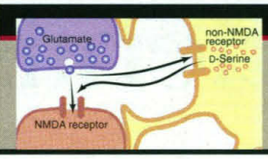

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GENETIC DISEASE

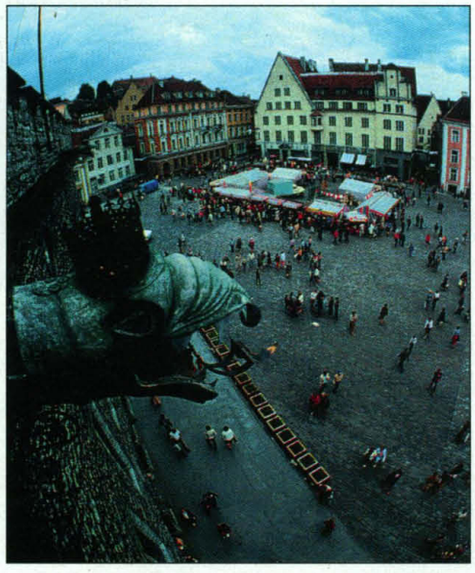
Storm Brews Over Gene Bank Of Estonian Population

TALLINN, ESTONIA—The Icelanders do it, the Swedes do it, and now the Estonians want to do it: A group of Estonian geneticists is hoping to catalog information on the health status and genetic makeup, or genotype, of more than 70% of Estonia's population of 1.4 million. The researchers, who have organized themselves under the auspices of a not-for-profit organization called the Genome Center Foundation, presented the plan late last month to the Estonian government and the scientific council of the University of Tartu. Over the next 10 years, they propose to collect extensive health questionnaires and blood samples and commit the information to a database that will be used for research as well as individual health care purposes.

The Genome Center estimates that collecting data on 1 million people will cost $90 million to $150 million over 10 years, but it expects that more than half the costs will be covered by companies buying rights to use the data for genetic research. The project is already gathering considerable momentum: According to the Genome Center, the approval won last month by the scientific council sends out an important signal, as Tartu University is home to the country's only medical faculty. The government also reacted favorably, naming the gene bank proposal one of three large-scale national projects to receive state funding next year. Chair of the Genome Center Jaanus Pikani says this government funding will help the team refine its methods of data and sample collection, prepare legislation to win formal parliamentary approval, and inform the public about the project. Assuming that governmental and public approval is forthcoming, the researchers hope to begin gathering data and sampling blood from consenting Estonians by 2001.

But the proposal may not get an easy ride: As news of the plan begins to leak out, it is provoking a heated reaction in some medical circles. "With an underfunded health care system and a population that would benefit more from a focus on lifestyle factors, such as smoking and abuse of alcohol and drugs, we should not enter into expensive high-tech endeavors," says Tiina Tasmuth, a professor of medical education at the University of Tallinn.

Andres Metspalu, a professor of biotechnology at the University of Tartu and a key figure in developing the idea of a gene bank, says there are two main goals: One is to identify disease genes, particularly those involved in multifactorial diseases—such as asthma and heart disease—by comparing genotypes within a group of patients with a given disease. The second goal is to set up a health care database that would give Estonians access to their own data, so they can benefit from the personalized medicine of the future. "Medical treatment will increasingly be tailored to specific genotypes, and this database would allow individuals to gain knowledge of disease risks and to receive the most effective medication," says Metspalu. His colleague, geneticist Toomas Veidebaum of Tallinn's Institute for Experimental and Clinical Medicine, adds that it is "necessary for us to start implementing modern technologies if we are not to fall hopelessly behind."



Sample population. Researchers plan to take blood samples from 1 million Estonians.

The disease pattern of the Estonian population is quite similar to that of Western Europe in general, but Metspalu is not concerned about overlap with other genomic projects. "With 80,000 genes to discover, and with the multigenic nature of many diseases, optimal results will come from coordination of various projects," he says. The Genome Center team is seeking to collaborate with the Icelandic company deCODE Genetics, which has recently embarked on a similar project. DeCODE president and former Harvard University geneticist Kari Stefansson told *Science* he is open to collaboration, adding that "the idea behind the Estonian project is interesting, and although specifics have not been discussed, I think working together would allow us to solve some technical problems and explore possible synergies."

But deCODE's experience does not bode well for the Estonians. Stefansson's project provoked fierce debate in Iceland and around the world. Researchers, medical ethicists, and data-protection specialists in many countries unsuccessfully lobbied the Icelandic government last year not to pass a law giving deCODE access to the health records of the entire country (*Science*, 1 January, p. 13). Since then, some physicians and patients have refused to cooperate in building up deCODE's database.

Some critics question whether the issues raised by the Estonian proposal will be fully addressed. "Creating an informed public debate about the ethics of genetics is a major challenge, because our countries have not yet developed the professional bioethics seen in the West," says Eugenijus Gefenas of Vilnius University, chair of the Lithuanian National Committee on Biomedical Ethics. The "paternalistic tradition" of the postcommunist Baltic states makes it difficult to ensure that informed consent and nondirective counseling of individuals are carried out properly, Gefenas says. "[It is] irresponsible to provide genetic information that may have profound implications for the individual as well as family members and unborn children" if it may not be properly understood, adds Tasmuth.

