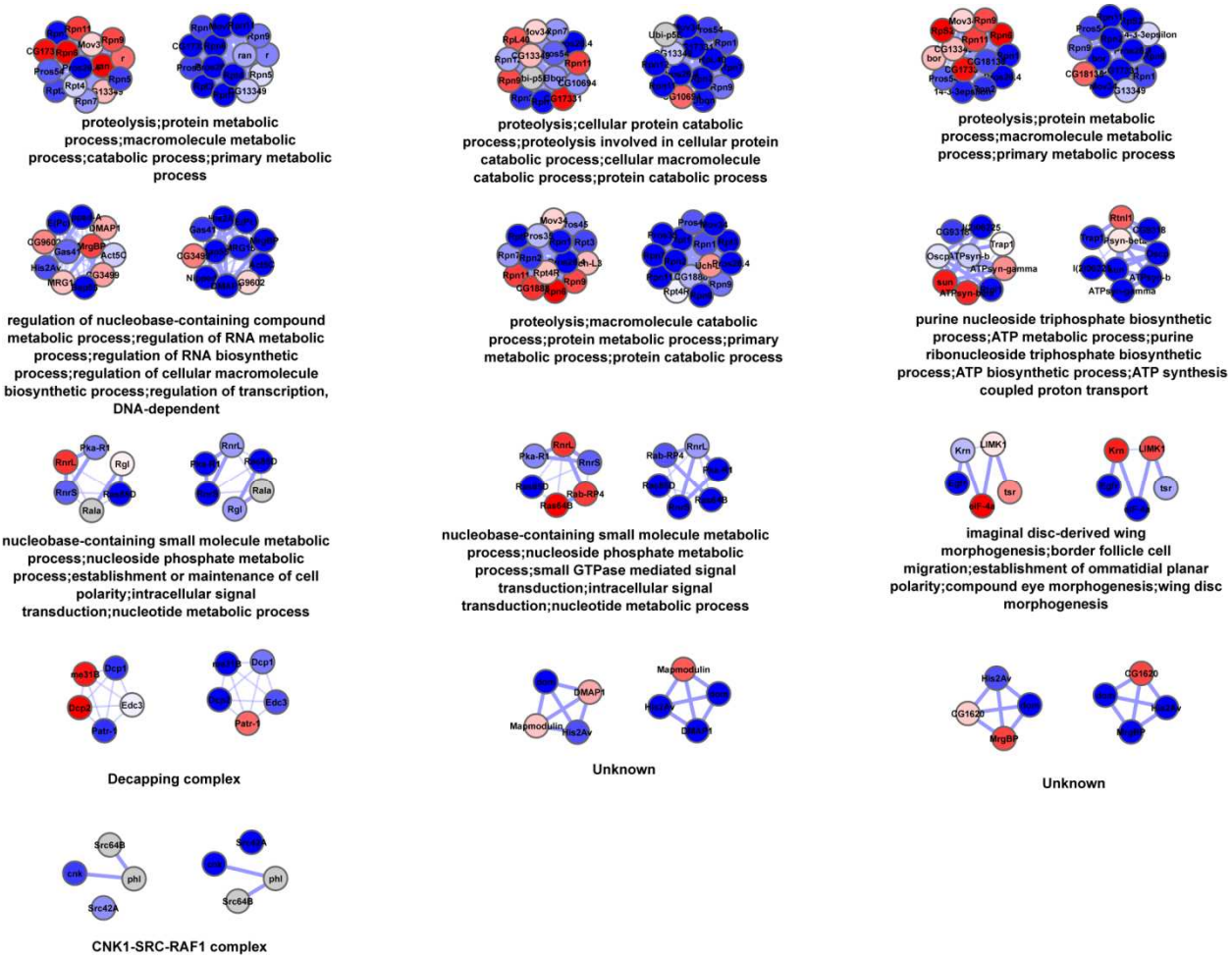


Figure S7: Baseline compared with EGF stimulus: stimulus-specific dynamic complexes. Non-redundant complexes corresponding to table S17 are shown. Node color and edge style are as described in figure S4.

