**Supplementary Table S1.** The top 46 TF pairs with *p*-values less than are regarded as the statistically significant cooperative TF pairs

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Rank** | **TF1** | **TF2** | **p-value** | **Existing algorithms which also predict this potential cooperative TF pair** | **Physical PPI evidence from BioGRID database** |
| 1 | IFH1 | SFP1 | 7.96E-109 | **Novel PCTFP** |  |
| 2 | IFH1 | RAP1 | 2.26E-94 | **Novel PCTFP** | Y |
| 3 | STE12 | TEC1 | 6.11E-72 | [1][4][8][10][14] | Y |
| 4 | RAP1 | SFP1 | 3.56E-69 | [1][4][8][11][14][15] |  |
| 5 | MSN2 | YAP1 | 2.58E-55 | [1][4] |  |
| 6 | MSN2 | SOK2 | 8.41E-55 | [14] | Y |
| 7 | MET32 | MET4 | 2.38E-53 | [1][4][8][14] | Y |
| 8 | MSN2 | MSN4 | 5.02E-43 | [1][4][8][10][14] |  |
| 9 | PDR1 | PDR3 | 4.46E-42 | [1][10][14][16] | Y |
| 10 | MET31 | MET32 | 1.88E-35 | [1][4][8][10][14] |  |
| 11 | MSN2 | SKN7 | 3.36E-35 | [1][4] |  |
| 12 | ACE2 | SWI5 | 4.94E-33 | [1][2][3][4][5][6][8][10][14][15][16] | |
| 13 | SOK2 | TEC1 | 1.26E-30 | [1] |  |
| 14 | CIN5 | MSN2 | 1.76E-29 | [1] |  |
| 15 | HAP2 | HAP4 | 5.22E-29 | [8][14][15][16] | Y |
| 16 | MSN2 | STE12 | 9.90E-29 | **Novel PCTFP** |  |
| 17 | MSN2 | TEC1 | 7.13E-28 | **Novel PCTFP** |  |
| 18 | MET28 | MET32 | 1.21E-27 | [1][14] |  |
| 19 | CBF1 | MET4 | 1.40E-26 | [1][4][8][14] | Y |
| 20 | FHL1 | IFH1 | 2.97E-26 | **Novel PCTFP** | Y |
| 21 | SWI4 | SWI6 | 8.45E-26 | [1][2][3][4][5][6][8][10][12][13][14][15][16] | Y |
| 22 | MET31 | MET4 | 8.98E-26 | [1][4][8][14] | Y |
| 23 | MET28 | MET4 | 1.21E-25 | [1][14] | Y |
| 24 | SKN7 | SOK2 | 2.35E-25 | [1][8] |  |
| 25 | MET28 | MET31 | 3.49E-25 | [1] |  |
| 26 | MSN4 | YAP1 | 1.44E-24 | [1][4] |  |
| 27 | MBP1 | SWI4 | 1.60E-24 | [1][3][4][5][6][8][9][10][14][15][16] | Y |
| 28 | CBF1 | MET32 | 1.55E-23 | [1][4][8][14] | Y |
| 29 | AFT1 | AFT2 | 7.38E-22 | [1][4][8][14] |  |
| 30 | MSN2 | PDR1 | 2.28E-21 | **Novel PCTFP** |  |
| 31 | ARG80 | ARG81 | 5.72E-21 | [1][2][4][11][14][15] | Y |
| 32 | CIN5 | SOK2 | 8.09E-21 | [1][8][16] |  |
| 33 | MSN2 | SKO1 | 8.62E-21 | [1] |  |
| 34 | SOK2 | SWI4 | 2.42E-20 | [1][16] |  |
| 35 | PDR1 | SOK2 | 6.23E-20 | [1][16] |  |
| 36 | HSF1 | MSN2 | 6.67E-20 | [1] | Y |
| 37 | MBP1 | SWI6 | 1.60E-19 | [1][2][3][4][5][6][8][10][12][13][14][16] | Y |
| 38 | OAF1 | PIP2 | 1.71E-19 | [1][4][14] | Y |
| 39 | ADR1 | CAT8 | 3.05E-19 | [1][14] | Y |
| 40 | SOK2 | YAP1 | 7.55E-19 | [1] |  |
| 41 | SKN7 | YAP1 | 1.24E-18 | [1][9][11][14] | Y |
| 42 | SOK2 | STE12 | 1.57E-18 | **Novel PCTFP** |  |
| 43 | INO2 | INO4 | 1.73E-17 | [1][4][8][14][16] | Y |
| 44 | RAP1 | TUP1 | 1.82E-17 | **Novel PCTFP** |  |
| 45 | MSN2 | PDR3 | 4.33E-16 | [14] |  |
| 46 | MSN2 | RAP1 | 5.67E-16 | **Novel PCTFP** |  |

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| **References** | |  |  |  |
| [1]: Balaji S, Babu MM, Iyer LM, Luscombe NM, Aravind L: Comprehensive analysis of combinatorial regulation using the transcriptional regulatory network of yeast. J Mol Biol. 2006, 360(1):213-227. | | | | |
