

1130 R

L. D. MacKay, Director
Finance Division

November 22, 1954

Herman M. Roth, Director
Research and Medicine Division

CONTRACT NO. AT-(40-1)-1081 - DUKE UNIVERSITY SCHOOL OF MEDICINE

H. M. Roth
J. R. Moore

SYMBOL: OR:JER

This is to advise you that the work under Contract No. AT-(40-1)-1081 with the Duke University School of Medicine has been completed and the final report has been submitted.

The contract should therefore be closed out.

ORIGINAL SIGNED BY
HERMAN M. ROTH
Herman M. Roth

cc: J. R. Moore
F. E. Matherson

Roussaville:lr

REPOSITORY Oak Ridge Operations
COLLECTION Records Holding area
Documents 1944-94
BOX No. 3 of 3 Bldg. 2714-H
AT-(40-1)-1081
FOLDER Duke Univ.

1110665

DC:JR

Oak Ridge, Tennessee
February 5, 1953

Duke University
School of Medicine
Durham, North Carolina

Attention: Mr. A. S. Brewer, Business Manager and Comptroller

Subject: MODIFICATION NO. 2 TO CONTRACT NO. AT-(40-1)-1081

Gentlemen:

Enclosed, for your retention, you will find one duly signed copy and one conformed copy of Modification No. 2 to your Contract No. AT-(40-1)-1081.

Very truly yours,

John R. Moore
Director, Contract Division
Oak Ridge Operations

JNF
Enclosure:
Mod. 2 (in dup.)

Nicholson: ja

OFFICE	<i>Contracts</i>	<i>Asst. Dir. Contract Div.</i>	<i>Asst. Dir. Contract Div.</i>			
SURNAME	<i>Nicholson</i>	<i>Langham</i>	<i>Evans</i>			
DATE	<i>2-5-53</i>	<i>2-5-53</i>	<i>2-5-53</i>			

1110666

Mod. 2 to Cont. AT-(LC-1)-1081

Duke University

Distributed February 5, 1970

Washington
Contract files
Finance (2)
Research & Medicine (2)
Washington (BB-2)
extra copies

1110667

Office of the
Business Manager and Comptroller

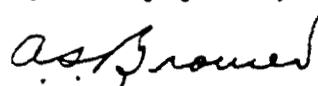
January 30, 1953

Atomic Energy Commission
Oak Ridge
Tennessee

Gentlemen:

Enclosed herewith I am returning three executed copies of Contract No. AT-(40-1)-1081. As soon as they have been executed by you, it will be appreciated if you will return one signed copy and one conformed copy for our files.

Very truly yours,



Business Manager and
Comptroller

ASB/ps
Encl.

1110668
1570
11-6-53

1110668

DC:JN

Oak Ridge, Tennessee
January 23, 1953

Duke University
School of Medicine
Durham, North Carolina

Attention: Dr. R. Wayne Rundles

Subject: MODIFICATION NO. 2 TO CONTRACT NO. AT-(40-1)-1081

Gentlemen:

Enclosed, in triplicate, is Modification No. 2 to the contract numbered as shown in the subject line above, which incorporates in a revision to Appendix "A" the program and budget for the third period of performance beginning January 1, 1953 and ending December 31, 1953.

If the modification, as submitted, is satisfactory to you it is requested that you sign the three copies thereof in the space provided for the Project Leader and have the modification signed by the proper official of the University, returning the three copies to this office. After signature on behalf of the Commission, one duly signed copy and one conformed copy of the modification will be returned to you for your retention.

Very truly yours,

R. C. Humphries
Acting Director
Contract Division
Oak Ridge Operations

[Handwritten initials]
Enclosure
Mod. 2 (in trip.)

Nicholson:jn

OFFICE	<i>Contracts</i>				
SURNAME	<i>Nicholson Humphries</i>				
DATE	<i>1-23-53</i>	<i>1-23-53</i>			

1110669

J. W. Caid, Jr., Assistant General Counsel

January 5, 1953

R. G. Humphries, Assistant Director, Contract Division

REQUEST FOR PREPARATION OF RENEWAL CONTRACT FOR ONE YEAR WITH
DUKE UNIVERSITY, SCHOOL OF MEDICINE, DURHAM, NORTH CAROLINA
CONTRACT NO. AT-(14-1)-1081, DR. WAYNE RUNDLES, PROJECT ILLNESS

SUBJECT: AD-103

Forwarded is an approved proposal for renewal of subject contract
for one year beginning January 1, 1953. The approval is covered by
Procurement Directive No. HM-53-109, dated December 15, 1952, in
the amount of \$10,000.00.

It is requested that you prepare an appropriate modification to
extend this contract for another year and provide for the payment
of \$10,000.00 in accordance with the enclosed revised budget.

Dr. C. S. Shoup will act as Technical Advisor on this contract.

R. G. Humphries

- 1. Memo to Kasechen, 12/30/52.
- 2. Memo to Washington, 12/15/52.
- 3. Ltr to Dr. Rundles, 12/24/52.
- 4. Proposal.
- 5. Resume.

CC: C. S. Shoup
L. B. Mackay
Ed Flagler
J. Nielsen

From: rfb

OFFICE ▶	<i>Contract Div.</i>				
SURNAME ▶	<i>Humphries</i>				
DATE ▶	<i>1-6-53</i>				

UNITED STATES ATOMIC ENERGY COMMISSION
OAK RIDGE OPERATIONS

MEMORANDUM OF OBLIGATION TRANSFERS

Memorandum No. OR-52-W-18

Date: February 8, 1952

TO : Lindsley H. Noble, Controller, Washington
FROM : L. D. Mackay, Director of Finance, Oak Ridge
SUBJECT: TRANSMITTAL OF OBLIGATING DOCUMENTS

Enclosed are the following contracts, purchase orders and/or other obligating documents executed pursuant to Procurement Directives issued by your office:

<u>Document</u>	<u>Proc. Dir.</u>	<u>Allegation Chargeable</u>	<u>Amount</u>
AT-(40-1)-1081	EM-52-96	260-00-01	\$3,544.00

L. D. Mackay

Enclosures:
As above

Martinelli:ncx

cc: Accts. Payable w/cpy of Contract (W/D)
Contract Section ✓

1110671

DC:JN

Oak Ridge, Tennessee
February 7, 1952

Duke University
School of Medicine
Department of Medicine
Durham, North Carolina

Attention: Dr. Wayne Rundles

Subject: MODIFICATION NO. 1 TO CONTRACT NO. AT-(40-1)-1081

Gentlemen:

Enclosed, for your retention, you will find one duly executed copy and one conformed copy of Modification No. 1 to your Contract No. AT-(40-1)-1081.

Very truly yours,

[Signature]
John R. [unclear]
Chief, Contract Division
Oak Ridge Operations

✓ Enclosures: *[initials]*
Mod. 1 (in dup.)
Nicholson:jn

OFFICE ▶	Contract and Gen. B.					
SURNAME ▶	Nicholson		<i>[initials]</i>			
DATE ▶	2-7-52	2-7-52	2-7			

H 500

1110672

Mod. 1 to Cont. AT-(LO-1)-1081

Duke University

Distributed February 7, 1952

GAC

Washington

Contract files

Finance (2)

Research & Medicine (2)

Washington (B&M-2)

extra copy

1110673

DC:JN

Oak Ridge, Tennessee
January 18, 1952

Duke University
School of Medicine
Department of Medicine
Durham, North Carolina

Attention: Dr. Wayne Rundles

Subject: MODIFICATION NO. 1 TO CONTRACT NO. AT-(40-1)-1061

Gentlemen:

Enclosed, in triplicate, is Modification No. 1 to the contract numbered as shown in the subject line above, which incorporates in a revision to Appendix "A" the program and budget for the second period beginning January 1, 1952 and ending December 31, 1952.

If the modification, as submitted, is satisfactory to you it is requested that you sign the three copies thereof in the space provided for the Project Leader and have the modification signed by the proper official of the University, returning the three copies to this office. After execution on behalf of the Commission, one duly executed copy and one conformed copy of the modification will be returned to you for your retention.

Very truly yours,

John R. Moore
John R. Moore
Chief, Contract Division
Oak Ridge Operations

VNF
Enclosure:
Mod. 1 (in trip.)