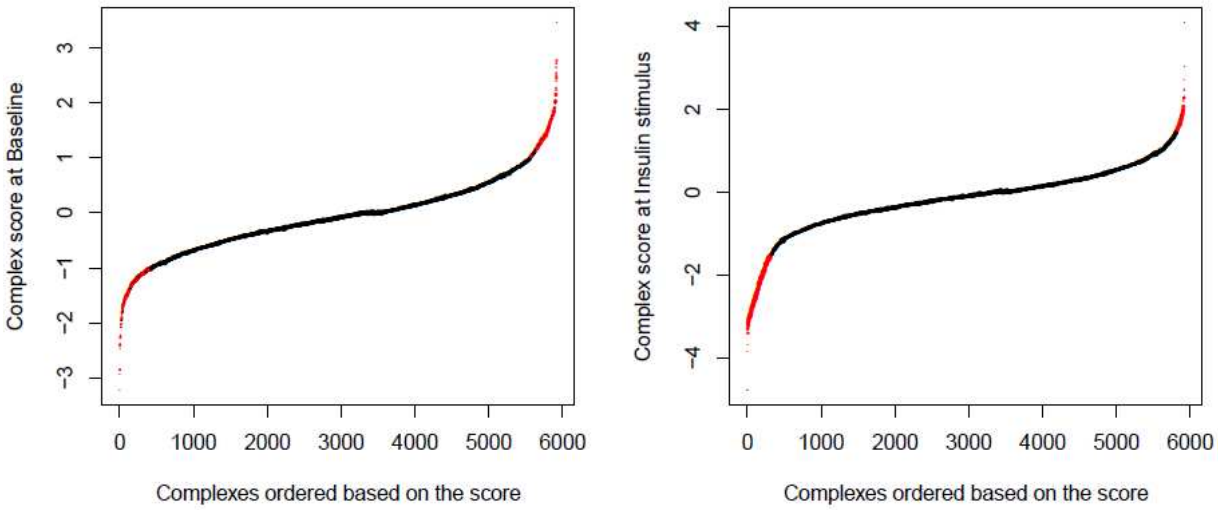
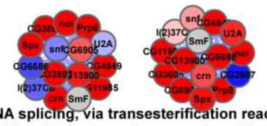
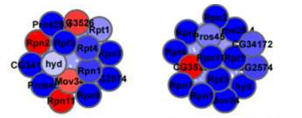


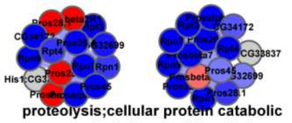
Figure S8: Complex enrichment results of baseline and insulin stimulus. (A) Baseline complex scores distribution. Significant complexes are highlighted in red (p-value ≤ 0.01 and score ≥ 1 or ≤ -1). (B) Complex score distribution from insulin stimulus data. Significant complexes are shown in red (p-value ≤ 0.01 and score ≥ 1.5 or ≤ -1.5). The point size is proportional to the complex size.



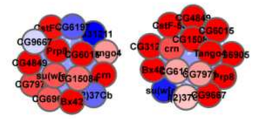
RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;mRNA processing;RNA splicing



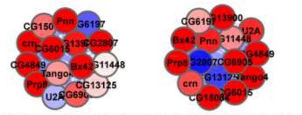
proteolysis;macromolecule catabolic process;protein metabolic process;catabolic process;protein catabolic process



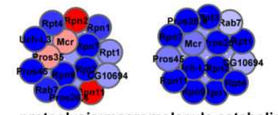
proteolysis;cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;cellular macromolecule catabolic process;protein catabolic process



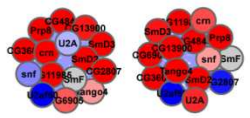
RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;mRNA processing;RNA splicing



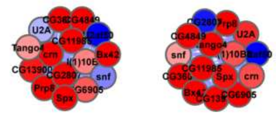
RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;mRNA processing;RNA splicing



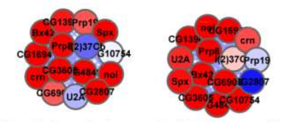
proteolysis;macromolecule catabolic process;protein metabolic process;macromolecule metabolic process;protein catabolic process



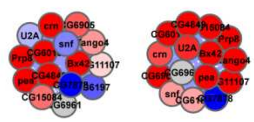
RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;mRNA processing;RNA splicing



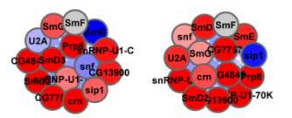
RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;mRNA processing;RNA splicing



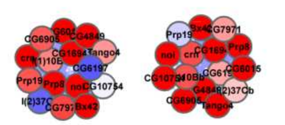
RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;mRNA processing;RNA splicing



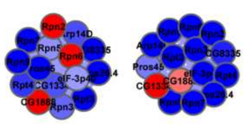
RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;mRNA processing;RNA splicing



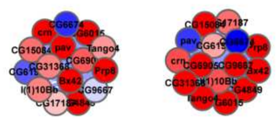
mitotic spindle organization;RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;RNA splicing



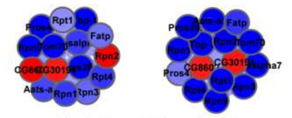
RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;mRNA processing;RNA splicing



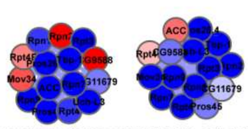
proteolysis;protein metabolic process;macromolecule metabolic process;primary metabolic process;metabolic process



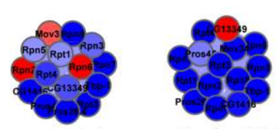
RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;mRNA processing;RNA splicing



