Computational identification of de-centric genetic regulatory relationships from functional genomic data.


Summary: We developed a new computational technique to identify de-centric genetic regulatory relationship candidates. Our technique takes advantages of functional genomics data for the same species under different perturbation conditions, therefore making it complementary to current computational techniques including database search, clustering of gene expression profiles, motif matching, structural modeling, and network effect simulation methods. It is fast and addressed the need of biologists to determine activation/inhibition relationship details often missing in synthetic lethality or chip-seq experiments. We used GEO microarray data set GSE25644 with 158 different mutant genes in S. cerevisiae. We screened out 83 targets with 610 activation pairs and 93 targets with 494 inhibition pairs. In the Yeast Fitness database, 33 targets (40%) with 126 activation pairs and 31 targets (33%) with 97 inhibition pairs were identified. To be identified further are 50 targets with 484 activation pairs and 62 targets with 397 inhibition pairs. The aggregation test confirmed that all discovered de-centric regulatory relationships are significant from random discovery at a p-value=0.002; therefore, this method is highly complementary to others that tend to discover hub-related regulatory relationships. We also developed criteria for rejecting genetic regulator candidates x as a candidate regulator and assessing the ranking of the regulator-target relationship identified. The top 10 high suspected regulators determined by our criteria were found to be significant, pending future experimental verifications.

Keywords: genetic regulation relationship; functional genomics; Yeast; computational prediction
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