Genetic networks map a functional wiring diagram of the cell

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Genome sequencing projects are providing an unprecedented view of human genetic variation. There is a growing awareness that genetic interactions, involving combinations of polymorphic alleles, may play a major role in determining phenotypes. Yet, our understanding of the genetic networks relevant to human disease remains rudimentary. Our group has focused on identifying genetic interactions in a model eukaryote, the budding yeast Saccharomyces cerevisiae, which provides a unique format for exploring genetic networks. We developed the ‘synthetic genetic array’ (SGA) method, which automates yeast genetics and enables systematic mapping of genetic interactions. We used SGA to complete a reference genetic interaction map for yeast. In total, we examined ~23 million pairs of deletion mutants and mutant strains carrying temperature-sensitive (ts) alleles of essential genes, mapping nearly 1 million genetic interactions. This network provides an unprecedented view of the functional organization of a cell and elucidates the fundamental properties of genetic networks. We have leveraged these insights to predict genetic backgrounds and environments that lead to changes in network structure and topology. We have also carried out mapping and analysis of genetic suppression and triple mutant genetic interactions.