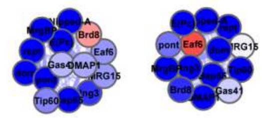
proteolysis;protein metabolic process;macromolecule metabolic process;primary metabolic process;metabolic process



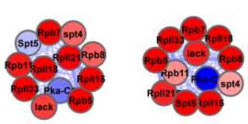
proteolysis;macromolecule catabolic process;protein metabolic process;macromolecule metabolic process;protein catabolic process



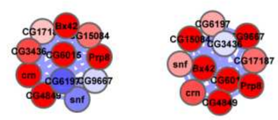
proteolysis;macromolecule catabolic process;protein metabolic process;primary metabolic process;protein catabolic process



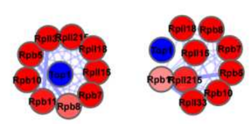
NuA4/Tip60 HAT complex;NuA4/Tip60-HAT complex A



G2/M transition DNA damage checkpoint;DNA damage checkpoint;mitotic cell cycle G2/M transition DNA damage checkpoint;mitotic cell cycle G2/M transition checkpoint;transcription from RNA polymerase II promoter



RNA splicing, via transesterification reactions with bulged adenosine as nucleophile;RNA splicing, via transesterification reactions;nuclear mRNA splicing, via spliceosome;mRNA processing;RNA splicing



DNA-directed RNA polymerase II, core complex

Figure S9: Continued…

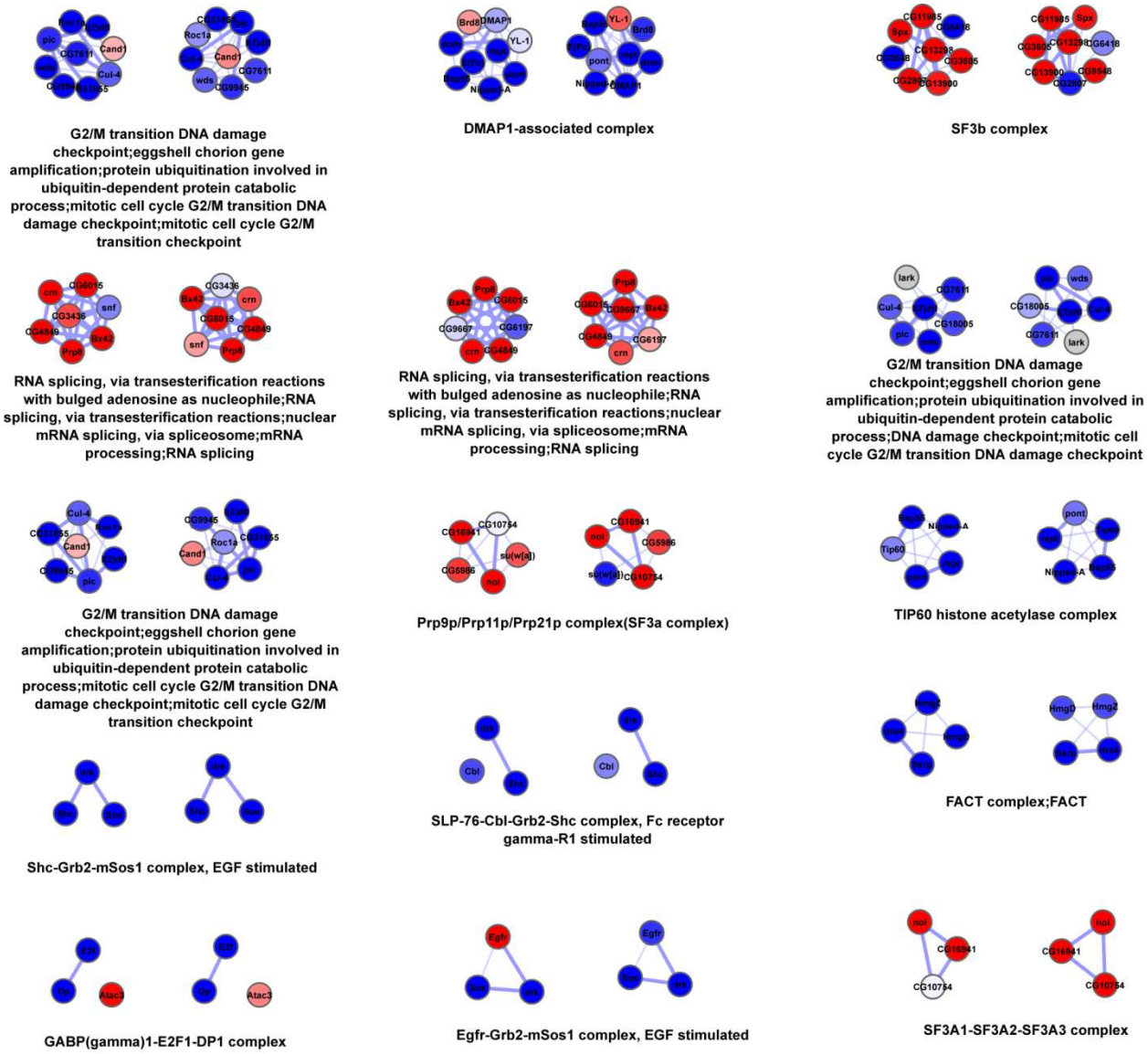
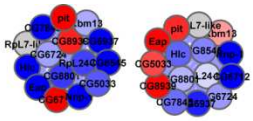
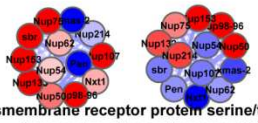


