DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

APPLICATION
FOR CONTINUATION GRANT

REVIEW GROUP	TYPE	PROGRAM	GRANT NUMBER (INSERT ON ALL PAGES)
IMB	5	R01	GM14650-06

TOTAL PROJECT PERIOD
FROM: 12/01/69 THROUGH: 11/30/74

REQUESTED BUDGET PERIOD
FROM: 12/01/71 THROUGH: 11/30/72

TO BE VERIFIED BY APPLICANT. CHECK INFORMATION IN ITEMS 1 THROUGH 6. IF INCORRECT, FURNISH CORRECT INFORMATION IN ITEM 13.

1. TITLE

GENETICS OF HUMAN TISSUE ~~XXXXXXX~~ ANTIGENS

2A. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR *(Name and Address, Street, City, State, Zip Code)*

LEDERBERG, JOSHUA
DEPT OF GENETICS
STANFORD UNIVERSITY SCH OF MED
STANFORD, CALIF 94305

4. APPLICANT ORGANIZATION *(Name and Address, Street, City, State, Zip Code)*

STANFORD UNIVERSITY
STANFORD, CALIFORNIA 94305

2B. DEGREE: Ph.D.

2C. SOCIAL SECURITY NO.: [redacted]X

5. PHS ACCOUNT NUMBER: 458210

2D. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT

GENETICS

2E. MAJOR SUBDIVISION

SCHOOL OF MEDICINE

3. ORGANIZATIONAL COMPONENT TO RECEIVE CREDIT FOR INSTITUTIONAL GRANT PURPOSES

01 SCHOOL OF MEDICINE

6. TITLE AND ADDRESS OF OFFICIAL IN BUSINESS OFFICE OF APPLICANT ORGANIZATION

CONTROLLER
STANFORD UNIVERSITY
STANFORD, CALIFORNIA 94305

COMPLETE THE FOLLOWING (See Instructions)

7. RESEARCH INVOLVING HUMAN SUBJECTS *(See Instructions)*
☐ NO ☐ YES APPROVED: _____ DATE

8. INVENTION CERTIFICATION *(See Instructions)*
☒ NO ☐ YES-NOT PREVIOUSLY REPORTED
☐ YES-PREVIOUSLY REPORTED

9. PERFORMANCE SITE (S)

Genetics Department
Stanford University School of Medicine
Stanford, California

TELEPHONE INFORMATION

	AREA CODE	TELE. NO. & EXT.
11A. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (ITEM 2A)	415	321-1200 5801
11B. NAME OF BUSINESS OFFICIAL (ITEM 6) K. D. Creighton	415	321-2300 2251
11C. NAME AND TITLE OF ADMINISTRATIVE OFFICIAL (ITEM 15B)		

10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD
$14,439

12A. CONGRESSIONAL DISTRICT OF APPLICANT ORGANIZATION SHOWN IN ITEM 4
Tenth

12B. COUNTY OF APPLICANT ORGANIZATION SHOWN IN ITEM 4
Santa Clara

13. USE THIS SPACE FOR CORRECTIONS TO ITEMS 1 THROUGH 6. INDICATE THE NUMBER(S) WHERE ANSWER(S) APPLY

Note correction of spelling in title, Item 1. Item 2B - add degree.
Item 2C - Dr. Lederberg's Soc. Sec. No. added.

14. CERTIFICATION AND ACCEPTANCE. WE, THE UNDERSIGNED, CERTIFY THAT THE STATEMENTS HEREIN ARE TRUE AND COMPLETE TO THE BEST OF OUR KNOWLEDGE AND ACCEPT AS TO ANY GRANT AWARDED, THE OBLIGATION TO COMPLY WITH PUBLIC HEALTH SERVICE TERMS AND CONDITIONS IN EFFECT AT THE TIME OF THE AWARD.

