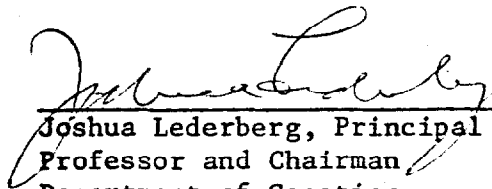


A proposal to  
National Science Foundation  
(U.S./Italy Science Cooperation)

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

May 1, 1972 - April 30, 1973  
(GB-29094)

Submitted by:

  
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Joshua Lederberg, Principal Investigator  
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U.S./Italy Science Cooperation

Proposal for Renewal: May 1, 1972 - April 30, 1973

(GB 29094)

Professor Cavalli-Sforza is now a permanent member of the Stanford faculty, and he has undertaken a major role in the coordination of the exchange of students and faculty between Stanford and Pavia. Professor Cavalli-Sforza maintains very close ties with his parent institution in Pavia. For our part, the visiting scientists have been inspiring and enthusiastic guests who have contributed a great deal to the élan and productivity of the Genetics Department of Stanford. We look forward to working with them in the future and know they share these expectations.

The collaboration will be, as in the past years, connected with the entire research program of the Genetics Department, with the assignments to individual professors made in accordance with the special interests of the visitor. The experimental facilities of the Department (including modern analytical instrumentation for biochemical genetics research, reference room, information retrieval aids, and access to a time-shared, remote-terminal computer system, with system programming support) will be freely available to the visiting scientists.

Among the programs supported in part by this grant is one dealing with neuron transplantation. During his stay at Stanford in 1968-69, Prof. Cavalli-Sforza started some experiments on brain transplantation in newborn mice, using cells marked with tritiated thymidine. This work is now continuing and shows transplants have a good probability of taking. Mostly glial cells have been observed to take in the transplant procedure, but cells that have neuron like activities may also occasionally show a take. This work is being continued but has been made slow by the necessity of leaving autoradiographic material under exposure for very long periods of time. The project was stimulated originally by a suggestion made by Professor Joshua Lederberg in an article appearing in the Washington Post.

Another project underway was begun by Prof. A. S. Santachiara-Benerecetti, who visited Stanford for six months in 1971, and is being continued by Dr. Pier Franco Pignatti, currently visiting at Stanford. This project deals with the biochemical genetics of nervous disorders. An attempt is being made to identify by electrophoretic techniques the brain enzymes which are important for the metabolism of neuro-transmitters. So far the enzymes analyzed with some success are monoaminooxidase, 5HTP decarboxylase as well as Dopa to dopaamine. Species differences have been found for the latter enzymes for the enzymes obtained from beef, rats, and mice. This result has been found by utilizing new techniques which increase the resolution of electrophoresis. The aim of the project is to study these same enzymes in man and to look for correlations between differences in these enzymes and abnormal behavior (in particular schizophrenia and other mental diseases).

Dr. K. Kidd (who has spent a year and a half in Pavia) and Dr. L. Sgaramella-Zonta (from Pavia) are working on an analysis of human and cattle genetic data on a population genetics project. The analysis of human genetic data is centered on discovering interactions between cultural and biological evolution. In particular, work is directed to the study of populations that may be the outcome of the demographic expansion that took place when agriculture was discovered and spread outward from its point of origin. (This links up with work carried out by Prof. Cavalli-Sforza and Dr. Albert Ammerman on the spread of the Neolithic. Dr. Ammerman is also at Stanford at the moment.)

Work carried out by Dr. Kidd on Icelandic cattle has shown that Icelandic cattle show the greatest genetic similarity to Norwegian cattle (in line with the belief that Icelandic cattle are historically descended from Norwegian cattle breeds). A closer analysis of these data carried out with Prof. Cavalli-Sforza

shows that the amount of differentiation observed between Icelandic and Norwegian cattle can be explained if drift alone is responsible for the differences. This study was made possible by the fact that enough demographic data are available on cattle in Iceland and in Norway to compare (with a reasonable amount of error) the amounts of drift in the two populations.

Mark Skolnick (a graduate student shortly to return to Pavia) is doing record linkage studies of Parma Valley parish registers. This research has grown out of work conducted over the past sixteen years, during which time much data on the demography of the Parma Valley have been collected. Mark Skolnick is currently at Stanford; he spent two years in Pavia developing a program which will allow the reconstruction of genealogies by computer in spite of differences arising from ambiguities in the original records. He will return to Pavia to complete part of this work and will base his Ph.D. thesis on this study.

Dr. Vittorio Sgaramella is working on a project aiming at establishing conditions to covalently join different DNA molecules by means of a recently discovered property of the T4 polynucleotide ligase ("terminal joining activity"), as well as to perfect methods to obtain completely base-paired DNA duplexes, which seem to be the substrate for this reaction.