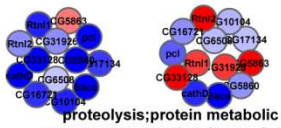
Figure S9: Baseline compared with insulin stimulus: common complexes. Non-redundant complexes corresponding to table S18 are shown. Node color and edge style are as described in figure S4.



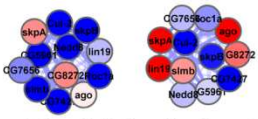
rRNA metabolic process;ncRNA metabolic process;ncRNA processing;rRNA processing;RNA processing



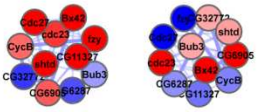
transmembrane receptor protein serine/threonine kinase signaling pathway;protein targeting;nuclear import;protein import into nucleus;SMAD protein import into nucleus



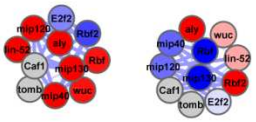
proteolysis;protein metabolic process;macromolecule metabolic process;primary metabolic process;metabolic process



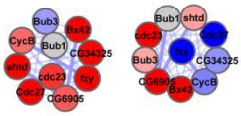
regulation of mitotic cell cycle;proteolysis involved in cellular protein catabolic process;modification-dependent protein catabolic process;modification-dependent macromolecule catabolic process;ubiquitin-dependent protein catabolic process



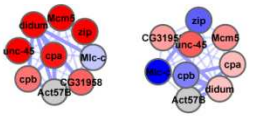
mitosis;nuclear division;M phase of mitotic cell cycle;regulation of cell cycle process;M phase



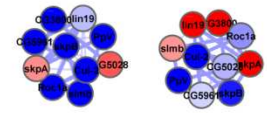
LINC complex, quiescent cells



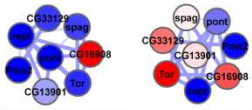
mitosis;nuclear division;organelle fission;M phase of mitotic cell cycle;M phase



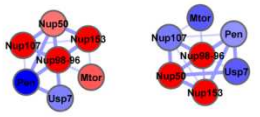
cellular component organization at cellular level;cellular process involved in reproduction;cytoskeleton organization;organelle organization;actin cytoskeleton organization



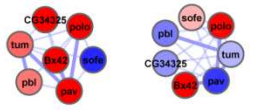
cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;modification-dependent protein catabolic process;modification-dependent macromolecule catabolic process;ubiquitin-dependent protein catabolic process



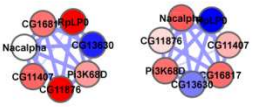
G2/M transition DNA damage checkpoint;G2/M transition checkpoint;DNA damage checkpoint;mitotic cell cycle G2/M transition DNA damage checkpoint;mitotic cell cycle G2/M transition checkpoint



transmembrane receptor protein serine/threonine kinase signaling pathway;protein targeting;nuclear import;protein import into nucleus;SMAD protein import into nucleus



mitotic spindle organization;cytokinesis, actomyosin contractile ring assembly;assembly of actomyosin apparatus involved in cell cycle cytokinesis;spindle organization;spindle assembly



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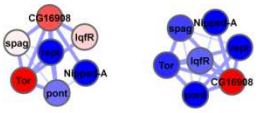
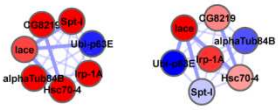


G2/M transition DNA damage checkpoint;G2/M transition checkpoint;response to DNA damage stimulus;mitotic cell cycle G2/M transition DNA damage checkpoint;mitotic cell cycle G2/M transition checkpoint



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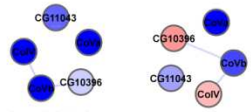
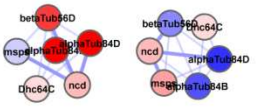
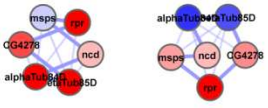


mitochondrial electron transport, cytochrome c to oxygen;oxidative phosphorylation;mitochondrial ATP synthesis coupled electron transport;ATP synthesis coupled electron transport;respiratory electron transport chain



purine ribonucleoside triphosphate metabolic process;purine nucleoside triphosphate catabolic process;purine ribonucleoside triphosphate catabolic process;GTP metabolic process;GTP catabolic process



ribonucleoside triphosphate catabolic process;purine nucleoside triphosphate catabolic process;purine ribonucleoside triphosphate catabolic process;GTP metabolic process;GTP catabolic process