SIGNATURES *(Signatures required on original copy only. Use ink. "Per" signatures not acceptable.)*		DATE
	15A. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR	8/16/71
	15B. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION	DATE

PHS 2590-1 OPTIONAL
REV. 1-70

RETURN COMPLETED APPLICATION TO PHS BEFORE: 1 OCTOBER 1971

SECTION II—BUDGET (USUALLY 12 MONTHS)	FROM	THROUGH	GRANT NUMBER
	12/1/71	11/30/72	GM 14650-06

A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD

PERSONNEL — NAME (Last, First, Initial) (a)	TITLE OF POSITION (b)	TIME OR EFFORT %/HRS. (c)	SALARY REQUESTED (d)	FRINGE BENEFITS (See Instructions) (e)	TOTAL (f)
Lederberg, J.	PRINCIPAL INVESTIGATOR		none		
Hwang, J.	Scientific Programmer	25%	3,600	561	
Wang, L.	Sr. Res. Asst.	16%	2,000	467	
Leo, M.	Computer Operator	35%	3,000	311	
Staff benefits:					
9 mo. @ 15.2%					
3 mo. @ 16.7%					
	Subtotals →		$ 8,600	$ 1,339	
(Indicate cost of each item listed below)	TOTAL (Columns (d) and (e)) →				$ 9,939
CONSULTANT COSTS (See Instructions)					$
EQUIPMENT					$
SUPPLIES Culture medium and chemicals				300	$ 300
TRAVEL — DOMESTIC					$
TRAVEL — FOREIGN					$
PATIENT COSTS (See instructions)					$
ALTERATIONS AND RENOVATIONS					$
OTHER EXPENSES (Itemize): Computer Time $4,000; Communications, Publication Costs 200					$ 4,200
TOTAL DIRECT COST (Enter on Page 1, Item 10)					$ 14,439

INDIRECT COST (See Instructions)

46 % S&W* / % NTDC*

Date of DHEW Agreement: 2/24/71

☐ Not Requested

☐ Under negotiation with.

*If this is a special rate (e.g. off-site), explain.

SECTION II—BUDGET (Continued)

Grant Number

GM-14650-06

B. Supplemental information regarding ITEMS in the proposed budget for the next period which require explanation or justification. (See Instructions)

The major emphasis of the work supported will be in connection with the continuing computer analysis of our serological data on the HL-A system. Mrs. Hwang has been largely responsible for the development of our system of programs and continues, with the help of Mrs. Leo, to supervise the analysis of our data. During the coming year we will be obtaining data on the frequencies of HL-A antigens in a variety of populations,and also different disease states, specifically Hodgkin's disease and systemic lupus erythematosus. The experimental work is being done in collaboration with Drs. McDevitt and Grumet of the Department of Medicine. In addition, our system of programs is used by Dr. Rose Payne of the Department of Medicine, who was closely associated with Dr. Bodmer when he was at Stanford.

A small amount of experimental work connected with the correlation of HL-A typing on fibroblasts and lymphocytes is being carried on by Mrs. Wang. This represents a continuation of the studies started by Dr. Bodmer when he was at Stanford.

Because the staff benefit rate has increased over that previously anticipated, total direct costs are slightly more than the previously recommended amount.

SECTION III—FISCAL DATA FOR CURRENT BUDGET PERIOD (USUALLY 12 MONTHS)	FROM	THROUGH	GRANT NUMBER
	12/1/71	11/30/72	GM-14650-06

The following pertains to your CURRENT PHS budget. Do not include cost sharing funds. This information in conjunction with that provided on Page 2 will be used in determining the amount of support for the NEXT budget period.

A. BUDGET CATEGORIES	CURRENT BUDGET (As approved by awarding unit) (1)	ACTUAL EXPENDITURES THRU 7/31/71 (Insert Date) (2)	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD (3)	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3) (4)	ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1) (5)
Personnel (Salaries)	13,890	7,338	6,552	13,890	0
Fringe Benefits	1,952	1,020	955	1,975	-23
Consultant Costs					
Equipment					
Supplies	3,000	2,400	900	3,300	-300
TRAVEL — Domestic					
TRAVEL — Foreign					
Patient Costs	1,000	200	0	200	800
Alterations and Renovations					
Other	12,100	6,335	6,242	12,577	-477
Total Direct Costs	31,942	17,293	14,649	31,942	0
Indirect Costs (If included in award)	8,195	4,329	3,866	8,195	0
TOTALS →	$40,137	$21,622	$18,515	$40,137	$ 0

Use space below to:

B. List all items of equipment purchased or expected to be purchased during this budget period which have a unit cost of $1000 or more.

