

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION
SPONSORED PROJECT INITIATION

Date: 7/18/79

Project Title: Organ Specific Tumor Localizing Antibody

Project No: G-32-C01

Green Card

Project Director: Dr. William P. Bale

Sponsor: DHEW/PHS/NIH - National Cancer Institute

Agreement Period: From 7/1/79 Until 6/30/80

Type Agreement: Grant No. 1 R01 CA25958-01

Amount: \$110,014 New PHS Funds (G-32-C01)
5,790 GIT Contribution (G-32-329)
\$115,804 Total

Reports Required: Annual Progress Report with Continuation Applications
Terminal Progress Report upon Grant expiration

Sponsor Contact Person (s):

Technical Matters

David Kiskiss, Ph.D.
Division of Cancer Biology
and Diagnosis
National Cancer Institute
Bethesda, MD 20014

Contractual Matters

(thru OCA)

Leo F. Buscher, Jr.
Grants Management Officer
National Cancer Institute
Bethesda, MD 20014

Mary Kirker
Grants Management Contact
301/496-7444

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)

Library, Technical Reports Section
EES Information Office
EES Reports & Procedures
Project File (OCA)
Project Code (GTRI)
Other _____

Jgers ✓ Reports Coordinator (OCA) *PEC 7/24/79*
Property Coordinator (OCA)

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION
SPONSORED PROJECT TERMINATION

Date: July 14, 1980

Project Title: Organ Specific Tumor Localizing Antibody

Project No: G-32-C01

Project Director: Dr. William P. Bale

Sponsor: DHEW/PHS/NIH - National Cancer Institute

Effective Termination Date: June 30, 1980 (01 year)

Clearance of Accounting Charges: ---

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 Annual Report of Expenditures (01 year)

NOTE: Continued by G-32-C02 (02 year).

Assigned to: Biology (School/Laboratory)

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Project File (OCA)
Project Code (GTRI)
Other _____

Reports Coordinator (OCA)
Research Property Coordinator (OCA)

SECTION IV

G-32-001

APPLICANT: REPEAT GRANT NUMBER SHOWN ON PAGE 1 →	GRANT NUMBER	
SECTION IV—SUMMARY PROGRESS REPORT	CA25958-02 <i>Interim Progress Report</i> <i>Submitted w/ Proposal</i> <i>March 25, 1980</i>	
	PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Last, First, Initial)	
Bale, William F	PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION	FROM	THROUGH
Georgia Institute of Technology	7/01/79	6/30/80
TITLE (Repeat title shown in item 1 on first page)		
Organ Specific Tumor Localizing Antibody		

1. List publications: (a) published and not previously reported; (b) in press. Provide five reprints if not previously submitted.
2. List all additions and deletions in professional personnel and any changes in effort.
3. Progress Report. (See Instructions)

1. (a) M. A. Contreras and W. F. Bale. Measurement of organ and tissue specific antigen and antibody. Fed. Proc. 39, 1141, 1980 (Abstract).
- (b) W. F. Bale, M. A. Contreras, and E. D. Grady. Factors influencing labeled antibody localization in tumors. Cancer Research. In Press.

2. No changes.

3. This research is based on the premise that tumors originating in organs not essential to life and well-being sometimes express cell surface antigens unique to these organs, and that antibodies to these antigens may be useful in the treatment of such tumors. In particular, antibodies able to localize in these tumors might be used as carriers of therapeutic doses of radioactive isotopes or of chemotherapeutic agents directly to tumor tissue, sparing to a greater or lesser extent normal tissues from the toxic effects of these agents.

The direct aim of this research is to develop methods for preparing large amounts of radioactive antibody that will localize with high specificity in one or more types of rat tumor. It is hoped that data and procedures so developed will be an aid in achieving the ultimate goal of effective treatment of human cancer when substantial tumor burdens exist.

Research under this grant is planned for a rat system, utilizing malignant tumors of mammary, pancreas, thyroid and large intestine origin.