Nicholson: ja

OFFICE ▶	<i>Contract. Cont. Div. (3)</i>					
SURNAME ▶	<i>Nicholson</i>			<i>AD</i>		
DATE ▶	<i>1-18-52</i>	<i>1-18-52</i>	<i>1-18</i>			

1110674

4221

J. Wallace Culp, Jr., Assistant General Counsel

January 11, 1952

R. G. Humphries, Chief, Contract Coordination Branch

RENEWAL OF CONTRACT AT-(10-1)-1002 - DUKE UNIVERSITY SCHOOL OF MEDICINE

ATTENTION: **REVISION**

Forwarded is an approved proposal for extending research under Contract No. AT-(10-1)-1002 with Duke University with Dr. E. Wayne Rundles as Project Leader, as covered by Procurement Directive 10-78-96.

Washington has suggested and the Contractor has consented in its reduction in the proposed capital equipment item to \$500 and the communications and travel item to \$200. With these adjustments the budget set forth in the Contractor's proposal is in the amount of \$9300 before adding overhead at 6%, or \$9858, making a total of \$10,858 for the second year. The Contractor's letter dated December 26, 1951, attached, reports there will be a balance at the end of the year of \$1500. Deducting this balance from the approved budget leaves a net payment due for the second year in the amount of \$8,558.

It is requested that you prepare an appropriate notification to extend the term of the contract to cover the research program and provide for a lump sum payment in the amount of \$8,558.

Dr. G. S. Shoup will act as technical advisor on this contract action.

R. G. Humphries

Encls.:

memo in Lanchester 12-13-51 w/

memo in Tuttle 11-26-51

Contractor's proposal dtd. 10-1-51 & ltr 12-26-51

- cc: C. E. Shoup
- L. B. Hooker
- Ed. Hooper
- J. Nicholson

Humphries:lm

OFFICE	<i>Contract Coordination Br.</i>				
SURNAME	<i>R. G. Humphries</i>				
DATE	<i>1-14-52</i>				

1110675

CONTRACTOR'S STATEMENT AND AGREEMENT REGARDING
CONTINGENT OR OTHER FEES FOR SOLICITING OR
SECURING GOVERNMENT CONTRACTS

(REFERENCE: General Services Administration General Circular
No. 2, dated May 1, 1950, Section 4)

_____ 0 _____

CONTRACTOR: Duke University

CONTRACT NO.: AT-(40-1)-1081

DATE OF CONTRACT: December 14, 1950

_____ 0 _____

I, A. Hollis Edens, representing Duke University, do hereby state that said
(Contractor)

Duke University has, has not, employed or
(Contractor)

retained a company or person (other than a full-time employee) to solicit
or secure this contract, and said Duke University
(Contractor)

hereby agrees that it will furnish such information relating thereto as may
be requested by the Atomic Energy Commission.

Duke University
(Contractor)

(SIGNED) BY: A. Hollis Edens

TITLE: A. Hollis Edens,
President.

DATE: January 12, 1951.

CONTRACTOR'S STATEMENT AND AGREEMENT REGARDING
CONTINGENT OR OTHER FEES FOR SOLICITING OR
SECURING GOVERNMENT CONTRACTS

(REFERENCE: General Services Administration General Circular
No. 2, dated May 1, 1950, Section 4)

————— 0 —————

CONTRACTOR: Duke University

CONTRACT NO.: AT-(40-1)-1081

DATE OF CONTRACT: December 14, 1950

————— 0 —————

I, A. Hollis Edens, representing _____

Duke University, do hereby state that said
(Contractor)

Duke University has, has not, employed or
(Contractor)

retained a company or person (other than a full-time employee) to solicit
or secure this contract, and said Duke University
(Contractor)

hereby agrees that it will furnish such information relating thereto as may
be requested by the Atomic Energy Commission.

Duke University
(Contractor)

(SIGNED) BY: _____

A. Hollis Edens,
President.

DATE: January 12, 1951.

1110677

GC:JN

Oak Ridge, Tennessee

JAN 9 1951

Duke University
School of Medicine
Durham, North Carolina

Attention: Mr. A. S. Brewer

Subject: CONTRACT NO. AT-(40-1)-1882

Dear Mr. Brewer:

Enclosed, in accordance with your letter dated December 11, 1950, you will find one duly executed and three conformed copies of the subject contract for your retention.

There is also enclosed, in duplicate, Contractor's Statement and Agreement Regarding Contingent or Other Fees For Soliciting or Securing Government Contracts. This statement is required by the Commission in accordance with established Government procedures. It is requested that both copies of the statement be properly executed and returned to this office.

Very truly yours,

JW
J. W. Old, Jr.
Assistant General Counsel

NFF
Enclosures:
Contract (in quad.)
CSA (in dup.)

Nichols:jn

OK CC: Contracts

J. W. Old, Jr.

Legal Reading File

OFFICE ▶	<i>Contracts</i>				
SUPNAME ▶	<i>Nichols:jn</i>				
DATE ▶	<i>1-8-51</i>	<i>1/9</i>			

1110678

Contract No. AT-(40-1)-1081

Duke University

Distributed January 2, 1951

GAO

Washington

Contract files

Finance (2)

Research & Medicine (2)

Contractor (1 sgnd & 3 conformed)

Washington (Tuttle)

Duke University
DURHAM
NORTH CAROLINA

Office of the
Business Manager and Comptroller

December 11, 1950

U. S. Atomic Energy Commission,
Oak Ridge, Tennessee.

Attention: Mr. C. Vanden Bulck,
Assistant to the Manager,
Oak Ridge Operations.

Dear Mr. Vanden Bulck:

Attached hereto we are returning three copies of Contract No. AT-(40-1)-1081, which have been properly signed by the President of the University and witnessed.

As soon as the contract has been executed by you for the Atomic Energy Commission, it will be appreciated if one of the signed copies is returned to us and, in addition, three conformed copies sent us for use in the administration of the contract.

Very truly yours,



Business Manager and
Comptroller.

ASB:jpj
cc: Dr. Wayne Rundles.

CONTRACTS

1110680

Office Memorandum • UNITED STATES GOVERNMENT

TO : J. W. Calk, Jr., Assistant General Counsel DATE: January 5, 1953

FROM : A. G. Humphries, Assistant Director, Contract Division

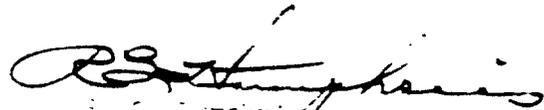
SUBJECT: REQUEST FOR REPLENISHMENT OF ANNUAL CONTRACT FOR ONE YEAR WITH
DUKE UNIVERSITY, SCHOOL OF MEDICINE, DURHAM, NORTH CAROLINA
CONTRACT NO. AD-(40-1)-1081, DR. WAHNE RUMBLES, PROJECT LEADER

SYNCL: AD:ARB

Forwarded is an approved proposal for renewal of subject contract for one year beginning January 1, 1953. The approval is covered by Procurement Directive No. EM-53-109, dated December 15, 1952, in the amount of \$10,000.00.

It is requested that you prepare an appropriate modification to extend this contract for another year and provide for the payment of \$10,000.00 in accordance with the enclosed revised budget.

Dr. C. S. Shoup will act as Technical Advisor on this contract.


A. G. Humphries

1. Memo fm Wassonau, 12/30/52.
2. Memo fm Washington, 12/25/52.
3. Ltr fm Dr. Rumbles, 12/22/52.
4. Proposal.
5. Resume.

CC: C. S. Shoup
L. D. MacKay
Ed Ziegler
J. Nicholson

Brown:arb

1110681

Office Memorandum • UNITED STATES GOVERNMENT

TO : John Moore, Director, Contract Division

DATE: December 30, 1952

FROM : Kenneth Kasschau, Director, Research and Medicine Division

SUBJECT: REQUEST FOR PREPARATION OF A RENEWAL CONTRACT FOR ONE YEAR WITH DUKE UNIVERSITY, SCHOOL OF MEDICINE, DURHAM, N. C. CONTRACT NO. AT-(40-1)-1081, DR. WAYNE RUNDLES, PROJECT LEADER.