C. Explain any significant balance or deficit shown in any category of Column 5.

D. List all other research support for Principal Investigator by source, project title, and annual amount.

The taking of blood and tissue samples has for the most part been completed, so there will be a balance left in the "Patient Cost" allocation. However, this is more than offset by costs related to the analysis of the samples and computerization of the data.

Research Support:

(NIH) AI-5160 Genetics of Bacteria $56,000 p.a.

APPLICANT: REPEAT GRANT NUMBER SHOWN ON PAGE 1 →	GRANT NUMBER
SECTION IV—SUMMARY PROGRESS REPORT	GM-14650-06
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Last, First, Initial)	PERIOD COVERED BY THIS REPORT
Lederberg, Joshua	FROM: 12/1/71 — THROUGH: 11/30/72
NAME OF ORGANIZATION: Stanford University	
TITLE (Repeat title shown in Item 1 on first page): Genetics of Human Tissue Antigens	

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. Publications.

Santachiara, A.S., M. Nabholz, V. Miggiano, A. J. Darlington and W. F. Bodmer, 1970. Genetic analysis with man-mouse hybrids: linkage between human lactate dehydrogenase B and peptidase B. Nature 227: 248-251.

Bodmer, J.G. and W. F. Bodmer, 1970. Studies on African Pygmies. IV: A comparative study of the HL-A polymorphism in the Babinga Pygmies and other African and Caucasian populations. Am. Journ. Hum. Genet. 22: 396-411.

Miggiano, V.C., M. Nabholz and W. F. Bodmer, 1970. Detection of HL-A and other antigens on fibroblast micro-monolayers using a fluorochromatic cytotoxicity assay. Histocompatibility Testing, 1970, 623-629.

Gabb, B.W. and W. F. Bodmer, 1970. A micro complement fixation test for platelet antibodies. Histocompatibility Testing, 1970, 543-547.

Bodmer, J., A. Coukell, W. F. Bodmer, R. Payne and E. Shanbrom, 1970. A new allele for the LA series of HL-A antigens: the analysis of a complex serum. Histocompatibility Testing, 1970, 175-185.

Bodmer, W. F., J. G. Bodmer and M. Tripp, 1970. Recombination between the LA and 4 loci of the HL-A system. Histocompatibility Testing 1970, 187-191.

Mattiuz, P. L., D. Ihde, A. Piazza, R. Ceppellini and W. F. Bodmer, 1970. New approaches to the population genetic and segregation analysis of the HL-A system. Histocompatibility Testing 1970, 193-205.

Hulett, R., A. Coukell and W. F. Bodmer, 1970. Tissue typing instrumentation using the fluorochromatic cytocoxicity assay. Transplantation 10: 135-137.

Payne, R., J. Bodmer, W. F. Bodmer and E. Shanbrom, 1970. Production of defined human leukocyte typing sera. Histocompatibility Testing, 1970, 207-220.

Coukell, A., J. G. Bodmer and W. F. Bodmer, 1971. HL-A types of forty-four Hodgkins patients. Transplantation Proc. (in press)

McDevitt, H.O. and W. F. Bodmer, 1971. Histocompatibility antigens, immune responsiveness and susceptibility to disease. American Journal of Med. (in press)

Grumet, F.C., A. Coukell, J. G. Bodmer, W. F. Bodmer and H.O. McDevitt, 1971. Histocompatibility antigens associated with systemic lupus erythematosis: A possible genetic predisposition to disease. New England J. Med. (in press)

2. Per budget.

3. Progress Report (GM-14650-05)

During the current grant year, the major part of Dr. Bodmer's activities was transferred to the University of Oxford where he has taken up a position as Professor of Genetics. Experimental work was continued at Stanford by Mrs. Anne Coukell, and the Stanford Medical School's ACME computer facility continued to be used for our data analysis, while Professor Lederberg took over as principal investigator on the project from January 1, 1971.

