Supplementary information S1 (table). Sources of molecular interaction and 'omics' profiling data

	Interaction type(s)	Detection methodologies	Databases
Physical	Protein-protein	Yeast-2-hybrid (Y2H)[1-3], co-immuno-precipitation (Co-IP)[4], mass spectroscopy[5,6]}, affinity purification coupled with mass spectroscopy (AP/MS)[7,8]	BioGRID[9], IntAct[10], APID[11], STRING[12], MINT[13], DIP[14], HPRD[15], MIPS-MPPI[16], Netpath[17], DroiD[18]
	Protein-DNA (e.g., regulatory networks)	Yeast-1-hybrid (Y1H)[19], chromatin immuno-precipitation based methods (CHIP-CHIP)[20], DNA-footprinting[21]	TRANSFAC[22], UniProbe[23], DroiD[18], BioGRID[9], TcoF-DB[24], BIPA[25], hPDI[26], EDGEdb[27], NPIDB[28,29]
	Protein-RNA	RNA electro-mobility shift (RNA-EMSA)[30], RNA-pull down[31]	PRID[32], BIPA[25] NPInter[33], RBPDB[34], PRIDB[35], StarBase[36]
	Metabolic (e.g., enzyme-substrate, ligand-receptor)	Mass spectroscopy based selective reaction monitoring (SRM)[6,37], NMR[38], affinity purification[8], co-IP[3], fluorescence spectroscopy[39]	Reactome[40], KEGG [41], BioCyc and MetaCyc[42], HMDB[43,44], EcoCyc[45], HumanCyc[46], ConsensusPathDB[47]
	Protein/gene-compound (e.g., drug-target, chemical-protein)	Chemical structure[48,49], forward or reverse chemo-genomic/proteomic profiling[50-52], in silico predictions[53]	SuperTarget[54], Matador[54], DrugBank[55] ChemProt[56], STITCH[57], AffinDB[58], MatrixDB[59], PSMDB[60], PDB-Ligand[61], ChEMBL[62], ConsensusPathDB[47]
Functional	Genetic (gene-gene)	Synthetic genetic array (SGA)[63], Epistatic Miniarray Profiling (E-MAP)[64], co-expression profiling[65,66]	BioGRID[9], DRYGIN[67], CYGD[68], DroID[18], ConsensusPathDB[47]
	Gene-Disease	Literature curation, clinical and sequence information	OMIM[69], HuDiNe[70], Diseasome[71]
Omics data type		**Detection methodologies**	**Databases**
Transcriptomics		Microarray[72], RNASeq[73]	GEO[74], SMD[75], TCGA[76], GXD[77], ONCOMINE[78], ArrayExpress[79],
RNAi (phenomics)		RNAi interference assay[80]	RNAiDB[81], GenomeRNAi[82], siRecords[83]
Epigenomics		Methylation profiling[84]	DAnCER[85], DiseaseMeth[86], PubMeth[87], MethDB[88], MethCancerDB[89], MethyCancer[90]
Mutation / SNP		SNP Array[91], genome sequencing[92]	TCGA[76], dbSNP[93], dbQSNP[94], GWAS Central [95], OMIM[69]
Proteomics		CHIP [11,2,96], Mass Spectrometry[5,6]	PDB[97], ExPASy[98], InterPro[99], World-2DPage[100], JASPAR[101]
Phosphorylation profile		Mass Spectrometry[5], literature curation	PhosphoGRID[102], PhospoELM[103], PHOSIDA[104]

For more information and databases, visit www.pathguide.org

References

1. Fields, S. High-throughput two-hybrid analysis. The promise and the peril. *FEBS J* **272**, 5391-9 (2005).
2. Ito, T. et al. A comprehensive two-hybrid analysis to explore the yeast protein interactome. *Proc Natl Acad Sci U S A* **98**, 4569-74 (2001).
3. Pandey, A. & Mann, M. Proteomics to study genes and genomes. *Nature* **405**, 837-46 (2000).
4. Phizicky, E.M. & Fields, S. Protein-protein interactions: methods for detection and analysis. *Microbiol Rev* **59**, 94-123 (1995).
5. Ho, Y. et al. Systematic identification of protein complexes in Saccharomyces cerevisiae by mass spectrometry. *Nature* **415**, 180-3 (2002).
