Date: June 18, 1979

Project Title: Developmental - Genetic Regulation of Brain Tryptophan Transport

Project No: G-32-658

Project Director: Dr. James A. Diez

Sponsor: National Science Foundation

Agreement Period: From 6/15/79 Until 11/30/82 (Grant Period)

Type Agreement: Grant No. BNS-7905601, dated 6/8/79

Amount: $85,000 NSF
        4,474 GIT (G-32-327)
        $89,474 TOTAL

Reports Required: Annual Progress Reports; Final Project Report

Sponsor Contact Person(s):

Technical Matters

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Contractual Matters

(thru OCA)

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EES/SE Branch
Division of Grants and Contracts
Directorate for Administration
National Science Foundation
Washington, D. C. 20550
202/632-7496

Defense Priority Rating: n/a

Assigned to: Biology (School/Laboratory)

COPIES TO:

Project Director
Division Chief (EES)
“School/Laboratory Director”
Dean/Director – EES
Accounting Office
Procurement Office
Security Coordinator (OCA)
Reports Coordinator (OCA)

Library, Technical Reports Section
EES Information Office
EES Reports & Procedures
Project File (OCA)
Project Code (GTRI)
Other
SPONSORED PROJECT TERMINATION SHEET

Date July 12, 1983

Project Title: Developmental - Genetic Regulation of Brain Tryptophan Transport

Project No: G-32-658

Project Director: Dr. James A. Diez

Sponsor: National Science Foundation

Effective Termination Date: 11/30/82

Clearance of Accounting Charges: 11/30/82

Grant/Contract Closeout Actions Remaining:

- Final Invoice and Closing Documents
- Final Fiscal Report
- Final Report of Inventions
- Govt. Property Inventory & Related Certificate
- Classified Material Certificate
- Other

Assigned to: Applied Biology (School/Laboratory)

COPIES TO:

Administrative Coordinator
Research Property Management
Accounting
Procurement/EES Supply Services

Research Security Services
Reports Coordinator (OCA)
Legal Services (OCA)
Library

EES Public Relations (2)
Computer Input
Project File
Other Diez
The major aim of this project was to determine whether the system which transports tryptophan (TRP) across the neuronal cell membrane shows significant physiological variation due to genotype of developmental age. TRP is the precursor of the neurotransmitter serotonin; variations in TRP availability can alter serotonin synthesis, and thereby affect the many behaviors modulated by serotonin.

The membrane transport system for TRP was studied in synaptosomes (nerve endings) prepared from whole mouse brain; the accumulation of radioactive TRP was used to characterize the maximum transport rate (Vmax) and the affinity of the carrier for TRP (Km). The transport constants were measured in preparations from several strains of mice which show differing behavioral traits; developmental changes in the constants were studied from birth to sexual maturity (approx. 8 wks.).

The major hypotheses of this study were confirmed: significant genetic differences in the Vmax and developmental changes in both the Km and Vmax for TRP transport were identified. Attempts to find a hormonal basis for the differences were not successful.

Experiments on the mechanism by which TRP is accumulated in synaptosomes have helped to resolve a controversy about how many carrier systems move TRP across the membrane. Our results indicate the existence of one system with relatively high affinity; the "low affinity" system which also appears in most TRP uptake studies seems to result from intra-cellular binding rather than movement across the membrane. These experiments also led to the discovery of a TRP-binding "phenomenon" in brain cell membrane fragments. This binding appears to behave much like a receptor for TRP, except that its dissociation constant (Kd) is relatively high (1 μm). The binding we measure could be to the carrier which transports TRP, except that it does seem to be unique to brain (we have not been able to measure it in liver, kidney, heart, erythrocytes, or platelets).