A major emphasis of our work during the year has been on the association between HL-A and diseases, specifically lupus erythematosis and Hodgkins disease. In collaboration with Drs. McDevitt and Grumet, we have confirmed the very significant increase in the frequency of the antigen W15 in patients with lupus erythematosis. There were some puzzling anomalies in the typing of these patients which will be followed up by family studies to confirm their antigen phenotype and further serological studies on the nature of the autolymphocytotoxic antibody present in the sera of many of these patients.

Typing of forty-four Hodgkins patients from Dr. Henry Kaplan's clinic at Stanford did not indicate the previously reported increase in the antigens W5 or HL-A5 in these patients. However, it appears likely that this may be because the distribution of types of Hodgkins is different in the patients that we typed. Specifically, these seemed to include a much higher frequency of the nodular sclerosing type of the disease than is normally found in other series.

We are again participating in the next International Histocompatibility Testing Workshop, whose aim is to obtain as comprehensive information as possible on the distribution of the HL-A antigens in different populations. We took part in the testing of sera to be used by the participants in this Workshop and prepared a specially absorbed serum for the detection of a component of one of the newer antigens of the LA series.

We have greatly simplified our procedures for collecting, storing and shipping lymphocytes for typing so that they now require a minimum of processing in the field. This has enabled us to collaborate much more easily with workers in out-of-the-way places in order to obtain blood samples for HL-A typing.

Prepared for the Science Information Exchange.

Not for publication or publication reference.

U. S. Department of
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

NOTICE OF RESEARCH PROJECT

PROJECT NO. (DO NOT USE THIS SPACE)

TITLE OF PROJECT

Genetics of Human Tissue Antigens

GIVE NAMES, DEPARTMENTS, AND OFFICIAL TITLES OF PRINCIPAL INVESTIGATORS OR PROJECT DIRECTORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT.

Joshua Lederberg, Professor, Department of Genetics
Walter F. Bodmer, Professor, Laboratory of Genetics, Oxford University
Rose Payne, Sr. Research Associate, Department of Medicine
[illegible]

NAME AND ADDRESS OF APPLICANT INSTITUTION

Stanford University, Stanford, California 94305

SUMMARY OF PROPOSED WORK – *(200 words or less – Omit Confidential data.)*

In the Science Information Exchange summaries of work in progress are exchanged with government and private agencies supporting research in the bio-sciences and are forwarded to investigators who request such information. Your summary is to be used for these purposes.

The main aim of this research program is to further the understanding of the inheritance of antigenic differences of human leukocytes and other human tissues and to use these antigens for studies in somatic cell genetics. Cytotoxicity assays are being used together with intensive absorption studies of sera reacting with human leukocytes for the investigation of the genetics of the major human leukocyte antigen polymorphisms. Studies on the distribution of these antigens in various racial groups will also be undertaken. The specificities of antigens carried by permanent and primary cell culture lines are being investigated. The use of these antigens for studies in somatic cell genetics are being explored.

PROFESSIONAL SCHOOL *(medical, dental, etc.)* WITH WHICH THIS PROJECT SHOULD BE IDENTIFIED	SIGNATURE OF PRINCIPAL INVESTIGATOR	DATE
School of Medicine		8/16/71

DO NOT WRITE BELOW THIS LINE – FOR OFFICE USE ONLY

SUPPORTING AGENCY

METHOD OF SUPPORT *(Check one)*

☐ Agency Staff (Intramural) ☐ Negotiated Contract ☐ Special Project Grant ☐ Research Grant ☐ Other (Specify)

FUNDS OBLIGATED CURRENT F.Y.	NUMBER OF FUTURE YEARS TENTATIVELY ASSURED BEYOND CURRENT FISCAL YEAR	BEGINNING DATE	ESTIMATED COMPLETION DATE

PHS-166
REV. 5-70