Figure S10: Continued…

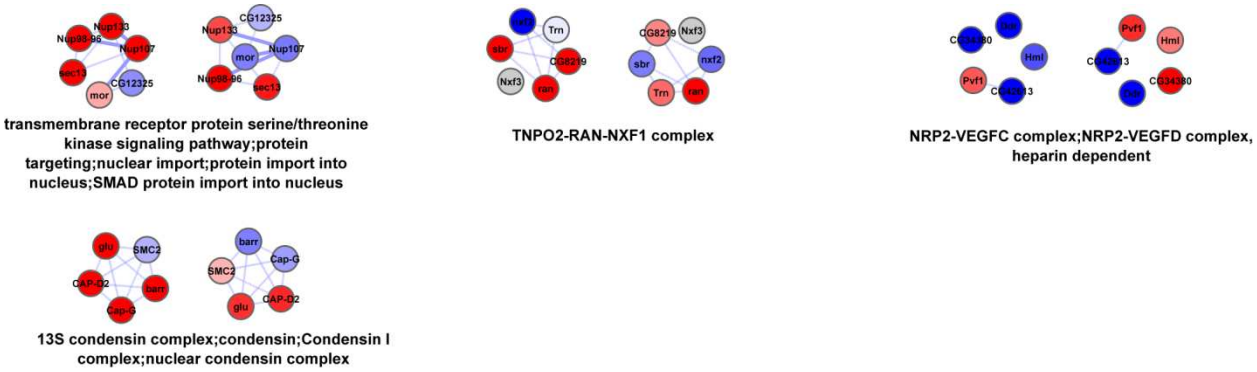
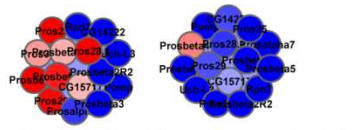
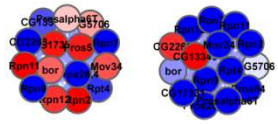


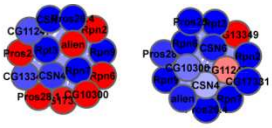
Figure S10: Baseline compared with insulin stimulus: baseline-specific dynamic complexes. Non-redundant complexes corresponding to table S19 are shown. Node color and edge style are as described in figure S4.



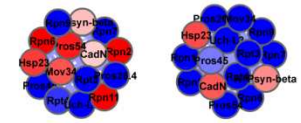
cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;modification-dependent protein catabolic process;modification-dependent macromolecule catabolic process;ubiquitin-dependent protein catabolic process



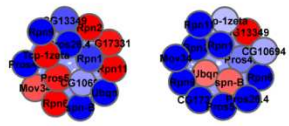
proteolysis;protein metabolic process;macromolecule metabolic process;primary metabolic process;metabolic process



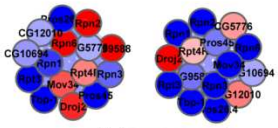
proteolysis;cell cycle phase;protein metabolic process;response to DA damage stimulus;protein catabolic process



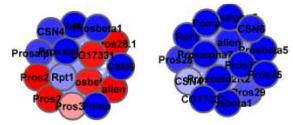
proteolysis;protein metabolic process;macromolecule catabolic process;primary metabolic process;protein catabolic process



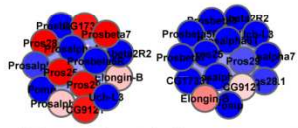
cellular response to stress;proteolysis;protein metabolic process;cellular macromolecule metabolic process;response to DNA damage stimulus



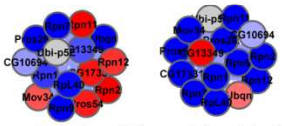
cellular response to stress;proteolysis;macromolecule catabolic process;protein catabolic process;response to DNA damage stimulus



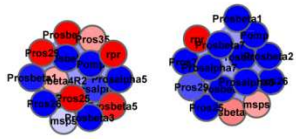
proteolysis;cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;response to DNA damage stimulus;protein catabolic process



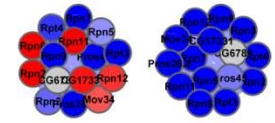
cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;modification-dependent protein catabolic process;modification-dependent macromolecule catabolic process;ubiquitin-dependent protein catabolic process



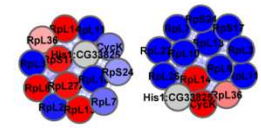
proteolysis;cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;cellular macromolecule catabolic process;protein catabolic process