SYMBOL: ORB:CSS

We are in receipt of approval by the Division of Biology and Medicine for renewal for one year of the subject contract, and Procurement Directive No. BM-53-109 in the amount of \$10,000. The budget submitted called for the sum of \$12,420. On December 23, 1952, Dr. C. S. Shoup asked Dr. Rundles to submit a new revised budget in line with Washington recommendations.

The revised budget has now been received from Dr. Rundles under date of December 24, and is enclosed herewith. In the revised budget, Dr. T. Arends is to be on the project only until March, 1953, since soon after that time he will return to Venezuela. From March onward the main body of the technical work will be carried by additional personnel to be supplied who are trained in clinical biochemistry. It will be noted that the items under capital equipment in the original budget in the amount of \$1000 are removed from the revised budget.

Dr. Rundles reports no remaining unobligated balance. We would appreciate the assistance of your office in preparation of this renewal contract in the amount of \$10,000 including 8% overhead.

Dr. C. S. Shoup will serve as Technical Advisor for this Division. A summary of the research program is enclosed.

Kenneth Kasschau
Kenneth Kasschau

5 Encls.:

1. Memo frm Wash.
2. Pro. Dir.
3. Ltr dtd 12/24/52 frm Dr. Rundles.
4. Proposal.
5. Resume.

Shoup:ec

Approved by
FD- BM-53-109
\$10,000
12/15/52
1289

UNITED STATES ATOMIC ENERGY COMMISSION
DIVISION OF BIOLOGY AND MEDICINE
WASHINGTON, D. C.

DATE: _____

TO : Kenneth Kasschau, Director, Office of Research and Medicine
Oak Ridge Operations Office
FROM : James F. Haggerty, Medical Branch
SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION
SYMBOL : BMM:JFH

This letter with enclosures, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University - School of Medicine
2. Investigator (s): R. Wayne Rundles, M. D.
3. Title: "Study of the Metabolism of the Human Bone Marrow"
4. () New Contract or (X) Renewal of Contract No. AT(40-1)1081
5. Duration - From: January 1, 1953 To: December 31, 1953
6. AEC Technical Supervision: Medical Branch
7. Recommended Support: \$10,000.00, including overhead at 8%
Authorized by Procurement Directive No. EM53-109
Issued _____ \$ 10,000.00
Activity No. 6300
8. Other Comments:

It is recommended that the budget be revised at a level of \$10,000.00, with deletion of funds for purchase of manometers and analytical balance.

Since this constitutes the third year of support, there is no assurance of support beyond this contract year. ~~_____~~

1110683

8. Comments (Continued)

9. Security Requirements:

In accordance with the provisions of GM-93 (Revised March, 1950), and the requirements of the Declassification Guide, the Division of Biology and Medicine has determined that the following security precautions should be taken in connection with the proposed research contract.

Since there is essentially zero chance that restricted data will be required or developed, no personnel security requirements should be imposed.

10. Reports: (X) Reports are to be required as provided for by Memorandum Instruction of November 9, 1949, on subject "Direct Research Contract Reports".
- () Special Reports Instructions are as follows:

- Enclosures: (X) "A" - Proposal, dated Undated
- () "B" - Notification letter, dated 11/10/49
- () "C" - Other correspondence, _____ letters
- (X) "D" - Procurement Directive BM53-109

Distribution:

Addressee: Original (w encl.)	Division File: Yellow Copy (w encl.)
1st Copy (" ")	Pink Copy (w/o encl.)
2nd Copy (" ")	Green Copy (" ")
Program Analysis	Branch File: White Copy (w ")
Branch: White Copy (w/o encl.)	

DUKE UNIVERSITY

December 24, 1952

Dr. Sam Shoup
U.S. Atomic Energy Commission
Office of Research and Medicine
P.O. Box E
Oak Ridge, Tennessee

Dear Dr. Shoup:

I appreciate very much your telephone call yesterday, regarding the budget for our AEC research project, "Study of the Metabolism of the Human Bone Marrow", for the calendar year, 1953. I have gone over our research program again in the light of the revisions suggested by your Committee. Some items of durable nature may be required during the course of the year, but we shall likely be able to obtain them from other sources. There will be some changes in our technical personnel during the course of the year.

The funds allotted for our work during the year, 1952, have been expended completely.

Enclosed is a revision of the budget for the coming year, which I believe will allow us to operate with close to maximum efficiency. We appreciate very much the support and interest of your Commission in our work here.

Very sincerely yours,

/s/ Wayne Rundles, M. D.

WR:mc
CC: Dr. James F. Haggerty
Enclosure

COPY

enc = c

1110685

U. S. Atomic Energy Commission

Research Contract No. AT - (40-1) - 1081

Budget, January 1, 1953 - December 30, 1953

Professional assistance (Dr. T. Arends, January-March, 1953)	\$ 825.00
Technical assistance (Mrs. E. Sallenberger)	3400.00
Part-time technical assistance	2759.00
Expendable apparatus and supplies, chemicals, reagents, glassware, photographic material, electrodes, filters, blood from donors, blood packs, etc.	2000.00
Communications and travel	<u>275.00</u>
	<u>\$9259.00</u>
Unexpended, 1952	<u>0.00</u>
	<u>\$9259.00</u>
University Overhead, 8%	<u>741.00</u>
	<u>710.72</u>
	<u>\$9999.72</u>
	<u>1,000.00</u>

s/s Wayne Hundles

WR:mc

COPY

1110686

copy

PROGRESS REPORT

ON

Research Project Sponsored by the Atomic Energy Commission
Metabolism of Human Bone Marrow, R. W. Rundles, M. D.,
Duke University School of Medicine, October 1, 1952

During the past year, our major effort in this project has been expended in perfecting technical procedures required for the study of leukocytes in vitro, and in studying certain aspects of the metabolism of normal human leukocytes. The latter has been necessary to provide reference data with which to compare the metabolic activities of immature leukocytes and bone marrow.

Technical Procedures: The method of separating viable leukocytes from normal blood without exposing them to anti-coagulants, wettable surfaces, or excessive gravitational force, as outlined in last year's Progress Report, has proved to be satisfactory. In patients with myelogenous leukemia, an adequate number of leukocytes has been obtained for metabolic studies, in the Warburg apparatus from as little as 50-100 ml. of whole blood. In preparing leukocytes for incubation, the concentrated cells have been resuspended in the donor's plasma, diluted 1/5 with a buffered electrolyte solution containing no divalent ions. It is possible that metabolic effects may be produced by small molecules, unstable proteins, or enzymes in the plasma. This will be studied in coming months by substituting for the plasma in which the leukocytes are suspended a dialyzed solution of albumin and alpha-globulins (SPPS, Cohn).

1110687

5 Oct #4

The preparation of aspirated human bone marrow tissue for metabolic study involves additional technical problems. The use of Dowex-50 cation exchange resin to prevent coagulation appears to be impractical. The use of the soluble chelating compound, ethylene diamine tetracetate (EDTA) is more promising. Before it can be adopted, however, its effect on the metabolism of leukocytes, if any, will have to be studied.

The separation of immature marrow cells from erythrocytes appears to be feasible if a high density protein solution (SPPS) containing lactose is used. The effect of this medium on the metabolism of leukocytes after they have been exposed to it for varying periods of time awaits study.

Another technical problem involves the determination of the quantity of the marrow tissue being utilized for metabolic measurements. We have found that cell counts are impractical. The possibility of using the nucleic acid content of marrow as a measure of the amount of tissue involved in a given metabolic process is being explored.

Studies on Mature Leukocytes: A number of fundamentally important observations have been made during the last year by Dr. Gordon McKinney and collaborators on the metabolism of mature leukocytes. Three activities in particular have been studied: respiration, glycolysis, and the utilization of carbohydrates. The effects of certain sugars, metabolic intermediates and inhibitors on these processes were also studied.

Some findings from this study were presented at the Federation meeting in New York City in April, 1952. Reprints of the Federation abstract are enclosed. (McKinney, Gordon R., Rundles, R. Wayne, Martin, Samuel P.: Respiratory activity of human leukocytes in vitro. Federation Proceedings. Vol. 11: 256, 1952.) The complete studies have recently been accepted for publication. (McKinney, Gordon R., Martin, Samuel P., Rundles, R. Wayne, Green, Rosalie: Respiratory and glycolytic activities of human leukocytes in vitro. Journal of Applied Physiology. In press.)

