

SUMMARY OF MATERIAL FOR THE STANFORD-PAVIA GRANT RESEARCH PROJECTS

1) Under direction of Professor Luca Cavalli-Sforza.

Genetic Study of Metabolism of Neurotransmitters
Supported by NIMH Grant #NS 10711-01

- 1A This investigation aims at finding genetic differences in enzymes metabolizing neurotransmitters and in proteins storing them. Electrophoretic mobilities have been found among various species for the enzyme 5-hydroxytryptophan decarboxylase. The enzyme investigated has been found identical to that decarboxylating DOPA, confirming earlier work in the literature. It is planned to extend this to further investigations on differences between mouse strains and to human material. This work has been started and should in the future be continued in collaboration with Silvana Santachiara of Pavia. Electrophoretic techniques have been set up for the study of proteins that show an affinity for serotonin in platelets. Mechanisms of storage of serotonin in platelets may be similar to those in brain cells. A search for a polymorphism in these proteins is in progress. This work is being carried out by Dr. Pier Franco Pignatti of Pavia.

1B Gene Diffusion and Natural Selection in Man

This problem was started as a project funded in part by local funds and it is hoped that it will obtain increased support by grants that have been requested from NSF and NIH. On the basis of a preliminary announcement by NSF, part of the request will be funded starting September 1, 1973. The decision of NIH should be communicated at the end of this month. In this project it is planned to test the possibility that the introduction of plant and animal breeding has determined a demographic explosion, which has resulted in a population expansion, well outside the limits of origin of these technological changes. An analysis of archeological data by Ammerman and L. Cavalli-Sforza has shown agreement with this hypothesis. It is planned to test the genetic consequences of this hypothesis, namely the spread of genes from the areas of origin of domestication, by using data on genetic markers collected in Europe, North Africa and Asia, that is, in the areas surrounding the major centers of origin of domesticates, the Middle East. Dr. Laura Sgaramella-Zonta of Pavia is working on this project.

1C Mutation Rates and Mutation Loads in Man USAEC AT(04-3)326

It is planned to examine Italian census data of 1962 obtained by L. Cavalli-Sforza which may help in estimating the age dependence of spontaneous mutation rates to sex linked recessive lethals. The data consist of the sex ratios among still borns and among live borns of women whose ages, as well as the ages of her parents at her birth are

known. This approach has been used in the past (see, for references, Cann and Cavalli-Sforza) with various results. The new data should have some advantage over earlier ones, being probably more reliable and certainly much more extensive. This project is carried out by Dr. Dr. Gianna Zei, presently at Pavia, under the supervision of Dr. Cavalli-Sforza.

1D

Reconstruction of Genealogies in the Parma Valley
NIH Training Grant GM295(16)

Barrai, Cavalli-Sforza, and Moroni have made a start in record linking by computer data on parish books of births, deaths and marriages. Material used was collected in the upper Parma Valley, a region that was also investigated earlier from a genetic point of view. The more ambitious task of reconstructing genealogies for the thirteen generations of data that are available has also been started (Skolnick, Moroni, Cannings and Cavalli-Sforza, 1971 "The reconstruction of genealogies from Parish Books"). Most of the latest work is due to Mark Skolnick, a Ph.D. student under the NIH Training Grant, who hopes to complete a full reconstruction for the upper Parma Valley during this year. This will allow us to study the inheritance of longevity, fertility and twinning, in addition to giving a considerable wealth of demographic material. M. Skolnick is presently in Pavia and Parma (Italy) to complete the computer conversion of the data and the reconstruction programs. He is expected to be back in Stanford by April, 1973. This work will form the subject of his thesis.

Professor J. Lederberg

2A Terminal joining of DNA molecules.

NIH Research Grant AI-5160

Dr. Vittorio Sgaramella is studying the enzymatic processes by which double-stranded DNA molecules can be joined together end-to-end. With the ligase from bacteriophage T4, he has demonstrated this as a new activity, and that it can be applied to the formation of di-, tri-, and polymers of the phage P22 DNA. The most important application of this method would be to the insertion of new genetic information from, say, mammalian cells into the DNA of a bacterial or virus chromosome-- experiments that are now under way with promising preliminary results. While this work is continuing here, cognate experiments are being pursued at Pavia by Ciferri and Falaschi, with whom we are in close communication.

(Additional funds are urgently required, however, to support brief visits to this laboratory by our colleagues in Pavia -- visits that cannot be so readily funded or justified within the framework of grants to the Stanford research program per se.

ESTIMATED LEVELS OF FUNDING

The following sums are fair estimates of the allocations to the programs in which visiting colleagues from Pavia are directly involved: These are direct costs for the calendar year 1973:

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|----|----------|----|----------|----|---------|----|---------|----|----------|
| 1A | \$13,750 | 1B | \$15,000 | 1C | \$3,000 | 1D | \$5,000 | 2A | \$25,000 |
|----|----------|----|----------|----|---------|----|---------|----|----------|

Total: \$61,750. Add indirect costs, approx. \$35,000 \$86,750.