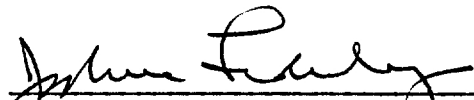


A proposal for submission to
National Science Foundation
(Italy/U.S. Science Cooperation)

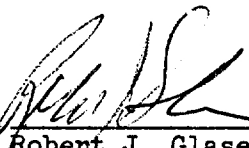
An Exchange Program in Genetics and Molecular Biology
Between Research Scientists from the Departments of Genetics of the
Universities of Stanford and Pavia


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Italy/U.S. Science Cooperation

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The Departments of Genetics of Stanford and Pavia, Italy, respectively, wish to undertake a formal collaborative project in genetics and molecular biology.

The present proposal from Stanford closely parallels one submitted by Pavia to the Consiglio Nazionale delle Ricerche of Italy.

The two departments have enjoyed a very close de facto relationship in the past, as exemplified by the exchanges listed on page 3. These repeated exchanges have resulted in the elaboration of a number of joint research projects in genetics and molecular biology in which both U.S. and Italian scientists participate. It will be very useful for the continuation of these projects if they could be corroborated by an even stronger exchange of people and ideas from the two departments.

These enterprises have been financed by charges to regular research budgets, funds which are becoming more difficult to release for this purpose. The cooperative program would enable us to move from an occasional interchange to a systematic coordination of research programs.

There should be two research units involved in this collaborative research, one at Stanford and one at Pavia. Each of the two would be engaged mostly, but not exclusively, in one of the two major research programs which are explained below. In particular, at least one pair of visits each year will involve the head of one department or his deputy, making an intensive consultation with the entire research program of the other. However, because of teaching and other duties, the senior scientists would be able to spend only comparatively short periods of time away from their main laboratories. On the other hand, younger

scientists could spend longer periods of time in the other department. In addition, other people may be engaged on a more or less permanent basis in either laboratory to ensure the continuity of the work.

Stanford, then, will furnish one or more senior and associate scientists so that the Pavia laboratory will have, on the average, one or two visitors in residence at any one time, and correspondingly will offer the facilities of the Stanford laboratory to two visitors, one a senior scientist, who may be different individuals during different parts of the year. The respective departments will endeavor to identify and certify scientists from other institutions as well who might go under Stanford's (or Pavia's) auspices, to represent special skills and interests needed to fulfill the program.

The following faculty and staff members from the Genetics Departments of Pavia and Stanford have been associated with the other department for periods of time ranging from a few weeks up to two years:

Dr. J. Lederberg (Stanford) in Pavia in 1962;

Dr. L. L. Cavalli-Sforza (Pavia) in Stanford in 1962, 1964, and 1965;

Dr. W. Bodmer (Stanford) in Pavia in 1963 and 1966;

Dr. A. Edwards (Pavia) in Stanford in 1964;

Dr. O. Ciferri (Pavia) in Stanford in 1966.

Presently, one junior scientist from Pavia, Dr. S. Barlati, is working in the Stanford Department of Genetics.

Further exchanges have taken place between Pavia and Stanford:

Dr. A. Falaschi, presently in Pavia, has spent four years in the Stanford Department of Biochemistry;

Dr. H. M. Cann, formerly a fellow in the Stanford Department of Genetics and now in the Stanford Department of Pediatrics, has spent one year in Pavia;

Dr. G. Milanesi will soon be spending several months in the Stanford Biochemistry Department.

Dr. Ruth T. Gross, then at Stanford, spent part of 1959-60 at Pavia. She is now Chief of Pediatrics at Mount Zion Hospital.

PROPOSED JOINT RESEARCH PROGRAMSMolecular Genetics (MG, to be carried out mostly at Stanford)

It is proposed to study the integration of synthetic deoxypolyribonucleotides and of DNA of widely different biological origin into the genome of Bacillus subtilis, and their genetic translation in vivo. Two models can be given as examples of a first experimental approach:

- 1) the uptake and integration of synthetic deoxypolyribonucleotides such as poly-dAdT into the genome of Bacillus subtilis;
- 2) the uptake and translation of synthetic ribopolynucleotides such as poly-rU into Bacillus subtilis.

Among other things, the second type of experiment, if successful, could permit the verification of the validity in vivo of the genetic code.

The ultimate goal of this research is the controlled modification of the genome of an organism.

Scientists from Pavia have already made an important contribution to the foundations of this problem, through their earlier visits having become familiar with the biochemical techniques developed mainly in the U.S. for molecular biology research.

A special laboratory and office has been designated at Stanford for the regular use of the Italian visiting scientists. In addition, the experimental facilities of the Department will be freely available, including modern analytical instrumentation for biochemical genetics, library, information retrieval aids, and access to a time-shared, remote-terminal computer system, with system programming support.

Human Populations Genetics (HPG)

A theoretical analysis shows that for an understanding of human variation, in particular of the mechanism of action of selection and genetic drift, work on populations must be conducted:

- 1) at a larger scale than so far, with the adoption whenever feasible of automated techniques for the analysis of a large number of characters;
- 2) refining further the mathematical and numerical tools presently available for the study of human populations.

The program is to set up a collection center starting with what techniques are already available and use it for the study of populations on which the Pavia and Stanford Departments are already engaged. Such an analysis is at present carried out in part in other departments for lack of the required facilities at Pavia and Stanford. One of the major aims in mind is to carry out the study of the inheritance of complex quantitative characters by way of linkage to the standard chromosome markers. This seems to be one of the best ways, so far untried, to study the inheritance of characters which otherwise escape analysis, such as behavioral ones. This will also involve much computer work.

While Pavia will be the primary center for these activities during its operational phase, Stanford has a specially competent instrumentation development laboratory. This is mainly dedicated to instrumentation for experiments in space biology, but its engineers and physicists will be available for consultation for the development of specialized automated equipment for immunological survey work. Stanford also has one of the most advanced computer systems in the world dedicated to medical research laboratory work, and its facilities will also be available for this project, giving Italian scientists an unusual opportunity to become familiar with these advanced techniques.

Other research support:

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|------|--------------|---|---------------------------|
| NSF | GB-4430X1 | (Jointly with faculty members of Genetics Department) A Program in Genetics and Molecular Biology 10/15/66 - 10/15/67 | \$63,600 |
| NIH | AI-5160-09 | Genetics of Bacteria | 9/1/66 - 8/31/67 \$52,174 |
| NIH | FR 00311-01 | (Jointly with Medical School faculty) Advanced Computer for Medical Research 9/1/66 - 7/31/67 | \$444,534 |
| NASA | NsG 81-60 S7 | Cytochemical Studies of Planetary Microorganisms. 9/1/66 - 8/31/67 | \$448,850 |