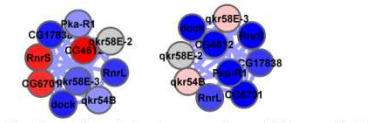
cellular protein catabolic process;proteolysis involved in cellular protein catabolic process;modification-dependent protein catabolic process;modification-dependent macromolecule catabolic process;ubiquitin-dependent protein catabolic process



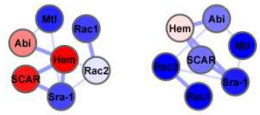
proteolysis;protein metabolic process;macromolecule metabolic process;primary metabolic process;metabolic process



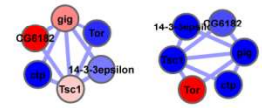
mitotic spindle organization;centrosome organization;centrosome cycle;centrosome duplication;mitotic spindle elongation



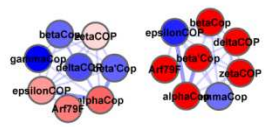
activation of cysteine-type endopeptidase activity involved in apoptotic process;regulation of cysteine-type endopeptidase activity involved in apoptotic process;activation of cysteine-type endopeptidase activity;positive regulation of cysteine-type endopeptidase activity;positive regulation of cysteine-type endopeptidase activity involved in apoptotic process



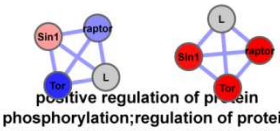
Wave-2 complex (Rac-activated)



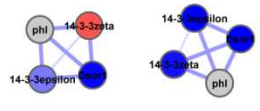
negative regulation of insulin receptor signaling pathway;regulation of GTPase activity;regulation of purine nucleotide catabolic process;regulation of GTP catabolic process;regulation of nucleotide catabolic process



Coatomer-Arf1 complex



positive regulation of protein phosphorylation;regulation of protein phosphorylation;positive regulation of protein modification process;positive regulation of phosphorylation;regulation of protein modification process



BRAF-MAP2K1-MAP2K2-YWHAE complex;RAF1-MAP2K1-YWHAE complex

Figure S11: Continued…

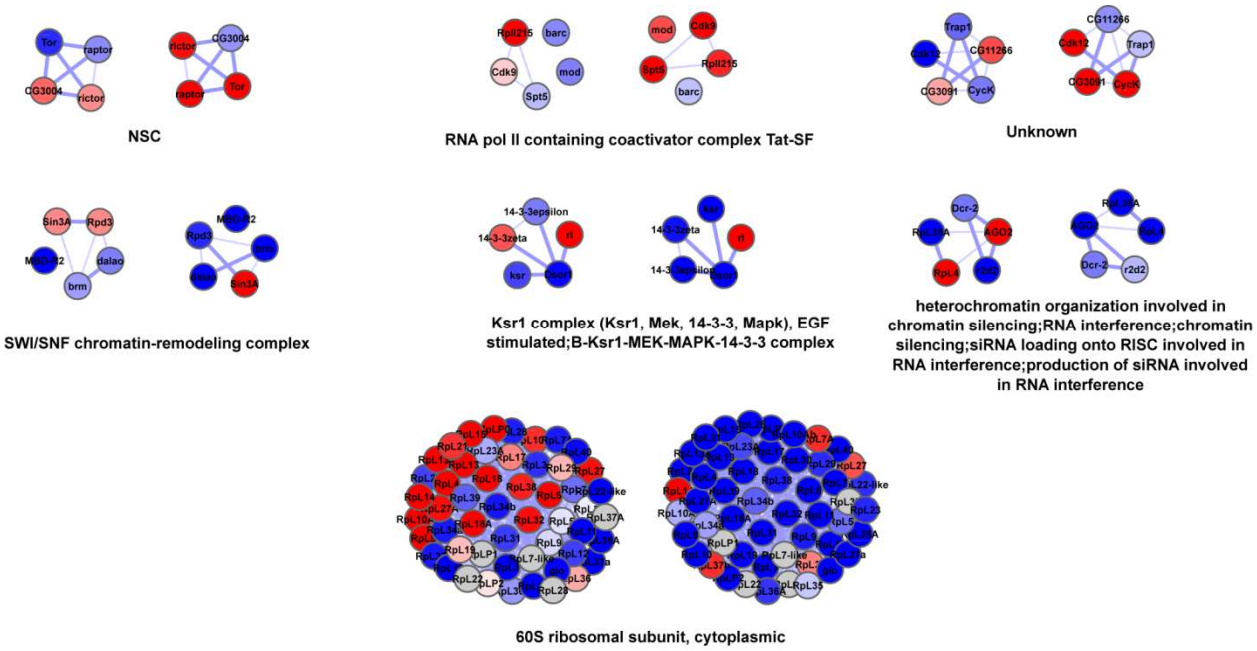


Figure S11: Baseline compared with insulin stimulus: stimulus-specific dynamic complexes. Non-redundant complexes corresponding to table S19 are shown. Node color and edge style are as described in figure S4.