6. Aebersold, R. & Mann, M. Mass spectrometry-based proteomics. *Nature* **422**, 198-207 (2003).
7. Collins, M.O. & Choudhary, J.S. Mapping multiprotein complexes by affinity purification and mass spectrometry. *Curr Opin Biotechnol* **19**, 324-30 (2008).
8. Rigaut, G. et al. A generic protein purification method for protein complex characterization and proteome exploration. *Nat Biotechnol* **17**, 1030-2 (1999).
9. Stark, C. et al. BioGRID: a general repository for interaction datasets. *Nucleic Acids Res* **34**, D535-9 (2006).
10. Kerrien, S. et al. The IntAct molecular interaction database in 2012. *Nucleic Acids Res* **40**, D841-6 (2012).
11. Prieto, C. & De Las Rivas, J. APID: Agile Protein Interaction DataAnalyzer. *Nucleic Acids Res* **34**, W298-302 (2006).
12. Szklarczyk, D. et al. The STRING database in 2011: functional interaction networks of proteins, globally integrated and scored. *Nucleic Acids Res* **39**, D561-8 (2011).
13. Chatr-aryamontri, A. et al. MINT: the Molecular INTeraction database. *Nucleic Acids Res* **35**, D572-4 (2007).
14. Salwinski, L. et al. The Database of Interacting Proteins: 2004 update. *Nucleic Acids Res* **32**, D449-51 (2004).
15. Keshava Prasad, T.S. et al. Human Protein Reference Database--2009 update. *Nucleic Acids Res* **37**, D767-72 (2009).

16. Pagel, P. et al. The MIPS mammalian protein-protein interaction database. *Bioinformatics* **21**, 832-4 (2005).
17. Kandasamy, K. et al. NetPath: a public resource of curated signal transduction pathways. *Genome Biol* **11**, R3 (2010).
18. Yu, J., Pacifico, S., Liu, G. & Finley, R.L., Jr. DroID: the Drosophila Interactions Database, a comprehensive resource for annotated gene and protein interactions. *BMC Genomics* **9**, 461 (2008).
19. Reece-Hoyes, J.S. et al. Yeast one-hybrid assays for gene-centered human gene regulatory network mapping. *Nat Methods* **8**, 1050-2 (2011).
20. Mockler, T.C. et al. Applications of DNA tiling arrays for whole-genome analysis. *Genomics* **85**, 1-15 (2005).
21. Hampshire, A.J., Rusling, D.A., Broughton-Head, V.J. & Fox, K.R. Footprinting: a method for determining the sequence selectivity, affinity and kinetics of DNA-binding ligands. *Methods* **42**, 128-40 (2007).
22. Matys, V. et al. TRANSFAC: transcriptional regulation, from patterns to profiles. *Nucleic Acids Res* **31**, 374-8 (2003).
23. Newburger, D.E. & Bulyk, M.L. UniPROBE: an online database of protein binding microarray data on protein-DNA interactions. *Nucleic Acids Res* **37**, D77-82 (2009).
24. Schaefer, U., Schmeier, S. & Bajic, V.B. TcoF-DB: dragon database for human transcription co-factors and transcription factor interacting proteins. *Nucleic Acids Res* **39**, D106-10 (2011).
25. Lee, S. & Blundell, T.L. BIPA: a database for protein-nucleic acid interaction in 3D structures. *Bioinformatics* **25**, 1559-60 (2009).
26. Xie, Z., Hu, S., Blackshaw, S., Zhu, H. & Qian, J. hPDI: a database of experimental human protein-DNA interactions. *Bioinformatics* **26**, 287-9 (2010).
27. Barrasa, M.I., Vaglio, P., Cavasino, F., Jacotot, L. & Walhout, A.J. EDGEdb: a transcription factor-DNA interaction database for the analysis of C. elegans differential gene expression. *BMC Genomics* **8**, 21 (2007).
28. Kirsanov, D.D. et al. NPIDB: Nucleic acid-Protein Interaction DataBase. *Nucleic Acids Res* **41**, D517-23 (2013).
29. Spirin, S., Titov, M., Karyagina, A. & Alexeevski, A. NPIDB: a database of nucleic acids-protein interactions. *Bioinformatics* **23**, 3247-8 (2007).
30. Smith, A.J. & Humphries, S.E. Characterization of DNA-binding proteins using multiplexed competitor EMSA. *J Mol Biol* **385**, 714-7 (2009).
