

December 27, 1950

Proposals to the Atomic Energy Commission for a Contract in
aid of a Research Project on

CYTOGENETIC EFFECTS OF RADIATIONS ON BACTERIA

at the Department of Genetics, UNIVERSITY OF WISCONSIN.

Project Leader: Joshua Lederberg, Ph.D., Associate Professor of Genetics

Scope, status, and motivation of project:

Support is requested from the Atomic Energy Commission for the preliminary exploration of a subject which may throw fundamental light on the mechanism of biological action of ionizing radiations. The material to be studied is diploid cells of Escherichia coli. Work in progress has shown that this material can be used to test the significance of recessive lethal mutations in the bactericidal effects of chemical mutagens such as nitrogen mustard or physical agents such as ultra-violet light. In diploid cells, lethal mutations can be detected owing to their temporary masking by the unmutated genome; in haploid cells, of course, lethal mutations result in cell death, and are thus not amenable to study.

Work in progress indicates that, contrary to expectation, lethal mutations play an insignificant role in bacterial killing by nitrogen mustard or ultraviolet light. Bactericide by these, and a large number of other agents, including hydrogen peroxide, formaldehyde, and X-rays (in a single preliminary experiment) is, however, accompanied by complex genetic reorganizations, not completely understood as yet, but including

the production of cells with haploid, rather than diploid constitution. It is also apparent that these changes are accompanied by disturbances in the division and distribution of the nuclear bodies in the treated bacteria.

The present project concerns the extension of this genetic and cytological work with special reference to the effects of X-rays (and subsequently, of other ionizing radiations). Because the project is already under way to some extent, with respect to chemical and ultraviolet effects, a modest request is made for the first year, as the major aim of the project during this interval is to determine the advisability of a concerted attack upon this problem. It is anticipated that increased working space for research will be available to the investigator in 1952, if an expansion of the program in the areas of interest to the Atomic Energy Commission appears desirable, both ^{to} the Commission and the investigator.

In this interval of exploration, probably no new personnel will be required. The genetic work will be continued by the investigator, with the assistance, particularly in cytological aspects, of graduate student research assistants already in residence or possibly of an additional assistant later. Financial support will be required primarily for the purchase of roentgen-dosimetric equipment needed for kinetic studies on the comparative rates of sterilization of diploid and haploid cells, and for additional supplies incidental to the project.

The University of Wisconsin has a number of X-ray machines on the campus, although none of these is primarily suited to biological research. However, for the present, the purchase of a new machine for the current project does not seem to be justified, and it is hoped that the present facilities will be adequate. A radioactive Co source will be available

to a project in another research group, and the installation of a betatron is anticipated. Basic apparatus and facilities for bacteriological research have already been established.

Relevant literature:

- Lederberg, J. 1947 Gene recombination and linked segregations in *Escherichia coli*. *Genetics* 32:505-525.
- _____ 1949 Aberrant heterozygotes in *Escherichia coli*. *Proc. Nat. Acad. Sci.* 35:178-84.
- _____ 1951 Genetic experiments on bacteria. In "Fifty Years of Genetics." MacMillan: New York, in press.
- Delaporte, B. 1949 Cytology of Bacteria. *Carnegie Inst. Yrbk.* 48: 166-170.
- Newcombe, H. B. and Scott, G. W. 1949 Factors responsible for the delayed appearance of radiation-induced mutants in *Escherichia coli*. *Genetics* 34:475-492.

Scientific Personnel: In this preliminary period, no new scientific personnel are contemplated, and the project will be handled directly by the principal investigator, with the assistance of various graduate students already in residence. If necessary, an additional graduate assistant may be employed during the latter half of the contract term, but no specific person is under consideration.

Proposed budget. (For March 1, 1951 to February 29, 1952)

The University of Wisconsin will provide basic working facilities for bacteriological research. Because the proposed project interlocks with other work already in progress, glassware, reagents, and bacteriological media will also be provided, as well as the services of the principal investigator. X-ray equipment already on the campus will be used as required, but fees routinely charged in connection with certain such services when provided by other departments will be paid from the contract.

The Commission will be asked to provide for the following:

Equipment and Supplies;	350
Roentgen meter for calibration of X-ray doses	250
Accessories for photomicrography	100
Service Fees for X-ray equipment	50
Salary, for 1/2 time graduate assistant for 6 months	600
Total	<u>1000</u>
Overhead, at 8%,	80
Grand Total	<u>1080</u>

The proposed term for the preliminary project is March 1, 1951 to February 29, 1952. However, if research results or other factors intervene which make further action advisable, the investigator may apply for subsidiary support prior to the expiration of this term. The probable term of an extended project would be about four years, unless full-time employees displace our graduate students.

Responsibilities of investigator: The principal investigator is in charge of all laboratory devoted to microbial genetic research, and housing, at present, three graduate research assistants, one postdoctoral research associate and a number of undergraduate assistants. His teaching duties, aside from those incidental to the laboratory, are minimal. A number of research projects are under way in the laboratory, dealing primarily with (a) formal and physiological genetics of *Escherichia coli*; (b) host-parasite relationships in lysogenic bacteria; (c) screening for genetic recombination in *Salmonella* and other bacteria; (d) cytological studies of haploid and diploid *E. coli*, and (e) mechanism of action of bactericidal agents.

The laboratory's program receives part of its support from other federal agencies as follows:

For 1950-51: National Institutes of Health \$4,320
(Genetics of Salmonella)

Chemical Corps 6,000 (15 mos.)
(Lysogenic Bacteria)

Requests anticipated for 1951-52

National Institutes of Health 9,000
(Genetics of Bacteria)

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