Table S1: Compilation of literature protein complexes for humans, *Drosophila*, and yeast. Complex source are either from literature curation (LC) or high confidence complexes reported in literature based on high-throughput MS-pull down data (HT). Source organism: the organism in which the protein complex is reported in the database or publication. Ortholog mapping: the protein complexes were mapped to other organism using DIOPT (17), an ortholog mapping tool.

Database/dataset	Source	Source organism	Ortholog mapping	Human	Drosophila	Yeast
CORUM (15)	LC	Human, mouse	Human, *Drosophila*, yeast	2363	2162	1395
PINdb (13)	LC	Human, yeast	Human, *Drosophila* and yeast	286	280	276
CYC2008 (14)	LC	Yeast	Human, *Drosophila*	358	346	408
	HT	Yeast	Human, Drosophila	343	333	400
Gene Ontology (2)	LC	Human, *Drosophila*, yeast	No mapping	282	146	304
Drosophila AP-MS pull-down complexes (16)	HT	Drosophila	Human, yeast	511	556	331
KEGG module (3)	LC	Human	*Drosophila*, yeast	210	196	193
SignaLink (32)	LC	Human, *Drosophila*	yeast	14	14	14
FlyReactome (52)	LC	*Drosophila*	Human, yeast	9	9	9
All literature complex				3638	3077	2173

Table S2: PPI data sets used to construct integrated PPI networks for humans, *Drosophila*, and yeast. Name of the data set, publication reference, URL, number of PPIs and proteins in the data set are given. All the PPI datasets are downloaded from the corresponding Website and the database version corresponds to the March 2012 release. For humans and yeast, the protein or gene identifiers are mapped to NCBI Entrez gene identifier. In case of *Drosophila*, the gene or protein identifiers are mapped to Flybase gene identifier.

Database/datasets	**Human**		**Drosophila**		**Yeast**	
	PPIs	Proteins	PPIs	Proteins	PPIs	Proteins
BioGrid (33) http://thebiogrid.org/	59226	12529	23916	7305	60062	5374
IntAct (53) http://www.ebi.ac.uk/intact/	40368	9468	25385	7530	76147	5555
DIP (54) http://dip.doe-mbi.ucla.edu/dip/Main.cgi	2860	1855	19753	6584	22028	4675
MINT (55) http://cbm.bio.uniroma2.it/mint/	19048	6315	17336	5917	27680	5104
HPRD (35) http://www.hprd.org/	39172	9670	-	-	-	-
DroID (36) http://www.droidb.org/	-	-	87070	9068	-	-
Drosophila AP-MS dataset (16)	-	-	10964	2296	-	-
MasterNet (integrated network)	108059	14495	98500	9373	118603	5729

Table S3: Predicted protein complexes for humans, *Drosophila*, and yeast. CFinder (38) was applied for humans, *Drosophila* and yeast filtered PPI networks. NetworkBLAST (19) was applied to identify protein complexes by aligning human and *Drosophila*, human and yeast, and *Drosophila* and yeast PPI networks.

Prediction source	**Human**		**Drosophila**		**Yeast**	
	Complexes	Proteins	Complexes	Proteins	Complexes	Proteins
CFinder / Human PPI	713	2046	-	-	-	-
CFinder / *Drosophila* PPI	-	-	433	1419	-	-
CFinder / Yeast PPI	-	-	-	-	423	1465
NetworkBLAST / Human vs. Drosophila PPI	1722	2665	1722	2638	-	-
NetworkBLAST / Human vs. Yeast PPI	3820	4369	-	-	3820	2712
NetworkBLAST / *Drosophila* vs. Yeast PPI	-	-	1532	2279	1532	1840
All predicted complexes	6251	6334	3639	3933	5551	3366

Table S4: Redundancy in the protein complex resource. A protein complex is defined as redundant if it is a subset, superset or shares 80% of proteins with the other complexes in the resource. Non-redundant complexes are constructed at 80%, meaning that no two complexes share more than 80% similarity. This table corresponds to Figure 2B.

Complexes	Human	Drosophila	Yeast
All complexes	9881	6703	7713
Non-redundant	5164	3399	3183
Redundant complexes	4717	3304	4530

Table S5: Overlap of the literature and predicted complexes at the protein level.

Organism	Literature specific		Predicted specific		Common		Total
	Proteins	Percentage	Proteins	Percentage	Proteins	Percentage	Proteins
Human	2959	31.8%	1769	19%	4565	49.1%	9293
Drosophila	2603	39.8%	917	14%	3016	46.1%	6536
Yeast	628	15.7%	714	17.9%	2652	66.4%	3994

Table S6: Proteome covered by the protein complex resources. This table corresponds to the Figure 2E.

