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Supplemental Information

**Changes of Cell Biochemical States Are Revealed
in Protein Homomeric Complex Dynamics**

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Table S5. Significance of the overlap between metformin hits and homologs in the budding yeast for genes associated to different diseases in *Homo sapiens* (related to Figure 3).

Disease	GWA studies (#)	Associated SNPs (#)	Mapped <i>Homo sapiens</i> genes (#)	Homolog ORFs in yeast (#)	Tested ORFs in metformin <i>hdPCA</i> (#)	Common ORFs with metformin <i>hdPCA</i> hits (#)	Hyper-geometric test (<i>P</i> -value)
Breast cancer	30	135	138	41	26	3	0.937
Breast cancer (early onset)	1	18	11	10	8	1	0.852
Colorectal cancer	20	82	75	22	19	4	0.599
Epithelial ovarian cancer	2	22	54	16	11	3	0.424
Lung cancer	11	27	43	11	9	1	0.883
Ovarian cancer	5	15	44	13	10	2	0.661
Pancreatic cancer	6	48	121	28	20	2	0.946
Prostate cancer	23	142	313	69	42	15	0.021
Type 2 diabetes Type 2 diabetes and other traits	42	231	185	45	26	11	0.012

Table S6. Common ORFs between metformin hits and homologs in the budding yeast for genes associated with type 2 diabetes in *Homo sapiens* (related to Figure 3).

Yeast ORF	Yeast Name	Homologs in <i>Homo sapiens</i>	GWAS # showing disease association	Pubmed ID	Description
<i>YBR164C</i>	<i>ARL1</i>	<i>ARL15</i>	1	24509480	Soluble GTPase with a role in regulation of membrane traffic
<i>YOL016C</i>	<i>CMK2</i>	<i>CAMK1D</i>	3	18372903 20862305 22961080	Calmodulin-dependent protein kinase
<i>YGL190C</i>	<i>CDC55</i>	<i>PPP2R2C</i>	1	19734900	Non-essential regulatory subunit B of protein phosphatase 2A (PP2A)
<i>YOR316C</i>	<i>COT1</i>	<i>SLC30A8</i>	12	17293876 17460697 17463246 19056611 19401414 17463248 17463249 19734900 20581827 22693455 23945395 24509480	Vacuolar transporter that mediates zinc transport into the vacuole
<i>YHR132C</i>	<i>ECM14</i>	<i>CPA6</i>	1	25102180	Putative metalloprotease with similarity to zinc carboxypeptidases
<i>YIL097W</i>	<i>FYV10</i>	<i>MAEA</i>	2	22158537 23945395	Subunit of GID complex
<i>YKL101W</i>	<i>HSL1</i>	<i>HUNK</i>	1	21490949	Nim1p-related protein kinase
<i>YMR165C</i>	<i>PAH1</i>	<i>LPIN2</i>	1	21490949	Mg ²⁺ -dependent phosphatidate (PA) phosphatase
<i>YER165W</i>	<i>PAB1</i>	<i>RBMS1</i>	1	20418489	Poly(A) binding protein
<i>YLR403W</i>	<i>SFP1</i>	<i>JAZF1</i>	3	20581827 24509480 18372903	Regulates transcription of ribosomal protein and biogenesis genes
<i>YIL030C</i>	<i>SSM4</i>	<i>MARCH1</i>	1	21490949	Ubiquitin-protein ligase involved in ER-associated protein degradation

Table S7. Common ORFs between metformin hits and homologs in the budding yeast for genes associated with prostate cancer in *Homo sapiens* (related to Figure 3).

Yeast ORF	Yeast Name	Homologs in <i>Homo sapiens</i>	GWAS # showing disease association	Pubmed ID	Description
YJR057W	CDC8	DTYMK	1	23535732	Thymidylate and uridylate kinase
YKR034W	DAL80	GATA5	1	23535732	Negative regulator of genes in multiple nitrogen degradation pathways
YKL002W	DID4	LINC00506 / CHMP2B	1	19767753	Class E Vps protein of the ESCRT-III complex
YJL110C	GZF3	GATA5	1	23535732	GATA zinc finger protein
YAL029C	MYO4	MYO6	1	25217961	Type V myosin motor involved in actin-based transport of cargos
YBR055C	PRP6	PRPF6	1	23535732	Splicing factor
YGR132C	PHB1	PHB	1	23535732	Subunit of the prohibitin complex (Phb1p-Phb2p)
YER095W	RAD51	RAD51B	1	23535732	Strand exchange protein
YJL026W	RNR2	RRM2	1	23535732	Ribonucleotide-diphosphate reductase (RNR), small subunit
YJL080C	SCP160	HDLBP	1	23535732	Essential RNA-binding G protein effector of mating response pathway
YLR403W	SFP1	JAZF1	1	18264096	Regulates transcription of ribosomal protein and biogenesis genes
YDR523C	SPS1	STK25	1	23535732	Putative protein serine/threonine kinase
YIL030C	SSM4	MARCH8	1	25217961	Ubiquitin-protein ligase involved in ER-associated protein degradation
YDL185W	VMA1	ATP6V1A	1	23535732	Subunit A of the V1 peripheral membrane domain of V-ATPase
YFL021W	GAT1	GATA5	1	23535732	Transcriptional activator of nitrogen catabolite repression genes