31. Keene, J.D., Komisarow, J.M. & Friedersdorf, M.B. RIP-Chip: the isolation and identification of mRNAs, microRNAs and protein components of ribonucleoprotein complexes from cell extracts. *Nat Protoc* **1**, 302-7 (2006).
32. Morozova, N., Allers, J., Myers, J. & Shamoo, Y. Protein-RNA interactions: exploring binding patterns with a three-dimensional superposition analysis of high resolution structures. *Bioinformatics* **22**, 2746-52 (2006).
33. Wu, T. et al. NPInter: the noncoding RNAs and protein related biomacromolecules interaction database. *Nucleic Acids Res* **34**, D150-2 (2006).
34. Cook, K.B., Kazan, H., Zuberi, K., Morris, Q. & Hughes, T.R. RBPDB: a database of RNA-binding specificities. *Nucleic Acids Res* **39**, D301-8 (2011).
35. Lewis, B.A. et al. PRIDB: a Protein-RNA Interface Database. *Nucleic Acids Res* **39**, D277-82 (2011).
36. Yang, J.H. et al. starBase: a database for exploring microRNA-mRNA interaction maps from Argonaute CLIP-Seq and Degradome-Seq data. *Nucleic Acids Res* **39**, D202-9 (2011).
37. Picotti, P. & Aebersold, R. Selected reaction monitoring-based proteomics: workflows, potential, pitfalls and future directions. *Nat Methods* **9**, 555-66 (2012).
38. Blaise, B.J. et al. Metabotyping of Caenorhabditis elegans reveals latent phenotypes. *Proc Natl Acad Sci U S A* **104**, 19808-12 (2007).
39. Huang, T. et al. Analysis and prediction of the metabolic stability of proteins based on their sequential features, subcellular locations and interaction networks. *PLoS One* **5**, e10972 (2010).
40. Vastrik, I. et al. Reactome: a knowledge base of biologic pathways and processes. *Genome Biol* **8**, R39 (2007).
41. Kanehisa, M., Goto, S., Kawashima, S., Okuno, Y. & Hattori, M. The KEGG resource for deciphering the genome. *Nucleic Acids Res* **32**, D277-80 (2004).
42. Caspi, R. et al. MetaCyc: a multiorganism database of metabolic pathways and enzymes. *Nucleic Acids Res* **34**, D511-6 (2006).
43. Wishart, D.S. et al. HMDB: the Human Metabolome Database. *Nucleic Acids Res* **35**, D521-6 (2007).
44. Wishart, D.S. et al. HMDB: a knowledgebase for the human metabolome. *Nucleic Acids Res* **37**, D603-10 (2009).
45. Keseler, I.M. et al. EcoCyc: a comprehensive database of Escherichia coli biology. *Nucleic Acids Res* **39**, D583-90 (2011).
46. Romero, P. et al. Computational prediction of human metabolic pathways from the complete human genome. *Genome Biol* **6**, R2 (2005).
47. Kamburov, A. et al. ConsensusPathDB: toward a more complete picture of cell biology. *Nucleic Acids Res* **39**, D712-7 (2011).
48. Bender, A. et al. Analysis of pharmacology data and the prediction of adverse drug reactions and off-target effects from chemical structure. *ChemMedChem* **2**, 861-73 (2007).
49. Mizutani, S., Pauwels, E., Stoven, V., Goto, S. & Yamanishi, Y. Relating drug-protein interaction network with drug side effects. *Bioinformatics* **28**, i522-i528 (2012).
50. Hillenmeyer, M.E. et al. The chemical genomic portrait of yeast: uncovering a phenotype for all genes. *Science* **320**, 362-5 (2008).
51. Bredel, M. & Jacoby, E. Chemogenomics: an emerging strategy for rapid target and drug discovery. *Nat Rev Genet* **5**, 262-75 (2004).
52. Fliri, A.F., Loging, W.T., Thadeio, P.F. & Volkmann, R.A. Analysis of drug-induced effect patterns to link structure and side effects of medicines. *Nat Chem Biol* **1**, 389-97 (2005).
53. Yamanishi, Y., Kotera, M., Kanehisa, M. & Goto, S. Drug-target interaction prediction from chemical, genomic and pharmacological data in an integrated framework. *Bioinformatics* **26**, i246-54 (2010).
54. Gunther, S. et al. SuperTarget and Matador: resources for exploring drug-target relationships. *Nucleic Acids Res* **36**, D919-22 (2008).