The principal conclusions of the latter manuscript are as follows:

(1) The respiration, glycolysis, and the utilization of carbohydrates by mature leukocytes obtained from the blood of humans was studied by methods which avoided exposing the cells to anti-coagulants, excessive gravitational force, or wettable surfaces.

(2) Increasing the glucose concentration from low levels to a physiologic range increased lactate formation proportionately to the amount of glucose added. In the presence of added glucose, oxygen consumption diminished.

(3) Fructose did not increase lactic acid production comparably to glucose and was without effect on respiration. Both fructose and glucose reduced glycogenolysis.

(4) Low oxygen tension did not alter the high rate of aerobic glycolysis of mature leukocytes.

(5) The effect of metabolic inhibitors and intermediates indicated the existance of Krebs cycle activity in the human polymorphonuclear leukocyte.

During the first year of work on this project, circumstances beyond our control prevented the full utilization of our hematology technicians' time on this project. This additional technical assistance enabled us to carry out a study of the effect of triethylene melamine in neoplastic diseases, which has provided an abundance of leads for further study and reference to marrow function. Certain aspects of these studies are being continued at this time. A publication acknowledging the sponsorship of the Atomic Energy Commission in this project has been published. (Rundles, R. Wayne, Barton, W. Bruce: Triethylene melamine in the treatment of neoplastic disease. Blood. Vol. 7: 483-507, 1952.)

Plans for the Remainder of This Year: Technical problems which await solution and on which work is being done were outlined above. We now plan on proceeding with studies comparable to those performed with mature human leukocytes utilizing immature granulocytes and lymphocytes obtained from the blood of patients with leukemia, and bone marrow aspirated from normal persons and from patients with proliferative diseases involving hemopoietic tissues. After these tissues have been studied, we can approach the problem of investigating the gross alterations in the cellular metabolism of leukocytes from blood and bone marrow which may be produced by chemotherapeutic agents and by ionizing irradiation.

Wayne Rundles, M. D.

PERSONNEL

Gordon H. McKinney, Ph.D., has worked full time on this project since July 1, 1951. He is supported by an American Cancer Society Fellowship.

Ray Schipke, M. D., continued work on this project as outlined before through February, 1952, when he began the private practice of pediatrics in Hartford, Connecticut.

Tulio Arends, M. D., took over Dr. Schipke's work at first on a part-time basis in January, 1952. He assists us with the clinical supervision of patients whom we use for investigation, with the development of protein solutions in which to study leukocyte metabolism, and with other chemical determinations.

Mrs. Elaine Sullenberger was transferred to this project to work full time, January 1, 1952. She has been our chief technician, performing cell counts, processing blood, doing lactate analyses, etc. She has been helped part time by Miss Bobby J. Callahan and Clinton Talley.

1110691

EXPENDITURES: (through August 31, 1952)

<u>Salaries:</u>	Dr. Gordon R. McKinney	\$ 0.00
	Dr. Ray Scripke, \$150/mo., 6 mos.	200.00
	Dr. Tulio Arends, \$100/mo., 6 mos.	600.00
	\$275/mo., 2 mos.	550.00
	Mrs. Elaine Sullenberger, \$250/mo.	2,000.00
	Miss B. J. Callahan, \$210/mo.	840.00
	Mr. Clinton Talley, \$200/mo.	400.00
<u>Social Security:</u>		17.56
<u>Capital Equipment:</u>		279.86
<u>Expendable Equipment and Supplies:</u>		1,283.31
<u>Communications and Travel:</u>		20.10
<u>University Overhead:</u>		535.97
		<hr/> \$7,176.84

We estimate that the total amount of the grant, \$10,800, will be expended by December 31, 1952.

Summary: The first two years' work on this project has revealed the difficulties involved in this type of work. Progress has been satisfactory and should become more rapid as work continues. Plans have been outlined for another 1-2 years' work in this field.

PUBLICATIONS:

Rundles, R. Wayne, Barton, W. Bruce: Triethylene melamine in the treatment of neoplastic disease. *Blood*. Vol. 7: 483-517, 1952.

McKinney, Gordon R., Rundles, R. Wayne, Martin, Samuel P.: Respiratory activity of human leukocytes in vitro. *Federation Proceedings*. Vol 11: p.256, March, 1952.

McKinney, Gordon R., Martin, Samuel P., Rundles, R. Wayne, Green, Rosalie: Respiratory and glycolytic activities of human

leukocytes in vitro. Journal of Applied Physiology. In press.

Martin, Samuel P., Chaidhuri, S. M., Green, Rosalie, McKinney, Gordon R.: The effect of cortisone on lysoytic rate of human leukocytes in vitro. To be published.

October 1, 1952

Proposal for Extension of Research Project Supported by the
Atomic Energy Commission

1. Title. Metabolism of Human Bone Marrow.
2. Institution: Duke University School of Medicine.
3. Investigators. R. Wayne Rundles, Ph.D., M. D.
Gordon R. McKinney, Ph.D., and others.
4. Scope and Present Status. Summarized in Progress Report dated October 1, 1952.
5. Outline of work to be undertaken: Our plans for the coming winter have been outlined in our Progress Report. We plan to extend our studies now to the investigation of the respiration, glycolysis, and the utilization of carbohydrates of immature leukocytes obtained from the blood of patients with leukemia and from the bone marrow.

In addition to the metabolic measurements already being carried out in our laboratory, which pertain to carbohydrate metabolism largely, we shall need to develop methods for study in fatty acid and amino acid utilization. The latter will necessitate the use of isotopes. To attain our goal, a comprehensive study of the metabolism of the human bone marrow in normal people, in disease states, and following chemical and physical injury, will obviously require intensive and continued work for some period of time.

1110693

Proposed Budget for the Study of the Effects of
Cadmium on the Growth of *Chlorella*, 1964

<u>Salaries:</u>	Professional (Dr. Willie Arnold),	10,000.00
	Technical (Mrs. E. Sollenberger)	3,400.00
	Others, part time	1,800.00

Capital Equipment:

Manometers, analytic balance, centrifuge accessories \$ 1,000.00

Expendable Equipment and Supplies:

Chemicals, reagents, glassware, bio. & from volunteer donors. 1,500.00

Communications and Travel:

200.00
200.00
400.00

Institutional Overhead, 25%:

999.00

Total:

17,000.00

Principal Investigator

Willie Arnold
Willie Arnold, Ph.D.
Department of Biology
The University of North Carolina

Administrative Director

The University

Department of Biology
The University of North Carolina

Respiratory activity of human leukocytes in vitro.

GORDON R. MCKINNEY, R. WAYNE RUNDLES
AND SAMUEL P. MARTIN (introduced by FRED-
ERICK BERNHEIM). *Dept. of Medicine, Duke
Univ. School of Medicine, Durham, N. C.*

Leukocytes were separated by gravity sedi-
mentation with dextran (C. P. Emerson) from
the blood of healthy individuals after it had been
passed through a decalcifying resin and handled
without exposure to wettable surfaces. After 60
minutes' sedimentation at 4° C., the leukocytes
were concentrated by centrifuging 15 minutes at
50 times gravity and decanting the supernatant
plasma. The white cells were resuspended in
plasma and Hanks' solution, modified to contain
no divalent cations. The Q_{O_2} of these cells, deter-
mined by Warburg's direct method and reported
as microliters $O_2/10^7$ cells/hour, was 6.3, a value
which did not change upon the addition of citrate,
alpha-ketoglutarate, succinate, fumarate, malate,
oxalacetate or glutamate in final concentration of
0.01 M. Exogenous cytochrome *c* (0.00005 M) did
not stimulate nor did malonate (0.01 M) inhibit
respiration with or without added succinate. KCN
and *p*-chloromercuribenzoate in a final concen-
tration of 0.0001 M markedly depressed respira-
tion, but 0.001 M DNP was without effect. When
cells were broken by grinding with alumina gel,
however, stimulation with succinate, *alpha*-keto-
glutarate, oxalacetate, cytochrome *c*, and DNP,
and inhibition with malonate were observed.
This indicates the existence of succinoxidase and
an active Krebs cycle in mature leukocytes. It
was evident that an intact cellular membrane
prevented the usual stimulation by Krebs cycle
intermediates and the inhibition by malonate.