Current active research involves studies of 7, 12-Dimethylbenz(a)anthracene (DMBA) induced rat mammary tumors, and antibodies produced in rabbits against this tumor and against normal rat pancreas.

Goals for the current year are largely those of developing appropriate experimental procedures. We do expect to have prepared antibody able to localize in considerable amounts preferentially in normal rat pancreas, and to have carried out studies of antibody localization in carcinogen induced mammary tumors.

In vitro studies: Much of our experimental work in the past 8 months has been concerned with the development of satisfactory methods of following in vitro antibody purification before and after labeling. A method that we currently believe satisfactory for use in titrating unlabeled rabbit antisera or sera fractions to rat organs or tumors uses ¹²⁵I-labeled purified goat antibody to rabbit γ -globulin as a Coomb's type reagent. Equal portions of insoluble or insolubilized antigen are incubated with a fixed dilution of immune serum or serum fraction. The washed portions of antigen now binding rabbit antibody, are incubated with the ¹²⁵I-labeled goat antibody containing progressively increasing amounts of the same but unlabeled goat antibody to rabbit γ -globulin. The extent to which binding of labeled goat antibody is depressed by the

increasing amounts of unlabeled goat antibody provides a measure of the amount of rabbit γ -globulin bound to rat tissue or tissue fractions. Conditions may be set to measure either the amount of reactive antibody present in antibody preparations of the abundance of antigen expressed by tissue or membrane fractions. This technique and related procedures have been used to develop methods, combining mildness with efficiency for antibody purification.

Studies with antibodies to normal rat pancreas: By using such procedures to determine optimal conditions we have absorbed rabbit antiserum to rat pancreas with a mixture of rat liver, spleen and small intestine antigens, prepared γ -globulin from this absorbed antiserum and labeled it with ^{125}I , and further purified this antibody by absorption and elution from insolubilized rat pancreas membrane antigen. This labeled antibody showed some specificity for localizing in rat pancreas after intravenous injection. Final ratio of ^{125}I -labeled antibody to ^{131}I -labeled normal IgG in pancreas was higher than in any other tissue except spleen.

Our studies indicate that labeled antibody with specificity for binding in pancreas does so rather slowly, as though antibody must first reach extravascular spaces before finding organ specific antigens with which it can bind. This result is similar to the results of our antibody binding studies in tumor where only tumor expresses the corresponding antigen and contrasts, for example, with studies of certain antibodies to kidney where binding in the kidney glomeruli occurs very rapidly.

On the other hand we have found that the ^{125}I -label of antibody to histocompatibility antigen expressed on tumor, or to tumor specific antigen, was rapidly degraded after attachment to tumor (half life of about 24 hours) while the ^{125}I -label of antibody bound to pancreas was much more stable, with a half life after attachment there of several days.

Studies with rat mammary tumors: On August 3, 1979 we administered DMBA by stomach tube to 14 F-344 rats. The first mammary tumor was noted on 9/28/79 and a portion was removed for transplantation and histological study on 10/8/79. From microscopic examination it appeared a moderately well differentiated adenocarcinoma. Additional transplants have been made from the primary tumor and from first generation transplants of this tumor into F-344 rats. It has, with one transplant exception, remained a slow growing tumor. A few apparently spontaneous regressions have occurred. However, 5 rabbits have been immunized with fractions of this tumor, and growing tumor is now available for antibody titration, purification, and in vivo localization studies that are just now getting underway.

Three additional tumors have now appeared in the 5 surviving rats to which DMBA was administered on 8/3/79. In addition we have available for our use two additional lines of DMBA tumors induced by one of us (MAC) about 4 years ago, carried as a transplant in F-344 rats for two years, and stored since then frozen in a tumor bank. During this two year transplant period these tumors each increased greatly in growth rate and lost most of the characteristic cellular architecture that identified them as adenocarcinomas.

