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Project NKULIRA 122

Purpose: To develop a technique for the preparation and characterization of purified Haurokinin. This study is closely related to the work of

Initiated: September 1960.

Contractor:

as a grantee of

Cost: \$2,000.00

Status: Unknown.

March 21, 1963

Memorandum to

Finances

Subject:

Attached is an accounting of one of the ones they are waiting for.

March 21, 1963

Q.

Accounting from

Received from

\$2,000.00

#### Expenditures:

1. Materials imported from 2 Kymographys with drums of 6 and 12 in.

2 infusion pump

1 kymograph with 6 in drum

()

1 time maker record

\$ 896.91

2. Material purchased with Money Exchange \$900 \$203.09 2

Using an average rate of the the following were purchased at the approximate \$ value of

1 Deep freezer	325.00
1 Tonometer of	21.00
1 tape record with acessories	120.00
l oxigenator for water bath	7.00
l oven and surgical material and syringes	117.00
drugs	64.00
Physiological material:	
Levers, cannules, mercury manometers from IBECC	212.00
l balance (to o.lg)	67.00
Picture rolls	25.00
Paper cutter	26.00
Mercury	23.00
Surgical material	57.00
Animals (cets, fowls, rabbits and dogs)	32.00
	7.09
Food for animals	and the second s
	\$2 000 00

\$2,000.00

This is a true statement of expenditures as reported to the fund.

Footly that services or materials have seen cattefacterly received and the expenditures were incurred on official testiness.

Pato: 3/27/63





(When I	illed	In)
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Cost Account 1125. 1039- 1902

Object Class

Date	Remarks and References	Obligations Incurred	Obligations Liquidated	Unliquidated Balançe
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29 SEr 1966	Dre &		200.00	Concessor (1997)
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1226:

9 Stemptember 1960

MEMORANDUM FOR: COMPTROLLER

ATTENTION

FINANCE DIVISION

SUBJECT

MKULTRA, Subproject 122

Under the authority granted in the memorandum dated 13 April 1953 from the DCI to the DD/A, and the extension of this authority in subsequent memoranda, Subproject 120 has been approved and \$2,000 of the over-all MKULTRA project funds has been obligated to cover the subproject's expenses. This obligation of funds should be charged to Allotment 1525-1009-1902.

Chief
TSD/Research Branch

APPROVED	FOR OBLIGATION OF FUNDS:
•	WAR THE STATE OF T
An American descriptions	Receirch Director

	• .		
Date			
No. of the Party o	THE OWNER WHEN THE PARTY	ARTECOPE A CONTRACT	desire some of state p

DELIGATION REFERENCE NO. 256

AUTHORIZING OFFICER

Distribution:

Orig & 2 - Addressee

1 - TSD/CC 1 - TSD/RB



(When Filled In)

I certify that the expenditures listed heroon and on any attachments were incurred for official purposes of a confidential nature, that payment or credit therefor has not been received, and that 00.000 S 500 W CREDIT AMOUNT (Finance use only) 71-80' AMOUNT this accounting is true and correct. HONEY ORCER T1830 はなる いかなのいのな なのかのかいのかいのからの VOUCHER NO. TOTAL EXPENSES VOUCHER NO. 7-12 DESCRIPTION CK. NO. CEJECT X REF. NO. CLASS CERCE 68.70 DVE SHGNATURE OF PAYEE DISBURSEMENTS TOTAL ACCOUNTED FOR ALLOT, OR CUST CASH CASH ON HAND END OF PERIOD OF FINANCE DIVISION WALL WARE the state bearing a triple SIGNATURE OF CERTIFYING OFFICER SIGNATURE OF APPROVING OFFICER REFUNDED HEREWITH CERTIFIED FOR PAYMENT OR CREDIT DATE GAT-62 GAT-66 GAT-66 ACT-NO. TRACT. NO. PERIOD OF ACCOUNTING 3 - VOUCHER USE APPROVED 4 R) 8 SPACE BELOW FOR EXCLUSIVE 2,000.co 3,80,0 CODE S C rosca \*\* EXPEND CODE はないない REVIEWED BY 3 DATE SUBMITTED DATE STATION COOE FROM FILE SIGNATURE OF AUTHORIZING OFFICER See States DESCRIPTION の名の名がある。 8 DBLIGATION REFERENCE NO. CHARGE ALLOTMENT RECEIPTS CERTIFY FUNDS ARE AVAILABLE DESCRIPTION W-ALL OTHER ACCOUNTS 13.33 TOTAL TO ACCOUNT FOR ACCOUNTING BY INDIVIDUAL FOR ADVANCE Follow Instructions on Reverse 8 HAND BEGINNING OF PERIOD Contract to DESCRIPTION - ADVANCE ACCOUNTS 13-27 3 DATE Ž. CASH ON REPARED BY NOTE: લું

