Identification And Characterization Of New Drosophila Mitotic Genes By Co-expression Analysis And Rna-mediated Interference.

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Based on the principle that genes involved in the same biological process tend to be significantly co-expressed, we exploited the extant microarray data to order the Drosophila genes according to their co-expression with known mitotic genes. We verified that the first 1000 genes of our co-expression list include more than one half of the known mitotic functions. With the aim of identifying novel genes involved in mitotic cell division, we performed RNAi experiments to inactivate each of these 1000 genes. Drosophila S2 cells were treated with double stranded RNA for three days and then analyzed for the normality of the chromosomes and the mitotic spindle. This screen led to identification of over 70 genes that have not previously been implicated in mitosis. Ablation of these genes resulted in a variety of mitotic phenotypes: (a) chromosome breakage, (b) abnormal chromosome condensation, (c) precocious sister chromatid separation, (d) defective spindle assembly, (e) metaphase arrest, (f) abnormal chromosome segregation, and (g) failures in cytokinesis. Most of the Drosophila genes identified in our screen have homologues in other eukaryotes including humans, thus providing a putative function for a fraction of the human genome.