

PROJECT ADMINISTRATION DATA SHEET

ORIGINAL REVISION NO. _____

Project No. G-32-627 R5949-1A0 GTRC/~~GR~~ DATE 6 / 24 / 86

Project Director: Dr. David B. Dusenbery School/~~US~~ Applied Biology

Sponsor: DHHS/PHS/NIOSH/Centers for Disease Control

Type Agreement: Grant No. 5R03 OH02095-02

Award Period: From 6/1/86 To 5/31/87 (Performance) 8/31/87 (Reports)

Sponsor Amount:	<u>This Change</u>	<u>Total to Date</u>
Estimated: \$	_____	\$ _____
Funded: \$	<u>14,748</u>	\$ <u>14,748</u>

Cost Sharing Amount: \$ _____ Cost Sharing No: _____

Title: Test for Neurotoxins Using Caenorhabditis Elegans

ADMINISTRATIVE DATA

OCA Contact E. Faith Gleason X4820

1) Sponsor Technical Contact:

2) Sponsor Admin/Contractual Matters:

Roy M. Fleming, SC.D.

Betty Feeley 262-6575

Chief, Grants Administration and Review

Grants Management Branch

Branch, NIOSH

Procurement and Grants Office

Centers for Disease Control Building,

Centers for Disease Control

Room 3053

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Atlanta, Georgia 30333

Atlanta, Georgia 30305

(404) 262-3343

Defense Priority Rating: N/A

Military Security Classification: N/A

(or) Company/Industrial Proprietary: _____

RESTRICTIONS

See Attached NIH Supplemental Information Sheet for Additional Requirements.

Travel: Foreign travel must have prior approval - Contact OCA in each case. Domestic travel requires sponsor approval where total will exceed greater of \$500 or 125% of approved proposal budget category.

Equipment: Title vests with GIT

COMMENTS:

COPIES TO:

SPONSOR'S I. D. NO. 02.108.002.86.001

Project Director
Research Administrative Network
Research Property Management
Accounting

Procurement/GTRI Supply Services
Research Security Services
Reports Coordinator (OCA)
Research Communications (2)

GTRC
Library
Project File

SPONSORED PROJECT TERMINATION/CLOSEOUT SHEET

14
SR-300

Date December 8, 1987

Project No. G-32-627

School/~~KIM~~ Applied Biology

Includes Subproject No.(s) N/A

Project Director(s) Dr. David ^{Dusenberry}~~Dusenbery~~ GTRC /~~KIM~~

Sponsor DHHS/PHS/NIOSH/Centers for Disease Control

Title Test for Neurotoxins Using Caenorhabditis Elegans

Effective Completion Date: 5/31/87 (Performance) 8/31/87 (Reports)

Grant/Contract Closeout Actions Remaining:

- None
- Final Invoice or Final Fiscal Report
- Closing Documents
- Final Report of Inventions Form 568 sent to P.I.
- Govt. Property Inventory & Related Certificate
- Classified Material Certificate
- Other _____

Continues Project No. G-32-620

Continued by Project No. _____

COPIES TO:

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- GTRC
- Research Communications (2)
- Project File
- Other Duane Hutchison
- Angela DuBose
- Russ Embry

FINAL PERFORMANCE REPORT

TITLE:

Screening Test for Neurotoxins Using Caenorhabditis elegans

GRANT NUMBER:

5 RO3 OHO 2095-02

PRINCIPAL INVESTIGATOR:

David B. Dusenbery, Ph.D.

School of Applied Biology

Georgia Institute of Technology

Atlanta, Georgia 30332

SUMMARY:

A promising screening test for neurotoxicity has been developed using a computer tracking system and a species of nematode, Caenorhabditis elegans. It is viewed in dark-field illumination, by a video camera interfaced directly to an IBM AT micro-computer. Several hundred nematodes are tracked simultaneously and rates of locomotion and frequency of change of direction are reported in real time. This system can rapidly obtain reliable data on a variety of behavioral parameters relating to locomotion and response to sensory stimulation. Initial testing has examined the effects on locomotion of six chemicals. Four

metals have been studied: copper, beryllium, mercury, and lead. Two organophosphate pesticides have been studied: malathion and vapona. Copper and beryllium were chosen as chemicals that have not been shown to be neurotoxins and the other four chemicals as substances known to be neurotoxins. Our findings for these six chemicals show that the rate of movement of exposed nematodes compared to the rate of movement of vehicle controls can be used as an indicator of neurotoxicity.

Acute lethality studies also have been performed with eight metals: HgCl_2 , $\text{BeSO}_4 \cdot 4\text{H}_2\text{O}$, $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$, $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, ZnCl_2 , $\text{Pb}(\text{NO}_3)_2$, CdCl_2 , and $\text{Sr}(\text{NO}_3)_2$. The LC50 values were compared to published mammalian oral LD50 values for salts of the same metals. Within this set of chemicals C. elegans was found to be a predictor of mammalian acute lethality, generating LC50 values comparable with the rat and mouse LD50 values. The total expenses for this testing are about 10 percent of the cost for mammalian lethality testing. The method is considered to have great promise, but further study is needed.

SIGNIFICANT RESULTS:

- * Screening test for neurotoxicity was developed using C. elegans.
- * The data generated from the screening test can be used to distinguish between neurotoxins and non-neurotoxins (within the set of chemicals tested).
- * The acute lethality data generated for eight metals can be used to predict acute lethality for mammalian species.
- * The costs of both types of toxicological testing (acute lethality and neurotoxicity) are less than 10 percent of the costs for similar tests using mammalian species.
- * Although the results are very promising, much additional testing is needed to verify the data.

PUBLICATIONS RESULTING FROM THIS GRANT:

Williams, P. L. and D. B. Dusenbery. 1987. Screening Test for Neurotoxins Using Caenorhabditis elegans. In Model Systems in Neurotoxicology: Alternatives Approaches to Animal Testing (A. Shahar and A. Goldberg, eds.). pp. 163-170. Alan R. Liss, New York.

Williams, P. L. and D. B. Dusenbery. Using the Nematode, Caenorhabditis elegans, To Predict Mammalian Acute Lethality to Metallic Salts. Submitted to Toxicology and Industrial Health, under review.

Williams, P. L. and D. B. Dusenbery. Behavioral Changes in the Nematode, Caenorhabditis elegans, As A Predictor of Neurotoxicity. Submitted to Fundamental and Applied Toxicology, under review.

PRESENTATIONS RESULTING FROM THIS GRANT:

Williams, P. L. and D. B. Dusenbery. "Screening Test for Neurotoxins Using Caenorhabditis elegans," Israel Institute for Biological Research, 31st OHOLO Conference, Tiberias, Israel, November 7, 1986.

Williams, P. L. and D. B. Dusenbery. "New Types of Toxicological Screening Tests Using A Nematode Species, Caenorhabditis elegans," American Industrial Hygiene Conference, Montreal, Quebec, Canada, June 2, 1987.