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Research proposal for a group of geneticists at Fort Detrick

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The dismantling of Ft. Detrick and the potential takeover of part of its facilities and personnel offers the opportunity to utilize the knowledge, skill, and facilities of a group of geneticists and tissue culture specialists. Some of these scientists (their names are given below) have worked on the isolation of mutants and their genetic alteration by transforming DNA, by virus transduction, and by virus transfection in bacteria. Others have utilized tissue cultures in nutritional studies and grown animal viruses in these cultures. I have discussed with these scientists the need for health-related research as a requirement for their possible association with NIH. They have agreed to change their direction and to work on the following program that should be of immediate interest to the NIH:

Curing of Hereditary Diseases by Genetic Transfer

An increasing fraction of diseases are due to hereditary defects. In most cases, the deficient compounds are phosphorylated, of high molecular weight, or for other reasons unable to enter cells. A cure of these diseases by addition of the missing compounds can therefore not be expected. But it can be anticipated that the transfer of genetic material into some of the deficient cells will be able to transform them into functionally normal cells which, owing to their selective advantage, may become the predominant cell population in a growing organism or among those cells of an adult organism that are still turning over. The existence of several mechanisms of genetic transfer has been demonstrated in microorganisms, mostly for bacteria, and the Ft. Detrick genetics group has importantly contributed to this development and has published more than 20 papers on their work in the last six years. In cells of higher organisms only scanty information is available, because the genetics of tissue cultures required several discoveries that have been made in the last few years. As Puck and Chu have shown in Chinese hamster cells, biochemical mutations in tissue cultures can be readily isolated. In addition, Harris and Ephrussi have demonstrated the genetic potential of cell fusion experiments. There is some indication that transformation by DNA may be feasible (Szybalski) and that animal viruses carry host DNA (Apotian for polyoma), which may render transduction feasible; the well-known phenomenon of virus "transformation" has clearly shown that some viral genetic information can be expressed and maintained inside tissue culture cells.

The research proposed here would involve the following types of development:

1. Isolation of biochemical or temperature-sensitive mutants in tissue cultures.

2. Measurements of genetic transfer of point mutations and larger alterations by transformation with DNA, transduction of genetic material by viruses with minimal or no health hazard, and transfection with the DNA of such viruses. If any one of these methods of genetic transfer succeeds, the conditions for ideal genetic transfer would be investigated and the incorporation of the transferred DNA into cellular DNA would be established.

3. Investigation of mechanisms restricting growth of viruses or of genetic transfer in different tissue culture lines. Very powerful restriction mechanisms have been discovered for bacteriophages, and their molecular origin has been attributed to DNA base methylation (Arber) and breakdown by specific DNAases (Meselson).

4. Viruses containing very specific nonviral information for the curing of genetic diseases could be isolated by techniques developed for bacteriophages, such as the growth of viruses in large quantities in cells in which recombination is impossible, by defective viruses carrying the desired gene linked to defective viral DNA, or by replicating viral DNA in vitro and then wrapping it into the viral protein coat which enables the entry of the nucleic acids into cells.

5. Examination of the sensitivity to viral infection and to genetic transfer for cells at different states of differentiation. This work would show whether viral or genetic transfer could be limited to specific differentiated tissue.

6. Since microorganisms develop antibiotics during their time of differentiation (sporulation), it is possible that specific compounds with antibiotic activities against other cells are also produced by tissue cultures. This would be easy to verify.

It is realized that experiments involving animal or human viruses and other genetic transfer of cells have to be performed with great caution, both because the viruses themselves may contaminate the surrounding areas and because inadvertently a mutant virus culture may grow up and start a new virus disease. However, experiments on the much more dangerous cancer viruses are presently performed under laboratory conditions which are not as ideally suited for protection as are the laboratories

of Ft. Detrick. The latter laboratories are held under reduced pressure and their air is exhausted through elaborate filter systems which permit no infectious particles to escape. The potential alleviation or curing of some genetic diseases, which should be accompanied by genetic family counseling, would render this research eminently worthwhile. Apart from eugenics, the transfer of genetic information seems to be the only hope for the curing of most hereditary diseases.

The names of scientists (all with Civil Service positions) currently involved in genetic and tissue culture work at Ft. Detrick are:

Dr. Robert A. Altenbern
Dr. Ivan D. Goldberg
Dr. William D. Lawton
Dr. Milton W. Slein
Dr. Franklin J. Tyeryar
Dr. Robert Zsigray

and their technical support staff of 15 people. This group now occupies a laboratory space of 15,000 square feet.

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