A *C. elegans* phenome project: Profiling and cluster analysis of RNAi phenotypes

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The genome of each organism contains the developmental program by which a fertilized egg develops into an individual animal with a complex body structure. To understand the developmental program at a molecular level, we have been performing a systematic analysis of gene functions in the nematode *C. elegans* by a high-throughput RNA interference (RNAi). In order to uncover multiple gene functions in the course of development, stage-specific RNAi is performed by a "soaking method", in which worms at particular developmental stages are soaked in the double-stranded RNA solutions, and both embryonic and post-embryonic phenotypes are analyzed. To record the phenotype information comprehensively in a manner readily usable for computer-assisted analyses, we have developed a methodology to systematically describe the developmental phenotypes by using a combination of pre-determined vocabulary sets in multiple independent criteria (e.g., cell number, cellular morphology, body morphology, tissue differentiation, cell death...). Next, these phenotype profiles were used to classify genes based on their similarities: The RNAi phenotype profiles were converted to binary datasets, then subjected to a principal component analysis, followed by a hierarchical cluster analysis. In the resulting dendrogram, genes with known common functions were closely clustered, confirming the validity of this method. Thus, gene clustering using RNAi phenotype profiles is an effective way to identify genes that might function in the same genetic pathways or protein complexes. Furthermore, integration of the RNAi phenotypic profiles with other genome-wide datasets (e.g., DNA microarray or yeast two-hybrid assays) will facilitate understanding of the genetic networks in developmental processes. Since over 70% of the genes in humans have their counterparts in *C. elegans*, these analyses will contribute to the further understanding of the evolutionarily conserved developmental processes. Characterization of some of the genes identified in our RNAi screen will also be presented.