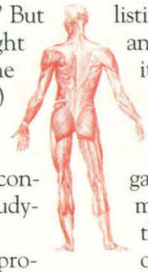
HUMAN GENETICS

NRC OKs Long-Delayed Survey Of Human Genome Diversity

A proposed international survey of genetic variation across the entire human population just got a cautious nod of approval from the National Research Council (NRC), after having been mired in controversy for several years. In a report released on 21 October, a 17-person NRC committee of scientists, ethicists, and lawyers concluded that the Human Genome Diversity Project (HGDP), first suggested by Stanford University population geneticist Luca Cavalli-Sforza in 1991, is worth pursuing because it can lead to a better understanding of the origin and evolution of humans.

But the committee recommended a less international, less technically ambitious project than some of its planners had envisioned. In particular, it said project organizers should set aside secondary goals, such as searching for new disease genes. Those goals would complicate the logistics of the project, the report said, and make it more difficult to protect the privacy and other rights of those who donated DNA. "[The HGDP] is meritorious and warrants support," says the committee's chair, William Schull, a geneticist at the University of Texas School of Public Health in Houston. "But we could see that the ethical and legal issues might be the ultimate stumbling block that would doom the project."

Both proponents of the HGDP and potential backers welcomed the report's conclusion. The original intent had been to study human evolution, they note, and they had always intended to take whatever steps are necessary to be fair to study participants. "We agree with the concept of instituting a variety of safeguards for individuals and their communities," says biological anthropologist Dennis O'Rourke of the National Science Foundation (NSF). Adds Cavalli-Sforza, "This is the strategy that we have already chosen." But while he considers the report a green light for the HGDP, neither the NSF nor the National Institutes of Health (NIH) are close to putting up the estimated $10 million to $30 million such an endeavor might cost. NIH may even consider supporting other approaches to studying variation in the genome.



Cavalli-Sforza and his colleagues proposed the HGDP as a way of getting a handle on questions ranging from human migration patterns to customs influencing patterns of human reproduction. Along the way, it might find mutated genes associated with diseases. The project would involve collecting DNA samples—from blood, hair, or cheek cells—from up to several hundred members of some 500 well-defined populations around the world. DNA from some families would be included. A predetermined set of genes—or markers—from each sample would be analyzed and compared to see how closely the populations are related. Then 25 of the samples would be immortalized in cell lines and the rest of the DNA would be banked for future use by researchers seeking to answer genetic, evolutionary, or anthropological questions.

But the idea precipitated heated discussion among geneticists and anthropologists about which populations should be studied and how the research should be carried out—what markers should be analyzed, for example (*Science*, 20 November 1992, p. 1300). In addition, the project drew strong protests from groups concerned that indigenous populations would be exploited because researchers might try to patent their DNA for use in medical tests or other products without sharing the profits with the original donors (*Science*, 4 November 1994, p. 720). Taken aback by the furor, in 1996, the NSF and the NIH—two possible HGDP funders—asked the NRC to help make sense of all the conflicting views.

SUPERSTOCK

Spice of life. Studying genetic variation can shed light on humankind's diverse origins.

In its report, entitled "Evaluating Human Genetic Diversity," the committee came up with five possible strategies for the project, listing the potential legal, ethical, scientific, and economic pitfalls of each. Ultimately, it recommended one that would limit the biomedical value of the HGDP. "If the primary goal is to get some feel for [human] diversity, then to obligate investigators to a very [strong] biomedical commitment would stultify the program from the outset," says Schull. "Let's focus on one target rather than focus on too many and have none of them be satisfied."

For example, in order to get a broad picture of diversity as economically as possible, with a minimum of ethical and legal complications, the report suggests that the project obtain samples from unrelated individuals within a given population and make sure the identities of the donors could not be linked to the samples. Besides protecting privacy, this approach would also free researchers from having to obtain further consent from donors for each new study done.

But that strategy would mean that the data wouldn't be very helpful to researchers hunting disease genes. Gene hunting requires knowing what diseases the donors had and examining DNA from as many members of affected families as possible. But precisely because it is ill-suited to making discoveries with potential commercial value, anonymous DNA collection raises fewer ethical and legal concerns.

The NRC report also recommended leaving open which genes or markers to analyze. New technologies under development, the committee pointed out, will allow researchers to do comprehensive analyses, even on small samples that could have many markers in common. "It seems to be shortsighted to fix on a set of markers when a year from now we could do much more," says Schull. And the report concluded that establishing and maintaining cell lines would be so costly, and create such logistical problems, that the fledgling HGDP would do best to avoid them.

Nor should the project try to set up a truly international effort until after the complex negotiations required to safeguard the rights of study participants are completed. For now, the committee concluded, the work should be limited to studies originating in the United States.

On the whole, HGDP planners are relieved to have the panel's endorsement. Now, says NSF's O'Rourke, he and his colleagues can start figuring out how to make the HGDP become reality. Nothing will happen before fiscal year 1999 because no funding was budgeted for HGDP in 1998.

But the report has raised further questions about whether NIH will participate. "NSF from the start was more committed to the idea because of the clear benefit for anthropology," says Judith Greenberg, a developmental biologist with the National Institute of General Medical Sciences in Bethesda, Maryland. She and her NIH colleagues will be weighing their options. "It might be possible that you don't have to collect lots and lots of samples from populations all over the world," she notes. "There might be alternative ways that might be more cost effective and [that] avoid some of the legal and ethical issues."

–Elizabeth Pennisi