## STANFORD/PAVIA EXCHANGE PROGRAM

Budget

May 1, 1972 - April 30, 1973PERSONNEL

## Genetics Dept., Stanford:

J. Lederberg (2% time) *		—
L. Cavalli-Sforza (3% time)		—
Louise Wang	(6 mo.)	\$ 5,800
Secretary (50% time)	(9 mo.)	2,700

## Visiting Fellows from Pavia:

S. Santachiara	(5 mo.)	6,000
P. Pignatti	(6 mo.)	4,200
O. Ciferri	(3 mo.)	5,000
C. Matessi	(6 mo.)	4,200
A. Cori	(3 mo.)	2,000

Total Salaries		29,900
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Staff Benefits (@ 15.7%)		4,694
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TOTAL PERSONNEL		34,594
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## TRAVEL (Stanford visitors to Italy)

L. Cavalli-Sforza	\$1,034
J. Lederberg	1,033
E. Shooter	1,033

Total Travel	3,100
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LABORATORY SUPPLIES	1,902
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COMPUTER TIME (ACME)	1,500
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TOTAL DIRECT COSTS	\$41,096
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INDIRECT COSTS (46% Total Direct Costs)	18,904
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TOTAL AMOUNT REQUESTED	<u>\$60,000</u>
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\* Time formally committed for cost sharing purposes.

Faculty and staff from Pavia who visited Stanford during the term of the Stanford/Pavia Grant, GB 29094

Prof. Orio Ciferri, Research Associate (9/71 - 12/71)

Dr. A. S. Santachiara-Benerecetti, Research Associate (7/71 - 12/71)

Dr. P. Pignatti, Research Fellow (1/72 - 6/73)

Dr. V. Sgaramella, Research Associate (9/71 - 8/72)

Dr. L. Sgaramella-Zonta, Research Associate (9/71 - 8/72)

Dr. C. Cannings, Research Associate (5/71 - 8/71)

Stanford faculty and staff who have visited and collaborated on projects in Pavia during last grant period.

Prof. L. Cavalli-Sforza

Dr. Kenneth Kidd

Dr. A. J. Ammerman

Mark Skolnick

Department of Genetics - Stanford University School of Medicine

Joshua Lederberg - (1) Incorporation of foreign genomes into B. subtilis DNA; control mechanism for precise and distorted DNA replication; novel processes of genetic recombination in bacteria; effects of chlorine and other environmental mutagens on DNA. (2) Computer simulation of human cognitive processes--mechanized hypothesis formation and suggestion of experimental tests; application to organic analysis.

L. L. Cavalli-Sforza - Research and teaching in human population genetics, involving a combination of genetic, demographic, anthropological and medical analysis; use of computers in medical analysis; transplantation of neurons; biochemical genetics of behavioral diseases.

Alan Duffield - Analysis of the organic chemical constituents of urine, using gas chromatography-mass spectrometry; fundamental studies in mass spectrometry of organic compounds; reaction of aqueous chlorine with organic compounds and DNA.

A. T. Ganesan - Genetic control of chromosome replication in B. subtilis; genetic chemistry of DNA replication; nature of attachment of the chromosome to the cell membrane; mechanism of genetic recombination during DNA mediated transformation; mode of phage replication in B. subtilis; chromosome replication in mammalian cells with reference to the role of nuclear membrane.

L. A. Herzenberg - Genetic and structural studies of immunoglobulins; mammalian cell genetics; mechanism and control of antibody synthesis; computer controlled instrumental methods of cell analysis and separation; genetics and immunology of tissue transplantation; automated cytochemistry.

E. C. Levinthal - Cytochemical studies of planetary microorganisms - Mars orbiter and lander photography and related image analysis - explorations in exobiology; development of computer-managed instruments, present emphasis being on mass spectrometry with specialized input systems such as gas-liquid chromatographs or laser volatilization of solids; optical methods of cell analysis and separation.

Eric M. Shooter - Biochemistry of the nervous system and its development; protein and nucleic acid synthesis in nervous system tissue; structure and mechanism of action of the Nerve Growth Factor protein. Genetic control of hemoglobin; subunit structure of hemoglobin and other proteins; interactions of protein subunits.

Publications arising from Stanford/Pavia Research

- Bodmer, W. F., and L. L. Cavalli-Sforza, 1971. Variation in fitness and molecular evolution. Proceedings of the Sixth Berkeley Symposium on Mathematical Statistics and Probability, Conference on evolution, April, 1971. In press
- Bodmer, W. F., and L. L. Cavalli-Sforza, 1971. Migration matrices. IV Int. Congr. Human Genetics, Paris, Proceedings. In press.
- Cavalli-Sforza, L. L., and W. F. Bodmer, 1971. The Genetics of Human Populations. W. H. Freeman & Co., San Francisco.
- Cavalli-Sforza, L. L., and K. K. Kidd, 1972. Considerations on genetic models of schizophrenia. Neurosciences Research Program Bulletin, in press.
- Kidd, K. K., P. Astolfi, L. L. Cavalli-Sforza, 1971. Error in the reconstruction of evolutionary trees. In Genetic Distance, Ed., J. F. Crow, in press.
- Kidd, K. K., and L. L. Cavalli-Sforza, 1971. An analysis of the genetics of schizophrenia. IV Int. Congr. Human Genetics, Paris, Proceedings. In press.
- Skolnick, M. H., A. Moroni, and L. L. Cavalli-Sforza, 1971. The population structure of Parma Valley, Italy, IV Int. Congr. Human Genetics, Paris, Proceedings. In press.
- Mazza, G., H. M. Eisenstark, M. C. Serra, and M. Polsinelli, 1971. Effect of caffeine on the recombination process of B. subtilis. Molecular and General Genetics, in press.