Whole-Animal High-Throughput Screens: The *C. elegans* Model

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Summary

The nematode *Caenorhabditis elegans* shows a high degree of conservation of molecular pathways related to human disease, yet is only 1-mm long and can be considered as a microorganism. Because of the development of a simple but systematic RNA-interference (RNAi) methodology, *C. elegans* is the only metazoan in which the impact of "knocking-down" nearly every gene in the genome can be analyzed in a whole living animal. Both functional genomic studies and chemical screens can be carried out using *C. elegans* in vivo screens in a context that preserves intact cell-to-cell communication, neuroendocrine signaling, and every aspect of the animal's metabolism necessary to survive and reproduce in lab conditions. This feature enables studies that are impossible to undertake in cell-culture-based screens. Although genome-wide RNAi screens and limited small-molecule screens have been successfully performed in *C. elegans* , they are typically extremely labor-intensive. Furthermore, technical limitations have precluded quantitative measurements and time-resolved analyses.

In this chapter, we provide detailed protocols to carry out automated high-throughput whole-animal RNAi and chemical screens. We describe methods to perform screens in solid and liquid media, in 96 and 384-well format, respectively. We describe the use of automated handling, sorting, and microscopy of worms. Finally, we give information about worm-adapted image analysis tools to quantify phenotypes. The technology presented here facilitates large-scale *C. elegans* genetic and chemical screens and it is expected to help shed light on relevant biological areas.

Key words: 384-well plate , 96-well plate , Agar , Antimicrobial , Automation , *C. elegans* , Chemical , Fluorescent marker , High-throughput , In vivo , Quantitative , RNAi , Screen , Whole-animal . *Caenorhabditis*