Drug Discovery & Development

Understanding and Treating Nervous System Dysfunction Using Modified Fly Models

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WARF: P120334US02

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in using prolonged larval stage *Drosophila* to model neurological disorders and screen possible treatments *in vivo*.

Overview

Neurological disorders—ranging from spinal cord injuries to Alzheimer's disease—are among the most challenging health issues. There is an ongoing need for disease models and screening systems to elucidate underlying mechanisms and identify effective treatments.

The nervous system of *Drosophila* larvae has proven to be a powerful experimental model for studying the growth and function of neurons and synapses. Significantly, key molecular mechanisms are conserved between *Drosophila* and vertebrates. Unfortunately, the third instar larval stage of these flies lasts only about three days. This short timeframe has hampered research into longer-term processes such as nerve regeneration and neurodegeneration.

The Invention

UW–Madison researchers have developed new methods to study such time-dependent neurological mechanisms and to screen for potentially therapeutic small molecules using extended third instar stage (ETI) *Drosophila* larvae. These flies have been genetically modified to remain in the larval period for up to 30 days but are otherwise normal. Given the longer time window, these ETI larvae can be utilized to identify agents that stimulate nerve regeneration, confer neuroprotection or prevent synaptic degeneration.

For such studies, the ETI larvae are fed test compounds (e.g., from a chemical library) and the functional consequences of the test agent on processes such as neuronal survival, axonal regrowth, and synaptic maintenance are assessed in appropriate assays.

Applications

- Drug screening, identification of targets and genetic studies

Key Benefits

- Provides a simple, convenient and rapid system for testing potential drugs
- Could help identify new genes and pathways for nerve regeneration and synaptic maintenance
- Enables live imaging, fast and inexpensive assays and definitive readouts

Stage of Development

The researchers have characterized the development, structure and function of the neuromuscular junction (NMJ) in the larvae. They have found that the time window for studying the flies' initial response to nerve injury has been increased from hours to multiple days. This has allowed the researchers to observe and characterize new phenomena following nerve damage, including degeneration of

synapses, glia proliferation and migration to the injury site, and robust nerve regrowth. They also have developed new models of age-dependent synaptic degeneration in the ETI background.

Additional Information

For More Information About the Inventors

- Barry Ganetzky

Related Technologies

- WARF reference number P02001US describes neurodegeneration mutants of *Drosophila*.
- WARF reference number P99190US describes a collection of temperature sensitive paralytic *Drosophila* mutants.

Publications

- Miller D.L., Ballard S.L. and Ganetzky B. 2012. Analysis of Synaptic Growth and Function in Drosophila with an Extended Larval Stage. J. Neurosci. 32, 13776-13786.

Tech Fields

- Drug Discovery & Development : Disease models

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854