55. Knox, C. et al. DrugBank 3.0: a comprehensive resource for 'omics' research on drugs. *Nucleic Acids Res* **39**, D1035-41 (2011).
56. Taboureau, O. et al. ChemProt: a disease chemical biology database. *Nucleic Acids Res* **39**, D367-72 (2011).
57. Kuhn, M., von Mering, C., Campillos, M., Jensen, L.J. & Bork, P. STITCH: interaction networks of chemicals and proteins. *Nucleic Acids Res* **36**, D684-8 (2008).
58. Block, P., Sotriffer, C.A., Dramburg, I. & Klebe, G. AffinDB: a freely accessible database of affinities for protein-ligand complexes from the PDB. *Nucleic Acids Res* **34**, D522-6 (2006).
59. Chautard, E., Ballut, L., Thierry-Mieg, N. & Ricard-Blum, S. MatrixDB, a database focused on extracellular protein-protein and protein-carbohydrate interactions. *Bioinformatics* **25**, 690-1 (2009).
60. Wallach, I. & Lilien, R. The protein-small-molecule database, a non-redundant structural resource for the analysis of protein-ligand binding. *Bioinformatics* **25**, 615-20 (2009).
61. Shin, J.M. & Cho, D.H. PDB-Ligand: a ligand database based on PDB for the automated and customized classification of ligand-binding structures. *Nucleic Acids Res* **33**, D238-41 (2005).
62. Gaulton, A. et al. ChEMBL: a large-scale bioactivity database for drug discovery. *Nucleic Acids Res* **40**, D1100-7 (2012).
63. Baryshnikova, A. et al. Quantitative analysis of fitness and genetic interactions in yeast on a genome scale. *Nat Methods* **7**, 1017-24 (2010).
64. Collins, S.R., Roguev, A. & Krogan, N.J. Quantitative genetic interaction mapping using the E-MAP approach. *Methods Enzymol* **470**, 205-31 (2010).
65. Stuart, J.M., Segal, E., Koller, D. & Kim, S.K. A gene-coexpression network for global discovery of conserved genetic modules. *Science* **302**, 249-55 (2003).
66. Vaske, C.J. et al. Inference of patient-specific pathway activities from multi-dimensional cancer genomics data using PARADIGM. *Bioinformatics* **26**, i237-45 (2010).
67. Koh, J.L. et al. DRYGIN: a database of quantitative genetic interaction networks in yeast. *Nucleic Acids Res* **38**, D502-7 (2010).
68. Guldener, U. et al. CYGD: the Comprehensive Yeast Genome Database. *Nucleic Acids Res* **33**, D364-8 (2005).
69. Hamosh, A., Scott, A.F., Amberger, J.S., Bocchini, C.A. & McKusick, V.A. Online Mendelian Inheritance in Man (OMIM), a knowledgebase of human genes and genetic disorders. *Nucleic Acids Res* **33**, D514-7 (2005).
70. Hidalgo, C.A., Blumm, N., Barabasi, A.L. & Christakis, N.A. A dynamic network approach for the study of human phenotypes. *PLoS Comput Biol* **5**, e1000353 (2009).
71. Goh, K.I. et al. The human disease network. *Proc Natl Acad Sci U S A* **104**, 8685-90 (2007).
72. Augenlicht, L.H. et al. Expression of cloned sequences in biopsies of human colonic tissue and in colonic carcinoma cells induced to differentiate in vitro. *Cancer Res* **47**, 6017-21 (1987).
73. Morin, R. et al. Profiling the HeLa S3 transcriptome using randomly primed cDNA and massively parallel short-read sequencing. *Biotechniques* **45**, 81-94 (2008).
74. Barrett, T. et al. NCBI GEO: archive for functional genomics data sets--10 years on. *Nucleic Acids Res* **39**, D1005-10 (2011).
75. Hubble, J. et al. Implementation of GenePattern within the Stanford Microarray Database. *Nucleic Acids Res* **37**, D898-901 (2009).
76. Cerami, E. et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. *Cancer Discov* **2**, 401-4 (2012).
77. Finger, J.H. et al. The mouse Gene Expression Database (GXD): 2011 update. *Nucleic Acids Res* **39**, D835-41 (2011).
78. Rhodes, D.R. et al. ONCOMINE: a cancer microarray database and integrated data-mining platform. *Neoplasia* **6**, 1-6 (2004).