1110695

Respiratory activity of human leukocytes in vitro.

GORDON R. MCKINNEY, R. WAYNE RUNDLES
AND SAMUEL P. MARTIN (introduced by FRED-
ERICK BERNHEIM). *Dept. of Medicine, Duke
Univ. School of Medicine, Durham, N. C.*

Leukocytes were separated by gravity sedi-
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passed through a decalcifying resin and handled
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respiration with or without added succinate. KCN
and *p*-chloromercuribenzoate in a final concen-
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cells were broken by grinding with alumina gel,
however, stimulation with succinate, *alpha*-keto-
glutarate, oxalacetate, cytochrome *c*, and DNP,
and inhibition with malonate were observed.
This indicates the existence of succinoxidase and
an active Krebs cycle in mature leukocytes. It
was evident that an intact cellular membrane
prevented the usual stimulation by Krebs cycle
intermediates and the inhibition by malonate.

Respiratory activity of human leukocytes in vitro.

GORDON R. MCKINNEY, R. WAYNE RUNDLES
AND SAMUEL P. MARTIN (introduced by FRED-
ERICK BERNHEIM). *Dept. of Medicine, Duke
Univ. School of Medicine, Durham, N. C.*

Leukocytes were separated by gravity sedi-
mentation with dextran (C. P. Emerson) from
the blood of healthy individuals after it had been
passed through a decalcifying resin and handled
without exposure to wettable surfaces. After 60
minutes' sedimentation at 4° C., the leukocytes
were concentrated by centrifuging 15 minutes at
50 times gravity and decanting the supernatant
plasma. The white cells were resuspended in
plasma and Hanks' solution, modified to contain
no divalent cations. The Q_{O_2} of these cells, deter-
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as microliters $O_2/10^7$ cells/hour, was 6.3, a value
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0.01 M. Exogenous cytochrome *c* (0.00005 M) did
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cells were broken by grinding with alumina gel,
however, stimulation with succinate, *alpha*-keto-
glutarate, oxalacetate, cytochrome *c*, and DNP,
and inhibition with malonate were observed.
This indicates the existence of succinoxidase and
an active Krebs cycle in mature leukocytes. It
was evident that an intact cellular membrane
prevented the usual stimulation by Krebs cycle
intermediates and the inhibition by malonate.

1110697

Office Memorandum • UNITED STATES GOVERNMENT

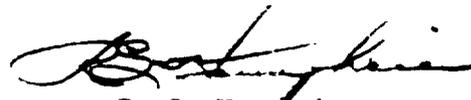
TO : J. Wallace Ould, Jr., Assistant General Counsel DATE January 14, 1952
FROM : R. G. Humphries, Chief, Contract Coordination Branch
SUBJECT: RENEWAL OF CONTRACT AT-(40-1)-1081 - DUKE UNIVERSITY SCHOOL OF MEDICINE
SYMBOL: DC:RGH

Forwarded is an approved proposal for extending research under Contract No. AT-(40-1)-1081 with Duke University with Dr. R. Wayne Rundles as Project Leader, as covered by Procurement Directive BM-52-96.

Washington has suggested and the Contractor has concurred in a reduction in the proposed capital equipment item to \$500 and the communications and travel item to \$200. With these adjustments the budget set forth in the Contractor's proposal is in the amount of \$9300 before adding overhead at 8%, or \$744, making a total of \$10,044 for the second year. The Contractor's letter dated December 28, 1951, attached, reports there will be a balance at the end of the year of \$1500. Deducting this balance from the approved budget leaves a net payment due for the second year in the amount of \$8,544.

It is requested that you prepare an appropriate modification to extend the term of the contract to cover the research program and provide for a lump sum payment in the amount of \$8,544.

Dr. C. S. Shoup will act as technical advisor on this contract action.



R. G. Humphries

Encls.:
Memo fm Kasschau 12-13-51 w/
Memo fm Tuttle 11-26-51
Contractor's proposal dtd. 10-1-51 & ltr 12-28-51

CC: C. S. Shoup
L. D. MacKay
Ed. Ziegler
J. Nicholson

Humphries:lm

1110698

Duke University
DURHAM
NORTH CAROLINA

School of Medicine
Department of Medicine
Reply to Undersigned

December 28, 1951

Dr. Sam Shoup
Atomic Energy Commission
Office of Research and Medicine
Post Office Box E
Oak Ridge, Tennessee

Dear Dr. Shoup:

In checking with the University business office regarding expenditures on our project "a study of the metabolism of the human base cation," sponsored by the A.E.C., we will have a balance at the end of the year of about \$1500. The bulk of this had been allocated for some laboratory equipment and supplies which could not be purchased due to temporary restrictions in our laboratory space. A new laboratory should be available for us to equip during the next three months.

I believe that our work can go on satisfactorily, however, during this next year with the budget reductions you mentioned, \$500 less for capital equipment and \$200 less for travel, or a total amount of \$10,100 for the year beginning January 1, 1952.

Very sincerely yours,


Wayne Rundles, M.D.

WR:jws

CC: Mr. Brower
Duke University

Atomic Energy Commission, Division of Biology and
Medicine, 1901 Constitution Ave. N.W., Washington, D.C.

1110699

JAN 2 1952

B-9

Office Memorandum • UNITED STATES GOVERNMENT

TO H. G. Humphries, Contract Coordinator

FROM John H. Roberson, Director of Research and Medicine

SUBJECT RESEARCH CONTRACT WITH DUKE UNIVERSITY, SCHOOL OF MEDICINE
(R. W. RUNDLES)

SYMBOL: RM:AMC

DATE: November 3, 1950

We are enclosing a request for a research contract with Duke University, School of Medicine together with a memo from L. W. Tuttle to Dr. Roberson for the following project:

"Metabolism of Human Bone Marrow"

The technical Advisor for this contract is Dr. R. H. Rucker.

John H. Roberson
John H. Roberson

Enclosures:

1. Req. for Research Contract
2. Memo fm LWT to JHR 10-18-50

Corley:oc

*Covered by Directive BM-51-44
Procurement dated 10/20/50 - \$12,042.00*

1110700

Office Memorandum • UNITED STATES GOVERNMENT

TO : John R. Moore, Chief, Contracts Division

DATE: December 13, 1951

FROM : Kenneth Kassensu, Acting Director, Office of Research and Medicine

SUBJECT: RENEWAL OF CONTRACT NO. AT-(LO-1)-1081 - DUKE UNIVERSITY SCHOOL OF MEDICINE

SYMBOL: RM:AMC

We are enclosing a memorandum from the Division of Biology and Medicine, Washington, dated November 26, 1951, authorizing the renewal of the subject contract for a period of one year, beginning January 1, 1952.

Dr. C. S. Shoup will act as technical advisor for this office. We would appreciate your assistance in negotiating this contract.

Kassensu
Kenneth Kassensu

Enclosure

- 1. Procurement Directive dtd 11-26-51
- 2. Memo fm LMT to NHM dtd 11-26-51
- 3. Proposal

Corley:oc

TRM

Note attached etc. dated Dec. 28th. 1951 indicating balance at end of yr. 1951 of \$1500

C. S. Shoup.

Covered by Procurement Directive EM-52-96 \$10,100

*10,044
1500
\$8,544*

cont. Part E-248.

UNITED STATES ATOMIC ENERGY COMMISSION
DIVISION OF BIOLOGY AND MEDICINE
WASHINGTON, D. C.

DATE: FEB 13 1951

TO : Dr. Nathan Woodruff, Director, Office of Research and Medicine
Oak Ridge
FROM : L. W. Tuttle, Assistant Chief, Medical Branch *LWT*
SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION
SYMBOL : BMM:LWT

This letter with enclosures, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University School of Medicine
2. Investigator (s): R. Wayne Rundles, M. D.
3. Title: "Metabolism of Human Bone Marrow"
4. () New Contract or (X) Renewal of Contract No. AT(40-1)-1081
5. Duration - From: January 1, 1952 To: December 31, 1952
6. AEC Technical Supervision: Medical Branch
7. Recommended Support: \$10,100.00, including overhead at 8%
Authorized by Procurement Directive No. EM52-96
Issued NOV 20 1951 \$ 10,100.00, including overhead at 8%
Activity No. 6300
8. Other Comments:

Due to limited funds available, it is suggested that the item for equipment be reduced to \$500.00, and the item for Communications and Travel be reduced to \$200.00.

