Genome study maps chemical sensitivity

[WASHINGTON] Details of a $60-million study of how 200 genes affecting susceptibility to chemicals vary across the population of the United States were unveiled last week at a conference organized by the US National Institute of Environmental Health Sciences (NIEHS).

During the meeting, held at the National Institutes of Health in Bethesda, Maryland, experts from fields including population science, genetics and epidemiology discussed the strategy of the Environmental Genome Project (EGP), which will study the DNA of about 1,000 individuals.

The meeting also heard concerns that genetic variations discovered by the project, and later found to be associated with disease risks, could be used to discriminate against individuals and groups, barring them from jobs and life or health insurance.

Commonly occurring variations (polymorphisms) in the genes that encode proteins which detoxify chemicals, repair DNA or regulate cell death are thought to increase the susceptibility of their carriers to damage from environmental toxins or carcinogens.

The EGP will seek to document the occurrence of selected polymorphisms. In a second stage, scientists will try to discover exactly how each polymorphism, combined with environmental exposures, increases disease risk. Ultimately, the goal is prevention, by allowing, for example, public health measures to be targeted more accurately at susceptible subpopulations.

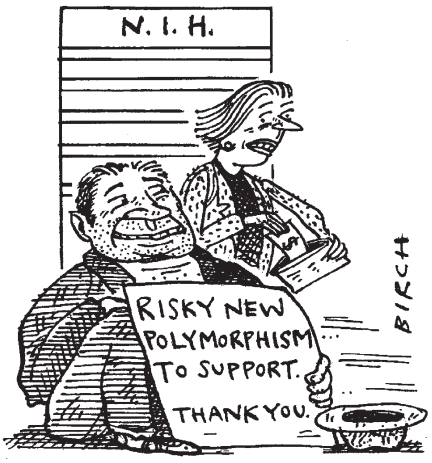
"More precise information would permit the best protection at the least cost," says Kenneth Olden, the director of NIEHS, who predicts that the project will have "a tremendous public-health impact".

The EGP does not aim to link polymorphisms to specific disease proclivities; that, NIEHS officials say, is a future project for extramural scientists, using the project's findings. Instead, it will seek to identify and catalogue the nature and distribution of the polymorphisms, and make the information available on an Internet database.

But the task is beset by complex and sometimes contentious questions, for example how to choose the most appropriate 200 genes to study (NIEHS has begun by soliciting gene nominations in journal advertisements), how to select the racial make-up of the sample population, and how to decide whether information on ethnic origins should be identifiable on the database.

NIEHS says that the database should not reveal this information. According to one conference participant, however, many scientists "think that's a really bad idea" because it would waste valuable data that could be used to help subpopulations.

But Francis Collins, the director of the National Human Genome Research Institute (NHGRI), who spoke at the conference on the project's ethical implications, disagrees. He says that while the goal may be laudable, ethically it is a minefield.



"How would Native Americans feel about having their DNA samples in this reference set and having somebody decide they want to look at genes that might be involved in alcoholism?" said Collins. "Would that be well received?" The NHGRI will host a conference in early December on how an appropriate reference set could be designed.

Charles Langley, a population geneticist at the University of California, Davis, says a separate concern is providing much of the impetus behind the EGP — and other, increasing efforts to identify polymorphisms throughout the genome. This is the fear that industry will begin to patent polymorphisms that could be useful markers for disease genes and drug sensitivities.

Those scientists opposed to such patenting say this would ultimately inhibit medical research and development. They hope that the EGP will pre-empt industry by rapidly identifying key polymorphisms of environmental relevance and making them public. "All of these variations have to be ultimately public. They can't be licensed, they can't be patented," insists David Cox, a geneticist at Stanford University who addressed the conference.

Cox says he has been personally told that the pharmaceutical company Glaxo has no interest in such patents. At a meeting last month of the NHGRI's Advisory Council, Alan Williamson, vice president for worldwide research strategy at Merck & Co., implied the same.

Olden has proposed spending $60 million on the EGP over six years, beginning in 1998. In a second phase, NIEHS will enlist extramural researchers nationwide to discover exactly how the polymorphisms interact with environmental exposures to cause — or sometimes forestall — disease. That understanding, it is hoped, will lead to preventive measures. Meredith Wadman

Diversity project 'does not merit federal funding'

[WASHINGTON] The proposed international Human Genome Diversity Project (HGDP) is not yet sufficiently feasible or well-defined to merit support from US government agencies, according to a study by the National Academy of Sciences.

The study, by a panel chaired by Jack Schull of the University of Texas Health Center at Houston, says the diversity of the human genome is of importance from both the anthropological and the biomedical point of view. But it says that the main focus of the study – a 'consensus document' prepared in 1993 by a human genome diversity subpanel of the Human Genome Organisation – meant different things to scientists from the two disciplines.

"Different participants in the formulation of the consensus document had quite different perceptions of the intent of the project, and even of its organisational structure," the panel found.

It therefore suggests that the National Institutes of Health and the National Science Foundation – the two agencies that asked for the report – should confine support of human genome diversity work to projects inside the United States. The panel says they should hold discussions with foreign agencies about how international projects should be structured before supporting any international work.

The academy's report is another setback for advocates of HGDP such as Luigi Luca Cavalli-Sforza, a population geneticist at Stanford University, who conceived the idea. Two years ago, the project received a cool response from the United Nations Educational Scientific and Cultural Organisation (see *Nature* **377**, 373; 1995).

Critics say that the project would exploit genetic information obtained from people of confined gene pools – for example, from small, isolated tribes – without giving anything back. They maintain that the information obtained from such studies could lead to genetic discrimination.

The academy found that the work the project would do has "substantial scientific merit and warrants support", but that ethical, legal and human-rights concerns, as well as organizational ones, must be met before it can proceed. Colin Macilwain