Tasmuth says she is outraged that the researchers presented the proposal to the government before there had been any public debate. She has published an article about it in an Estonian daily newspaper, and Genome Center researchers have been invited to discuss the proposal at a meeting on 13 November arranged by the Estonian Christian Physicians' Society, of which Tasmuth is head.

CREDIT: SOVFOTO/EASTFOTO

Metspalu recognizes the need to educate Estonians about genetics, but he believes that obtaining informed consent will not be a problem. "In a small pilot study, questioning 111 people resulted in a 90% acceptance rate, and I expect something similar for the general population," he says. **–LONE FRANK**

Lone Frank is a writer in Copenhagen, Denmark.

INFECTIOUS DISEASES

Malarial Genome Comes Into View

In 1986, Thomas Wellems set out on a seemingly narrow quest. He wanted to find the gene that enabled the malarial parasite *Plasmodium falciparum* to become resistant to chloroquine, the drug that had been a mainstay therapy for decades. But along the way, Wellems, a malaria expert at the National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland, accomplished what may be a more far-reaching feat. As reported on page 1351, he and his colleagues from NIAID and from the National Center for Biotechnology Information pinpointed a series of genetic landmarks across the entire 14-chromosome genome of this deadly parasite. It is one of two new maps of the parasite unveiled this month; the second, published in the November issue of *Nature Genetics*, shows a different type of landmark.

Richard Hyman of the Stanford DNA Sequencing and Technology Center in Palo Alto, California, says that the new maps will be "really useful" for researchers working to sequence the parasite's genome, because the landmarks will enable them to align short stretches of sequenced DNA in the correct order along *P. falciparum*'s chromosomes. Producing that sequence is a top target, Hyman notes. There's no preventive vaccine for malaria, which kills about 2 million people a year, and in the past 2 decades the organism has become resistant to other key antimalarial drugs in addition to chloroquine. The completed sequence may reveal potential targets for antimalaria vaccines or drugs.

A sequenced genome seemed an impossible dream when Wellems first started his project. "At the time, we didn't even know how many chromosomes there were," he recalls. He and his colleagues planned to home in on the location of the chloroquine-resistance gene by identifying genetic landmarks in the genome and seeing which of them were inherited along with the drug resistance. The team did this by tracking down microsatellites, short, easily identifiable bits of repetitive DNA that could serve as these landmarks.

For that effort, they also spent more than 5 years developing new resistant and sensitive parasites and then cross-breeding them. Only then could they trace the inheritance of the markers and the drug-resistance trait in the offspring of the hybrids to glean clues to the gene's location.

The map naturally emerged from this effort, as the group determined the patterns of microsatellites in the offspring of the crosses. Markers that are close to one another on a chromosome are more likely to be inherited together than those far apart, and so the team could establish the relative orders of the markers—901 in all—along the chromosomes and the approximate distances between them.

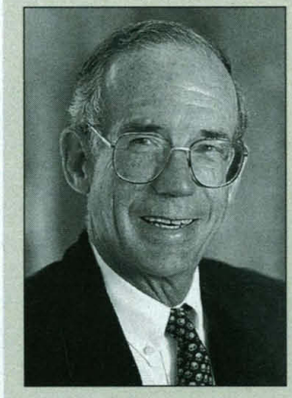
The second map, produced by David Schwartz of the University of Wisconsin, Madison, and his colleagues, pins down the physical locations of its markers. These researchers used a technique called optical mapping, which Schwartz devised while at New York University (NYU) in New York City. It uses electrostatic forces to hold pieces of fluorescently labeled *P. falciparum* DNA stretched out on glass. Then, for this

Getting the picture. Computer software merges fluorescence microscopy images to reveal cuts in long stretches of the malarial parasite's DNA.

CREDIT: (TOP) SCHWARTZ *ET AL.*

PUBLISHING

Kennedy Named Editor-in-Chief of *Science*



Donald Kennedy, president emeritus of Stanford University and a former commissioner of the Food and Drug Administration (FDA), has been appointed the next Editor-in-Chief of *Science*. A neuroscientist by training, Kennedy is currently Bing Professor of Environmental Science at Stanford.

Kennedy's appointment was announced on 9 November by the board of directors of the American Association for the Advancement of Science, which publishes *Science*. Board chair M.R.C. Greenwood, chancellor of the University of California, Santa Cruz, said in a statement: "He brings to this task a broad understanding of current science issues, a wealth of experience in government and university, and incomparable insight." He will take over the editorship on 1 June 2000 from Floyd Bloom, who announced last year that he would not seek a second 5-year term when his current appointment expires in May 2000. Kennedy will retain his Stanford faculty position through the 2000–01 academic year.

Kennedy, 68, received A.B. and Ph.D. degrees from Harvard and joined the Stanford faculty in 1960. His research focused on invertebrate neurobiology, in particular on how organisms generate and control patterned motor output. He served as FDA commissioner from 1977 to 1979, returned to Stanford as provost, and was appointed president in 1980, a position he held for 12 years.

His current research and teaching focuses on environmental policy. He co-chairs an interdisciplinary center at Stanford that explores the development of policies on issues such as land-use changes, shifts in agricultural practices, and global climate change.