find random variations—may miss most of the SNPs that alter the structure of the proteins they encode. Yet these are the SNPs that may directly influence disease risk.

Most SNPs, according to Chakravarti, are not likely to have a direct impact on their protein products. This is because they fall in the estimated 95% "noncoding" area of the genome, or because they behave in a "synonymous" or silent way, coding for the same protein an alternate SNP codes for. Nonsynonymous coding SNPs (cSNPS), in contrast, are very rare in the human gene pool. "There seems to be a strong selection against any change in protein structure. [Most of these changes] have been weeded out in the course of evolution," says Chakravarti.

In addition, Lander's study reports that a significant percentage of the relevant cSNP variants are found mainly in certain subpopulations, such as Asians or African-Americans. "What that tells us," says Leonid Kruglyak, a geneticist at the Fred Hutchinson Cancer Research Center in Seattle, "is that the [nonsynonymous cSNPs] are harder to find in the first place." Chakravarti agrees, adding that "to discover them you'll have to take as large and diverse a sample population as possible."

The scarcity of protein-altering SNPs will also make it difficult to tie them to a specific disease. Lander's study concludes that linking a disease to a very rare gene variant would require thousands of patients, way too many even for state-of-the-art tools for whole genome analysis. At present, says Chakravarti, "The right way to go is to take a set of candidate genes and assess them directly in as many patients as possible" for an association between SNPs and the disease.

This cautionary advice comes as the SNPs stampede is well under way. In January 1998, for instance, Francis Collins, director of the National Human Genome Research Institute (NHGRI) at the National Institutes of Health in Bethesda, Maryland, launched a $30 million project to create a collection of some 450 human DNA samples that aims to expand the number of SNPs from a few thousand known today to about 100,000 in the next 3 years. And in April, 10 large drug companies, the Wellcome Trust philanthropy of Britain, and a handful of academic laboratories teamed up to form a nonprofit alliance called the SNP Consortium, or TSC, that will create a SNP archive encompassing some 300,000 SNPs within the next 2 years. Like J. Craig Venter's sequencing factory Celera Genomics in Rockville, Maryland, TSC will collect random data across the entire genome.

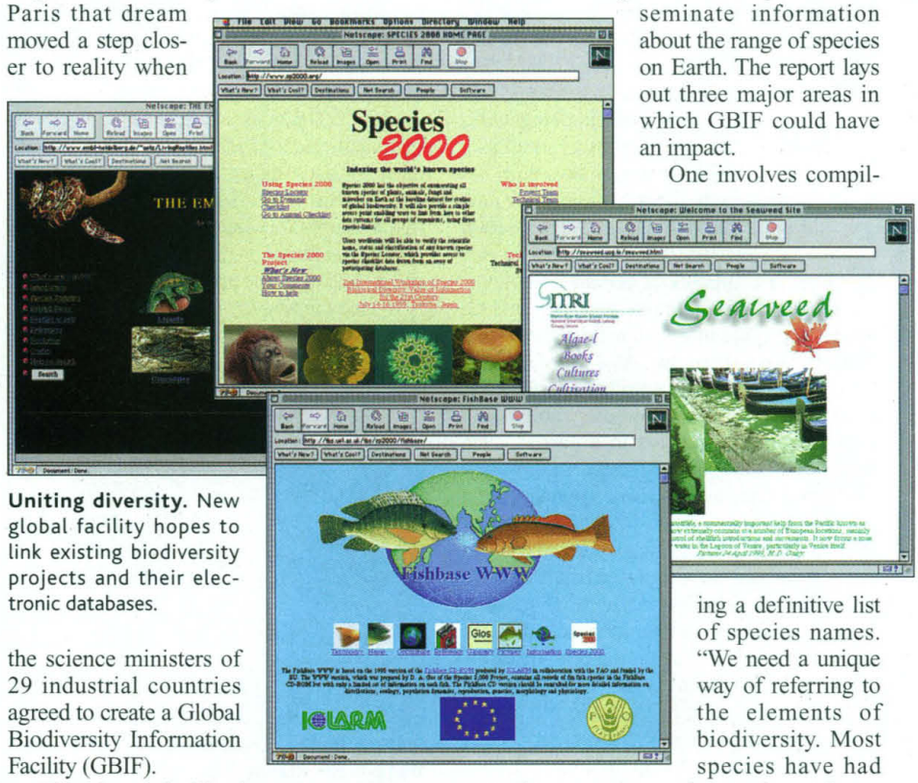
In combination, the gene-focused and random strategies for collecting SNPs should enable scientists to explore the human genome extensively. Celera geneticist Mark Adams says: "I really see [the two approaches] as complementary. The whole-genome strategy will give us a large number of SNPs, both within and outside of genes, and that's a very useful starting point." With this large SNP bonanza just ahead, says Lisa Brooks, program director of the SNP project at NHGRI, research sponsors need to develop new automated technologies that can rapidly "score the genotypes of many individuals." NHGRI is putting money into this area. But Brooks notes that "even a standard screening of, say, 50 candidate genes is still a way off."