79. Parkinson, H. et al. ArrayExpress update--an archive of microarray and high-throughput sequencing-based functional genomics experiments. *Nucleic Acids Res* **39**, D1002-4 (2011).
80. Fire, A. et al. Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans. *Nature* **391**, 806-11 (1998).
81. Gunsalus, K.C., Yueh, W.C., MacMenamin, P. & Piano, F. RNAiDB and PhenoBlast: web tools for genome-wide phenotypic mapping projects. *Nucleic Acids Res* **32**, D406-10 (2004).
82. Gilsdorf, M. et al. GenomeRNAi: a database for cell-based RNAi phenotypes. 2009 update. *Nucleic Acids Res* **38**, D448-52 (2010).
83. Ren, Y. et al. siRecords: an extensive database of mammalian siRNAs with efficacy ratings. *Bioinformatics* **22**, 1027-8 (2006).
84. Heyn, H. & Esteller, M. DNA methylation profiling in the clinic: applications and challenges. *Nat Rev Genet* **13**, 679-92 (2012).
85. Turinsky, A.L. et al. DAnCER: disease-annotated chromatin epigenetics resource. *Nucleic Acids Res* **39**, D889-94 (2011).
86. Lv, J. et al. DiseaseMeth: a human disease methylation database. *Nucleic Acids Res* **40**, D1030-5 (2012).
87. Ongenaert, M. et al. PubMeth: a cancer methylation database combining text-mining and expert annotation. *Nucleic Acids Res* **36**, D842-6 (2008).
88. Amoreira, C., Hindermann, W. & Grunau, C. An improved version of the DNA Methylation database (MethDB). *Nucleic Acids Res* **31**, 75-7 (2003).
89. Lauss, M. et al. MethCancerDB--aberrant DNA methylation in human cancer. *Br J Cancer* **98**, 816-7 (2008).
90. He, X. et al. MethyCancer: the database of human DNA methylation and cancer. *Nucleic Acids Res* **36**, D836-41 (2008).
91. LaFramboise, T. Single nucleotide polymorphism arrays: a decade of biological, computational and technological advances. *Nucleic Acids Res* **37**, 4181-93 (2009).
92. Cirulli, E.T. & Goldstein, D.B. Uncovering the roles of rare variants in common disease through whole-genome sequencing. *Nat Rev Genet* **11**, 415-25 (2010).
93. Sherry, S.T. et al. dbSNP: the NCBI database of genetic variation. *Nucleic Acids Res* **29**, 308-11 (2001).
94. Tahira, T. et al. dbQSNP: a database of SNPs in human promoter regions with allele frequency information determined by single-strand conformation polymorphism-based methods. *Hum Mutat* **26**, 69-77 (2005).
95. Thorisson, G.A. et al. HGVbaseG2P: a central genetic association database. *Nucleic Acids Res* **37**, D797-802 (2009).

96. Jackson, V. Studies on histone organization in the nucleosome using formaldehyde as a reversible cross-linking agent. *Cell* **15**, 945-54 (1978).
97. Berman, H.M. et al. The Protein Data Bank. *Acta Crystallogr D Biol Crystallogr* **58**, 899-907 (2002).
98. Gasteiger, E. et al. ExPASy: The proteomics server for in-depth protein knowledge and analysis. *Nucleic Acids Res* **31**, 3784-8 (2003).
99. Hunter, S. et al. InterPro in 2011: new developments in the family and domain prediction database. *Nucleic Acids Res* **40**, D306-12 (2012).
100. Hoogland, C., Mostaguir, K., Appel, R.D. & Lisacek, F. The World-2DPAGE Constellation to promote and publish gel-based proteomics data through the ExPASy server. *J Proteomics* **71**, 245-8 (2008).
101. Portales-Casamar, E. et al. JASPAR 2010: the greatly expanded open-access database of transcription factor binding profiles. *Nucleic Acids Res* **38**, D105-10 (2010).
102. Stark, C. et al. PhosphoGRID: a database of experimentally verified in vivo protein phosphorylation sites from the budding yeast Saccharomyces cerevisiae. *Database (Oxford)* **2010**, bap026 (2010).
103. Dinkel, H. et al. Phospho.ELM: a database of phosphorylation sites--update 2011. *Nucleic Acids Res* **39**, D261-7 (2011).
104. Gnad, F., Gunawardena, J. & Mann, M. PHOSIDA 2011: the posttranslational modification database. *Nucleic Acids Res* **39**, D253-60 (2011).