FORM 282 USE PREVIOUS EDITIONS.

£13

TOTALS

# INSTRUCTIONS

- If funds, in the form of other than U.S. Dollars were on hand, received, or disbursed during the accounting If advances have been made to third parties, enter the total of such advances outstanding at the beginning of the accounting period period, all pertinent data, i.e., rate, method of acquisition, etc., must be shown. on line la. -4
- If more space is required to explain receipts, prepare receipt form, number and attach hereto. In every case, completely identify the source of receipts. તં
- and enter the total under 1 tem 3. If advances to third parties are outstanding at the close of the account-When a receipt is not obtained, prepare a certificate and attach as a sufficient to list all vouchers, prepare a listing on a separate sneet The voucher may be Attach a voucher for each expenditure and assign a number thereto in numerical sequence. ing period, attach an itemized list and enter the total on line 3a. the receipt obtained from the payee. When space on form is not voucher. 'n
- When accounting not be given for disbursements which are advances to be accounted for. for advances are obtained, list as expenditures or refund of cash, as appropriate. Final credit will ...
- to Account For" must agree with the total disbursements entered Total receipts entered on the line "Total the line following "Total Accounted For." ۲,

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19 September 1960

MINORANDOM POR: THE RECORD

VIA

: TSD/Budget Officer

SUMBER

: Managa, Subproject 122, Invoice #1. Allotsent 1125-1009-1902

1. Involce Ko. 1 is attached covering the above subproject. Payment should be used as follows:

Cashier's check in the amount of \$2,000.00 dream on a payable to

2. The check should be forwarded to Chief, TSD/Research Eranch, through TSD/Erdget Officer, no later than Manday, 3 Colober 1960.

3. This is a final invoice. However, since it is enticipated that additional finds will be obligated for this project, the files should not be closed.

Chicf TSD/Resporch Branch

Attached:

Involca & Cartifications

Distribution: ONE & 2 - Addresses

1 - TSD/FASS

RECEIVED.

5/5

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## INSTRUCTIONS

- or disbursed during the accounting If advances have been rade to third parties, enter the total of such advances outstanding at the beginning of the accounting period period, all pertinent data, i.e., rate, method of acquisition, etc., must be shown. If funds, in the form of other than U.S. Dollars were on hand, received,
- If more space is required to explain receipts, prepare receipt form, number and attach hereto. In every case, completely identify the source of receipts. તાં
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- When accounting advances to be accounted for. cash, as appropriate. for advances are obtained, list as expenditures or refund of which are not be given for disbursements Final credit will
- to Account For" must agree with the total disbursements entered on Total receipts entered on the line "Total the line following "Total Accounted For." 'n

11-88

#### RECEIPT

Receipt is hereby acknowledged of the following check:

Treasurer's Check , dated September 28, 1960, in the amount of \$2,000.00, drawn on the

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10-5-60



19 September 1900

METORYTHAM FOR: THE NACORD

VIA

: TSD/Budget Officer

SUBJUCT

1 Managa, Subproject 122, Involce fl

Allowent 1125-1009-1908

1. Involce No. 1 is attached covering the above subproject. Payment should be unde as follows:

Cashier's check in the ecount of \$2,000.00, drewn on a local bank, tayable to

2. The check should be forwarded to Chief, Tob/Research Breach, through Tab/Dulget Officer, no later than Monday, 3 Catcher 1960.

