

Tentative Proposals

11/15/50
A L C

Cytogenetic effects of radiations on bacteria

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Support is request^d 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 ultra-violet effects, a modest request is made for the first year, as the major aim of the project during this

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

Budget. For roentgen-dosimetric equipment, and other	
apparatus and supplies	\$500.00
Overhead.... (at established rate)	
Total	\$500.00 plus overhead.

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.

The principal investigator is in charge of all laboratory devoted to microbial genetic research, and housing, at present, three graduate research assistants and one postdoctoral research associate. His teaching duties, aside from those incidental to the laboratory, are minimal. A number of research projects are underway in the laboratory, dealing primarily with formal and physiological

a) ~~xxxxxxx~~ genetics of *Escherichia coli*; b) host-parasite relationships in lysogenic bacteria; c) screening for genetic recombination in *Salmonella* and other bacteria; d) cytological comparisons of haploid and diploid *E. coli*, and the effect of bactericides, and e) mechanism of action of bactericidal agents.

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

For 1951-52:	National Institutes of Health (Genetics of <i>Salmonella</i>)	\$ 4,320
	Chemical Corps (Lysogenic Bacteria)	6,000 (15 mos.)

Requests anticipated for 1951-52

National Institutes of Health (Genetics of Bacteria)	2,000.
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