1110703

8. Comments (Continued)

9. Security Requirements:

In accordance with the provisions of GM-93 (Revised March, 1950), and the requirements of the Declassification Guide, the Division of Biology and Medicine has determined that the following security precautions should be taken in connection with the proposed research contract.

Since there is essentially zero chance that restricted data will be required or developed, no personnel security requirements should be imposed.

10. Reports: (X) Reports are to be required as provided for by Memorandum Instruction of November 9, 1949, on subject "Direct Research Contract Reports".
- () Special Reports Instructions are as follows:

- Enclosures: (X) "A" - Proposal, dated October 1, 1951
- () "B" - Notification letter, dated _____
- () "C" - Other correspondence, _____ letters
- (X) "D" - Procurement Directive BMSC-96

Distribution:

Addressee: Original (w encl.)	Division File: Yellow Copy (w encl.)
1st Copy (" ")	Pink Copy (w/o encl.)
2nd Copy (" ")	Green Copy (" ")
Program Analysis	Branch File: White Copy (w ")
Branch: White Copy (w/o encl.)	

October 1, 1951

Proposal for Extension of Research Project Supported by
the Atomic Energy Commission.

1. Title. Metabolism of Human Bone Marrow.
2. Institution. Duke University School of Medicine.
3. Investigators. R. Wayne Rundles, Ph.D., M.D.,
Gordon R. McKinney, Ph.D., and others.
4. Scope and Present Status. Summarized in Progress Report dated
October 1, 1951.
5. Outline of work to be undertaken. As before.
6. Material, Equipment, and Facilities. As before.
7. Scientific Personnel. See Progress Report.
8. Budget, proposed for January 1-December 30, 1952, appended.
9. Other responsibilities of investigators, etc. (as previously given)

Proposed Budget to be supplied by the Atomic Energy Commission, Jan. 1-
Dec. 30, 1952.

<u>Salaries:</u>	Ray Shipke, M.D., professional assistant	3,800
	Technicians	4,000

Capital equipment:

Laboratory benches, Cabinets, Warburg vessels and manometers, blood centrifuge equipment, etc.	500 1,000
---------------------------------------------------------------------------------------------------	-------------------------

Expendable equipment and supplies:

Chemicals, reagents, glassware, etc.	1,000
--------------------------------------	-------

Communication and travel:

200
400
<hr/> 10,000
9300

Institutional Overhead @ 8% -

800	744
----------------	-----

Total

<hr/> 10,000	10,044
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Principal Investigator

R. Wayne Rundles, M.D.
Duke Hospital, Durham

Administrative Approval

Jas. Browner

Duke University

Business Manager & Comptroller
Duke University

1110705

Progress Report,

Research Project Sponsored by the Atomic Energy Commission,

Metabolism of Human Bone Marrow, R. W. Rundles, M.D.,

Duke University School of Medicine, October 1, 1961.

The loss of professional assistants from our Laboratory early in 1951, occasioned by the needs of the Armed Forces, delayed the beginning of our study on the metabolism of the human bone marrow. Nevertheless, considerable progress has been made during the last few months in this intrinsically difficult investigation.

Nearly all past studies of tissue metabolism have utilized organs and tissues other than bone marrow. A standard of reference for the metabolic processes of bone marrow was considered necessary. It appeared that a satisfactory comparison could best be made with normal human leucocytes. The technical problem of obtaining adequate quantities of normal, living leucocytes has been overcome. From previous work it was apparent that contact with wettable surfaces, anticoagulants, strong centrifugal force, etc., would have to be avoided. All surfaces coming in contact with the cells should be coated with silicone, or be made of plastic. Coagulation should be prevented by ion exchange resin decalcification. A satisfactory blood donor kit incorporating these essentials has recently become available (Fenwal Laboratory) and has proved eminently suitable for our purposes. To separate red from white cells, the most satisfactory method has proved to be the addition of one part in twenty of 5% Swedish Dextran of specific viscosity 0.46, suspending the plastic container in a closed water filled vessel at 4°C, and allowing the erythrocytes to sediment. After the red cells have sedimented in a matter of 45-60 minutes the supernatant plasma, which contains a large percentage of

the leucocytes, can be forced into a collecting jar by increasing the water pressure surrounding the plastic bag. By centrifugation at 50-60 G., or less, one can obtain concentrated suspension of leucocytes, 20,000,000-30,000,000 per cc., relatively free of red blood cells. Experiments were performed regarding the effect on respiration of different media in which white cells were suspended. It was found that leucocytes were injured if they were suspended in protein-free electrolyte solutions, or in solutions containing only albumin. Most satisfactory rates of respiration were obtained with leucocytes suspended in plasma diluted with a balanced electrolyte solution. After respiratory measurements have been completed, the leucocyte protein content is determined by nitrogen analysis by the micro-Kjeldahl method. Satisfactory respiratory quotients have been obtained with leucocytes obtained and studied by these procedures.

The handling of bone marrow after aspiration was patterned on the above principles. Several methods for separating bone marrow particles from blood, utilizing differences in specific gravity, were explored with little success. Concentrated albumin solutions and gelatins were mechanically faulty, if not fatally injurious, to surviving cells. While a final method for separating marrow particles for metabolic studies has not been adopted, it appears at this time that placing the marrow in a plasma solution containing Dextran, followed by differential centrifugation will be satisfactory. The use of other red cell agglutinating agents, a phycohemagglutinin, a dextran with a molecular weight of about 440,000 and specific viscosity of 0.64, and a dextrin will be studied.

Warburg equipment has been assembled, calibrated and is in active use. A micro-Kjeldahl nitrogen analysis method is in

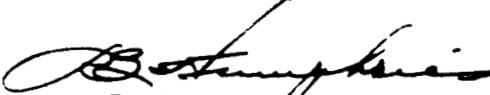
Office Memorandum • UNITED STATES GOVERNMENT

TO : J. Wallace Ould, Jr., Assistant General Counsel DATE: November 13, 1950
FROM : R. G. Humphries, Contract Coordinator
SUBJECT: REQUEST FOR PREPARATION OF LUMP SUM RESEARCH CONTRACT WITH DUKE UNIVERSITY
SYMBOL: CO:RGH

Forwarded is an approved research project in the amount of \$12,042 with Duke University School of Medicine.

It is requested that you prepare an appropriate lump sum contract to cover this work. The portion of Section 3, Appendix "B" in the lump sum research contract form requiring clearance of the project leader should be deleted since the work is to be conducted on an unclassified basis.

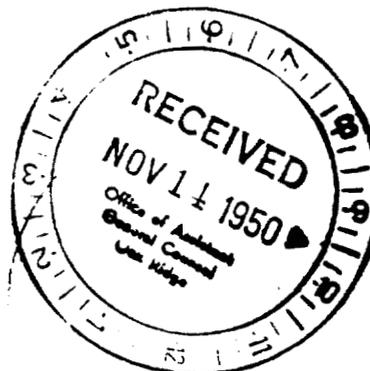
Dr. R. H. Rucker, Office of Research and Medicine, has been designated technical advisor on this contract. Please contact him on any technical questions.


R. G. Humphries

Enclosures:
Memo fm Roberson 11-3-50
Memo fm Tuttle 10-18-50 w/
Approved Project

CC: Dr. R. H. Rucker
Mr. S. Sobol
Mr. W. Stockburger (Finance)

Humphries:lm



1110708

UNITED STATES ATOMIC ENERGY COMMISSION
DIVISION OF BIOLOGY AND MEDICINE
WASHINGTON, D. C.