3. This is a final involce. However, since it is enticipered that additional funds will be obligated for this project, the files should not be closed.

> Catef Top/Research Branch

Attenhed: Invoice & Cortifications

Distribution: Orly 8, 2 - Addressee

1 - TSD/FASS

>2 - TSD/RB

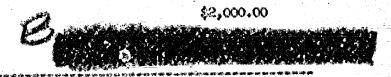
rsd (19 Sept. 60)





INVOICE

For Services



#### CERTIFICATIONS

(1) It is hereby certified that this is Invoice No. 1 applying to Subproject No. 122 of MANARA, that performence is satisfactory, that services are being accomplished in accordance with nutual agreements, that a detailed agenda of the payments and receipts is on file in TSD/RB, that this bill is just and correct and that payment thereof has not yet been made.

Chief, FED/Research Branch

Pates

(2) It is hereby certified that this invoice applies to Subproject No. 122 of MONERA which was duly approved, and that the project is being carriedout in accordance with the memorandum of 13 April 1953 from the DOI to the DD/A, and the extension of this authority in subsequent memoranda.

Research Director

Date:





9 September 1960

NEMORANDUM FOR: COMPTROLLER

HOLLMAKLY

: Pinence Division

SUBJECT

AMULINA, Subproject 122

Under the authority granted in the removandum dated 13 April 1953 from the DCI to the DD/A, and the extension of this authority in subsequent removanda, Subproject 122 has been approved and \$2,000 of the over-all MAULIEM project funds has been obligated to cover the subproject's expenses. This obligation of funds should be charged to Allotment 1525-1009-1902.

American

TSD/Research Brench

APPROVED	FOR	OBLIG	ation	O3	FUIDS:
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DRAFT/S 1900 A

MEMORANDUM FOR: THE RECORD

SUBJECT.

Project MKULTRA, Subproject 122

1. It is requested that Subproject 122 te approved to support in part the research project of University

in accordance with the attached proposal.

"stress" reaction. Its nature and function are not well understood.

Purification and chemical characterization are a necessary preliminary to exploring its biological function. Thas until recently been associated with research program dealing with human stress reactions at Success by in the present study could support materially project, MKULTRA, Subproject 61.

has been briefed fully on this project.

h. This project will be funded through the for security and cover purposes.

The accounting for funds expended shall conform to the established procedures of that organization. Title to any permanent equipment shall remain with an inversity in lieu of overhead charges.

5. The total cost of this project for a period of one year is estimated to be \$2,000 as indicated in the attached budget. Charges





should be made against Allotment Number 1525-1009-1902.

6. No cleared or witting persons are concerned with the conduct of this project.

Chief
TSD/Research Branch

APPROVED FOR OBLIGATION OF FUNDS:

A

el milio

Attachment: Proposal

Distribution: Original Only





August 15, 1960

MEMORANDUM TO:

SUBJECT: Project Proposal entitled:

Principal Investigator.

This proposal has been circulated to
and All comments appear favorable, particularly those
of who is a professor of pharmacology at the
It would appear from his evaluation that this research could constitute a
tine scientific contribution as you may know, has worked with
here at and recently returned to

My only comments are: 1) I do not feel personally able to judge the significance of the research except from a general point of view and, from that standpoint, it appears to be very important; and 2) my only other reaction is the same as is the robservation by which questions the immediate relevance of this proposal to the field of this observation can be rationalized, then I would feel that the positive comments of the Directors and Advisers can lead only to recommendation for approval to support this project.

Program Director

Enc: 2 copies of Proposal

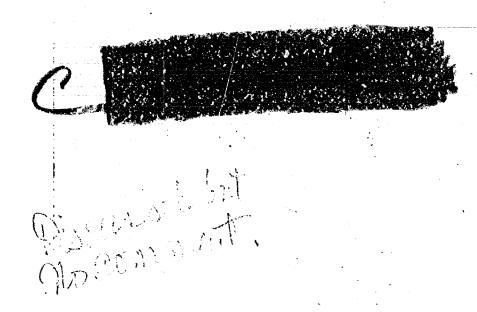
May 1, 1960.



