Updated regulation curation model at the *Saccharomyces* Genome Database

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The *Saccharomyces* Genome Database (SGD) provides comprehensive, integrated biological information for the budding yeast *Saccharomyces cerevisiae*, along with search and analysis tools to explore these data, enabling the discovery of functional relationships between sequence and gene products in fungi and higher organisms. We have recently expanded our data model for regulation curation to address regulation at the protein level in addition to transcription, and are presenting the expanded data on the 'Regulation' pages at SGD. These pages include a summary describing the context under which the regulator acts, manually curated and high-throughput annotations showing the regulatory relationships for that gene, and a graphical visualization of its regulatory network and connected networks. For genes whose products regulate other genes or proteins, the Regulation page includes Gene Ontology enrichment analysis of the biological processes in which those targets participate. For DNA-binding transcription factors, we also provide other information relevant to their regulatory function, such as DNA binding site motifs and protein domains. As with other data types at SGD, all regulatory relationships and accompanying data are available through YeastMine, SGD's data warehouse based on InterMine.

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YOX1 / YML027W Regulation

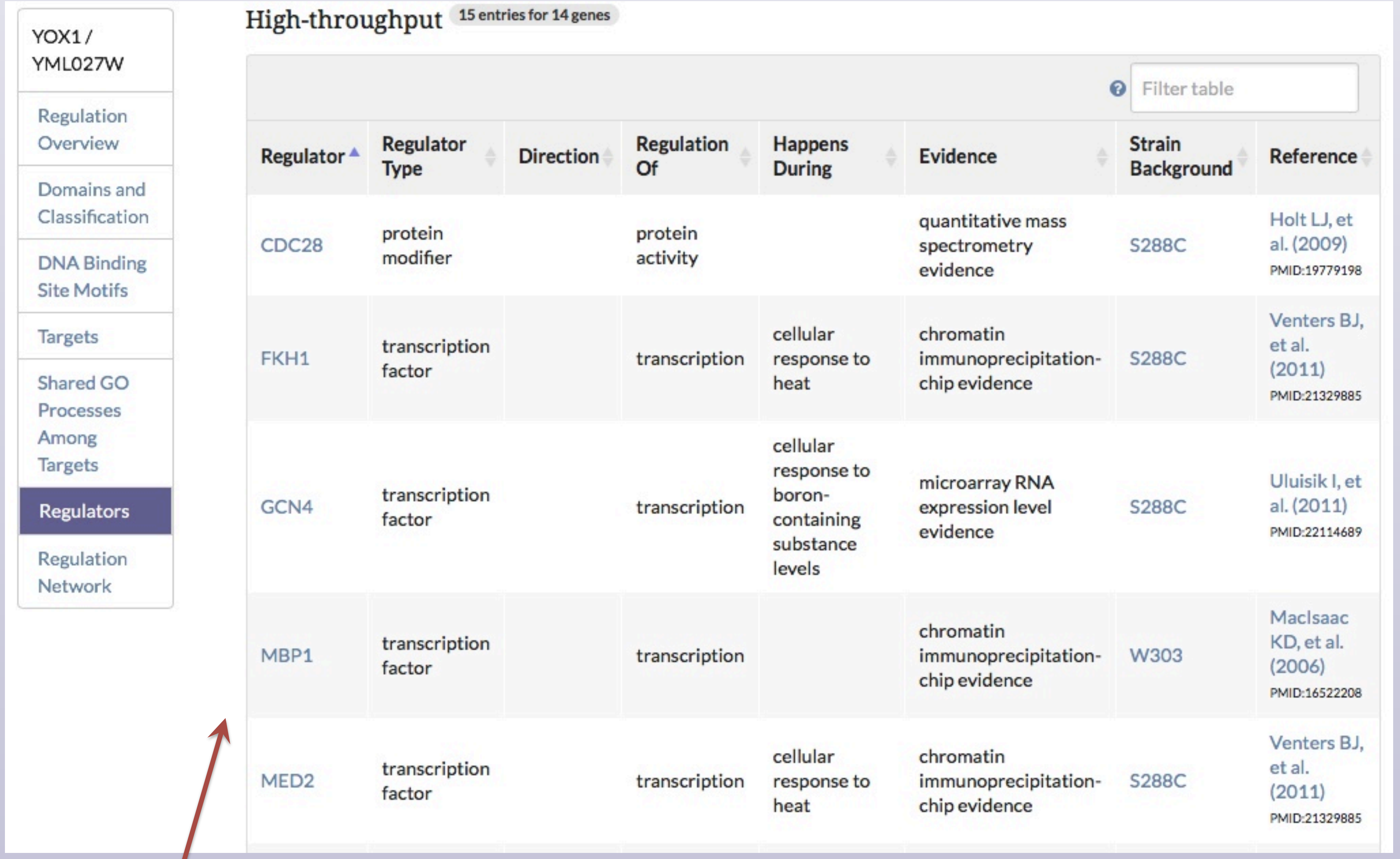
YOX1 encodes a helix-turn-helix transcriptional repressor of the homeodomain family. Yox1p restricts transcription of genes containing early cell cycle boxes (ECBs) to M-G1 phase. Yox1p is an ancillary transcription factor that binds alongside Mcm1p on promoters. Examples include important cell cycle genes such as SWI4 and CLN3, themselves rate-limiting for cell cycle progression, and essential for the control of subsequent waves of gene expression at G1-S. Yox1p binds upstream of genes involved in spindle function, DNA synthesis and repair, and also associates with a small portion of intergenic regions adjacent to tRNA genes. Removal of Yox1p from promoters allows gene expression at M-G1. YOX1 is under transcriptional regulation by SBF, and Mcm1p controls the expression of SWI4 which encodes a component of SBF, thereby setting up a negative feedback loop. The transcription of the CDC20 APC (anaphase promoting complex) activator is repressed by Yox1p and kept very low during S phase. Upon mitotic onset, Yox1p abundance declines and the CDC20 gene is actively transcribed. Cdc28p negatively regulates YOX1 transcription, thereby keeping intracellular levels of Yox1p low, and promoting the transcription of CDC20. Yox1p is an unstable protein, so that suppression of its transcription results in rapid reduction of intracellular protein levels.