TO : Dr. John Roberson, Dir. Research and Medicine, Oak Ridge Operations Office
FROM : L. W. Tuttle, Asst. Chief, Medical Branch
SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION

REFER TO: BMM:LWT
SYMBOL:

This letter with enclosures, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University, School of Medicine, Durham, N.C.
2. Investigator(s): R. W. Rundles
3. Title: "Metabolism of Human Bone Marrow"
4. Duration - From: To: One year with provision for renewal
5. AEC Technical Supervision: Medical Branch
6. Recommended Support: \$12,042.00 Procurement Directive BM-51-44 including 8% overhead
7. Other Comments

The scope of the scientific work has been examined in the light of the requirements of the Declassification Guide and GM-93 (par. 4c Revised March 2, 1950). It is determined that the work falls in a category where there is essentially zero chance that restricted data will be required or developed during the investigations. It is recommended that the contract be set up on a completely unclassified basis.

Note
no clearance
necessary.

1110709

35
79-7307

hope to be able to use for studying the utilization and incorporation into cellular protein of amino acids.

Mrs. Ella Hardy Shipke, a graduate medical technologist, has worked full time but is now working part time.

Miss Betty Simpson, a graduate medical technologist, was transferred to this project July 1, 1961, working full time.

Expenditures. (January 1, 1961 to September 15, 1961).

Capital equipment			\$1,249.88
Salaries			
Dr. Gordon McKinney	\$ 0.00	\$ 0.00	
Dr. George Chase	800.00/mo.	1,000.00	
Dr. Ray Shipke	300.00/mo.	750.00	
Miss Betty Simpson	185.00/mo.	462.50	
Mrs. Ella H. Shipke	185.00/mo. 8 mos.		
	130/mo. currently	1,545.00	
		<u>\$3,837.50</u>	\$3,837.50
Expendable Supplies			462.09
Travel			186.98
			<u>\$5,706.46</u>
	University Overhead		456.44
	Total Expenditure		\$6,161.89

Salaries at the above rate will continue throughout this year. It is estimated that \$800-\$1,000 will remain unexpended at the end of the year.

Summary. Satisfactory progress has been made on this project so far and continued work should result in significant scientific advances.

Wayne Rundles, M.D.
Wayne Rundles, M.D.

GC:JN

Oak Ridge, Tennessee
November 28, 1950

Duke University
School of Medicine
Durham, North Carolina

Attention: Dr. E. W. Rundles

Subject: CONTRACT NO. AT-(40-1)-1061

Dear Dr. Rundles:

Your research project which was submitted to the Commission's Division of Biology and Medicine, Washington, D. C., has been approved by that office in the amount of \$12,042.00 and has been forwarded to this office for preparation of an appropriate contract covering the Commission's support of your project.

Enclosed in three copies, is a contract numbered as shown in the subject line above, which incorporates in Appendix "A" a description of your project and the budget for the first period which you are to follow as a general guide.

It is requested that you sign each copy of the contract in the space provided for the Project Leader on the signature page of the contract and have the contract signed by the proper official of the University. All copies should then be returned to this office. After the Contracting Officer has signed the contract for the Commission a fully executed copy of the contract together with one conformed copy, will be returned for the use of the University.

It will be noted that the contract provides for payment in Article III of a lump sum in consideration of your performance of the research activities described in Appendix "A". The first payment, representing one-half the amount of the agreed compensation, will be paid to you upon your submission of a properly certified voucher on or before the first date established in Article II of the contract. The remaining 50% of the agreed compensation will be paid to you within six months from the date of the first payment.

Performance of a cost audit of your expenditures has been eliminated through this lump sum payment for your research services. It is believed that this will save you considerable time and trouble in detailing your expenditures on cost reimbursement vouchers.

1110711

operation. Methods for measuring lactic acid production, aerobic and anaerobic glucose utilization are being standardized. Filter paper chromatography methods for amino acid analysis are being set up. Our hematology technicians have acquired skill in methods utilized in bone marrow examinations, cell counting, staining. They have not had all of their time fully occupied on this project to date, but have helped maintain access to clinical material. They have, in addition, assisted with a research project begun earlier on the effects of Triethylene melamine in neoplastic disease. A publication dealing with our investigations in this field will be completed during the coming months, in which partial support by the Atomic Energy Commission will be acknowledged.

Personnel.

Gordon B. McKinney, Ph.D. Dr. McKinney finished his [REDACTED] [REDACTED] He has worked full time on this project since July 1. He is supported this year by an American Cancer Society Fellowship.

George Chase, M.D. Dr. Chase finished [REDACTED] [REDACTED] He was able to assist us with the early phases of this work from Jan.-June, 1961, before beginning his internship July 1, 1961.

Ray Shipke, M.D. Dr. Shipke finished his [REDACTED] [REDACTED] Since July, 1961, he has assisted us in obtaining blood from donors, in preparing leucocyte suspensions, processing marrow specimens, and setting up chemical methods. He is now familiarizing himself with paper chromatographic methods which we

August 16, 1950

Proposal for the Support of Research Project by the Atomic
Energy Commission

1. Title. Metabolism of Human Bone Marrow.
2. Institution. Duke University School of Medicine.
3. Investigators. R. Wayne Rundles, Ph.D., M.D.
Robert W. Willett, M.D.
Gordon R. McKinney, Ph.D. (July '51)

4. Scope and Present Status.

The bone marrow differs from most organs and tissues in the body in that its main product is blood cells. Comparatively few studies have been made of its metabolism (Warren, J. Biol. Chem. 167:543, 1947; Guzman Barron, et al, J. Biol. Chem. 171:801, 1947, J. Exp. Med. 87:489 and 503, 1948, J. Gen. Physiol. 32:537 and 595, 1949, Bird and Evans, J. Biol. Chem. 178:289, 1949). Most investigators have used rabbit bone marrow. The findings in general indicate that oxygen utilization is 5 times less than that of highly respiring tissues. Glucose, pyruvate, acetate, and amino acids are utilized vigorously. Some evidence suggests that fatty substances may be especially important nutrients.

No attempts appear to have been made to study the metabolism of the human bone marrow. Since cellular morphology varies from species to species it is possible that metabolic activity does also.

The hemopoietic tissues furthermore are among the most vulnerable to the action of some destructive agents that may be employed in warfare and are frequently involved in clinical diseases.

1110713

The latter include nutritional deficiencies (megaloblastic cell development), chemical or drug damage (aplastic anemia, agranulocytosis some types of thrombocytopenic purpura and hemolytic anemia), radiation depression or damage, and malignant diseases (leukemia, sub-leukemia, multiple myeloma, etc.)

5. Outline of work to be undertaken.

Preliminary studies indicate that bone marrow cells can be aspirated from human subjects in sufficient quantity for in vitro studies using the Warburg apparatus. Adequate methods are available for separating the primitive blood cells from the erythrocytes, and for determining the rate of many metabolic processes/mg. of fat free tissue.

We wish to determine first the conditions for optimal survival of the marrow cells, or better growth and proliferation, if possible in a chemically defined medium. ^(then a) We can then study ^{the} the rate of O₂ consumption, the utilization of glucose, pyruvate, acetate, and amino acids, essential and otherwise in normal and abnormal marrow as influenced by roentgen irradiation, the presence of P 32, urethane and other agents which have a well defined influence on marrow function.

Studies on amino acid uptake will require studies with synthetic radioactive amino acids, as well as amino acid analyses employing filter paper chromatography and microbiological assay.

The hematologic effects of urethane have been investigated in our laboratory for 3 years. The compound suppresses the growth of myeloid elements in myelogenous leukemia and plasma cells in multiple myeloma selectively and beneficially. An

[REDACTED]

Gordon R. McKinney. U. S. Public Health Fellow, 1949-51,
Department of Physiology and Pharmacology (Dr. Frederick
Bernheim).

[REDACTED]

[REDACTED]

Publications:

McKinney, G. R.: A study of the action of a nitrogen mustard
on cytochrome oxidase. *Anat. Record*, 101:34, 1948.

McKinney, G. R.: The effect of a nitrogen mustard on certain
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Expendable Equipment and Supplies, (Chemicals, reagents,
glassware, experimental animals, etc.) 2,500.00

Communication and Travel 300.00

11,150.00

Institutional Overhead @ 8% 892.00

Total \$12,042.00

Principal Investigator

Approved by Executive Committee,
Duke University School of Medicine

R. Wayne Rundless, M.D.

Approved by Administration,
Duke University

A. B. Brower

Business Manager and
Comptroller

Rundles, R. W.