Research for the coming year will include (a) preparation of labeled antibody showing high specificity for localizing in rat pancreas. Success will indicate the

Bale, William F.
CA25958-02

probable feasibility of preparing labeled antibody able to localize in the human pancreas as a diagnostic aid in nuclear medicine. (b) As a major goal the determination of the feasibility of preparing labeled "organ specific" antibody localizing preferentially in DMBA-induced malignant mammary neoplasms. When produced, such an antibody will be used as an immunological probe in detecting organ specific antigen expressed in mammary tumor in tumor cell fractionation studies. (c) Preparation of antisera to other rat tumors and preliminary studies with these antisera.

The undersigned agrees to accept responsibility for the scientific and technical conduct of the project and for provision of required progress reports if a grant is awarded as the result of this application.

5/21/80

Date

Principal Investigator

DEPARTMENT OF HEALTH AND HUMAN SERVICES

(Instructions are on reverse)

Grant No.
1 R01 CA25958-01

DATE OF THIS REPORTING PERIOD

NAME AND ADDRESS OF GRANTEE INSTITUTION

Georgia Institute of Technology
Atlanta, Georgia 30332

TRANSACTION NO.

(08)R1CA25958A

INSTITUTIONAL ID NO.

G-32-C01

FROM 7/1/79 TO 6/30/80

PROJECT PERIOD

7/1/79 6/30/82

FROM TO

CHECK IF FINAL REPORT

1. Expenditures of DHHS Funds for this Reporting Period

a. Personnel	\$.	h. Alterations and renovations	
b. Consultant services		i. Other	
c. Equipment			
d. Supplies		j. Total direct costs	68,927.93
e. Travel, domestic		k. Indirect costs:	
f. Travel, foreign		Rate * % <input checked="" type="checkbox"/> S&W <input type="checkbox"/> TDC	
g. Patient care costs		Base \$ 52,824.78	40,138.72
		l. TOTAL	\$ 109,066.65
2. Expenditures from Prior Periods (previously reported)			-0-
3. Cumulative Expenditures			109,066.65
4. Total Amount Awarded -- Cumulatively			110,014.00
5. Unexpended Balance (Item 4 less Item 3)			947.35
6. Unliquidated Obligations			-0-
7. Unobligated Balance (Item 5 less Item 6)			947.35
8.a. Cost Sharing Information -- Grantee Contribution This Period			5,788.51
b. % of Total Project Costs (Item 8a divided by total of Items 1 and 8a)			% 5.0
9.a. Interest/Income (enclose check)			-0-
b. Other Refundable Income (enclose check)			-0-

10. Remarks * 7/1/79-6/30/80 \$52,554.78 @ 76% = \$39,941.62
 as of 7/1/80 270.00 @ 73% = 197.10
 (charges incurred prior to 6/30/80) \$52,824.78 \$40,138.72

I hereby certify that this report is true and correct to the best of my knowledge, and that all expenditures reported herein have been made in accordance with appropriate grant policies and for the purposes set forth in the application and award documents.

Dr. W. F. Bale

Professor

Date

10/7/80

DATE

David V. Welch, Manager, Grants & Contracts Acctg.

Formerly HEW-459 404/894-4624

REPORT OF RESEARCH GRANT
EXPENDITURES

GEORGIA INSTITUTE OF TECHNOLOGY
ATLANTA, GEORGIA 30332

OFFICE OF
THE
COMPTROLLER

October 7, 1980

Grants Management Officer
National Cancer Institute
DHHS/PHS/NIH
Bethesda, Maryland 20205

Dear Sir or Madam:

Enclosed is the Report of Research Grant Expenditures for
Grant No. 1 R01 CA 25958-01 for the period 7/1/79 - 6/30/80.

If you have any questions or require additional information,
please let us know.

Sincerely,

David V. Welch, Manager
Grants & Contracts Accounting

DVW/BITS/jb
Enclosure

cc: Dr. W. F. Bale
Dr. J. W. Crenshaw
Mr. H. Dean
Mr. O. H. Rodgers ✓
File G-32-C01