Acker J, et al. (2013) Yeast RNA polymerase III transcription factors and effectors. Biochim Biophys Acta 1829(3-4):283-95 PMID:23063749
SGD Paper PubMed DOI full text

Surana U, et al. (2012) Staging a recovery from mitotic arrest: Unusual ways of Cdk1. Bioarchitecture 2(2):33-37 PMID:22754627
SGD Paper PubMed PMC full text

McInerny CJ (2011) Cell cycle regulated gene expression in yeasts. Adv Genet 73:51-85 PMID:21310294
SGD Paper PubMed DOI full text

Transcriptional Targets and Regulators for YOX1 (includes high-throughput predictions)

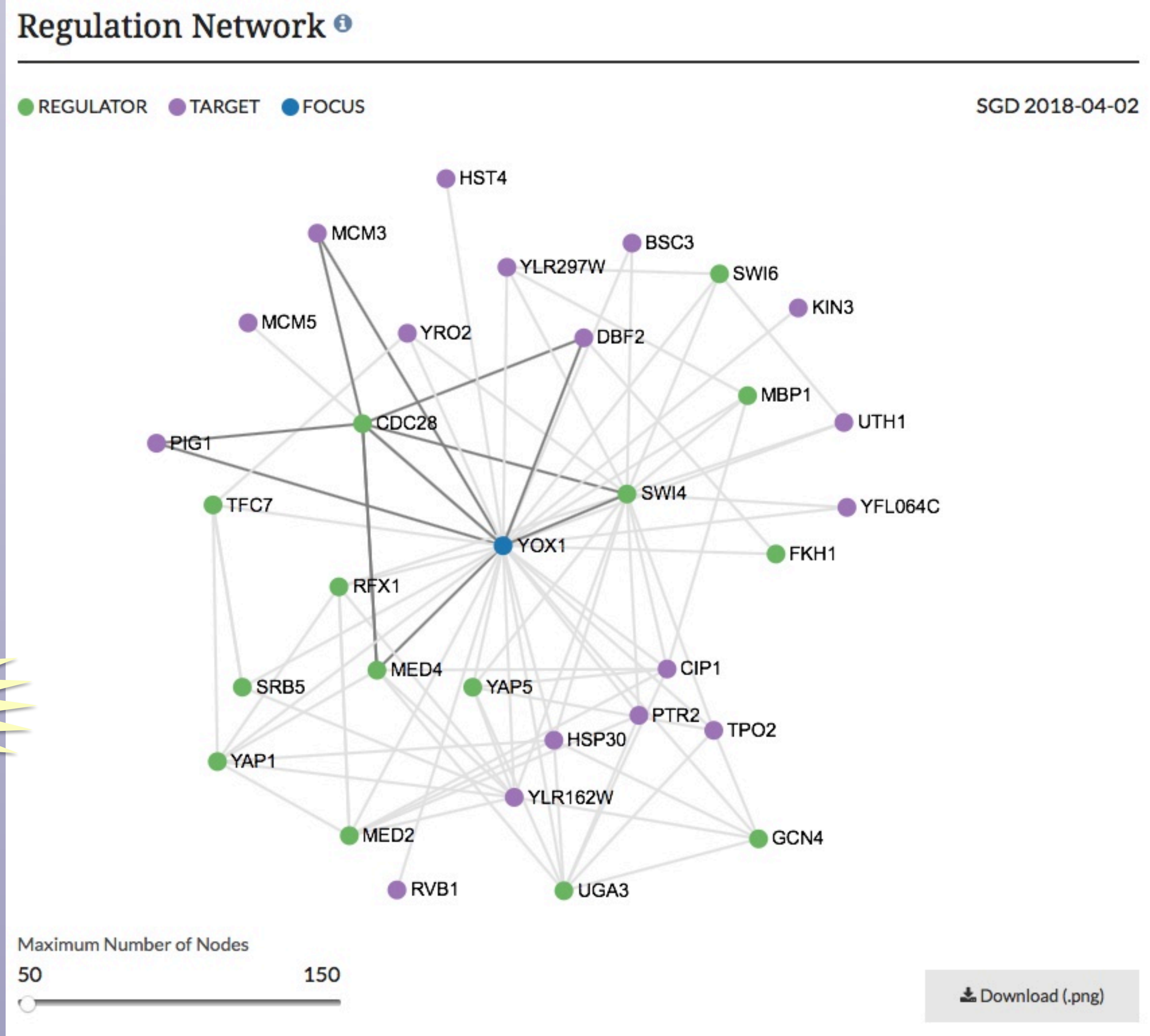


High-throughput

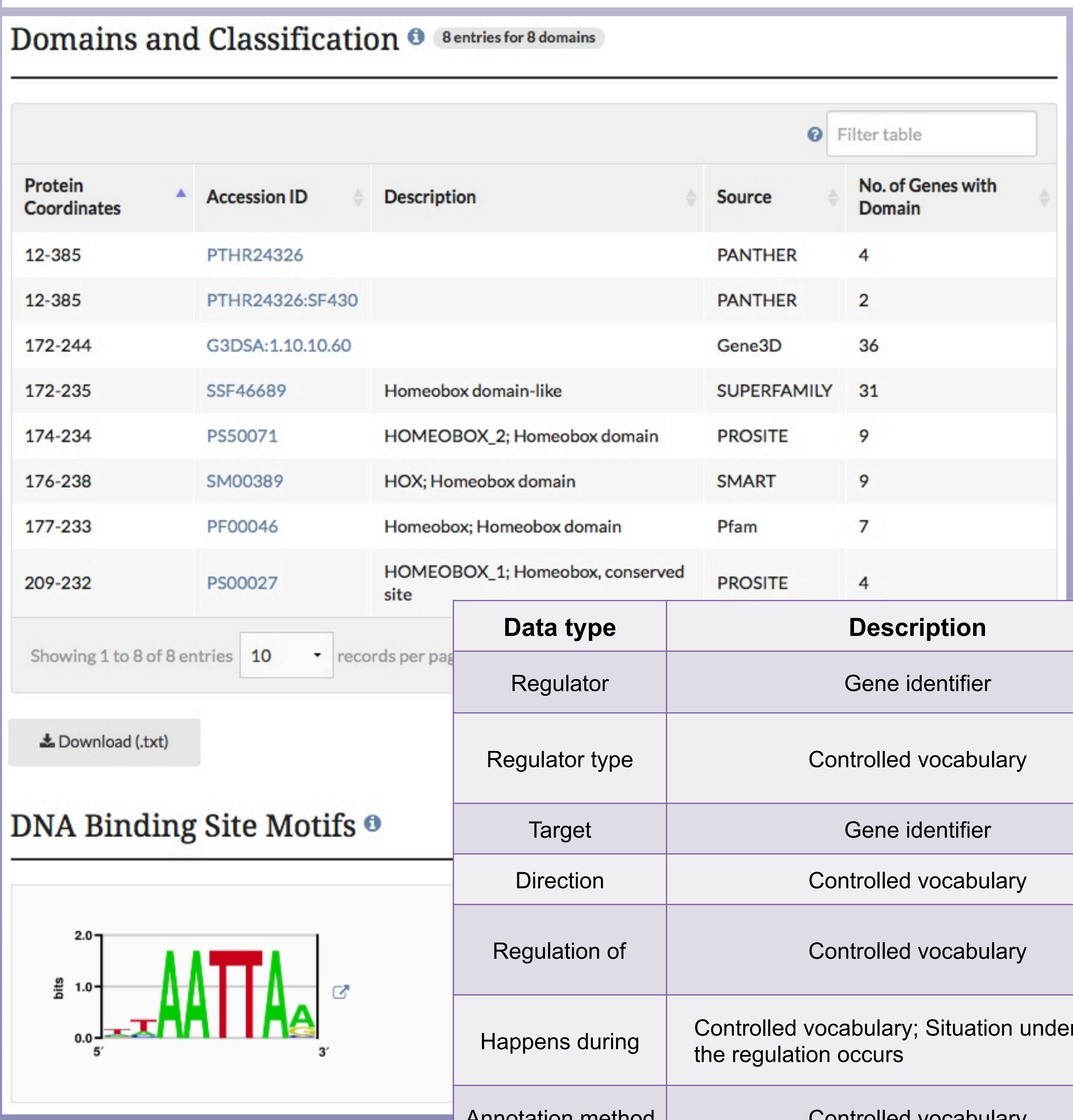
15 entries for 14 genes

Regulator	Regulator Type	Direction	Regulation Of	Happens During	Evidence	Strain Background	Reference
CDC28	protein modifier		protein activity		quantitative mass spectrometry evidence	S288C	Holt LJ, et al. (2009) PMID:19779198
FKH1	transcription factor		transcription	cellular response to heat	chromatin immunoprecipitation-chip evidence	S288C	Venters BJ, et al. (2011) PMID:21329885
GCN4	transcription factor		transcription	cellular response to boron-containing substance levels	microarray RNA expression level evidence	S288C	Uluisik I, et al. (2011) PMID:22114689