Dear Sirs:

I have enclosed a proposal for consideration by the for support for a series of studies conce med with Neurokinin, a substance that appears to be of great importance in the pathological mechanisms by which man's relationship to his environment influences health.

Sincerely yours,



#### PROPOSAL

Author:
Institution: Department of Pharmacology, University of

The central nervous system evokes, integrates, and modulates
the body's adaptive responses to the environment. These responses, necessary to
survival when appropriate, are implicated in the etiology and course of disease of
many categories when inappropriate. It is well established that reactivity to noxious
stimulation can be modulated by the central nervous system through control of the
timing and amount of adrenal cortical stimulating hormone (AC IH) from the pituitary
gland. Recent experiments at the have shown that another major
route for central nervous system modulation of the inflammatory response exists. This
latter route is through vasemoter control and through modification of the magnitude of
local, neuronal reflexes. A potent vasodilator substance is implicated in these reactions.

The applicant has been one of the ho has defined this biochemical substance as neurokinin. Neurokinin apparently is a vasodilator polypeptide formed by the splitting of a protein (globulin) present in extracellula r fluid. This splitting is due to the action of a proteclytic enzyme (neurokinin forming enzyme), possibly an intraneuronal protects. The same enzyme has been observed

in the cerebrospinal fluid and in perfusate of the cerebral ventricle during stimulation of the brain, thus giving a source of the material for study. A crude preparation of powdered neurolekinin has been prepared by incubation of globulin with cerebrospinal fluid collected from patients with schizophrenia, which contain large amounts of neurokinin-forming enzyme.

The application has worked with and and in the preparation of clude neurokinin.

#### e) Immediate Objectives --

To prepare and characterize highly purified neurokinin by chromatographic chemical methods.

### f) Long Range Objectives

To define the pharmacologic properties, and contribute to understanding of the physiological and pathological significance of neurokinin.

## II. Methods

- a) Obtain neurokinin forming enzyme from human cerebrospinal fluid and from perfusate of cerebral ventricles of laboratory animals during stimulation of the brain.
- b) Preparation of crude neurokinin by incubation of cerebrospinal fluid with globulin, precipitation, and extraction with alcohol.
- c) Eurification of the crude preparation by paper and column chromatographic separation of the components in the crude preparation.
  - d) Pharmacologic studies to identify the active fraction
    - a. isolated rat uterus, rat duodenum bioassay
      and assay of depressor action on the blood pressure.

- e) Pharmacologic characterization of the properties of pulific neurokinin.
- I) Electroencephalographic changes induced by intraventricular and intercarotid injection in the cat.
- 2) Behavioral changes induced by intraventricular injections of neurokinin into unanesthetized cats with implanted intraventricular cannulae.

  It is expected that these studies will require one year to complete.

IV. Budget

a) Apparatus to augment equipment available in the

	$\mathcal{F}/\mathcal{B}$	
	1) Stereotoxic (Horsely Clark) apparatus for perfusion	of cerebral
ventricle	es and for placement of introventricular connulae	\$900.00
	2) Perfusion pump	200.00
	3) Small polyethylene Tubing	50.00
	4) Recording kimograph for smooth muscle bioassay	250.00
	5) Miscellançous equipment, manameter, clamps, cannulae	100.00
	<ul> <li>b) Drugs and supplies for electrophoresis and for pharmacologic studies</li> </ul>	300.00
	c) Animals, animal food, and cages	200,00

TOTAL

\$2,000.00

The author is

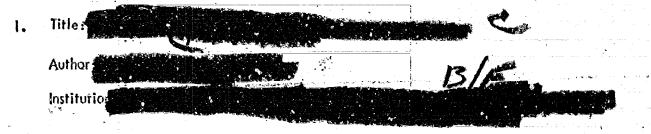
The author is engaged in full time research and teaching. He has worked as a professional or years and has worked specifically with vasodilator polypeptides with . He has recently completed a fellowship with tithe working with neurokinin and becoming acquainted with the point of view of the program.

is a tax exempt organization of the

VI and VII:

This project has not been undertaken previously and no support has been our is being requested of other foundations.

