

HARVARD UNIVERSITY
Office of Technology Development



High-Throughput Screening Tools for Disruptors of Meiosis and Fat Homeostasis

Principal Investigator

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Technology

Despite the devastating outcomes of genetic anomalies stemming from problems during the cell division program meiosis, screening of environmental toxicants for their ability to disrupt meiosis has revealed to be very challenging. Meiosis is a complex process that cannot be recapitulated in a tissue culture setting, and occurs at specific stages of development over a period of several months to years. Time, cost, and experimental constraints therefore limit *in vivo* screening of environmental toxicants that disrupt biological processes such as meiosis.

Dr. Colaiacovo and Dr. Allard developed an inexpensive and reliable, high-throughput screen to identify compounds or mixtures of compounds that disrupt meiosis. The lab additionally developed a screening method to identify compounds that affect fat homeostasis. They chose to use the nematode *C. elegans* as a model system for their screens because many cellular and molecular pathways for meiosis and fat metabolism are evolutionarily conserved between worms and mammals. This technology uses a fluorescent reporter, green fluorescent protein (GFP), which is only expressed in the progeny of worms where meiosis has been disrupted. The effect of a compound on meiosis can then be quickly quantified using fluorescent microscopy of live worms.

The Colaiacovo lab also evaluated the effects of an environmentally relevant toxicological agent to further validate *C. elegans* as a model system to analyze their effects on reproductive biology of worms. The lab further plans to use their screening technology to screen the "1408" library from the National Toxicology program.

Market and Applications

Disruption of meiosis in humans has been linked to a number of genetic disorders such as Down and Turners syndrome, and abnormal fat homeostasis is thought to be an underlying cause of obesity and related diseases. This high-throughput screening method identifies whether a compound has a toxic effect on these important biological processes. Samples, such as drug candidates, agrochemicals, industrial chemicals, soil and water samples, may be used to evaluate:

- Safety of pre-clinical drug candidates. Toxicity screening in *C. elegans* may be used to rapidly and inexpensively test compounds earlier in the pipeline.
- Safety of household and industrial chemicals.
- Environmental effects of compounds. By testing samples of soil and water, the effects of agrochemicals and industrial chemicals can be analyzed in high-throughput manner.
- Molecular toxicology of compounds. Localization of GFP-tagged proteins combined with the powerful genetic approaches available in *C. elegans* make it possible to identify the mechanism of action of any known or newly discovered toxins.

Product Advantages

These screens have a number of important advantages over current screening methods:

- Inexpensive model system
- High-throughput approach enables screening using 96-well plates
- Short reproductive and life cycle of *C. elegans* enables completion of screens in days
- Transparency of worm simplifies image analysis of disrupted biological processes
- Powerful genetic approaches available for follow-on studies

Licensing Opportunity:

This technology is available for worldwide, exclusive licensing.

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