MBP1	transcription factor		transcription		chromatin immunoprecipitation-chip evidence	W303	MacIsaac KD, et al. (2006) PMID:16522208
MED2	transcription factor		transcription	cellular response to heat	chromatin immunoprecipitation-chip evidence	S288C	Venters BJ, et al. (2011) PMID:21329885

Regulation Network



Domains and Classification



8 entries for 8 domains

Protein Coordinates	Accession ID	Description	Source	No. of Genes with Domain
12-385	PTHR24326		PANTHER	4
12-385	PTHR24326:SF430		PANTHER	2
172-244	G3DSA:1.10.10.60		Gene3D	36
172-235	SSF46689	Homeobox domain-like	SUPERFAMILY	31
174-234	PS50071	HOMEOBOX_2; Homeobox domain	PROSITE	9
176-238	SM00389	HOX; Homeobox domain	SMART	9
177-233	PF00046	Homeobox; Homeobox domain	Pfam	7
209-232	PS00027	HOMEOBOX_1; Homeobox, conserved site	PROSITE	4

Showing 1 to 8 of 8 entries 10 records per pag

DNA Binding Site Motifs

Revised data model

Data type	Description	Value	
Regulator	Gene identifier	Gene name or systematic name	
Regulator type	Controlled vocabulary	Transcription factor Chromatin modifier Protein modifier	*Future:* *RNA-binding protein* *RNA modifier*
Target	Gene identifier	Gene name or systematic name	
Direction	Controlled vocabulary	Positive, Negative, [null]	
Regulation of	Controlled vocabulary	Transcription Protein activity	*Future:* *RNA stability* *Protein stability*
Happens during	Controlled vocabulary; Situation under which the regulation occurs	Defined subset of Gene Ontology terms: descendent terms of Biological Process 'cellular response to stimulus' GO:0051716 and 'cell cycle phase' GO:0022403	
Annotation method	Controlled vocabulary	Manually curated High-throughput	
Evidence	Type of experiment used to test for and/or demonstrate the regulatory relationship	Evidence & Conclusion Ontology (ECO) term	
Strain background	Controlled vocabulary	Strain name	
Reference	Publication in which the regulatory relationship is described	PubMed ID	

Future directions

- regulatory complexes
  - *in addition to single protein regulators*
- other types of regulators
  - *RNA-binding proteins*
  - *RNA modifiers*
  - *other protein-binding entities*
- other types of regulation
  - *RNA stability*
  - *protein stability*

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