#### PROPOSAL



The central nervous system evokes, integrates, and modulates
the body's adaptive responses to the environment. These responses, necessary to
survival when appropriate, are implicated in the etiology and course of disease of
many categories when inappropriate. It is well established that reactivity to noxious
stimulation can be modulated by the central nervous system through control of the
timing and amount of adrenal cortical stimulating hormone (::AC TH)from the pituitary
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have shown that another major
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### e) Immediate Objectives.

To prepare and characterize highly purified neurokinin by chromatographic chemical methods.

#### f) Long Range Objectives

To define the pharmacologic properties, and contribute to understanding of the physiological and pathological significance of neurokinin.

### II. Methods

- a) Obtain neurokinin forming enzyme from human cerebrospinal fluid and from perfusate of cerebral ventricles of laboratory animals during stimulation of the brain.
- b) Preparation of crude neurokinin by incubation of cerebrospinal fluid with globulin, precipitation, and extraction with alcohol.
- c) Rurification of the crude preparation by paper and column chromatographic separation of the components in the crude preparation.
  - d) Phermacologic studies to identify the active fraction
    - a. isolated rat uterus, rat duodenum bioassay
       and assay of depressor action on the blood pressure.

- e) Pharmacologic characterization of the properties of pulific neurokinin.
- I) Electroencephalographic changes induced by intraventricular and intercarotid injection in the cat.
- 2) Behavioral changes induced by intraventricular injections of neurokinin into unanesthetized cats with implanted intraventricular cannulae.

It is expected that these studies will require one year to complete. 111.

IV. Budget

a) Apparatus to augment equipment available in the



1) Stereotoxic (Horsely Clark) apparatus for perfusion of cerebral ventricles and for placement of intraventricular cannulae \$900:00 200.00 2) Perfusion pump 50,00 3) Small polyethylene Tubing 4) Recording kimograph for smooth muscle bioassay 250:00 100.00 5) Miscellangous equipment, manometer, clamps, cannulae b) Drugs and supplies for electrophoresis and for 300.00 pharmacologic studies 200.00 c) Animals, animal food, and cages

\$2,000.00 TOTAL

The author is

is a tax exempt organization of the State

The author is engaged in full time research and teaching. He has worked as a professional for years and has worked specifically with vasodilator polypeptides with the has recently completed as fellowship with at The working with neurokinin and becoming acquainted with the point of view of the program.

VI and VII.

٧.

This project has not been undertaken previously and no support has been or: is being requested of other foundations.

(2,2-

26 August 1960

122-16

ELMORANDUM FOR: THE RECORD

SUBJECT

Approval of Dr

Proposal

ATTENDANCE

Drs. Gottlie

III FII Y

Request for \$2000.00 to provide equipment and supplies for study was approved. Neurokinin is presumed to be a major mediator in the "stress" reaction. Its nature and function are not well understood. Purification and chemical characterization is a necessary preliminary to exploring its biological function. This proposal has received the strong endorsement of

2. The funding mechanism will be the Title to permanent equipment

3. A name check of proved negative. He will remain unwitting of true Sponsor

TSD/Research Branch

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(TSD/RB)

Rec'd. Full.

See July 60

See

WHI.



182-17

23 August 1960

MEMORANDUM FOR: THE RECORD

SUBJECT

Discussion with on Proposal

1. At 1100 that with Mr.

to brief him on the proposal washined doubt derable

echanism, its origin and its the colon (Stemming in partition his participation in the old I assured him, in answer to his question, that arrangements could be made to approach grantees to undertake imissions. Further, if his division needed a funding mechanism with sound cover to promote any that could be fitted into the cover, the was available to help out.

2. Although saw no immediate need, he was genuinely enthusiastic and wished to make division brass aware of the possibilities.



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for file