DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

APPLICATION
FOR CONTINUATION GRANT

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 ANTIGENS

2. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR

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

3. DEGREE

Ph.D.

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

STANFORD UNIVERSITY
STANFORD, CALIFORNIA 94305

5. PHS ACCOUNT NUMBER

458210

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

GENETICS
CONTROLLER
STANFORD UNIVERSITY
STANFORD, CALIFORNIA 94305

COMPLETE THE FOLLOWING (See Instructions)

7. RESEARCH INVOLVING HUMAN SUBJECTS (See Instructions)

YES

8. INVENTION CERTIFICATION (See Instructions)

YES-PREVIOUSLY REPORTED

9. PERFORMANCE SITE (SI)

Genetics Department
Stanford University School of Medicine
Stanford, California

10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD

$14,439

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)

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

Tenth

12B. COUNTY OF APPLICANT ORGANIZATION SHOWN IN ITEM 4

Santa Clara

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.)

14A. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR

15A. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION

DATE: 8/16/71

RETURN COMPLETED APPLICATION TO PHS BEFORE: 1 OCTOBER 1971
SECTION II—BUDGET (USUALLY 12 MONTHS)

A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD

FROM 12/1/71 THROUGH 11/30/72

GRANT NUMBER GM 14650-06

PERSONNEL

<table>
<thead>
<tr>
<th>NAME (Last, First, Initial)</th>
<th>TITLE OF POSITION</th>
<th>TIME OR EFFORT</th>
<th>SALARY REQUESTED</th>
<th>FRINGE BENEFITS</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lederberg, J.</td>
<td>PRINCIPAL INVESTIGATOR</td>
<td>none</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hwang, J.</td>
<td>Scientific Programmer</td>
<td>25%</td>
<td>3,600</td>
<td>561</td>
<td></td>
</tr>
<tr>
<td>Wang, L.</td>
<td>Sr. Res. Asst.</td>
<td>16%</td>
<td>2,000</td>
<td>467</td>
<td></td>
</tr>
<tr>
<td>Lee, M.</td>
<td>Computer Operator</td>
<td>35%</td>
<td>3,000</td>
<td>311</td>
<td></td>
</tr>
</tbody>
</table>

Staff benefits:
9 mo. @ 15.2%
3 mo. @ 16.7%

Subtotals $18,600 $1,339

CONSULTANT COSTS (See Instructions)

EQUIPMENT

SUPPLIES

Culture medium and chemicals 300

TRAVEL

DOMESTIC

FOREIGN

PATIENT COSTS (See instructions)

ALTERATIONS AND RENOVATIONS

OTHER EXPENSES (Itemize):

Computer Time $4,000
Communications, Publication Costs 200

TOTAL DIRECT COST (Enter on Page 1, Item 10) $14,439

INDIRECT COST

(See Instructions)

% SEW*
46

Date of DHEW Agreement: 2/24/71

PHS 2590-1 (All previous editions obsolete)

PAGE 2

Rev. 1-70
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
(USUALY 12 MONTHS)

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

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.
## SECTION IV—SUMMARY PROGRESS REPORT

<table>
<thead>
<tr>
<th>Applicant: Repeat Grant Number Shown on Page 1</th>
<th>Grant Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GN-14650-06</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Principal Investigator or Program Director (Last, First, Initial)</th>
<th>Stanford University</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lederberg, Joshua</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of Organization</th>
<th>Title (Repeat title shown in Item 1 on first page)</th>
<th>Genetics of Human Tissue Antigens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
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</tbody>
</table>

**PERIOD COVERED BY THIS REPORT**

<table>
<thead>
<tr>
<th>From</th>
<th>Through</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/1/71</td>
<td>11/30/72</td>
</tr>
</tbody>
</table>

1. **Publications.**


2. **Per budget.**
Application for Continuation Grant
GM-14650-06

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 Genomics. 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 erythematosus and Hodgkin's 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 erythematosus. 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 Hodgkin's 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 Hodgkin's 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.
Genetics of Human Tissue Antigens

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

NAME AND ADDRESS OF APPLICANT INSTITUTION
Stanford University, Stanford, California 94305

SUMMARY OF PROPOSED WORK
In the Science Information Exchange, summaries of work in progress are exchanged with government and private agencies supporting research in the biosciences 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.