[REDACTED] Assistant Instructor in Anatomy, Cornell University Medical College, 1933-37; Interne, Assistant Resident and Resident in Medicine, University of Michigan Hospital, 1940-43; Instructor in Internal Medicine, and Research Assistant, Simpson Memorial Institute, 1943-45; Duke University, 1945-49; Assistant Professor of Medicine, Duke University, 1949-

Partial Bibliography:

- Rundles, R. Wayne: Fiber and cellular degeneration following temporal lobectomy in the monkey, Cornell Thesis, 1937.
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- Rundles, R. Wayne: Prognosis in the neurologic manifestations of pernicious anemia. Blood, 1:209, 1946.
- Rundles, R. W., and Falls, Harold F.: Hereditary (sex-linked ?) anemia. Am. J. Med. Sci., 211:641, 1946.
- Hodges, Fred J., Rundles, R. Wayne, and Hanelin, Joseph: Roentgenologic study of the small intestine. Radiology, 49:587 and 659, 1947.

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- Loge, J. P., and Rundles, R. W.: Urethane (ethyl carbamate) therapy in multiple myeloma. *Blood*, 4:201, 1949.
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UNITED STATES ATOMIC ENERGY COMMISSION
DIVISION OF BIOLOGY AND MEDICINE
WASHINGTON, D. C.

TO : Dr. John Roberson, Dir. Research and Medicine, Oak Ridge Operations Office
DATE: October 18, 1950
FROM : L. W. Tuttle, Asst. Chief, Medical Branch
SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION

REFER TO
SYMBOL: EMM:LWT

This letter with enclosures, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University, School of Medicine, Durham, N.C.
2. Investigator(s): R. N. Rundles
3. Title: "Metabolism of Human Bone Marrow"
4. Duration - From: To: One year with provision for renewal
5. AEC Technical Supervision: Medical Branch
Including 8% overhead
6. Recommended Support: \$12,042.00 Procurement Directive BM-51-44
7. Other Comments

The scope of the scientific work has been examined in the light of the requirements of the Declassification Guide and GM-93 (par. 4c Revised March 2, 1950). It is determined that the work falls in a category where there is essentially zero chance that restricted data will be required or developed during the investigations. It is recommended that the contract be set up on a completely unclassified basis.

August 16, 1960

Proposal for the Support of Research Project by the Atomic
Energy Commission

1. Title. Metabolism of Human Bone Marrow.
2. Institution. Duke University School of Medicine.
3. Investigators. R. Wayne Rundles, Ph.D., M.D.
Robert W. Willett, M.D.
Gordon R. McKinney, Ph.D. (July '61)

4. Scope and Present Status.

The bone marrow differs from most organs and tissues in the body in that its main product is blood cells. Comparatively few studies have been made of its metabolism (Warren, J. Biol. Chem. 167:543, 1947; Guzman Barron, et al, J. Biol. Chem. 171:801, 1947, J. Exp. Med. 87:489 and 503, 1948, J. Gen. Physiol. 32:537, and 595, 1949; Bird and Evans, J. Biol. Chem. 178:269, 1949). Most investigators have used rabbit bone marrow. The findings in general indicate that oxygen utilization is 5 times less than that of highly respiring tissues. Glucose, pyruvate, acetate, and amino acids are utilized vigorously. Some evidence suggests that fatty substances may be especially important nutrients.

No attempts appear to have been made to study the metabolism of the human bone marrow. Since cellular morphology varies from species to species it is possible that metabolic activity does also.

The hemopoietic tissues furthermore are among the most vulnerable to the action of some destructive agents that may be employed in warfare and are frequently involved in clinical diseases.

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The latter include nutritional deficiencies (megaloblastic cell development), chemical or drug damage (aplastic anemia, agranulocytosis, some types of thrombocytopenic purpura and hemolytic anemia), radiation depression or damage, and malignant diseases (leukemia, sub-leukemia, multiple myeloma, etc.)

5. Outline of Work to be Undertaken.

Preliminary studies indicate that bone marrow cells can be aspirated from human subjects in sufficient quantity for in vitro studies using the Warburg apparatus. Adequate methods are available for separating the primitive blood cells from the erythrocytes, and for determining the rate of many metabolic processes, e.g. of fat free tissue.

We wish to determine first the conditions for optimal survival of the marrow cells, or better growth and proliferation, if possible in a chemically defined medium. We can then study the rate of O_2 consumption, the utilization of glucose, pyruvate, acetate, and amino acids, essential and otherwise in normal and abnormal marrows as influenced by roentgen irradiation, the presence of P 32, urethane and other agents which have a well defined influence on marrow function.

Studies on amino acid uptake will require studies with synthetic radioactive amino acids, as well as amino acid analyses employing filter paper chromatography and microbiological assay.

The hematologic effects of urethane have been investigated in our laboratory for 3 years. The compound suppresses the growth of myeloid elements in myelogenous leukemia and plasma cells in multiple myeloma selectively and beneficially. An understanding

of its metabolic effect in bone marrow is an important matter which may be studied advantageously in vitro and in vivo with the aid of the radioactive urethane.

6. Material, Equipment and Facilities.

The facilities of a small but well equipped Hematology Laboratory, organized and staffed as a consultation service for Duke Hospital patients, is available for this investigation. An abundance of clinical material is available. An additional laboratory is available in the Medical Research Building where electrophoretic and physico-chemical studies of proteins are being carried out. Expanded laboratory quarters in Duke Hospital are planned when construction under contract is completed.

Warburg equipment has been purchased from available funds. Additional equipment and supplies requested from the A.E.C. to be used in this investigation are itemized below.

7. Scientific Personnel.

R. W. Rundles, Assistant Professor of Medicine, Duke University.

Outline of research experience and publications appended.

Robert W. Willett. Damon Runyon Clinical Research Fellow, 1950-51.

[REDACTED]

[REDACTED] Interns, Duke Hospital, April-June

1948, Interns, Syracuse University Hospital, 1948-49;

Assistant Resident in Medicine, Duke Hospital, 1949-1

Publications:

Willett, R. W., and McPherson, H. T.: Some observations on intraocular ovarian transplants with special reference to the effects of progesterone. Thesis, Duke University, 1948.

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Department of Physiology and Pharmacology (Dr. Frederick
Bernheim).

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Duke University School of Medicine

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Duke University

P. Wayne Russell, M.D.

a.s. Brewer

Business Manager and
Comptroller

[REDACTED] etc
in Anatomy, Cornell University Medical College, 1933-37; Intern, Assistant Resident, and Resident in Medicine, University of Michigan Hospital, 1940-43; Instructor in Internal Medicine, and Research Assistant, Simpson Memorial Institute, 1943-45, Duke University, 1945-49, Assistant Professor of Medicine, 1949-

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November 28, 1950

In order to assist you in preparing an appropriate voucher there is enclosed an instruction sheet containing numbered instructions corresponding with numbers appearing on a specimen copy of the voucher form. Vouchers should be submitted to the Oak Ridge Operations office in one original (white) and four copies (yellow) addressed as shown in Article IV of the contract. It is assumed that you will give your business office the benefit of these instructions.

Your attention is called to the reporting requirements outlined in Appendix "C" to the contract, especially to Item No. 2 requiring the immediate submission of a 200 word summary statement describing the purpose and scope of your project.

For your information and guidance in purchasing isotopes through the Commission, in accordance with the provisions of Article VII, there is enclosed a copy of the latest radiisotope catalog, together with a set of application forms, which you will use in making purchases of isotopes.

Your particular attention is invited to Appendix "E", Section 12 - Fellowships.

It is believed that the remaining portions of the contract are self-explanatory, however, if you have any questions concerning the application or interpretation of any of the contract provisions I will be glad to furnish you with additional information pertaining thereto.

Very truly yours,

CB

for C. Vanden Bulck
Assistant to the Manager
Oak Ridge Operations

Enclosures:
Contract (in trip.)
Vouchers & Instr. Sheets
Isotope Catalog & Applic. form w/instr. sheet

Nicholson:ja

CC: Contracts ✓ C. Vanden Bulck A. M. Corley L. W. Tuttle (Washington)

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