

Researchers reveal types of genes necessary for brain development

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Researchers from Harvard Medical School and Brandeis University have successfully completed a full-genome RNAi screen in neurons, showing what types of genes are necessary for brain development. Details of the screen and its novel methodology are published July 4th in the open-access journal *PLoS Genetics*.

Recent advances in genomics, such as the sequencing of entire genomes and the discovery of RNA-interference as a means of testing the effects of gene loss, have opened up the possibility to systematically analyze the function of all known and predicted genes in an organism. Until now, this type of functional genomics approach has not been applied to the study of very complex cells, such as the brain's neurons, on a full-genome scale.

Dr. Katharine Sepp and her fellow researchers took fresh neuronal cells extracted from embryos of the fruit fly genus *Drosophila* and screened them using RNA interference techniques. The team tested all genes, one by one in a rapid manner, for their potential role in neuronal development. The team then validated the method in mice.

A combination of live-cell imaging and quantitative analysis allowed Sepp et al to characterize neurons' morphological phenotypes in response to RNAi-mediated gene knockdown. The researchers focused on 104 evolutionary conserved genes that, when downregulated by RNAi, have morphological defects. The team developed algorithms to help streamline the analysis of the thousands of images created in the process.

The analysis revealed unexpected, essential roles in neurite outgrowth for genes representing a wide range of functional categories including signaling molecules, enzymes, channels, receptors, and cytoskeletal proteins. Results also determined that genes known to be involved in protein and vesicle trafficking show similar RNAi phenotypes.

The researchers believe that this study provides an effective method for future studies of a large variety of genes, including those with important functions in the nervous system.

Citation: Sepp KJ, Hong P, Lizarraga SB, Liu JS, Mejia LA, et al. (2008) Identification of Neural Outgrowth Genes using Genome-Wide RNAi. PLoS Genet 4(7): e1000111. doi:10.1371/journal.pgen.1000111

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