–MICHAEL HAGMANN

BIOINFORMATICS

OECD to Set Up Global Facility on Biodiversity

Researchers studying the diversity of life have dreamed of pooling all they know in a single electronic compendium. Last week in Paris that dream moved a step closer to reality when the science ministers of 29 industrial countries agreed to create a Global Biodiversity Information Facility (GBIF).



Uniting diversity. New global facility hopes to link existing biodiversity projects and their electronic databases.

The virtual facility hopes to convert a growing tower of biodiversity Babel, replete with incompatible databases, confusing terminology, and uncatalogued material, into a transparent source of information that is accessible to anyone, anywhere. But before it tackles that challenge, GBIF will have to be transformed from an attractive notion into a real facility with a staff and a budget.

GBIF is the fruit of a 2-year effort by a working group of the Megascience Forum, a body created by the industrialized-country members of the Organization for Economic Cooperation and Development (OECD) to explore possible collaborations in building large scientific facilities. Last week the science ministers agreed it should be renamed the Global Science Forum to better address scientific issues of global significance that do not necessarily involve major construction—such as biodiversity. Last year the parties to the 1992 United Nations Convention on Biological Diversity (CBD) urged OECD to come up with a program like GBIF to give individual countries access to the scientific information they need to carry out the terms of the convention. "GBIF is a very important international undertaking to ensure we can all share openly information about biodiversity," says Neal Lane, science adviser to U.S. President Bill Clinton and vice-chair of last week's meeting.

The new facility incorporates the recommendations of a bioinformatics working group, many of whose members are also leaders of existing efforts to compile and disseminate information about the range of species on Earth. The report lays out three major areas in which GBIF could have an impact.

One involves compiling a definitive list of species names. "We need a unique way of referring to the elements of biodiversity. Most species have had more than one name and some dozens," says Stephen Blackmore, keeper of botany at Britain's Natural History Museum, who served on the bioinformatics working group that proposed GBIF. To produce such a list, GBIF will work closely with Species 2000, an effort just under way to enumerate all known species of plants, animals, fungi, and microbes. "Its endorsement may also help us in obtaining additional funding," says Frank Bisby of the U.K.'s Reading University, who chairs Species 2000.

Another goal is to coordinate the development of new software to link databases that

embrace the full range of biodiversity information including geographical, ecological, genetic, and molecular data. A third activity will be to digitize all biodiversity information, now usually embodied specimens in museums continents away from where the samples were collected. "Repatriation of data is a major impetus," says Meredith Lane, vice president for biodiversity at the Academy of Natural Sciences in Philadelphia and a member of the bioinformatics working group. But that process, by which the host country would obtain electronic access to information stored in another country, will require an enormous and sustained effort. "We have 30 million insects on pins, many very small and fragile with tiny hand-written labels. At our current rate of progress, [cataloguing these specimens electronically] would take centuries," says Blackmore.

Of course, all this will take money. And despite the official go-ahead, none has yet materialized for GBIF. The working group has estimated that GBIF will end up coordinating some $40 million a year in ongoing work within member countries, and that GBIF itself can make an important contribution at an annual cost of $8 million a year. But such a budget, paid by member nations, is probably a few years away.

As a first step, science ministers from Australia, Denmark, the United Kingdom, and the United States have signaled their intention to contribute toward the $2 million to $3 million needed to set up a six-person secretariat at a site to be determined. Australia and the United Kingdom are seen as likely bidders for the administrative headquarters, to open next year. Although the United States is unlikely to put in an application, says James Edwards of the National Science Foundation, it is strongly committed to the project. "There is some activity going on now to mobilize data, and there are sporadic efforts to put it on the Internet," he says. "But there's no capacity for the one-stop shopping needed for nations to carry out the CBD and to develop their own biodiversity programs. That's what GBIF will do."

–JUDY REDFEARN

Judy Redfearn writes from Bristol, U.K.