Complexes	**Human**		**Drosophila**		**Yeast**	
	Covered	Total	Covered	Total	Covered	Total
All proteins	9293	20402	6536	13776	3994	5882
Conserved proteins	5161	6203	4009	5249	3184	3551

Table S7: Comparison of protein complexes with GO and KEGG with respect to co-citation. Significant and total protein complexes, GO categories and KEGG pathways are shown. Significant protein complexes, GO, and KEGG refers to significantly co-cited protein complexes compared to 1000 random sets of the same size ($p < 0.05$). This table corresponds to Figure 2G.

Resource	**Human**		**Drosophila**		**Yeast**	
	Significant	Total	Significant	Total	Significant	Total
Complexes	8757	9125	4545	5817	6708	7098
GO	5119	5994	2170	2457	1901	2036
KEGG	100	102	110	129	167	178

Table S8: Comparison of protein complexes with GO and KEGG with respect to protein colocalization. Significant and total protein complexes, GO categories and KEGG pathways are shown. Significant protein complexes, GO, and KEGG refers to significantly colocalized protein complexes compared to 1000 random sets of the same size ($p < 0.05$). This table corresponds to Figure 2H.

Resource	**Yeast**	
	Significant	Total
Complexes	3518	6682
GO	511	1976
KEGG	77	177

Table S9: Comparison of protein complexes with GO and KEGG with respect to gene coexpression. Significant and total protein complexes, GO categories and KEGG pathways are shown. Significant protein complexes, GO, and KEGG refers to significantly coexpressed genes compared to 1000 random sets of the same size ($p < 0.05$). This table corresponds to Figure 2H.

Resource	**Human**		**Drosophila**	
	Significant	Total	Significant	Total
Complexes	5364	8450	4015	5491
GO	2082	6293	1787	2628
KEGG	126	175	159	189

Table S10: Annotation of the protein complex resource. Literature annotation corresponds to the annotation from the source database. GO enrichment was performed if the complex was predicted or if the annotation was available from the literature. Unknown complexes are new complexes for which no functional theme is associated. This table corresponds to Figure 2I.

Complexes	**Human**	**Drosophila**	**Yeast**
Literature annotation	3784	3372	2838
GO enrichment	5721	2614	4613
Unknown	376	717	262
Total	9881	6703	7713

Table S11: Gene or protein input identifiers supported by the COMPLEAT.

Identifier type	Human	Drosophila	Yeast
Symbol	Entrez gene symbol	Flybase gene symbol	Entrez gene symbol
Gene identifier	Entrez gene identifier	Entrez gene identifier	Entrez gene identifier
Protein identifier	Uniprot identifier	Uniprot identifier	Uniprot identifier
Species specific identifier	Entrez gene identifier	Flybase gene identifier	Locus tag

Table S20: Dynamic phosphosites changing in response to insulin treatment. A systematic investigation of insulin-induced phosphorylation using mass spectrometry and isobaric labeling of S2R+ cells identified dynamic phosphorylation of Moira and MBD-R2 following a 10-minute insulin stimulus including the Akt/RSK/S6 consensus motifs on Moira. This observation is consistent with human data, where Akt phosphorylates the human ortholog of Moira (BAP155) (48). Method: Biological duplicates of two conditions (no treatment or 10 minutes insulin treatment) were analyzed. Cells were lysed in 8 M urea, 75 mM NaCl, 50 mM Tris, pH 8.2, protease inhibitors cocktail (Roche), 1 mM NaF, 1 mM β-glycerophosphate, 1 mM sodium orthovanadate, 10 mM sodium pyrophosphate, 1 mM PMSF. 1mg of protein from each replicate was digested with trypsin (Promega) and processed as reported by Dephoure and Gygi (56). 12 strong cation exchange (SCX) fractions were subjected to phosphopeptide enrichment using IMAC-Select Affinity Gel (Sigma-Aldrich) and subsequent peptide desalting with Stagetips (57). Samples were analyzed on an LTQ OrbiTrap Velos mass spectrometer (Thermo Fisher Scientific) using a data-dependent Top10-MS2 method using (higher-energy collisional dissociation) HCD for reporter ion quantitation. Peptide identification and filtering was performed following the methods of Dephoure and Gygi (56) but using a composite *Drosophila melanogaster* protein database. Data normalization and phosphosite localization was performed as previously described (58). The phosphorylation sites indicated above for Moira and MBD-R2 were localized with near certainty using the Ascore algorithm (Ascore > 19).

Protein identifier	Symbol	Phosphosite	Fold change Log2(10'/0')	Akt/RSK/S6 consensus motif (RxxS/T) (47)	Phosphosite
FBpp0082692	Mor	PGKRKRS#PAVVHK	0.30	Yes	Ser^{327}
FBpp0082081	MBD-R2	KRASTGS#LGGSSG	0.26	No	Ser^{288}