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F A X C O V E R S H E E T

To: *Prof. M. Meulman*

From: *Marty Kaplan*

Number of pages, including cover sheet: *4*

Date: *27 Jan '92*

Dear Matt,

Message:

- 1. The enclosed was prepared on request from Student Pugwash USA for inclusion in their "Tough questions" section of their Newsletter. Please let me know if there are any factual errors.*
- 2. Remind Jack Gold of the dates of our Berlin Conference. I believe he wanted to attend as an accompanying person (with you or me).*
- 3. I think I have arranged a slot for you to report on the CNE at a plenary in Berlin.*
- 4. Dudley Wright died a few days ago.*

Some Comments on the Human Genome Project (HUGO)

by

Martin M. Kaplan

(see footnote at end of paper)

In considering the Human Genome Project (HUGO), I will only touch on the technical aspects, and will stress the importance of some of the social questions that arise.

The deoxyribonucleic acid (DNA) constituting the human genome consists of sequences of some three billion base pairs in the 50,000 or more genes which govern our body processes. ^{More than} Some 2,000 of these genes have been mapped (located) so far. (James Watson and Francis Crick identified the structural arrangement of the chemicals in their formulation of the double helix in the early 1950s which won them the Nobel prize.) With recently developed sequencing technology it is possible to obtain the sequence of 300-500 base pairs in a single experiment. It is generally estimated that it will take about 15 years to map the entire human genome at a cost of about five billion dollars.

Proponents of HUGO have emphasized that priority would be given to the pursuit and delineation of malfunctioning genes that cause human disease, especially those diseases where a genetic predisposition (e.g. breast cancer) or a specific genetic deficit (e.g., cystic fibrosis) is involved. Other genetically determined diseases include hemophilia, sickle cell anemia and muscular dystrophy.

As James Watson, a prime mover of HUGO, put it:

"When finally interpreted, the genetic messages encoded within our DNA molecules will provide the ultimate answers to the chemical underpinnings of human existence. They will not only help us understand how we function as healthy human beings, but will also explain, at the chemical level, the role of genetic factors in a multitude of diseases, such as cancer, Alzheimer's disease, and schizophrenia, that diminish the individual lives of so many millions of people."

Molecular genetic and physical maps of human DNA are first needed to help locate disease genes. This will require preliminary work on model organisms such as the colibacillus, yeast, fruit fly and the mouse. There is little difference of opinion amongst biological scientists about proceeding with this preliminary work which, along with parallel research on human DNA, is estimated will take about five years.

There is ~~is~~ disagreement, however, within the scientific community about the second stage of the project which involves completing the physical maps of human DNA and

the sequencing of selected genes in the 24 different chromosomes. Part of this disagreement is technical in nature. For example, is it necessary ^{and worthwhile} to include non-functional parts (perhaps the most) of the DNA which are remnants of the evolution process. A more serious reservation is that sequencing is now largely an ~~automatic~~ ^{ad} technology, and may not attract good scientific minds to the extended years of work required. After the sequencing of an identified gene is accomplished it will be necessary to determine how the gene functions to produce its physiological or pathological effect - a complex, difficult and time-consuming ~~task~~ ^{task} ~~problem~~. Also, scientific opponents to the project consider that the funds required for a crash program would divert resources and personnel from investigator-initiated research, and would slow down high quality medical and biological research.

Both scientists and non-scientists are deeply concerned by some of the social issues involved. These problems have been recognized by the early and present forceful promoters of the project, and they have advocated that three to four percent, and later ~~up to~~ ^{up to} ten percent of funds of the project be allocated to study such questions. An important question is the use to be put of the acquired information about an individual's genetic constitution, for example, by insurance companies or by "security" forces. The lack of a right to privacy is morally objectionable, and society should limit as far as possible the potential misuse of genetic information. We need only recall the ~~tragic~~ misuse of incomplete genetic information for "eugenics" ~~by some delusional scientists and others during the present century~~ ^{by some delusional scientists and others during the present century} ~~either this century~~ not to speak of how the Nazis exploited some German ~~human geneticists and psychiatrists for their~~ ^{scientists to support their} genocide programs, ~~first against the mentally handicapped and then the Jews and Gypsies.~~ Efforts should be started as soon as possible by lawyers and other experts on data protection to formulate plans for regulation.

Another vexing question concerns the future product of genetic engineering. There is the fear of altering human germlines (ovum and sperm) and its unpredictable longer term consequences. Perhaps an exception here would be the genetically determined immune-deficiency diseases. But it has been argued that this could be the start of a slippery slope argument (once started, when does it stop?) that bedevilled the debate over embryo research. However, further research could be blocked (as was done in the embryo research field) by legislation at any stage. It has ^{also} been suggested that a list of disorders be compiled as allowable targets for gene therapy, whether germline or somatic ^{the latter} (affecting body cells - liver

kidney, etc., but not the ovum or sperm). The list could be changed periodically, but only through legislation or a ruling by a statutory body.

It should be ~~kept~~ ^{kept} in mind that curiosity about nature is the motor of scientific endeavor, and research in science is virtually impossible to stop. This is especially true, as Robert Openheimer put it in relation to the atomic bomb when the research is technically sweet ~~and would be socially important~~ ^{It may add, revealed, monitored, (admittedly) and}

The pace of research, however, can be slowed down by a restriction of funds, and perhaps this is advisable until the ~~social~~ ^{closest of} questions ~~involved~~ ^{and other problems} are better resolved. In any event, the social issues ^{arising from N000} must be debated and confronted urgently by expert groups and the public at large.

Footnote - Dr Kaplan, a former Secretary-General of Pugwash (1976-1988) is a microbiologist. He is presently serving as a consultant to the World Health Organization where he was previously employed as a director of research.