| [2]: Banerjee N, Zhang MQ: Identifying cooperativity among transcription factors controlling the cell cycle in yeast. Nucleic Acids Res 2003, 31:7024-7031. | | | | |
| [3]: Chang YH, Wang YC, Chen BS: Identification of transcription factor cooperativity via stochastic system model. Bioinformatics 2006, 22:2276-2282. | | | | |
| [4]: Chen MJ, Chou LC, Hsieh TT, Lee DD, Liu KW, Yu CY, Oyang YJ, Tsai HK, Chen CY: De novo motif discovery facilitates identification of interactions between transcription factors in Saccharomyces cerevisiae. Bioinformatics 2012, 28:701-708. | | | | |
| [5]: Chuang CL, Hung K, Chen CM, Shieh GS: Uncovering transcriptional interactions via an adaptive fuzzy logic approach. BMC Bioinformatics 2009, 10:400. | | | | |
| [6]: Datta D, Zhao H: Statistical methods to infer cooperative binding among transcription factors in Saccharomyces cerevisiae. Bioinformatics 2008, 24:545-552. | | | | |
| [7]: Elati M, Neuvial P, Bolotin-Fukuhara M, Barillot E, Radvanyi F, Rouveirol C: LICORN: learning cooperative regulation networks from gene expression data. Bioinformatics 2007, 23:2407-2414. | | | | |
| [8]: Harbison CT, Gordon DB, Lee TI, Rinaldi NJ, Macisaac KD, Danford TW, Hannett NM, Tagne JB, Reynolds DB, Yoo J, Jennings EG, Zeitlinger J, Pokholok DK, Kellis M, Rolfe PA, Takusagawa KT, Lander ES, Gifford DK, Fraenkel E, Young RA: Transcriptional regulatory code of a eukaryotic genome. Nature 2004, 431:99-104. | | | | |
| [9]: He D, Zhou D, Zhou Y: Identifying synergistic transcriptional factors involved in the yeast cell cycle using Microarray and ChIP-chip data. In Proceedings of the Fifth International Conference on Grid and Cooperative Computing Workshops:21-23 October 2006; Hunan. Edited by Xiao N, Buyya R, Liu Y, Yang G. Los Alamitos: IEEE Computer Society; 1996:357-360. | | | | |
| [10]: Lai FJ, Jhu MH, Chiu CC, Huang YM, Wu WS: Identifying cooperative transcription factors in yeast using multiple data sources. BMC Systems Biology 2014, 8(Suppl 5):S2. | | | | |
| [11]: Nagamine N, Kawada Y, Sakakibara Y: Identifying cooperative transcriptional regulations using protein-protein interactions. Nucleic Acids Res 2005, 33:4828-4837. | | | | |
| [12]: Tsai HK, Lu HHS, Li WH: Statistical methods for identifying yeast cell cycle transcription factors. Proc Natl Acad Sci USA 2005, 102:13532-13537. | | | | |
| [13]: Wang J: A new framework for identifying combinatorial regulation of transcription factors: a case study of the yeast cell cycle. J Biomedical Informatics 2006, 40:707-725. | | | | |
| [14]: Wang Y, Zhang XS, Xia Y: Predicting eukaryotic transcriptional cooperativity by Bayesian network integration of genome-wide data. Nucleic Acids Res 2009, 37:5943-5958. | | | | |
| [15]: Yang Y, Zhang Z, Li Y, Zhu XG, Liu Q: Identifying cooperative transcription factors by combining ChIP-chip data and knockout data. Cell Res 2010, 20:1276-1278. | | | | |
| [16]: Yu X, Lin J, Masuda T, Esumi N, Zack DJ, Qian J: Genome-wide prediction and characterization of interactions between transcription factors in Saccharomyces cerevisiae. Nucleic Acids Res 2006, 34:917-927. | | | | |
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