DEVELOPMENTAL BIOLOGY

How to Get a Heart in The Right Place

CHARLOTTESVILLE, VIRGINIA—Like a child learning to put her hand over her heart for the Pledge of Allegiance, a developing embryo needs to know its right from its left. The heart goes on the left and the liver on the right, but how the embryo knows which is which is a long-standing puzzle. At the annual meeting of the Society for Developmental Biology here last month, one promising theory—that twirling "hairs" on embryonic cells set up the left-right distinction—gained strength.

Scientists first proposed a connection between cilia—whiplike protrusions that can propel cells and help keep airways clear—and organ placement nearly 25 years ago. In 1976, Bjorn Afzelius described how human patients with a genetic defect called Kartagener's syndrome have immotile sperm and defective cilia in their airways—and about half have their organs on the wrong side (*Science*, 23 July 1976, p. 317). That connection led to speculation that cilia might somehow help to direct organ placement, but no one knew whether Kartagener's syndrome disables the cilia in the embryo as well.

Turn, turn, turn. Twirling cilia on the node cells of a developing embryo may distinguish its left from its right.

CREDIT: S. POTTER, UNIVERSITY OF CINCINNATI AND J. DUNLAP, UNIVERSITY OF TENNESSEE

The old theory was resurrected 6 months ago, after cell biologist Nobutaka Hirokawa of the University of Tokyo and his colleagues reported that when they knocked out a gene involved in cilia assembly in mice, about half the animals had reversed left-right organ placement, and all lacked cilia on so-called node cells. These cells produce many of the signals that direct the early patterns in a mouse embryo, and the node is the site of some of the first molecular differences between left and right.

When the team made microscopic videos of normal node cells, they found that their cilia rotated counterclockwise, unlike the back-and-forth motion of cilia on sperm or in airways. By tracking fluorescently labeled beads, the scientists determined that the cilia somehow swept the fluid surrounding the cells to the left. That might cause an as yet unknown signal to accumulate, eventually leading to asymmetric organ development. The lack of this lateral cue in the mutant strain could explain the 50% rate of organ reversal.

But other researchers had trouble repeating the technically difficult observations, and many remained unconvinced. One concern was that the mice without cilia on their node cells might have other defects as well, so that something other than the cilia themselves could be the cause of the left-right disturbances. Even Yale University pediatric cardiologist Martina Brueckner, who had been working with a different strain of mutant mice that also suffer a 50% chance of left-right reversal, had her doubts. "It just seemed so weird," she says.

But, at the meeting, she announced that her team has taken a close look at the node cells in their mutant embryos, too. They found that these cells do have cilia, but they stand rigid and straight, instead of twirling. Without that motion, evidently, the signal drifts randomly left or right, which could explain the reversals.

The observation boosts the theory that twirling cilia cause asymmetry, says cell biologist Chris Wright of Vanderbilt University. "Showing that they're rigid is tantalizing," he says. But to really clinch the case, he says, someone needs to show that the cilia in yet another mutant mouse strain called *inv*, in which almost all the animals have reversed organs, twirl backward.

–GRETCHEN VOGEL

SCIENTIFIC MISCONDUCT

EMF Researcher Made Up Data, ORI Says

In a blow to a research area hungry for credible findings, the federal Office of Research Integrity (ORI) reported last month that a biochemist "engaged in scientific misconduct ... by intentionally falsifying and fabricating data and claims" in two studies on how electromagnetic fields (EMFs)—the kind shed by power lines and home appliances—affect living cells. The researcher, Robert P. Liburdy, formerly of the Lawrence Berkeley National Laboratory (LBNL) in California, has agreed to ask the journals to retract the results. "There's a lot of acrimony in the [EMF] debate, and this won't calm things down," says Richard G. Stevens, a cancer epidemiologist at the Pacific Northwest National Laboratory in Hanford, Washington.

Liburdy's findings were among the first to offer a plausible mechanism for a possible link between EMF exposure and cancer or other diseases. In a pair of 1992 papers of which he is the sole author, Liburdy offered evidence that EMFs increase the flow of calcium into lymphocytes, a kind of immune cell produced in the thymus. The papers created a stir, as calcium ions signal cells to turn genes on and off, and play a role in cell division. Because tumor growth is tied to cell proliferation, an alteration in calcium signaling could conceivably lead to cancer. But in an analysis obtained by *Science*, ORI states that "Liburdy's claims that EMF causes cellular effects related to calcium signaling [in three figures in the two journal articles] are